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3 Pharmacovigilance Risk Assessment Committee (PRAC)

4 **Good practice guide on recording, coding, reporting and**  
5 **assessment of medication errors**  
6 **Draft**

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8 Comments should be provided using this [template](#). The completed comments form should be sent to [medicationerrors2013@ema.europa.eu](mailto:medicationerrors2013@ema.europa.eu) by 14 June 2015.

Keywords	<i>Medication errors, pharmacovigilance, good practice, ICSR reporting, intercepted error, potential error, adverse reaction, MedDRA coding, PSUR, RMP, patient safety;</i>
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11 **As part of the public consultation of the good practice guide on recording, coding, reporting**  
12 **and assessment of medication errors the European Medicines Agency (EMA) would also like**  
13 **to take the opportunity to obtain stakeholder feed-back on the following questions:**

- 14 1. With regard to recording medication errors in ICSRs, please provide comments on the proposal in  
15 Annex 4 for a business process for using the ICH E2B (R3) ICSR data element 'Additional  
16 Information on Drug' (G.k.10.r) and the data elements 'Sender's diagnosis' and 'Sender's  
17 comments'.
- 18 2. With regard to reporting medication errors in ICSRs do you consider the proposed disclaimer in  
19 chapter 5.7.2 useful to address potential conflicts between marketing authorisation holders'  
20 pharmacovigilance obligations and potential exposure to liability when classifying medication errors  
21 in suspected adverse reaction reports to national competent authorities or the Agency?
- 22 3. With regard to signal detection activities would you consider the development of methodological  
23 guidance on the detection of signals of medication errors in EudraVigilance useful, taking into  
24 account the Standard MedDRA Query (SMQ) for medication errors currently under development?
- 25 4. With regard to pharmacovigilance activities would stakeholders consider making available collated  
26 medication error reports via the EudraVigilance Data Analysis System (EVDAS) and/or the public  
27 adrreports.eu website in line with the revised EudraVigilance Access Policy useful? Please note that  
28 for the general public such reports would be presented by EEA and non-EEA geographic origin and  
29 based on a filter using coded MedDRA terms in combination with the data element 'Additional  
30 Information on Drug' (G.k.10.r) once the ICH E2B (R3) standard is implemented.

31 Good practice guide on recording, coding, reporting and  
32 assessment of medication errors  
33

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## 88 **Executive summary**

89 The European Union (EU) pharmacovigilance legislation has introduced a number of changes related to  
90 medication errors which affect the operation of pharmacovigilance systems in EU Member States. To  
91 support implementation of the new legal provisions amongst the stakeholders involved in the  
92 reporting, evaluation and prevention of medication errors the European Medicines Agency (EMA) in  
93 collaboration with the EU regulatory network was mandated to develop specific guidance for  
94 medication errors, taking into account the recommendations of a stakeholder workshop held in London  
95 in 2013.

96 This good practice guide is one of the key deliverables of the Agency's medication error initiative to  
97 clarify specific aspects related to recording, coding, reporting and assessment of medication errors in  
98 the context of EU pharmacovigilance activities with the objective to improve reporting and learning  
99 from medication errors for the benefit of public health.

## 100 **1. Introduction (background)**

101 Errors associated with the use of medicinal products are a major public-health burden. Medication  
102 errors generally refer to unintended mistakes in the processes of prescribing, dispensing or  
103 administering of medicinal products in clinical practice. An estimated 18.7 - 56% of all adverse drug  
104 events among hospitalised patients result from medication errors that would be preventable and are  
105 thus a concern at all stages of health care delivery in European health care systems<sup>1</sup>.

## 106 **2. Scope**

107 The scope of this good practice guide includes the recording, coding, reporting and assessment of  
108 medication errors associated with suspected adverse reaction(s) in the context of EU  
109 pharmacovigilance obligations applicable to competent authorities in EU Member States, marketing  
110 authorisation holders and the Agency.

111 The primary purpose is to support competent authorities in EU Member States, marketing authorisation  
112 holders and the Agency to comply with their pharmacovigilance obligations detailed in Title IX of  
113 Directive 2001/83/EC and Regulation (EC) 726/2004, Chapter 3, Article 28 with regard to the  
114 recording, reporting and assessment of suspected adverse reactions (serious and non-serious)  
115 associated with an error in the prescribing, dispensing, preparation or administration of a medicinal  
116 product for human use authorised in the EU.

117 The recording, reporting and assessment of events associated with intentional overdose, abuse,  
118 misuse, occupational exposure and off-label use of medicines is outside the scope of this guidance.

119 EU good pharmacovigilance practices (GVP) require marketing authorisation holders to summarise  
120 information on medication errors regardless of whether they are associated with adverse reaction(s) in  
121 periodic safety update reports (PSUR) and to reflect the current knowledge about the risk of  
122 medication errors in risk management plans (RMP) for the purpose of continuous benefit-risk  
123 evaluation of medicinal products. This guide therefore also provides recommendations for marketing  
124 authorisation holders on the recording, coding, reporting and assessment of medication errors brought  
125 to their attention and which are not associated with adverse reaction(s).

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<sup>1</sup> von Laue NC, Schwappach DL, Koeck CM. The epidemiology of preventable adverse drug events: a review of the literature. *Wien Klin Wochenschr* 2003; 115:407–415.

126 The scope of this guide also includes the Medical Dictionary for Regulatory Activities (MedDRA) coding  
127 conventions for medication error reports. Specific coding examples complementary to the guidance  
128 provided in the MedDRA Term Selection Points to Consider (MTS:PTC) document are provided.

129 The guidance acknowledges the fundamental role of patient safety reporting systems established in  
130 several EU Member States is to enhance patient safety by learning from potential failures of the  
131 healthcare system, including from medication errors which do not result in adverse reaction(s).  
132 However, authorities, bodies, organisations and/or institutions responsible for patient safety within EU  
133 Member States are outside the remits of Directive 2001/83/EC and Regulation (EC) No 726/2004 and  
134 medication errors not associated with adverse reaction(s) are not required to be reported as individual  
135 case safety reports (ICSR) in line with EU pharmacovigilance obligations.

136 In line with the provisions of Article 107a (5) of Directive 2001/83/EC one of the objectives of this  
137 guidance is the establishment of good practice for sharing information on medication errors associated  
138 with adverse reaction(s) between national competent authorities responsible for pharmacovigilance of  
139 medicinal products and authorities, bodies, organisations and/or institutions responsible for patient  
140 safety reporting and learning systems in EU Member States. A model of collaboration and exchange of  
141 information is introduced as an example for good practice acknowledging that EU Member States may  
142 use different models that best fit their national requirements for the exchange of information on  
143 medication errors.

### 144 **3. Legal basis**

145 Article 1(11) of Directive 2001/83/EC provides the definition of an adverse reaction (see chapter 4.2. )  
146 which covers noxious and unintended effects resulting not only from the authorised use of a medicinal  
147 product at normal doses, but also from medication errors and uses outside the terms of the marketing  
148 authorisation, including misuse and abuse of a medicinal product.

149 Recital (17) of Directive 2010/84/EC provides that Member States should operate a pharmacovigilance  
150 system to collect information that is useful for the monitoring of medicinal products, including  
151 information on suspected adverse reactions arising from use of a medicinal product within the terms of  
152 the marketing authorisation as well as from use outside the terms of the marketing authorisation,  
153 including overdose, misuse, abuse and medication errors, and suspected adverse reactions associated  
154 with occupational exposure.

155 Accordingly, Article 101(1) of Directive 2001/83/EC lays down EU Member States' requirements to  
156 operate a pharmacovigilance system for the fulfilment of their pharmacovigilance tasks and to collect  
157 information on the risks of medicinal products as regards patients' or public health. That information  
158 shall in particular refer to adverse reactions in humans, arising from use of the medicinal product  
159 within the terms of the marketing authorisation as well as from use outside the terms of the marketing  
160 authorisation, and to adverse reactions associated with occupational exposure.

161 Article 107a (5) of Directive 2001/83/EC further requires EU Member States to ensure that reports of  
162 suspected adverse reactions arising from an error associated with the use of a medicinal product that  
163 are brought to their attention are made available to the Eudravigilance database and to any  
164 authorities, bodies, organisations and/or institutions, responsible for patient safety within that EU  
165 Member State. They shall also ensure that the authorities responsible for medicinal products within  
166 that Member State are informed of any suspected adverse reactions brought to the attention of any  
167 other authority within that EU Member State. From a public health perspective, it is good practice that  
168 competent authorities in EU Member States are also aware of adverse reactions associated with  
169 medication errors which may have been reported to a national patient safety organisation (PSO) or any  
170 other authorities, bodies, organisations and/or institutions responsible for patient safety within that EU

171 Member State. The provisions of Article 107a (5) of Directive 2001/83/EC recognise the broader remit  
172 of PSOs to tackle medication errors by introducing appropriate changes to clinical practice which is  
173 outside the legal remit of competent authorities in EU Member States.

174 Article 107a(5) of the Directive further requires that suspected adverse reaction reports arising from  
175 an error shall be appropriately identified in the standard web-based structured forms for the reporting  
176 of suspected adverse reactions by healthcare professionals and patients referred to in Article 25 of  
177 Regulation (EC) No 726/2004.

178 Each marketing authorisation holder is responsible for submitting PSURs for its own products according  
179 to Article 107b of Directive 2001/83/EC and Article 28 (2) of Regulation (EC) 726/2004. The legal basis  
180 for the submission of RMPs is provided in Article 8(3) (iaa) of Directive 2001/83/EC requiring that the  
181 application for a marketing authorisation shall be accompanied by a summary of the applicant's  
182 pharmacovigilance system and a risk management plan which describes the risk management system  
183 for the concerned product. The format and content requirements for PSUR and RMP are described in  
184 Articles 30 to 35 of the European Commission Implementing Regulation (EU) No 520/2012.

185 With regard to medication errors occurring in the context of clinical trials, Regulation (EU) No  
186 536/2014 on clinical trials on medicinal products for human use, which will repeal Directive  
187 2001/20/EC, lays down the reporting requirements for adverse events and serious adverse events by  
188 the investigator to the sponsor (Article 41) and the reporting requirements for suspected unexpected  
189 serious adverse reactions by the sponsor to EudraVigilance (Article 42). In addition, Annex III of  
190 Regulation (EU) No 536/2014 on safety reporting clearly states that medication errors, pregnancies  
191 and use outside what is foreseen in the protocol, including misuse and abuse of the product, shall be  
192 subject to the same obligation to report as adverse reactions.

## 193 **4. Definitions**

194 The definitions provided in Article 1 of Directive 2001/83/EC should be applied for the purpose of this  
195 guidance; of particular relevance for ICSR recording, reporting and assessment activities are the  
196 definitions provided in GVP module VI together with this chapter which include general principles  
197 presented in the ICH E2A and E2D guidelines<sup>2</sup> and WHO guidance<sup>3</sup>. Also the definitions provided in the  
198 complementary guidance in chapter 4.5. should be adhered to.

### 199 **4.1. Adverse event**

200 Article 2 (32) of Regulation (EC) 536/2014 on clinical trials on medicinal products for human use,  
201 which will repeal Directive 2001/20/EC, defines an adverse event (AE) as any untoward medical  
202 occurrence in a subject to whom a medicinal product is administered and which does not necessarily  
203 have a causal relationship with this treatment.

204 A similar definition is provided in Annex I (Rev 3) of the GVP guideline: any untoward medical  
205 occurrence in a patient or clinical trial subject administered a medicinal product and which does not  
206 necessarily have a causal relationship with this treatment.

207 An adverse event can therefore be any unfavourable and unintended sign (including an abnormal  
208 laboratory finding, for example), symptom, or disease temporally associated with the use of a  
209 medicinal product, whether or not considered related to the medicinal product. For the purpose of this

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<sup>2</sup> <http://www.ich.org/products/guidelines/efficacy/article/efficacy-guidelines.html>

<sup>3</sup> WHO draft guidelines for adverse event reporting and learning systems (2005)  
([http://www.who.int/patientsafety/events/05/Reporting\\_Guidelines.pdf](http://www.who.int/patientsafety/events/05/Reporting_Guidelines.pdf))

210 guidance medication related adverse events should be distinguished from other adverse events (e.g.  
211 fall, surgery on wrong body site etc.).

212 WHO defines an adverse event as an injury related to medical management, in contrast to  
213 complications of disease. Medical management includes all aspects of care, including diagnosis and  
214 treatment, failure to diagnose or treat, and the systems and equipment used to deliver care. Adverse  
215 events may be preventable or non-preventable.

## 216 **4.2. Adverse reaction**

217 An adverse reaction (ADR) is a response to a medicinal product which is noxious and unintended  
218 (Directive 2001/83/EC, Article 1(11)). This includes adverse reactions which arise from:

- 219 • the use of a medicinal product within the terms of the marketing authorisation;
- 220 • the use outside the terms of the marketing authorisation, including overdose, off-label use,  
221 misuse, abuse and medication errors;
- 222 • occupational exposure.

223 This definition is provided in GVP Module VI.A.2.1 'Management and reporting of adverse reactions to  
224 medicinal products'.

## 225 **4.3. Medication error**

226 For the purpose of ICSR reporting in the EU, GVP Module VI.B.6.3 defines a medication error as any  
227 unintended error in the prescribing, dispensing or administration of a medicinal product while in the  
228 control of the healthcare professional, patient or consumer. This definition is focused on the  
229 management and reporting of adverse reactions to medicinal products and does not cover all stages of  
230 the medication use process where an error may occur and where there is an adverse reaction, e.g.  
231 preparation for administration.

232 For the purpose of this guidance and building on the GVP VI principles the following **conceptual**  
233 **definition** of a medication error is provided to allow for a common approach to recording, coding,  
234 reporting and assessment of errors in the drug treatment process regardless of whether the error is  
235 associated with adverse reaction(s):

236 *A medication error is an unintended failure in the drug treatment process that leads to, or has the*  
237 *potential to lead to, harm to the patient.*

238 The concepts of intentional overdose, off-label use, misuse and abuse as defined in GVP Module  
239 VI.A.2.1.2 are outside the scope of this guidance and should be clearly distinguished from medication  
240 errors.

241 For EU specific regulatory processes and pharmacovigilance reporting requirements for medication  
242 errors associated with ADRs please refer to chapter 5.3.

