EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Session 2 Reporting

Operational definition of medication error for EU reporting requirements

Medication-errors workshop
London, 28 February – 1 March 2013

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European Medicines Agency

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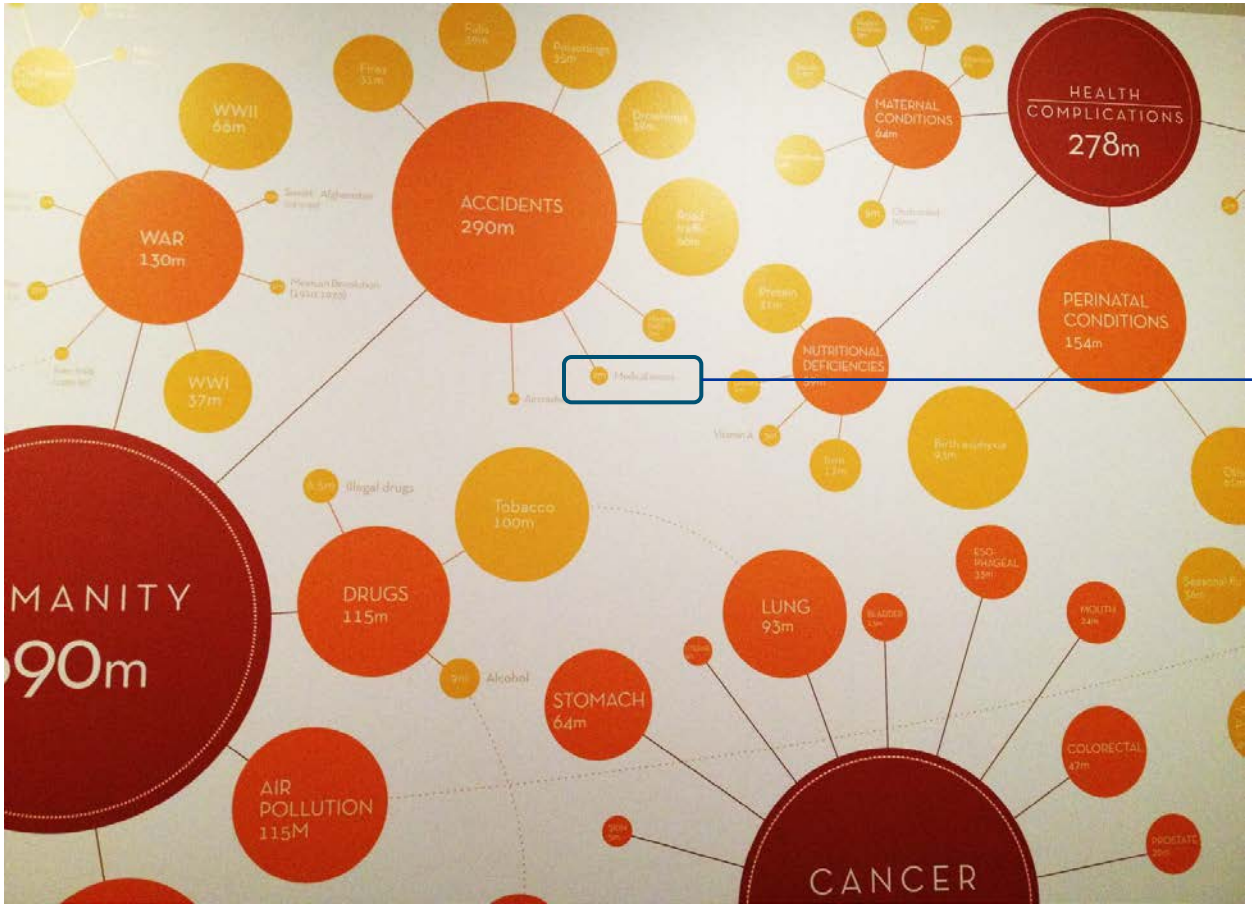
What were the most common causes of death in the 20th century?



Medication errors account for 2m deaths globally!

From David McCandless' graphic commissioned to accompany the exhibition '*Death – A Self Portrait*' at the Wellcome Collection London, November 2012.

The Facts about Medication Errors

- 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

1 Creation of a better medication safety culture in Europe: Building up safe medication practices. Council of Europe Expert Group on Safe Medication Practices (2006).

