EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Overview of key principles of the EU Good Practice Guide on medication errors

Session 1 – Pharmacovigilance of Medication Errors – Regulatory and Industry Perspective

DIA Information Day on Medication Errors, London, 20 October 2016

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An agency of the European Union

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The Facts about 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* (GPG definition);
- Most common single preventable cause of adverse events in medication practice;
- Major public-health burden with an estimated annual cost between 4.5 - 21.8 billion € (World Alliance for Patient Safety 2010);
- 18.7 - 56% of all adverse drug events among hospital patients result from medication errors that would be preventable[1];
- Medication-error rates in EU[1]:
  - Ambulatory care: 7.5% at prescription, 0.08% at dispensing
  - Hospital care: 0.3–9.1% at prescription, 1.6–2.1% at dispensing

Medication errors cost the NHS up to £2.5bn a year

The Pharmaceutical Journal, 20 OCT 2014 **By** Ingrid Torjesen

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

EudraVigilance reporting trends

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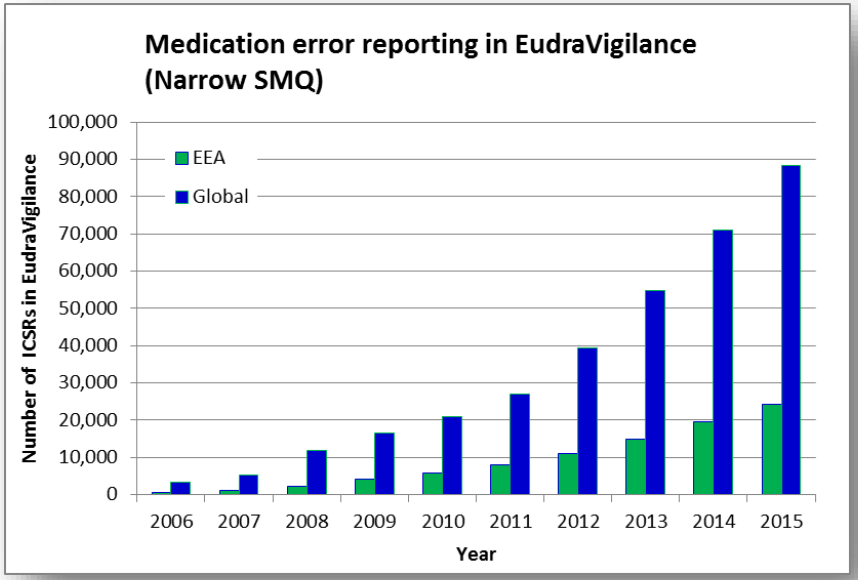
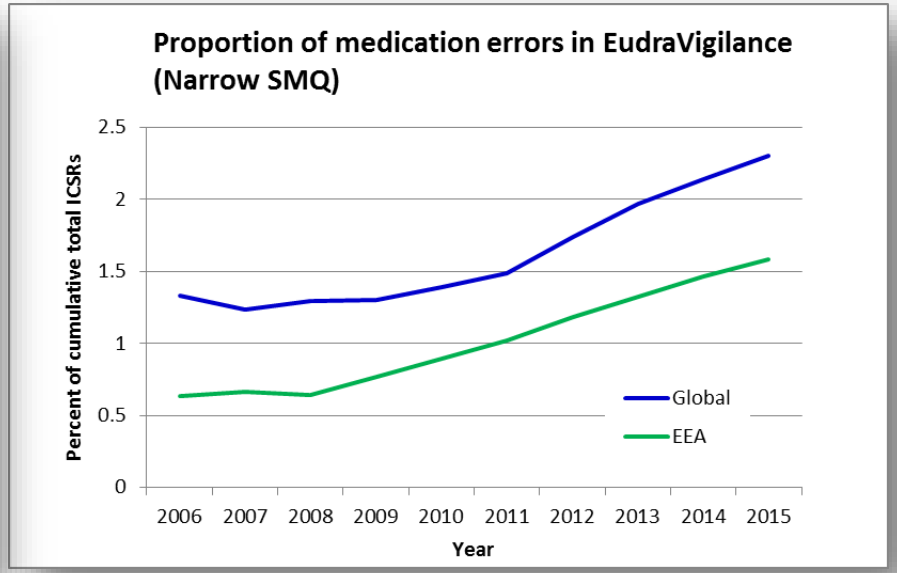
- Medication error reporting trends are increasing, 1.6% of all EEA and 2.3% of globally reported ICSRs in EudraVigilance are related to medication errors* by end of 2015;





