Creation of a better medication safety culture in Europe:
Building up safe medication practices

Expert Group on Safe Medication Practices (P-SP-PH/SAFE)

The views expressed in this report do not necessarily reflect the offical opinions of the Council of Europe

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Executive summary

The Council of Europe Committee of Experts on Pharmaceutical Questions established the Expert Group on Safe Medication Practices in 2003 to review medication safety and to prepare recommendations to specifically prevent adverse events caused by medication errors in European health care.

This work is complementary to the work of the Council of Europe Committee of Experts on Management of Safety and Quality in Health Care (SP-SQS) that prepared recommendations on management of patient safety and prevention of adverse events in health care. The recommendations were adopted by the Committee of Ministers on 24 May 2006 (Council of Europe Recommendation Rec(2006)7).

As medication errors are the most common single preventable cause of adverse events, a specific strategy to promote medication safety was established as a part of the Council of Europe Recommendation Rec(2006)7, see Appendix E. "Medication safety – A specific strategy to promote patient safety" of Recommendation Rec(2006)7 of the Committee of Ministers to member states on management of patient safety and prevention of adverse events in health care in Appendix 1.

Aim of the report

This report essentially deals with medication errors and their prevention. It presents the work carried out by the Expert Group on Safe Medication Practices and represents the first international report on this topic with a special focus on Europe.

Although the development of this document meets the challenge of the great variation in the different European countries regarding medication regulations, clinical practices, procedures for the use of medication and organisational cultures, as well as the lack of information on medication errors occurring in member states of the Partial Agreement, the Expert Group on Safe Medication Practices proposes a multidisciplinary and integrated approach to enhance medication safety in Europe. The members of the expert group are health professionals committed to medication safety by their academic qualification and/or day-to-day practice in the medication use system. No conflict of interest with public health has been disclosed during the preparation of this report.

According to the vision statement agreed in November 2003 (see Appendix 2 of the report), the Council of Europe's Expert Group on Safe Medication Practices carried out its work according to the following essential objectives:

- to enhance awareness of medication errors across the European countries and recognition as an important system-based public health issue;
- to provide guidance for reducing medication errors and preventable adverse drug events in all the processes of the medication use system, both in hospital and ambulatory care settings, based on reporting, analysing and active learning from the medication errors and on evidence-based strategies already recommended;
- to help European Health Authorities, governments and regulatory agencies, pharmaceutical companies, organisations and professional societies, health professionals and patients selecting top safety practices for implementation both at

national and local levels and building up Europe-wide standards for safe medication practices;
- to foster the development of a safe medication practices agenda shared at European level.

Furthermore, the Expert Group aims at encouraging collaboration between the stakeholders in order to improve the quality of the use of medication and patient safety.

The report is divided into six sections:
- Introduction: provides the scope of the report
- Chapter I: explores how to prevent errors by learning from medication errors
- Chapter II: outlines how to measure and evaluate medication safety
- Chapter III: explains how the design of medicinal products used in Europe can be developed to improve the in use -safety of medicinal products
- Chapter IV: describes methods for improving safe medication practices
- Chapter V: explores how medicine information practices contribute to medication safety

When considering medication safety there is frequently confusion and misunderstanding because the different terms used are not clearly defined and used uniformly. Therefore, the Expert Group has established a glossary (see Appendix 3 of the report).

Seriousness of the problem in European health care

Medication safety is considered as one of the fundamental areas of patient safety since adverse drug events are the most frequent single type of adverse events. Several national multi-centre studies on adverse events in different countries revealed that between 6.3 – 12.9% of hospitalised patients have suffered at least one adverse event during their admissions and that between 10.8 – 38.7% of these adverse events were caused by medicines. It should be noted that 30.3% to 47.0% of these adverse drug events appear to be consequences of medication errors and therefore, may be considered as preventable.

Available data show that the morbidity and mortality associated with medication errors in Europe are of a similar magnitude as in the United States and other countries (see Introduction §2.1 and Appendix 4 of the report). The reported incidence of preventable adverse drug events in European hospitals range from 0.4 to 7.3% of all hospitalisations. In primary care, adverse events are caused by errors in prescription and administration or lack of compliance with therapy and are probably more frequent than in hospital settings, because drug consumption is greater, although information is scarce. European research studies about preventable adverse drug events occurring in primary care and leading to hospital admissions have shown that between 0.9% and 4.7% of all hospital admissions to internal medicine and intensive care wards are caused by medication errors.

Risks from medication errors are poorly managed in Europe. Safe medication practices at both local and national levels are poorly developed and implemented in the majority of European countries (see Appendix 5 of the report).

Top level actions recommended to European health care organisations

The following list of top level actions summarises the key messages derived from the report that the Expert Group on Safe Medication Practices recommends to be taken into account by European health care organisations with a view to promoting medication safety.

Medication safety is one of the fundamental areas of patient safety since medication errors are the most common single preventable cause of adverse events. European Health Authorities should recognise the high incidence of preventable adverse drug events and the important increase of health care costs by harm to patients. Risks from medication errors should be correctly understood and managed in Europe.