### 243 **4.3.1. Medication errors and correlation with harm and preventability**

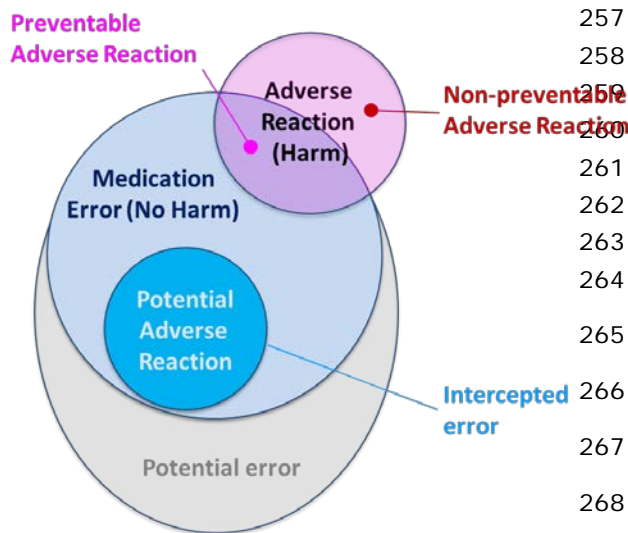
244 Figure 1 below outlines the correlation of medication errors with harm and preventability from a  
245 patient safety perspective. An adverse reaction as a consequence of an error in the medication use  
246 process is considered preventable, in contrast to a non-preventable adverse reaction which may be  
247 labelled e.g. in SmPC section 4.8 as an undesirable effect of a medicine, i.e. the probability of harm to  
248 the patient is known and accepted and will likely occur depending on the frequency of the adverse  
249 reaction. There are also medication errors which do not necessarily result in harm (no ADR) but which



250 may have other unwanted effects e.g. from an economic or environmental point of view (e.g. drug  
251 prescribed and dispensed but not taken). If an error occurred but was identified and intercepted before  
252 reaching the patient, a potential adverse drug reaction was prevented and this is referred to as  
253 'intercepted error'.

254 For learning purposes "potential errors" may also be relevant, e.g. if there are circumstances or  
255 information capable of leading to an error which are considered worthwhile to be recorded.

256



257 Figure 1: Correlation between medication errors,  
258 preventable and non-preventable adverse reactions  
259 and intercepted errors (modified according to  
260 Morimoto et al., Qual Saf Health Care 2004; 13:306-  
261 314). This figure is intended for illustrative purposes  
262 only to explain the concept of medication errors from  
263 a *patient safety* perspective without implications for  
264 pharmacovigilance reporting requirements.

265

266

267

268

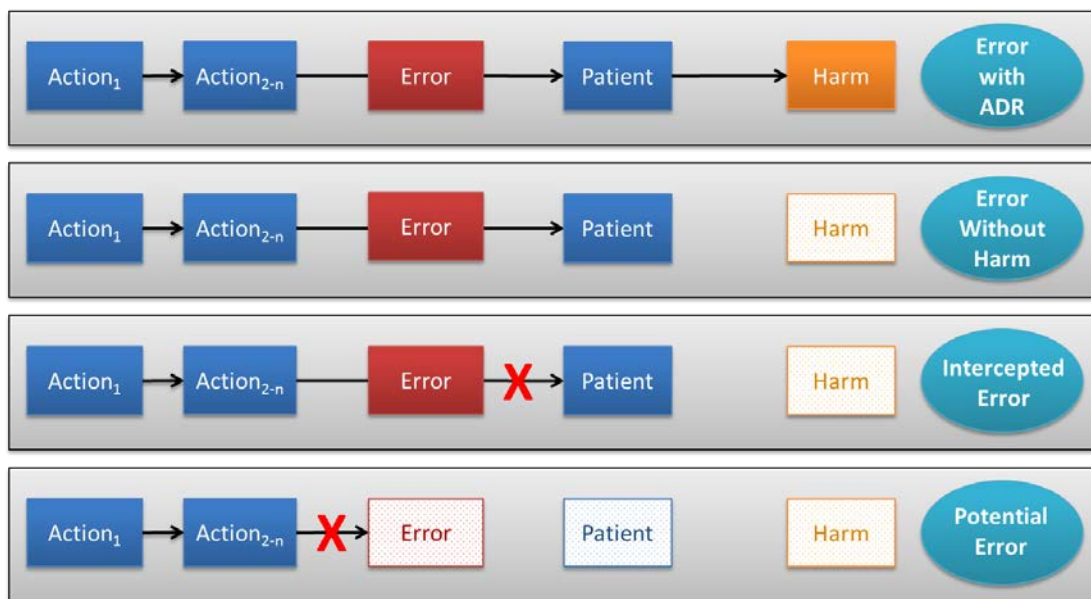
269

#### 270 4.3.2. Classification of medication error reports

271 For the purpose of this guide, the objective of which is to support the implementation of the EU  
272 pharmacovigilance requirements outlined in chapter 3. adverse reactions arising from medication  
273 errors (i.e. resulting in harm to the patient) should be recorded, reported and assessed.

274 Medication errors brought to the attention of MAHs but not resulting in harm, i.e. not associated with  
275 adverse drug reaction(s), may be relevant for the scientific evaluation and interpretation of safety data  
276 and of the benefit-risk profile of a medicinal product and should therefore be recorded and assessed in  
277 line with the recommendations of GVP Module VI.B.6.3, and GVP Module VII.B.5.9 and V.B.8.6.4 on  
278 periodic safety update reports and risk management planning respectively (see chapter 5.4. ).

279 To facilitate this process it is important to adequately classify medication errors. Depending on where  
280 the break occurs in the chain of events leading to the error and its consequences for the patient, a  
281 clear distinction should be made between medication errors associated with adverse reaction(s),  
282 medication errors without harm, intercepted medication errors and potential medication errors as  
283 shown in figure 2. The definitions for intercepted and potential medication errors are provided in  
284 chapter 4.3.3. and 4.3.4. respectively.



285

286 Figure 2: Concept for the classification of medication error reports for pharmacovigilance purposes. Depending on  
 287 the break in the chain of events (represented by X), medication errors may be classified as error with ADR, error  
 288 without harm, intercepted error and potential error.

### 289 4.3.3. Intercepted medication error ('near miss')

290 In the context of pharmacovigilance an intercepted error indicates that an intervention caused a break  
 291 in the chain of events that would have resulted in a 'potential ADR' and the intervention has prevented  
 292 actual harm being caused to the patient, e.g. a wrongly dispensed medicine was actually not taken by  
 293 the patient because the error was noticed.

294 In the context of patient safety reporting systems the term 'near miss' is used for describing what is  
 295 termed 'intercepted error' for pharmacovigilance purposes. A near miss from a patient safety  
 296 perspective is a random break in the chain of events leading up to a potential adverse event which has  
 297 prevented injury, damage, illness or harm, but the potential was nonetheless very near.

### 298 4.3.4. Potential medication error

299 According to GVP Module VII.B.5.9 a potential medication error is the recognition of circumstances that  
 300 could lead to a medication error, and may or may not involve a patient.

301 The term potential medication error refers to an error which has the potency for various mistakes and  
 302 may become reality at any time or it has already occurred. This includes all possible mistakes in the  
 303 prescribing, dispensing, administration or preparation of a medicinal product by all persons who are  
 304 involved in the medication process.

305 The potential error could lead or has led to

- 306 a) a medication error with harm, but without the awareness of the actual cause,
- 307 b) a medication error without harm, but without the awareness of the actual cause, or
- 308 c) a medication error without harm, but with the awareness of the actual cause and the subsequent  
 309 prevention (intercepted error, see chapter 4.3.3. ).

310 Following this approach the various mistakes could be clearly assigned to one or two of these  
 311 categories (a, b or c). For example, the indication of the strength of the active substance of oral

312 solutions (drops) may vary between different marketing authorisation holders. Sometimes the strength  
313 on the label of oral solutions refers to 'mg/ml' sometimes to 'mg/dose'. Therefore it is necessary -  
314 before change of medication – to calculate these dose regimes to ensure that the dose applied remains  
315 unchanged. Otherwise, a patient could be exposed to an accidental overdose due to a misinterpretation  
316 with regard to the concentration and the real amount of active substance per dose. In accordance with  
317 the classification proposed this might have led to a medication error with or without harm in  
318 accordance with categories a) or b). If a pharmacist notices a false calculation before delivering the  
319 drug to the patient this case would fall under category c). The borders between these categories are  
320 fluent as described. In another example a pharmacist noticed that the names of two medicines are  
321 similar and could clearly lead to drug name confusion in practise, but there was no involvement of a  
322 patient actually taking the drug. This potential medication error could be assigned to above category  
323 c). Since no patient was involved consequently no harm could occur, but the potential for error exists  
324 and such potential cases of medication error should be included in the relevant PSUR sections to allow  
325 regulators to take action to minimise the risk of drug name confusion. In this example the MAH is  
326 encouraged to also inform the Agency's Name Review Group (see chapter 5.3.1. ) if the medicine is  
327 authorised through the centralised procedure.

#### 328 **4.4. Root cause analysis**

329 WHO International Classification for Patient Safety (ICPS) defines root cause analysis as a reactive  
330 form of risk assessment to inform the development of actions taken to reduce risk, as a systematic  
331 iterative process whereby the factors that contribute to an incident (error) are identified by  
332 reconstructing the sequence of events and repeatedly asking "why" until the underlying root causes  
333 (contributing factors or hazards) have been elucidated.

334 For the purpose of conducting root cause analysis where appropriate chapter 5.5.1. describes  
335 important parameters which may have contributed to the occurrence of a medication error and which  
336 should be taken into account for case follow-up.

#### 337 **4.5. Complementary guidance**

338 This guidance should be read in conjunction with the following EU and international guidance:

- 339 • GVP Module V (rev. 1) on risk management
- 340 • GVP Module VI (rev. 1) on the management and reporting of adverse reactions to medicinal  
341 products
- 342 • GVP Module VII (rev. 1) on Periodic Safety Update Report
- 343 • ICH E2B (R3) Implementation Guide for Electronic Transmission of Individual Case Safety  
344 Reports
- 345 • ICH E2C (R2) Periodic Benefit Risk Evaluation Report (PBRER) the contents of which are  
346 consistent with GVP Module VII Periodic Safety Update Report
- 347 • ICH E2F Development Safety Update Report (DSUR)<sup>4</sup>
- 348 • ICH-Endorsed Guide for MedDRA Users: MedDRA® Term Selection: Point to Consider (latest  
349 version)

350 <sup>4</sup> ICH E2F guidance on Development Safety Update Reports (DSUR) requires that for an investigational medicinal product which has been approved for marketing in any country, safety findings from marketing experience relating to the approved indication but also on off-label use, administration to special populations (e.g. pregnant women), medication errors, overdose and abuse are included. Relevant points to consider for the evaluation of risks include (where applicable) evidence of clinically significant medication errors.

## 351 **5. Structure and processes**

352 This chapter highlights the general principles in relation to the recording, coding, reporting and  
353 assessment of medication error reports associated with medicinal products for human use, which are  
354 applicable to competent authorities responsible for medicinal products in EU Member States and  
355 marketing authorisation holders. The definitions provided in chapter 4. should be followed. EU  
356 requirements are presented in chapter 6.

### 357 **5.1. Recording of medication error reports**

358 In line with the scope of this guidance, recording medication errors associated with suspected adverse  
359 reaction(s) in the context of EU pharmacovigilance obligations applies to competent authorities in the  
360 EU Member States, marketing authorisation holders and the Agency, and includes the collection and  
361 collation of such case reports.

362 EU Member States are required by Article 102 of Directive 2001/83/EC to encourage healthcare  
363 professionals and consumers to report suspected adverse reactions to national competent authorities.  
364 Medication errors associated with the use of a medicinal product which result in harm may be reported  
365 spontaneously as unsolicited communication by a healthcare professional or consumer to a competent  
366 authority, a marketing authorisation holder or other organisation (e.g. regional pharmacovigilance  
367 centre, poison control centre, etc.). In this context GVP VI.A.2.3 defines a healthcare professional as a  
368 medically-qualified person such as a physician, a dentist, a pharmacist, a nurse, a coroner or as  
369 otherwise specified by local regulations. A consumer is a person who is not a healthcare professional  
370 i.e. a patient, a lawyer, or a friend, a relative or a carer of a patient.

371 If the error is associated with adverse reaction(s), the legal requirements for recording, reporting and  
372 assessment of suspected adverse reactions (serious and non-serious) associated with medicinal  
373 products for human use authorised in the EU as detailed in Title IX 'Pharmacovigilance' of Directive  
374 2001/83/EC and Chapter 3 of Regulation (EC) No 726/2004 apply. Marketing authorisation holders and  
375 national competent authorities should therefore record medication errors associated with adverse  
376 reaction(s) as ICSR in ICH E2B format in the local (MAH) or national (NCAs) pharmacovigilance  
377 database.

378 It is good practice to also record cases of medication errors not associated with adverse reaction(s) in  
379 the format of an ICSR, however these cases should not be reported as valid individual cases in  
380 accordance with GVP VI (see chapter 5.3. ). Marketing authorisation holders and national competent  
381 authorities may use alternative formats as appropriate or if required by national legislation to record  
382 cases.

383 From a patient safety perspective, errors in treatment and care may be the result of faulty procedures  
384 or systems and may or may not involve the use of medicines. Such errors may be reported  
385 spontaneously by healthcare professionals or consumers to the local healthcare provider organisation  
386 (e.g. a hospital, a nursing home, a general practitioner) where the patient has been treated. Such  
387 cases may be recorded and reported as 'patient safety incident' to regional and/or national patient  
388 safety organisations (PSO) where they exist in EU Member States.

389 Patient safety incident reports involving an error in the use of a medicine which are associated with  
390 adverse reaction(s) brought to the attention of a national patient safety organisation should also be  
391 *made available* to the competent authorities in EU Member States responsible for the supervision of  
392 medicines (see also chapter 6.2. ).

393 In line with the ICH E2C (R2) guideline and GVP Module VII.B.5.9 on PSURs, marketing authorisation  
 394 holders should summarise relevant information on patterns of medication errors and potential  
 395 medication errors, even when not associated with adverse outcomes, in the PSUR sub-section on  
 396 medication errors for the interpretation of safety data and for the benefit-risk evaluation of medicinal  
 397 products.

