EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

23 October 2015
EMA/190895/2015
Pharmacovigilance Risk Assessment Committee

Overview of comments received on draft 'Good practice guide on recording, coding, reporting and assessment of medication errors' (EMA/762563/2014)

Interested parties (organisations or individuals) that commented on the draft document as released for consultation.

Stakeholder no.	Name of organisation or individual
1	AstraZeneca
2	Dr Roberto Frontini, Universitätsklinikum Leipzig
3	Swissmedic
4	Foundation Portal for Patient Safety/CMR
5	Standing Committee of European Doctors / Comité Permanent des Médecins Européens (CPME)
6	PHARMIG – Association of the Austrian pharmaceutical industry
7	AESGP
8	Gilead Sciences International Ltd.
9	Vaccines Europe
10	Drug Commission of the German Medical Association (DCGMA)
11	Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM)
12	EFPIA
13	German Pharmaceutical Industry Association (BPI)
14	Sanofi Pasteur MSD
15	Novo Nordisk
16	European Association of Hospital Pharmacists (EAHP)
17	Dr David Gerret, NHS England
18	Angela van der Salm, DADA Consultancy
19	Dr Yogini Jani, NHS England
20	Pharmaceutical Group of the European Union (PGEU)
21	Actelion Pharmaceuticals Ltd
22	Bristol-Myers Squibb

30 Churchill Place ● Canary Wharf ● London E14 5EU ● United Kingdom
Telephone +44 (0)20 3660 6000 **Facsimile** +44 (0)20 3660 5555
Send a question via our website www.ema.europa.eu/contact

Stakeholder no.	Name of organisation or individual
23	Novartis
24	Guild of Healthcare Pharmacists
25	Croatian Agency for Medicinal Products and Medical Devices (HALMED)
26	Medicines Evaluation Board, The Netherlands
27	Italian Society of Hospital Pharmacists (SIFO)
28	Dr Mirko Petrovic

1. General comments – overview

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1	Pregnancy exposures are a special type of medication error. If a case report describes a neonatal adverse event after gestational exposure, then two ICSRs need to be created, one for the maternal exposure during pregnancy and the second for the neonate's experience.	
1	Several references are made to 'potential' medication errors (section 4.3.4, lines 393-397, Table 1, lines 1154-1159, lines 1246-1248) and the need for these to be summarized in the PSUR and RMP. It would be helpful to have some clarification of the expectations of the agency in terms of how to capture these data. For example this could be through the MedDRA PT that could be used to capture' potential' medication errors: CIRCUMSTANCE OR INFORMATION CAPABLE OF LEADING TO MEDICATION ERROR; or through the PT INTERCEPTED MEDICATION ERROR that covers situations where an error occurred but the patient didn't actually take the wrong drug / dose. This requirement also needs to be aligned with the instruction in lines 746-747 that 'medication errors should not be inferred unless specific information is provided' in which case source information has to clearly state that an error occurred.	
2	Good practice guide on recording, coding, reporting and assessment of medication errors and Good practice guide on risk minimisation and prevention of medication errors as well as Risk minimisation strategy for high strength and fixed combination insulin products, addendum to the good practice guide on risk minimisation and prevention of medication errors are useful documents and fulfill the scope. The addendum to insulin contains the remarks already made. Nevertheless I strongly suggest to add to the documents a list of the used abbreviations. Some of them are common, some are explained but unfortunately not all. Abbreviations are useful but – as remarked in the text – can also be misleading if not clear.	
3	(1) Document 762563 is very relevant, fills an important gap. Tables, figures, examples	

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	are especially valuable.	
3	(2) In contrast to the unifying approach of EMA to all drug-related safety problems, there is a very strict distinction between medication errors with and without ADR.	
3	(3) The document, read in isolation, could give the impression that the legal responsibility for medication errors without ADR would be outside the responsibility of competent authorities and the EMA; we therefore propose to introduce a short cross reference to the guide on risk management which clearly mentions these responsibilities.	
3	(4) Consider revising that medication errors without ADRs are “not reportable” as ICSRs to and from competent authorities. However, reporting ICSRs of intercepted or potential medication errors**, if they point to a serious safety signal**, to competent authorities should be encouraged in order to take action as early as possible. Precious time could be lost, if the completion of lists by third parties (SPOs e.g.) and full documentation of a signal is awaited.	
3	(5) There should be a separate chapter on urgent reporting of important safety signals relating to medication errors. The relevant text (lines 642-646) is in subsection 5.4 on “periodic reporting” and could easily be missed.	
4	We understand that ME’s are divided in ME+ADR and ME-ADR. The emphasis is on ME+ADR and these reports (ISCR) are internationally shared (via EudraVigilance), also with PSO. This doesn’t count for ME-ADR. These (trend) reports are shared nationally, some items internationally between NCA’s and not (obligatory) with PSO’s. In common: PSO’s emphasize on risks and not primarily on outcome. That’s a big difference. We think EMA / NCA’s should emphasize more on risks. We compare it with safety in traffic where the government tries to improve safety by (also and more than in pharmacovigilance) focussing on risks instead on harm. You get the	

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	most penalties for risks (neglecting red traffic light) and not for accidents (risks with harm). The accent has to focus on risks as much as on harm and both should be shared (inter)nationally and with PSO's.	
5	CPME welcomes the opportunity to comment on the EMA the good practice guide on recording, coding, reporting and assessment of medication errors. In January 2015, CPME had commented on a preliminary draft of the Guide in the framework of the Patient Safety and Quality of Care Working Group (PSQC WG) of the European Commission. Part of these comments were taken into account, therefore CPME reiterates the following points that have not been included into the new draft version of the Guide.	
6	The document introduces many new processes, tables and information. It would be most helpful to establish a point of information/functional email address where FAQ can be placed.	
7	The whole guidance is based on medication errors examples based on prescribed drugs (guidance and examples). Specific chapters should be dedicated to generic and well-established non-prescription medicines for completeness of the guidance. Consumers and healthcare professionals need to be sensitised – for example through the patient leaflet or educational materials – about reporting medication errors with or without adverse event, intercepted errors, potential errors, and how to report data to ensure the assessment of medication errors (reporting of mitigation factors and ameliorating factors).	
8	This document impacts mostly the data entry and case assessment personnel, who need to have MedDRA knowledge and expertise to appropriately implement this guidance. Furthermore, coders will need to have equal understanding of MedDRA medication errors criteria in order to apply appropriate coding outcome as intended in this guidance.	
10	According to the draft of the "Good practice guide on recording..." only medication errors (ME) which have caused harm to the patient are to be reported to the NCAs. ME without harm, intercepted and potential errors are recorded only by the MAH and evaluated in the	

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	PSUR / RMP. In order to improve risk minimisation all cases of ME (including ME without harm, intercepted and potential errors) should be recorded in a central database and analysed systematically.	
10	A new section should be created and it should include providing advice on how to handle ADR reports which - in the first place - did not specify whether or not an ME is suspected but where - in the second place - the respective analysis may be performed and could result in the notion that the ADR was due to an ME. The reason for this suggestion is as follows: The assumption that the cause of an ADR might have been an ME is based on patient and treatment details as well as on the knowledge of the authorisation status of the suspected drug and relevant co-medications. In many cases, particularly in the event of serious ADRs, the physician who is in charge of treating the patient because of an ADR did not prescribe the (suspected) medicine. This was probably done by a specialist for the respective field. If e.g. an orthopaedist prescribes a NSAID to a patient who also takes some other drugs including herbals and an upper GI bleeding occurs, the patient will then probably be treated by a gastroenterologist or a GI surgeon. Indeed – and on the contrary – a medical specialist will be particularly cautious and less likely than other physicians to prescribe a medicine which may cause an ADR in the field of his or her speciality. While the prescribing physician may usually know the treatment details the physician who treats the patient because of the ADR and who may be motivated to report it, will often not have the information about the relevant medical history and also not about the authorisation status of the respective drugs. This is, however, a prerequisite for the judgement whether or not the original treatment was on-label or outside the authorisation status and possibly an ME. Such information may only be collected as a second step, if at all, by contacting several persons (prescriber, nurse, patient) and reading relevant material (patient records, SPCs).	

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	This second step may take a lot of work and time and hence not fit into interval of 15 days between the detection of a serious ADR and its reporting (to which MAHs and regulatory authorities are obliged). With regard to the workload it will often not be feasible and from the medical and regulatory viewpoint it will often not be worthwhile. If this secondary analysis results in the notion that the ADR was caused by an ME several consequences will have to be considered. It is important to give detailed guidance on how to proceed in these cases: - Criteria for starting an analysis - Methods of analysis - Consequences of such an analysis: data base, labelling, risk assessment, communication The current draft guideline emphasises the handling of reports where an ADR was recorded and immediately judged as being caused by an ME and on situations where an error was observed and identified as such but where this error did not cause any harm. While these issues are important to mention they should be complemented by a major section on the handling of ADR reports where the causation by an ME seems possible but unclear, as suggested above.	

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12	EFPIA welcome the opportunity to comment on this guidance which is generally well-written. Our comments are intended to improve the Guide when it is finalized. Currently available GVP guidance already requires MAHs to collect and report on medication errors. The scope of this draft Good Practice Guide extends these requirements considerably with collection and reporting (categorization) expectations of information in a level of detail industry does not have and will likely not be able to collect through follow up (especially when no AE is associated). The guidance relies on HCPs to report medication errors, which, given experience, is unlikely unless there is an associated (serious) adverse event. We propose considerations for NCAs to work with their local healthcare systems to encourage reporting. In addition it would be appreciated to have further discussions at one of the upcoming authority/industry meetings before finalizing the good practice guides. The guidance changes/broadens the definition of a medication error: “A medication error is an unintended failure in the drug treatment process that leads to, or has the potential to lead to, harm to the patient”. The guidance also introduces different types of medication errors for PV classification purposes: (1) medication error with AE/harm, (2) medication error without AE/harm, (3) intercepted medication error (“near miss”), and (4) potential medication error. Safety databases may not have the technical ability to differentiate these different ‘types’ of medication errors. Our suggestion would be that EMA synchronise the implementation of these changes in line with R3 requirements, as the database will require additional changes at that time. The document is quite repetitive and repeats the guidance outlined in existing GVP modules several times. This could cause issues if the other modules are updated. This guidance should not repeat any coding examples but only refer to the MTS:PTC document which is updated with each version of MedDRA.	