It is recommended that European health care organisations and other stakeholders take steps to:

- Establish **medication errors reporting systems** as a component of or to complement patient safety incident reporting systems for incidents involving medicines. Such systems must include primary care as well as hospital settings and should be developed at local, national and European levels.
- Establish and use a common **terminology** concerning harm to patients caused by medication and promote a common taxonomy to facilitate the sharing of safety information in Europe. A clear distinction has to be made between two different aspects of medication safety: medication errors, linked to the safety of practices, and adverse drug reactions, linked to the safety of products.
- Create a **culture of safety** at local, national and international levels with political, financial and logistical support of public health and in particular by medication safety initiatives.
- Set up a **nationally recognised focal point for safe medication practices** in a collaborative and complementary way to pharmacovigilance systems, based on a national system for reporting medication errors, analysing causes and disseminating information on risk reduction and prevention. The focal point's annual reports to identify risks and methods that have been used effectively to manage these risks could be collated at European level and used to inform the health care organisations in individual European countries.

Current European medicines regulations concerning the naming, packaging and labelling including patient information leaflets and datasheets (Summary of product characteristics; SmPC) (in particular technical information for injectable medicines) for medicinal products do not consider all aspects pertaining to patient safety adequately. Medication errors frequently occur in Europe because of sound-alike or look-alike drug names, similarities in the outer appearance of medicines' packages and labelling as well as unclear, ambiguous or incomplete labelling information.

European directives on other types of health care products require user testing, but regrettably, user testing is required by the European directives for medicinal products only for patient information leaflets (PILs). Possible risks occurring at every stage of the medication use system including storage, dispensing, preparation and administration of medicines by health professionals and also the preparation and use of medicines by carers and patients in the ambulatory setting should be taken into account.

Although there is a wide consensus that medicine information is an integral part of health care, few actions have been taken to ensure easy access to balanced and ready-to-use information both to practitioners and patients.

It is recommended that European health care organisations and other related stakeholders take steps to:

- Update the European legislative framework applied by the European Medicines Agency and National Drug Regulatory Authorities to take into account the need for good design with a view to minimising the risks of medication errors when using medicinal products in practice, as well as to include a requirement that packaging and labelling should be subject to specific human factor assessment and **user testing including medicine information in the hospital/ ambulatory setting** by the manufacturers prior to marketing authorisation.
- Update the national and European legislative framework to require pharmacies and other persons authorised for dispensing medicines to ambulatory patients to put a typewritten label on the container of the medicinal product at dispensation. This **dispensing label** is intended to assist patients, carers and health professionals to use the medicines as intended and to minimise errors. Labelling of medicinal products should foresee adequate space for a dispensing label.
- Update the national and European legislative framework to require **complete and unambiguous labelling of every single unit of use** of all licensed medicines products (e.g. tablet, vial and nebules), including the international nonproprietary name (INN), trade name, strength, expiry date, batch number and a data matrix bar code. The data matrix bar code should contain a GS1 Global Trading Index Number (GTIN) identifier in addition to the expiry date and batch number.
- Update the national and European legislative framework dealing with **professional (datasheet, summary of product characteristics) and patient information**. This information should be considered as a communication tool between public health authorities, health care professionals and patients. European states and international organisations should allocate parts of their health care and research budgets to clinical trials meeting defined public health needs, to the development of balanced information based on these trials and for providing regulatory agencies and medicine information centres with adequate means to fulfill defined public health needs.
- Support national centres for safe medication practices which should identify through **post-marketing monitoring** problems related to poor naming, labelling and packaging and medicine information caused by medicines already in use and work closely with national drug regulatory authorities and manufacturers to respond appropriately and timely to resolve the problems detected. Co-ordination at European level is required.

It is possible to improving the safety of the medication use system: solutions are available, many of them have a focus on the improvement of medication use practices.

It is recommended that European health care organisations and other related stakeholders take steps to:

- Include multidisciplinary medication practice procedures in undergraduate **education**, induction and refresher training for all health care staff responsible for using medicines.
- Put into practice the concept of **concordance** wherever possible. All health professionals involved in patient counselling should have a good basic and continuing education that covers drug therapies, therapeutic guidelines and communication skills, including human

relations. They should be educated to communicate about medicines with patients in an empowering way so as to involve them in their own care as active partners and experts of their disease/symptoms and finally check that patients receive the information they need.

- Delegate the responsibility for the management of local medication use systems in both primary and secondary care to **multidisciplinary safe medication practices committees**. These committees should include physicians, nurses, pharmacists, quality managers and administrators.
- Use systematically appropriate methods to **detect medication incidents** and evaluate the effect of safe medication practices and initiatives intended to minimise risks. Each organisation should use the method(s) that fits best to its aims.
- Develop multidisciplinary teams to develop **working procedures on safe medication practices**. These procedures should be audited annually and results from these audits, medication incident reports and other data should be used to plan and report on safe medication practice for health care institutions.
- Ask prescribers to evaluate the patient's total health status and to review all existing medication before prescribing new or additional medication to ascertain possible drug-related problems. Prescription information should be written legibly, preferably printed and should be complete.
- Use **electronic prescribing systems** including clinical decision support and electronic alerts that have been proven to reduce errors in prescribing, dispensing and administration.
- Enable pharmacists to review on a regular basis medication orders and the patient health record before medication is dispensed and/or to identify and correct medication errors and to discuss problems with the prescriber, if needed.
- Provide **essential and up-to-date medicine information and therapeutic guidelines** in a ready-to-use form at the point of care for health professionals who prescribe, prepare, dispense and administer medicinal products. Sources of objective comparative medicine information should be easily accessible, using the most appropriate information technology.
- Promote the key role of complete and appropriate interpersonal and interdisciplinary, oral and written **communication between health professionals and patients**, particularly at the key stages of prescribing, dispensing, counselling and transfer of information about the medication of an individual patient between organsiations. In particular, providers and health professionals should review the patient's list of medicines at every encounter. The reconciliation of medication history should be done at every transition of care in which new medication is prescribed or existing prescriptions are renewed.