398 In addition, GVP module V on risk management systems requires that the potential for medication  
 399 errors is addressed in module SVI 'Additional EU requirements for the safety specification' providing  
 400 cumulative data.

401 For the purposes outlined above marketing authorisation holders should therefore record, report and  
 402 assess all medication errors which are brought to their attention, regardless of whether associated with  
 403 an adverse reaction(s), in their pharmacovigilance system or equivalent system for medication error  
 404 reports not associated with adverse reaction(s). This should allow the generation of summary  
 405 tabulations and of listings of individual cases to support assessment (see chapter 5.4. and 6.5. ), and  
 406 apply the classification described in chapter 4.3.2. of this guidance. Based on this classification, table 1  
 407 below provides an overview how medication errors are recorded both from a pharmacovigilance and  
 408 patient safety perspective. In addition, table 1 shows the reporting requirements for marketing  
 409 authorisation holders in line with EU pharmacovigilance obligations and GVP recommendations.

410 Table 1: Recording medication errors occurring in the EU.

			Patient Safety	Pharmacovigilance	
Medication Error Type	Error Occurred	Harm (ADR)	Recording	Recording	Report Type
Error with ADR	✓	✓	Incident with harm	Medication error with clinical consequence(s)	ICSR reportable to NCA and/or EV <sup>3</sup> ; PSUR summary <sup>1</sup> ; RMP;
Error Without Harm	✓	✗	Incident	Medication error without clinical consequence(s)	PSUR summary <sup>1</sup> ; RMP;
Intercepted Error	✓	N/A	Prevented incident ('near miss')	Intercepted medication error	PSUR summary <sup>1</sup> ; RMP;
Potential Error	✗	N/A	N/A <sup>2</sup>	MedDRA PTC: use of Term 'Circumstance or information capable of leading to medication error'	PSUR summary <sup>1</sup> ; RMP;

423

424 ✓ Indicates event did happen; ✗ indicates event did not happen; N/A not applicable; EV EudraVigilance

425 <sup>1</sup> The PSUR summary information includes interval and cumulative summary tabulations in line with GVP VII, and on  
 426 request of the competent authority or the Agency additional listings of cases of medication error of special interest  
 427 relevant for the benefit-risk evaluation. See chapters 5.3. and 5.4.

428 <sup>2</sup> Not in line with the definition of a patient safety incident which is any unintended or unexpected incident which  
 429 could have or did lead to harm for one or more patients receiving e.g. NHS England care. Report prevented patient  
 430 safety incidents (known as 'near misses'). Therefore a potential error is not an incident because it has not occurred  
 431 and is not a near miss because it cannot be said that it has been prevented.

432 <sup>3</sup> Only applicable after successful EudraVigilance audit, see chapter 5.3. and Annex 1.

## 433 **5.2. Terminologies for coding purposes**

434 In line with the scope of this guidance the terminology stakeholders will use for recording and coding  
435 medication errors will depend on the purpose, i.e. compliance with EU pharmacovigilance reporting  
436 requirements or compliance with national, regional or local patient safety reporting systems where  
437 established in EU Member States. This chapter briefly describes the terminologies applied to either  
438 context.

### 439 **5.2.1. Context of pharmacovigilance**

440 The Medical Dictionary for Regulatory Activities (MedDRA) is used worldwide by regulatory authorities,  
441 pharmaceutical companies, clinical research organisations and health care professionals for sharing  
442 information concerning medicinal products for regulatory purposes.

443 In line with Article 25 of the Commission Implementing Regulation (EU) No 520/2012 on the  
444 performance of pharmacovigilance activities, the classification, retrieval, presentation, risk-benefit  
445 evaluation and assessment, electronic exchange and communication of pharmacovigilance and  
446 medicinal product information, EU Member States, marketing authorisation holders and the Agency  
447 shall apply the MedDRA terminology.

448 The definition of medication error provided in chapter 4.3. is close to the definition provided in the  
449 MedDRA Term Selection: Point to Consider (MTS:PTC) and introductory guide. Subcategories of  
450 medication errors covered by this definition would include *prescribing errors* of physicians or other  
451 healthcare professionals who have the authority to prescribe, or *dispensing errors* which are not limited  
452 to pharmacists, but may also include nurses and physicians who dispense medicines. Also *documented*  
453 *hypersensitivity to administered drug* is a subcategory of medication error referring to the situation  
454 when a patient is administered a medicinal product that is documented in the patient's medical file to  
455 cause a hypersensitivity reaction in the patient.

456 The concept of intercepted errors referred to in chapter 4.3.3. is also reflected in MedDRA providing  
457 several terms for coding and data retrieval purposes under the *HLT Medication Errors NEC*. For further  
458 information please refer to MTS:PTC.

459 Medication errors should be clearly distinguished from *off-label use* which according to GVP module VI  
460 refers to situations where the medicinal product is *intentionally* used for a medical purpose not in  
461 accordance with the authorised product information.

462 Medication errors should be distinguished from *misuse*, which is defined as *intentional and*  
463 *inappropriate* use of the medicinal product not in accordance with the authorised product information.

464 Also *product quality issues* which are abnormalities that may be introduced during the  
465 manufacturing/labelling, packaging, shipping, handling or storage process of a medicinal product  
466 should be distinguished and not included in the definition of a medication error provided in chapter 4.3.  
467 of this guidance. For example, the splitting of a scored tablet in two differently sized parts is  
468 considered a product quality complaint and not a medication error.

### 469 **5.2.2. Context of patient safety**

470 Errors may happen when patients receive healthcare services for preventive, diagnostic, curative or  
471 rehabilitative purposes which may or may not involve the use of a medicine. If medication errors  
472 happen with a pattern or at an unacceptable frequency or result in serious consequences for the  
473 patient and public health, it is essential to understand the causes, contributory factors as well as



474 consequences of the error, and the possible mitigating actions and solutions which could prevent the  
475 error from happening again.

476 There is currently no commonly agreed terminology used for classifying patient safety incident reports  
477 in national reporting and learning systems of EU Member States where they exist.

478 The World Health Organization (WHO) has been leading in examining patient safety incident reporting  
479 and learning systems. A major milestone was the launch of the Conceptual Framework for the  
480 International Classification for Patient Safety (WHO ICPS) as the basis for a common language. WHO  
481 ICPS defines an error as a failure to carry out a planned action as intended or application of an  
482 incorrect plan. Errors may manifest by doing the wrong thing (commission) or by failing to do the right  
483 thing (omission), at either the planning or execution phase. In the context of medication practice the  
484 plan or intended action is directed towards successful treatment of the patient's condition.

485 To facilitate learning from patient safety incident reports, WHO is currently undertaking work aimed at  
486 drafting a Minimal Information Model (WHO MIMS) which will be universally applicable to patient safety  
487 incident reporting. For more information please refer to the WHO [website](#).

### 488 **5.3. Reporting requirements for medication errors associated with adverse** 489 **reactions**

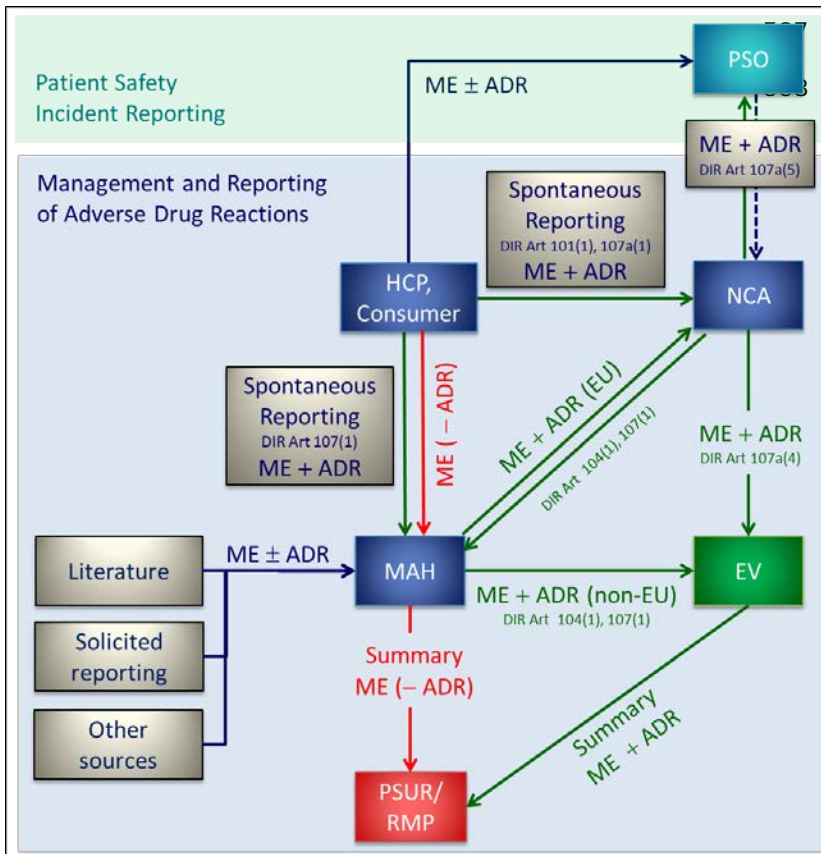
490 Medication errors associated with adverse reaction(s) may be reported spontaneously as unsolicited  
491 communication by a healthcare professional or consumer to a competent authority, a marketing  
492 authorisation holder or other organisation (e.g. regional pharmacovigilance centre, poison control  
493 centre) or described in the scientific literature.

494 GVP module VI.C.6 highlights the requirements for the electronic exchange of information on  
495 medication errors associated with adverse reaction(s) between competent authorities in EU Member  
496 States, marketing authorisation holders and the Agency through EudraVigilance, the data processing  
497 network to collate and share pharmacovigilance information electronically as defined in Articles 24(1)  
498 and 24(3) of Regulation (EC) No 726/2004.

499 Medication errors may also be reported in the context of solicited reports of suspected adverse  
500 reactions derived from organised data collection systems, which include clinical trials, observational  
501 studies, registries etc. The general reporting rules for suspected adverse reactions occurring in  
502 organised data collection systems conducted in the EU under the scope of Directive 2001/83/EC,  
503 Regulation (EC) No 726/2004 or Regulation (EU) No 536/2014<sup>5</sup> apply accordingly. Figure 3 outlines  
504 the information flow for medication error reporting in line with EU pharmacovigilance reporting  
505 requirements of Directive 2001/83/EC and taking into account the role of national patient safety  
506 organisations as referred to in Article 107a(5) of Directive 2001/83/EC.

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<sup>5</sup> REGULATION (EU) No 536/2014 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC.



522 Figure 3: The graph shows the information flow (green arrows) for medication errors reports associated with  
 523 suspected adverse reaction(s) (+ ADR) in line with EU reporting requirements of Directive 2001/83/EC, and the  
 524 stakeholders involved: marketing authorisation holders (MAH), national competent authorities (NCA) and  
 525 authorities, bodies, organisations and/or institutions responsible for patient safety (PSO) where they exist within a  
 526 Member State in accordance with Article 107a(5) of Directive 2001/83/EC. The red arrows represent medication  
 527 error reports not associated with suspected adverse reactions (- ADR) brought to the attention of MAHs and/or  
 528 NCAs which are outside the scope of EU reporting requirements of Directive 2001/83/EC and should therefore not  
 529 be submitted as ICSR, however such reports should be included as summary information in periodic safety update  
 530 reports (PSUR) and risk management plans (RMP) in line with GVP. From a public health perspective, it is good  
 531 practise that NCAs in Member States are also informed of adverse reactions associated with medication errors which  
 532 have been brought to the attention of a PSO in that EU Member State (dotted line).

533 Annex 1 provides the above information flow reflecting the simplified adverse reaction reporting rules  
 534 in accordance with Regulation (EC) No 726/2004 which will enter into force six months after the  
 535 announcement by the EMA Management Board that based on an independent audit report, the  
 536 EudraVigilance database has achieved full functionality in line with the provisions of Article 24(2) of  
 537 Regulation EC No 726/2004.

538 For the purpose of this guidance as shown in figure 4, all reports of suspected (serious and non-  
 539 serious) adverse reaction(s) associated with medication errors should be reported by MAHs and  
 540 competent authorities in EU Member State as individual case safety reports in line with definition  
 541 provided in GVP VI.A.2.5 and the requirements detailed in GVP Module VI.C.3 and VI.C.4 regarding  
 542 reporting time frames and reporting modalities. A valid ICSR should include at least one identifiable  
 543 reporter, one single identifiable patient, at least one suspect adverse reaction and at least one suspect  
 544 medicinal product in order to be reportable to competent authorities (GVP VI.B.2). In addition, the



545 reporting requirements for ICSRs to EudraVigilance apply, please refer to GVP VI.C.4 'Reporting  
546 modalities for serious and non-serious ICSRs' in connection with GVP VI Appendix 3.

547



548

549 Figure 4: MAHs and NCA reporting requirements for spontaneous reports of suspected (serious and non-serious)  
550 adverse reaction(s) associated with medication errors.

551

552 In line with the provisions of GVP Module VII.B.5 the PSUR includes cumulative and interval summary  
553 tabulations of data relevant for the benefit-risk evaluation of a medicinal product, including data on  
554 medication errors associated with spontaneous (serious and non-serious) adverse reaction reports  
555 (ICSRs) from post-marketing data sources. This includes reports from healthcare professionals,  
556 consumers, scientific literature, competent authorities and from solicited non-interventional studies, as  
557 well as medication errors which may constitute for example a safety signal or a safety concern. Serious  
558 adverse events from clinical trials and serious adverse drug reactions from non-interventional studies  
559 and other non-interventional solicited sources associated with medication errors may also be included  
560 in the relevant PSUR sections.

561 Once the EudraVigilance database has achieved full functionality following a successful audit and is  
562 accessible to marketing authorisation holders to the extent necessary to comply with their  
563 pharmacovigilance obligations<sup>6</sup>, summary tabulations from EudraVigilance supporting the assessment  
564 of medication errors in PSURs may be created using reports by means of the EudraVigilance data  
565 analysis system and complemented with additional data on medication errors held in the marketing  
566 authorisation holder's own pharmacovigilance system (i.e. non-serious cases of medication errors  
567 which occurred outside the EEA and medication errors not associated with adverse drug reactions).  
568 Alternatively marketing authorisation holders may create summary tabulations from their own  
569 pharmacovigilance system provided the system contains all relevant information on medication errors.  
570 A report on medication errors will also be made available on the European database on suspected  
571 adverse drug reaction reports ([www.adrreports.eu](http://www.adrreports.eu)) in line with the revised EudraVigilance access  
572 policy<sup>7</sup>.