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	We note that the MedDRA® HLGT *Product quality issues* is under revision and is anticipated to reflect major changes that will impact coding starting with MedDRA version 19.0. In addition, CIOMS is in the process of developing a Standardized MedDRA Query (SMQ) for Medication Errors (ME) that should drive changes in ME-associated data retrieval and display. Definitions of medication errors and neighbouring concepts should be handled consistently throughout the document and other regulatory guidance (EMA, MTS:PTC, MSSO) to achieve a common understanding and a reliable classification of these events. Guidance focusses on medication errors but could more clearly define the differentiation from product use issues (the new PTs *Intentional product use issue* and *Product use issue* are not mentioned at all), off label use, drug misuse/ abuse/ dependence and accidental exposure. Because of the newly available vague “product use issue” terms, it has to be made very clear how much “interpretation” is regarded acceptable for case classification. This guidance has considerable detail and is helpful. However there are examples where more information is provided by the reporter than is often the case. The coder is left to decide whether to follow the example as MTS:PTC and this guidance advise coding what is reported without making any assumptions. The document is clear about the fact that the stage where the medication error occurred (prescribing, dispensing) and potential contributing factors are to be captured (plus potential adverse reactions), together with the fact whether the error actually leads to incorrect administration: “intercepted” medication error terms should be used when a medication error does not lead to an incorrect administration. But it is not made clear if splitting of terms is required when a medication error reaches the patient, to capture both the “stage” (e.g. the dispensing or prescribing error) and the specific administration error. If one ICSR contains an event that is related to medication error and also other events that are considered as valid SAE/AE but not related to medication error, further guidance is needed to the MAH on how to record/split such ICSRs. For all special situation cases it	

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	seems that splitting has to be done even if one ICSR is reported to MAH, in order to ensure proper classification of medication error and associated AE/SAE and other distinct AE/SAE not linked to medication error. Several terms in HLGT *Product quality issues* describe concepts that are potential medication errors, e.g. PTs *Product commingling*, *Product dropper issue*, etc. It would be appreciated if this guidance could address usage of these PTs in the context of medication errors. Furthermore the guidance should clearly have a recommendation to use the SMQ medication errors that will include relevant product quality terms. More specific and comprehensive guidance on coding of medication errors with devices and differentiation from other device issues (e.g. quality issues, incidences) would be highly appreciated. Whilst the inclusion of examples is helpful it is felt that many of the examples given are product / quality issues associated with labelling, which is defined in the guidance as being a quality issue, not a medication error. The examples in this guidance should focus on medication errors, and acknowledge that product complaints, especially those without an associated ADR, are captured in quality / manufacturing databases and are subject to different requirements. MTS: PTC suggests that additional codes be used to note 'No AE' and 'Drug not take in context of intercepted ME'. To enable this, will the EMA be requesting these two new MedDRA codes to be issued in conjunction with this guideline so that only a single code has to be assigned? There is no mention of medication monitoring errors (and the corresponding definition) in the guidance? Based on the MedDRA hierarchy, they are to be considered medication errors. According to the MedDRA Concept descriptions "a medication monitoring error is an error that occurs in the process of monitoring the effect of the medication through clinical	

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	assessment and/or laboratory data. It can also refer to monitoring errors in following instructions or information pertinent to the safe use of the medication." Is this applicable to HCPs and patients/ consumers (for OTC drugs) who do not follow instructions for the safe use of the medication in the label (e.g. regarding concomitant medications, pre-existing diseases etc.)? More guidance would be helpful. Question 1: We agree with the proposal Question 2: We would question whether this is required in the EU and whether it makes pharma companies appear unnecessarily defensive Question 3: Yes, for signal detection purposes, especially due to fact that in version 18.0 of MedDRA there are two HLGTs which might be used for the selection of cases, SMQ will be very useful. Further detailed methodological guidance on the detection of signals of medication errors in EudraVigilance would be much appreciated to provide a standardised approach across different MAHs and other stakeholders. SMQ should be rather hierarchical to cover at least medication errors/intercepted errors/potential errors and once the G.k.10.r. will be introduced they can be very helpful for cumulative presentation of different categories of medication errors. Question 4: Yes this would be useful and would encourage a culture of reporting errors	
13	We appreciate the thorough work that was done in collating the Good Practice Guide (GPG). Nevertheless, a major part of it deals with reporting requirements for medication errors with an ADR (ME + ADR). Since the handling of such case reports is sufficiently detailed in the applicable GVP modules the entire topic should be significantly shortened in	

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	this GPG in order to improve readability and particularly in order to avoid possible deviations from the applicable GVP modules whenever these are updated.	
13	While striving to enhance medication safety for patients a key aspect is to identify the appropriate addressee. Marketing authorisation holders are surely the ones to be the most easily compelled to adhere to guidelines, they are, however, probably not the ones to gain the most knowledge about medication errors, especially those without ADRs (ME – ADR). In this respect the content of this GPG should be reconsidered. Neither Directive 2001/83/EC nor Regulation (EC) 726/2004 require MAHs to put special emphasize on the handling of ME – ADR. The requirements detailed for the PSUR sub-section 9.2 “Medication errors” in connection with the new possibilities provided by the implementation of ICH E2B(R3) are deemed perfectly adequate to ensure appropriate evaluation of reports of ME – ADR received by MAHs.	
13	As EudraVigilance is the most extensive database within EU the availability of collated medication error reports would be very helpful to stakeholders. These reports may form the basis for measures regarding design, presentation, labelling, naming, and packaging of a drug to reduce the risk for medication errors. The data should be available as MedDRA terms as well as on basis of SMQ for medication errors, which is currently under development.	
13	**Answer to question 1 (line 14-17):** The MAH can implement the proposed business process for electronic recording of ME. Nevertheless, the work load rises enormously and supposed benefits are doubtful. **Answer to question 2 (line 18):** There is no chapter 5.7.2 in the guide. Assuming that the lines 934 - 939 in section 5.7.1 are meant (not 5.7.2), we think the use of a fixed disclaimer is useful when reporting medication errors. The proposed wording seems to be fine. **Answer to question 3 (line 22):** Standard MedDRA Queries (SMQs) are very useful in the detection of signals. Therefore we appreciate the development of SMQ for medication errors. However, we assume that **no additional guidance on signal detection** with special	

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	emphasize on medication errors is necessary. **Answer to question 4 (line 25):** We do not see any additional benefits in collated medication error reports once ICH E2B (R3) is implemented. It should be noted that even if the reports are anonymized, the content reflects specific and individual data of patients, that should **not be public available** neither on EVDAS nor on adrreports.eu website in not appropriate format. Maybe it is more useful to establish a more general statistically orientated system (focusing on the specific reaction and the active substances only) to present these cases of medication error to the public.	
15	Please consider aligning the tables for medication errors with those included in the RMP (SV1.4.1 in RMP template section SCV.4) and PSUR VII.B.5.9 2. (PSUR sub-section "Medication errors").	
16	The European Association of Hospital Pharmacists (EAHP) welcomes the opportunity to respond to the EMA's consultation on "Good practice guide on recording, coding, reporting and assessment of medication errors". Overall, EAHP supports the guidance document and considers it can make a positive contribution to: • reporting of adverse reaction(s) associated with medication errors; • reporting medication errors **not** associated with adverse reactions; • wider sharing information about medication errors among stakeholders; • bringing about standard web-based formats for reporting adverse reactions by healthcare professionals and patients/consumers; • protecting individual personal data and anonymous based reporting. EAHP also welcome the use of visual tools and diagrams within the document (e.g. figures 1, 2 and 3) to underpin the communication of key points and concepts. This is especially valuable in respect of pan-European guidance in so far as much of the primary audience	

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	will be non-native English speakers. We encourage EMA to utilise this approach widely across its production of public documentation. While commenting on the topic of reporting medication error, EAHP takes the opportunity to raise with EMA some potential points for improvement in relation to the accessibility and usability of the repository databases to which errors are reported. For example, there are several different landing pages in this area of EMA pharmacovigilance and reporting activity including: • www.adrreports.eu/ • https://eudravigilance.ema.europa.eu • http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/general/general_content_000537.jsp& Yet the pages do not immediately clearly link or reference to each other. A single EMA pharmacovigilance landing page that briefly explains the roles of the different websites and links could more easily help the irregular or first time visitor (e.g. hospital pharmacist in practice, or interested patient) to access the correct page and find the information they are looking for (and indeed other information resources they were not previously aware of).	
17	As a general point the definition of Medication error inconsistently omits those errors of compounding or preparation. This is especially significant for local IV and aseptic production in hospitals. I would propose altering the formal definition from to include 'preparation'. This term is inconsistently included in the consultation documentation, and it must be consistently included. *Medication errors are unintended mistakes in in the prescribing, dispensing and administration of a medicine that could cause harm to a patient. They are the most common preventable cause of undesired adverse events in medication practice and*	

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	present a major public health burden. to *Medication errors are unintended mistakes in in the prescribing, preparation, dispensing and administration of a medicine that could cause harm to a patient. They are the most common preventable cause of undesired adverse events in medication practice and present a major public health burden.*	
17	Overall I would agree that standardisation will lead to pooling of data and better understanding of the latent errors involved with use of medicines. My major comments are that: a. there is an assumption that MedDRA coding will be understood by those that report Patient Safety Incidents. I have grave concerns regarding the time taken and the validity and reliability of healthcare practitioners to do this. In England we have Medication Safety Officers who could accurately code PSIs according to MedDRA but, given the number of errors involved, this could only be a solution for serious harm events; b. similarly there is an expectation to report errors with associated health status. In England we are moving to SNOMED CT for clinical health terminology (The International Health Terminology Standards Development Organisation (IHTSDO)). Again I have huge concerns that those reporting PSI will be able to apply the coding structured for SNOMED CT. I feel the best that can be expected is for reporters to provide qualitative descriptions of what happened and for these to be inspected for learning and trends; c. There needs to be a staggered expectation for what is possible to code and report. For serious harm ADRs then it is right to expect greater detail and to work towards MedDRA coding. But for all other levels of harm a far more pragmatic approach must be taken with simplicity and a minimal expectation on healthcare practitioners, PSOs, MAHs and manufacturing industry to report;	

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	d. Noting section 5.7.1 (line 920>), if the PSO and member state takes the view that anonymised reporting will lead to improve learning, then this must be allowed to supersede the requirement individual identification. Use of a disclaimer is noted. Furthermore, in the UK it is currently a criminal offence to dispense incorrectly. This is in the process of being addressed though legal channels. Until this is finalised, it would compromise professional practice to mandate identification. Also noted is page 35, line 1133> 'The reporting of medication errors by healthcare professionals and consumers is in no way intended, nor should it be interpreted or construed by a marketing authorisation holder, national competent authority or any other third party as an admission, al legation or claim for Potential liability, but for the sole purpose of the pharmacovigilance tasks as described in Title IX of Directive 2001/ 83/ EC'; and, a. Full support for the process described in figure 6, page 33.	
17	PC Questions 1. Q: With regard to recording medication errors in ICSRs, please provide comments on the proposal in Annex 4 for a business process for using the ICH E2B (R3) ICSR data element 'Additional Information on Drug' (G.k.10.r) and the data elements 'Sender's diagnosis' and 'Sender's comments'. A: This nuance of coding/reporting will simply not be understood within practice, it only serves to introduce uncertainty and variation in interpretation. 2. Q: With regard to reporting medication errors in ICSRs do you consider the proposed disclaimer in chapter 5.7.2 useful to address potential conflicts between marketing authorisation holders' pharmacovigilance obligations and potential exposure to liability when classifying medication errors in suspected adverse reaction reports to national competent authorities or the Agency? A: yes it is very helpful. The wording is comprehensive.	