Introduction

Key points:

- Patient safety is defined as the freedom from accidental injuries during the course of medical care. Safety is a key component of a quality system within any health care organisation.
- Several national multi-centre studies on adverse events reveal that 6.3 – 12.9% of hospitalised patients experience at least one serious adverse event. There is little research in primary care and so the incidence of patient safety incidents in this sector is only known through the frequency of admissions caused by adverse events. Studies indicate that adverse events involving medication practice range from 10.8 to 38.7% of patients under medicine therapy.
- Operating at strategic level, the World Alliance for Patient Safety and the European Union are focusing on broader actions concerning patient safety and are not carrying out specific initiatives on safe medication practices.
- The Council of Europe European Health Committee established a Committee of Experts on Management of the Safety and the Quality in Health Care (SP-SQS) to review broader patient safety issues in Europe and the Council of Europe‘s Committee of Experts on Pharmaceutical Questions established the Expert Group on Safe Medication Practices in order to review specifically the prevention of medication errors in European health care.
- This report on the creation of a better medication safety culture in Europe through building up safe medication practices is the first international report on this topic and aims at complementing the Council of Europe Recommendation Rec(2006)7 of the Committee of Ministers to member states on management of patient safety and prevention of adverse events in health care.
- The Expert Group has established a glossary to prevent confusion and misunderstanding caused by the use of the different terms related to medication safety (see Appendix 3).
- Adverse drug events are injuries related to the use of medicines. They are the most common single type of serious adverse events and are caused by adverse drug reactions (linked to product safety) or medication errors (linked to the safety of practices). If an adverse drug event is caused by a medication error, the event is preventable.
- A medication error is any non-intentional deviation from ordinary standards of the medicine therapy and is preventable by definition. A medication error may occur at one or several stages of the medication use system, such as formulary selection, prescription, dispensing, validation, preparation, storage, delivery, administration, therapeutic monitoring and information. It may occur also at its interfaces through communication and transcription. 30.3% to 47.0% of all adverse drug events are preventable and most of the serious adverse drug events are caused by medication errors.
- Medication errors should not be confused with adverse drug reactions which need to be reported within the pharmacovigilance system. Pharmacovigilance evidences the adverse effects of the medicinal product which are pharmacological effects. Medication error reporting systems evidence the adverse effects of the medication use system, in particular of associated practices.
- Medication error rates should be considered as indicators of the quality of the different processes of the medication use system. Even if there are still too few reliable data on the

frequency of medication errors in European countries, the available studies carried out in Europe reveal that medication errors are of a similar magnitude as in the United States and other countries.

- Risks from medication errors are poorly managed in Europe. Safe medication practices at both local and national levels are poorly developed and implemented in the majority of countries in Europe.
- European Health Authorities should recognise the high incidence of preventable adverse drug events and the important increase of health care costs by health damages to the patient.

Summary of Chapter 1 - From patient safety to medication safety

Patient safety is defined as the freedom from accidental injuries during the course of medical care and encompasses the activities aimed to avoid, prevent or mitigate adverse outcomes which may result from health care.[1,2] Safety is a key component of quality within any health care organisation.

A number of research studies in different countries indicate that patient safety is a major problem for health care worldwide. Several national multi-centre studies on adverse events have underlined the epidemiological importance of the problem (see Table 1). These studies reveal that between 6.3 – 12.9% of hospitalised patients in the United States of America experience at least one serious adverse event. little research has been done in primary care and so the incidence of patient safety incidents in this sector is only known through the frequency of the admissions caused by adverse events (i.e. 4.0% in the French adverse event ENEIS study).

Table 1: Main results of national multi-centre studies on adverse effects

Studies	Year of data collection	No of patients	Stays with at least one serious adverse event	Adverse drug events		
				Part of adverse events	preventable	death
Harvard Medical Practice Study (HMPS) [3,4]	1984	30,195	3.7%	19.4%	17.7%	
Quality Australian Health Care Study (QAHCS) [5]	1992	14,179	16.6%	10.8%	43.0%	8.0%
Thomas et al. (UCMPS) [6]	1992	14,732	2.9%	19.3%	35.0%	
Schioler et al. (Denmark) [7]	1998	1,097	9.0%			
Davis et al. (New Zealand) [8]	1998	6,579	12.9%	15.4%		
Vincent et al. (United Kingdom) [9]	1999	1,014	10.8%			
Canadian Adverse Events Study (CAES) [10]	2000	3,745	7.5%	23.6%		
French Adverse Event Study (ENEIS) [11] - prospective study in hospitalised patients - cause of hospitalisation	2004	8,574	6.6‰ 4.0%	19.5% 38.7%	31.0% 47.0%	
Spanish Adverse Event Study (ENEAS)[12]	2005	5,624	9.3%	37.4%	34.8%	

Research studies indicate that the proportion of adverse events involving medication practice may be between 10.8 – 38.7%. Adverse drug events are often the first type of serious adverse events. 30.3% to 47.0% of the adverse drug events detected in these studies are preventable and appear to be the consequences of medication errors.