*based on Narrow SMQ Medication Errors

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;
  - Facilitation of patient reporting [*DIR 2010/84/EU Recital 21 and DIR 2001/83/EC Article 102*];
- 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);

Stakeholder Workshop in London, 2013

Key recommendations:

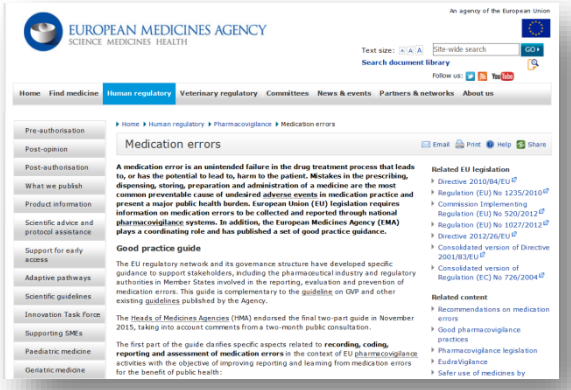
- Harmonisation and further development of terminologies and definitions at EU and international level.
- Establishment of collaborative relationships between national patient safety authorities, national regulators, the EMA and the European Commission.
- Development of new methods to identify medication errors from a patient safety and pharmacovigilance perspective through data pooling and analysis.
- Systematic assessment and prevention of the risk of medication errors during the product life-cycle (pre and post MA) through the EU risk-management planning process.
- Active engagement and capacity building with patient consumer groups and healthcare professionals to improve safe medication practices.
- Support to research into safe medication practices.

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 EU Regulatory Network's action plan:

- **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** (*GPG II Addendum*)

→ Published 25 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;

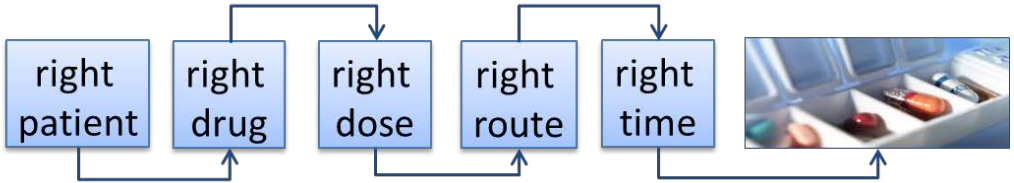
Not in scope:

- **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.)

What is a medication error?



Medication error involves the unintended failure to uphold one or more of the five "rights" of medication use in line with SmPC/PIL, but may also involve

- dose omission
- dispensing or use of expired medication
- use of medication past the recommended in-use date
- dispensing or use of an improperly stored medication
- use of inappropriate dosage form or administration technique
- instructions for use of cartridges and/or prefilled pens not followed
- etc.

Definition of 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".

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 error is **unintended**. 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.
- 'Drug treatment process' includes prescribing, storing, dispensing, preparation for administration and administration of a medicine in clinical practice.
- Definition in GVP VI (Rev. 2) has been aligned.