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	3. Q: With regard to signal detection activities would you consider the development of methodological guidance on the detection of signals of medication errors in EudraVigilance useful, taking into account the Standard MedDRA Query (SMQ) for medication errors currently under development? A: yes guidance would be useful. Signal detection relies on judgement. The better informed the judgement the stronger the signal 4. Q: With regard to pharmacovigilance activities would stakeholders consider making available collated medication error reports via the EudraVigilance Data Analysis System (EVDAS) and/or the public adrreports.eu website in line with the revised EudraVigilance Access Policy useful? Please note that for the general public such reports would be presented by EEA and non-EEA geographic origin and based on a filter using coded MedDRA terms in combination with the data element 'Additional Information on Drug' (G.k.10.r) once the ICH E2B (R3) standard is implemented. This is for national debate and agreement, it is not something that is consulted on. If you ask, should national bodies debate this, then the answer would be yes.	
18	PC Questions: Reply to point 1 (line 14): Good idea, would be helpful in identifying the reports. Reply to point 2 (line 18): Disclaimer is listed in 5.7.1 rather than in 5.7.2. MAHs would need to incorporate this in their working procedures with the sole purpose of being protected against claims of HCPs who believe they have been done injustice? I think the purpose of pharmacovigilance in itself is to share information on a product and I think there should be a more fundamental disclaimer somewhere that MAHs when reporting ICSRs never aim to point a finger at anyone. Reply to point 3 (line 22): I would be very much in favour of an SMQ for medication errors	

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	to facilitate signal detection. Usability of guidance on how to do this in EudraVigilance would depend on the access level (current public level would not help very much). Reply to point 4 (line 25): Yes from a transparency point of view, less positive considering potential lack of trust	
19	Overall, the principle of a good practice guide for this topic is a commendable. However the guidance focuses heavily on regulatory aspects and appears to overlook practitioner input and the work over the decade of learning from reporting, and the influence of human factors in medication errors. Lessons from improved reporting indicate that involvement of end-users in the design stage, especially for product labelling and packaging could greatly reduce the risk of error. The focus is also on newly licensed medication and does not address existing licensed medicines. Many of the reporting requirements are captured in the voluntary national reporting and learning system. Requires alignment with [and ideally extraction from] these to ensure healthcare practitioners are not burdened by reporting to multiple systems.	
21	Specificity regarding follow-up is unrealistic. We are unlikely to be able to obtain this kind of information when following up with reporters, especially if consumer reports.	
21	When is the expected publication time of a final guidance? Will this document be implemented at the same time as E2B (R3)?	
21	Is this expected to be prospective implementation or retrospective to ensure we include all information for periodic reports? Flagging of these cases in the database?	
22	1. With regard to recording medication errors in ICSRs, please provide comments on the proposal in Annex 4 for a business process for using the ICH E2B (R3) ICSR data element 'Additional Information on Drug' (G.k.10.r) and the data elements 'Sender's diagnosis' and 'Sender's comments'.	

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	"Once implemented after a successful EudraVigilance audit, the ICH E2B (R3) data element G.k.10.r 'Additional information on drug (coded)' should always be populated with the respective code for medication error at drug level (i.e. code 7) if the primary source has indicated that any type of medication error may have occurred. As this is a repeatable field, other codes may be used as appropriate. **The use of field G.k.10.r to record "medication error" on the drug-level would facilitate aggregate data retrieval in case there is more than one suspect medication reported but the medication error itself is not associated with all suspect products; as well as potentially facilitating identification of "medication errors" independent of MedDRA term selection describing the nature of medication error. The disadvantage of using this field may be that the recording of "medication error" both as a reaction as well as on the "additional information on drug (G.k.10.r)" field may be redundant and result in potential inconsistency in populating field G.k.10.r and hence may not ultimately serve the purpose of aggregate data retrieval vs. having MedDRA terms used as the basis of the aggregate data search criteria.** If there is no explicit indication of a medication error by the primary source which would clearly transpose into a MedDRA term in the reaction section but there is a hint that there may have occurred an error in the context of the clinical course description, the sender may choose to populate data element G.k.10.r at their discretion to 'flag' a medication error. The case should be followed up to confirm if there was actually a medication error. The use of G.k.10.r also refers to intercepted errors where the cases are recorded as ICSRs in the database for PSURs. **It may be useful; however, there are points to consider for implementation. 1. Individual interpretation of ICSRs should be considered for the assessment of**	

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	"potential medication error", which may have an impact on aggregate assessment of such reports. 2 Due to the possibility of inconsistent assessment and thus population of field G.k.10.r, the value of the same in aggregate data assessment/ signal detection should be considered. In addition to the flag, an appropriate MedDRA term should be selected in reaction (E.i.2.1b) or sender's diagnosis (H.3.r.1b) as applicable (see MedDRA Term Selection: Points to Consider). **The Company agrees that the most appropriate MedDRA term describing medication error should be coded on the reaction field (E.i.2.1b) or sender's diagnosis (H.3.r.1b) as per MedDRA Points to Consider.** 2. With regard to reporting medication errors in ICSRs do you consider the proposed disclaimer in chapter 5.7.2 useful to address potential conflicts between marketing authorisation holders' pharmacovigilance obligations and potential exposure to liability when classifying medication errors in suspected adverse reaction reports to national competent authorities or the Agency? **If the disclaimer language were included in some but not all ICSRs, this could imply that any report without the disclaimer is indeed an allegation that a third party was responsible for the occurrence of a medication error, particularly since there would be guidance advocating use of the disclaimer language. Thus, the omission of the disclaimer language in a particular case would increase the likelihood of potential conflicts between marketing authorisation holders' pharmacovigilance obligations and potential exposure to liability.** **If the ICSR forms will not be revised to ensure that the disclaimer language is on**	

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	every form, then another solution would be to include within the GVP guidance itself an express statement that the classification of an occurrence by an MAH as a medication error is not to be interpreted or construed as an allegation that a third party contributed to the occurrence. This would have the effect of importing the principle of the disclaimer language into every single ICSR of a medication error, so there would be no risk of an MAH inadvertently omitting the disclaimer on a particular report and thus increasing their potential exposure. 3. With regard to signal detection activities would you consider the development of methodological guidance on the detection of signals of medication errors in EudraVigilance useful, taking into account the Standard MedDRA Query (SMQ) for medication errors currently under development? **Yes, Bristol-Myers Squibb is in agreement that the development of a methodological guidance on the detection of signals involving medication errors in EudraVigilance would be useful. As the Good Practice Guide on Recording, Coding, Reporting and Assessment of medication errors points out, there are various classifications of medication error such as:** ***Intercepted errors*** ***Potential medication errors*** ***Prescribing errors*** ***Medication errors without harm*** ***Incorrect dose administered*** ***Incorrect drug administered*** ***Unintentional overdose*** ***Drug dose omission*** ***Labeling/Packaging errors*** ***Drug contamination errors*** ***Accidental exposure (due to incorrect drug/device use)***	

Stake-holder no.	General comments	Proposed change by stakeholder, if any
	Therefore, a guidance document, taking into account the Standard MedDRA Query (SMQ) for medication errors for search criteria and methodology currently under development, would prove to be beneficial to ensure consistency within the pharmaceutical industry and healthcare community for the detection of signals involving medication errors. 4. With regard to pharmacovigilance activities would stakeholders consider making available collated medication error reports via the EudraVigilance Data Analysis System (EVDAS) and/or the public adrreports.eu website in line with the revised EudraVigilance Access Policy useful? Please note that for the general public such reports would be presented by EEA and non-EEA geographic origin and based on a filter using coded MedDRA terms in combination with the data element 'Additional Information on Drug' (G.k.10.r) once the ICH E2B (R3) standard is implemented. **While not opposed to providing aggregate medication errors, it is important to note that a company's collated reports should not be considered the definitive source on the matter—the information originates from third parties, is most likely incomplete and under-reported, and therefore could be misleading about the true occurrence of the errors. Additionally, it should be taken into consideration whether the collated report would include ICSRs based on the MedDRA coding of medication error or would be intended to be more comprehensive and include cases flagged as medication error only by choosing "code 7" on the "Additional information on Drug (G.k.10.r) field. Another concern is whether the collated report would include/ be required to include the MAH's assessment of medication error cases, so that a meaningful evaluation is provided to the reporter. Personally identifiable information would need to be removed for compliance with Privacy requirements if the collated medication error report would be**	

Stake-holder no.	General comments	Proposed change by stakeholder, if any
	required to include individual case details. Also, the current draft guidance does not include any description re: the content of these collated medication error reports, which has limitation on the ability to comment on the proposed requirement/ activity.	
24	Introduction talks about errors and is blame ridden not enough emphasis on creating a learning culture.	
24	The definition of harm and severity are not well defined and seem to cause a lot of confusion because they are so subjective for example a missed dose of insulin leads to blood glucose monitoring and seeking medical advice some people will class this as low harm whilst other class this as no harm. My main concern is that we need to improve data quality and this is an area in which we need a clear steer.	
26	The guide considers a lengthy document (43 pages). Some information is repeated several times, but in slightly different ways. In conclusion, a more concise document would be appreciated.	
26	The guide states to be intended to provide guidance. In order to further clarify its status to the general public, it may be considered to reposition the guide as a guideline or reflection paper.	
26	The guide is subject to confusion for pharmaceutical assessors with respect to the definition on medication error. Some information in the guide is not fully consistent with the definition of medication error made in the beginning of the document. This is also the case for some information provided in the good practise guide on risk minimisation and prevention of medication errors which is also currently open for consultation on the EMA-website. As a consequence, it is not clear - if the definition on medication errors would exclude o any off-label use, regardless as to whether it is related to the indication, dose, user group, or medication handling or whether off-label use would only be excluded in relation to a specific scope e.g. indication;	

Stake-holder no.	General comments	Proposed change by stakeholder, if any
	o any off-label use or intentional off-label use only o any misuse or overdose, or intentional misuse or overdose only • the definition on medication errors would include any handlings to be conducted to make the preparation ready for administration e.g. dissolving powder for reconstitution, breaking tablets, measuring oral liquids with a measuring device, diluting concentrates for infusion and. o If so, if a different approach would be applicable depending on the person by whom the handling was conducted (pharmacist, nurse or other professional caregiver, non-professional caregiver, patient itself); o If so, if a different approach would be applicable as to whether the handling was intended or not-intended by the prescriber; o If so, if a different approach would be applicable as to whether or not the handling was authorised or not authorised in the SmPC. It is suggested to clarify these issues at the beginning of the document to have a clear understanding of the definition of medication error and the issues covered.	
26	The PRAC is reminded that medication errors may not only be substance related, but rather trademark as the excipient composition, tablet size etc. may differ among companies.	
28	Create a list of medications with high risk potential Differentiate between sound-alike and look-alike medications (pay attention to separate storage) Record carefully all medications: importance of in-depth medication review (history taking followed by evaluation of medication used) as the first step Register substitution of medications taken at home during hospital stay Seamless pharmaceutical care: assure information flow between different settings (and different ward during hospital stay) regarding medications prescribed in addition to medication related problems in general and medication errors in particular	