573 In line with the provisions of GVP VII.C.4.2.2, the assessment of the causes and circumstances that led  
574 to a medication error may be supported by additional listings of individual cases of medication errors of  
575 special interest upon request by the competent authority or the Agency. Listings of individual cases  
576 should be provided by the marketing authorisation holder within an established timeframe to be  
577 included in the request. This may be accompanied by a request for an analysis of individual cases of  
578 medication errors associated with adverse reaction(s) where necessary for the scientific evaluation,  
579 including information on numbers of serious cases, details on the causes and circumstances that led to  
580 the medication error, mitigating and ameliorating factors and as necessary, analysis of non-serious  
581 cases. The MedDRA coding principles in section 5.6. should be applied.

582 A template for summary tabulation and additional listing of individual cases of medication errors of  
583 special interest upon request is provided in Annex 2.

<sup>6</sup> Article 24(2) of Regulation (EC) No 726/2004.

<sup>7</sup> [http://www.ema.europa.eu/docs/en\\_GB/document\\_library/Other/2011/07/WC500108538.pdf](http://www.ema.europa.eu/docs/en_GB/document_library/Other/2011/07/WC500108538.pdf)

### 584 **5.3.1. Medication errors related to invented names**

585 The checking of invented names is part of the EMA's role in evaluating the safety of medicinal products  
586 within the centralised authorisation procedure, since the proposed invented name(s) could create a  
587 public health concern or potential safety risk. Regardless of the association with adverse reaction(s)  
588 medication errors related to the invented name of a medicinal product (e.g. product name confusion)  
589 should be notified to the Agency's Name Review Group via the dedicated mailbox  
590 ([nrg@ema.europa.eu](mailto:nrg@ema.europa.eu)) for centrally authorised products. The [guideline on the acceptability of names](#)  
591 [for human medicinal products processed through the centralised procedure](#) (EMA/CHMP/287710/2014  
592 – Rev. 6) applies. For nationally authorised medicinal products competent authorities in Member States  
593 should be contacted for national guidance on checking invented names.

594 For ICSRs reporting a name confusion, the names of both medicinal products involved in the confusion  
595 should be provided in the drug section regardless whether the sender holds a marketing authorisation  
596 for both products. In ICH E2B (R3) format the product which the patient received by mistake should be  
597 given the drug characterisation 'suspect' and the product which was not received (because of the  
598 error), should be assigned the characterisation 'drug not administered'. The coding for 'additional  
599 information on drug' should also be applied as outlined in section 5.5.2. The MedDRA terms selected  
600 should indicate the name confusion and any other associated medication errors and adverse reactions.

### 601 **5.4. Periodic reporting of medication errors without an adverse reaction**

602 Information on medication errors where no suspected adverse reaction has occurred, or in other words  
603 where the error did not result in clinical consequences or harm to the patient, do not fall in the  
604 definition of a reportable individual case provided Article 1(11) of Directive 2001/83/EC.

605 By analogy, intercepted errors (see definition 4.3.3. ) and potential medication errors (see definition  
606 4.3.4. ) which may occur in the context of the use of a medicinal product are not reportable as  
607 individual case safety reports to competent authorities responsible for medicinal products or to  
608 EudraVigilance. However, it is good practice that competent authorities systematically record  
609 information about medication errors without adverse reaction(s) which may be brought to their  
610 attention through exchange agreements with national patient safety organisations as outlined in  
611 chapter 6.2.

612 The information on medication errors without suspected adverse drug reaction brought to the  
613 marketing authorisation holder's attention may be relevant for the scientific evaluation and  
614 interpretation of safety data and of the overall benefit-risk profile of the medicinal product and should  
615 therefore be systematically recorded and assessed by marketing authorisation holders for  
616 pharmacovigilance purposes.

617 In line with the recommendations of GVP Module VII, patterns of medication errors regardless of  
618 whether associated with adverse reaction(s) should be included as summary information in the PSUR  
619 sub-section VII.B.5.9 2. on 'Medication errors' as shown in figure 5.

620 Marketing authorisation holders should make all reasonable efforts to include in the PSUR summary  
621 relevant information on patterns of medication errors, taking into account the reports brought to their  
622 direct attention by healthcare professionals and consumers and those published in the scientific  
623 literature, in addition to information either made public as single case reports, listings of individual  
624 cases or otherwise aggregated data or evaluations from national competent authorities and patient  
625 safety organisations if not presented elsewhere in the PSUR.

626 To support the assessment of the causes and circumstances of medication errors brought to the MAH's  
627 attention which are not associated with adverse reaction(s) including intercepted and potential errors,

628 listings of individual cases should be provided upon request by the competent authority or the Agency  
629 if the medication errors constitutes an area of special interest with relevance for the overall benefit-risk  
630 evaluation of the medicinal product (e.g. where a signal has arisen) or if the medication error is a  
631 safety concern in the risk management plan. A template for additional listings of individual cases of  
632 medication errors of special interest upon request is provided in Annex 2.

633 For the purpose of reporting medication errors in PSURs, marketing authorisation holders should apply  
634 the classification proposed in chapter 4.3.2. accordingly.

635



636

637 Figure 5: GVP requires MAHs to summarise information on patterns of medication errors in PSUR and RMP  
638 regardless of whether associated with adverse reaction(s).

639 PSUR section VII.B.5.9 should also include cross-references to other relevant PSUR sections (see  
640 chapter 5.3. ) where case reports of medication errors associated with an adverse reaction are  
641 discussed.

642 If the medication error constitutes an important safety concern which impacts on the overall benefit-  
643 risk balance of the medicinal product or on public health, such case regardless of whether associated  
644 with an adverse reaction should be notified in line with the recommendations of GVP Module VI.C.2.2.6  
645 as an emerging safety issue to National Competent Authorities and the Agency via a dedicated  
646 mailbox: [P-PV-emerging-safety-issue@ema.europa.eu](mailto:P-PV-emerging-safety-issue@ema.europa.eu).

647 In line with the recommendations of GVP Module V.B.8.6.4, the risk management plan Part II, Module  
648 SVI.4 "Potential for medication errors" should include a stand-alone summary of aggregated data on  
649 medication errors which occurred during the clinical trial programme and/or post-marketing period  
650 regardless of whether associated with adverse drug reaction(s), as shown in figure 5. The following  
651 information should be provided based on the summary tabulations or listings of individual cases  
652 provided in the PSUR (see Annex 2):

- 653
- Description of error (i.e. type or category as applicable)
  - Number of occurrences up to data lock point
  - Analysis of cause (based on the parameters described in chapter 5.5.1. )
  - Steps taken to prevent the error
  - Comments
- 654  
655  
656  
657

658 Where available, the information from failure mode and effects analysis (FMEA) conducted during the  
659 development programme for new medicines should be taken into account to evaluate the risk of  
660 medication errors in normal clinical practice and to identify knowledge gaps in the safety profile where  
661 additional pharmacovigilance activities may be required. FMEA may be able to detect issues related for  
662 example to the invented name, product presentation, labelling, product user groups, translation into  
663 Braille or accidental ingestion by children.

## 664 **5.5. Follow-up of medication error reports**

665 GVP module VI.B.3 provides detailed guidance on how ICSRs should be followed-up to obtain as  
666 comprehensive information as required for the scientific evaluation and causality assessment of the  
667 reported case, in addition to any effort to collect the minimum information for an ICSR to be valid  
668 (please refer to GVP VI.B.2). GVP VI.B.2 also provides that reports, for which the minimum information  
669 for a valid ICSR remains incomplete, should nevertheless be recorded within the pharmacovigilance  
670 system to support on-going safety or benefit-risk evaluation activities.

671 Where medication errors are monitored events of special interest (e.g. where a signal has arisen) or  
672 safety concerns in the risk management plan of a medicinal product, or where the error resulted in  
673 serious harm to the patient, as a general rule the case should always be followed-up with the primary  
674 reporting source.

### 675 **5.5.1. Parameters to follow-up when reporting medication errors**

676 To ensure better learning from medication errors for the development and promotion of safe  
677 medication practice, it is good practice that marketing authorisation holders and national competent  
678 authorities follow-up essential information in relation to medication errors brought to their attention  
679 regardless of whether the error was associated with adverse reaction(s). Table 2 below provides an  
680 overview of parameters which may support the scientific evaluation of individual case reports or of  
681 aggregated data on medication errors.

682 For medication errors which are associated with serious adverse reaction(s), marketing authorisation  
683 holders and national competent authorities should make all reasonable efforts to collect the essential  
684 information provided in table 2 through appropriate case follow-up, unless national requirements for  
685 anonymous reporting of medication errors prevent follow-up.

686 It is good practice that national competent authorities perform follow-up activities in collaboration with  
687 national patient safety organisations based on the exchange agreements for information and reports  
688 on medication errors referred to in chapter 6.2.

689 Contributing factors are particularly relevant for the analysis of root causes which led to the error (see  
690 chapter 4.4. ) and should be discussed in the relevant PSUR sections (e.g. GVP VII.B.5.9) to support  
691 the assessment of signals and the selection of adequate risk minimisation measures intended to  
692 prevent or reduce the occurrence of medication errors in RMPs. Follow-up is particularly important to  
693 enable learning from cases with a potential for harm to the patient and from cases involving errors of  
694 omission resulting in adverse reaction(s). Table 2 also provides guidance on the respective ICH E2B  
695 ICSR data elements where the essential follow-up information should be reported in an ICSR.

696 Case reports of medication errors should include where possible the following information:

- 697 • Category (type) of medication error (see chapter 4.3.2. )
- 698 • Stage of medication process where the error occurred
- 699 • Contributing factor(s)
- 700 • Reported adverse reaction(s) if the error affected the patient or consumer with clinical  
701 consequences (error with ADR)
- 702 • Potential risk(s) for the patient or consumer if the error did not happen (potential error) or did not  
703 reach the patient or consumer (intercepted error, error without harm)
- 704 • Medicinal product(s) involved

- 705 • Batch number if the error is due to device failure

706 Table 2: Parameters to follow-up when reporting medication errors

Parameter	Description	ICSR Data element E2B (R2)	ICSR Data element E2B R(3)
Setting	<p>Inpatient (hospital, nursing home, care home), outpatient (general practitioner, specialist practice, ambulatory), pharmacy, drug store, private home, etc.</p> <p>Since this information is sensitive due to possible legal implications in the context of HCP liability, anonymisation of HCP personal data should be guaranteed, see chapter 5.7.1. )</p>	<p><b>A.2</b> Primary source</p> <p><b>B.5</b> Narrative  (Narrative information should only provide general setting not reporter information)</p>	<p><b>C.2.r</b> Primary source</p> <p><b>H.1</b> Narrative</p> <p><b>H.5</b> Case narrative in native language (Narrative information should only provide general setting not reporter information)</p>
Stage of medication process	<p>If <b>NOT</b> clearly derived from MedDRA coded reaction term(s) (single term or combination of terms), the stage of the medication process where the error occurred should be provided in the narrative:</p> <ul style="list-style-type: none"> <li>• Prescribing</li> <li>• Dispensing</li> <li>• Preparation for administration</li> <li>• Administration</li> </ul>	<p><b>B.5</b> Narrative</p>	<p><b>H.1</b> Narrative</p> <p><b>H.5</b> Case narrative in native language</p>
Category (type) of medication error	<p>The appropriate MedDRA LLT term(s) (either single term or combination of terms) (see chapter 5.6. ) should be selected to reflect the category (type) of error.</p>	<p><b>B.2.i.1.b</b> Reaction/ event in MedDRA terminology</p> <p><b>B.5.3.b</b> Sender's diagnosis</p>	<p><b>E.i.2.1</b> Reaction/event</p> <p><b>H.3.r.1.b</b> Sender's diagnosis</p>
	<p>If the type of error cannot be coded with a specific MedDRA LLT term, the LLT 'Medication error' should be used and further detail on the category (type) of medication error should be provided in the narrative.</p>	<p><b>B.2.i.1.b</b> Reaction/ event in MedDRA terminology</p> <p><b>B.5</b> Narrative</p>	<p><b>G.k.10.r</b> Additional information on drug</p> <p><b>H.1</b> Narrative case summary and</p>

Parameter	Description	ICSR Data element E2B (R2)	ICSR Data element E2B R(3)
			further information <b>H.5</b> Case narrative in native language
Contributing factor(s)	<p>Covariates, actions or influences which are thought to have played a part in the origin or the development of the medication error (or to increase the risk of error) related to:</p> <ul style="list-style-type: none"> <li>• Patient or healthcare professional staff related human factors such as behaviour (e.g. distraction, fatigue), performance (e.g. breach of standard of care) or communication issues (e.g. illegible handwriting on prescriptions, discharge recordings);</li> <li>• Work, e.g. system factors such as work environment, staffing issues, workload, shift work;</li> <li>• Organisation, e.g. healthcare policy, transition of patient care;</li> <li>• External factors beyond the control of the healthcare professional or patient, e.g. medication unavailability;</li> </ul> <p>This information may be provided by the primary reporter, or if the information is missing the ICSR sender should perform case follow-up. This is necessary information to conduct root cause analysis (see 4.4. ) where appropriate.</p>	<p><b>B.5.2</b> Reporter's comments</p> <p><b>B.5.4</b> Sender's comments</p>	<p><b>H.1</b> Narrative case summary and further information</p> <p><b>H.2</b> Reporter's comments <i>or</i></p> <p><b>H.4</b> Sender's comments</p> <p><b>H.5</b> Case narrative in native language</p>
Medicinal product(s) involved	<p>The medicinal product information should be coded in the ICSR drug section.</p> <p>If the patient did not receive the actual prescribed drug but another one, in <b>E2B (R3)</b> repeatable ICSR sections G should be completed with the information about the prescribed drug and the term '<i>Drug not administered</i>', as well as the information on the dispensed drug as the 'suspect' drug. In <b>E2B (R2)</b> the free text field 'additional information on drug' can also be used. The medication error should be captured with the appropriate MedDRA LLT code in section E.i Reaction(s)/Event(s).</p>	<p><b>B.4.k</b> Drug information</p> <p><b>B.4.k.1</b> Characterisation of drug role</p> <p><b>B.4.k.19</b> Additional information on drug</p>	<p><b>G.k.1</b> Characterisation of drug role +</p> <p><b>G.k.2</b> Drug identification +</p> <p><b>G.k.10.r</b> Additional information on</p>

