EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Good Practice Guide on Medication Errors – Highlights and EU Regulatory Initiatives

6th Industry Stakeholder Platform on the Operation of the EU Pharmacovigilance Legislation

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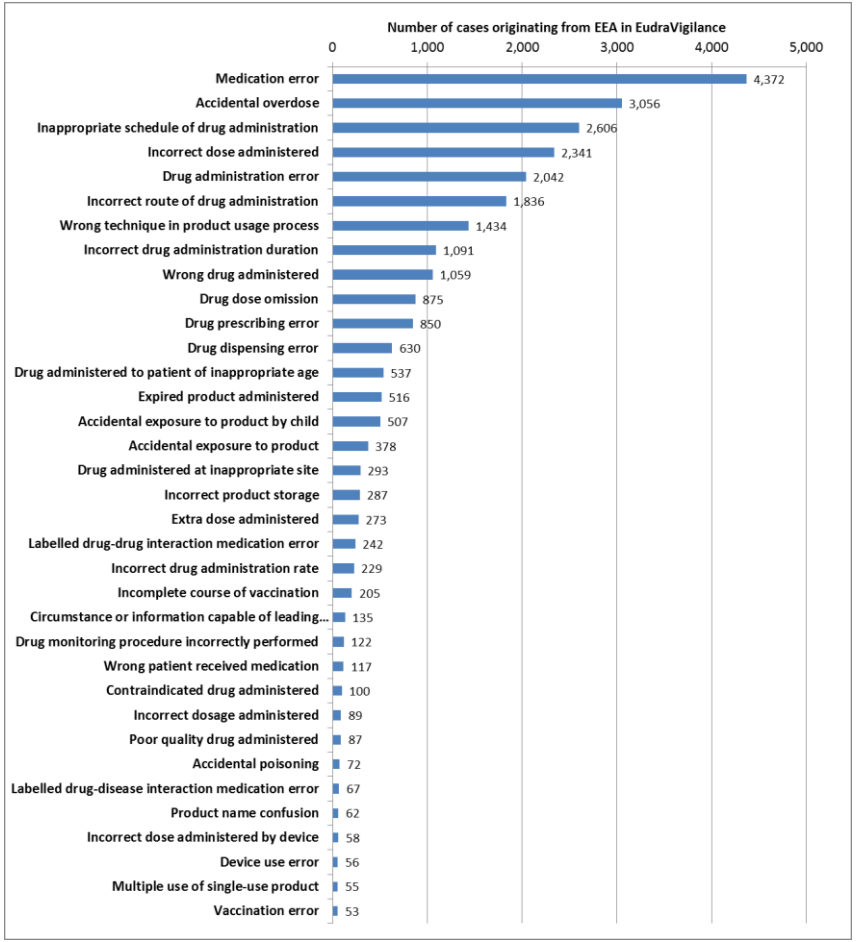
Motivation for EU Initiative on Medication Errors

- EU pharmacovigilance **legislation** requires:
  - Reporting of adverse reactions (ADR) associated with medication errors to EudraVigilance [*DIR 2010/84/EU Recital (5) and (17), DIR 2001/83/EC Article 1(11) and 101(1)*];
  - National competent authorities to liaise with national patient safety organisations [*DIR 2001/83/EC Article 107a (5)*] for exchange of ADRs caused by errors;
- To support implementation of these provisions, the EU regulatory network organised a **stakeholder workshop** on medication errors in 2013 which resulted in key recommendations for tackling medication errors from a regulatory perspective;
- Based on these recommendations, a **medication error action plan** was agreed by EU Heads of Medicines Agencies (HMA);

EudraVigilance reporting (EEA)

10 most commonly reported errors - MedDRA preferred terms (PT) (15/11/15)[1]:

1. Medication error
2. Accidental overdose
3. Inappropriate schedule of drug administration
4. Incorrect dose administered
5. Drug administration error
6. Incorrect route of drug administration
7. Wrong technique in product usage process
8. Incorrect drug administration duration
9. Wrong drug administered
10. Drug dose omission



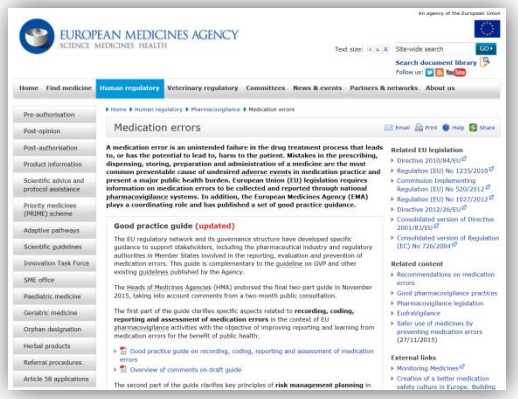
[1]Based on SMQ Medication Errors narrow terms list under development