2. Specific comments on text

Stake-holder no.	Line no.	Stakeholder comments	Proposed change by stakeholder, if any
1	22-24	We cannot assess the need for methodologic guidance on a new SMQ until it's finished.	
1	82, 847, 1234	Complimentary should be Complementary	Additional coding examples for medication errors complementary to MTS:PTC document
1	58, 675, 678, 706, 1160	Follow up should not have a hyphen in multiple locations when it's a verb, e.g., We should follow up on this question.	Follow up, rather than follow-up
1	301-304	"Potency for various mistakes…" is not clear.	The term potential medication error refers to ~~an error which has the potency for various mistakes and may become reality at any time or it has already occurred. This includes~~ all possible mistakes in the prescribing, dispensing, administration or preparation of a medicinal product by all persons who are involved in the medication process.
3	14	The proposal for a business process in annex 4 is welcome and valuable.	
3	18	The proposed disclaimer is considered useful.	
3	22	Yes, developing methodological guidance would probably be useful, as medication errors do have specific features	
3	25	Making this information public could increase awareness of the problem and may help prevent medication errors. Special consideration should be given to data protection in the context of liability questions	

Stake-holder no.	Line no.	Stakeholder comments	Proposed change by stakeholder, if any
3	246	The wording of section 4.3.1 and figure 1 could be misinterpreted (ADRs principally not preventable).	Replace not preventable e.g. by “not generally preventable”.
3	378	Medication errors without ADR should be recorded but not reported as ICSR according to GVP VI, chapter 5.3 -> should be reconsidered (can delay signal detection, see general comment 3).	
3	642	Ad hoc reporting of important safety signals should not be mentioned in the chapter on periodic reporting, but in a separate chapter (see 5).	
3	983	Medication errors without ADR brought to the attention of competent authorities should be recorded by them, transmitted to national SPOs and taken into account for risk management activities. What precludes exchanging reports pointing to signals with MAHs and other competent authorities (see also comment to line 378 and general comment 4).	
4	119	MAH’s have to summarize Medication Errors (ME’s) with and without AR’s in PSUR’s. What is the effort MAH’s are obliged to make to obtain this information/ these risks of medication errors. Do they have the obligation to collaborate with PSO? Otherwise? See 274, 620 (should make all reasonable efforts to include….).	Where HCP report only once (PSO OR MAH) the MAH has to make all reasonable efforts to get reports / trends from the PSO (which is not obliged to give (all) the information).
4	134-136	Medication Errors not associated with adverse reaction(s) are not required to be reported as individual case safety reports (ICSR). And further in 136: ME’s with harm: do share with NCA. 1. But how to share ME’s with AR’s is not described in the text. 2. ME’s without AR’s, but with evident risk, are not internationally shared at all. In the interest of patient safety we have the opinion that these incidents should be shared as well.	See also general comments.
4	378	ME’s without AR’s have not to be reported as ICSR; only shared nationally? Why are these ME’s not shared internationally? It’s in the	See general comments.

Stake-holder no.	Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		interest of patient safety to share the risks.	
4	389-392	S*hould* be made available	NCA's are obliged to make all reasonable efforts to get an agreement with PSO's to collect all reports of ME's.
4	410	Clinical consequence = harm ?? All clinical consequences (missed dose insulin, higher blood glucose) are considered as harm? Clear definition is needed.	Add clear definitions.
4	520	No relation between MAH and PSO in scheme. Incidents often reported to one organisation. It's important that MAH and PSO share the information, in order to analyse the risks. See line 620. (Compare with the link between NCA and PSO).	See comment 119.
4	559	And other non-interventional solicited sources associated with medication errors **may** also be included We have the opinion that in the interest of patient safety this may be not strong enough.	Must be
4	584	Only Medication Errors related to invented names, why are generic names not mentioned in this document? See Good practice guide on risk minimization and prevention of medication errors)	
4	587	ME's related to the invented name regardless of the association with adverse reactions reported as ICSR AND reported via dedicated mailbox? Do you have to report twice? We think that's not advisable.	
4	608	How do PSO's share intercepted and potential errors with NCA?	Describe a proposition in a way the risks can be internationally shared.
4	642-646	Who can use the dedicated mailbox mentioned in 646? We think it is in the interest of Patient Safety that PSO's too have access to this dedicated	PSO's should also have access to this dedicated mailbox.

Stake-holder no.	Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		mailbox. If ISMP Spain had access to this mailbox, and the information was sent to PSO's and NCA's, the Jevtana-problem in the Netherlands could have been solved earlier.	
4	686-688	It is good practice that NCA's perform follow-up activities in collaboration with national PSO bases on the agreements for information and reports on medication errors referred to in chapter. What is the exact meaning of this sentence? Good practice: how to organise this.	
4	706 table	Stages of medication process are not complete; missing is storing/logistics. For example in case the fridge where the insulin is stored has problems in keeping the good temperature, can result in a medication error (blood glucose too high).	To add storing and logistics as stage of medication process.
4	706	Contributing factors: information technology is missing. The thesis "Learning from medication errors through a nationwide programme" says in Chapter 6 that 1 in 6 medication errors were related to IT. See also Journal of American Medical Informatics Association 2014;21(e1):e63-e70	Add IT and software as contributing factor.
4	1038-1040	What do you share and how? ME's with harm: NCA has to share these ME's as individual reports with the PSO. How? It is good practice that PSOs provide the NCA with information regardless of whether the error is associated with adverse reaction(s): how do they provide this information?	
4	1113-1114	….to report any suspected adverse reaction in accordance……	HCP and patients should report all risks, not only ADR (preventable or not preventable) to the national spontaneous reporting system(s). See also general comments.
4	1270-1291 (Annex 4)	In our opinion it is important to develop a (more) detailed coding system for medication errors with the aim of the analysis of the risks and to improve patient safety.	

Stake-holder no.	Line no.	Stakeholder comments	Proposed change by stakeholder, if any
5	199	Adverse event often refers to as "medication related adverse event" - to make a difference with other kind of adverse events (e.g. falls, infections, wrong side surgery).	The document should make the distinction between “adverse events” and “medication related adverse events”.
5	206	The categorisation of off-label use as a potential adverse drug reaction is questionable. If the possible negative effects are taken into account from the very beginning, they should not be considered as adverse reactions.	
5	236	The definition of medication error as proposed in the current draft document is as follows: “A medication error is an unintended failure in the drug treatment process that leads to, or has the potential to lead to, harm to the patient”. In a previous draft document, the definition included a reference to medications errors caused by either omissions or commissions. We would advise to keep this reference to omissions and commissions.	The definition should read: “A medication error is an unintended failure in the drug treatment process that leads to, or has the potential to lead to, harm to the patient. It can include an act or acts of omission or commission.” Indeed, omissions are among the most serious medication errors (for example omission of anti-coagulants) therefore the last part of the sentence should not be deleted.
5	328	The EMA document refers to Root cause analysis (RCA). Different methods are used for the analysis of medication errors and RCA is not always the most appropriate method.	A systems analysis or a patient safety analysis may in some cases be more appropriate.
5	401	The guide envisages that Marketing authorisation holders (MAH) should learn from errors which come to their knowledge, but it does not envisage anything about how MAH should try to find those error reports. The national authorities should forward all reports (after anonymisation) to the companies, when they can be identified. For generics or other situations where MAH cannot be identified, the national authorities should publish anonymous trends for the use of the MAHs. This is important for the staff and patients who report- to know that the reports will then be used.	
5	547	The Eudravigilance coding on medication errors should be revisited and amended to European work flows. We welcome categorisation of	

Stake-holder no.	Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		medication errors in a common database. The categories for medication errors in the Eudravigilance database is to our knowledge mainly based on pharmacist work flows. Other workflows should be covered so that the database categories reflect relevant error types.	
5	706	Table 2 outlines the parameters to be followed when reporting medication errors. The table doesn't provide with the possibility to code into the reporting process that the substitution of a drug was done. Due to substitution, the actual product cannot always be identified. This should be taken into account when coding. Furthermore, the coding list is very long. Neither clinical staff nor hospital administrative staff will or can spend too much time on reporting and classifying. The most important is a good and simple system for harm reporting, including potential harm.	
5	1066	The role of PRAC: Since medication errors are a problem with the same magnitude as other adverse reactions, PRAC should include members with this expertise. The same goes for EMA staff and staff in national authorities.	
6	378-382	"It is good practice to also record cases of medication errors not associated with adverse reaction(s) in the format of an ICSR, however these cases should not be reported as valid individual cases in accordance with GVP VI (see chapter 5.3.). Marketing authorisation holders and national competent authorities may use alternative formats as appropriate or if required by national legislation to record cases." It would be best practice that only one format is used and to avoid too many alternative formats.	
6	507-521; 1178-1180	The flow chart is a bit confusing. Please use numbers for starting points and the flow of information. Please use a larger format (e.g. whole page) and structure the information more intuitive.	

Stake-holder no.	Line no.	Stakeholder comments	Proposed change by stakeholder, if any
6	531	Practise The language changes between American and British English. For better readability a consistent style should be used.	Practice
6	101	"Errors associated with the use of medicinal products…" Are cosmetics and food supplements also concerned?	
6	270	For generic and well established non-prescription medicines, the most frequent reported medication error types are Errors with ADR or Errors without harm. For completeness, an example of Intercepted Error and Potential Error should be provided for OTC drugs. Is it applicable?	
7	303	Please clarify whether 'preparation of a medicinal product' may refer to the manufacturing process or only to preparation of the marketed product.	Possible rewording to clarify.
7	506 (Figure 3) and previous references	Multiple references to safety incident reports – should this be reworded? Incident reports are currently predominantly associated with the submission of ICSRs associated with medical devices (as per the MEDDEV guidelines) – may cause confusion.	Possible reword – AE/ADR reports?
7	561-572	The preference would be to define one database to be used by all MAH, either EudraVigilance or the MAH's own database.	
7	592-593	Could the EMA contact national competent authorities on behalf of MAHs? It would save a lot of time and would avoid duplicated efforts from MAHs.	
7	627-628	Please define the search criteria to be used for consistency amongst MAHs (HLGT: Medication errors).	
7	684-685	Could the EMA prepare standard questionnaires for following-up on medication errors associated case reports?	
7	724-725	"Flag medication errors at drug level using code 7 which stands for	Please clarify in lay language what 'code 7' exactly

Stake-holder no.	Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		medication error."	means.
7	902	"But also may also be related"	"But also may be related"
7	1234-1267	Coding examples for medication errors are all based on prescribed medicines. Some examples should also be provided for OTC drugs.	Some factice examples: - a three-month-old baby was inadvertently given an ibuprofen syrup quantity measured for a 3-year-old child. - a patient inadvertently used pholcodine for runny nose and complained that the nose was still congested - a patient inadvertently used pholcodine for runny nose and reported that he was feeling better. - a patient took painkiller medication for headache once a day for two days and complained of headache worsening - a patient taking a cough and cold combination of actives including paracetamol together with a paracetamol containing product, complained about abnormal feeling. - an adult patient was smoking while on the nicotine patch and became nervous. - an adult patient applied two nicotine patches at the same time on his arm and reported dizziness. - a patient used xylometazoline nasal drops for 7 weeks every day and one drop inadvertently fell in his eye. No adverse reaction was reported. - a father administered one paracetamol suppository to his child without knowing that the child already had received the suppository 10 minutes before.

