REPORTING AND LEARNING SYSTEMS FOR MEDICATION ERRORS: THE ROLE OF PHARMACOVIGILANCE CENTRES

World Health Organization

Reporting and learning systems for medication errors: the role of pharmacovigilance centres

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Contents

Foreword

This publication has been developed as part of the "Monitoring Medicines" project (http://www.monitoringmedicines.org/) funded by the Research Directorate of the European Union under its Seventh Framework Programme. It aims to enable readers to learn more about why adverse events occur with medicines, and what can be done to reduce patient deaths and negative health impacts arising from undetected problems with medicines safety globally. It provides a framework for advancing the application, coordination and optimal use of pharmacovigilance evidence, sharing that evidence and strengthening the links between national pharmacovigilance centres and other patient safety networks, to prevent medicines-related adverse events. The publication is expected to:

- increase the capacity of national pharmacovigilance centres to analyse reports of medication errors;
- increase the capacity of national pharmacovigilance centres to identify preventable medication errors; and
- support action to minimize the occurrence of preventable medication errors.

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Abbreviations

The following abbreviations are used in this publication. For further explanations of terminology used, see the glossary.

ADE	adverse drug event
ADR	adverse drug reaction
EU	European Union
FMEA	failure mode and effects analysis
HCP	health-care practitioner
ICPS	International Classification for Patient Safety
IMSN	International Medication Safety Network
ISMP	Institute of Safe Medication Practice (USA)
LASA	look-alike, sound-alike
MAE	medicine administration error
ME	medication error
MERS	medication error reporting system
NPSA	National Patient Safety Agency (England)
NRLS	National Reporting and Learning System
PCC	poison control centre
PSO	patient safety organization
PVC	pharmacovigilance centre
RCA	root cause analysis
UMC	Uppsala Monitoring Centre (WHO Collaborating Centre for International Drug Monitoring)
WHO	World Health Organization

1. Objectives

This publication is intended to strengthen the capacity of national pharmacovigilance centres (PVCs) to identify, analyse and issue guidance to prevent or minimize medication errors (MEs) that harm patients. In addition it is intended to stimulate cooperation between national PVCs and patient safety organizations (PSOs) to work together in order to minimize preventable harms from medicines.

Background and technical guidance are provided on the principles and methods of ME incident reporting and learning. This information is intended to assist PVCs and PSOs to begin using the same philosophy, terminology and processes when undertaking this work.

2. Burden of medication errors on public health

2.1 Patient safety incidents

Patient safety incident is a term used by PSOs when referring to an event or circumstance that could have resulted, or did result, in unnecessary harm to a patient.

Estimates show that in developed countries as many as one in 10 patients is harmed while receiving hospital care (Bates, 2010). The harm can be caused by a range of errors or adverse events. In developing countries, the probability of patients being harmed in hospitals is higher than it is in industrialized nations. The economic benefits of improving patient safety are compelling. Studies show that additional hospitalization, litigation costs, infections acquired in hospitals, lost income, disability and medical expenses have cost some countries between US$ 6 billion and US$ 29 billion per year. Industries with a perceived higher risk, such as aviation and nuclear power plants, have a much better safety record than health care (World Alliance for Patient Safety).

2.2 Medication incidents

The term medication incident is used by PSOs when an adverse event is linked to the use of a medicine. A medication incident can be described as any undesirable experience that a patient has while taking a medicine, but which may not be related to the medicine.

Medication error (ME) is a commonly used term which has a similar meaning. The definition used in this document is "a failure in the treatment process that leads to, or has the potential to lead to, harm to the patient" (Ferner & Aronson, 2006).

It is acknowledged that children are at the greatest risk for MEs. A systematic review of published research on MEs in children found, as with studies on adults, that the definition of ME was non-uniform across the studies (Miller et al., 2007).

The first studies on adverse drug events (ADEs) date back to 1984 with the Harvard Medical Practice Study. Of the 30 195 patients included, 19.4% experienced an ADE and 17.7% of these ADEs were considered preventable. Safe medication practice is concerned with minimizing preventable errors

that harm or have the potential to harm patients when medicines are prescribed, supplied, dispensed, prepared, and administered clinically.

In the United States a list of high alert medicines and therapeutic groups of medicines has been developed based on error reports submitted to the Institute for Safe Medication Practices (ISMP)'s National Medication Errors Reporting Program, reports of harmful errors in the literature, and input from practitioners and safety experts (Institute for Safe Medicine Practices, 2012). These medicines pose a higher risk of causing significant harm to patients when they are used in error. The clinical consequences resulting from an error with these medicines are more likely to lead to fatal or serious harm. Additional safeguards should be included in practice to minimize errors with these medicines.

Box 1 (page 4) illustrates the concept of high alert therapeutic groups. The list will change over time with the emergence of new therapeutic principles and others falling out of clinical practice.

Box 2 (page 5) illustrates the concept of high alert medicines and is not exhaustive. The list will change over time with the emergence of new medicines and others falling out of clinical practice.

2.3 Examples of medication error incidents

2.3.1 Prescribing error

Inappropriate starting dose of morphine tablets: A 70-year-old male patient weighing 60 kg was prescribed slow-release oral morphine tablets, 60 mg twice a day, for arthritic pain. He had not been taking any opioid medicines. His previous analgesia medicine was oral tramadol tablets, 50 mg three times a day. After taking four doses of the oral morphine the patient was confused, hallucinating and drowsy. He was admitted to hospital where he remained for six days after receiving naloxone.

All doctors, both junior doctors and experienced senior doctors, commit prescribing errors; and the mean error rates can be as high as 8.9 per hundred medication orders (Dornan et al., 2009).

2.3.2 Dispensing error

Mis-selection of propranolol for prednisolone tablets: A 65-year-old female patient with a history of obstructive airways disease was seen by her general practitioner and prescribed an oral penicillin product and prednisolone, 40 mg daily for seven days. The community pharmacist misselected a 28-day patient pack of propranolol 40 mg tablets instead of prednisolone 5 mg tablets and labelled the pack of propranolol with a

Box 1. High alert therapeutic groups[a]

- Adrenergic agonists, intravenous (IV) (e.g. epinephrine, phenylephrine, norepinephrine)
- Adrenergic antagonists, IV (e.g. propranolol, metoprolol, labetalol)
- Anaesthetic agents, general, inhaled and IV (e.g. propofol, ketamine)
- Antiarrhythmics, IV (e.g. lidocaine, amiodarone)
- Antithrombotic agents, including:
  - anticoagulants (e.g. warfarin, low-molecular-weight heparin, IV unfractionated heparin)
  - factor Xa inhibitors (e.g. fondaparinux)
  - direct thrombin inhibitors (e.g. argatroban, bivalirudin, dabigatran etexilate, lepirudin)
  - thrombolytics (e.g. alteplase, reteplase, tenecteplase)
  - glycoprotein IIb/IIIa inhibitors (e.g. eptifibatide)
- Cardioplegic solutions
- Chemotherapeutic agents, parenteral and oral
- Dextrose, hypertonic, 20% or greater
- Dialysis solutions, peritoneal and haemodialysis
- Epidural or intrathecal medications
- Hypoglycaemics, oral
- Inotropic medications, IV (e.g. digoxin, milrinone)
- Insulin, subcutaneous and IV
- Liposomal forms of drugs (e.g. liposomal amphotericin B) and conventional counterparts (e.g. amphotericin B desoxycholate)
- Moderate sedation agents, IV (e.g. dexmedetomidine, midazolam)
- Moderate sedation agents, oral, for children (e.g. chloral hydrate)
- Narcotics/opioids IV, transdermal, oral (including liquid concentrates, immediate and sustained-
- release formulations)
- Neuromuscular blocking agents (e.g. succinylcholine, rocuronium, vecuronium)
- Parenteral nutrition preparations
- Radiocontrast agents, IV
- Sterile water for injection, inhalation, and irrigation (excluding pour bottles) in containers of 100 mL or more
- Sodium chloride for injection, hypertonic, greater than 0.9% concentration

[a] Institute for Safe Medicine Practices (2012).

Box 2. High alert medicines[a]

- Epoprostenol (Flolan), intravenous (IV)
- Magnesium sulfate injection
- Methotrexate, oral, non-oncologic use
- Opium tincture
- Oxytocin, IV
- Nitroprusside sodium for injection
- Potassium chloride for injection concentrate
- Potassium phosphates injection
- Promethazine, IV
- Vasopressin, IV or intraosseous

[a] Institute for Safe Medicine Practices (2012).

dispensing label with instructions to take eight tablets daily. The same manufacturer supplied both the prednisolone and propranolol tablet packs and the labelling and packaging of the two products were very similar in appearance. The patient took the first dose and soon afterwards had difficulty breathing, became hypotensive and lost consciousness. She was rushed to hospital where she subsequently died.

A systematic review of research on dispensing errors found the incidence of such errors in community pharmacies ranged between 0.01% and 3.32%; in hospital pharmacies the figures were 0.02–2.7% (James et al., 2009). It is useful to report not only "unprevented" dispensing errors but also those dispensing errors that were in fact prevented from occurring. The latter serve as useful learning experiences and can form the basis for approaches that can be taken to prevent dispensing errors. A useful systematic review of prevented and unprevented error rates in different countries, was conducted by James et al. (2009) and includes data from Australia, Brazil, Denmark, Spain and the UK.

2.3.3 Medicine preparation error

Two male patients receiving treatment for multiple myeloma were prescribed intravenous amphotericin 5 mg/kg body weight as part of their anti-infective regimen. Two formulations of amphotericin were available in the clinical area: amphotericin deoxycholate (Fungizone) and amphotericin as a lipid complex (Abelcet). The Fungizone formulation was prepared and then administered by clinical staff. The two patients

subsequently died of amphotericin overdose. The maximum daily dose for Fungizone is 1.5 mg/kg.

2.3.4 Administration error

A patient was admitted following a traffic accident. He had sustained bilateral lower limb fractures, but was recovering well. Cardiac arrest followed with symptoms consistent with a large pulmonary embolus. The patient was resuscitated long enough to enable him to be transferred to a critical care unit, but died shortly afterwards despite intensified treatment. On his drug chart, the prophylactic heparin injections were not signed as being administered on several occasions.

What constitutes a medicine administration error (MAE) varies from study to study making comparisons difficult. Some studies include time errors: for example, the medicine is given one hour earlier or later than it was prescribed for, while other studies ignore them. The focus of MAE research on the number of errors can be misleading and may overestimate the problem. Many researchers consider the severity of the errors which are important from the patient's perspective (Kelly & Wright, 2011).

2.3.5 Monitoring error

A 42-year-old male patient had an emergency admission to hospital with lithium toxicity. Unfortunately his blood lithium levels were out of date. The last level that had been recorded (5 months earlier) was within the therapeutic range; hence his oral lithium prescription was re-authorized. His two most recent outpatient appointments had been cancelled and his lithium levels were not being regularly monitored. At the time of reporting, the patient was being ventilated.

2.4 Root causes of medication errors

MEs include errors of omission as well as errors of commission. MEs, like other types of patient safety incidents, usually arise from human factors and poorly designed health-care products and systems rather than the individual performance of a single practitioner. This can be seen clearly if medication incident reports are collected together in an individual hospital or across a health-care system. Similar medication incidents occur involving different health-care staff. Disciplining one member of the health-care team involved in an ME does not prevent an identical error recurring. It is important to identify and address the root causes of errors to enable these risks to be minimized.

Ensuring safe medication practice requires an understanding of human factors (the reasons why humans make errors), and that health-care products and systems should be designed to minimize the risks of MEs harming patients.

Published research indicates that MEs occur frequently but that not all errors cause harm or have the potential to cause harm. It is important to understand what is meant by the terms ME, ADE and adverse drug reaction (ADR) when reviewing published literature (Morimoto et al., 2004).

2.5 Medication error reporting and learning systems

The most important knowledge in the field of patient safety is how to prevent harm to patients during treatment and care. The fundamental role of a patient safety reporting system is to enhance patient safety by learning from failures of the health-care system. Health-care errors are often provoked by weak systems and often have common root causes which can be generalized and corrected. Although each event is unique, there are likely to be similarities and patterns in sources of risk which may otherwise go unnoticed if incidents are not reported and analysed.

The *WHO draft guidelines for adverse event reporting and learning systems* were published by the World Alliance for Patient Safety in 2005 to help countries develop or advance reporting and learning systems in order to improve the safety of patient care.

Reporting is fundamental to detecting patient safety problems. However, on its own it can never give a complete picture of all sources of risk and patient harm. The guidelines also suggest other sources of patient safety information that can be used both by health services and nationally.

Figures from the United Kingdom, one of the countries that is active in implementing ME reporting and learning systems may illustrate the level and type of reporting performance that can be achieved. Between January 2005 and December 2010, 517 415 medication incident reports were received from England and Wales, constituting about 10% of all patient safety incidents. Of the medication incidents 75% came from acute general hospitals, while smaller numbers, 8.5%, came from primary care. Some 16% of the medication incidents reported actual patient harm and 0.9% of these incidents resulted in death or severe harm. The process steps involved in the largest number of error reports were

- medicine administration, 50%;
- prescribing, 18%;
- omitted and delayed medicine, 16%; and
- wrong dose, 15% (Cousins et al., 2012).

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3. Organizations involved in medication error prevention

Patient safety has been defined as "freedom from accidental injury in health care". Patient safety is a serious global public health issue and many countries are increasingly recognizing the importance of improving patient safety. Health authorities ought to put systems in place to collect, analyse and prevent MEs, be it at the local, national or international level. This section aims to present the different models committed to patient safety.

3.1 International level

3.1.1 World Health Organization

3.1.1.1 The pharmacovigilance programme

As a consequence of the thalidomide tragedy, World Health Organization (WHO) created a collaborative system for international collection of individual reports of suspected ADRs in 1968. The system is based on national pharmacovigilance centres (PVCs) collecting case reports, initially from health-care professionals, but later also from patients and marketing authorization holders, and submitting them to WHO. The network of national PVCs submitting individual case safety reports (ICSRs) to the WHO database, Vigibase, maintained by the Uppsala Monitoring Centre (UMC) in Sweden, has expanded from 10 participants originally to considerably more than 100.

One of the main objectives of establishing the global database was, and still is, to facilitate the identification of rare incidents of medicine-related problems in clinical practice that were not identified during the pre-marketing development phase of a medicine. Such early signals identified by national PVCs or UMC are shared between countries in the network. Initially the focus of this signal analysis process was on harm caused by the pharmacological properties of medicines or hypersensitivity or idiosyncratic reactions experienced by patients. Over time it became evident that many of the recorded injuries to patients were due to failure of health-care systems and/or failure of health-care professionals to ensure that applicable instructions or guidelines for use of medicines were being followed. Quite often patient harm, as recorded in adverse reaction databases, can be linked to e.g. overdose, inappropriate route of administration or use of contraindicated medicine combinations. It has become evident that the WHO ICSR database, VigiBase™, which held 7.5 mil-

lion case records in 2012, collected since it was set up in 1968, is also a rich source of information for the study of MEs.

Initially the WHO Adverse Reaction Terminology (WHO-ART) did not include specific terms that allowed reporters to indicate that a medicine-related reaction might be due to an error, but over time more such terms have been included in the terminology. Currently a considerable number of ICSRs submitted to VigiBase contain terms that indicate the adverse effect may be due to a ME; this also demonstrates that many national PVCs have become engaged in identifying MEs.

3.1.1.2 Patient safety

In 2002, the World Health Assembly (WHA) adopted a resolution on patient safety (Resolution WHA55-18; WHO, 2002) that significant enhancement of health system performance can be achieved in Member States by preventing adverse events in particular, and by improving patient safety and health-care quality in general. The Resolution recognized the need to promote patient safety as a fundamental principle of all health systems and urged Member States to pay the closest possible attention to the problem of patient safety, to establish and strengthen the science-based systems that are necessary for improving patient safety and the quality of health care, including the monitoring of medicines, medical equipment and technology.

An effective safety culture in health care will exhibit the following high-level attributes that health-care professionals strive to operationalize through the implementation of strong safety management systems:

- where all workers (including front-line staff, physicians and administrators) accept responsibility for the safety of themselves, their co-workers, patients and visitors;
- that prioritize safety above financial and operational goals;
- that encourage and reward the identification, communication, and resolution of safety issues;
- that provide for organizational learning from accidents; and
- that provide appropriate resources, structure, and accountability to maintain effective safety systems.

3.1.2 The World Alliance for Patient Safety

WHO's World Alliance for Patient Safety was launched in October 2004, to confirm and endorse the objectives of the WHA Resolution (Resolution WHA55-18; WHO, 2002). The rationale behind this initiative was mainly

to introduce a concrete health policy designed to prevent patient harm. The Alliance focuses on assessing and understanding problems caused by unsafe care by producing guidelines on reporting and learning for patient safety, the International Classification for Patient Safety (ICPS) and by enhancing research for patient safety guidance.

- First challenge: *clean care is safer care*
- Second challenge: *safe surgery saves lives*

The Alliance is also promoting innovation and encouraging commitment through initiatives such as "Patients for Patient Safety" as well as launching the Safety Prize and building skills for patient safety worldwide.

The Alliance has developed a range of patient safety education and training materials including "A multi-professional patient safety curriculum guide" with slides and workshop materials (WHO, 2011).

3.1.3 International Medication Safety Network

At the international level, studies have shown that collaboration is needed between all parties dedicated to medication safety and patient safety (Bencheikh & Benabdallah, 2009). In 2006, the International Medication Safety Network (IMSN) was founded with the following objectives:

- to avoid duplication of ME cases;
- to develop a common terminology; and
- to share and exchange cases of ME and prevention strategies so as to avoid making the same errors again.