Definition

- **Potential error**

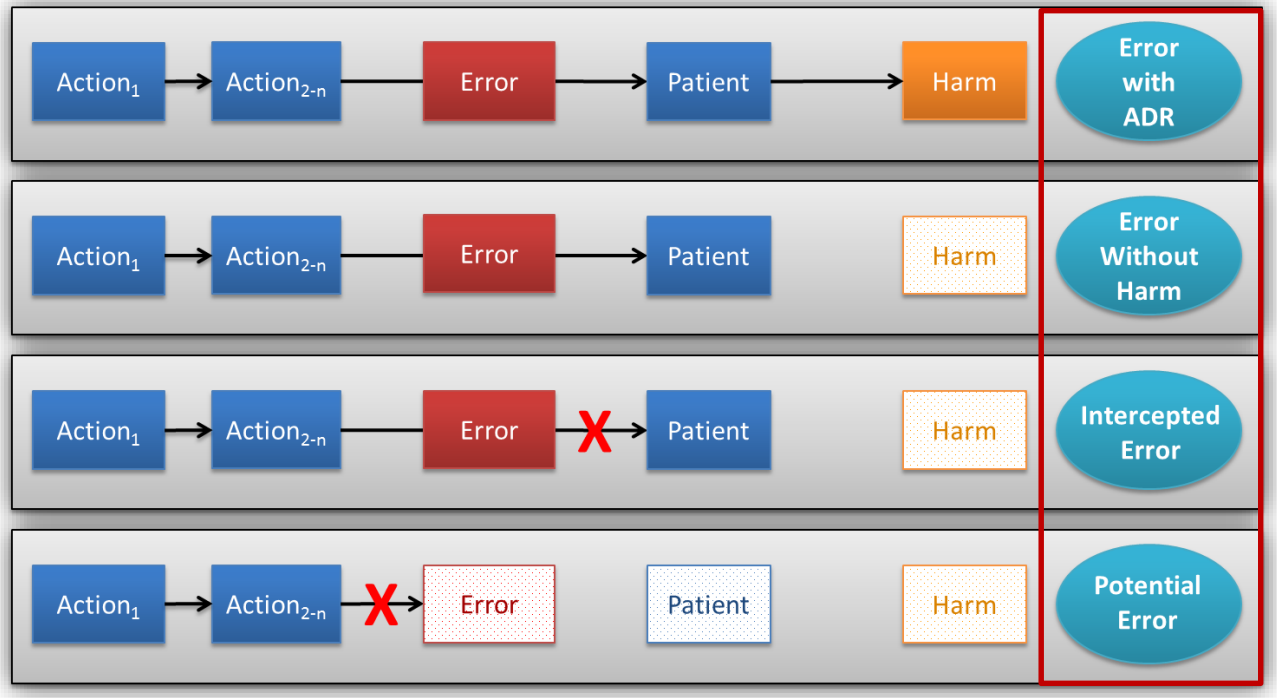
  “A potential error is the recognition of circumstances that could lead to a medication error, and may or may not involve a patient” (GVP Module VII.B.5.9);

- **Intercepted error**

  “An intercepted error indicates that an intervention caused a break in the chain of events in the treatment process before reaching the patient which would have resulted in a potential ADR” (Good Practice Guide).

  The intervention has prevented actual harm being caused to the patient, e.g. a wrongly prepared medicine was actually not administered to the patient because the error was noticed by the nurse.

Classification of medication errors



MEs should be **recorded and classified** for pharmacovigilance and risk management purposes.

Recording Requirements for Pharmacovigilance Purposes

			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;