Stake-holder no.	Line no.	Stakeholder comments	Proposed change by stakeholder, if any
			- a patient crushed his pills and dissolved them in water before oral use. - a patient ate 4cm dimetindene cream
8	128, 847	Regulatory agencies recode data according to their conventions if they believe coding outcomes are in question	It is recommended to add the following: 'There may be examples that do not reflect practices and requirements in all regions (per ICH MTS: PTC version 4.9) and **all companies'**
8	467	To add an example to distinguish between the product quality issue and medication in splitting the table.	For example, the splitting of a scored tablet in two differently sized parts is considered a product quality complaint and not a medication error. **However 'Tablet split incorrectly' is a wrong technique in drug usage process which is a medication error**.
8	761	Substitute 'but' with 'and'.	
8	862-870	There is agreement with the provided definition of "off-label use"; however, "off-label use" can be interpreted differently by individuals and companies in various global regions.	
8	1242	Example (first row) - Patient experienced paraplegia after an epidural… Suggest to remove the first LLT term selected (Accidental exposure to product) as it doesn't appear to fit the reported criteria	At the LLT Term Selected column there should be only the following LLTs: Exposure to contaminated device; Paraplegia
8	1242	Example (fourth row) - Patient was prescribed different insulin product… The reported verbatim does not mean or indicate that this was a drug prescribing error or wrong drug administered. Suggest remove the first LLT Term Selected: Wrong drug administered.	At the LLT Term Selected column, there should be only the following LLTs: Drug prescribing error; Hypoglycaemia
8	1242	Example (fifth row) - Patient was prescribed 10 fold higher strength… There were no drug prescribing error and accidental overdose indicated in the reported term.	Either add language that reflects that an error occurred or remove the two LLT: "Drug prescribing error" and "Accidental overdose" at the column LLT Term Selected

Stake-holder no.	Line no.	Stakeholder comments	Proposed change by stakeholder, if any
8	1242	Example (sixth row) - Patient well controlled on antiepileptic medicines… This verbatim text gives different interpretations: 1) patient did not go to get the drug, and 2) there is an interruption of supply which can be coded to LLT/PT: Product distribution issue. Reconsider to reword the example more clearly.	
8	1253	Example (second row) - Product preparation requires two pre-filled syringes to be… Suggest to remove the first LLT term selected (Inappropriate preparation of medication) because the reported verbatim stated it is a difficult procedure and will 'likely' result in problems in preparation of medication but it did not result in an inappropriate preparation of medication.	At the LLT Term Selected column, there should be only the LLT: Circumstance or information capable of leading to medication error
8	1260	Example: A child died after accidental exposure to a fentanyl patch… Suggest to remove the second LLT term selected (Medicinal patch adhesion issue), because the reported term lends to different interpretations.	At the LLT Term Selected column, there should be only LLT: Accidental exposure to product by child
9	667	Please clarify "in addition to any effort to collect the minimum information for an ICSR to be valid". Concerns only medication errors associated with adverse reactions (medication errors not associated with adverse reactions considered as not valid)?	
9	702-703	Please clarify "Potential risk(s) for the patient or consumer if the error did not happen (potential error) or did not reach the patient or consumer (intercepted error, error without harm)".	
9	706	Table 2, page 24, Seriousness, Description "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"	Proposal to discuss in the periodic safety update reports, and not on individual basis in ICSRs.
9	743-751	*"Inferred medication errors"* There may be instances where the initial primary reporter has not specifically stated there was a 'medication error'	

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		but it is clear from the information provided that there has been an error. MedDRA coding principles advise that medication errors should not be inferred unless specific information is provided." Even if not clearly reported as "medication error" by the reporter, "medication error" is added by the MAH if the product is not administered according to the SmPC".	
9	706	Table 2, page 23, "Covariates defining the treated population (CIOMS V)": "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~~ **adequate** information in the SmPC".	
10	207-211	In the section defining an adverse event no differentiation should be made between medication-related AEs and other AEs. Such a differentiation requires causality assessment and – if the result is 'yes, possibly medication-related' – would generate an ADR, not a sub-type of an AE! We should keep in mind that many AEs which, in the first instance, had been considered as not medication-related (e.g. car accident) were later on recognised as still causally related to drug treatment (in this example: reduced attention).	
10	212	It is not correct that the 'WHO defines an adverse event as an injury related to medical management …'. Apart from being problematic (see comment above) it is not the official definition of the WHO but only written in a ***draft*** guideline of the World Alliance on Patient Safety as a quotation of Hiatt et. al. (NEJM 1989, 321: 480-4).	
10	225-237	It is confusing that two different definitions are presented, i.e. one 'for the purpose of ICSR reporting in the EU' and another one 'for the purpose of this guidance'.	*)*

Stake-holder no.	Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		The omission of a necessary and already prescribed drug therapy (for example, by not taking necessary and prescribed medication by the patient) is just like not prescribing a necessary concomitant therapy (for example, no prescription of calcium folinate with high-dose methotrexate therapy) to be regarded as medication error. Also not providing necessary information for a patient and omission of monitoring may be a medication error.	
10	243-269	While it is true that ADRs due to MEs are preventable the absolute notion is not correct that ADRs which are not due to MEs are non-preventable. Often there are options to carry out 'on-label' treatments (i.e. non-ME-treatments) in a way that well-known and SmPC-labelled ADRs are mostly avoided (e.g. co-medication of a PPI to a patient treated with high doses of an NSAID for which the SmPC does not demand such co-medication may still reduce the risk of GI bleeding).	
10	254-255, 267-269, 283-284	Making 'potential errors' subject of a guideline seems inappropriate, because those situations where an error did not occur but could have occurred are too difficult to define with any practical specificity and hence to be regulated.	
10	305	It does not seem logical to write that a potential error has led to a medication error. A real mistake is not a potential one any more.	
10	307; 990	Comment: Introducing a specific sub-class of MEs characterised by the two criteria that a) no harm had occurred and b) nobody was aware of the error, and carrying this ME class through the guideline does not seem appropriate, because it is a merely theoretical construct without any consequence.	
	369-370	The definition of a consumer seems awkward. Defining a consumer as someone 'who is not a healthcare professional i.e. a patient, a lawyer, or	

Stake-holder no.	Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		a friend, a relative or carer of a patient' is absurd, because a lawyer, friend or caretaker typically does not consume drugs and because – on the other hand – a healthcare professional may well consume drugs.	
10	664-717 and Table 2	In a guideline on '…assessment of medication errors' one would expect an outline of appropriate root cause analyses (RCAs). This, though paramount, is not provided here. Table 2 is just a checklist of some points to be considered but in no way a guide to RCA. Apart from this the table doesn't mention safeguards like co-medication of protective drugs or monitoring by lab tests. (See also the respective comments on the guideline on risk minimisation and prevention of MEs 'EMA/606103/2014').	
10	706	The item "Category (type) of medication error" is understood differently in table 2 as in section 4.3.2. (referenced at line 697). The item "Stage of medication error" should also follow the steps transcription and monitoring.	
10	745-747	Comment: Medication errors should not be inferred unless specific information is provided. The term "specific information" should be explained.	
10	808-809	The wording "Other than monitoring errors, all medication errors which reach the patient are de facto administration errors" is misleading: One could understand here that medication errors do not include monitoring errors. However, since monitoring is part of the medication process, monitoring errors are consequently to be regarded as medication errors. The statement 'all medication errors which reach the patient are de facto administration errors' is not appropriate, because it implies an overstretching of the meaning of the term 'administration'. 'Administration' is normally used synonymously with 'application' and	

Stake-holder no.	Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		means just the physical procedure of placing a drug into or on the body. Thus, a wrong drug or a drug at an inappropriate dosage may well be administered correctly (i.e. within the terms of the SmPC), so that the administration as such should not be considered as ME.	
10	920-943	It may be assumed that physicians fear legal consequences of spontaneous reporting of medication errors. Therefore, the "good practice guide on the recording…" should address the possibility of anonymous reporting. Although this is contrary to the requirements for a valid case report (as defined in section 5.3. "Reporting requirements for medication errors associated with adverse reactions"), the possibility of anonymous reporting in the sensitive context of medication errors seems sensible.	
11	862	Intentional o*verdosing/under-dosing* should be part of a wider definition of *off-label use*, because both scenarios are outside of the authorized product information and they happen with a special intention of health care professionals. To avoid confusion between the three terms (*Overdosing/under-dosing* versus *medication error*, *off-label use or even misuse*) it would be much easier to differentiate only between *off-label use* and *medication errors.*	The definition in the GVP Annex I should also be taken into account.
12	144-192	The legal basis for all requirements concerning medication errors without an AE is unclear. It is unclear throughout the document what is legally binding and what is recommended. The use of 'should' is most prominent.	Cite specifically/separately the legal basis / articles referring to ME without an associated AE/ADR
12	185-192	This paragraph outlines that for clinical trials, reporting of medication errors, pregnancies and use outside of what is foreseen in the protocol … shall be subject to the same obligation to report as adverse reactions. Proposed change (if any): Please clarify the expectations here. Is the MAH expected to train the	

Stake-holder no.	Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		sites on reporting of MEs of all categories or to use data from the CRF to detect medication errors and process those without further information from the investigator, e.g. use of the wrong drug package during randomisation which would typically be a protocol violation or compliance issues where patient did not take drug for a day, this would usually be documented in the compliance section of a CRF and not reported as a medication error. Also, for each category, it would be good to specify what the related AE data fields are supposed to be completed with. E.g. is a potential medication error serious and related? Also, please include clear examples of medication errors in clinical trials which can be used for investigator training, e.g. patient took wrong tablet (background med instead of IMP) due to similarity of tablets – is that a medication error?	
12	207-211 and 271-273	The guidance refers to both adverse events and adverse reactions e.g. lines 207-211: For the purpose of this guidance medication related adverse events should be distinguished from other adverse events (e.g. fall, surgery on wrong body site etc.).and lines 271-273: For the purpose of this guide, the objective of which is to support the implementation of the EU pharmacovigilance requirements outlined in chapter 3. adverse reactions arising from medication errors (i.e. resulting in harm to the patient) should be recorded, reported and assessed. It is unclear whether there is an expectation for a causality assessment to be performed as prerequisite to assess a medication error and preventability, e.g. AEs occurring in conjunction with a medication error and deemed not related are not be recorded?	