The Network now includes members from more than 20 countries, independent agencies, scientific societies, government agencies, associations, PVCs and the ISMP. The IMSN also focuses on the prevention of MEs and contributes to safer health care by supporting dissemination and implementation of medication-related patient safety solutions. The Network is also supporting safe medication practice centres and effective collaboration between PVCs and safe medication practice centres by sharing data and knowledge to build up expertise. It serves WHO and national agencies as an expert stakeholder organization responding to patient safety initiatives.

The IMSN is hosted by The Institute of Safe Medication Practices, in Pennsylvania, USA. The network operates as a cooperative of safe medication practice centres that operate reporting and learning systems for ME incidents. The Network has an executive committee, a website (www.intmedsafe.net) and holds an international annual meeting.

IMSN issued a position statement on pharmacovigilance and medication in 2009 (International Medication Safety Network, 2009).

3.2 National level

3.2.1 Patient safety organizations

Patient safety organizations (PSOs) undertake medication safety activities. In the mid-nineteen-seventies the PVCs focused on collecting and detecting ADRs. It was at this time that PSOs were founded, at first to take charge of patient incidents occurring in hospitals, and later in all health-care communities. Many, but not all, countries have PSOs.

In the USA, many agencies are dedicated to safe medication practice. These include the ISMP (ISMP, 1975) as well as the Joint Commission and Joint Commission International for Patient Safety, also designated as a WHO Collaborating Centre for Patient Safety Solutions. The agency in the United Kingdom is the National Reporting and Learning Service (NRLS) (and previously the National Patient Safety Agency). In Australia there is the Commission on Safety and a Health Care Quality Council.

PSOs undertake a range of activities to promote safer practice. These activities may include the collection and analysis of ME reports, root cause analysis (RCA), development and promotion of prevention strategies and dissemination of information leading to improvement of patient safety and a decrease in MEs (*see also section 7.2*). Prevention strategies and tools for health-care professionals can include training materials, seminars and e-learning. PSOs collaborate to share knowledge, expertise and prevention strategies. Examples of activities and products of some PSOs are shown in Table 1.

3.2.2 National pharmacovigilance centres

According to the WHO definition, pharmacovigilance is the science and activities related to the detection, assessment, understanding and prevention of adverse effects or any other medication-related problem (WHO, 2002). Since the outset, PVCs have been concerned with minimizing the risks of adverse reactions. Over the past forty years, pharmacovigilance has had an increasing focus on detecting and preventing MEs. It is possible to detect MEs from within the ICSRs that are received by national PVCs.

In 2006, WHO, UMC and the Moroccan National Pharmacovigilance Centre initiated a joint pilot project that systematically addressed aspects of this extended function for a PVC; the project reviewed the collection and analysis of information on adverse events related to MEs. The pilot project demonstrated that while some PVCs regularly collected reports of adverse events that were

Table 1. Examples of activities and products of some PSOs

Institute of Safe Medication Practice (ISMP) (USA)	National Reporting and Learning Service (NRLS)/ National Patient Safety Agency (NPSA) England	Australia
Patient safety brochure	Patient safety toolkits and e-learning	Safety Patient safety recommendations and implementation resources
Posters	Seven steps to patient safety	Improvement National standardization, e.g. National Inpatient Medication chart
Teleconferences	Root cause analysis (RCA) report writing tools and templates	Program for RCA National standardization, e.g. National Inpatient Medication Chart
Video conferences	Design for Patient Safety: medication topics	E-learning programmes
Medication safety pocket guide		

due to MEs, there were other PVCs that "inadvertently" collected this information, as ADR reports (Alj et al., 2007; Benkirane et al., 2009; Benabdallah et al., 2011). The project also investigated the presence of other systems for collecting ME reports in selected countries, and whether there was any collaboration between these structures and the PVCs (see Table 2). The project led to the conclusion that it would be useful to develop a tool and a strategy to strengthen the capacity of PVCs to detect MEs from within ICSRs.

More recently the Monitoring Medicines project, with funds from the European Commission, provided the opportunity to build on the first results of

Table 2. PVCs and PSOs: models and collaborations

Available models	Percentage of respondents *n* = 21
Countries with PVC, but no PSO	28.5
Countries with PVC and PSO	71.4
Collaboration between PVC and PSO	28.5
No collaboration between PVC and PSO	23.8
PVC plays the role of PSO	19.0

Source: Benabdallah et al. (2011).

the pilot project. Based on the hypothesis that capturing comprehensive data (what, how and why) as a source of learning is the basis for identifying areas of change (Canadian Patient Safety Institute, 2006), the Monitoring Medicines project has focused on:

- developing useful tools, such as the P Method to detect preventable ADRs in national databases (see section 6.1.1);
- undertaking a retrospective analysis of ADRs in the pharmacovigilance databases of candidate PVCs, by applying the P method, to detect preventable ADRs;
- proposing improvements to existing ADR reporting forms to optimize ME detection;
- organizing training courses and seminars for health-care practitioners (HCPs) on the importance of reporting ADRs, and on the use of the P method to analyse ADRs.

The Monitoring Medicines project concluded that:

- Although primarily set up to collect and investigate ADR reports, the fields that are necessary for optimal capture of adverse events due to MEs either already exist in the PVCs' ADR reporting forms, or can be easily added to the forms.
- Seminars and training courses should be organized to improve reporting of ADRs and MEs by HCPs.
- Special skills are needed and should be made available at the PVC for assessing the causal relationship between the medicine and the adverse reaction, and for assessing the preventability of an adverse event.
- Effective communication between PVC staff and HCPs, patients and PSOs is of paramount importance for collective learning to prevent MEs and to promote patient safety.

3.2.3 Poison control centres

There are few mechanisms for collecting data on MEs that exist and/or are managed outside hospital settings. Poison control centres (PCCs) remain an underutilized source of information on ADRs and MEs, and could help to detect and understand MEs. A Canadian study showed that one third of the calls (1525) to one Canadian Poison Centre about unintentional exposures involved medications (Ackroyd-Stolarz et al., 2011). Of those, 470 calls reported unintentional therapeutic errors and 61 ADRs. MEs represented 10.6% of

drug poisoning cases reported to the Moroccan PCC. PCCs are better known to the public than PVCs, often operating around the clock, 7 days a week, and the staff are well trained, and may include physicians, pharmacists, nurses or other experts with training in toxicology, history taking and risk assessment.

PCCs have the advantage that they are contacted by telephone immediately after the event, and therefore, compared with PVCs, the information gathered by a PCC is more detailed and current, and often first-hand (reported by the patients themselves or by their families) (Volans et al., 2007).

Some PCCs carry out a systematic follow-up to learn of the outcome of the incident, and gather more information, if needed. When PCCs are staffed by physicians, they can provide immediate treatment advice. When the staff are not physicians (e.g. in Canada), they can have a consultation with a physician when it is needed (Ackroyd-Stolarz et al., 2011). It would be very useful to share data between PCCs and PVCs to optimize ME detection and to better understand the causes of MEs.

There are also many practical advantages of linking PVCs and PCCs. These include:

- sharing the same resources (administrative staff, communication material, databases, secretary, library, facilities, computer resources, personal competences, and laboratory support);
- sharing technical competencies in pharmacology and toxicology, causality assessment, regular updates on signals and alerts, epidemiology, statistics and communication.

3.3 Local level

3.3.1 Hospitals

Almost all hospitals have ME reporting systems. The most commonly used reporting methods are: incident report review, review of patient charts, direct observation, interventions by pharmacists and ADE trigger tools. For more detailed information, see section 6.2 (Detecting medication errors in practice).

3.3.2 Consumer and patient organizations

Patient and consumer organizations are dedicated to patient or consumer welfare. Almost all countries have consumer and patient organizations. They may be active at the local or national level, but can also play a role at the international level. They generally target one kind of disease and focus on all

aspects relating to it, leading to provision of help for patients in their daily life and improvement of their quality of life. Patients and consumers also need to be more involved in pharmacovigilance networks.

In recent years, the role of the patient in reporting ADRs has been increasing. Several studies (van Grootheest et al., 2004; Mclernon et al., 2010; Krska et al., 2011; Mayor, 2011; van Hunssel et al., 2010, 2011) have shown the importance of patient reports, the quality of patient reports of ADRs and MEs, and the growing interest shown by patients in their drug therapy. Involving patients in pharmacovigilance is important because:

- patients are better informed about their conditions and treatment; and
- patients or their relatives will be the first to notice any observable problems resulting from the medication.

"Patients for patient safety" (PFPS), a programme of the WHO World Alliance for Patient Safety, focuses on preventing MEs by educating patients about the concept of patient safety and by increasing patient awareness. This programme emphasizes the central role patients and consumers can play in efforts to improve the quality and safety of health care around the world. PFPS works with a global network of patients, consumers, caregivers and consumer organizations to support patient involvement in the patient safety programmes of WHO Patient Safety.

Local patient and consumer organizations are a valuable resource for collecting data on ADRs and MEs in the local environment. They also organize workshops for educating patients on:

- awareness of ADRs and MEs
- the importance of the culture of patient safety
- the importance of the culture of patient engagement to provide safer care
- strengthening patient awareness about the importance of reporting ADRs and MEs
- effective communication about drug safety.

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4. Terminology and definitions

PVCs worldwide have been working with harmonized terms and tools that are developed, managed and maintained through the coordinated efforts of WHO and the UMC. Pharmacovigilance focuses on medication safety, with patient safety as its ultimate goal. The terms and definitions in pharmacovigilance have thus been "medicine centred". On the other hand, in the field of patient safety, terminologies are applied in the context of improvement in the quality of health-care delivery systems. Medication safety is one aspect of patient safety which bridges the patient safety and pharmacovigilance activities.

Terms and definitions need to evolve continuously to cover a widening framework and scope of work. Because the scope of pharmacovigilance has broadened to deal with MEs, some new terms belonging to the "patient safety" aspect are now being used by PVCs; furthermore, some old terms in pharmacovigilance are being redefined to address its broadened scope. For example, according to its original definition, an ADR is "a response to a medicine which is noxious and unintended, and which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease or for the modification of a physiological function". But the widening scope of pharmacovigilance has led to a new definition being proposed for an ADR as "any noxious and unintended effect resulting not only from the authorized use of a medicinal product at normal doses, but also from medication errors and uses outside the terms of the marketing authorization, including the misuse and abuse of the medicinal product" (Yu, Nation & Dooley, 2005). This definition thus also includes MEs.

Medication safety is a broad and complex area within patient safety. Organizations (outside PVCs) that are involved in reporting MEs and/or are linked to networks such as IMSN (see section 3), use different terms and definitions in their work. In the past, such organizations worked separately from PVCs, with little communication or coordination. But since 2006, efforts have been made to bring the two together, thanks to the WHO pilot project on MEs and, more recently, the EC-funded Monitoring Medicines project (see section 3.2.3).

For a successful collaboration between the PVCs and other medication safety organizations, there needs to be a common "language", with harmonized

terms and definitions. Yu and colleagues (2005) summarize the problems arising from the multiplicity of terms, their definitions and functional meanings. A comparison of some terms and how they are interpreted and used by PVCs and other medication safety organizations is shown in Table 3.

Table 3. Some terms and how they are interpreted and used by pharmacovigilance centres (PVCs) and patient safety organizations (PSOs)[a]

Term	Meaning in PVC	Meaning in PSO	Comment
Patient safety incident	Currently not used	Event or circumstance which could have resulted, or did result, in unnecessary harm to a patient	PVCs could adopt this term
Medication incident	Currently not used	Any undesirable experience that has happened to the patient while taking a drug but which may or may not be related to the drug	PVCs could adopt this term
Potential patient safety incident	Currently not used	A patient safety incident without harm	Commonly referred to as "near miss" PVCs could adopt this term
Adverse event	Any untoward medical occurrence temporally associated with the use of a medicinal product, but not necessarily causally related	An injury related to medical management, in contrast to complications of disease	PSO meaning not restricted to medicines
Adverse drug event	Currently not used	Any injury resulting from medical interventions related to a drug	PVCs could adopt this term instead of "adverse event" (see section 4.1)
Potential adverse drug event	Currently not used	No harm occurred even if error occurred or was intercepted	Commonly referred to as "near miss"
Preventable adverse drug event	Currently not used	Injury that is the result of an error at any stage of the medication use process.	= medication error PSOs could replace this term with "medication error" (see below under "medication error")

Table 3. Continued

Non-preventable adverse drug event	Currently not used	Event that does not result from an error, but reflects the inherent risk of drugs and cannot be prevented given the current state of knowledge	= adverse drug reaction PSOs could replace this term with adverse drug reaction
Adverse drug reaction (ADR)	A response to a medicine which is noxious and unintended, and which occurs at doses normally used in humans for the prophylaxis, diagnosis, or therapy of disease or for the modification of a physiological function	Any noxious effect resulting from the use of the medicinal product at normal doses within optimal conditions of use (non-preventable events)	
Preventable ADR	Injury that is the result of an error at any stage of the medication use process	Currently not used	= medication error This term was defined using a Delphi method by PVC and PSO representatives. PSOs could consider adopting the term
Medication error	A failure in the treatment process that leads to, or has the potential to lead to, harm to the patient	A preventable adverse drug event	Meaning essentially the same PSOs could consider using this term instead of preventable adverse drug event (see above)

[a] These definitions reflect the current understanding of terms by representatives of PVCs and PSOs. The definitions are expected to evolve with their broader use and adaptation and should be revisited at an appropriate time in the future.

4.1 Harmonization of terminology and definitions

Understanding and exchange of information between PVCs and PSOs at the local, national and international levels would improve if terms and definitions could be harmonized. A first attempt to reach consensus started with a Delphi method, organized by the Moroccan PVC but the process needs to be strengthened and widened through the inclusion of other comments and suggestions. The group considered various terms including *adverse event, adverse drug event, adverse drug reaction, medication error, potential adverse drug event, preventable adverse drug event and preventable adverse drug reaction.*

The first recommendation of the process was for PVCs to adopt the use of the term adverse drug event instead of adverse event (see Table 3) when referring to a medication-related event.

In conclusion, a critical factor for establishing efficient and standardized reporting systems between pharmacovigilance and PSOs is undoubtedly a common terminology.

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5. Classification

Patient safety is the reduction of risk of unnecessary harm associated with health care to an acceptable minimum. A patient safety incident is an event or circumstance that could have resulted, or did result, in unnecessary harm to a patient. The use of the term "unnecessary" in this definition recognizes that errors, violations, patient abuse and deliberately unsafe acts occurring in health care are unnecessary incidents, whereas certain forms of harm, such as an incision for a laparotomy are necessary (Runciman et al., 2009).

MEs are a subset of patient safety incidents. The same classification and analysis systems used for other patient safety incidents should be used for ME reports. It is recommended that centres operating a system for reporting and learning from MEs should use the WHO International Classification for Patient Safety (ICPS) (World Alliance for Patient Safety Drafting Group, 2009; WHO/World Alliance for Patient Safety, 2009).

5.1 The conceptual framework for ICPS

The conceptual framework for the ICPS was designed to provide a much needed method of organizing patient safety data and information so that it can be aggregated and analysed to:

- compare patient safety data across disciplines, between organizations and across time and borders;
- examine the roles of system and human factors in patient safety;
- identify potential patient safety issues; and
- develop priorities and safety solutions (Donaldson, 2009).

5.2 ICPS drafting principles

The principles used for drafting the ICPS were as follows:

- The classification should be based upon concepts as opposed to terms or labels.
- The language used for the definitions of the concepts should be culturally and linguistically appropriate.

- The concepts should be organized into meaningful and useful categories.
- The categories should be applicable to the full spectrum of health-care settings in developing, transitional and developed countries.
- The classification should be complementary to the WHO Family of International Classifications (http://www.who.int/patientsafety/implementation/taxonomy/en/).
- The existing patient safety classifications should be used as the basis for developing the conceptual framework for international classifications.
- The conceptual framework should reflect a genuine convergence of international perceptions of the main issues related to patient safety.

5.3 The ICPS data structure

Categories of characteristics of patient safety incidents include origin, discovery, reporting of the incident and the personnel involved, as well as when and where the incident occurred (see Figure 1).

Patient factor categories include demographics and the reason for the health-care encounter. The most important categories in the ICPS are contributory factors. By having sufficient information about the circumstances of an incident, these categories can be documented, and the greater understanding gained enables targeted actions to minimize the risk of similar incidents in the future.

Contributory factor categories include those concerning the patient, staff, work, organization and external factors. Mitigating factors are immediate actions or circumstances which prevent or moderate the progression of an incident towards harming a patient (Thompson et al., 2009).

Ameliorating actions take place after the incident has already caused harm to the patient. An example would be the resuscitation of a patient who has suffered a cardiac arrest as a result of inadvertent injection of high-concentration potassium chloride or treatment of a post-operative wound infection with antibiotics (Thompson et al., 2009).

An overview of the ICPS data structure is provided in Figure 1 (WHO World Alliance for Patient Safety, 2009). Note that several description headings have been added to the figure that were not included in the version proposed in 2009 (WHO World Alliance for Patient Safety 2009): "organizational and service factors," "external factors", "work and environmental factors" and "staff and patient factors".