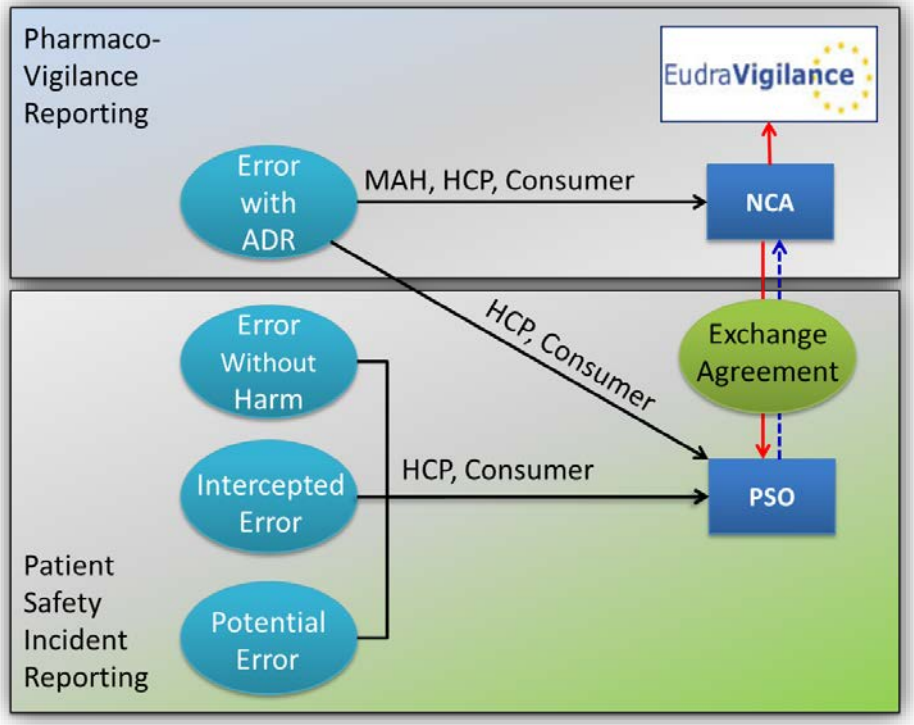
[1] Summary tabulations and on request additional listings of cases of medication error of special interest

[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

Collaboration with Patient Safety Organisations

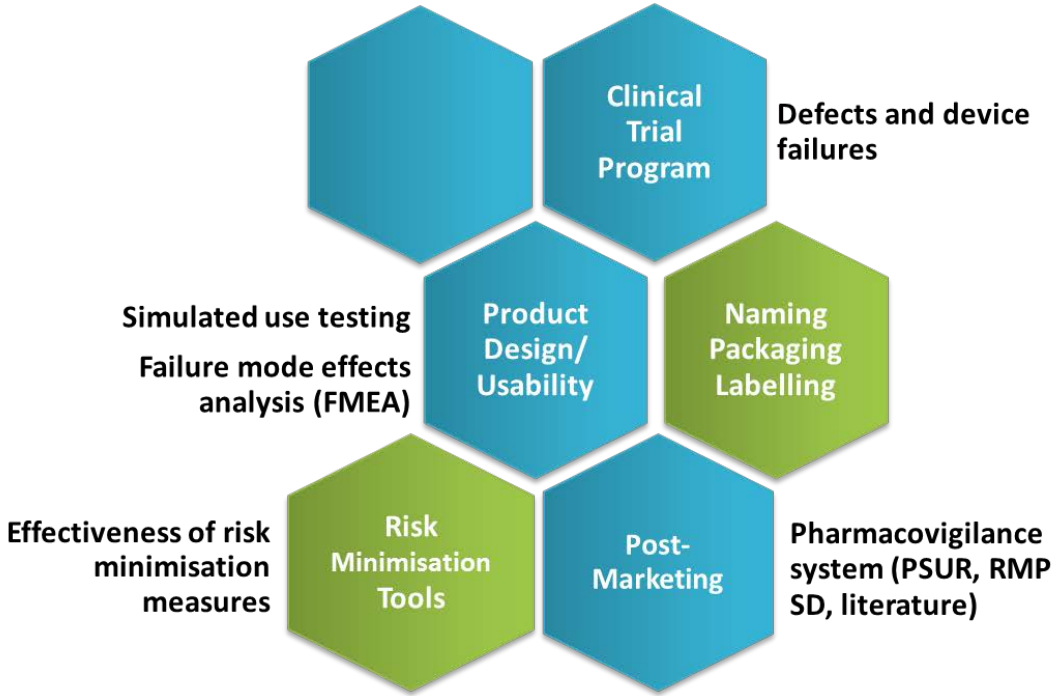
Model for collaboration between **National Competent Authorities (NCA)** and **national patient safety organisations (PSO)** for the exchange of ME. The red line between NCA and PSO refers to the legal provision to make medication error reports associated with ADR(s) *available*. The blue dotted line 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