Parameter	Description	ICSR Data element E2B (R2)	ICSR Data element E2B R(3)
	The additional information on drug (coded) data element G.k.10.r should be populated (7= <i>medication error</i> ) for E2B (R3).		drug
Covariates defining the treated population (CIOMS V)	<ul style="list-style-type: none"> <li>For paediatric population: consider factors linked to the need for individualised doses depending on age, weight and body surface area, age-related weight increase over time; lack of inadequate information in the SmPC and PIL for dose calculation and of appropriate paediatric formulations; specific drug combinations in neonates, transitions of care such as admission and discharge.</li> <li>For the elderly: consider higher risk of inappropriate prescribing associated with multiple morbidities and poly-pharmacy, medication reconciliation issues, poor adherence to treatment regimen (e.g. through impaired vision product label/PIL cannot be read) and increased susceptibility to ADRs e.g. through renal and hepatic functional decline.</li> <li>Disease/Condition: indication treated, disease severity, acute/chronic, co-morbidities</li> <li>Relevant medical history: risk factors, diet, alcohol use, tobacco use, concomitant therapy/treatment</li> <li>Pharmacology-related: blood or tissue levels; pharmacodynamic, pharmacokinetic and pharmacogenetic information</li> <li>Miscellaneous: prescriber (generalist vs specialist), pregnancy/nursing status, organ impairment</li> </ul>	<p><b>B.5</b> Narrative case summary and further information</p> <p><b>B.5.2</b> Reporters comments</p> <p><b>B.5.4</b> Senders comments</p> <p><b>B.1.7</b> Medical history</p> <p><b>B.3</b> Tests</p> <p><b>B.4</b> Concomitant drugs</p>	<p><b>H.1</b> Narrative case summary and further information</p> <p><b>H.2</b> Reporter's comments <i>or</i></p> <p><b>H.4</b> Sender's comments</p> <p><b>D.7.1.r.5</b> Comments +/-</p> <p><b>D.7.2</b> Text for relevant medical history and concurrent conditions +/-</p> <p><b>D.8</b> Relevant past drug history</p> <p><b>F.r.2.2.b</b> Test name</p>
Patient outcome	Patient outcome should be recorded for each MedDRA term coded. Strictly speaking the outcome of a medication error is not applicable if the medication error did occur. As this outcome is not available in E2B, the outcome should match the outcome of the consequential suspected ADR.	<p><b>B.2.i.8</b> Outcome of reaction/ event at the time of last observation</p>	<p><b>E.i.7</b> Outcome of reaction/event at time of last observation</p>
Seriousness	Coded according to ICSR seriousness criteria (refer to GVP VI.A.2.4 seriousness criteria: results in death, is life-threatening, requires inpatient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant		<p><b>E.i.3.2</b> Seriousness criteria at event level</p>



Parameter	Description	ICSR Data element E2B (R2)	ICSR Data element E2B R(3)
	<p>disability or incapacity, is congenital anomaly/birth defect) for serious adverse drug reactions.</p> <p>For medication errors associated with non-serious adverse drug reaction(s) the patient outcome should be reported accordingly.</p>		
	<p>For medication errors without ADR (i.e. intercepted errors, errors not resulting in harm, potential errors) the potential for harm should be described in the narrative of the case in the organisation's database. These reports are not reportable in the EU.</p>		<p><b>H.1</b> Narrative case summary and further information</p>
Mitigating factors	<p>Actions or circumstances which prevented or moderated the progression of an error towards harming the patient.</p> <p>Such actions could be taken with the medicinal product as a result of the reaction(s)/event(s), e.g. drug withdrawn, dose reduced, dose increased, etc. There may be other mitigating actions or circumstances which should be reported in the narrative accordingly.</p>	<p><b>B.5</b> Narrative case summary and further information + <b>B.4.k.16</b> Action(s) taken with drug</p>	<p><b>G.K.8</b> Action(s) taken with drug +/- <b>H.1</b> Narrative case summary and further information</p>
Ameliorating factors	<p>Corrective actions which took place after the medication error has already caused harm to the patient.</p> <p>Such actions could be taken with the medicinal product as a result of the reaction(s)/event(s), e.g. drug withdrawn, dose reduced, dose increased, etc. There may be other corrective actions or circumstances which should be reported in the narrative accordingly, e.g. administration of an antidote.</p>	<p><b>B.5</b> Narrative case summary and further information + <b>B.4.k.16</b> Action(s) taken with drug</p>	<p><b>G.K.8</b> Action(s) taken with drug +/- <b>H.1</b> Narrative case summary and further information</p>

707

708 If the information about a medication error received directly from a consumer/patient is incomplete,  
709 attempts should be made to obtain the consumer/patient's consent to contact a nominated healthcare  
710 professional to obtain further follow-up information. When the occurrence of the reaction/event of such  
711 case, initially reported by a consumer/patient, has been confirmed (totally or partially) by a healthcare  
712 professional, this information should be highlighted accordingly in the report.

713 Follow-up of medication error cases should be tailored towards optimising the collection of important  
714 missing information which may in exceptional cases involve targeted questionnaires in local language.  
715 Marketing authorisation holders are encouraged to discuss the content of medication error specific  
716 follow-up questionnaires with national competent authorities and to provide a copy in the risk  
717 management plan Annex 7 as appropriate.



## 718 **5.5.2. ICH E2B (R3) 'Additional information on drug' data element**

719 For the new ICH E2B (R3) standard options for medication error flagging are available. For the current  
720 ICH E2B (R2) standard please refer to GVP VI.

721 *ICH E2B (R3) - Additional Information on Drug (coded) (G.k.10.r)*

722 The ICH E2B (R3) standard for the electronic transmission of ICSRs provides the option of coding  
723 additional information which is not covered elsewhere in the E2B (R3) data elements under the data  
724 element 'Additional Information on Drug (coded) (G.k.10.r)' in order to 'flag' medication errors at drug  
725 level using code 7 which stands for medication error. The case details still have to be MedDRA coded in  
726 the relevant data fields as described in chapter 5.6. In this data element further scenarios may be  
727 coded which are however outside the scope of this guidance. A business process for using ICH E2B  
728 (R3) for recording medication errors in ICSRs is provided in Annex 4.

729 There may be situations where in this data element more than one code can be selected, for example if  
730 a medication error led to unintentional overdose both codes for the medication error (code 7) and for  
731 the overdose (code 2) should be selected. In addition to the flag, a MedDRA Lowest Level Term (LLT)  
732 should also be provided in data element Reaction(s)/Event(s) (E.i.2.1) selecting the most specific code  
733 possible to provide details on the type of medication error at case level, and where this information  
734 cannot be coded it should be provided in the narrative (H.1). In addition, data element G.k.11 can be  
735 used to provide further information in free text format where it cannot be specified by G.k.10.

736 *ICH E2B (R3) - Characterisation of drug role G.k.1*

737 For medication errors where the patient did not receive the actual prescribed medicinal product but  
738 another medicinal product, repeatable 'Sections G' should be completed with the information about the  
739 prescribed drug (selecting the characterisation of drug role as 'drug not administered'), as well as the  
740 information on the dispensed drug as the 'suspect' drug. The appropriate medication error should be  
741 captured with the appropriate MedDRA Lowest Level Term (LLT) code for the associated reaction/event  
742 in data element Reaction(s)/Event(s) (E.i.2.1).

743 *Inferred medication errors*

744 There may be instances where the initial primary reporter has not specifically stated there was a  
745 'medication error' but it is clear from the information provided that there has been an error. MedDRA  
746 coding principles advise that medication errors should not be inferred unless specific information is  
747 provided.

748 For cases clearly associated with a medication error based on specific information but where the term  
749 'medication error' has not been stated by the primary source, marketing authorisation holders and  
750 national competent authorities potentially exposed to liability in accordance with EU Member States'  
751 national law may provide a disclaimer (see chapter 5.7. ) in the 'senders comment' section.

## 752 **5.6. Coding medication errors with MedDRA**

753 To ensure consistency in how MedDRA terms are assigned to *verbatim* reports of medication errors and  
754 related information on the type of error, its causes (i.e. contributing factors related to human  
755 behaviour), clinical consequences (i.e. adverse reactions), symptoms and diseases, this guidance  
756 should be read in conjunction with the ICH-Endorsed Guide for MedDRA Users 'MedDRA Term  
757 Selection: Points to Consider' (MTS:PTC) document. The MTS:PTC guide promotes accurate and  
758 consistent term selection and can be downloaded from the [MedDRA website](#). The MTS:PTC guide  
759 should also be used by healthcare professionals, researchers, and other parties (e.g. patient safety

760 organisations) involved in the reporting of medication errors. The focus of the current MedDRA  
761 terminology is on coding clinical consequences of medication errors but to support the analysis of the  
762 causes why the error occurred in the first instance. Discussions on the expansion of MedDRA e.g. to  
763 include human use factors are ongoing.

### 764 **5.6.1. General coding principles**

765 GVP Module VI, chapter VI.C.6.2.3.3 on “suspected adverse reactions related to overdose, abuse, off-  
766 label use, misuse, medication error or occupational exposure” provides that if a case of medication  
767 error is reported with clinical consequences, the MedDRA Lowest Level Term (LLT) code, corresponding  
768 to the term closest to the description of the reported medication error should be added to the term for  
769 the suspected adverse reaction(s) in the data element ‘Reaction/event in MedDRA terminology (Lowest  
770 Level Term)’ (ICH-E2B(R2) B.2.i.1), in line with the recommendations of MTS:PTC in its latest version.

771 As a guiding principle MedDRA coders should only code what can be read in the report, without adding  
772 or subtracting any information, and coders should not infer a medication error unless specific  
773 information is provided by the primary source (the same principle applies to intentional overdose, off-  
774 label use, misuse and abuse). In line with GVP VI.C.2.2.3 where a competent authority or marketing  
775 authorisation holder disagrees with the diagnosis reported by the primary source, an alternative  
776 diagnosis can be provided in the ICH-E2B (R2) data element B.5.3 ‘Sender’s diagnosis/syndrome  
777 and/or reclassification of reaction/event’ in addition to the reported diagnosis provided in the ICH-  
778 E2B(R2) section B.2 ‘Reaction(s)/event(s)’.

779 For the purpose of summarising medication error reports in PSUR and RMP, the MedDRA structure  
780 allows for aggregation of reported terms in medically meaningful groupings to facilitate analysis of  
781 safety data. MedDRA can also be used to produce summary tabulations or listings of individual cases  
782 as referred to in chapter 5.4. to compute frequencies and to capture and analyse related data such as  
783 indications, investigations, medical and social history.

### 784 **5.6.2. Special situations**

785 This chapter provides guidance for MedDRA coders in special situations which may be associated with  
786 medication errors.

787 a) Is intentional re-challenge considered a medication error?

788 The concept of challenge, de-challenge and re-challenge to a medicinal product is one of the standard  
789 means of assessing adverse reactions. The administration of a suspect product to a patient, its  
790 subsequent withdrawal from the patient’s regimen with partial or complete disappearance of an  
791 adverse reaction (positive de-challenge) and subsequent reintroduction of the suspected product is by  
792 definition an intentional process. Therefore intentional re-challenge to a medicinal product should not  
793 be considered a medication error and not be coded as such.

794 b) Differences in term selection from *HLT Maladministrations* vs *HLT Medication Errors NEC*

795 There are some differences in selecting terms from the two HLTs. As the name suggests the  
796 maladministration HLT terms are associated with errors in administration. A term in the *HLT Medication*  
797 *Error NEC* may indicate that there was an error but not specify that it ended up as an administration  
798 error.

799 Some terms may require some consideration e.g. ‘Wrong patient received medication’ versus ‘Drug  
800 dispensed to wrong patient’. The latter is a dispensing error which may or may not have reached the

801 patient whereas the other term clarifies that the patient received the medication but the term does not  
802 specify the stage at which the error occurred.

803 c) Coding at different stages of medication error

804 Medication errors can be a series of events as shown in figure 2 at prescribing, dispensing, preparation  
805 or administration. As shown in chapter 4.3.2. there may be more than one stage in the drug  
806 treatment process where for example a prescription error if not intercepted would lead to a dispensing  
807 error, and consequently result in an administration error.

808 Other than monitoring errors, all medication errors which reach the patient are de facto administration  
809 errors. For coding purposes it is most important to capture the primary point in the chain of events. It  
810 is preferable to code other downstream errors in addition to provide as much information as possible.

811 d) Treatment non-compliance of the patient

812 Patient non-compliance with prescribed treatment or course of medication may result from a variety of  
813 factors with the most common scenarios being:

- 814 • *Intentional non-compliance* if the patient decides not to take the prescribed medicine because  
815 he feels better (e.g. antibiotic course not completed);
- 816 • *Medication error* if the patient is not capable of complying without supervision (e.g. Alzheimer's  
817 patient forgets to take drug or patient treated with antipsychotics);

818 In general if there is an element of intention implied, similar to the concept of intentional  
819 overdose/underdose and off-label use described in chapter 5.6.6. , this would be outside the scope of a  
820 medication error. The example of a patient not completing the course of antibiotics may be considered  
821 a misuse in accordance with the definition in GVP VI.

822 Circumstances of treatment non-compliance which cannot be coded with appropriate MedDRA terms  
823 should be provided in the narrative.

824 e) Medicinal product unavailability

825 If a patient is unable to get a (repeat-) prescription (e.g. from pharmacy or from emergency supplies)  
826 or due to a manufacturing defect and as a consequence the patient experiences a deterioration of the  
827 underlying condition, this is not considered a medication error. In this context MAHs should consider  
828 notification of any withdrawal, suspension or cessation of marketing of a human medicinal product to  
829 the competent authority as applicable<sup>8</sup>.

### 830 **5.6.3. MedDRA term selection**

831 The latest version of MedDRA terminology ([www.meddra.org](http://www.meddra.org)) should always be used and  
832 corresponding changes to the MedDRA term hierarchy taken into account. Within the *SOC Injury,*  
833 *poisoning and procedural complications* the *HLGT Medication Errors* provides HLTs which are most  
834 relevant for coding medication errors.