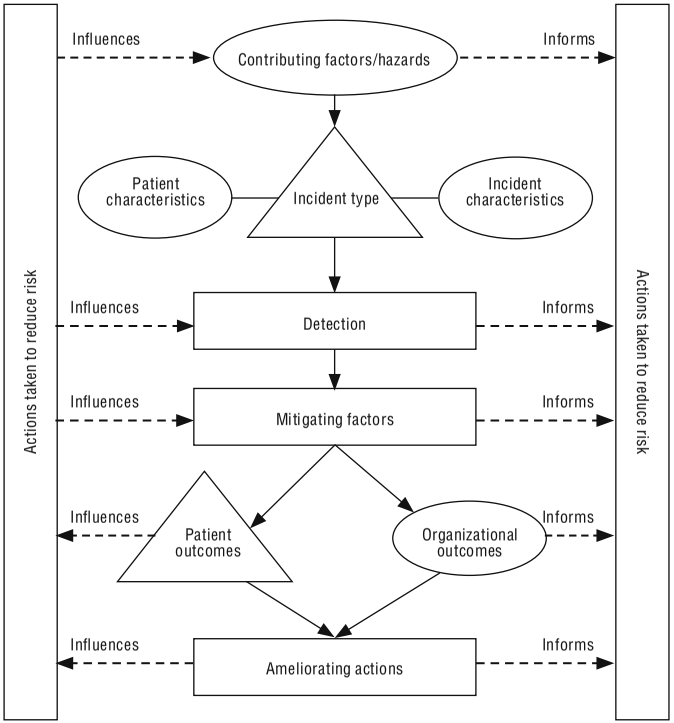
Figure 1. WHO International Classification of Patient Safety

Incident types
- Clinical administration
- Clinical process procedure
- Documentation
- Health-care associated infection
- Medication/intravenous fluids
- Blood/blood products
- Nutrition
- Oxygen/gas/vapour
- Medical device equipment
- Behaviour
- Patient accidents
- Infrastructure/building fixtures
- Resources/organizational management

Patient and incident characteristics
- Patient factors
- Staff factors
- Work/environmental factors
- Organizational/service factors
- External factors
- Other

Staff and patient factors
- Cognitive
- Performance
- Behaviour
- Communication
- Pathophysiological/disease-related
- Emotional
- Social factors

Work and environmental factors
- Physical environment/infrastructure
- Remote/long distance from service
- Environmental risk assessment/ safety evaluation
- Current code specifications/ regulation



Organizational outcomes
- Media management/public relations – Complaint management
- Claims/risk management – Stress debriefing/staff counselling
- Local notification and resolution – Reconciliation/mediation
- Culture change – Education and training

Organizational and service factors
- Protocols/policies/procedures/process
- Organizational decisions/culture
- Organization of teams
- Resources/workload

External factors
- Natural environment
- Products, technology and infrastructure
- Services, systems and policies

Detection
- Error recognition
- Change in patients status
- By machine/environmental change/alarm
- By count/audit/review
- Proactive risk assessment

Mitigating factors
- Directed to patient
- Directed to staff
- Directed to organization
- Directed to an agent
- Other

Patient outcome
- Type of harm
  International classification diseases
- Degree of harm
  Fatal
  Severe
  Moderate
  Mild
  None
- Social/economic impact
  International classification of functioning, disability and health

Ameliorating actions
- Patient-related
- Organization-related
- Actions to reduce risk

5.3.1 Medication incident subcategories of the ICPS

There are two useful subcategories in the ICPS for medication incidents.

5.3.1.1 The medication use process subcategory

The medication use process category identifies ordinal steps in the use of a medicine, i.e. prescribing, dispensing, administering and monitoring medicines. It is important to allocate only one of these categories for any incident. The step during which an error first occurred should be the one that is used, i.e. if a prescribing error occurred, then this category should be used, regardless of whether dispensing error and administration errors occurred later.

5.3.1.2 The medication problem subcategory

The medication problem category identifies medication incidents involving wrong patient, wrong medicine, wrong dose, strength or frequency, wrong formulation, wrong route, wrong quantity, wrong storage, omitted medicine or dose, or expired medicine, among others. Again, for ease of analysis *it is best to select the most descriptive single category* for each incident report.

5.4 Medicines and IV fluids involved

The ICPS does not provide a classification system for medicinal products or medical devices. National or regional classification systems for medicines and medical devices used for ADR and medical device vigilance programmes should be used for ME reporting programmes.

5.5 ICPS terms and pharmacovigilance classification systems

Virtually all PVCs use either the WHO Adverse Reaction Terminology (WHO-ART) or the Medical Dictionary for Drug Regulatory Activities (MedDRA) for coding and classification of clinical information recorded on ICSRs. Many, but not all, ICPS terms can be mapped to one of these terminologies. Many new terms have been included in both MedDRA and WHO-ART during the past few years with the specific aim of recording ME in a more consistent and complete fashion. However, additional work is required to better support ME reporting and analysis within pharmacovigilance systems.

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6. Identifying and reporting medication errors

It is well known that patients undergoing medical, pharmaceutical and paramedical interventions run a risk of MEs. Identifying MEs and finding their underlying causes are the first steps in establishing prevention strategies to avoid their recurrence. In certain situations, MEs are easily recognized by practitioners, but in other cases MEs are not clearly visible and are then reported as ADRs.

The objective of this section is to outline the different methods that could be used to identify an ME through ICSRs that are sent to a PVC. This section also aims to describe methods for collecting and reporting MEs. Reports of both ADRs and MEs could be collected from HCPs, the pharmaceutical and medical devices industry or patients and carers.

6.1 Identifying MEs through individual case safety reports

Over the years, PVCs have found that a small but important number of ICSRs that were reported as "ADRs" were possibly due to some aspect of ME and were thus "preventable" ADRs. According to the literature, the rate of preventable ADRs may vary from 18.7% to 80% (Yu, Nation & Dooley, 2005).

PVCs should develop their tools and their skills to identify MEs from ADR reports and to investigate their preventability. Currently, two aspects of pharmacovigilance could be enhanced to address these objectives: the reporting form for ICSRs and a tool for assessing the preventability of ADRs.

6.1.1 The yellow card and other individual case safety reporting forms

The yellow card ADR reporting scheme was launched in the United Kingdom in 1964 to stimulate ADR reporting and to improve communication between health-care professionals regarding health products.

The information contained in the yellow card and in other forms of ICSRs is of great value for PVCs in establishing a causal relationship between the observed adverse effect and the medicine. At a minimum, an ICSR should contain information on the following (Uppsala Monitoring Centre, 2012):

- the patient
- adverse event
- suspected drug(s)
- all other drugs used (including self-medication)
- risk factors
- name and address of reporter.

Over the years, reporting forms have been redesigned as the information required has changed.

There are many adaptations of the original yellow card. In some PVCs, there are particular adaptations to capture information on specific types of health products (e.g. herbals or medical devices) or targeted for public health programmes (e.g. tuberculosis, malaria and AIDS). The reporting forms allow PVCs to operate and provide continuous safety monitoring throughout the lifespan of a medicinal product. Initially, there was only a paper version, but with the advent of email and the Internet, electronic and web-based versions of reporting forms are now also available.

Recently, the scope of pharmacovigilance has widened in some countries to include identification of MEs. In view of this development, some centres may consider reviewing the forms they use for ICSRs. The forms for ICSRs should be structured to help PVCs capture more information on MEs. The form should combine relevance and simplicity, for a user-friendly design.

A working group, convened under the aegis of the Monitoring Medicines project, has reviewed the existing elements in common ICSR reporting forms and examined their value in detecting and assessing MEs. The group considered that the following elements are important for the identification of MEs from ICSRs and for the assessment of preventability of MEs (Figure 2, page 30):

- Patient weight, to detect dose errors: this is particularly important for children, for whom the dose prescribed is calculated according to their weight, and also for adults when the dose for the prescribed drug is weight-dependent.
- "Relevant medical history", this should include: current medical condition, co-morbidities and previous history of allergy, to help understand whether underlying pathology and known history of allergy were considered when prescribing.
- Strength of the formulation, to detect prescribing errors.

Figure 2. A model ICSR reporting form with important data fields to support ME detection

National Pharmacovigilance Centre

REPORTING ADVERSE EVENTS RELATED TO DRUGS AND OTHER HEALTH PRODUCTS

Patient

Name:
Age:
Sex: M ☐ F ☐ unknown ☐
Weight (kg):
If pregnant, gestation term:
Locality/city:
Phone number:

Relevant medical history
Current medical condition:
Comorbidities:
Previous history of allergy: yes ☐ no ☐ unknown ☐
If yes, please specify to which drug:

Adverse events(s)

Clinical and paraclinical description of adverse event:

Date of start of reaction: ☐☐/☐☐/☐☐☐☐ Date of end of reaction: ☐☐/☐☐/☐☐☐☐
Occurrence delay: hours ☐☐ days ☐☐ months ☐☐
Relevant laboratory test:
Differential diagnosis eliminated:
Action taken: drug withdrawn ☐ dose reduced ☐ treatment of reaction (please specify): .....
Other: .....
Seriousness: hospitalization ☐ prolonged hospitalization ☐
Outcome: favourable ☐ sequelae ☐ not recovered ☐ death ☐ unknown ☐

Drugs and other health products administered by patient

Name and form	Suspected/ concomitant drug	Dosage and route of administration	Batch number	Date therapy started	Date therapy ended	Indication	Status of dispensing and use(*)	Action taken (**)

Please specify if it is:
(*) medical prescription 1; self-medication 2; medication error 3; defective product 4; drug interaction 5.
(**) drug withdrawn a; dose reduced b; dose increased c; dose not changed d; unknown e.
If vaccine: Number of administration:
Setting of administration: public sector ☐ private sector ☐ vaccination drive ☐
If herbal medicine: Quantity:
Part used: Preparation: infusion ☐ decoction ☐ soaking ☐ other ☐
Rechallenge with drug or health product: yes ☐ no ☐ which one :
Recurrence of adverse event: yes ☐ no ☐ please describe:

Reporter

Name: ..... **phone no.:** ..... **email:** .....
Postal address: .....
physician ☐ specialist dentist ☐ pharmacist ☐ nurse ☐ other health-care professional:
Workplace: teaching hospital ☐ public sector ☐ private sector ☐
City: .....
Receive more information about this reporting? yes ☐ no ☐

Signature

To be transmitted by post, phone, fax or email

- Legal status of the medication (such as, over-the-counter, prescription only, specialist use) and its approved use, to help understand whether the drug responsible for the ME is prescribed by a physician, taken on the advice of a pharmacist, or a result of self-medication, and to detect problems of misuse.

The form should include:

- the question "Was this a medication error?" ME is already a reportable term, in the WHO-ART. To overtly include a question on ME in the reporting form will provide an opportunity to build the culture of reporting MEs as a standard practice;
- information on suspected and concomitant drugs: to understand the relevance of all drugs taken by the patient and their interactions;
- the "case narrative", which is a source of considerable information about the circumstances in which ADRs/MEs occur;
- results from relevant laboratory tests to allow detection of drug monitoring errors.

6.1.2 The P method

Some of the ADRs reported to the PVC are in fact due to MEs. It has been estimated that 10–80% of all ADRs may be preventable (Tudoux, 2004). Not all MEs will lead to patient harm. Preventable ADRs represent MEs that led to actual harm to the patient. It is therefore important to support PVC staff with a good tool and appropriate training to help them to identify preventable ADRs, as a first step to identifying the underlying MEs.

Several methods are available for evaluating the preventability of ADRs, but there is no gold standard in this field. A systematic review by Ferner and Aronson (2006) pointed out that the different approaches so far developed to assess ADR preventability were not satisfactory. These approaches rely either on the judgement of the investigators, which is not easily reproducible, or the use of predefined criteria that cannot always be applied to any individual case. Hence, the authors proposed an approach based on the analysis of the ADR mechanisms.

In the light of these approaches, and under the aegis of the Monitoring Medicines project, a new method has been developed which relies on preventability criteria and is therefore named the "P method". The P method is used to systematically detect MEs in ICSRs sent to PVCs. The method can be applied to any reported adverse event once a reasonable link between the event and the suspected drug has been validated by causality assessment. It is also important to emphasize that the intended purpose of the P method is not to classify MEs

or to perform RCA. The reference documents that should be used when assessing the case are: the summary of product characteristics (SmPC) and the international or national recommendations on the use of the medicine.

The P method allows us to explore the whole medication use process from prescription to drug use monitoring, aiming to identify preventable risk factors that increase the likelihood of an ADR. The P method is based on the identification of any risk factor that increases the likelihood of an ADR occurring.

These risk factors constitute the twenty criteria used to assess preventability of ADRs. The method explores risk factors in relation to health-care professional practices (criterion 1 to criterion 16), patient behaviour (criteria 19 and 20) and drug quality (criteria 5, 6, 17 and 18) (Table 4).

The P method requires a "yes or no or not-applicable or unknown" response to each of the 20 criteria to be completed for each ADR (Table 4). Answering "yes" to any one of the criteria involved in the occurrence of the ADRs deems the event preventable. This implies that the cause of the ADR is known, which facilitates the identification of the critical criteria that are potentially involved in the ADR's occurrence. These critical criteria vary according to the ADRs' causes. For example if the ADR's cause is linked to dose, the critical criteria to be explored are criteria 1, 2, 3, 4, 9, 10, 12, 13 and criterion 16. If the ADR is time-related, the critical criteria are criteria 3, 4, 7 and 15. Criteria 9, 10 and 11 are the critical criteria for an ADR that is related to patient susceptibility. Patient behaviour and drug quality should be explored systematically; they could increase the likelihood of any ADR (criteria 5, 6, 17, 18, 19, 20).

A criterion is considered as "not applicable" when it is not critical (e.g. the prescription of two medicines with similar ingredients does not influence the occurrence of an allergy). More than one criterion could be detected. The outcome of preventability assessment will result in one of three possible scores: "preventable", "non-preventable", and "not assessable". The ADR is categorized as preventable if at least one critical criterion is identified. The ADR is deemed non-preventable if none of the critical criteria are identified in the ICSR. The case is categorized as "not assessable" if there are no data or insufficient data for assessment (e.g. an anaphylactic reaction due to penicillin is deemed "not assessable" if the patient's previous history of drug allergy is not documented), or the situation is controversial (e.g. a drug that does not have a paediatric indication but is commonly used in children).

The SmPC, updated international or national standard guidelines and similar reference documents should be used to assess the ADR's preventability.

Table 4. Criteria for assessment of the preventability of ADRs

Factors related to	Preventability criteria	Yes	No	UK	NA
Professional practice "Pr"	1. Incorrect dose?				
	2. Incorrect drug administration route?				
	3. Incorrect drug administration duration?				
	4. Incorrect drug dosage formulation administered?				
	5. Expired drug administered?				
	6. Incorrect storage of drug?				
	7. Drug administration error (timing, rate, frequency, technique, preparation, manipulation, mixing)?				
	8. Wrong indication?				
	9. Inappropriate prescription according to characteristics of the patient (age, sex, pregnancy, other)?				
	10. Inappropriate prescription for patient's clinical condition (renal failure, hepatic failure …), or underlying pathology?				
	11. Documented hypersensitivity to administered drug or drug class?				
	12. Labelled drug–drug interaction?				
	13. Therapeutic duplication? (prescription of 2 medicines or more with similar ingredient)				
	14. Necessary medication not given?				
	15. Withdrawal syndrome? (due to abrupt discontinuation of treatment)				
	16. Incorrect laboratory or clinical monitoring of medicine?				
Product/drug "Pd"	17. Poor quality drug administered?				
	18. Counterfeit drug administered?				
Patient "Pa"	19. Non-compliance?				
	20. Self-medication with non over-the-counter drug?				

UK: unknown; NA: Not applicable

Some investigators consider the P method too resource-intensive and time-consuming and prefer to use alternative methods for the assessment of the preventability of ADRs (Kunac & Tatley, 2011).

6.2 Detecting medication errors in practice

The detection of MEs represents an essential step towards making progress in patient safety by elaborating prevention strategies and improving medication use at each stage of the system. Different approaches have been set up in response to the difficulty of getting clinicians to voluntarily report MEs. Another big challenge has been to develop methods that can detect any failure in the medication-use system even if the ME does not reach the patient (potential ADE). Examining potential ADEs helps to identify both where the system is failing (the error) and where it is working (the interception).

The methods most commonly used are:

- incident report review
- patient chart review
- direct observation
- interventions by pharmacists
- ADE trigger tools.

These methods are complementary, and none of them is able to detect all the medication incidents that occur, given the considerable complexity of the medication-use system.

6.2.1 Incident reports

The most frequently used approach in the health-care system is incident reporting, which is based on voluntary reporting of incidents by HCPs, patients or parents of patients. Reporting can be done using a paper form, by email, fax, telephone or an interactive computer-based mechanism. It is easy to implement and generally inexpensive. However, under-reporting is a major drawback of this method, which relies on the awareness and willingness of the HCPs to report incidents.

6.2.2 Patient chart review

Patient chart review encompasses concurrent or retrospective medical record review including, but not limited to, medical records, discharge summaries, pharmacy databases and laboratory data. The review is conducted by trained HCPs. This method can be used to detect all types of incidents, although it is

more useful for detecting ADEs and potential ADEs, mainly those generated in the prescription and monitoring processes. The method is less effective in detecting errors in the dispensing and administration processes, unless they cause harm to the patient.

6.2.3 Direct observations

This method consists of observation of the administration of medicines at the patient's own bedside in order to detect any difference between what the patient receives and the medical prescription. This is the most reliable and effective method to detect and to quantify the administration errors and is also valuable for the detection of dispensing errors, but it is not useful to detect errors in the prescription and monitoring processes.

6.2.4 Interventions by pharmacist

Hospital pharmacists need to demonstrate their ability to monitor and improve the use of medicines and that they have a role in medical audit, working with clinicians identifying problems with medicines, setting standards and monitoring practice.

Reporting their interventions can help with the identification and measurement of medication risks and in tracking changes over time. This method is efficient for detecting MEs during the prescription process and also for intercepting errors before they affect the patient. In this sense, it can be used both for detecting MEs and potential ADEs.

Intervention reporting can also be used to measure the effectiveness of automation. For instance, the effectiveness of a computerized order-entry system can be evaluated by measuring changes in how often and what types of interventions pharmacists make, or in terms of error reduction.

This method is easy to set up, but it may pose a time management problem to pharmacists who have to make so many interventions each day that they may not have sufficient time to record them all.