EU Good Practice Guide (GPG) on Medication Errors

Developed by the EU Regulatory Network's governance structure for the implementation of the pharmacovigilance legislation, the 2-part guidance is a key deliverable of the HMA action plan on medication errors agreed in 2013:

- **Good practice guide on recording, coding, reporting and assessment of medication errors** (*GPG I*)
- **Good practice guide on risk minimisation and prevention of medication errors** (*GPG II*), including
  - **addendum on risk minimisation strategy for high-strength/fixed combination insulins** *II Addendum*)

Published on EMA website on 27 Nov 2015



Scope of GPG

- **Regulatory guidance** on recording, coding, reporting and assessment, and risk minimisation and prevention of medication errors (regardless of whether associated with adverse reactions) occurring with **authorised medicinal products**, including those supplied with drug delivery devices (if applicable) in everyday medical practice;
- **Risk management activities** in relation to medication errors, including those related to the design, presentation, labelling, naming, device component (if applicable) and packaging **during the product-life cycle** of medicines;

Not in scope:

- **Reporting** of medication errors in context of interventional **clinical trials**, to be addressed in context of implementation of clinical trials Regulation 536/2014;
- Medication errors with **medical devices** authorised in accordance with Directive 93/42/EEC (remit of EU Member States' national legislation);

Contents - GPG I Recording, coding, reporting, assessment

- **Scope & legal basis**
- **Definitions** and **classification** of ME
- **Recording** of medication error reports
- **Coding** medication error reports with **MedDRA**
- **Reporting requirements** for medication errors associated **with** adverse reactions
- **Periodic reporting** of medication errors without adverse reaction(s)
- **Follow-up** of medication error reports (typical parameters required for RCA)
- Rules of **anonymisation** of personal data and **liability disclaimer**
- **Collaboration** between national competent authorities (**NCA**) and patient safety organisations (**PSO**) for exchange of information on medication errors
- Annexes (templates, coding examples, business process for ICH E2B R3 etc.)