Adverse Reaction Reporting for Medicines and EudraVigilance

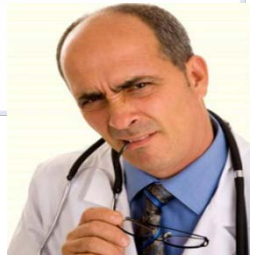
Secure electronic data processing network

Report adverse reactions

- Patient

Report adverse reactions

- Healthcare professional



Report adverse reactions

- Medicines Authority Member State
- Pharmaceutical Company

Monitoring of safety of medicines

- European Medicines Agency

EudraVigilance

Since 2012

Quality Assurance + Data Protection

European database of suspected adverse drug reaction reports

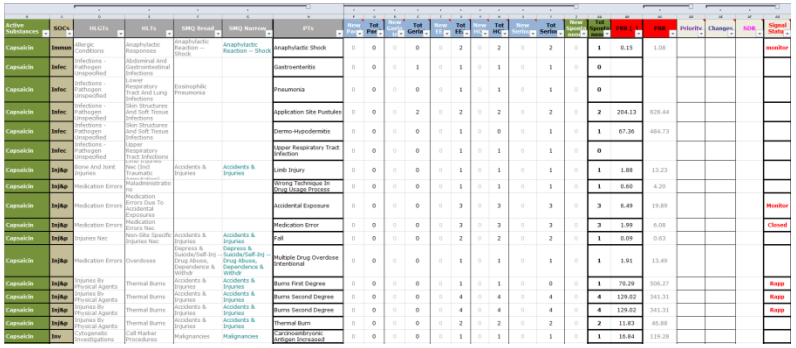
http://www.adrreports.eu

Legal basis: Title IX of Directive 2001/83/EC and Chapter 3 of Regulation (EC) 726/2004

Safety Monitoring in EudraVigilance

Electronic reaction monitoring reports

- EMA



Signal (safety) review

- EMA
- Medicines Regulatory Authorities in EEA

Assessment of benefit risk balance

- PRAC

Reporting Requirements for Medication Errors

- New pharmacovigilance legislation requires reporting of **medication errors that result in adverse reactions** to EudraVigilance
- Legal basis:
  - Directive 2010/84 (EC) Recital (5) and (17)
  - Directive 2001/83/EC Articles 1(11) and 101(1)
  - Directive 2001/83/EC Article 107a (5)

Legal Basis I

Directive 2010/84 (EC) Recital (5)

For the sake of clarity, the definition of the term 'adverse reaction' should be amended to ensure that it covers noxious and unintended effects resulting not only from the authorised use of a medicinal product at normal doses, but also from medication errors and uses outside the terms of the marketing authorisation, including the misuse and abuse of the medicinal product.

Directive 2010/84 (EC) Recital (17)

Member States should operate a pharmacovigilance system to collect information that is useful for the monitoring of medicinal products, including information on suspected adverse reactions arising from use of a medicinal product within the terms of the marketing authorisation as well as from use outside the terms of the marketing authorisation, including overdose, misuse, abuse and medication errors, and suspected adverse reactions associated with occupational exposure.

Directive 2001/83/EC Article 1(11) - Definition

Adverse reaction: A response to a medicinal product which is noxious and unintended.

Legal basis II

Directive 2001/83/EC Article 101(1)

Member States shall operate a pharmacovigilance system……to collect information on the risks of medicinal products as regards patients' or public health. That information shall in particular refer to adverse reactions in human beings, arising from use of the medicinal product within the terms of the marketing authorisation as well as from use outside the terms of the marketing authorisation….

Directive 2001/83/EC Article 107a (5)

Member States shall ensure that reports of suspected adverse reactions arising from an error associated with the use of a medicinal product that are brought to their attention are made available to the Eudravigilance database and to any authorities, bodies, organisations and/or institutions, responsible for patient safety within that Member State.

They shall also ensure that the authorities responsible for medicinal products within that Member State are informed of any suspected adverse reactions brought to the attention of any other authority within that Member State.

These reports shall be appropriately identified in the forms referred to in Article 25 of Regulation (EC) No 726/2004.