6.2.5 Adverse drug event trigger tools

The trigger tool uses an efficient sampling technique to identify potential adverse events through an audit of medical records. Each tool includes a limited number of triggers that signal the most common types of adverse events or those that are most likely to cause serious harm. Triggers are included based on a literature review, expert opinion and testing for feasibility. When a trigger is found, the chart is reviewed to determine whether an adverse event has occurred. There are three types of triggers:

1. use of specific drug antidotes used to treat ADEs, for example, the use of vitamin K to treat over-anticoagulation with warfarin, or the prescription of flumazenil for over-sedation with benzodiazepines;
2. results from laboratory tests that may indicate an ADE; and
3. clinical events that may indicate an ADE.

6.2.6 Comparison of methods

6.2.6.1 Stage of medication use system

Each method has specific advantages for detecting errors in certain processes. For instance, chart review allows mainly for the detection of prescription errors, but not transcription or administration errors, while the observation methods are the most appropriate for detecting administration errors (see Table 5, page 37).

6.2.6.2 Potential and actual ME

Some methods only capture incidents that cause damage to the patients, e.g. methods using adverse event triggers, while others usually detect errors that do not cause damage, as in the case of the observation methods.

6.2.6.3 Estimation of ME rate

It has been shown that direct observation detected administration errors at a much higher rate and more accurately than either chart review or incident report review (Morimoto et al., 2004).

The ADE Prevention Study Group has highlighted that solicited reporting by health workers was inferior to chart review for identifying ADEs but was effective for identifying potential ADEs (Flynn et al., 2002).

Considering the lack of overlap and the ability of each method to identify different medication errors, the use of a combination of methodologies is strongly recommended.

All the methods mentioned above are useful to support health workers in their daily practice. However, findings collected at local levels (e.g. wards or hospitals) are not shared at the national or international levels. Ideally, MEs collected by PVCs and hospitals should be reported to PSOs to allow exchange of experiences concerning management and prevention of recurrent MEs and to avoid occurrence of known MEs.

6.3 Reporting medication errors

Systems for reporting MEs can operate where there is a high level of patient safety culture. Health workers report MEs observed or suspected in their daily

Table 5. Comparison of the methods to detect medication errors (MEs) in practice

Method	Advantages	Disadvantages	Efficacy/explored stage	Feasibility
Spontaneous reporting	* captures actual ME * promotes a culture of safety	* underreporting * no quantitative data * data incomplete and inaccurate	* reports and alerts * feedback and corrective actions	* easy to set up * inexpensive * necessity for a culture of notification
Direct observation	* accurate * captures actual and potential error	* time-consuming * training difficult	* good quality data about administration errors * does not explore prescription and monitoring stage	* nurse training * labour intensive
Chart review	* retroactive * available data * commonly used standardized criteria * captures more than incident reporting	* difficult * time-consuming * labour intensive * planning criteria/ indicators necessary	* gold standard to detect adverse events * fewer MEs detected * does not detect potential adverse drug events * less effective for detecting errors in the dispensing and administration processes	* depends on the training of the reviewers * depends on quality of documentation of medication incidents in the clinical history
Pharmacist intervention reporting system	* detects actual and potential MEs * improves prescription	* not all interventions are usually recorded * time-consuming * pharmacists do not always have access to patients or to clinical notes	* detects prescribing, transcribing and monitoring errors * less effective in detecting dispensing and administration errors	* time needed to make records
ADE trigger tools	* allows detection of actual ME * automatic detection	* limited detection according to the triggers used		* computerized documentation system needed * detection bias depending upon triggers used: only certain ADEs are detected

practice to the PSO using the ME reporting form available in their workplace. If there is no PSO in the country where the ME occurs, the report is sent to the PVC. In all cases, close collaboration between PSOs and PVCs should be put in place so that data can be shared.

The ME reporting form should be made available for HCPs, producers of pharmaceuticals and medical devices and patients. Some ME reporting forms exist as electronic versions either for downloading or for web-based data submission. ME reporting forms usually contain the following elements:

- identifiable reporter
- date of incident
- error description
- name of drug(s) involved.

An example of a medication error report form is shown in Figure 3.

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Figure 3. A model form for reporting medication errors to a patient safety organization

PATIENT INFORMATION

Patient identifier (confidential)	Age/date of birth	Sex ☐ Female ☐ Male ☐ Unknown	Address

INCIDENT

Date of incident: ☐☐|☐☐|☐☐☐☐
☐ Holiday ☐ Weekend

Time of error

Setting of error

☐ Public hospital ☐ Prescriber's office ☐ Unknown
☐ Teaching hospital ☐ Pharmacy
☐ Private hospital ☐ Patient's home
Please specify the ward: …… ☐ Other (please specify) ……

Description of medication error: Free text entry field (narrative description of the incident including relevant information such as patient's medical history, laboratory tests results, concomitant therapy, work environment)

PATIENT OUTCOME – ACTUAL

Tick the appropriate patient outcome
☐ Fatal
☐ Severe (permanent harm)
☐ Moderate harm (requiring active treatment)
☐ Mild harm (requiring monitoring)
☐ No harm

PATIENT OUTCOME – WHERE NO HARM

Tick the appropriate patient outcome
☐ Potentially fatal
☐ Potentially severe (permanent harm)
☐ Potentially moderate harm (requiring active treatment)
☐ Potentially mild harm (requiring monitoring)

PRODUCT INFORMATION

NAME AND FORM	STRENGTH	FREQUENCY AND ROUTE	DATES OF THERAPY		DIAGNOSIS
			START	END	

PERSONNEL INVOLVED

Staff or health care professional who made the error
☐ Physician ☐ Health professions student ☐ Pharmacist ☐ Patient/caregiver ☐ Dentist ☐ Nurse ☐ Unknown
☐ Other (please specify): .....

STAGE OF ME IN THE MEDICATION USE SYSTEM

☐ Prescribing ☐ Transcription ☐ Dispensing ☐ Administration ☐ Monitoring
☐ Other (specify): .....

TYPE OF ME

☐ Wrong patient ☐ Wrong medicine ☐ Contraindication including known allergy
☐ Wrong dose, strength or frequency ☐ Wrong quantity ☐ Wrong duration
☐ Wrong rate (too fast/too slow) ☐ Wrong dosage form ☐ Wrong formulation
☐ Wrong route of administration ☐ Wrong preparation method ☐ Expired medicine
☐ Wrong method of administration ☐ Wrong time of dose administration ☐ Dose omitted or delayed
☐ Poor quality or counterfeit medicine ☐ Monitoring error clinical or laboratory
☐ Other (please specify): .....

7. Analysing medication error incident reports

In order to learn from ME incident reports, review and analysis is required. Aggregate analysis of multiple incident reports is usually conducted to develop an ME signal. However, detailed analysis of an individual report is sometimes required, where there is an outcome of death or serious harm from a new risk and where timely action is required. Feedback to reporters and stakeholders requires both quantitative and qualitative analysis. Prioritizing risks that have caused harm or have the greatest potential to cause harm is an important part of the process as health-care professionals and organizations have a finite capacity to make changes to their medicine systems to improve patient safety each year. Root cause analysis helps identify system design improvements that can be targeted by effective ME prevention strategies and guidance.

7.1 Summarizing and prioritizing medication error reports (quantitative analysis)

ME reports can be summarized and prioritized for action using categories listed by the Institute for Safe Medication Practices (2006).

The most useful categories for initial analysis and prioritization are:

- patient outcome
- medication use process
- medication problem
- therapeutic group or individual medicine.

7.1.1 Analysis by patient outcome

MEs occur frequently in clinical practice, but only a small percentage of these errors cause (or have the potential to cause) serious harm. Analysing medication incidents by actual patient outcome is helpful to identify those risks that have caused serious harm and therefore require further analysis. The ICPS category is for actual patient outcome; this is important to note since reporters often classify incidents for potential outcome, and these classifications need to be adjusted for actual outcome. For an example of how more than 500 000 medication incidents reported over six years were analysed using patient outcomes see Table 6 (page 41).

Table 6. Medication incidents reported by patient outcome

Actual clinical outcome	Incidents	Percentage of medication incidents
Death	271	0.05
Severe	551	0.10
Moderate	17 421	3.31
Low	68 578	13.03
No harm	439 318	83.46
N/A	240	0.05
Total	**526 379**	**100.00**

Source: Cousins, Gerrett & Warner(2012). Reproduced with permission.

Having identified those risks that have caused serious harm, a more comprehensive understanding of the risk can be obtained by analysing similar incidents with less serious clinical outcomes. For an example of how all reported incidents involving medication loading doses were analysed to identify ME types see Tables 7 (page 42) and 8 (page 43).

7.1.2 Analysis by medication process

Analysing MEs by medication process is helpful to identify specific risks relating to prescribing, preparing, dispensing, administration and monitoring medicines. For an example of how more than 500 000 medication incidents reported over six years were analysed using medication process see Table 9 (page 43).

7.1.3 Analysis by medication problem

Using the ICPS classification of medication problems is a very helpful method of analysis that can help identify cross-cutting risks affecting two or more medication process stages, medicines and therapeutic groups associated with a medication risk. For an example of how more than 500 000 medication incidents reported over six years were analysed using medication incident category see Table 10 (page 44).

7.1.4 Analysis by therapeutic group or medicine

Using the medicine name or therapeutic group can help identify high-risk medicines associated with preventable harms in practice. An example of how 377 medication incidents with patient outcomes of death or severe harm reported over six years were analysed to identify high-risk medicines or therapeutic groups is provided in Table 11 (page 45).

Table 7. Analysing incidents involving errors with loading doses to gain further understanding of the error types that can occur

Error type following review	Degree of harm (checked and corrected by clinical review)					Total	
	Death	Severe	Moderate	Low harm	No harm	Total (n)	Total (%)
Incorrect loading dose prescribed or administered	1	1	46	112	313	**473**	**41**
Omitted and delayed administration of loading dose		2	30	71	182	**285**	**24**
Communication and documentation of loading dose and/ or subsequent maintenance dose			6	17	78	**101**	**9**
Maintenance dose prescribed/ administered at an incorrect time			5	15	72	**92**	**8**
Loading dose repeated in error			6	23	51	**80**	**7**
Loading dose continued for maintenance without dose change	1	1	5	6	39	**52**	**4**
Maintenance dose not prescribed/ administered after loading dose			1	6	21	**28**	**2**
Loading dose given but not required			2	6	20	**28**	**2**
Administration rate of maintenance Dose delivered as per loading dose			1	7	18	**26**	**2**
Total	**2**	**4**	**102**	**263**	**794**	**1165**	

Source: National Patient Safety Agency (2010a). Reproduced with permission.

Table 8. Analysing incidents involving medicine loading doses to gain further understanding of the range of medicines associated with this type of error

	Degree of harm (checked and corrected by clinical review)					Total
	Death	Severe	Moderate	Low harm	No harm	
Warfarin		2	13	33	97	**145**
Amiodarone			11	26	75	**112**
Digoxin			15	25	59	**99**
Phenytoin	2		13	14	34	**63**
Metronidazole			1	7	54	**62**
Caffeine			6	13	41	**60**
Aminophylline			6	18	35	**59**
Heparin			4	17	27	**48**
Other medications or unknown (62)						**209**
Total						**1165**

Source: National Patient Safety Agency (2010a). Reproduced with permission.

Table 9. Medication incidents by medication process

Medication process	Incidents	Percentage of medication incidents
Administration of medicines	263 228	50.01
Prescribing of medicines	97 097	18.45
Preparation/dispensing of medicines	87 057	16.54
Other	48 410	9.20
Monitoring/follow-up of medicine use	23 648	4.49
Advice	3 537	0.67
Supply or use of over-the-counter medicine	3 045	0.58
N/A	240	0.05
(blank)	117	0.02
Other/unspecified	48 410	9.20
Total	**526 379**	**100.00**

Source: Cousins, Gerrett & Warner, 2012. Reproduced with permission.

Table 10. Medication incidents by category of error reported

Category of error	Incidents	Percentage of medication incidents
Omitted and delayed medicine	82 028	15.58
Wrong dose or strength	80 170	15.23
Wrong medicine	48 834	9.28
Wrong frequency	44 165	8.39
Wrong quantity	28 764	5.46
Mismatching between patient and medicine	21 915	4.16
Wrong/transposed/omitted medicine label	13 755	2.61
Patient allergic to treatment	11 695	2.22
Wrong formulation	11 254	2.14
Wrong/omitted/passed expiry date	10 998	2.09
Wrong storage	10 447	1.98
Unknown	10 024	1.90
Wrong method of preparation/supply	9 840	1.87
Wrong route	7 934	1.51
Contraindication to the use of the medicine in relation to medicine or condition	7 632	1.45
Adverse drug reaction (when used as intended)	5 939	1.13
Wrong/omitted verbal patient directions	1 383	0.26
Wrong/omitted patient information leaflet	1 156	0.22
Blank	129	0.02
Other/not specified	118 317	22.48
Total	**526 379**	**100.00**

Source: Cousins, Gerrett & Warner, 2012. Reproduced with permission.

Table 11. Medicines/therapeutic groups identified in incident reports with clinical outcomes of death and severe harm

Medicine or therapeutic group	Death	Severe	Total	Percentage of medication incidents with fatal and severe harm outcome
Opioids	46	43	89	10.83
Antibiotics	10	38	48	5.84
Warfarin	15	30	45	5.6
Low-molecular-weight heparin	23	23	46	5.6
Insulin	9	37	46	5.6
Benzodiazepines	15	12	27	3.28
Nonsteroidal anti-inflammatory drugs (NSAIDs)	1	17	18	2.19
Total	**142**	**235**	**377**	**45.99**

Source: Cousins, Gerrett & Warner, 2012. Reproduced with permission.

7.2 Root cause analysis (qualitative analysis)

Reports of MEs that have caused (or have the potential to cause) serious harm should be analysed to understand their contributory factors and root causes. An understanding of human error and human factors is required to do this.

Contributory factors are those which affect the performance of individuals whose actions may have an effect on the delivery of safe and effective care to patients, and hence the likelihood of a patient safety incident occurring. Contributory factors may be considered either to influence the occurrence or the outcome of an incident, or to actually cause it. The removal of the influence may not always prevent incident recurrence but will generally improve the safety of the care system whereas removal of causal factors or "root causes" will be expected to prevent or significantly reduce the chances of recurrence.

"**Care delivery problems** are due to the direct provision of care. They arise in the process of care, usually actions or omissions by members of staff. They have two essential features a) care deviated beyond safe limits of practice b) the deviation had at least a potential direct or indirect eventual adverse outcome for the patient" (Vincent et al., 1999).

These problems are sometimes called active failures.

"**Service delivery problems** are failures identified during the analysis of the patient safety incident, which are associated with the way a service is delivered and the decisions, procedures and systems that are part of the whole process of service delivery. Service delivery problems are usually due to latent failures that arise from well intentioned but (with hindsight) wrong management decisions that go unrecognised" (Vincent et al., 1999).

7.2.1 Human error and human factors and systems

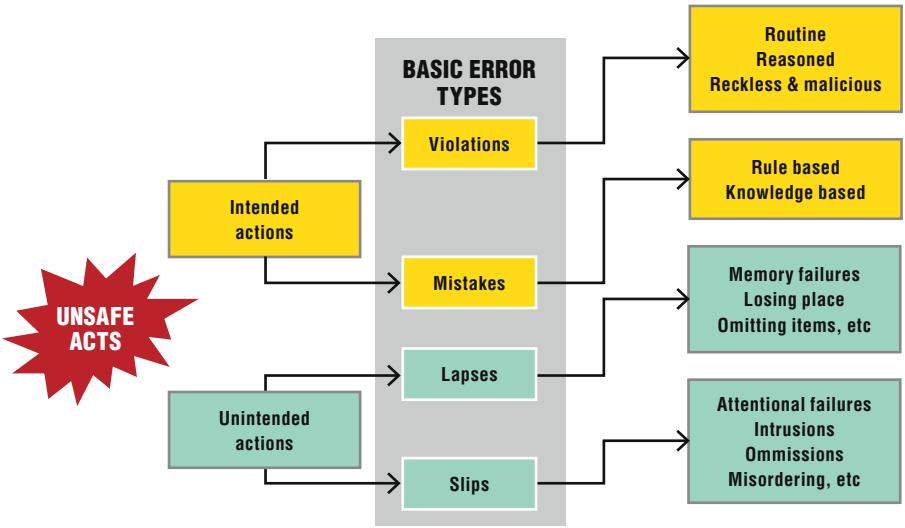
"All those occasions in which a planned sequence of mental or physical activities fails to achieve its intended outcome, and when these failures cannot be attributed to some change agency" (Reason 1990).

"Action by human operators can fail to achieve the goal in two different ways. The actions can go as planned, but the plan can be inadequate or the plan can be satisfactory but the performance can be deficient" (Hollagel, 1993).

Reason has identified various different types of human error (see Figure 4).

In addition to slips, lapses, mistakes and violations, Reason also describes an additional error type called latent error. These errors are due to systems or

Figure 4. Types of human error



Source: James Reason, Human Error, © Cambridge University Press, 1990, reproduced with permission.

routines that are formed in such a way that humans are predisposed to make these errors.

Having classified human error, what are the underlying causes of these errors? Human factors (also known as ergonomics) describe many underlying causes including; environmental, organizational and job factors as well as human and individual characteristics which influence behaviour at work. These elements influence the performance of people operating equipment or systems; they include behavioural, medical, operational, task-load, machine interface and work environment factors. Understanding human factors will help to address two myths of human performance in health care.

- *The perfection myth*. That is if we try hard enough we will not make any errors. Or that it is possible for humans to be 100% accurate, 100% of the time.
- *The punishment myth*. If we punish people when they make errors they will make fewer of them. This myth fails to take into account that other practitioners are likely to make the same error if there is no learning.