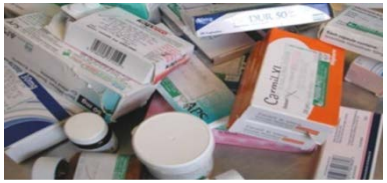
Product life-cycle approach



High risk groups – paediatrics

- Due to **change in body surface area, body weight and size** depending on degree of development dosing errors are most common in paediatric patients;
- **Pharmacokinetic profile** during early childhood also changes quickly which contributes to **over-** but also **under-doses**;
- Dosing instructions are often by body weight rather than age in months or years which requires **dose recalculation**;
- Risk of **dilution / reconstitution errors** in absence of appropriate paediatric formulations with medicines authorised for adults only;
- Dosing issues with liquid formulations if no or **wrong oral dosing device** (e.g. syringe) is provided and the liquid formulation exists in different strengths;
- **Accidental ingestion** by children is a common error;

High risk groups - elderly



- Polypharmacy in the elderly patient is a common cause for mix-ups, interactions and administration errors;
- Difficulties in handling products (opening bottles, blisters, swallowing tablets/capsules, dividing tablets or counting drops, use of asthma inhalers etc.);
- Impaired eye sight (e.g. difficulties reading labels, dialling insulin units on pen or administration of eye drops) leading to errors;

- Patients with low literacy have difficulties following the instructions for use (i.e. use of pictograms and diagrams to visualise the correct use of the product is preferred);

Key recommendations for error prevention

- The **potential for medication errors** should be assessed **at all stages of the product life-cycle**, particularly during product development taking into account root cause analysis (RCA) and human factor testing methods;
- **Adverse reactions** related to medication errors in the post marketing period should be discussed in the RMP and ways of limiting the errors proposed;
- Errors without ADR should be discussed in PSUR regional appendix as appropriate;
- 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.

EU Initiative on Medication Errors – further achievements

- **ICH M1: MedDRA** (v.18.1) expanded with new terms for data retrieval and assessment, including updated MedDRA Term Selection Points to Consider (MTS:PTC) documents;✓
- New ICH endorsed **Standardised MedDRA Query (SMQ)** for medication errors developed to support signal detection activities;✓
- PRAC **Signal Management Review Technical Working Group** (SMART WG) has developed a tool to flag medication errors in the **electronic Reaction Monitoring Reports (eRMR)** made available to EU Regulatory Network to support signal detection;✓
- Collaboration with European Commission's **Patient Safety Quality of Care Working Group** (PSQCWG) to support collaboration amongst national competent authorities and patient safety organisations (PSO) in Member States; ✓

EMA Webpages on Medication Errors

- **Medication Errors dedicated web page**

  Home ▶ Human Regulatory ▶ Pharmacovigilance ▶ Medication errors

- **Promoting the safe use of medicines**: EMA has launched a webpage to communicate to patients and HCPs any additional measures to prevent medication errors
  - Increase awareness of the additional measures recommended by EMA;
  - Ensure that a specific medicine is used correctly and to reduce the risk of medication errors;
  - Accessible via the European public assessment reports (EPAR) of these medicines;

  Home ▶ Find Medicine ▶ Human Medicines ▶ Recommendations on Medication errors

Challenges ahead

- **Launch of the new EudraVigilance system** with enhanced functionalities:
  - Implementation of new ICSR ICH E2B (R3) standard with option for **medication error flagging** [*Additional Information on Drug (coded) (G.k.10.r)*]
  - MAH access to EudraVigilance data (revised EudraVigilance Access Policy) (2017)
- **Exchange of medication error reports without ADR** brought to the attention of NCAs with MAHs and PSOs;
- Clarifications on the responsibilities for conduct of **root cause analysis (RCA)** at Member State level, i.e. extent of RCA conduced for pharmacovigilance purposes;

Thank you for your attention

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

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