Definition of ‘Adverse Reaction’

GVP Module VI – Management and reporting of adverse reactions to medicinal products

An adverse reaction is a response to a medicinal product which is noxious and unintended [DIR Art 1].
This includes adverse reactions which arise from:

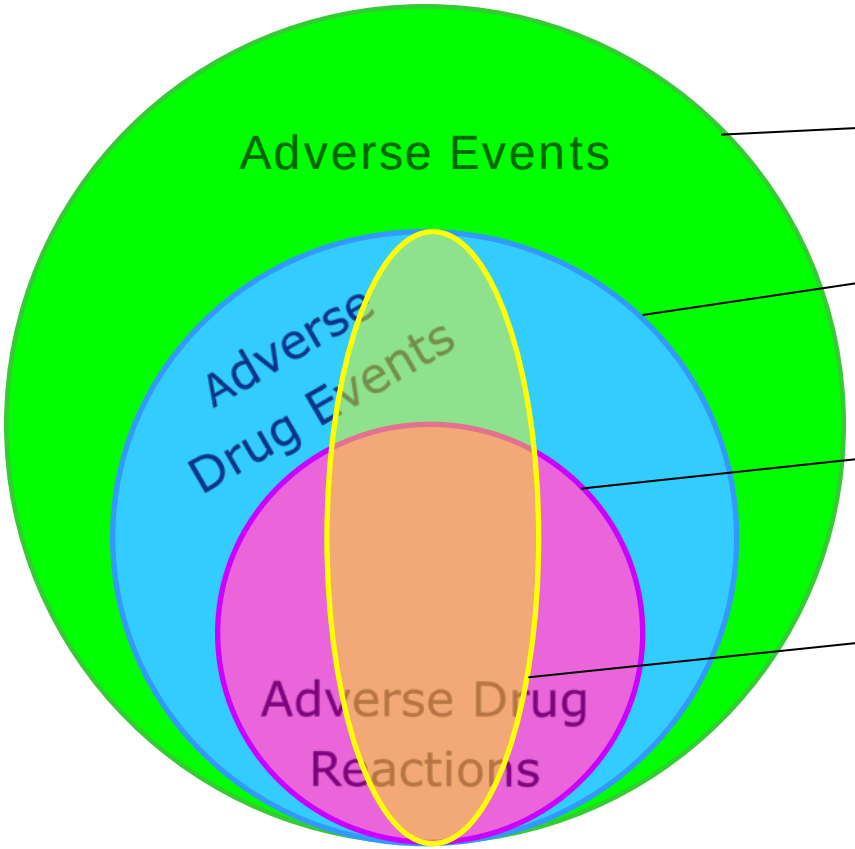
- the use of a medicinal product **within the terms of the marketing authorisation**;
- the use **outside the terms of the marketing authorisation**, **including** overdose, off-label use, misuse, abuse and **medication errors**;
- occupational exposure.

Definition of ‘Medication Error’

GVP Module VI – Management and reporting of adverse reactions to medicinal products

“Medication error refers to any **unintentional error** in the **prescribing**, **dispensing**, or **administration** *[including preparation for administration]* of a medicinal product while in control of the healthcare professional, patient or consumer.”

Context of Adverse Event, Adverse Drug Event and Adverse Drug Reaction



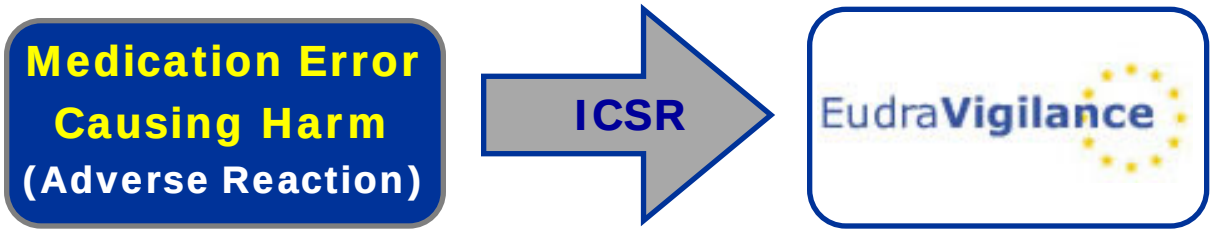
AE: Any occurrence or injury related to management of a disease

ADE: Any occurrence or injury related to medication (involving a medicinal product)

ADR: An adverse (drug) reaction is a response to a medicinal product which is noxious and unintended [DIR Art 1]

Medication Errors

Reports of Medication Error Associated with Adverse Reaction(s)