1.1. International efforts for improving patient safety

The report "To Err Is Human: Building a Safer Health System" of the US Institute of Medicine (IOM) of the US National Academy of Sciences, published in November 1999, had galvanized a suddenly expanded level of concern about patient injuries and safety in health care both in the United States and abroad.[1]

Over the last years, the awareness politicians and health professionals about patient safety has been raised in many countries all over the world through important reports proposing recommendations for improvement, e.g. in the UK,[13,14,15] in Canada, [16] in Switzerland.[17] National and local professional initiatives for improving patient safety have been reactivated or started In several countries.

In May 2002, the World Health Assembly adopted a resolution (WHA55.18) urging World Health Organization (WHO) and member states to pay the closest possible attention to the problem of patient safety.[18] In October 2004, the WHO launched the World Alliance for Patient Safety to raise awareness and political commitment to improve the safety of care and to facilitate the development of patient safety policies and practice in all WHO member states, as stated by the London Declaration published on 17 January 2006.[19]

In November 2002 during its 52nd meeting, the European Health Committee (CDSP), Council of Europe, decided to establish and approved the terms of references of the Committee of Experts on Management of Safety and Quality in Health Care (SP-SQS) to prepare recommendations for the prevention of adverse events in health care by a system approach. The Recommendation Rec(2006)7 of the Committee of Ministers to member states on management of patient safety and prevention of adverse events in health care was adopted on 24 May 2006 by the Committee of Ministers (see Appendix 1).[20]

Under the aegis of the Luxembourg European Union Presidency and the European Commission, the first European Union Conference on patient safety "Patient Safety – Making it happen – The European perspective" was organised on 4 and 5 April 2005. Focusing on the interest in and the challenges to patient safety at European Union level, the conference endorsed the "Luxembourg Declaration on Patient Safety" which is in line with the Council of Europe approach.[21]

The Council of Europe is contributing to the European Commission co-funded project SIMPATIE "Safety Improvement For Patients In Europe", which aims at establishing a tool box of terms, indicators, internal and external instruments for improvement of safety in health care which are harmonised across Europe.[22] This project started on 15 February 2005 for a two-year duration and constitutes a vehicle for promoting the stipulations laid down in the above-mentioned Council of Europe Recommendation Rec(2006)7.

The above-mentioned recommendation considers that the culture in place in the system and organisations delivering health care to a community is the key to improved patient safety (see Appendix 1). Therefore a definition of safety culture; requirements for strong leadership and changes at all levels of the system has been prepared in co-operation with the Expert Group on Safe Medication Practices. There is a link between quality- and risk management. Laws and resources, incentives and educational programmes, recognised national focal points for patient safety and communication are of great importance.

A safety culture is a culture where everyone has a permanent and active awareness of situations prone for errors. A safety culture creates an environment where it is accepted that people will make mistakes and processes and equipment will fail, where individuals are allowed to make errors, where problems and errors are treated openly and fairly in a non-blame, non-punitive atmosphere at all levels, where problem analysis focuses on organisational performance, where the whole organisation is able to learn from safety incidents and then put things right.[20]

Giving credibility at the highest level of a health care system is the key factor for developing a safety culture. Government and other policy makers should support measures to allow health care organisations to develop a safety culture (e.g. through policies and political support of public health and patient safety issues, financial and logistical resources, individual and team incentives and rewards, mandatory risk management). The highest level of a health care organisation should take the lead in quality and risk management and translate the results at all levels into shared values, norms and behaviour at all levels.[20]

A system approach is the best way to improve patient safety. Risk management should be based on an integrated in quality management and take into account of human factor engineering in the development of structure and human factor principles in the development of processes. At all levels, staff should be educated in human behaviour (human factor) and risk management principles. Solutions to prevent harm should be implemented through changes in structure and processes.[20]

Health care staff should be encouraged to both proactively assess and reactively report risks. Actions that could go wrong should be proactively identified and assessed. At all levels, actual and potential problems and errors should be reported when they occur, locally and nationally to a national board. Health care organisations should introduce systems allowing them to regularly conduct safety culture assessments and learn from them. Safety should be expressed by quality indicators and followed up.[20]

1.2. Medication safety: an unrecognised issue

Risks from medication errors are poorly managed in Europe. Safe medication practices are poorly developed and implemented in the majority of European countries.

1.2.1. Current patient safety efforts ignore medication safety

Heads of agencies, health policy makers, patient groups and the World Health Organization came together to improve patient safety. The World Alliance for Patient Safety intends to:

- co-ordinate and facilitate international expertise and learning on patient safety in order to reduce duplication of efforts and minimise the waste of resources, particularly in the developing countries;
- collate patient safety information from many sources and consider the merits of global reporting. The development of national/subnational reporting systems in countries could also be facilitated;
- design a process by which countries can decide whether a solution is appropriate for use in their health economy;
- share work in progress in relation to problem specification or solution development and where appropriate, to co-ordinate international work in specific areas;

- assist countries in developing patient safety research programmes to solve specific problems in the health care systems.