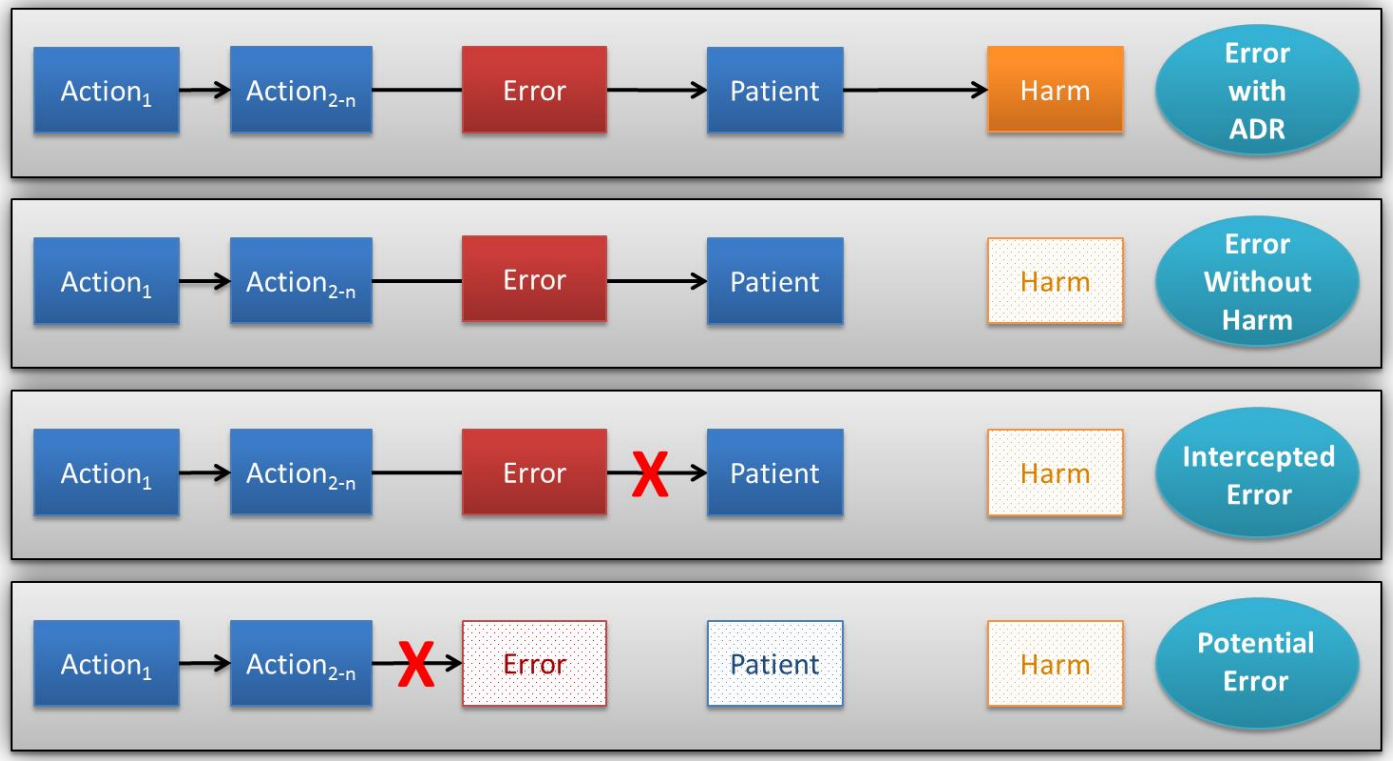
Focus: Definition of medication errors

"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".

Important considerations:

- A 'failure in the drug treatment process' does not refer to lack of efficacy of the drug, rather to **human or process mediated failures**.
- The concepts of intentional **overdose, off-label use, misuse and abuse** as defined in GVP Module VI.A.2.1.2 are **outside scope** and should be clearly distinguished from medication errors.
- The current definition of medication errors in GVP VI on management and reporting of adverse reactions will be aligned with the next revision.

Focus: Classification of Medication Errors



Focus: Recording Requirements

			Patient Safety	Pharmacovigilance	
Medication Error Type	**Error Occurred**	**Harm (ADR)**	**Recording**	**Recording**	**Report Type**
Error with ADR	✓	✓	Incident with harm	Medication error with adverse reaction(s)	ICSR reportable to NCA and/or EV[3]; PSUR summary[1]; RMP;
Error Without Harm	✓	✗	Incident	Medication error without adverse reaction(s)	PSUR summary[1]; RMP;
Intercepted Error	✓	N/A	Prevented incident ('near miss')	Intercepted medication error	PSUR summary[1]; RMP;
Potential Error	✗	N/A	N/A[2]	MTS:PTC guidance: PT 'Circumstance or information capable of leading to medication error'	PSUR summary[1]; RMP;

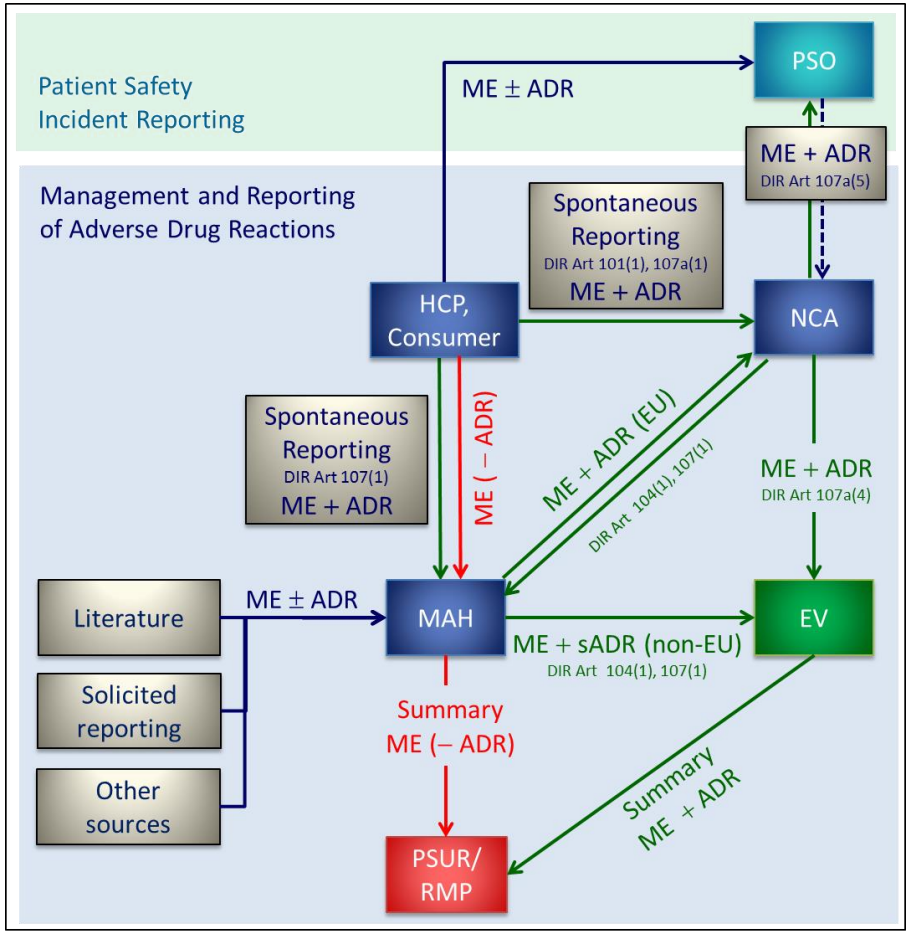
[1] Summary tabulations and on request additional listings of cases of medication error of special interest