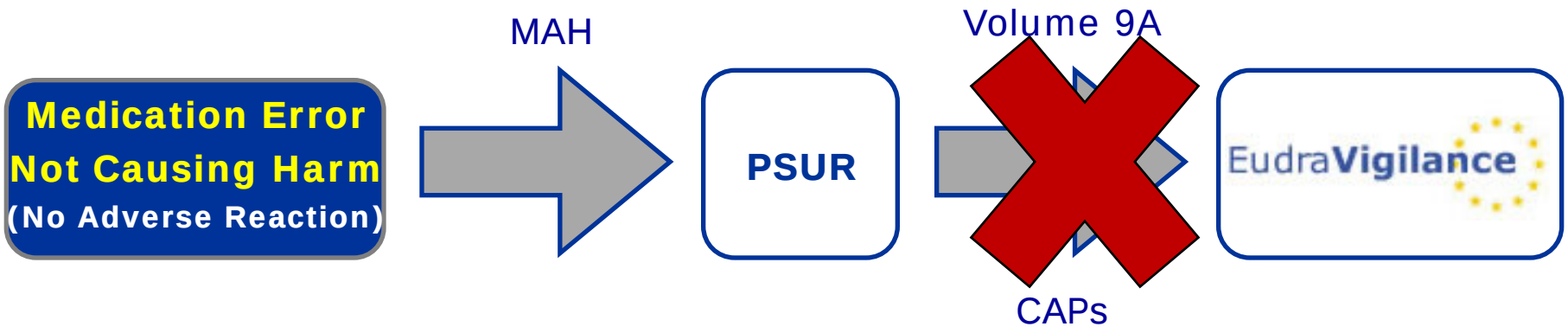
GVP Module VI.B.6.3 on reports of medication error:

The normal reporting rules for ICSRs apply. They apply equally to

- Overdose (administered quantity above recommended dose)
- Abuse (persistent or sporadic, intentional excessive use + harmful effects)
- Misuse (intentionally and inappropriately used outside terms of MA)
- Off-label use (intentionally used outside terms of MA)
- Occupational exposure (medicinal products exposure as result of profession)

if associated with an adverse reaction.

If There Is No Associated Adverse Reaction



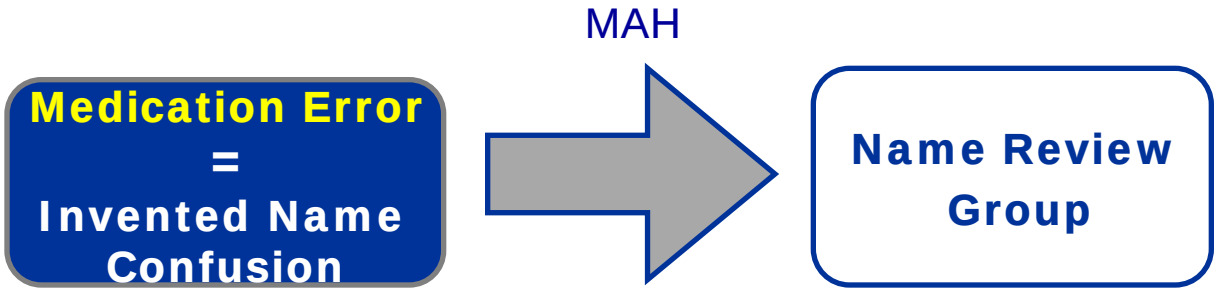
GVP Module VI.B.6.3 and GVP Module VI.C.2.2.6:

For medication errors which do not fall in the definition of a reportable ICSR, **MAHs** should consider them in **PSURs** and if constituting a safety concern

- impacting on the B/R balance of the medicinal product *or*
- impacting on public health

→ Notification as **emerging safety issue** to NCAs and EMA via dedicated mailbox P-PV-emerging-safety-issue@ema.europa.eu.

Medication Errors due to Name Confusion



Guideline on the acceptability of names for human medicinal products processed through the centralised procedure

(CPMP/328/98, Revision 5, 2007)

Prescription errors/medication errors due to the invented names of medicinal products which are **NOT** associated with an adverse reaction

→ Notification to EMA Name Review Group via dedicated mailbox nrg@ema.europa.eu

The guideline was last reviewed in December 2007.