The World Alliance for Patient Safety has not announced safe medication practice initiatives and is operating at a more strategic level.

According to its current programme, the World Alliance for Patient Safety should take forward pilot work to collect and analyse information about adverse drug reactions related to prescribing, dispensing and administration, in conjunction with the WHO Foundation Collaborating Centre for International Drug Monitoring. Furthermore, the WHO Collaborating Centre on Patient Safety Solutions, the Joint Commission on Accreditation of Health Care Organisation and the Joint Commission International should provide existing solutions disseminated by these organisations.[23]

The Luxembourg Declaration on Patient Safety published on 5 April 2005 by the European Commission recognises that patient safety has a significant and high place on the political agenda of the European Union (EU), nationally in European Union member states and locally in the health care sector. The declaration recommends to

- establish an European Union forum with the participation of relevant stakeholders to discuss European and national activities regarding patient safety;
- work together in the frame of the World Alliance for Patient Safety and with the Council of Europe towards a common understanding on patient safety issues, and to establish an 'EU solution bank' and 'best practice' examples and standards;
- create the possibility of support mechanisms for national initiatives regarding patient safety projects, acknowledging that patient safety is embraced by the programme of the Health and Consumer Protection Directorate General;
- ensure that European Union regulations with regard to medical goods and related services are designed with patient safety in mind.

The European Union has not announced any safe medication practice initiatives and is again operating at a more strategic level.

These organisations are focusing on broader patient safety actions and have no specific initiatives concerning safe medication practices.

1.2.2. Council of Europe initiative for improving medication safety

The use of medicines is the most frequent intervention among all health care interventions in developed countries. "To Err Is Human: Building a Safer Health System", referring to the Harvard Medical Practice Study, recalled that adverse drug events (ADE) are also the most common single type of serious adverse events.[1,3] More than half of these ADEs are caused by medication errors and would be preventable.[3]

In 2002, the Committee of Experts on Pharmaceutical Questions (P-SP-PH), Council of Europe, decided to establish the baseline about medication errors in Europe in a survey. Based on the survey results, the P-SP-PH organised in collaboration with the World Health Organization/Regional Office for Europe the first Scientific Expert Meeting in The Hague in November 2002 the first Scientific Expert Meeting to share experiences, create a network and establish a forward work programme across Europe.[24] Participants agreed on a consensus

document about medication safety and the establishment of a multidisciplinary Expert Group to carry out the programme.[25]

In November 2003, the Expert Group on Safe Medication Practices held its first meeting. Inspired by the Scientific Expert Meeting's consensus document, the Expert Group agreed on a vision statement (see Appendix 2).

For these reasons, this report will essentially deal with medication errors and their prevention.

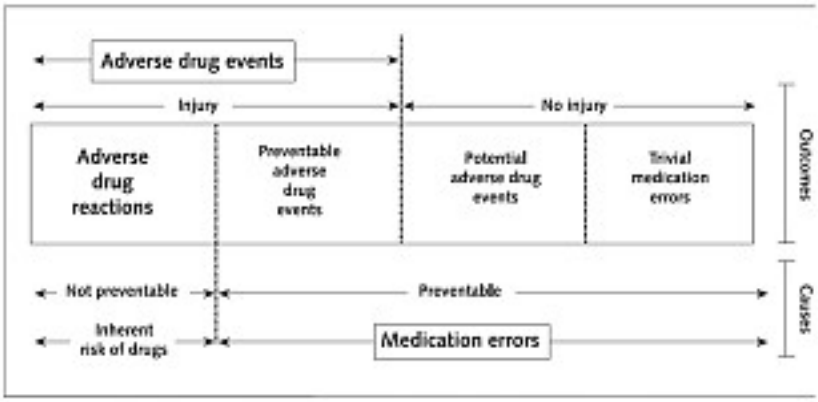
Summary of Chapter 2 - Medication safety: what do we know

The very first problem when considering medication safety is that confusion and misunderstandings occur frequently because the different terms used for medication safety are not clearly defined and not used in the same way. But for a correct understanding of evidence-based data on preventable adverse drug events an accurate use of specific terms is fundamental.

Based on different available definitions of terms related to medication safety in seminal publications and public reports, the Expert Group on Safe Medication Practices has established a glossary to facilitate the use of terms in the same way (see Appendix 3).

Although **medication safety** comprises both medication errors and adverse drug reactions, a clear distinction has to be made between them: medication errors are linked to the safety of health care service, whereas adverse drug reactions are linked to product safety (see Figure 1). This distinction between safety of practices and product safety was clearly assumed by the Resolution WAH55.18 and adopted by WHO's 55th World Health Assembly in May 2002 and its associated report.[18]

Figure 1: Terminology for adverse drug events [26,27]



(Original figure: Figure 2 - Otero MJ, Dominguez-Gil A. Acontecimientos adversos por medicamentos: una patología emergente. Farmacia Hospitalaria 2000; 24(4):258-266. Reproduced with the permission of the journal *Farmacia Hospitalaria*.)