[2] Not in line with the WHO ICPS definition of a patient safety incident

[3] For ICSR reporting modalities interim and final arrangements after successful Eudra-Vigilance audit refer to GPG I Annex 1

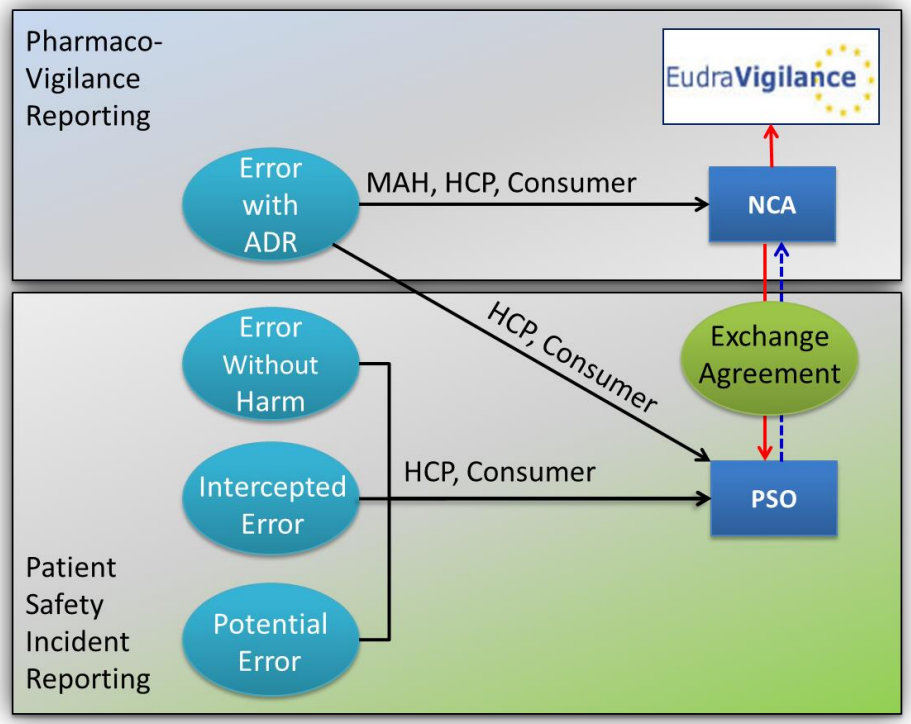
Focus: EU Reporting

- **Green arrows** refer to medication error reports associated with (serious and non-serious) **suspected adverse reaction(s) (+ ADR)**, including non-EU suspected serious adverse reaction(s) (+ sADR) MAHs have to report to EudraVigilance (EV).
- **Red arrows** represent medication error reports not associated with suspected serious adverse reactions (- ADR).
- **Blue dotted arrow** represents adverse reactions associated with medication errors brought to the attention of a PSO.