835 The [MedDRA Introductory Guide](http://www.meddra.org/how-to-use/support-documentation) (<http://www.meddra.org/how-to-use/support-documentation>)  
836 provides concept descriptions of MedDRA Preferred Terms (PT) for interpretation and coding purposes.  
837 Other relevant terms may be included under other MedDRA SOCs. It is recommended to use the  
838 MedDRA browser to identify available terms.

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<sup>8</sup> For further information please refer to Q&A on withdrawn-product notifications:  
[http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q\\_and\\_a/q\\_and\\_a\\_detail\\_000143.jsp&mid=WCOB01ac0580745911](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000143.jsp&mid=WCOB01ac0580745911)

839 The ICH-endorsed guide for MedDRA users 'MedDRA Term Selection: Points to Consider' (MTS:PTC)  
840 document provides comprehensive guidance including examples of how medication errors should be  
841 coded in the following scenarios and the MTS:PTC latest version should always be consulted.

842 If a case of medication error is reported with clinical consequences, the MedDRA Lowest Level Term  
843 (LLT) codes, corresponding to the term closest to the descriptions of both the reported medication  
844 error and the clinical consequences should be added to the observed suspected adverse reaction(s) in  
845 the data element 'Reaction/event in MedDRA terminology (Lowest Level Term)' (ICH-E2B(R2) B.2.i.1  
846 or ICH-E2B(3) E.i.2.1), in line with recommendations included in the latest version of the MTS:PTC.

847 Annex 3 provides additional coding examples for medication errors complimentary to the MTS:PTC.

#### 848 **5.6.4. Accidental and occupational exposures versus medication error**

849 In GVP VI.A.2.1.2 occupational exposure refers to the exposure to a medicinal product as a result of  
850 one's professional or non-professional occupation. For the purposes of MedDRA term selection and  
851 analysis of MedDRA-coded data, the MedDRA Introductory Guide version 17.0 encompasses under  
852 occupational exposure the 'chronic' exposure to an agent (including therapeutic products) during the  
853 normal course of one's occupation, and could include additional scenarios in specific regulatory regions.  
854 For example, occupational exposure may additionally relate to a more acute, accidental form of  
855 exposure that occurs in the context of one's occupation (e.g. occupational exposure of healthcare  
856 workers to a product). In contrast, accidental exposure is not defined in GVP or MTS:PTC and may  
857 refer to 'acute', sudden exposure in context of an accident which could also be the result of a  
858 medication error depending on the circumstances. In the wider context, occupational exposure is not  
859 normally considered to be associated with a medication error, although for pharmacovigilance purposes  
860 the majority of cases of occupational exposure would likely to be more of the acute/accidental type and  
861 therefore fall into the medication error category.

#### 862 **5.6.5. Off-label use versus medication error**

863 In line with GVP VI.A.2.1.2 off-label use relates to situations where the medicinal product is  
864 *intentionally* used for a medical purpose not in accordance with the authorised product information.  
865 The focus is on the intention of the healthcare professional to use a product outside the authorised  
866 indication for other medical purposes. Medication error however refers to any *unintentional* error in the  
867 prescribing, dispensing, or administration of a medicinal product while in the control of a healthcare  
868 professional, a patient or a consumer. To determine when the use of medicine is outside of an  
869 authorised indication it is paramount to establish what are the authorised indications in a country or  
870 regulatory region, e.g. within the EU.

#### 871 **5.6.6. Overdose/underdose versus medication error and off-label use**

872 Overdoses are not necessarily considered to be medication errors unless unintentional overdose  
873 occurred as a consequence of an error. In this situation it is important to code both concepts in order  
874 to facilitate case identification. Intentional overdose is not considered a medication error.

875 For the purposes of term selection and analysis of MedDRA-coded data, 'overdose' is more than the  
876 maximum recommended dose (in quantity and/or concentration), i.e., an excessive dose and  
877 underdose is the administration of less than the minimum recommended dose (in quantity and/or  
878 concentration).

879 Both over- and underdose may unintentionally be the result of a preceding medication error and  
880 relevant terms from either HLT *Overdose* or HLT *Maladministration* which currently includes the terms  
881 for underdose, may be chosen in combination with the associated medication error term.

### 882 **5.6.7. Coding of medication errors with medical devices**

883 For pharmacovigilance purposes device issues will be associated with drug delivery devices rather than  
884 medical devices although the MedDRA hierarchy contains a wide granularity of terms for those  
885 organisations/agencies/regions which also regulate medical devices.

886 There are separate concepts to consider when selecting device terms associated with medication error:

887 1. Device medication error terms falling into maladministration HLT in MedDRA hierarchy. These terms  
888 are most likely to be appropriate in pharmacovigilance for where a medication error has clearly  
889 occurred relating to a medicinal product delivery device.

890 2. Other terms in the device issues HLT may relate to medication errors from device  
891 error/failure/quality issues or into user errors (e.g. device difficult to use). There are also some terms  
892 which are clearly medication errors (e.g. wrong device dispensed) which are uniaxial terms within the  
893 Device issues HLT and not linked to medication error section of the hierarchy. For pharmacovigilance  
894 purposes the device will be a medicinal product delivery device and the consequence will be a  
895 medication error related to the drug. The example in the PTC TS shows a 'Wrong device used' (In  
896 device section of hierarchy only) and also recommends to code 'Accidental overdose' which falls into  
897 the medication error section of hierarchy.

898

Insulin was given using the wrong syringe resulting in the administration of an overdose. The patient developed hypoglycaemia.	Wrong device used Accidental overdose Hypoglycaemia	If an overdose is reported in the context of a medication error, the more specific term <i>LLT Accidental overdose</i> can be selected
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899

900 The PT 'Device misuse' has subordinate LLTs which may be analogous to the concept of PT 'Intentional  
901 product misuse' which is recommended to be used for coding cases falling within the definition in  
902 section 1.3.8 but also may also be related to medication error, for example the LLT 'Device use beyond  
903 labelled duration' may be either intentional misuse or a medication error. The LLT 'Intentional device  
904 misuse' should only be used where there is information to confirm that it is intentional. Where no  
905 information is available if it is intentional or unintentional the LLTs without intention should be used  
906 (E.g. 'Inappropriate device therapy'. In circumstances where it is clear that it was an unintentional  
907 device use, LLTs should be selected subordinate to the PT 'Device use error'.

### 908 **5.6.8. Standard MedDRA Query (SMQ) for medication errors**

909 Following approval of the ICH advisory panel in September 2014 a SMQ for medication errors is  
910 currently being developed to support data retrieval, signal detection and assessment of medication  
911 errors in pharmacovigilance databases.

## 912 **5.7. Rules of anonymisation of personal data**

913 Directive 95/46/EC on the protection of individuals with regard to the processing of personal data and  
914 on the free movement of such data provides the legal basis for the processing of personal data within  
915 the European Union. Regulation (EC) No 45/2001 regulates the protection of individuals with regard to

916 the processing of personal data by Community institutions and bodies, including the European  
917 Medicines Agency.

918 The provisions of GVP VI.C.6.2.2.8 regarding the processing of personal data within the EudraVigilance  
919 database for the purpose of safeguarding public health should also be applied to medication errors.

### 920 **5.7.1. Anonymous reporting**

921 Given the lack of EU harmonised legislation which protects healthcare professionals from potential  
922 liability claims in relation to reporting medication errors for pharmacovigilance purposes, some EU  
923 Member States have either implemented a no-blame policy or introduced anonymous reporting for  
924 medication errors.

925 In accordance with the national laws of relevant EU Member States the potential liability may result  
926 from claims that the classification of a suspected adverse reaction as a medication error made by the  
927 marketing authorisation holder may be interpreted as implying that a third party (the healthcare  
928 professional) has contributed to the occurrence of a medication error.

929 There is, therefore, a conflict between this potential liability and the implied pharmacovigilance  
930 obligation of the marketing authorisation holder to classify medication errors as such when reporting  
931 suspected adverse reactions to national competent authorities or the Agency. This conflict could be  
932 potentially addressed by including a 'disclaimer' in the suspected adverse reaction report (ICSR)  
933 submitted by the marketing authorisation holder to the national competent authority or the Agency:

934 *This suspected adverse reaction report is submitted and classified as a medication error solely and*  
935 *exclusively to ensure the marketing authorisation holder's compliance with the requirements set out in*  
936 *Directive 2001/83/EC and Module VI of the Good Pharmacovigilance Practices. The classification as a*  
937 *medical error is in no way intended, nor should it be interpreted or construed as an allegation or claim*  
938 *made by the marketing authorisation holder that any third party has contributed to or is to be held*  
939 *liable for the occurrence of this medication error.*

940 The inclusion of this disclaimer may help minimise the potential exposure of the marketing  
941 authorisation holder to claims that the classification of a suspected adverse reaction as a medication  
942 error may be interpreted as implying that a third party has contributed to the occurrence of a  
943 medication error.

944



## 945 **6. Operation of the EU regulatory network**

946 This chapter highlights the roles of key stakeholders involved in the collection, management and  
947 reporting of reports of medication errors regardless of whether associated with suspected adverse  
948 reactions.

949 The EU specific requirements, as defined in Directive 2001/83/EC, applicable to competent authorities  
950 in EU Member States and to marketing authorisation holders in relation to suspected adverse reactions  
951 associated with an error in the use of human medicinal products are explicitly highlighted.

952 The roles of consumers, healthcare professionals and patient safety organisations responsible for  
953 national patient safety incident reporting and learning systems in EU Member States in context of  
954 medication error reporting is also explained.

955 This chapter should be read in conjunction with the definitions and general principles detailed in  
956 chapter 1 and 2 of this guidance.

### 957 **6.1. The role of competent authorities in EU Member States**

958 The general provisions of GVP VI.C.2.1 regarding EU Member States' responsibilities for the collection  
959 and recording of reports of suspected adverse reactions apply.

960 Articles 107 and 107a of Directive 2001/83/EC impose a legal obligation on marketing authorisation  
961 holders and EU Member States to record and report suspected adverse reactions. For this purpose EU  
962 Member States operate a pharmacovigilance system to collect information on the risks of medicinal  
963 products with regard to patients' or public health, including suspected adverse reactions arising from  
964 use of the medicinal product within the terms of the marketing authorisation as well as from use  
965 outside the terms of the marketing authorisation, and to adverse reactions associated with  
966 occupational exposure [Directive 2001/83/EC, Article 101(1)]. This includes suspected adverse  
967 reactions arising from errors with human medicinal products.

968 EU Member States should also take all appropriate measures to encourage consumers (including  
969 patients) and healthcare professionals to report suspected adverse reactions, including those arising  
970 from medication errors, to the national competent authority (Directive 2001/83/EC, Article 102). For  
971 this purpose patient reporting should be facilitated through the provision of alternative reporting  
972 formats in addition to web-based formats which Competent Authorities provide on their national  
973 websites. National competent authorities should consider the recommendations<sup>9</sup> for minimum data  
974 elements to facilitate the implementation of web-based reporting forms to support consumer reporting  
975 of medication errors within their territory.

976 Furthermore, EU Member States have the obligation to evaluate the information received in the  
977 pharmacovigilance system scientifically, to detect any change to a medicine's risk-benefit balance, to  
978 consider options for risk minimisation and prevention and to take regulatory action concerning the  
979 marketing authorisation as necessary.

980 For this purpose competent authorities in EU Member States should systematically record and report  
981 medication errors associated with adverse reaction(s) which are brought to their attention in line with  
982 the ICSR general reporting requirements in GVP VI.B.7.

983 It is good practice that medication errors which do not fall in the definition of a reportable ICSR (i.e.  
984 intercepted errors, medication errors without harm and potential errors) which may be brought to the

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<sup>9</sup> Reflection Paper on standard web-based structured forms for the reporting of suspected adverse reactions by healthcare professionals and patients (EMA/137945/2011)

985 competent authority's attention through exchange agreements with national patient safety  
986 organisations as outlined in chapter 6.2. are systematically recorded and the information taken into  
987 account e.g. for risk management activities as appropriate.

988 Complementary to the provisions of GVP module VI for the management and reporting of adverse  
989 reactions to medicinal products, EU Member States should promote the classification of medication  
990 errors proposed in chapter 4.3. to support the performance of their pharmacovigilance obligations, i.e.  
991 to evaluate medication error reports scientifically, to detect any change to a medicine's risk-benefit  
992 balance related to its erroneous use and to implement appropriate risk minimisation measures in a  
993 timely and efficient manner.

994 Accurate classification and coding of information pertinent to medication errors (see chapter 5.5.1. )  
995 will help to achieve the intended objectives of the pharmacovigilance legislation to strengthen the  
996 supervision of medicinal products and to enhance the protection of public health. The recommendation  
997 in GVP VI.C.6.2.3.3 to explicitly code medication errors in addition to the suspected adverse drug  
998 reaction(s) therefore reflects the intention of the EU legislator and the objectives of the revised  
999 pharmacovigilance legislation.

## 1000 **6.2. Collaboration with National patient safety organisations**

1001 The pharmacovigilance legislation includes provisions intended to stimulate co-operation between EU  
1002 national pharmacovigilance centres and patient safety organisations (PSO) or any other authorities,  
1003 bodies, organisations and/or institutions responsible for patient safety including patient safety incident  
1004 reporting and learning systems established in Member States. The objective of this collaboration is to  
1005 minimise preventable harm from medication errors by learning from failures of the healthcare system.  
1006 The term 'patient safety incident' in this context refers to an event or circumstance which could have  
1007 resulted, or did result, in unnecessary harm to a patient. The scope of this term encompasses the  
1008 entire health care process whereas the scope of adverse reactions in pharmacovigilance refers to the  
1009 use of medicines by a patient or healthcare professional. Patient safety incidents may occur in hospitals  
1010 or other health care communities and may or may not involve a medicinal product. The harm to the  
1011 patient may be caused by an error resulting in an adverse event or adverse reaction. Medication error  
1012 incidents provide a valuable source of information regardless of whether or not the error is associated  
1013 with adverse reaction(s). In some EU Member States there may be other mechanisms to collect data  
1014 on medication error incidents outside of hospital settings, for example through poison control centres.

1015 As explained in chapter 3. , Article 107a (5) of Directive 2001/83/EC requires EU Member States to  
1016 ensure that adverse reaction reports arising from an error associated with the use of a medicinal  
1017 product that are brought to their attention are *made available* to any authorities, bodies, organisations  
1018 and/or institutions, responsible for patient safety within that EU Member State. EU Member States shall  
1019 also ensure that the authorities responsible for medicinal products within that EU Member State (i.e.  
1020 NCA) are *informed* of any suspected adverse reactions brought to the attention of any other authority  
1021 within that EU Member State.