The most widely used definition of a **medication error** is the one adopted by the U.S. National Coordination Council for Medication Error Reporting and Prevention (NCC MERP):

> "A medication error is any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. Such events may be related to professional practice,

> health care products, procedures, and systems, including prescribing; order communication; product labelling, packaging, and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use." [28]

Taking into account the knowledge related both to human error and the quality of health care, the French Society of Clinical Pharmacy has upgraded the NCC MERP definition with a view to making it more accurate and operational (see note[i]).[29]

Medication errors occur in ambulatory and hospital care settings or at the interface between them.

Medication errors should not be confused with **adverse drug reactions** that are defined differently according to the Chapter V a (Pharmacovigilance) of Directive 75/319/EEC (Article 29b) amended by Commission Directive 2000/38/EC of 5 June 2000:

> "An adverse drug reaction is a response to a drug 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 physiological function". [30]

These terms are similar to the WHO's definition.[31] With respect to the EMEA recommendations "adverse drug reaction" is an expression to be used only where there is a causal relationship with the use of the "medicinal product" (medicine).[32]

In consequence, **medication error reporting systems** (see Chapter I) evidence the adverse effects of the medication use system, with particular mention to the associated practices, whereas **pharmacovigilance** assess the adverse effects of the product itself which are pharmacological effects (adverse drug reactions are monitored by well-established product safety organisations, such as the WHO Foundation Collaborating Centre for International Drug Monitoring).

2.1. Incidence of adverse drug events

The information about the incidence of adverse drug events (ADEs) from all types of medicines is limited to the experience in some specific areas, leaving the incidence in outpatient care and the overall incidence of ADEs largely unexplored. A systematic review of the results issued from European studies on adverse drug events is available in the Appendix 4.1.

Although most health problems associated with the use of medicines are relatively minor, serious adverse events may lead to hospitalisation, disability or death. But because drug exposure is so high, even a very low ADE rate can lead to a large number of serious injuries or death.

[i] French Society of Clinical Pharmacy' definition: "A medication error is any deviation from ordinary standards of care appropriate for the time of the medicine therapy of a patient. A medication error is a non-intentional omission or failed activity related to the medication use system, which can be the cause of a risk or of an adverse event reaching the patient. By definition, a medication error is preventable because it evidences what should have been done and what was not during the medicine therapy of a patient. A medication error can concern one or several stages of the medication use system, such as: formulary selection, prescription, dispensing, validation, preparation, storage, delivery, administration, therapeutic monitoring; and information; but also its interfaces, such as communications and transcriptions".

2.1.1. Hospitals

Only a few studies examined **overall ADEs** among hospital inpatients. Prospective studies reported ADE incidence rates ranging from 2.4 to 6.5 ADEs per 100 admissions in the United States.[33,34,35] Two retrospective studies drawing on state-wide samples of hospital patients in the United States, focusing in the first place on negligence and **serious ADEs**, found a rate of 0.72 for every 100 patients admitted in New York[4] and of 0.62 in Colorado and Utah.[36] In France, a national multi-centre study on serious adverse events revealed an incidence of 6.6 ADEs per 1,000 patient days.[11]

According to the results of European studies (see Appendix 4.1), the incidences of ADEs varied between 2.1% and 19.8% for inpatients at internal medicine wards, 2.6% and 21.5% in paediatrics, and seem to be more important in geriatrics when comparative data are available.
ADEs may even be fatal. But there are too few data for a reliable estimate of **fatal ADEs** in European hospital settings.[37]

Risk factors for ADEs have been related to the medication use, particularly to dosing (OR: 1.2-3.7), nursing division (OR: 1.5-3.8), and administration route (OR: 1.4-149.9). When compared with the oral route of administration, intravenous administration was a risk factor (OR:1.5-14.4). The highest risk factors identified were patient-controlled analgesia (OR: 6.6-149.9) and epidural routes (OR: 3.0-64.2).[38]

2.1.2. Hospital admission

A meta-analysis of studies analysing the ADE rate leading to hospital admission are mostly based on North-American studies (of very different design), report ADE incidence rates ranging from 0.2 to 41.3 ADEs per 100 admissions, with mean values between 2.4% and 6.7%.[39,40,41,42,43]
European studies report incidence rates of admission caused by ADEs (see Appendix 4.1) ranging:

from 0.5 to 6.5 per 100 overall admissions, according to multi-centre studies,
from 0.2 to 13.8 per 100 admissions in medicine,
from 1.5 to 4.1 per 100 admissions in paediatrics,
from 5.3 to 18.4 per 100 admissions in geriatrics,
from 1.1 to 9.6 per 100 emergency admissions,
from 0.01 to 0.5 per 100 admissions after visits to emergency units.

ADEs cause between 0.3% and 20.2% visits to emergency units.