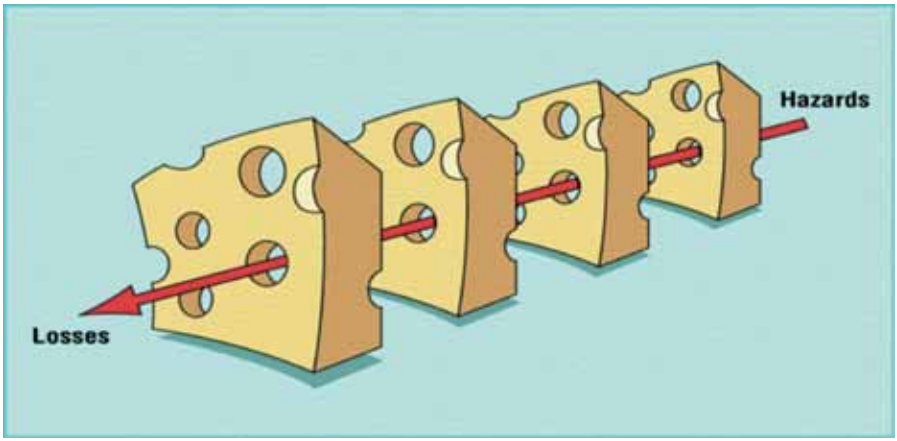
Like all myths, these two are untrue. Wide acceptance of these myths by the health-care community leads to systems where medication errors are likely to occur.

7.2.2 System barriers to prevent medication errors

Medicines use systems have various barriers to prevent harm to patients. Barriers include medicine regulations and standard operating procedures describing how medicine-related tasks should be undertaken, e.g. use of special documentation and information technology for prescribing, dispensing, administering and monitoring medicines, and independent checking by a second HCP, as well as restricted access to medicines, and defined professional training and competences, among others.

In 1990 Reason described barriers intended to minimize the risk of human errors as slices of Swiss cheese (see Figure 5, page 48). The barriers, or defences, intended to prevent errors from occurring do not provide complete protection from errors. Like slices of Swiss cheese the barriers have holes in them. Given a certain set of circumstances all the holes in these defences will line up and an ME occurs that seriously harms a patient (see Figure 5, page 48). When reviewing contributory factors to an ME, it is important to identify deficiencies in the design of barriers intended to prevent errors in medication use systems.

Figure 5. The "Swiss cheese" model to describe barriers intended to prevent errors



Source: James Reason, Human Error, © Cambridge University Press, 1990, reproduced with permission.

7.2.3 Identifying contributory factors to medication error incidents

It is important to consider all contributory factors to an ME. This will avoid the narrow focus on failings of individuals directly involved in the incident and enable a shift away from the culture of blame.

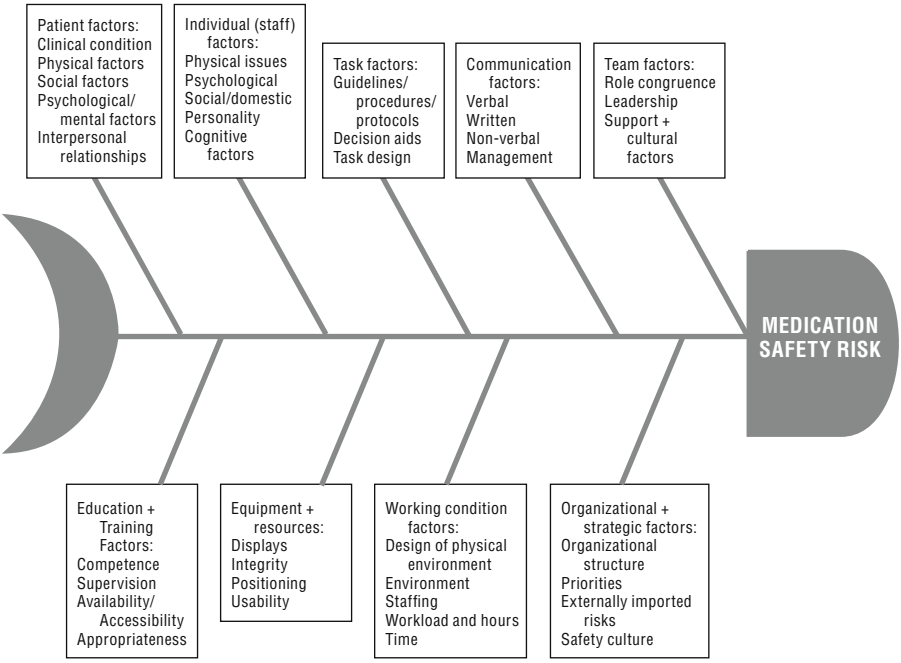
The WHO ICPS provides terms for contributory factors. These factors should be considered when analysing MEs. A fish diagram is often used as a tool to help classify all the possible contributory factors to an ME incident report (see Figure 6, page 49).

For each of the contributory factors a few examples are given below to illustrate how the classification system may be used.

a. Patient factors

- The patient had poor eyesight and could not read the medicine label to select the correct medicine or follow the dosage instructions.
- The patient had severe rheumatoid arthritis and could not easily open the medicine packaging and administer the medicine.
- The child was too young to swallow large tablets safely.
- The patient had a known allergy or contraindication to the medicine.

Figure 6. The fish diagram of contributory factors to a patient safety risk



Source: National Patient Safety Agency (2010). Reproduced with permission.

- The patient had renal failure and the dose of the medicine required reduction.

b. Staff factors

- A nurse had hearing difficulties and misheard a verbal instruction concerning a medicine to be administered intravenously.
- A pharmacist was going through a difficult divorce and was distracted at work and dispensed the wrong type of insulin to a patient.
- A doctor had a difficult personality and would not readily act on information provided by ward nursing staff and failed to prescribe an anticoagulant for a patient with a mechanical heart valve.

c. Work and environmental factors

- A dirty ward environment and poor aseptic technique led to contaminated injections being prepared and administered to patients leading to septicaemia.

- Poor storage facilities and separation of infusion fluids led to epidural bupivacaine infusion being mis-selected for a sodium chloride 0.9% infusion and being administered to a patient intravenously.
- Due to a computerized electronic prescribing system being offline and not available for use, medicine doses were omitted and delayed.
- Delays in receiving medicines from an off-site pharmacy led to medicine doses being omitted.

d. Organizational and service factors

- A doctor prepared and administered an overdose of insulin in an intravenous syringe rather than an insulin syringe. Medicine preparation and administration procedures only applied to nursing staff. There were no procedures for medical staff.
- A medical patient who was confined to bed for seven days did not have any medicines prescribed to prevent deep vein thrombosis (DVT), because DVT prevention policies were only available for surgical patients.
- Overdoses of amphotericin infusions were administered. There were inadequate dosing reference sources in clinical areas.

e. External factors

- A range of oral medicines from one manufacturer were supplied with look-alike labelling and packaging. These products were linked to a large number of dispensing and administration errors.
- A range of injectable medicines were provided from one manufacturer without any technical information in the pack and were prepared using an incompatible infusion fluid and volume and administered too quickly to the patient.
- A national chemotherapy protocol recommended an intravenous chemotherapy medicine to be administered on days 1 + 7. The protocol was misread and the chemotherapy was administered daily for seven days.

7.2.4 Identifying root causes

Having reviewed all possible contributory factors, one or more of these factors should be identified as a root cause. Actions intended to prevent recurrence of similar MEs should be directed to these root causes. Not all root causes will be amenable to solution development; however, action can and should be taken on most root causes.

The important thing is not to stop at intermediate causes. These are plausible and easily found. Working on remedying what are in fact intermediate

causes looks and feels productive. Intermediate cause solutions, more accurately called symptomatic solutions, may even work for a while. But failure to address the true root causes will inevitably lead to delay or circumvention, or may block, weaken, or even reverse the solutions, because intermediate causes are symptoms of deeper causes. It is important to strike at the root.

7.2.5 Example of a medication error report analysis form

An example design for an ME report analysis form is provided in Figure 7, page 53.

7.2.6 Full root cause analysis

There is a significant difference between the process for analysing MEs in reporting centres and that undertaken in the health-care organizations reporting the incident. A full RCA can only be undertaken in the organization where the incident took place. A full RCA should only be undertaken for fatal or serious incidents because of the time and expense involved. It is a structured process that should be undertaken by multidisciplinary teams under a team leader who has experience of RCA. This process will certainly take several days and in some cases weeks and even months. A great deal of information has to be collected, staff interviewed and patient notes reviewed. This cannot be done remotely in reporting centres. Incident reports are usually sent to reporting centres and this information can be supplemented by anonymized or summarized RCA reports when available. There is a great deal of knowledge to be obtained from full RCA reports and they are very useful resources for additional learning when they are shared by health-care provider organizations.

More details concerning full RCA can be found in other publications (National Patient Safety Agency, 2010b; Institute for Safe Medication Practices, 2006).

7.3 Summary

ME reports can be summarized and prioritized for action using categories in the ICPS. The most useful categories for initial quantitative analysis and prioritization are: patient outcome, medication use process, medication problem, therapeutic group or individual medicine.

Reports of MEs that have caused (or have the potential to cause) serious harm should be analysed to understand their contributory factors and root causes. An understanding of human error and human factors is required to do this.

Medicines use systems have various barriers to prevent harm to patients, but these barriers do not provide complete protection from errors. Given a certain set of circumstances all the holes in these defences line up (Figure 5) and an ME occurs that seriously harms a patient. When reviewing contributory factors to an ME, it is important to identify deficiencies in the design of barriers intended to prevent errors in medication use systems.

The WHO ICPS provide terms for contributory factors. These factors should be considered when analysing MEs. A fish diagram (Figure 6) is often used as a tool to help identify all the possible contributory factors to an ME incident report.

There is a significant difference between the process for analysing MEs in reporting centres and that undertaken in the health-care organization reporting the incident. A full RCA can only be undertaken in the organization where the incident took place, but as far as possible it should be done in collaboration with the reporting centre. There is a great deal of learning to be obtained from full RCA reports and these are invaluable resources for additional learning when they are shared by health-care provider organizations.

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Figure 7. Example of a medication error (ME) analysis form intended to be used with an ME report form

Medication error analysis form: Part 1

The purpose of reporting is for learning and systems improvement.

Date of incident: ..... Your incident identification number: .....

Patient details: Sex: M ☐ F ☐ Age: ..... (years) Ethnicity: .....

Patient factors (tick those factors that apply)

Cognitive factors	Perception/understanding	
	Knowledge based/problem solving	Failure to synthesize/act on available information
		Problems with causality
		Problems with complexity
	Illusory correlation	
	Halo effect	
Performance factors	Technical error in execution (physical-skill based)	Slips/lapse error
	Rule based	Misapplication of good rules
		Application of bad rules
	Selectivity	
	Bias	Biased reviewing
		Confirmed bias
Behaviour	Attention issues	Distraction/inattention
		Absent-mindedness/forgetfulness
		Overattention
		Out of sight, out of mind
	Fatigue/exhaustion	
	Overconfidence	
	Non-compliance	
	Routine violation	
	Risky behaviour	
	Reckless behaviour	
	Sabotage/criminal act	
Communication factors	Communication method	Paper based
		Electronic
		Verbal
	Language difficulties	
	Health literacy	
	With whom	With staff
		With patient
Disease related	International classification of diseases	
	International classification of primary care	
	Problems with substance abuse	
Emotional factors		
Social factors		

Medication error analysis form: Part 2

The purpose of reporting is for learning and systems improvement.

Date of incident: ..... Your incident identification number: .....

Patient details: Sex: M ☐ F ☐ Age: ..... (years) Ethnicity: .....

Staff factors (tick those factors that apply)

Cognitive factors	Perception/understanding	
	Knowledge based/problem solving	Failure to synthesize/act on available information
		Problems with causality
		Problems with complexity
	Illusory correlation	
	Halo effect	
Performance factors	Technical error in execution (physical-skill based)	Slips/lapse error
	Rule based	Misapplication of good rules
		Application of bad rules
	Selectivity	
	Bias	Biased reviewing
		Confirmed bias
Behaviour	Attention issues	Distraction/inattention
		Absent-mindedness/forgetfulness
		Overattention
		Out of sight, out of mind
	Fatigue/exhaustion	
	Overconfidence	
	Non-compliance	
	Routine violation	
	Risky behaviour	
	Reckless behaviour	
	Sabotage/criminal act	
Communication factors	Communication method	Paper based
		Electronic
		Verbal
	Language difficulties	
	Health literacy	
	With whom	With staff
		With patient
Disease related	International classification of diseases	
	International classification of primary care	
	Problems with substance abuse	
Emotional factors		
Social factors		

Medication error analysis form: Part 3

The purpose of reporting is for learning and systems improvement.

Date of incident: ..... Your incident identification number: .....

Patient details: Sex: M ☐ F ☐ Age: ..... (years) Ethnicity: .....

Work/environmental factors (tick those factors which apply)

Physical environmental or infrastructure
Remote and long distance from service
Environmental risk assessment or safety evaluation
Current code, specification or regulations

Organizational/service factors (tick those factors that apply)

Protocols, policies, procedures and processes
Organizational decision or culture
Organization of teams
Resources or workload

External factors (tick those factors that apply)

Natural environment	
Products, technology or infrastructure	Medicine name
	Medicine labelling
	Product information (e.g. summary of product characteristics; SPC)
	Patient information leaflet
	Administration devices
	Electronic infusion device
	Technical information
Services, systems or policies	

Other factors (please specify)

Medication error analysis form: Part 4

The purpose of reporting is for learning and systems improvement.

Date of incident: .....

Your incident identification number: .....

Patient details: Sex: M ☐ F ☐ Age: ..... (years)

Ethnicity: .....

Root cause or causes

Possible actions to address root cause(s)

Name

Job title

Signature

Date

8. Medication error prevention strategies

8.1 Country strategy for managing medication errors (MEs)

The first global prevention strategy to minimize harm from ME was adopted at the 55th World Health Assembly in 2002 (see section 3.1.1).

Each country should develop a strategy for ME reporting and learning to promote evidence-based policies.

This strategy should recognize a national organization dedicated to safe medication practice. This safety medication practice organization could be part of a patient safety organization or part of a PVC. It could be a centralized or decentralized organization, and should work in a harmonized way for patient safety.

8.1.1 Basic steps to develop a national organization dedicated to safe medication practice

The first step is to make contact with health authorities and with local, regional or national institutions such as PSOs and patient safety groups, PVCs, PCCs, patient and consumer organizations, and groups working on clinical medicine, pharmacology and toxicology, outlining the importance of the project, its purposes and the importance of close collaboration.

A patient incident reporting form may need to be designed and its use implemented. However, it is recommended to adapt and use any existing form (e.g. an ADR reporting form, see section 6.1). Adequate training should be provided to all relevant staff in patient safety methods and tools.

Material to promote awareness and inform HCPs, patients, and consumers should be produced, printed, and sent. This material should contain all relevant information about the aims and methods of the medication safety system.

Seminars and meetings for HCPs should be organized in hospitals, academic institutions and professional organizations on the importance of reporting MEs, of analysing the data collected, of the culture of patient safety, and on the magnitude of the problem.

Close collaboration between international medication safety organizations and PVCs should be fostered to enable them to share data and prevention strategies.

8.1.2 Practical methods to minimize harm from medication errors

All levels of the medicine delivery process would require strategies to prevent MEs and will normally include actions by one or more of the following:

- industry
- regulators
- health-care professionals
- patients and carers.

Guidance should include practical methods to make practice safer.

In general, national programmes are created to enhance the safety of patients. ME prevention strategies include, among others, three complementary actions: preventing MEs, making them visible, and mitigating their effects when they occur (sections 8.1.3–8.1.5).

8.1.3 Preventing medication errors

MEs can be prevented if the following aims are aspired to:

- increased ability to learn from mistakes through better reporting systems, skilful investigation of incidents, and responsible sharing of data;
- greater capacity to anticipate mistakes and probe systemic weaknesses that might lead to an adverse event;
- improving the prescribing process for medicines by ensuring that handwriting is legible, avoiding oral prescription, collaborating closely with the clinical pharmacist, using medication reconciliation, and applying the Situation, Background, Assessment, Recommendation (SBAR) technique. SBAR is an easy to remember mechanism to clearly communicate critical information between members of the team (Beckett & Kipnis, 2009).

8.1.4 Making them visible

Reduction of MEs by making them visible can be achieved by:

- making it easier to discover errors and take corrective action, with independent double-checks, alerts and warnings, poster campaigns and empowerment of patients and carers;
- use of forcing functions to eliminate or reduce the risk that a medicine can be prescribed, dispensed or administered in a potentially lethal manner.

8.1.5 Mitigating their effect when they occur

When MEs do occur their effects can be mitigated by:

- facilitating correct actions, use of antidotes and use of appropriate guidelines;
- use of forcing functions – safer design to make wrong actions more difficult, simplifying processes or products, and improving task or product information;
- sensitization, education, training and improving work competencies.

8.1.6 Raising awareness, education and training

A Multi-professional Patient Safety Curriculum Guide for patient safety education has been published. This comprehensive guide assists universities and schools in the fields of dentistry, medicine, midwifery, nursing and pharmacy to teach patient safety. It also supports the training of all health-care professionals on important patient safety concepts and practices (WHO, 2011). PVCs and/or the medication safety organization should organize and undertake sensitization education and training on patient safety for health-care providers, patients and carers and consumer and patient organizations (Box 3).

8.1.6.1 Training and educating patients, carers and consumer and patient organizations

Patients, carers and consumer and patient organizations should be educated:

- to be aware of the importance of reporting ADRs and MEs;

Box 3. Safety culture

An effective safety culture in health care will exhibit the following five high-level attributes that health-care professionals strive to achieve through the implementation of strong safety management systems:

- All workers (including front-line staff, physicians and administrators) accept responsibility for the safety of themselves, their co-workers, patients and visitors.
- Safety is prioritized above financial and operational goals.
- Identification, communication and resolution of safety issues are encouraged and rewarded.
- Provision is made for organizational learning from accidents.
- Provision is made for appropriate resources, structure and accountability to maintain effective safety systems.