Stake-holder no.	Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		Usually medication errors are reported spontaneously. As per Module VI any AEs are deemed related unless the report explicitly assess the AE as unrelated. Please clarify whether this principles is valid for medication errors	
12	230-231	Comment: Chapter 4.3 says that GVP Module VI.B.6.3 definition of a medication error does not cover all stages of the medication use process and the guide therefore provides a conceptual definition. The example for not falling into the GVP definition (preparation for administration) might not be well chosen. There are several products which will be prepared for administration by the pharmacist, doctor or the patient himself (e.g. reconstitution of antibiotics by parents - wrong amount of liquid will change the strength of the solution; reconstitution of antigene preparation in allergy hyposensibilisation) that are not clearly outside of the GVP definition of a medication error.	The definition needs to be consistent with the definition in other GVP documents (e.g. Module VI) in order to promote a common approach. If examples are to be given it should be one which is only done during the manufacturing process
12	250-251	The example provided sounds more like noncompliance on the patient side or a conscious decision not to take the drug (e.g. after reading the PIL) rather than a medication error. It should be clarified to include the error Proposed change (if any).	E.g. drug prescribed ~~and~~ but wrong drug dispensed but not taken by patient
12	249-251	In the example of medication errors with 'other unwanted effects… (e.g. drug prescribed and dispensed but not taken)', in some circumstances, for example within Patient Support Programs, such information may be extractable from data to which the MAH could have access yet this may not have been within the design/objectives. To what extent would MAHs be expected to 'extract' such events?	It should be made clear that the MAH can only collect factual information provided.
12	285	Figure 2 and the related classification assume information that the MAH usually does not have.	It should be made clear that a classification can only be made when the factual data allow doing so.
12	305-327	The information relating to potential errors and what they could or have	The potential error could lead ~~or has led~~ to

Stake-holder no.	Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		led to (from line 305 onwards) is quite confusing. How can a 'potential error' have already led to a), b) or c) yet still be 'potential' for the particular event in question?	
12	312-313	The fact that strength of oral solutions vary between MAH confuses the medication error. In line 464-468 states that issues with labelling are product quality issues. Therefore, a reference to some labels referring to mg/ml and sometimes mg/dose seems to be a quality issue rather than a medication error. In this instance, it would be expected that the reported potential error would be captured as a product complaint rather than reported to safety. The same holds true for the example of the pharmacist noting that the names of two medications were similar. In addition, the medication name is submitted and approved by regulatory authorities and the same with product labelling. Therefore, these 2 examples may be out of MAH control and it seems that regulators have more information to compare across products to prevent labelling issues such as those described.	
12	380-381	It is unclear which alternative formats for recording ICSRs of medication errors not associated with AEs are meant?	Further specification would be appreciated.
12	389-393	It is unclear if the term 'patient safety incident' is a generally recognised term amongst HCPs and national/regional PSOs or indeed other potentially impacted bodies. Perhaps inclusion in the definition section of this guidance would be useful. In addition it is unclear what mandated requirement is in place to ensure that 'patient safety incidents' associated with adverse reactions *are* 'made available' to EU NCAs by PSOs?	Please provide further information on MAH access to such information.

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		In order to facilitate the MAH ability to summarize patterns of medication errors and potential medication errors in PSURs will information brought to the attention of EU member states by patient safety organisations be made available to MAH? For example will it be included into EudraVigilance for download by the MAH?	
12	410	Table 1 specified the recording medication errors occurring in the **EU.**	Please clearly specify the expectations for recording all types of medication errors occurring outside of the EU.
12	464-468	The text makes reference to a product quality issue that should be distinguished from a medication error and not included in the definition of a modification error. However, the text does not make clear reference to scenarios where a product complaint may lead to a medication error. The ICH MedDRA Points to Consider v.18.0, section 3.28.3 provides the following example: "The mother administered an underdose of antibiotic because the lines on the dropper were hard to read". The suggestion provided is to co-code to LLT: 'Product dropper calibration unreadable' and 'Accidental underdose'.	Consider clarifying by expanding the explanation by using examples. Also, more clarity could be provided around the distinction between product complaint vs. medication error. As the text appears at present, it is too high level and could be misread in that any product complaint would never be linked to a medication error.
12	467	This states that "the splitting of a scored tablet in two differently sized parts is considered a product quality complaint and not a medication error". Use of the term "scored" can be misleading, as the use of "score-lines" may be cosmetic only, and not intended to indicate that the tablet may be broken.	Revise to read "the splitting of a ~~scored~~ tablet with a "break-line" in two differently sized parts is considered a product quality complaint and not a medication error".
12	469-487	The intent of section 5.2.2 (Context of patient safety) is unclear and appears to be for educational/information purposes rather than a requirement for MAH / NCA action.	Consider moving this section to the introduction section.
12	499-501,	Text seems to require to collect or report medication errors with	Make clear the requirement to collect or report

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	647-657	associated reactions (regardless of seriousness) from clinical trials. Elsewhere (Line 1193-1217 including Table A2-1), template for summary tabulations and listings of ICSR shown in Annex 2 denotes that these do **not** include interventional clinical trials.	medication errors from interventional clinical trials (e.g., medication error if associated with overdose and/or a serious adverse event).
12	521	Figure 3 indicates that MAHs should send ME + ADR from non-EU countries to Eudravigilance. This does not align with the final requirements laid out in GVP module VI which indicate that only non-serious ICSRs that occur in the EU should be submitted.	Update the diagram to indicate that ME + **SADRs** from non-EU countries should be submitted to Eudravigilance.
12	557	The statement 'medication errors which may constitute for example a safety signal or safety concern' will cause confusion. In the preceding lines, it was stated the MAH will present medication errors with associated ADRs from all post-marketing sources in the PSUR.	Suggest clearly stating that PSUR discussions will include discussions of the following: 1) Medication errors that are associated with ADRs from post-marketing sources 2) Other medication errors that were identified as a signal or safety concern Please also make this consistent with guidance stated in lines 617-619.
12	561-567	The text here does not align with Figure 3 but does align with the requirements laid out in GVP module VI.	Update figure 3 to align with GVP module VI.
12	561-572	Technical questions have been identified in operating this proposed process: • Is a reconciliation of data necessary in case EudraVigilance data and data from MAHs database is used to to provide summary tabulations for medication errors? (e.g. case creation date may differ making it difficult to receive the same cases for a defined reporting period) • Is data from EudraVigilance suitable to assess the association of medication errors and adverse events?	A more detailed consultation on this functionality would be welcomed.
12	585-590	Is it the expectation that the agency's name review group is informed of	Further clarification requested

Stake-holder no.	Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		each occurrence of medication error related to the invented name, or would this only be required on review of aggregate data a 'pattern' is suggested?	
12	664-674	It is not clear if ME reports should routinely be followed up if they are NOT events of special interest or a safety concern.	Add in a reference to GVP.VI.B.6.3 which is explicit about the requirement to follow up for special situation reports.
12	676-681	This paragraph introduces the concept around the good practice that marketing authorization holders and national competent authorities should gather essential information in relation to medication errors that are brought to their attention. This is regardless of whether the error was associated with the adverse reactions(s). Table 2 provides an overview of parameters which may support the scientific evaluation of ICSRs or aggregate data. The text immediately after lines 682-685 makes reference to follow-up activities for cases of medication error which are associated with serious adverse reactions. Still making reference to table 2 as a reference of parameters that should be followed-up. No difference between the two paragraphs is noted regarding the follow-up activities that should be performed. If the intention that table 2 is used for all scenarios whether the medication error is associated with an adverse reaction or not, then it is not clear why another paragraph focusing only to medication error associated with serious adverse reactions is written immediately after, basically repeating the same concepts.	The text going from 676 to 685 may be combined as follows (682 to 685): "To ensure better learning from medication errors for the development and promotion of safe medication practice, it is good practice that marketing authorization holder and national competent authorities should make all reasonable efforts to collect, through appropriate case follow-up, ~~follow-up~~ essential information in relation to medication error brought to their attention regardless of whether the error was associated with adverse reaction(s), unless national requirements for anonymous reporting prevent follow-up. Table 2 below provides an overview of parameters which may support the scientific evaluation of individual case safety reports or of aggregated data on medication errors.
12	682-685	When discussing follow-up activities, reference is made only to medication errors associated with serious adverse reactions (line 682).	Clarification is required for those medication errors associated with non-serious AEs.

Stake-holder no.	Line no.	Stakeholder comments	Proposed change by stakeholder, if any
12	706	Table 2 raises a number of questions. • Is splitting required to capture the stages in the medication process where an error occurred plus the resulting administration error? • Terms for coding of external factors leading to e.g. therapy interruption that are beyond the control of the HCP or patient (e.g. insurance issues etc.) are currently missing in MedDRA. Only option is PT *Therapy cessation* with underlying LLTs, which is considered a therapeutic procedure following MedDRA hierarchy. For appropriate classification, more options for coding of contributing factors are needed, with appropriate MedDRA hierarchical linkages.	
12	706	Typographical error changes the meaning of the sentence.	Strictly speaking the outcome of a medication error is not applicable if the medication error did not occur.
12	706	Table 2 indicates that all reports of medication error, including potential errors, should be entered as ICSRs. If it is a true potential error with no actual patient then this would not be considered as an ICSR.	Remove reference to potential errors. 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.
12	706	Table 2 contains very specific information regarding follow-up requirements. It suggests that the use of targeted follow-up questionnaires may be needed in order to gather such information. Is this the expectation for all instances of medication error, or only those that are 'of special interest' to the MAH on a per product basis? eg. as referenced in lines 713-714? It is perhaps unlikely that the reporters will respond to such a questionnaire and/or provide the details, in particular the 'contributing factors', in view of potential liability issues.	Please clarify expectations.