Meta-analyses performed in 2001 revealed that the odds of being hospitalised by ADR related problems is 4 times higher in the elderly than in younger people (16.6% vs. 4.1%).[42] Mean age is strongly associated with preventable drug-related admissions: a meta-analysis of studies in older patients (mean age >70) reported estimates of prevalence about twice as high as in studies on younger patients.[44]

2.1.3. After discharge from hospital

The transition from hospital-based care to community-based care is critical. Changes in medication are common during the transfer between hospital and nursing home and are a cause of ADEs.[45] Adverse events occurring after discharge from hospital reveal the extent of the gap in the continuity of care, particularly for medication management. Canadian studies show that the most common ADE experienced in discharged patients with adverse events (19 to 23%) were ADE's (66%-72% of the AEs).[46,47]

2.1.4. Nursing homes

There are even fewer studies on the incidence of ADE in nursing homes than in hospitals and none examined more than one or two institutions.As with hospital studies, the definition of what constituted an ADE varied substantially. One study with a narrower definition reported an incidence of 0.44 ADEs for every month that a patient spent in this institution.[48] compared with 0.71 ADEs reported in a second study with a much broader definition. This definition comprised ADRs in general.[49] These rates are overall comparable to the rates reported by one study of hospital ADEs that presented ADE incidence in terms of time spent in the hospital.[4]

2.1.5. Primary care

Studies on the incidence of ADEs among outpatients are extremely rare. A study reported an ADE incidence rate of 5.5 per 100 patients. [50] In a prospective cohort study, including a survey of patients and a chart review, 25% patients had at least one ADE, 16% of them requiring a visit to a clinical facility. 28% of the ADEs were reversible and 11% were preventable. Of the reversible events, 63% were attributed to the physician's failure to respond to medication-related symptoms and 37% to the patient's failure to inform the physician of the symptoms. [51]

The revision of electronic patient records in primary care using computerised queries shows potential for detecting preventable drug related morbidity (PDRM). A pilot study shows an overall incidence of 1.0% in the United-Kingdom.[52]

It is not surprising that with a broader definition of an ADE the incidence rate will be higher. However, if the same ADE definitions are applied rigorously and the same drug distribution system is used, ADE incidence rates are relatively similar.

2.2. Incidence of preventable adverse drug events

Medication errors may not systematically result in an adverse outcome. If they do, they would result in preventable ADEs and indicate a health damage to the patient (i.e., a clinically manifest adverse outcome).

2.2.1. Hospitals

By far most medication error studies have been carried out in hospitals in the United States. Medication errors occur in 5.15 per 100 admissions. The error affected adversely patient care outcomes (preventable ADE) only in 0.25 per 100 admissions .[53] The reported median incidence of preventable adverse drug events in United States hospitals is 1.8 per 100 admissions (range, 1.3-7.8%).[54] This range is similar to the reported incidence of preventable adverse drug events in European hospitals (0.4-7.3%: see Appendix 4.1). An estimated proportion of 18.7 - 56% of all ADEs among hospital patients result from medication errors and would be preventable.[55] The median preventability rate of ADEs is 35.2% (range, 18.7-73.2%). The more serious an ADE is, the higher is its preventability.[4,35]

Analysing the processes were preventable ADEs occurred,
- Leape found that 39% of the primary errors leading to a preventable adverse drug event occurred at prescribing, 38% at administration, 11% at dispensing and 12% at transcription;[56]
- Kaushal reported less than 30 preventable adverse drug events but showed a similar pattern: prescribing and administration stages were most often associated with preventable adverse drug events.[57]

When considering the organisation of the hospital drug use system, more preventable ADEs occur within traditional ward stock systems than in unit dose drug distribution systems (see Appendix 4.1, **Error! Reference source not found.**

2.2.2. Hospital admission

Preventable adverse drug events in primary care lead to hospital admissions, which are considered as an indicator of the seriousness of the clinical consequences. European research studies in the hospital sector indicate that the part of preventable ADEs in admissions caused by ADEs ranges from
47% to 72% according to multi-centre studies,
23.1% to 70.6% in medicine,
44.3% to 60.9% in intensive care,
30% to 79.6% in geriatrics,
32% to 66.7% in emergency admissions, and
37.9% to 46.8% of visits to emergency units caused by ADEs.

A considerable part of the hospitalisations due to adverse drug events are preventable. A subgroup analysis performed in 2001 revealed that up to 88% of the ADR related hospitalisations are preventable in the elderly. In the younger population this is only 24%.[42]

2.2.3. After discharge from hospital

In France, the incidence for post discharge ADRs in primary care was 0.4 per 100 admissions in a prospective study where general practitioners reported all cases of an adverse reaction to a medicine prescribed in hospital among patients who consulted them within 30 days of discharge. 59% of the ADRs they were considered preventable.[58]

Summarising the data presented above, it evident that preventable adverse drug events are a concern for all the European health care systems, revealing that medication practices are not safe. Moreover, adverse drug events are shared between each component of the health care system, due to the lack of safety at the interfaces.

2.3. Incidence of medication errors

Medication error rates should be considered as quality indicators of the different processes of the medication use system. Even if there are still too few reliable data on the frequency of medication errors in European countries, the available studies carried out in Europe reveal that medication errors have a similar magnitude as in the United States and other countries.

Medication error rates have often been played down because most of medication errors are minor and seemed to have little consequences. However, some dramatic errors that happened with high risk medicines showed that failures in the medication use system are very similar.