Focus: Collaboration with Patient Safety Organisations

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



Contents - GPG II Risk Minimisation and Prevention

- **Scope & legal basis**
- **General principles of risk management planning** and the tools used
  - Root cause analysis (RCA)
  - Use-related risk analysis and Human Factor/Usability Engineering
- **Assessing the potential for medication errors** during the product life-cycle
  - Typical errors during clinical trial programme, including defects and device failures
  - Errors in post-authorisation phase
- **Risk minimisation measures** (routine and additional, including their effectiveness)
- **Specific considerations in high risk groups** (paediatrics, elderly, visual impairment)
- **Annex –** real life examples of sources of error and error preventing design features
- **Addendum -** risk minimisation strategy for high-strength and fixed-combination insulin products

Focus: Key Recommendations for Risk Minimisation

- The **potential for medication errors** should be assessed **at all stages of the product life-cycle** but particularly during product development taking into account RCA and human factor testing methods;
- To minimise the risk of medication error:
  - Careful consideration of the **product name, drug product design, presentation** and **labelling** to minimise the risk of mix-ups between different products and different product presentations of the same brand;
  - **Product information** (SmPC and PIL) should inform healthcare professionals, patients and caregivers of the most **appropriate use** of the product.
- Corrective regulatory actions should be taken in response to medication errors which result in adverse outcomes;

Initiatives for collaboration on medication errors

- European Commission's **Patient Safety Quality of Care Working Group** (PSQCWG) on patient safety aspects to support collaboration amongst national competent authorities and patient safety organisations (PSO) in Member States;
- **ICH M1 Points to Consider** (PTC) working group for MedDRA aspects
  - MedDRA expanded with new terms for data retrieval and assessment;
  - MedDRA Term Selection Points to Consider (MTS:PTC) documents updated;
- **CIOMS** working group on **Standardised MedDRA Queries** (SMQ) for new SMQ on medication errors (development ongoing);
- PRAC **Signal Management Review Technical Working Group** (SMART WG) is developing statistical and methodological guidance for signal detection, including a chapter on qualitative methods for medication errors;

Questions to the industry

- Feedback on the outputs delivered to date?
- Reflections on implementation and challenges?
- Are there further gaps which, if addressed would, support safe and effective use of medicines?

Thank you for your attention

Further information: **ema.europa.eu**

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Public consultation summary

GPG I: 28 stakeholders

- 242 individual comments
- 61 pages overview document

GPG II: 42 stakeholders

- 365 individual comments
- 123 pages overview document

GPG II Addendum: 16 stakeholders

- 93 individual comments
- 23 pages overview document

GPG I: 7 responses to consultation questions:

1. Use of G.k.10.r data element (ME flag): supported (5/6)
2. Disclaimer: supported (5/6)
3. Signal detection guidance (SMQ): supported (6/7)
4. Collated ME reports in EVDAS and/or adrreports.eu (after EV audit): supported (4/7), but further debate needed

GPG II: 7 responses to consultation question:

1. Whether it is useful to include examples of medication errors resulting in harm during the post-authorisation phase: supported (6/7)

Further key topics addressed following consultation I

- MedDRA coding principles - *clarifications added to distinguish ME from concepts for off-label use, accidental exposure, product quality issues, product complaints, misuse/abuse etc.*
- Case management in ICH E2B(R3) - *no splitting of cases where several events are reported; code the primary of stage of medication process where error occurred + use of G.10.k.r flag at drug level as appropriate*
- Use of G.10.k.r ME-flag - *optional data element*
- Stakeholder access in context of E2B (R3) and revised EV Access Policy – *same as for any ADR in line with revised access policy*;
- Data reconciliation - *via worldwide unique case identifier*
- NRG notification - *for each error occurrence but does not replace PHV reporting obligations*

Further key topics addressed following consultation II

- Off-label use vs medication error - *MedDRA coding concepts clarified*
- Tools to improve product design - *clarification on FMEA, user testing etc. to be considered but not mandatory*
- Root cause analysis - *not expected as routine PhV activity of MAHs and NCAs, but by PSO; details to conduct RCA to be collected through case follow-up as appropriate*
- Product design recommendations for high strength/fixed combination insulins - *pre-filled pens preferred, other presentations such as vials only if justified*
- Structure and presentation of examples - *all product specific examples moved in Annex of GPG II*
- Consistency with Quality guidelines – *comments from QWP implemented*

EFPIA comments not addressed

- Remove MedDRA coding examples in GPG I – *examples not covered in MTS:PTC maintained*;
- PSO access to ESI mailbox – *PSO are not within remit of DIR/REG*;
- Mention of medication monitoring errors in definition – *rejected by PRAC*;
- Guidance on coding ME with devices and differentiation from other device issues (e.g. quality issues, incidences) – *out of scope*;