Stake-holder no.	Line no.	Stakeholder comments	Proposed change by stakeholder, if any
12	708-709	The guidance does not specify the number of attempts which should be made in order to obtain further information for a medication error.	Further guidance requested.
12	748-751	The current text: For cases clearly associated with a medication error based on specific information but where the term **'medication error'** has not been stated by the primary source, marketing authorisation holders and national competent authorities potentially exposed to liability in accordance with EU Member States' national law may provide a disclaimer (see chapter 5.7.) in the 'senders comment' section.	"Medication error" as a term is seldom reported by the primary source, so suggest using a more general sentence, e.g., "For cases clearly associated with a medication error based on specific information, code as such. Where a specific term indicating a medication error has not been stated by the primary source, this should not be assumed, consistent with the ICH Points to Consider document.
12	758-760	This guidance states that "The MTS:PTC guide should also be used by healthcare professionals, researchers and other parties (e.g. patient safety organisations) involved in the reporting of medication errors." Awareness and familiarity with MTS:PTC is a lot to ask of healthcare professionals who only occasionally report ADRs and medication errors; they are not part of the pharmaceutical industry. It also assumes that the databases they are using are utilising MedDRA (or is this only applicable to the EU regulatory databases that accept reports directly from these individuals?)	Reporters should be encouraged to give the most comprehensive description possible of the medication error. Use of MedDRA PTC should not be required.
12	787	It would be helpful if coding guidance for the following special situations was provided: 1) Patient is re-challenged because prescriber/caregiver is unaware of a previous adverse drug reaction; 2) A medication is prescribed and administered to a patient in whom it is contraindicated, because the prescriber/caregiver is unaware that there is a contraindication in the label; 3) A medication is prescribed and administered to a patient in whom it is contraindicated, because the prescriber/caregiver is unaware that the patient has a situation that causes the drug to be contraindicated; 4) The prescriber knows that a	Add these examples into Section 5.6.2 Special Situations and provide coding guidance for each situation.

Stake-holder no.	Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		medication is contraindicated, but intentionally prescribes it anyway.	
12	808-810	This suggests that multiple medication error events should be coded for the same exposure which could result in inappropriate analysis of the data at an aggregate level.	Remove the final sentence. Other than monitoring errors, all medication errors which reach the patient are de facto administration errors. For coding purposes it is most important to capture the primary point in the chain of events~~. It is preferable to code other downstream errors in addition to provide as much information as possible.~~
12	824-829	The guidance rightly indicates that this example is not a medication error. However guidance on how to code unavailability of the product would be appreciated.	Guidance added.
12	847	As stated in the General Comments above we have concerns over the statement “Annex 3 provides additional coding examples for medication errors complimentary to the MTS:PTC”. Examples will require updating for MedDRA versions as the terms could change. There is also a chance that an example may disagree with a future MTS:PTC example (as MTS:PTC is updated for each MedDRA Versions) causing confusion.	This guidance should refrain from repeating information in MTS:PTC.
12	848-861	It is not clear if accidental and occupational exposures should be considered as medication errors?	Guidance on how to code accidental and occupational exposures should be given.
12	880-881	Guidance in this section is already outdated, according to MedDRA v18.0 hierarchy. PTs *Accidental overdose* and *Accidental underdose* are in HLT *Maladministrations*; the non-accidental terms are now in HLT *Overdoses NEC* or HLT *Underdoses NEC*.	Please update.
12	909-911	The addition of a new SMQ is welcomed	Please add that the use of this SMQ is recommended when it is available.
12	920-943	Whilst there is some uncertainty as to the necessity for such a disclaimer (see General Comments above) if it is to be included the guidance should	Please provide E2B field code where this disclaimer should be included if used.

Stake-holder no.	Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		state in which field this disclaimer should be included	
12	1211-1212	This table format is too prescriptive; many organizations don't use HLTs and HLGTs in displaying data and may not have the programs set up to do so. Besides, footnoting other HLTs to be considered points out how the HLGT *Medication errors* is not sufficient to retrieve all cases which is why the SMQ is welcomed.	Delete this table and add a recommendation that SMQ Medication errors be used instead.
12	1224-1233	Table A2-2 and Table A2-3. These tables cannot be automatically populated from the majority of MAH safety databases because there are no associated fields in the database for these (ie. Medication stage, contributing factors, ameliorating factors etc.). These tables would therefore have to be manually generated. As such they should be requested only in exceptional circumstances.	
12	1236-1238	Inclusion of additional coding examples is not recommended unless they are unambiguous and are unlikely to change. If Annex 3 is to be retained but not updated for MedDRA versions, it is suggested to specify the MedDRA version of the examples here.	"This Annex includes specific examples of medication errors in addition to those provided in the MTS:PTC documents ~~to address~~. The examples in this annex are in MedDRA version XX.X and may not be appropriate for later versions. The MTS:PTC document in its latest version should always be consulted."
12	1242	Example 1: It is unclear why is this coded as accidental exposure to product as this is not what was reported. Suggest *Devise Use Error* be coded Example 2: Suggest LLT should be *Accidental dose increase* Example 3: Suggest use of the new PT *Dose calculation error* Example 4: Cannot be classified as medication error based on the information provided, but rather represents a product use issue. Could also represent a product substitution issue. Example 6: In contradiction to line 825ff where it is stated that such "events" are not to be considered a medication error. Why then extract	Based on the guidance provided around the classification of medication error reports (section 4.3.2) and the need to support the scientific evaluation and interpretation of safety data by coding the chain of incidents starting from where the first error occurred, the examples should have the coding reverted as follows (underlined LLTs are those proposed to be re-ordered): Proposed change: • Patient was prescribed different insulin product

Stake-holder no.	Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		and code Drug dose omission? PT/LLT *Drug supply chain interruption* to be used?	at same daily dose and experienced hypoglycaemia **LLT term selected**: Drug prescribing error; Wrong drug administered; Hypoglycaemia • Patient was erroneously prescribed 10 fold higher strength of an oral opioid and went into respiratory failure at home after having taken 3 doses **LLT term selected**: Drug prescribing error; Accidental overdose; Respiratory failure;
12	1249-1250	Preferred option in MTS:PTC is now to code only the medication error. We should not encourage to create an event that is coded to LLT *No adverse effect*.	Please delete these two lines.
12	1253	Example 2: LLT *Inappropriate preparation of medication* should not be selected because the preparation never happened.	Revise table.
12	1275	It is only stated that code 7 should be used for medication error, however rather than use of a general code, a more specific code should be proposed to correspond to the actual category of medication error. It would be also useful, as it is usually the case in the post-marketing setting, to define/assign a code for "POSSIBLE MEDICATION ERROR" when it cannot be established whether the use was intentional or unintentional, as the number of such cases can be very large. In addition, a separate code should be allocated for the cases where medication error was not reported as such but might be suspected by MAH. Indeed Sender's diagnose may be used as proposed but then too	Revise guidance.

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		many fields will be necessary to include in very simple grouping for cumulative analysis. Sender's comments should always be mentioned in all cases where subsequent AE/SAE occur due to medication error.	
13	1270-1290	Taking into account that the ICH E2B (R3) format for ICSRs is new and there is no practical experience, the proposal in annex 4 seems to be appropriate. Moreover the additional coding of specific related reactions (as described in section 5.7.1.) makes the system much more flexible.	
13	934-939	To our opinion, such a disclaimer seems to be very useful/necessary, especially if there is no explicit indication of a medication error by the primary source, which would clearly transpose into a MedDRA term in the reaction section, but there is a hint that there may have occurred a medication error in the context of the clinical course description.	
14	771	It is specified: "As a guiding principle MedDRA coders should only code what can be read in the report, without adding or subtracting any information, and coders should not infer a medication error unless specific information is provided by the primary source" The reporter may not be aware of the medication error at the time of the report but it could be identify upon receipt after MAH or NCA assessment. Therefore this is not relevant to not code the MAH /NCA assessment as medication error report may be missed.	"As a guiding principle MedDRA coders should only code what can be read in the report, without adding or subtracting any information, and coders should not infer a medication error unless **clear information provided by the primary source clearly described a medication error**"
14	289	For intercepted medication error it is specified: 'an intervention caused a break in the chain of events that would have resulted in a potential ADR ...' Definition should be more detailed on what should be considered intercepted error. For example a HCP calling to confirm information on the good use of a product (which route, which indication, which dosage): should this be considered as intercepted error considering that without	In the context of pharmacovigilance an intercepted error indicates that an intervention caused a break in the chain of events **from prescription to before it reaches the patient** and that would have resulted in a 'potential ADR' and the intervention has prevented actual harm being caused to the patient, e.g. a wrongly dispensed medicine was actually not taken by the

Stake-holder no.	Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		information the wrong product/dosage/administration could have been administered?	patient because the error was noticed.
15	1200-1201	With regards to tables A2-1/2/3, in line 1200-1201 it is stated that “the tables should be created automatically”. This may require major alternations to existing databases since fields included in these tables aren’t included in many safety databases.	Please add “preferably” to the sentence “the tables should be created automatically from the pharmacovigilance database……..”
15	1211	Table A2-1, it reads as if only medication errors with associated adverse reactions are to be included in table A2-1. This table will therefore not provide the full overview of all medication errors. Based on the safety databases in the various MAHs, this table may be difficult to generate, and may need to be compiled manually.	
15	1221-1223	“Listings of individual cases shown in table A2-1 should be included in GVP VII.C.5 as PSUR EU regional appendix, subsection on medication errors… ” Will GVP module VII be updated accordingly as this is currently not a requirement in GVP module VII?	Please align with GVP module VII.
15	1224	Table A2-2contains only medication errors of special interest.	Please consider to align with the table ”description of medication errors” in RMP (RMP template section SVI.4) Please consider to include all medication errors (i.e. with and without adverse reactions) to provide a full overview of all medication errors (i.e. combine tables A2-2 and A2-3)
15	1226	Table A2-3 contains only medication errors without adverse reactions.	Please consider to align with the table ”description of medication errors” in RMP (RMP template section SVI.4) Please consider to include all medication errors (i.e. with and without adverse reactions) to provide a full overview of all medication errors (i.e. combine tables

Stake-holder no.	Line no.	Stakeholder comments	Proposed change by stakeholder, if any
			A2-2 and A2-3)
15	1275-1279	The E2B (R3) field G.k.10.r is mentioned here as being mandatory to flag. However, in the "EU Individual Case Safety Report (ICSR)0F Implementation Guide EMA/51938/2013" (released 04-DEC-2014) this field is mentioned as being optional on page (table 32, page 74).	Please clarify if the field G.k.10.r is meant to be optional or mandatory and update relevant guideline accordingly.
16	320-323	Section 4.3 of the document makes reference to a pharmacist noticing the names of two medicines are similar which could lead to drug name confusion in practise. EAHP supports the reporting of this kind of potential medication error but considers some active steps may be required in European countries to encourage and stimulate such proactive notification of the potential for error. EAHP requests that the EU medicines agencies regulatory network give consideration to this matter in respect of its strategy to 2020 which is currently subject to consultation.	
16	362-363	*"EU Member States are required by Article 102 of Directive 2001/83/EC to encourage healthcare professionals and consumers to report suspected adverse reactions to national competent authorities."* EAHP is curious to be informed of if, and how, the degree to which the obligations of the Directive in this respect are being met, and encourage the EU medicines agencies regulatory network to regularly assure itself that such enactment of the Directive is taking place to a satisfactory level. EAHP considers encouraging of reporting to be a continuous exercise.	
16	401-404	"*For the purposes outlined above marketing authorisation holders should therefore record, report and assess all medication errors which are brought to their attention, regardless of whether associated with an*	