- to raise patient awareness on the importance of patient safety, emphasizing that patients are at the heart of patient safety, and that they have to be involved in their own care;
- to understand the importance of undertaking a medication education programme which reduces the risk of MEs.

8.1.6.2 Training courses for HCPs on medication safety

Training courses for HCPs should emphasize:

- the importance of identifying and reporting ADRs and MEs;
- the role of PVCs in improving patient safety;
- the importance of the use of material that is provided, such as guidelines, flyers and CDs;
- the importance of the culture of patient safety.

8.1.6.3 Training courses to enhance and strengthen efficient communication

Communication should be enhanced and strengthened between the following groups:

- *Between HCPs (team)*. Encourage fluid communication using the SBAR technique, and by applying efficient procedures and guidelines.
- *Between HCPs and patients*. Raise the awareness of both parties that good communication is at the heart of patient safety and clinical quality, using the medication reconciliation process and the medication education programme.
- *Between HCPs and PVCs*. Highlight the importance of the role of PVCs in improving patient safety and raise awareness of HCPs of their essential role in improving patient safety by reporting ADRs and MEs.

ME prevention strategies should address the root causes and contributory factors identified from the ME analysis. They are intended to reduce the risk of repetition of MEs. It is usual for more than one method (or solution) to be used to reduce the risk as part of an overall strategy.

It is not sufficient just to highlight the ME risks to practitioners, health-care providers, industry, patients and carers. Patient safety guidance to minimize the risks should be included together with a description of the ME risk. Guidance should include practical methods to make practice safer.

There is a hierarchy of effectiveness for patient safety methods:

- Facilitate correct actions
  - — forcing functions (techniques that eliminate the possibility that the ME can happen)
  - — safer design to make wrong actions more difficult,
  - — process/product simplification,
  - — improving task or product information.
- Make it easier to discover errors and take corrective action
  - — independent second checks,
  - — alerts and warnings,
  - — empower patients and carers .
- Offer education and training, and improve work competencies.

Education, training and improved work competencies are the least effective of the patient safety methods and wherever possible other methods should be included in addition to education and training to reduce risks and make medication practice safer.

8.2 Prevention strategies for medicine regulators and industry

8.2.1 The design of labelling and packaging of medicine products

The design of labelling and packaging of a medicine product may contribute to look-alike mis-selection errors in practice, resulting in the wrong medicine, wrong dose, wrong route or wrong formulation of medicine being administered.

The following statements are quoted from a Council of Europe report published in 2006.

"*Current European medicines regulations concerning naming, packaging and labelling for pharmaceutical products provide inadequate safeguards for patients.*"

"*There is little recognition of the importance of the human factor principles in selection and design of drug names, labels and packages in order to minimise the potential for error and enhance medication safety.*"

"*The current design for labelling and packaging prioritises industry concerns, such as trade dress, instead of considering the context where the pharmaceutical product has to be used. It is not patient-centred, but, rather, relies on an assumption of perfect performance by healthcare professionals and by patients.*"

For MEs where serious harm has been reported involving the wrong medicine, dose, route or formulation having been dispensed or administered, the labelling and packaging of the outer pack and unit of use pack (e.g. ampoule, vial or 28-day calendar pack) should be reviewed to determine if the design looks similar to that of other products from the same supplier or another supplier.

The importance of safe design of labelling and packaging needs to be emphasized. The medicine regulatory process in many countries does not require the design of the labelling and packaging to be formally reviewed. Manufacturers are only required to submit the written information they intend to include on the labelling and packaging of their medicine product. Information such as the font, text size, the use of colour and design is not formally considered as part of the medicine regulation process. This is unfortunate and leads to medicine products that may be mis-selected for other products, and to medicines with confusing presentation of information being placed on the market. Several organizations have produced design for safety guidance for the pharmaceutical industry to assist it to produce labelling and packaging that will promote safer use in practice (Medicines and Healthcare Products Regulatory Agency, 2003; Council of Europe, 2006; National Patient Safety Agency, 2006, 2008a). See Figures 8–10.

Figure 8. Unsafe and safer designs of oral medicine packs (National Patient Safety Agency, 2006). Reproduced with permission.

Figure 9. Unsafe and safer designs of injection vial labels (National Patient Safety Agency, 2008). Reproduced with permission.

Figure 10. Unsafe and safer designs of injection ampoules boxes (National Patient Safety Agency, 2008). Reproduced with permission.

SUGGESTED ACTION

Where incidents have been reported where one of the contributory factors is unsafe design of the labelling and packaging of medicine products, the centre reviewing the medication error incidents should contact the manufacturer and the medicine regulator and recommend that the design of the medicine product be improved to reduce the risk of similar errors being repeated.

Health-care providers and practitioners should also be alerted to the risk. "Purchasing for safety" initiatives have been undertaken by some health-care providers. This involves risk assessment of labelling and packaging as an integral part of medicine procurement, where the labelling and packaging of a medicine are assessed to identify any risks to patient safety. Where significant risks are identified, alternative medicine products with safer designs are pro-

cured if they are available. If there are no alternatives for a particular medicine product then the manufacturer is informed and caution in use measures are introduced into practice and an alternative medicine product is purchased when it becomes available (NHS National Pharmaceutical Quality Assurance Committee, 2004; Alldred, 2006).

8.2.1.1 An example of a design of labelling and packaging of medicine products strategy

An example of look-alike, sound-alike design of medicine products that led to MEs being reported involves the two vaccine products Revaxis® and Repevax® (see Figure 11) (National Patient Safety Agency, 2004).

Figure 11. Look-alike medicine products: Repevax® and Revaxis®
Reproduced with permission.

The NPSA in the UK issued a patient safety guidance concerning Repevax® and Revaxis® vaccine products (Aventis, Pasteur, MSD) (NPSA, 2004). These two vaccines with sound-alike names and look-alike labelling and packaging were involved in numerous ME reports. In one report 93 schoolchildren were vaccinated with Repevax® instead of Revaxis®. The manufacturer subsequently improved the design of the labelling and packaging to reduce the risk of mis-selection.

8.2.2 Medicine names

Medicine names can look or sound like other medicine names, which leads to confusion and poses a threat to patient safety.

The Institute for Safe Medication Practices (ISMP) in the USA publishes a periodically updated list with more than 700 pairs of similar drug names that have caused mix-ups (Institute for Safe Medication Practices, 2005). Likewise, ISMP-Spain in collaboration with the General Spanish Council of Pharmacists campaigns to prevent MEs caused by similarity in drug names in Spain and has produced a list of several thousand registered pairs of drug names that could lead to confusion (ISMP-Spain).

There are no studies available reporting the incidence of errors that result from confusing the names of medicines. A report on the errors communicated to the United States Pharmacopeia (USP)-ISMP ME reporting system indicates that look-alike and sound-alike drug names account for at least 15% of these errors (United States Pharmacopeia, 2004).

MEs related to name confusion arise between:

- look- and/or sound-alike trademark names;
- look- and/or sound-alike trademark and non-proprietary names;
- look- and/or sound-alike trademark and non-proprietary names;
- formulations with the same trademark name that contain different drugs (Hoffman & Proulx, 2003; Aronson, 2004).

The risk of error between two medicine products with similar medicine names increases substantially if they also have the same dosage strength and the same route of administration or dosage form, as well as if they are administered according to the same dosing schedule. Other factors that may increase the potential for confusion include similar packaging and labelling, and being stored close together on pharmacy shelves, in dispensing cabinets, in the ward unit, or in the patient's home.

ME prevention strategies related to similar medicine names require actions during both the pre- and post-marketing phases of the lifecycle of a medicine product and involve regulators, industry, ME reporting programmes, HCPs and patients (Lambert et al., 2005).

Pre-marketing strategies include the design of new medicine names that might not be confused with existing names and the assessment of each new name to test its vulnerability to confusion with existing names. Thus the aim is to ensure that products with confusing drug names do not enter the marketplace.

Post-marketing strategies are designed to minimize errors with medications that are already in use and comprise the implementation of specific practices that prevent errors due to name confusion, and the reporting and dissemination of MEs that occur in clinical practice with products with similar names, with the aim of changing practices and thus reducing the risks of recurrence (Lambert et al., 2005). Innovative labelling can be used to emphasize the difference between products with look-alike and sound-alike names, for example, the use of tall man (capital) letters to highlight those letters that distinguish medicine names, such as chlorproPAMIDE and chlorproMAZINE. The use of colour to draw attention to these different letters can increase the likelihood of products with similar names being distinguished from one another (US Food and Drug Administration, 2009).

SUGGESTED ACTION

Where name confusion is identified, health-care providers should be alerted to the risk and recommended to take additional safety precautions in practice.
Health-care organizations should actively identify and manage the risks associated with look-alike and sound-alike medications.

8.2.2.1 An example of a medicine name error prevention strategy

The WHO Collaborating Centre for Patient Safety Solutions issued guidance concerning look-alike and sound-alike medication names in 2007.

The existence of confusing drug names is one of the most common causes of ME and is acknowledged to be of concern worldwide. With tens of thousands of drugs currently on the market, the potential for error due to confusing drug names is significant (Table 12, page 67).

8.2.3 Technical information on medicine product

In many countries there is a regulatory requirement for patient information leaflets for medicine products to be user-tested to ensure that patients can find and clearly understand information about their medicines. There is no such requirement for user-testing of the specification of product characteristics or other technical information intended for health professionals. Technical information can sometimes be very long and complex and this can make it difficult for HCPs to find the required information quickly. The information may also be written to meet regulatory requirements rather than to be easily understood and meet the needs of HCPs in busy practice environments. In some cases

Table 12. Examples of confused medicines name pairs

Country	Brand name (nonproprietary name)	Brand name (nonproprietary name)
Australia	*Avanza* (mirtazapine)	*Avandia* (rosiglitazone)
	Losec (omeprazole)	*Lasix* (furosemide)
Brazil	*Losec* (omeprazole)	*Lasix* (furosemide)
	Quelicin (succinilcolina)	Keflin (cefalotina)
Canada	Celebrex (celecoxib)	Cerebyx (fosphenytoin)
	Losec (omeprazole)	*Lasix* (furosemide)
France	fluoxetine	Fluvoxamine
	Reminyl (galantamine hydrobromide)	*Amarel* (glimepiride)
Ireland	*Losec* (omeprazole)	*Lasix* (furosemide)
	morphine	hydromorphone
Italy	*Diamox* (acetazolamide)	*Zimox* (amoxicillina triidrato)
	Flomax (morniflumato)	*Volmax* (salbutamolo solfato)
Japan	*Almarl* (arotinolol)	*Amaryl* (glimepiride)
	Taxotere (docetaxel)	*Taxol* (paclitaxel)
Spain	*Dianben* (metformin)	*Diovan* (valsartan)
	Ecazide (captopril/hydrochlorothiazide)	Eskazine (trifluoperazine)
Sweden	*Avastin* (bvacizumab)	*Avaxim* (hepatitis A vaccine)
	Lantus (insulin glargine)	*Lanvis* (toguanine)

Brand name shown in italics; nonproprietary names shown in normal type.
Source: WHO Collaborating Centre for Patient Safety Solutions, 2007.

technical information is not made available in the medicine pack. If technical information on how an injectable medicine should be safely prepared and administered is not included in the medicine pack, MEs may result, as practitioners may not prepare and administer the medicine as recommended by the manufacturer. It is not practical to expect medical and nursing staff to gain access to a pharmaceutical company's website to obtain this information each time a medicine has to be prepared. Technical information may also be confusing, for example expressing the dose of a medicine as both a salt and base.

SUGGESTED ACTION

Where incidents have been reported in which a contributory factor is the medicine product technical information, the centre reviewing the medication error incidents should contact the manufacturer and the medicine regulator and recommend changes to the technical information to reduce the risk of similar errors being repeated. The centre should also alert health-care providers to the risk and recommend additional safety precautions in practice.

8.2.3.1 An example of an error prevention strategy for medicine product technical information

The International Medication Safety Network reported recently that there had been reports from several European countries (France, Spain and the United Kingdom) that the label on eribulin (Halaven®), a new drug recently authorized, via a centralized process by the European Medication Agency, for the treatment of metastatic or locally advanced breast cancer may lead to errors in dosing.

Authorization for this medication was based on the results of a global study in a phase III trial in which a dose of 1.4 mg/m^2 of eribulin mesylate was used; that is, the dose was expressed in terms of a salt (Cortes et al., 2011). In the USA, this medication was registered in 2010 as a solution for injection. Strength was expressed on the label also in terms of eribulin mesylate. It was marketed in 2 mL vials which contained a 1 mg dose of eribulin mesylate.

In Europe, however, the dose for this medication is expressed in terms of eribulin base, following European guidelines, where there are several discrepancies regarding some national translations. The label for the same vial as marketed in the USA indicates: 0.44 mg/mL, 2 mL. Below that it states: "Each 2 mL vial contains 0.88 mg of eribulin (in the form of mesylate)". The way this label is written could lead one to believe that the quantity given is for eribulin mesylate (Otero, 2013).

In the view of the International Medication Safety Network (IMSN) there is a risk of dosing errors occurring when this medication is used because of confusion between "salt" and "base". If the professionals did not know about this difference in the form of expressing the dose, and used the dose from the pivotal trial, as is frequently done, they might think that the dose of 1.4 mg/m2 corresponded to the amount indicated on the label. Also, when the professionals who prepare the medication read the label on it, they could easily believe that the 0.88 mg was eribulin mesylate instead of eribulin base. As a result they would prepare a higher dose than they should.

The IMSN considers that the dosing indication for a medication should always be expressed in terms of base, and accordingly, the European guideline would be correct. It is unfortunate that, in this case, this guideline is not in harmony with the guidelines in all other countries, which would avoid a large number of problems. Nevertheless, the IMSN also considers that the label authorized for use in Europe should be modified to contain the following text:

"Each 2 mL vial contains 0.88 mg of eribulin (equivalent to 1 mg of eribulin mesylate)."

In this way, there would be no ambiguities when health-care professionals read the label.

8.2.4 Formulation and presentation of medicine products

Medicine formulation and presentation may be identified as contributory factors in ME reports. For example, where a medicine is presented as a concentrate requiring dilution before administration there is a risk that the undiluted medicine could be administered. Where a medicine is presented as two liquids that have to be mixed together before they are administered, there is a risk that only one half of the medicine formulation (which may be the diluent) is prepared and administered. When a normal dose of a medicine is only a small percentage of the unit of use container, there is a risk that too large a volume or dose is measured and administered in error. This is a particular problem with paediatric doses.

Formulation and presentation in ready-to-administer concentrations, strengths and presentations are the safest to use in practice. If for technical reasons there is no alternative to requiring dilution, small dose measurement and mixing in practice, then additional safeguards and precautions should be included in the product labelling, packaging and technical information by the manufacturer. Additional safeguards will also be needed in practice by the health-care provider.

SUGGESTED ACTION

Where incidents have been reported in which a contributory factor is the formulation and presentation of a medicine product, the centre reviewing the medication error incidents should contact the company and the medicine regulator and recommend changes to the formulation and presentation to reduce the risk of similar errors being repeated.

8.2.4.1 An example of a medicine product formulation and presentation error prevention strategy

Conscious sedation is a technique in which the use of a medicine produces a state of depression of the central nervous system enabling treatment to be carried out, but during which verbal contact with the patient is maintained throughout the period of sedation. The medicine and techniques used to provide conscious sedation should provide a margin of safety wide enough to render loss of consciousness unlikely (British Society of Gastroenterology, 2003).

There have been reports of some adult patients being overdosed with midazolam injection when it is used for conscious sedation. The presentation of high-strength midazolam as 5 mg/ml (2 ml and 10 ml ampoules) or 2 mg/ml (5 ml ampoule) exceeds the dose required for most patients. There is a risk of the entire contents of high-strength ampoules being administered to the patient when only a fraction of this dose is required (National Patient Safety Agency, 2008b).

In practice, doses often exceed that required, are not titrated to meet the patient's individual needs, do not take into account concurrent medication (e.g. opioids) and may involve high-risk groups, for example, the frail or the elderly. There is frequent recourse to injectable flumazenil (antagonist/reversing agent) for reversal of sedation in patients who have been over-sedated.

8.2.5 Risk management plans

Clinical trials of medicines do not necessarily represent "real life" experience of using a medicine because of the:

- small numbers of subjects participating in clinical trials;
- restricted population (age, sex, ethnicity);
- restricted co-morbidity, co-administration of medications and conditions of use;
- relatively short duration of exposure and follow-up;
- statistical problems associated with looking at multiple outcomes;
- medicine products used in the trial not having the final labelling, packaging, technical information and range of formulations used for the medicine that is placed on the market.

For these reasons, regulators now often require a risk management plan with risk minimization activities to be developed by the market authorization holder.

The European Union (EU) and the European Medicines Agency (2013) have defined a "risk management plan" as a set of pharmacovigilance activities and interventions designed to identify, characterize, prevent or minimize risks relating to medicinal products, including the assessment of the effectiveness of these interventions.

The Food and Drug Administration in the USA has defined these plans (known as "risk evaluation and mitigation strategies" and formally called RiskMaps) as a strategic safety programme designed to meet specific goals and objectives in minimizing known risks of a product while preserving its benefits.

An EU risk management plan is required for specific defined situations, and particularly when there is a significant change in a marketing authorization, such as:

- for a medicine used in children
- a new dosage form
- a new route of administration
- a significant change in indication or patient population.

To anticipate MEs before they occur, the first step is to learn from past experiences and the second step is to take measures to identify risks and minimize them. Failure mode and effects analysis (FMEA) can be used to examine the use of new medicines and the design of processes to determine points of potential failure and what their effect would be. FMEA is a prospective tool that quantifies risks involved in different stages of a process, and includes activities in the minimization plan before any error actually happens (Institute for Safe Medicine Practices, Canada, 2007).