1022 Many but not all EU Member States have established patient safety organisations or national patient  
1023 safety reporting and learning systems; therefore the implementation of these legal provisions is a  
1024 national responsibility of the competent authority in each EU Member State and is limited to the  
1025 exchange of information on medication error reports associated with suspected adverse drug  
1026 reaction(s).

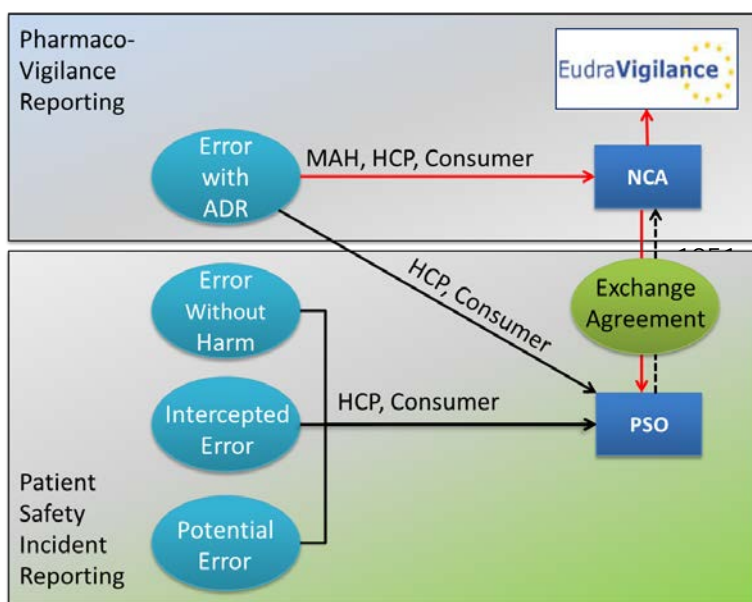
1027 In EU Member States where a national system for reporting patient safety incidents exist, the national  
1028 competent authority and the responsible patient safety organisation should work together to build  
1029 efficient working relationships with the aim to improve the quality and extent of reporting of



1030 medication errors and the resulting learning to maximize public health benefits of spontaneous  
 1031 reporting of medication errors. A formal exchange agreement between the two bodies should be signed  
 1032 to allow the exchange of information and of reports on medication errors. A good practice example for  
 1033 an exchange agreement is described in figure 6. It is acknowledged that individual EU Member States  
 1034 may use different models that best fit their national requirements.

1035 The exchange agreement in figure 6 should cover medication error reports associated with adverse  
 1036 reaction(s) brought to the NCA's attention which should preferably be exchanged (*made available*) as  
 1037 individual reports with the PSO or any other authority in that EU Member State responsible for patient  
 1038 safety. In addition, it is good practice that PSOs provide the NCA with *information* about medication  
 1039 errors brought to their attention in a suitable format (e.g. summary tabulation, listings of individual  
 1040 cases etc.) regardless of whether the error is associated with adverse reaction(s). However, medication  
 1041 error reports associated with adverse reaction(s) should preferably be exchanged as individual reports  
 1042 to allow further processing in national pharmacovigilance databases and subsequent transmission to  
 1043 EudraVigilance by the competent authority.

1044



1059

Figure 6: Model for collaboration between National Competent Authorities (NCA) and national patient safety organisations (PSO) for the exchange of medication errors. The red line between NCA and PSO refers to the legal provision to make medication error reports with ADR(s) *available*. The dotted line is a good practise recommendation to *inform* about medication errors regardless of whether associated with adverse drug reaction(s).

1060 As part of the Monitoring Medicines project funded by the Research Directorate of the European Union  
 1061 under its Seventh Framework Programme, WHO has published a report<sup>10</sup> intended to stimulate  
 1062 cooperation between national pharmacovigilance centres and patient safety organisations to streamline  
 1063 collaborative efforts to minimise preventable harm from medicines. The report provides background  
 1064 and useful technical guidance on the principles and methods of medication error incident reporting and  
 1065 learning and provides a framework for the coordination and sharing of pharmacovigilance evidence.

### 1066 **6.3. The role of the Agency's Pharmacovigilance Risk Assessment** 1067 **Committee**

1068 In accordance with EU legislation the Agency coordinates the scientific resources and expertise put at  
 1069 its disposal by Member States for the performance of pharmacovigilance activities, in particular the  
 1070 pharmacovigilance tasks performed by the Pharmacovigilance and Risk Assessment Committee (PRAC).  
 1071 The PRAC is responsible for providing recommendations in relation to the detection, assessment,

<sup>10</sup> [Reporting and learning systems for medication errors: the role of pharmacovigilance centres. World Health Organisation \(2014\)](#)

1072 minimisation and communication of risks of adverse reactions, including those arising from medication  
1073 errors associated with the use of medicinal products authorised in the EU regardless of the route of  
1074 authorisation (Article 61a(6) of Regulation (EC) 726/2004). During its monthly plenary meetings the  
1075 PRAC evaluates and provides recommendations to the Committee for Human Medicinal Products  
1076 (CHMP) or the Coordination Group for Mutual Recognition and Decentralised Procedures (CMDh) for  
1077 regulatory action on safety issues, including medication errors.

1078 The PRAC performs the initial analysis and prioritisation of signals of new risks or risks that have  
1079 changed or changes to the risk-benefit balance of a medicinal product, based on the evaluation of  
1080 pharmacovigilance data reported to EudraVigilance.

1081 In line with GVP module V.B.8.6.4 the RMP contains a dedicated section (Part II - SVI.4) which  
1082 specifically elaborates on the potential for medication errors based on pre- and post-authorisation  
1083 safety data reporting, including a review of preventive measures for the final product being marketed.  
1084 The PRAC is also responsible for monitoring the outcome of risk minimisation measures and conditions  
1085 of marketing authorisations for the safe and effective use of medicines which may be required to  
1086 manage the risk of medication errors (Article 56(1)(aa) of Regulation (EC) 726/2004). This may  
1087 include the design and evaluation of post-authorisation studies to further investigate medication errors  
1088 in clinical practice. In this context the PRAC may provide recommendations to MAHs on protocols to  
1089 study the utilisation of patterns of use of medicines under real life conditions with the objective to  
1090 quantify the risk of medication errors and to measure the impact of regulatory interventions.

1091 By analogy PSURs assessed by the PRAC include a dedicated section on aggregated data (summary  
1092 reports) of medication errors that occurred during the reporting interval in chapter VII.B.5.9. This  
1093 information is taken into consideration in the continuous evaluation of the benefits and risks of a  
1094 medicinal product.

1095 The specific pharmacovigilance tasks performed by the Agency are detailed in GVP module I.C.2.3  
1096 'Role of the European Medicines Agency' and corresponding GVP modules.

#### 1097 **6.4. The role of healthcare professionals, patients and consumers**

1098 Regardless of legal obligations related to reporting requirements for pharmacovigilance purposes,  
1099 consumers and healthcare professionals are critical stakeholders for successful learning from  
1100 medication errors acting as primary source for reporting and providing first-hand information on the  
1101 case. In accordance with the ICH E2D guideline a consumer is defined as a person who is not a  
1102 healthcare professional such as a patient, lawyer, or a friend, relative or carer of a patient. A  
1103 healthcare professional is defined as a medically-qualified person such as a physician, a dentist, a  
1104 pharmacist, a nurse, or as otherwise specified by local regulations.

##### 1105 Patient/consumer and healthcare professional reporting

1106 The pharmacovigilance legislation promotes and facilitates adverse reaction reporting by patients,  
1107 consumers and healthcare professionals through development and provision of standard web-based  
1108 structured forms. In accordance with Articles 102 and 107(a) of Directive 2001/83/EC each EU Member  
1109 State has the responsibility to record all suspected adverse reactions that occur in its territory which  
1110 are brought to its attention by consumers and healthcare professionals, including follow-up of case  
1111 reports, by means of national medicines web-portals or other means. To encourage reporting the  
1112 legislation requires that all medicinal products include a standard text in the SmPC asking both  
1113 healthcare professionals and patients to report any suspected adverse reaction in accordance with the  
1114 national spontaneous reporting system referred to in Article 107a(1) of Directive 2001/83/EC. For this  
1115 purpose the details (website URL and/or email address) of the national competent authorities' websites

1116 are included in section 4.8 'Undesirable effects' of the SmPC and section 4 'Possible side effects' of the  
1117 package leaflet accordingly.

1118 Medicinal products which are subject to additional monitoring in accordance with Article 23 of  
1119 Regulation (EC) 726/2004 include in addition a black triangle and a statement in both SmPC and  
1120 package leaflet asking healthcare professionals and patients to report any suspected adverse reactions  
1121 to allow quick identification of new safety information.

1122 As described in GVP module VI.B.1.1.1 consumers and healthcare professionals may report medication  
1123 errors as any other adverse reaction spontaneously to a competent authority, marketing authorisation  
1124 holder or other organisation (e.g. regional pharmacovigilance centre, poison control centre) as  
1125 unsolicited communication. Consumer reports should be documented and reported in accordance with  
1126 GVP VI.

#### 1127 No blame reporting culture for healthcare professionals

1128 Healthcare professionals should report errors of use of medicines which they either commit themselves  
1129 or which they are made aware of through consumers, patients or any other third party regardless of  
1130 whether the error is associated with suspected adverse reaction(s). As primary source of information  
1131 healthcare professionals play a key role in providing relevant information on the parameters required  
1132 for the scientific evaluation of the case (see chapter 5.5.1. ) by marketing authorisation holders and  
1133 regulatory authorities. The reporting of medication errors by healthcare professionals and consumers is  
1134 in no way intended, nor should it be interpreted or construed by a marketing authorisation holder,  
1135 national competent authority or any other third party as an admission, allegation or claim for potential  
1136 liability, but for the sole purpose of the pharmacovigilance tasks as described in Title IX of Directive  
1137 2001/83/EC.

### 1138 **6.5. The role of marketing authorisation holders**

1139 MAHs are required to operate their own pharmacovigilance system for the fulfilment of  
1140 pharmacovigilance tasks equivalent to the relevant EU Member State's pharmacovigilance system. This  
1141 includes the obligation to record, i.e. collect and collate all reports of suspected adverse reactions,  
1142 including those arising from use of the medicinal product within the terms of the marketing  
1143 authorisation as well as from use outside the terms of the marketing authorisation, and to adverse  
1144 reactions associated with occupational exposure [Directive 2001/83/EC, Article 104].

1145 MAHs are, therefore, legally required to report medication errors as part of their reporting obligation of  
1146 suspected adverse reactions if the adverse reaction is associated with an error.

1147 Directive 2001/83/EC does not explicitly require MAHs to classify suspected adverse reactions in  
1148 different categories provided for in the definition of an adverse reaction (i.e. medication errors,  
1149 overdose, occupational exposure, off-label use, use within the scope of the marketing authorisation,  
1150 etc.). However, GVP Module VI.C.6.2.3.3 on 'suspected adverse reactions related to overdose, abuse,  
1151 off-label use, misuse, medication error or occupational exposure' contains a recommendation for MAHs  
1152 to use the MedDRA Lowest Level Term (LLT) code to classify the medication error as such when  
1153 reporting in EudraVigilance (see 2.5.1.).

1154 For this purpose it is paramount that MAHs systematically record reports of medication errors which  
1155 are brought to their attention but which do not fall in the definition of a reportable ICSR (i.e.  
1156 intercepted errors, medication errors without harm and potential errors in line with chapter 4.3.2. ) in  
1157 their local pharmacovigilance database or equivalent system which allows for the collation of  
1158 medication error reports both with and without associated adverse reaction(s) in the summary reports  
1159 required for PSURs (see chapter 5.4. ). This includes reports from literature, solicited reporting and

1160 other sources. MAHs should make all reasonable efforts to follow-up the essential information referred  
1161 to in table 2 (chapter 5.5.1. ) for the analysis, scientific evaluation and interpretation of case reports of  
1162 medication errors in line with the general provisions in chapter 5.5. and to include an analysis of this  
1163 information in the summary report on medication errors provided for in GVP VII.B.5.9 in the PSUR.

1164 In addition, MAHs should provide additional listings of cases of medication errors not associated with  
1165 ADRs upon request of a competent authority or the Agency to support the scientific evaluation and  
1166 assessment of the summary reports provided in PSURs as outlined in chapter 5.4.

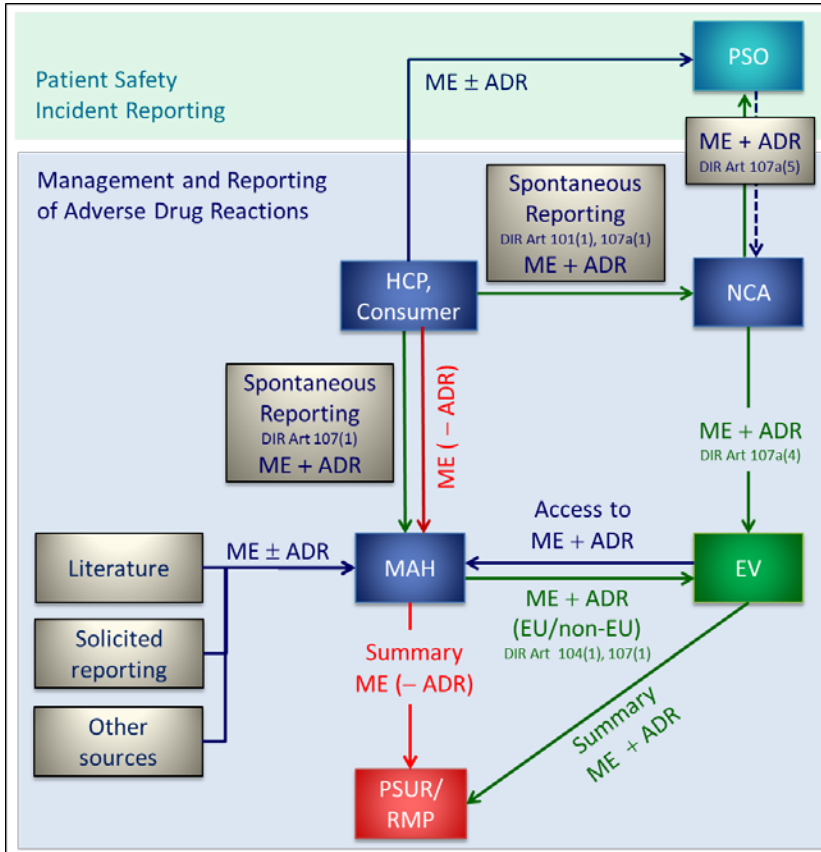
1167 According to GVP V.B.8.6.4, the MAH should discuss in RMP module SVI medication errors which  
1168 occurred both during the development phase and post-marketing, providing information on the errors,  
1169 their potential cause(s) and possible remedies given but also taking into account potential reasons for  
1170 medication errors. If adverse reactions occurred as a result of medication errors appropriate measures  
1171 to minimise the risk of medication errors should be proposed. In this context, MAHs should also take  
1172 into consideration the results of the analysis of the essential information referred to in table 2 (chapter  
1173 5.5.1. ) as appropriate.