Reporting of ICSRs

International Consensus Guideline ICH E2B(R2)

- Only **valid** ICSRs fulfilling minimum reporting criteria
  - Identifiable reporter
  - Identifiable patient
  - Suspected substance/medicinal product
  - **Medication error** + suspected adverse reaction

GVP Module VI – Reporting timeframe

- **15 days** for **serious** valid ICSRs (death, life-threatening, requires inpatient hospitalisation or prolongation of existing hospitalisation, persistent or significant disability or incapacity, congenital anomaly/birth defect)
- **90 days** for **non-serious** valid ICSRs

(During the transitional provisions [DIR Art 2] reporting of non-serious adverse reactions to EudraVigilance does not apply)

Causality (International Consensus Guideline ICH-E2A)

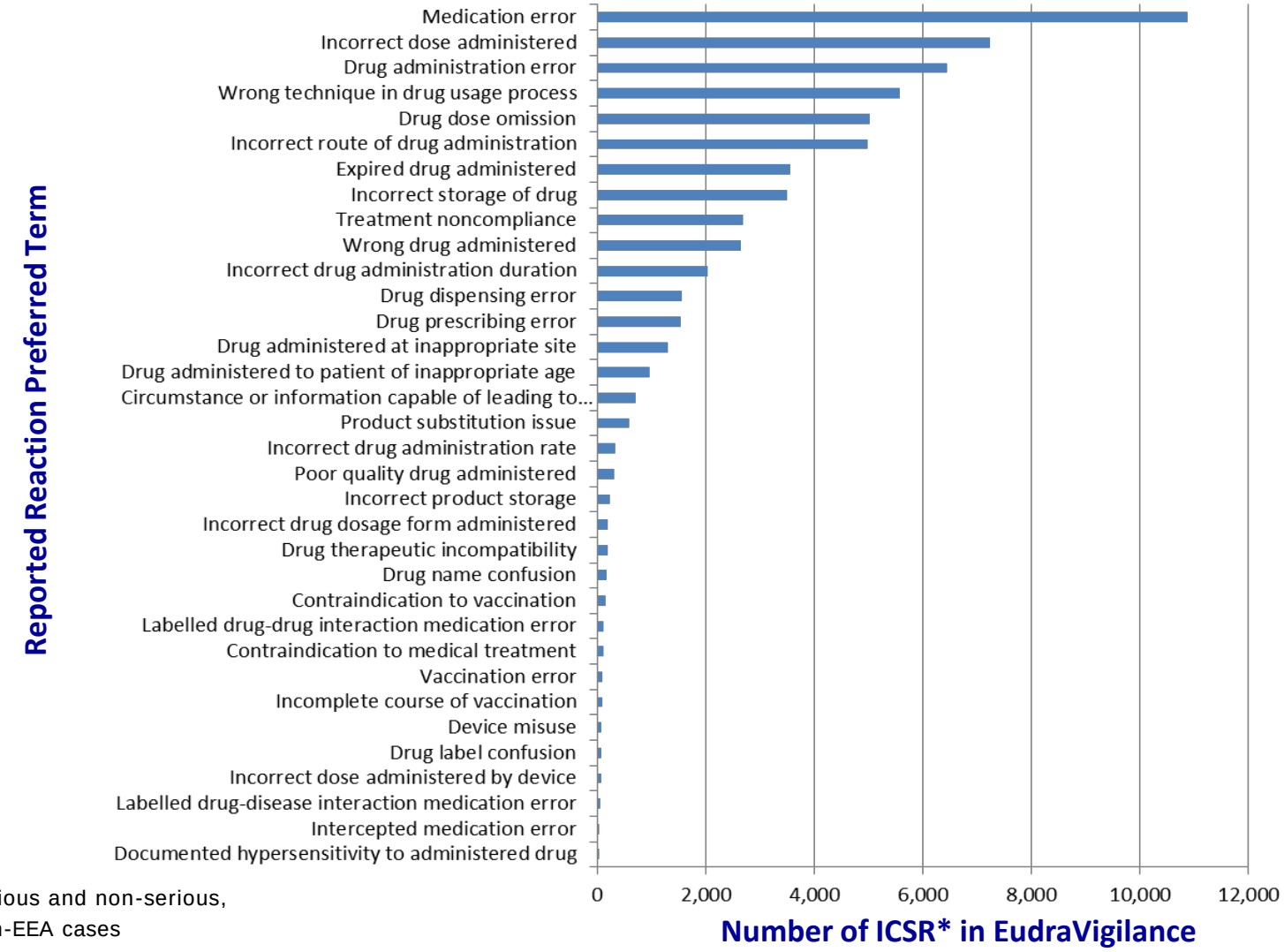
GVP Module VI – Management and reporting of adverse reactions to medicinal products

- The definition of an adverse reaction implies at least a **reasonable possibility of a causal relationship** between a suspected medicinal product and an adverse event.
- An adverse reaction, in contrast to an adverse event, is characterised by suspected causal relationship between a medicinal product and an occurrence.
- All **spontaneous reports** notified by healthcare professionals, patients or consumers are **considered suspected adverse reactions**, unless causal relationship is excluded by the reporter.