The tool requires the production of a detailed flow diagram of the steps in the use of the medicines, e.g. prescribing, dispensing, preparation, administration and monitoring. The failure modes, their causes and potential clinical outcomes for each step in the medicine's use should be identified and scored by a multidisciplinary group. Each failure mode is scored for clinical severity (values ranging from low (1) to high (5)); frequency of occurrence (values ranging from low (1) to high (5)); and detectability (values ranging from always (1) to never (4)). The three scores are then multiplied together to give a criticality score which has a maximum of 100. The higher the criticality score, the more critical the failure mode.

severity x frequency x detectability = criticality score (maximum 100)

SUGGESTED ACTION

Medicine manufacturers should use failure modes and effects analysis (FMEA), involving a small multidisciplinary group, to identify and prioritize risks associated with the use of a medicine and describe risk minimization actions that can help reduce these risks.

Failure modes are then prioritized according to their criticality scores. Additional risk reduction methods are identified for each failure mode and the new criticality score is recalculated. The risk reduction measures should reduce the overall criticality score to within acceptable limits.

Safe medication practice centres should share information about ME reports and risks to medicine regulators reviewing risk management plans.

8.3 Prevention strategies for reducing incidents with medical devices

Medical devices are frequently required for preparing, measuring and administering medicines. There are risks associated with the use of these devices with medicines.

- The wrong device may be used. For example a filter needle may be used when preparing an intravenous suspension of a medicine and the filter will remove the suspended drug.
- The calibration on the medical device may not be appropriate for the dose measurement required.
- The connector on the device may enable wrong route connections.
- Errors can be made in setting up and programming electronic infusion devices used to control the rate of administration of a medicine infusion.

SUGGESTED ACTION

Where a contributory factor for an incident is the use of a medical device with a medicine, the centre reviewing the medication error incident should identify practice and design issues and contact users, health-care providers, medical device manufacturers, and regulators and recommend changes in the use and design of the device to reduce the future risk of similar errors occurring.

8.3.1 Examples of strategies for the prevention of medical devices medication error

8.3.1.1 Preventing wrong route errors with oral liquid medicines, enteral feeds and flushes

Incorrect intravenous administration of oral liquid medicines and enteral feeds and flushes has resulted in deaths and severe harm. RCA identified that use of Luer connectors and infusion spikes, designed for intravenous devices, in devices intended for oral and enteral administration is a root cause of wrong route of administration errors.

In some countries, there are oral/enteral syringes and administration devices in a range of sizes with tips that are not compatible with intravenous or other parenteral devices. These devices are clearly labelled as being intended for oral/enteral use and may have coloured plungers or barrels to further help identification.

Guidance on how to minimize the risk of wrong route errors with oral and enteral feeds and flushes has been produced and is summarized below (National Patient Safety Agency, 2007).

Design, supply and use of oral/enteral syringes

- Only use labelled oral/enteral syringes that cannot be connected to intravenous catheters or ports to measure and administer oral liquid medicines.
- Do not use intravenous syringes to measure and administer oral liquid medicines.
- Make sure stocks of oral/enteral syringes are available in all clinical areas where it may be necessary to measure and administer oral liquid medicines with a syringe.
- When patients or carers need to administer oral liquid medicines with a syringe, supply them with oral or enteral syringes.

Design, supply and use of enteral feeding systems

- Enteral feeding systems should not contain ports that can be connected to intravenous syringes or that have end connectors that can be connected to intravenous or other parenteral lines.
- Enteral feeding systems should be appropriately labelled to indicate the route of administration.
- Three-way taps and syringe tip adaptors should not be used in enteral feeding systems because connection design safeguards can be bypassed.

Organizational procedures, training and audit

- Medicines and enteral feeding policies and procedures should identify and manage the risk of administering oral liquid medicines by the wrong route.
- These procedures should be part of the organization's training and competency assessment programmes.
- Annual medicines management audits should include a review of the measurement and administration of oral liquid medicines to ensure compliance with local policies and procedures.

8.3.1.2 Preventing wrong dose errors arising from insulin use with intravenous syringes

There have been fatal cases where subcutaneous doses of insulin have been measured and administered in an intravenous syringe rather than in a dedicated insulin syringe (100 units/ml). The calibration marks on an intravenous syringe are not appropriate for measuring doses of insulin and 10-fold and 100-fold errors have been reported arising from this practice.

Example guidance to minimize the risk of wrong dose errors arising from insulin administration with intravenous syringes is summarized below (National Patient Safety Agency, 2010a).

- All regular and single insulin (bolus) doses are measured and administered using an insulin syringe or commercial insulin pen device. Intravenous syringes must never be used for insulin administration.
- The term "units" is used in all contexts. Abbreviations, such as "U" or "IU", are never used.
- All clinical areas and community staff treating patients with insulin have adequate supplies of insulin syringes and subcutaneous needles, which staff can obtain at all times.
- An insulin syringe must always be used to measure and prepare insulin for an intravenous infusion. Insulin infusions are administered in 50 ml intravenous syringes or larger infusion bags. Consideration should be given to the supply and use of ready-to-administer infusion products, e.g. prefilled syringes of fast-acting insulin – 50 units in 50 ml sodium chloride 0.9%.
- A training programme should be put in place for all health-care staff (including medical staff) expected to prescribe, prepare and administer insulin. An e-learning programme is available (www.diabetes.nhs.uk/safe_use_of_insulin).

- Policies and procedures for the preparation and administration of insulin and insulin infusions in clinical areas are reviewed to ensure compliance with the above.

8.4 Prevention strategies for individual practitioners

Analysis of serious ME reports frequently shows that HCPs assume that other practitioners or specialist services are solely responsible for the safe use of medicines and do not sufficiently recognize their own role and responsibilities, and that patient safety and the safe use of a medicine is everyone's responsibility.

Examples of unsafe assumptions made by individual practitioners concerning medicines use include the following:

- Prescribers fail to check the dose of an infrequently used medicine with a reference source, as they assume a pharmacist or nurse will check the dose before dispensing or administering the medicine.
- A family doctor prescribes a non-steroidal anti-inflammatory medicine for a patient on long-term anticoagulant therapy and assumes the anticoagulant clinic will adjust the dose of the anticoagulant at a future (unspecified) clinical appointment.
- A pharmacist or nurse fails to check the medicine allergy status of a medicine assuming the prescriber has checked this with the patient before prescribing.
- A pharmacist dispenses a supply of warfarin to a patient in the community and assumes that the patient is routinely attending an anticoagulant clinic, knows what dose to take, and is self-monitoring for adverse effects of the therapy.

Suggestions on how to promote the safer use of medicines by individual practitioners frequently recommend that practitioners confirm the intended use, contraindications and dose of a medicine. Where possible this should include independent checking with an information source, another practitioner and the patient or carer. Safer practice by individual practitioners can be supported by well-designed medication systems, standard operating procedures and education and training programmes (see section 8.5).

SUGGESTED ACTION

Where incidents have been reported in which a contributory factor is identified as actions of individual practitioners, the centre reviewing the medication error incidents should identify practice issues and contact health-care providers to recommend changes in practice to reduce the risk of similar errors being repeated.

8.4.1 Examples of strategies for the prevention of medication errors involving actions for health-care practitioners

8.4.1.1 Reducing dosing errors with opioid medicines

Fatal MEs have been reported concerning patients receiving unsafe doses of opioid medicines, where a dose or formulation was incorrect based on the patient's previous opioid dose. Every member of the team has a responsibility to check that the intended dose is safe for the individual patient. Knowledge of previous opioid dose is essential for the safe use of these products. There is a wide variety of opioid medicines, and supply shortages may result in products being used which are unfamiliar to practitioners.

Example guidance to minimize the risks of dosing errors with opioid medicines has been produced (National Patient Safety Agency, 2008c).

When opioid medicines are prescribed, dispensed or administered, in anything other than acute emergencies, the HCP concerned, or their clinical supervisor, should:

- Confirm any recent opioid dose, formulation, frequency of administration and any other analgesic medicines prescribed for the patient. This may be done, for example, through discussion with the patient or their representative (although not in the case of treatment for addiction), the prescriber or through medication records.
- Where a dose increase is intended, ensure that the calculated dose is safe for the patient (e.g. for oral morphine or oxycodone in adult patients, not normally more than 50% higher than the previous dose).
- Ensure that HCPs are familiar with the following characteristics of the medicine in question and the formulation: usual starting dose, frequency of administration, standard dosing increments, symptoms of overdose, and common side-effects.
- Health-care organizations should ensure that local medicines and prescribing policies, including standard operating procedures, are reviewed to reflect this guidance.

8.5 Prevention strategies for health-care provider organizations

Organizational and management decisions concerning the medicine use process may be identified as contributory factors in ME reports. That is, risks may arise from how an organization manages medicine prescription, procurement, storing, dispensing preparation, administration and clinical monitoring, and how expired and unused medicines are disposed of.

Risks in the medicine use process may arise from organizations' policies and procedures being absent, incomplete, unclear, too complex, impractical or unknown and ignored by health-care professionals. There may be inadequate induction and training of practitioners on medicine policies and procedures. In addition there may be poor arrangements for clinical governance of medicine-related services and little local learning from incident reporting and quality and safety audits. These types of risks are called latent errors.

It is often helpful to produce a flow diagram of the part of the medicine use process linked to a specific ME or group of errors to identify the risks and safeguards in place at each step of the process. This helps to determine if there are sufficient safeguards in place to effectively manage all the risks identified and whether these safeguards are included in organizational policies and procedures, and are followed in day to day practice. This approach is derived from the FMEA technique. The full technique can only be applied by a multidisciplinary group in health provider organizations, but reporting centres can use some of the same approaches to help understand organization issues and risks better and to develop guidance and tools intended to address these issues.

PSOs have knowledge and expertise to advise on strategies to address the various contributory factors and PVCs should work with PSOs to develop and communicate advice.

SUGGESTED ACTION

Where incidents have been reported in which a contributory factor is identified as organization issues, the centre reviewing the medication error incidents should develop guidance and tools intended to assist health-care provider organizations to better manage and reduce the future risk of similar errors occurring.

8.5.1 Examples of medication error prevention strategies for health-care provider organizations

8.5.1.1 Reducing harm from omitted and delayed medicine doses in hospital

Medicine doses are often omitted or delayed in hospital for a variety of reasons. While these events may not seem serious, for some critical medicines or conditions, such as patients with sepsis or those with pulmonary embolisms, delays or omissions can cause serious harm or death. Patients going into hospital with chronic conditions are particularly at risk. For example, patients with Parkinson's disease who do not receive their medicines on time may recover slowly or lose function, such as the ability to walk.

Example guidance for organizations to minimize the risks from omitted and delayed medicines suggests the following measures (National Patient Safety Agency, 2010b):

- Identify a list of critical medicines where timeliness of administration is crucial. This list should include anti-infectives, anticoagulants, insulin, resuscitation medicines and medicines for Parkinson's disease, and other medicines identified locally.
- Ensure that medicine management procedures include guidance on the importance of prescribing, supplying and administering critical medicines, timeliness issues and what to do when a medicine has been omitted or delayed.
- Review and, where necessary, make changes to systems for the supply of critical medicines within, and out-of-hours to minimize risks.
- Review incident reports regularly and carry out an annual audit of omitted and delayed critical medicines. Ensure that system improvements to reduce harm from omitted and delayed medicines are made. This information should be included in the organization's annual medication safety report.

8.6 Prevention strategies for patients and carers

In the past, health-care culture has not encouraged recognition, incident reporting and communication about errors in health-care practice. It has been relatively uncommon for health-care professionals to communicate about errors with other professionals and even more uncommon for health-care professionals to communicate with patients and carers. It may even have been considered unprofessional to acknowledge the risk of an error in health-care delivery when communicating with patients and carers. Today health-care culture is changing and, increasingly, health care is considered a partnership between health-care professionals and patients and their carers. Patients are

encouraged to take an active role in their own care, to learn and understand about their medical condition and its treatment, and to be more aware of the risks involved in their treatment. This should include the risks arising from serious MEs.

The majority of medicines are administered by patients and carers in the community. In hospitals, patients are usually awake and give their consent for administration of medicines. Patients and carers may then be considered the last safeguard or barrier to prevent a serious ME from occurring. In order to do this effectively they need to be supplied with information on the risk of MEs (without alarming them) and provided with guidance on what actions they can take to minimize these risks.

Patients and carers can be empowered by providing them with suitable information to enable them to confirm that they are receiving the right medicine, in the right dose, by the right route at the right time and that the use of the medicine is being monitored appropriately.

If there are important risks arising from mis-selection of other medicine products, or the wrong dose, wrong route or wrong time, or the medicine is not adequately monitored, patients can be alerted to these risks and provided with information on how they can identify and manage them and can be encouraged to take an active part in ensuring safe medication practice.

SUGGESTED ACTION

Where incidents have been reported in which contributory factors have been identified and addressed by the prevention strategies described earlier, and medication errors are still occurring, the centre reviewing the medication error incidents should consider working with patients and carers to determine whether issuing guidance and information for patients and carers would provide additional safeguards to better manage and reduce the risk of similar errors being repeated.

8.6.1 Examples of strategies for prevention of medication errors for patients and carers

8.6.1.1 Safer use of insulin

Insulin is frequently included in the list of the top 10 high-alert medicines worldwide. Insulin treatment has been identified as an important cause of hospital admissions, mainly as a consequence of severe hypoglycaemia. The costs of managing hypoglycaemia are significant.

MEs involving the use of the wrong insulin product, omitted or delayed insulin doses, and wrong insulin doses are frequently reported. Look-alike and sound-alike insulin products, inadequate systems for insulin administration in hospitals and poor communication regarding dosing are important root causes of these errors.

Patient safety can be improved by empowering patients to take a more active role to ensure the safe use of insulin. This can be achieved with a patient information booklet and a patient-held record, which documents the patient's current insulin products and enables a safety check for prescribing, dispensing and administration (see Figure 12, page 81). Such an "insulin passport" can complement existing systems for ensuring key information is accessed across healthcare sectors.

Example guidance on safer insulin therapy for patients and carers states the following (National Patient Safety Agency, 2011):

- Adult patients on insulin therapy should receive a patient information booklet and an insulin passport to help provide accurate identification of their current insulin products and provide essential information across health-care sectors.
- Health-care professionals and patients are informed on how the insulin passport and associated patient information can be used to improve safety.
- When insulin is prescribed, dispensed or administered, health-care professionals cross-reference available information to confirm the correct identity of insulin products.
- Systems are in place to enable hospital inpatients to self-administer insulin where feasible and safe.

8.7 Summary

ME prevention strategies should address the root causes and contributory factors identified from the ME analysis. It is not sufficient just to highlight the ME risks to practitioners, health-care providers, patients and carers. Patient safety guidance to minimize these risks should be included alongside a description of the ME risk. There is a hierarchy of effectiveness for patient safety methods. Guidance should include practical methods to make practice safer. It is usual for more than one method (or solution) to be used as part of an overall strategy to reduce the risk. Strategies can include the industry, regulators, practitioners, health-care provider organizations, patients and carers.

More details of ME prevention strategies are available on the websites listed in Box 4 (page 82).

Figure 12. The insulin passport (National Patient Safety Agency, 2011).
Reproduced with permission.

Insulin passport

Instructions

You should complete as much information for your passport as possible, then fold it to credit-card size. Keep it with you for emergencies and for reference when insulin products are prescribed or dispensed.

The area below is not for use as a daily diary record.

In the table below you should record information on your current insulin products. Provide as much detail so that all your insulin products are clearly identified. A healthcare professional can help with this. If someone else has added information, ask them to sign it. You must keep this information up to date. Keep the passport with you and when you need to contact a healthcare professional, show it to them. They can use the information to help identify exactly what insulin products you use.

Date started	Date stopped	Insulin brand name	Presentation (for example, vial, cartridge, or prefilled pen) and devices for insulin administration	Signatures

Source: National Patient Safety Agency (2011).

Box 4. Websites providing information on medication error preventions strategies

American Society for Health System Pharmacists. Patient Safety Resource Centre
www.ashp.org/menu/PracticePolicy/ResourceCenters/PatientSafety.aspx

Australian Commission on Safety and Quality in Health Care
www.safetyandquality.gov.au/

Danish society for Patient Safety
www.patientsikkerhed.dk

Food and Drug Administration (USA)
www.fda.gov/drugs/drugsafety/medicationerrors/default.htm

Institute for Safe Medication Practices, Brazil
www.ismp-brasil.org/

Institute for Safe Medication Practices, Canada
www.ismp-canada.org

Institute for Safe Medication Practices, Spain
www.ismp-espana.org

Institute for Safe Medication Practices, USA
www.ismp.org

International Medication safety Network
www.intmedsafe.net

National Patient Safety Agency, UK
http://www.nrls.npsa.nhs.uk/resources/patient-safety-topics/medication-safety/

Patient Safety Authority, Commonwealth of Pennsylvania (USA)
http://patientsafetyauthority.org/ADVISORIES/AdvisoryLibrary/Pages/Home.aspx

WHO Collaborating Centre for Patient Safety Solutions
www.ccforpatientsafety.org/Patient-Safety-Solutions

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Beckett CD, Kipnis G (2009). Collaborative communication: Integrating SBAR to improve quality/patient safety outcomes. J Healthc Qual.31:19–28.

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Council of Europe (2006). Creation of a better medication safety culture in Europe. Building up safe medication practices (http://www.coe.int/t/e/social_cohesion/soc-sp/medication%20safety%20culture%20report%20e.pdf, accessed 6 April 2014).

Cortés J, O´Shaughnessy J, Loesch D, Blum JL, Vahdat LT, Petrakova K, on behalf of the EMBRACE investigators (2011). Eribulin monotherapy versus treatment of physician´s choice in patients with metastatic breast cancer (EMBRACE): a phase 3 open-label randomised study. Lancet.377:914–23.