Stake-holder no.	Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		adverse reaction(s), in their pharmacovigilance system or equivalent system for medication error reports not associated with adverse reaction(s).” EAHP strongly supports this section of the guidance and indeed consider it worthy of additional emphasis in the finalised version in order to fully underline the importance of recording and report errors that did not lead to harm, as well as those that did.	
16	476-477	*“There is currently no commonly agreed terminology used for classifying patient safety incident reports in national reporting and learning systems of EU Member States where they exist.”* This occurs to EAHP as a system deficiency to be overcome. EAHP advises that the EU medicines agencies regulatory network set itself the goal of addressing this matter within a defined timeframe e.g. by the end of 2017.	
16	578-580	*“Listings of individual cases should be provided by the marketing authorisation holder within an established timeframe to be included in the request. This may be accompanied by a request for an analysis of individual cases of medication errors associated with adverse reaction(s) where necessary for the scientific evaluation, including information on numbers of serious cases, details on the causes and circumstances that led to the medication error, mitigating and ameliorating factors and as necessary, analysis of non-serious cases.”* EAHP advises the document authors to be aware of the burden for the reporter in terms of fulfilling such a list of information fields (especially “details on the causes and circumstances that led to the medication	

Stake-holder no.	Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		error, mitigating and ameliorating factors"), and the potential unintended impact therefore of creating further disincentives to healthcare professional reporting if applied too bluntly. Careful attention is therefore required to ensure proportionality in approach, including defining the circumstances where such detailed reports are necessary (and, by extension, when not necessary), and the methods to collect information in the least burdensome way (e.g. well designed and user-tested web portals, mobile apps etc).	
16	758-759	The document states: *"The MTS:PTC guide promotes accurate and consistent term selection and can be downloaded from the MedDRA website. The MTS:PTC guide should also be used by healthcare professionals, researchers, and other parties (e.g. patient safety organisations) involved in the reporting of medication errors."* With this in mind, EAHP considers that there is further useful activity that might be conducted across Europe to promote the MTS:PTC guide to healthcare professionals in order to meet the aspiration for accurate and consistent reporting expressed in the guidance document. This might be helpfully taken up as an item for consideration by the EU medicines agencies network in the context of its Strategy to 2020, currently under consultation.	
17	236-7	A medication error is an unintended failure in the drug treatment process that leads to, or has the potential to lead to harm to the patient. There are knowedge-based errors that occur frequently. This is intended, but also failure in practice. Consideration should be given to changing this to, '….error is an unintended *or intended* failure in the drug	

Stake-holder no.	Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		treatment process.	
17	468	The Minimum Information Model (WHO MIMs) must be at a level where compliance does not compromise existing member state systems for pharmacovigilance, neither should it restrict those member states from evolving more in-depth mechanisms for determining learning and categorisation of error.	
17	521	Figure 3 did not make it immediately clear that it does allow for PSO to receive ME +/- ADRs and redirect them to MAHs. This is a significant route for error Patient Safety Incident reporting in England. The PSUR should be made available to the PSO, National competent Authority as well as the MAH, i.e the red arrow should be bi-directional	
17	563-566	….summary tabulations from EudraVigilance supporting the assessment of medication errors in PSURs may be created using reports by means of the EudraVigilance data analysis system and complemented with additional data on medication errors held in the marketing authorisation holder's own pharmacovigilance system. Who will be able to access this information? This needs to be made clear in the documentation. As a minimum this should include MARs, PSOs, NCAs and manufacturers.	
17	706	Table 2: The medicinal product information should be coded in the ICSR drug section. In England the Dictionary of Medication and Devices (DM&D) is the definitive description. MAHs and NCA will have ways of describing medicines and devices. It will be very difficult to standardise this across the EU as names vary across the EU.	
17	808	…..all medication errors which reach the patient are de facto	

Stake-holder no.	Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		administration errors. I disagree with this. The basis of error reporting is to identify the root cause of the error. If the root cause was a prescription error then that should be the coding, even if it progresses to reach the patient.	
18	232	To me it is not clear why this is a **conceptual definition** and how I should understand this. Will it replace the definition currently present in GVP Module VI?	Clarify the above.
18	305	If a potential medication error has led to harm, is it still a potential medication error?	The graph above clearly shows that a potential medication error is recognised before it even turns into an error, so would limit the description here to phrases as “could have” “might have” rather than has led. Therefore, example a) is also not very clear to me.
18	867	Old versus new definition	In line with remainder of document, include (preparation for) before “administration”.
18	1153, 1156, 1159	Typo’s in bookmarks	Line 1153 no reference to chapter, 1156 and 1159 space after. Applies to remainder of document where chapter x.x.x. is followed by a)
19	113-115 134	The focus is on adverse reactions as a result of error – this is missing serious near miss errors where there may on that occasion not be any adverse reaction but the potential remains in any other patient on any other occasion.	
19	117-118	Errors as a result of off-label use sometimes signal a need for alternative labelled/ licensed products e.g. in paediatrics and should be within scope.	
19	171-172	The emphasis us in changes it clinical practice, however there should be better communication and agreement between PSOs and EU member state regulatory and licensing authorities to review licensing processes and changes to licensed products on the basis of learning from	

Stake-holder no.	Line no.	Stakeholder comments	Proposed change by stakeholder, if any
		medication errors which have been reported to PSOs.	
19	230-231	Medication errors in the preparation for administration stage of the medicines use process should be within scope. The preparation is determined by the licensed formulation and presentation, and if not suitable for clinical use, should be addressed within the pre-licensing authorisation stage by involving practitioners in the review process.	
19	476	The UK have commonly agreed terminology for classifying patient safety incidents.	
19	599 and Table 2	Detailed levels of MedDRA terms and coding would not be known to or understood by health care practitioners who would be reporting the incidents. Reporting should be simple to allow practitioners to report in their own words so that detailed coding can take place at a later stage if necessary.	
19	682-684 708-709	Section 5.7.1: reasonable efforts should respect organisation and national requirements for patient confidentiality, and other information governance practices, so as not to adversely affect or prevent the reporting of serious incidents or near misses	
19	808-809	All medication errors that reach the patient should not automatically be coded as administration errors as that may result in missing the route causes in the case of prescribing, dispensing and preparation errors.	
21	226-235	This section refers to the definition of medication error provided in Module VI.B.6.3 and then provides a conceptual definition. Should we consider the two definitions mutually exclusive or is it foreseen that Module VI will be updated in line with the conceptual definition?	
21	706	Table 2, the 2nd paragraph "For medication errors associated with non-serious adverse drug reaction(s) the patient outcome should be reported accordingly", should this be under the Patient outcome parameter? The 3rd paragraph seems to be not linked to parameter of seriousness, does it	

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		need a separate parameter?	
21	761	Should this sentence read: "The focus of the current MedDRA terminology is NOT on coding…"?	
21	851	If the MedDRA Introductory Guide version 17.0 changes does it make sense to refer to this specific version?	
23	393-397	We question the requirement to include **intercepted medication errors and potential medication errors** in PSURs and RMPs, as many of these are not true adverse events but technical complaints. If the intent is to conceptually include technical complaints under the regulatory umbrella of adverse events, please consider a broader communication to industry of the change in AE definition.	
23	538-550	Please clarify if this text requires sponsors to expedite non-serious adverse reactions associated with medication errors in a 15-day window. If this is the intent, please clarify which ICH expediting criterion should apply.	
23	882-907	The EU Medical Device Directive 93/42/EEC and aligned MEDDEV guidances stipulate requirements for reporting device incidents to competent medical device agencies in Europe. This section of the draft guidance implies that they must also be reported under pharmacovigilance requirements for medicines. If this is the intent it may result in major policy and process issues for some sponsors. Please clarify the specific requirements in more detail and provide a reference to the directive or regulation supporting them.	
24	706	Patient outcome – this is the opposite of what happens now ie generally speaking it is making an assumption about the degree of harm which occurred when that could vary for all the reason described under	

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		covariates.	
24	800	There is no scope for the error where the correct medicines have been dispensed for the patient to take home but the nursing staff either forget to give the patient the medication or give the wrong patient's medication.	
24	934	This may cause problems if the healthcare professional is negligent- this proposal only address's problems of the regulatory body and not organisations who have to manage individuals and their competencies. This in turn has the potential to lead to very bureaucratic processes.	
24	1127	This is problematic given that some incidents will arise from negligence as fair blame approach is better.	
25	14-16	We analyzed medication errors (ME) among the spontaneously reported ADRs to the Croatian Agency for Medicinal Products and Medical Devices (HALMED) on 100 spontaneously reported ADRs in 2013. In twenty percent of reported ADRs suspected MEs was identified. In most cases (86%), ME was suspected only by assessor. In process of identifying a medication error in practice it is very hard to check that in particular case it was unintended failure in the drug treatment process. Process of identifying ME is very sensitive and relationship between reporter and national pharmacovigilance center as well as legal implications in the context of HCP liability in some countries must be taken into account. Our results indicate the need to capture suspected ME by assessor in databases as well as promoting reporting of ME and customizing ADR forms for reporting ME. Please see proposed changes below.	If possible, the case should be followed up to confirm if there was actually a medication error. Also it is important to develop search in Eudravigilance. Please see comment of Q3.
25	18-21	Agree.	
25	22-24	We find it very useful. The search should enable possibility to include cases with populated fields: G.k.10.r, E.i.2.1b and Sender's diagnosis.	
25	25-30	We are of the opinion that more experience with implementation of The Guidance should be gained before making decision about making data	

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		about ME available to public.	
26	561-566	We do not see the additional value of requesting MAHs to extract summary tabulations from Eudravigilance to discuss in their PSUR since not all medication errors report will be in Eudravigilance and they need to supplement with data from their database anyway. For this reason, this could be removed from the guidance.	
27	242; 336; 393; 600; 945;	We suggest to share at European level throught all state members a glossary that include all the definitions of ADE, ADR, Incident, Sentinel Event and so on to have a good standardisation of the comunication. In this way it is possible to prevent difformities throught the reporting coming from different countries (communication barrier). Point 4.4 line 336: we suggest to use audit metodology to evaluate ADRs. Point 5.3.1 line 600: we suggest to develope a National database on confondent factors asociated to drugs that can be included in an european database. Point 6: it is necessary to have a formal agreement between National agencies for pharmacovigilance and health ministers (that recieved aderse events in a structured manner) to establish efficient information exchange. Lines 393-395 regarding the PSURs, we believe that during clinical trials the drug packaging is different from the approved packaging introduced in the marketing so it will be an under reporting of possible medication	

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		errors caused by drug packaging or LASA. In general we believe that it is very important a communication feedback to all health care providers that have made a medication error or an ADR report. It is also important to share all the information on MEDICATION errors and ADRs at European level to prevent their recurrences.	