1174 MAH should apply the classification of medication errors referred to in chapter 4.3.2. to facilitate these  
1175 activities.

1176

1177 **Annexes**

1178 **Annex 1 - Simplified reporting rules for medication errors associated with**  
 1179 **adverse reactions post EudraVigilance audit**



1180

1181 The graph shows the simplified information flow (green arrows) for medication errors reports associated with  
 1182 suspected adverse reactions (+ ADR) in line with EU reporting requirements of Directive 2001/83/EC after a  
 1183 successful EudraVigilance audit, and the stakeholders involved: marketing authorisation holders (MAH), national  
 1184 competent authorities (NCA) and authorities, bodies, organisations and/or institutions responsible for patient safety  
 1185 (PSO) where they exist within a Member State. The red arrows represent medication error reports not associated  
 1186 with suspected adverse reactions (- ADR) brought to the attention of MAHs and/or NCAs which are outside the  
 1187 scope of EU reporting requirements of Directive 2001/83/EC and should therefore not be submitted as ICSR,  
 1188 however such reports should be included as summary information in periodic safety updated reports (PSUR) and  
 1189 risk management plans (RMP) in line with GVP. From a public health perspective, it is good practise that NCAs in  
 1190 Member States are also informed of adverse reactions associated with medication errors which have been brought  
 1191 to the attention of a PSO in that Member State (dotted line).

1192

1193 **Annex 2 - Template for summary tabulation and listing of individual cases**  
 1194 **of medication errors**

1195 In line with GVP VII.B.5.6 the PSUR includes interval and cumulative summary tabulations of adverse  
 1196 reactions including those associated with medication errors for the reporting interval. This annex  
 1197 provides a template for summary tabulations and for additional listings of individual cases of  
 1198 medication errors not included elsewhere in the PSUR, e.g. where medication errors are discussed as  
 1199 safety signal or safety concern.

1200 The tables should be created automatically from the pharmacovigilance database but marketing  
 1201 authorisation holders may modify the tables to suit specific requirements, as appropriate.

1202 For PSURs covering several medicinal products with the same active substance differences between  
 1203 indications, formulations and target populations may require separate tables (e.g. for medication  
 1204 errors with patches versus medication errors with oral formulation).

1205 A summary tabulation as shown in table A2-1 should be included in GVP VII.C.5 as PSUR EU regional  
 1206 appendix, sub-section on medication errors with cross-references to GVP VII.B.5.9 MedDRA  
 1207 terminology should be applied for coding medication error related terms at MedDRA Preferred Term  
 1208 (PT) and Higher Level Term (HLT) levels based on spontaneous ICSRs in line with the provisions in  
 1209 chapter 5.6.

1210

1211 **Table A2-1:** Summary tabulation - numbers of Preferred Terms (PT) in the HLT Medication Errors reported with  
 1212 serious or non-serious adverse reaction(s) from post-authorisation sources\* for <invented name>.

HLGT Medication Errors <sup>1</sup>	Spontaneous, including competent authorities (worldwide) and literature					Non-interventional post-marketing study and reports from other solicited sources **	
	Serious		Non-serious		Total Spontaneous	Serious	
	Interval	Cumulative	Interval	Cumulative	Cumulative	Interval	Cumulative
<HLT 1>							
<PT>							
<PT>							
<HLT 2>							
<PT>							
<PT>							

1213 <sup>1</sup> Consider MedDRA HLTs such as *Accidental exposures to Product, Maladministrations, Medication Errors NEC, Medication Monitoring*  
 1214 *Errors* and other relevant HLTs as applicable.

1215 \* Non-interventional post-authorisation studies, reports from other solicited sources and spontaneous ICSRs (i.e., reports from  
 1216 healthcare professionals, consumers, competent authorities (worldwide), and scientific literature)

1217 \*\* This does not include interventional clinical trials.

1218 Additional listings of individual cases of medication errors of special interest shown in table A2-2 below  
 1219 may be provided upon request by the PRAC Rapporteur or a EU Member State through the Agency to  
 1220 support the assessment of medication errors in PSURs, particularly for medication errors of special  
 1221 interest or if constituting a safety concern in the risk management plan. Listings of individual cases as

1222 shown in table A2-1 should be included in GVP VII.C.5 as PSUR EU regional appendix, sub-section on  
 1223 medication errors with cross-references to GVP VII.B.5.9 accordingly.

1224 **Table A2-2:** Listings of individual cases of medication errors of special interest for <invented name>.

Medication error of special interest MedDRA Preferred Term(s)	Reported adverse reaction(s) MedDRA Preferred Term(s)	Medication stage (prescribing, dispensing, preparation, administration, monitoring)	Contributing factors (e.g. human behaviour, system related, transition of care, external beyond HCP/patient control)	Patient risk factors (e.g. paediatric, elderly, pregnancy, lactation, disease)	Ameliorating factors and corrective action(s)
<PT 1>					
<case 1>					
<case 2>					
<PT 2>					
<case 1>					
<case 2>					

1225  
 1226

1227 **Table A2-3:** Listing of individual cases of medication error not associated with adverse reaction(s) from post-  
 1228 authorisation sources\*\*\*\* for <invented name>.

1229

Type of error	Brief description	Medication stage (e.g. prescribing, dispensing, preparation, administration, monitoring)	Contributing factors (e.g. human behaviour, system related, transition of care, external beyond HCP/patient control)	Patient risk factors if patient involved	Mitigating factors preventing or moderating the progression of an error
<b>Medication errors without harm</b>					
<case 1>					
<case 2>					
Totals					
<b>Intercepted errors</b>					
<case 1>					
<case 2>					
Totals					
<b>Potential errors</b>					
<case 1>					
<case 2>					
Totals					

1230  
 1231  
 1232

\*\*\*\* Reports from non-interventional post-authorisation studies and other solicited sources, reports from healthcare professionals and consumers and the scientific literature brought to the attention of the marketing authorisation holder

1233



1234 **Annex 3 - Additional coding examples for medication errors complimentary**  
 1235 **to MTS:PTC documents**

1236 This Annex includes specific examples of medication errors in addition to those provided in the  
 1237 MTS:PTC documents to address. The MTS:PTC document in its latest version should always be  
 1238 consulted.

1239 **A. Medication errors reported with clinical consequences**

1240 If a medication error is reported with clinical consequences (with ADR/ADE), select terms for both the  
 1241 medication error and the clinical consequences.

1242 Examples

Reported	LLT Term Selected	Comment
Patient experienced paraplegia after an epidural anaesthesia procedure was carried out with a needle contaminated with topical disinfectant	Accidental exposure to product; Exposure to contaminated device; Paraplegia;	This is a procedural error caused by the wrong use of the epidural needle as device.
Patent was inadvertently administered the higher strength of a calcium channel blocker and experienced hypotension	Incorrect dose administered; Hypotension;	Note the difference in concepts of dose, dosage and dosage form
Dose calculation error in an adolescent treated for growth failure results in insulin-like hypoglycaemia	Incorrect dose administered; Hypoglycaemia;	There is no term for coding dose calculation error but this information should be provided in the case narrative.
Patient was prescribed different insulin product at same daily dose and experienced hypoglycaemia	Wrong drug administered; Drug prescribing error; Hypoglycaemia;	
Patient was prescribed 10 fold higher strength of an oral opioid and went into respiratory failure at home after having taken 3 doses	Drug prescribing error; Respiratory failure; Accidental overdose	The PT Prescribed overdose should not be selected; the overdose is not intended and consequence of a medication error.
Patient well controlled on antiepileptic medicines failed to get repeat or emergency supply and was hospitalised with partial seizures	Drug dose omission; Partial seizures;	The fact that it is a supply issue cannot be coded and should be recorded in the narrative of the database.

1243 **B) Medication errors and potential medication errors reported without clinical consequences**

1244 Medication errors without clinical consequences are not adverse reactions, but as highlighted in chapter  
 1245 5.4. they should also be recorded by MAHs if brought to their attention. Select a term that is closest to  
 1246 the description of medication error reported. Also the potential occurrence of a medication error and  
 1247 intercepted errors (or near misses) should be recorded and the term which is closest to the description  
 1248 of the error should be selected.

1249 If specifically reported that no adverse effect has occurred, it is acceptable to select LLT No adverse  
 1250 effect.

1251 In instances where the medication did not reach the patient, it is acceptable to select LLT Drug not  
 1252 taken in context of intercepted medication error.



## 1253 Examples

Reported	LLT Term Selected	Comment
Patient was dispensed the wrong product due to confusion of packs. The product is available in two presentations, one colour coded and one not.	Product packaging confusion; Wrong drug dispensed;	The information that the product is available in 2 presentations with different colour code cannot be coded and should be provided in the case narrative.
Product preparation requires two pre-filled syringes to be mixed prior to administration in 15 steps to achieve homogenous solution for injection. This is a difficult procedure and will likely result in problems in preparation	Inappropriate preparation of medication Circumstance or information capable of leading to medication error;	This is an example for a potential medication error due the high number of preparation steps required.
Pharmacist reported confusion of product label of prolonged-release with immediate release formulation	Product Label confusion; Circumstance or information capable of leading to medication error;	This is an example of a potential medication error since the report does not state that the wrong product was actually dispensed. The most specific code for the reported potential medication error should be selected, and also the PT Circumstance or information capable of leading to medication error to capture that the error is a potential one.

1254 **C) Accidental exposure**

1255 Accidental exposure to medicines occurs if a medicinal product is used by someone other than the  
1256 person the medicine was prescribed for, or if a person becomes inadvertently exposed. It may be  
1257 harmful, and in some cases life-threatening. Adverse reactions following accidental exposure to a  
1258 medicinal product associated with a medication error should always be reported. The principles for  
1259 medication errors also apply to accidental exposures.

## 1260 Example

Reported	LLT Term Selected	Comment
A child died after accidental exposure to a fentanyl patch which had fallen off another person without noticing and got stuck to the child.	Accidental exposure to product by child; Medicinal patch adhesion issue;	In this example the poor adhesion could also be a quality issue, however poor visibility of the patch may be one of several possible contributing factors;

1261 **D) Accidental overdose**

1262 A medication error may be associated with accidental overdose, however overdose per se is not  
1263 considered a medication error. For the purposes of term selection and analysis of MedDRA-coded data,  
1264 overdose is defined as more than the maximum recommended dose (in quantity and/or concentration),  
1265 i.e. an excessive dose (see Appendix B, MedDRA Introductory Guide). If the report clearly states that  
1266 the overdose is the result of a medication error the *PT Accidental overdose* should be used.

## 1267 Examples

Reported	LLT Term Selected	Comment
Patient was administered a 20% overdose due to a reconstitution error of a medicine where both the concentrate and the diluent vials contained an overfill not adequately communicated in the posology section of the SmPC	Inappropriate preparation of medication; Accidental overdose;	This is an example for a common reconstitution issue resulting in a preparation error and consequential accidental overdose.
Infant was administered overdose of antipyretic solution for infusion due to a confusion of 'mg' with 'ml'	Drug administration error; Accidental overdose;	The fact that the administration error occurred through a human error confusing mg with ml cannot be coded and should be reported in the case narrative.
Patient exposed to life-threatening overdose due to confusion of dilution requirements for generic (higher concentrated solution for infusion) with requirements for originator	Inappropriate dilution of medication; Accidental overdose;	

1268

1269

1270 **Annex 4 - Business process proposal for using ICH E2B (R3) for recording**  
 1271 **medication errors in ICSRs**

1272 This draft proposal for recording medication errors in ICSRs using ICH E2B (R3) was finalised by the  
 1273 EudraVigilance Expert Working Group (EWG) in March 2015 and should be read in connection with  
 1274 chapter 5.5.2. of this guidance.

1275 Once implemented after a successful EudraVigilance audit, the ICH E2B (R3) data element G.k.10.r  
 1276 'Additional information on drug (coded)' should always be populated with the respective code for  
 1277 medication error at drug level (i.e. code 7) if the primary source has indicated that any type of  
 1278 medication error may have occurred. As this is a repeatable field, other codes may be used as  
 1279 appropriate.

1280 If there is no explicit indication of a medication error by the primary source which would clearly  
 1281 transpose into a MedDRA term in the reaction section but there is a hint that there may have occurred  
 1282 an error in the context of the clinical course description, the sender may choose to populate data  
 1283 element G.k.10.r at their discretion to 'flag' a medication error. The case should be followed up to  
 1284 confirm if there was actually a medication error. The use of G.k.10.r also refers to intercepted errors  
 1285 where the cases are recorded as ICSRs in the database for PSURs.

1286 In addition to the flag, an appropriate MedDRA term should be selected in reaction (E.i.2.1b) or  
 1287 sender's diagnosis (H.3.r.1b) as applicable (see MedDRA Term Selection: Points to Consider).

1288 The advantage of using the G.k.10.r flag is to identify medication error cases at drug level rather than  
 1289 only at case level.

1290 The fields should be populated as follows:

Scenario	Flag G.k.10.r	Reaction E.i.2.1b	Sender's comment H.4	Sender's diagnosis H.3.r.1.b
Reported as medication error, sender agrees	✓	✓	As applicable	
Reported as medication error, sender assessment provides alternative 'diagnosis'	✓	✓	✓	✓
Not explicitly reported as medication error but information and assessment of case leads to suspicion that a medication error was involved	At discretion	MedDRA PTC: Do not infer	Disclaimer* may be used as an option	✓

1291 \*Disclaimer as referred to in chapter 5.7.1.