Number of Cases with Medication Errors in EudraVigilance (EV)

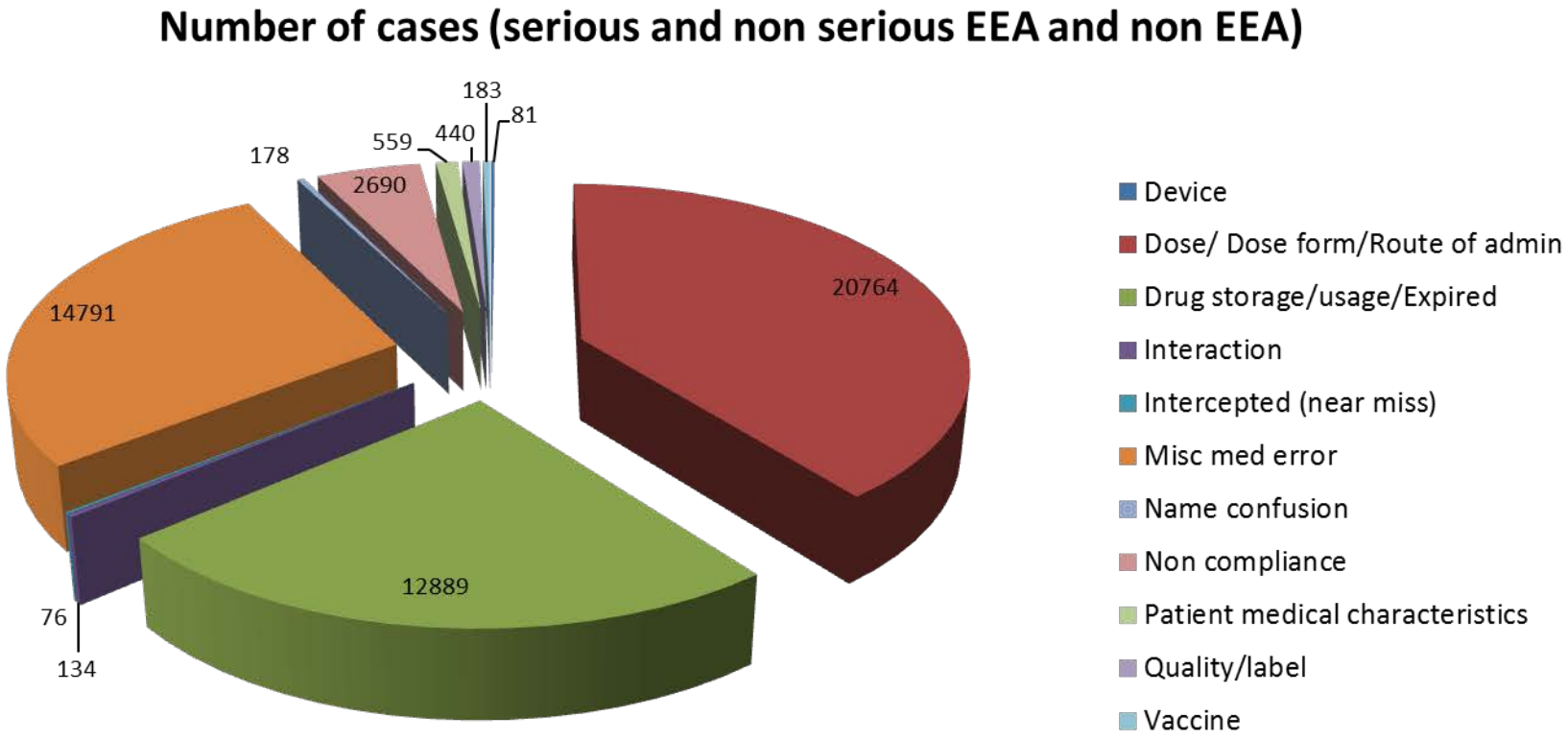
Origin	# Cases (serious and non serious)	% of total cases in EV	# Cases serious only	% of total serious cases in EV
EEA	14,099	1.18	9,373	0.99
Non EEA	45,895	2.37	27,245	1.7

The Most Frequently Reported Errors in EV



*Includes serious and non-serious, EEA and non-EEA cases

The Most Frequent Medication Errors in EV (Grouped by MedDRA Terms Coded)



Medication errors based on EMA internal grouping

Thank you for your attention.

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