European Medicines Agency (2013). Guidance on format of the risk management plan (RMP) in the EU – in integrated format (http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2012/11/WC500134650.pdf, accessed 6 April 2014).

Food and Drug Administration (2009). Guidance for industry format and content for risk evaluation and mitigation strategies (REMS) (http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/ucm184128.pdf, accessed 6 April 2014).

Hoffman JM, Proulx SM (2003). Medication errors caused by confusion in drug names. Drug Saf.26:445–52.

Institute for Safe Medication Practices (2005). ISMP´s list of confused drug names (www.ismp.org/Tools/confuseddrugnames.pdf, accessed 6 April 2014).

Institute for Safe Medication Practices, Canada (2002). Neuromuscular blocking agents – time for action. Safety Bulletin. 12 (http://ismp-canada.org/download/safetyBulletins/ISMPCSB2002-12NMB.pdf, accessed 6 April 2014).

Institute for Safe Medication Practices, Canada (2007). Failure modes and effects analysis framework (http://www.ismp-canada.org/fmea.htm, accessed 6 April 2014).

ISMP-Spain general de Colegios Oficiales de Farmacéuticos e Instituto para el Uso Seguro de los Medicamentos (ISMP-Spain). Campaña de prevención de errores de medicación causados por similitud en los nombres de los medicamentos [Campaign to prevent medication errors caused by similarity of drug names] (http://www.usal.es/ismp, accessed 6 April 2014).

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National Patient Safety Agency (2004). Patient safety notice. Ensuring safer practice with Repevax and Revaxis vaccines (http://www.nrls.npsa.nhs.uk/resources/?EntryId45=59795, accessed 6 April 2014).

National Patient Safety Agency (2006). Design for patient safety. A guide to the graphic design of medication packaging 2nd ed. (http://www.nrls.npsa.nhs.uk/resources/collections/design-for-patient-safety/?entryid45=63053, accessed 6 April 2014).

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National Patient Safety Agency (2008a). Design for patient safety. Labelling and packaging guidelines for injectable medicines (http://www.nrls.npsa.nhs.uk/resources/?entryid45=59831, accessed 6 April 2014).

National Patient Safety Agency (2008b). Rapid response report. Reducing the risk of overdose with midazolam in adults (http://www.nrls.npsa.nhs.uk/resources/patient-safety-topics/medication-safety/?entryid45=59896&p=2, accessed 6 April 2014).

National Patient Safety Agency (2008c). Rapid response report. Reducing dosing errors with opioid medicines (http://www.nrls.npsa.nhs.uk/resources/patient-safety-topics/medication-safety/?entryid45=59888&p=2, accessed 6 April 2014).

National Patient Safety Agency (2010a). Rapid response report. Safer administration of insulin (http://www.nrls.npsa.nhs.uk/resources/patient-safety-topics/medication-safety/?entryid45=74287&p=1, accessed 6 April 2014).

National Patient Safety Agency (2010b). Rapid response report. Safer ambulatory syringe drivers (http://www.nrls.npsa.nhs.uk/resources/patient-safety-topics/medication-safety/?entryid45=92908&p=1, accessed date Month year).

National Patient Safety Agency (2010). Rapid response report. Reducing harm from omitted and delayed medicines in hospitals (http://www.nrls.npsa.nhs.uk/resources/patient-safety-topics/medication-safety/?entryid45=66720&p=2, accessed 6 April 2014).

National Patient Safety Agency (2011). The adult patient's passport to safer use of insulin (http://www.nrls.npsa.nhs.uk/resources/?EntryId45=130397, accessed 6 April 2014).

NHS Pharmaceutical Quality Assurance Committee (2004). Quality assurance and risk assessment of licensed medicines for the NHS (http://www.qcnw.nhs.uk/docs/QA%20&%20Risk%20Assessment%20of%20licensed%20Medicines%20for%20the%20NHS.pdf, accessed 6 April 2014).

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United States Pharmacopeia (2004). Use caution – avoid confusion. USP Quality Review April 79:1–12.

US Food and Drug Administration (2009). Name differentiation project (http://www.fda.gov/NewsEvents/Newsroom/PressAnnouncements/2009/ucm184399.htm, accessed 6 April 2014).

WHO Collaborating Centre for Patient Safety Solutions (2007). Look-alike and sound-alike names (accessed 6 April 2014).

WHO (2011). Multi-professional Patient Safety Curriculum Guide (http://www.who.int/patientsafety/education/curriculum/tools-download/en/, accessed 6 April 2014).

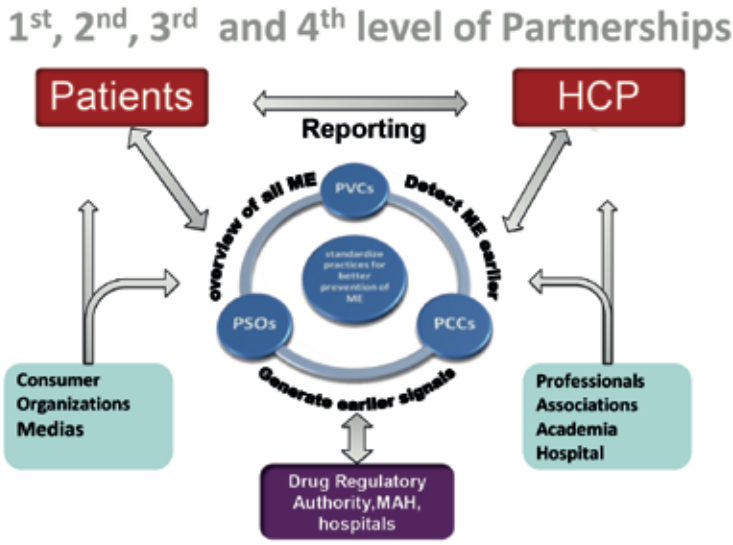
9. Collaborations

A model for collaboration is presented in Figure 13 based on the identification of all institutions and organizations totally or partially involved in patient safety promotion or in collecting, analysing and preventing MEs. It also deals with how they can collaborate for synergistic results. Four levels of partnership are identified for the benefit of patients.

9.1 First level of partnership

The first level of partnership is represented by PVCs, PCCs and PSOs. The aim of the partnership is to gain an overview of all MEs, to detect MEs, to generate signals early, to standardize practices and to share reporting systems and databases.

Figure 13. Schematic outline of partnerships between stakeholders engaged in tackling MEs



A partnership between PVCs, PCCs and PSOs with a mutual exchange of data will lead to optimized ME detection and allow better understanding of the causes of ME, leading to the implementation of prevention strategies. The competencies and positions of the different networks are complementary and can be used to strengthen data analysis, methodological development, learning and outreach activities for the implementation of ME prevention in direct interaction with health-care professionals, patients and their organizations.

9.2 Second level of partnership

The second level of partnership is between patients and HCPs. Patients and HCPs are the reporters, because patients are the first to experience the harm, and HCPs are at the frontline with the patients. This partnership could not be efficient without the combined involvement of levels 1 and 2, to notify ADRs and MEs to level 1, and to inform, train, sensitize, and educate partners to prevent MEs at level 2. Active and efficient collaboration between level 1 and level 2 will lead to prevention of MEs.

9.3 Third level of partnership

The third level of partnership is represented by academia, professional organizations, consumer organizations and the media.

Partnership of level 1 with level 2 could not be efficient without the collaboration of level 3, to promote, to teach and to train HCPs on the concept and culture of patient safety and on the importance of reporting ADRs and MEs, and to educate patients and consumers on the importance of patient safety and of patient engagement in preventing MEs.

The lack of engagement by academia in preventing MEs should be remedied with a strengthened partnership between PVCs, PSOs, PCCs and academia to:

- focus on teaching and training in clinical pharmacology;
- focus on teaching and training in the principles of safe medication practice for undergraduate and postgraduate medical, pharmacy and nursing students;
- schedule specific courses on patient safety focusing on medication safety;
- foster clinical research on methods to reduce the risk of harm from medication practice in all clinical settings.

Partnering with and gaining the confidence of the media is essential to promote, sensitize, strengthen and foster the patient safety concept in the community.

9.4 Fourth level of partnership

The fourth level of partnership is represented by the medicines regulatory authorities, marketing authorization holders and hospitals.

Including level 4 in the partnership is essential for the implementation and monitoring of preventive actions suggested by level 1, thus avoiding the recurrence of MEs.

Partnering with hospitals should include studies to be carried out in intensive care units and hospital wards and implementation of ME prevention strategies.

9.5 Collaboration between the four levels of partnership

To achieve a situation in health care where MEs are identified, reported, analysed and learned from, and where preventive measures are implemented in a timely manner, a system has to be created allowing the four levels of stakeholders to work together. Such partnerships can only be achieved through visionary political leadership driving patient safety as a primary objective and concern for everyone involved in health care (see Figure 14).

Figure 14. Conceptual diagram of the four levels of partnership required to achieve a system for good control and management of MEs

Annex 1. Glossary

Accident
An unplanned, unexpected, and undesired event, usually with adverse consequences.
Senders (1994)

An adverse outcome that was not caused by chance or fate. Most accidents and their contributing factors are predictable and the probability of their occurrence may be reduced through system improvements.
Canadian Patient Safety Dictionary (2003)

Adverse drug event (ADE)
Any injury resulting from medical interventions related to a drug. This includes both ADRs in which no error occurred and complications resulting from medications errors.
Bates et al. (1995)

Any untoward medical occurrence that may present during treatment with a medicine but which does not necessarily have a causal relationship with this treatment.
World Health Organization (2002)

Adverse drug reaction (ADR)
A response to a medicine which is noxious and unintended, and which occurs at doses normally used in humans for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function.
World Health Organization (2002)

Noxious and unintended effects resulting not only from the authorized use of a medicinal product at normal doses, but also from medication errors and uses outside the terms of the marketing authorization, including the misuse and abuse of the medicinal product.
Directive 2010/84/EU (December 2010)

Adverse event
Any injury related to medical management, in contrast to complications of disease.
Hiatt et al. (1989).

An unintended injury that was caused by medical management and that resulted in measurable disability.
Leape et al. (1993)

An incident in which harm resulted to a person receiving health care.
Patient Safety International (2009)

An unintentional outcome with injury which is caused by the health care system.
Cuperus-Bosma, Wagner &. van der Wal (2006)

An injury caused by medical management.
Patient safety: conducting a root cause analysis of adverse events (2007)

Cause
An antecedent factor that contributes to an event, effect, result or outcome. A cause may be proximate in that it immediately precedes the outcome, such as an action. A cause may also be remote, such as an underlying structural factor that influences the action, thus contributing to the outcome. Outcomes never have single causes.
Wade (2002)

An antecedent set of actions, circumstances or conditions that produce an event, effect, or phenomenon. A cause may be proximate (immediately precede) or remote (a factor in predisposing to) the event, effect, or phenomenon.
Canadian Patient Safety Dictionary (2003)

Contributing factors
An antecedent factor to an event, effect, result or outcome similar to a cause. A contributory factor may represent an active failure or a reason an active failure occurred, such as a situational factor or a latent condition that played a role in the genesis of the outcome.
Wade (2002)

The reason(s), situational factor(s), or latent condition(s) that played a role in the genesis of an adverse outcome.
Canadian Patient Safety Dictionary (2003)

Error
Failure of a planned action to be completed as intended, or the use of a wrong plan to achieve an aim.
Patient safety: conducting a root cause analysis of adverse events (2007)

Failure mode and effects analysis (FMEA)
A risk assessment method based on the simultaneous analysis of failure modes, their consequences and their associated factors. This systematic method is used to identify and prevent product and process problems before they occur.
Cohen, Davis & Senders (1994)

Forcing function
An aspect of a design that prevents a target action from being performed or allows its performance only if another specific action is performed first.
AHRQ Patient Safety Network

Harm
Temporary or permanent impairment of the physical, emotional, or psychological function or structure of the body and/or pain resulting therefrom requiring intervention.
National Coordinating Council for Medication Error Reporting and Prevention (NCC MERP) (1998)

Death, disease, injury, suffering, and/or disability experienced by a person.
Patient Safety International (2009)

Human error
The failure to complete a planned action as it was intended, or when an incorrect plan is used in an attempt to achieve a given aim.
Canadian Patient Safety Dictionary (2003)

Incident
An event or circumstance, which could have or did lead to unintended and/or unnecessary harm to a person, and/or a complaint, loss or damage.
Patient Safety International (2009)

An unintended event taking place during the care process with the possibility of injury for the patient.
Cuperus-Bosma, Wagner &. van der Wal (2006)

Injury
Harm caused by an external force or action.
Patient Safety: Conducting a Root Cause Analysis of Adverse Events (2007)

Latent error
An error that lies dormant in the system, usually removed from the direct control of the practitioner that may or may not become an active error.
Patient Safety: Conducting a Root Cause Analysis of Adverse Events (2007)

Medication error
A failure in the treatment process that leads to, or has the potential to lead to, harm to the patient.
Ferner & Aronso (2006)

Outcome
A product, result or practical effect. In health care, outcomes may be measured in a variety of ways, but tend to reflect the health and well-being of the patient and associated costs.
Canadian Patient Safety Dictionary (2003)

Patient safety
The identification, analysis and management of patient-related risks and incidents, in order to make patient care safer and minimize harm to patients.
Aspden, NPSA (2004)

The prevention of health-care errors, and the elimination or mitigation of patient injury caused by health-care errors.
National Patient Safety Foundation

A type of process or structure whose application reduces the probability of adverse events resulting from exposure to the health-care system across a range of diseases and procedures.
Shojania et al. (2001)

The process by which an organization makes patient care safer. This should involve: risk assessment, the identification and management of patient-related risks; the reporting and analysis of incidents; and the capacity to learn from and follow up on incidents and implement solutions to minimize the risk of them recurring.
National Patient Safety Agency (2004)

The reduction and mitigation of unsafe acts within the health-care system, as well as through the use of best practices shown to lead to optimal patient outcomes.
Canadian Patient Safety Dictionary (2003)

Pharmacovigilance
The science and activities related to the detection, assessment, understanding and prevention of adverse effects or any other possible drug-related problems.
World Health Organization (2002)

Potential adverse drug event or near miss
A medication error with the potential to cause injury but which does not actually cause any injury, either because of specific circumstances, chance or because the error was intercepted and corrected.
Morimoto et al. (2004)

Preventability
Implies that methods for averting a given injury are known and that an adverse event results from failure to apply that knowledge.
Leape et al. (1993)

Preventable
Potentially avoidable in the relevant circumstances.
Patient Safety International (2009)

Preventable adverse event
Adverse event that would not have occurred if the patient had received ordinary standards of care appropriate for the time of the study.
Michel et al. (2004)

Preventable adverse drug event
An injury that is the result of an error at any stage in the medication use process.
Morimoto et al. (2004)

Preventable adverse drug reaction
An injury that is the result of an error at any stage in the medication use process.
Consensus during Delphi surve

Process
A series of related actions to achieve a defined outcome. Prescribing, medication or administering medication are processes.
Leape et al. (1998)

A course of actions or sequence of steps, including what is done and how it is done. Examples of these interrelated activities within the health-care system include decision making, problem solving and communication.
Canadian Patient Safety Dictionary (2003)

Risk
The probability of danger, loss or injury within the health-care system.
Canadian Patient Safety Dictionary (2003)

Risk management

Clinical and administrative activities undertaken to identify, evaluate, and reduce the risk of injury to patients, staff, and visitors and the risk of loss to the organization itself.

Joint Commission on Accreditation of Healthcare Organizations (2002)

Identifying, assessing, analysing, understanding, and acting on risk issues in order to reach an optimal balance of risks, benefits and costs.

National Patient Safety Agency (2004)

Organizational activities designed to prevent patient injury or moderate the actual financial losses following an adverse outcome.

Canadian Patient Safety Dictionary (2003)

Root cause analysis (RCA)

Root cause analysis is a retrospective review of a patient safety incident undertaken in order to identify what, how, and why it happened. The analysis is then used to identify areas for change, recommendations and sustainable solutions, to help minimize the recurrence of the incident type in the future. This approach is equally applicable to complaints and claims.

National Patient Safety Agency (2004)

A systematic process to identify the factors which contributed to an incident.

Patient Safety International (2009)

Root cause analysis is defined as a systematic process of investigating a critical incident or an adverse outcome to determine the multiple, underlying contributing factors. The analysis focuses on identifying the latent conditions that underlie variation in performance and, if applicable, developing recommendations for improvements to decrease the likelihood of a similar incident in the future.

Canadian Patient Safety Dictionary (2003)

Safety

Freedom from accidental injury.

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Sentinel event

An incident, which should never have happened – which has a severe or potentially severe outcome. Sentinel events normally trigger a root cause analysis.

Patient Safety International (2009)

An unexpected event involving death or serious injury unrelated to the natural course of the individual's illness or underlying condition; a sentinel event is so called because it signals the need for investigation and remediation.

Patient Safety: Conducting a Root Cause Analysis of Adverse Events (2007)

System

A set of interdependent elements, both human and nonhuman, interacting to achieve a common aim.

Patient Safety: Conducting a Root Cause Analysis of Adverse Events (2007)

System is reserved for use when describing the entirety of health care and can be defined as a set of interdependent components interacting to achieve a common aim.

Canadian Patient Safety Dictionary (2003)

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This publication should enable readers to learn more about why adverse events occur with medicines, and what can be done to reduce patient deaths and negative health impacts arising from undetected problems with medicines safety globally. It should provide a framework for advancing the application, coordination and optimal use of pharmacovigilance evidence, sharing that evidence and strengthening the links between national pharmacovigilance centres and other patient safety networks, to prevent medicines-related adverse events. The publication aims to increase the capacity of national pharmacovigilance centres to analyse reports of medication errors, to identify preventable medication errors and also to support action to minimize the occurrence of preventable medication errors.

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