2.3.1. Medication administration errors

The direct observation technique, originally developed in 1962 in the United States, is the most effective method to quantify the administration errors (see II.1.1) and has been used in more than 50 studies which results are provided and discussed in detail in Appendix 4.2.[59,60] The evidence issued from comparative studies conducted during the 1960s and the 1970s led to establish unit dose dispensing of medication as a standard of practice in the hospitals in the United States since it supported nurses in medication administration, reduced the waste of expensive medicines and enabled patients to be more easily charged for inpatient doses.[61,62,63]

Research studies with the same direct observation technique have also been undertaken in Europe, mainly since the 1990s, providing the following medication administration error rates. Wrong-time medication errorswere excluded (see Appendix 4.2):

5.1% to 47.5% in traditional floor stock or ward stock systems;
2.4% to 8.6% in the UK ward stock system with original prescription and daily ward visits by pharmacists;
7.2% to 9.1% in patient prescription distribution systems;
10.5% in a unit dose drug distribution manual system;
2.4% to 9.7% in unit dose drug distribution computerised or automated systems.

Comparative studies support strongly that individualisation of drug distribution systems reduces the incidence of medication errors and of nosocomial adverse drug events.[64]

European studies indicate that the rate of errors concerning intravenous administration in hospitals are considerably higher than those involving medicines for oral use.[65,66,67,68,69,70] In one study, at least one error occurred in 49.3% of intravenous medicine doses prepared on hospital wards. 1% were considered errors with potentially severe consequences and 29% errors of potentially moderate severity.[71] This particular risk is mainly due to the lack of ready-to-use unit dose packages of injectable pharmaceutical forms on the European market and to inadequate human resources in hospital pharmacies.

2.3.2. Prescribing errors

Prescribing error rates vary widely among different prescribing systems and different hospitals, and are difficult to compare since definitions are not standardised. Studies suggest that prescribing errors occur in 0.3-9.1% of prescriptions issued for hospital inpatients, causing health damage to approximately 1% of inpatients.[72,73]

Less is known about prescription errors in primary care, the consequences of which may be reflected in medicine related hospital admissions. A British retrospective study survey indicates a 7.5% error rate in prescriptions issued in general practice.[74]

2.3.3. Dispensing errors

There was a small number of studies on dispensing errors which were identified at the final check stage of hospital pharmacies [75,76] (e.g. 1.65% in a Spanish hospital,[77] 2.1% in a British hospital pharmacy with an additional identification or 0.02% outside of the pharmacy).[78]

There is very little published evidence concerning dispensing error rates by community pharmacies:[79] A United States observational study in 50 community pharmacies revealed 1.7%.[80] A feasibility study for recording of dispensing errors and near misses in four British primary care pharmacies found respectively 0.08% and 0.48% rates.[81]

As a conclusion, available studies analysing the frequency and characteristics of medication errors in European countries show that medication error rates should be considered as quality indicators of the different processes of the medication use system (see Table 2).

Table 2: The incidence of medication errors in Europe

Stage in the medication use system	Ambulatory care	Hospital settings	Comments
Prescribing	**7.5%**	**0.3 - 9.1%**	% of medication orders
Dispensing	**0.08%**	**1.6 - 2.1%**	
Administration	Not available		Direct observation studies
		49.3%	- intravenous medicine doses prepared on wards
		5.1 - 47.5%	- traditional floor stock or ward stock systems
		2.4 - 8.6%	- ward stock system with original prescription and daily ward visits by pharmacists
		7.2 - 9.1%	- patient prescription distribution systems
		10.5%	- unit dose drug distribution manual system
		2.4 - 9.7%	- unit dose drug distribution computerised or automated systems

2.4. Costs of preventable adverse drug events

United States data

Several studies carried out in the United States have investigated ADEs in hospitalised patients and their impact on hospital costs. Four out of the five studies that specifically analysed the average excess hospital costs in the United States resulting from ADEs, estimated **$US1 939 to $2 595** per case.[33,82,83,84] The last study reported average ADE costs of $US783 per case.[85] The admissions caused by ADEs averaged $US6 885 to 7 857 per event.[83] By extrapolating the findings about ADEs to all hospital patients in the United States, the additional hospital costs were estimated $US 1.56-4 billion per year.[33,82]

Furthermore, research studies in different countries have quantified the incidence and economic consequences of adverse drug effects occurring in primary care and leading to hospital admission and emergency unit visits. They have shown that preventable ADEs constitute between 43.3% and 80% of all adverse events leading to emergency unit visits and hospital admissions and disproportionately increase health care costs. Finally, a recent estimation revealed that in the United States the costs of problems linked to medicines use in primary care exceeded $US177 billion in the year 2000.[86]

European data

Studies carried out in Spain have indicated that the 4.7% of hospital admissions caused by preventable ADEs caused on average costs of **€3 000 per event**.[87] In Germany, a study on medicine related hospitalisations on the basis of an average length of stay of 13 days at a reimbursement level of €287 , estimated the drug related hospitalisation cost to €3 700 and the annual direct cost for Germany to €400 million.[88]

In the UK, a study on ADR directly leading to the admission, most of them definitely or possibly avoidable (72.0%) with overall fatality in 0.15% estimated the annual cost of such admissions to the NHS to €706 million on the basis of a medium bed stay of 8 days, accounting for 4% of the hospital bed capacity and at average costs per medical bed day).[89] In France, the direct costs of ADEs admitted to emergency units to the French public hospital system is estimated about €636 million, i.e. about 1.8% of the annual budget in 2002.[90]

Table 3: The cost of preventable adverse drug events in European countries

Country	Additional hospital cost per preventable adverse drug event	Estimate of the national annual cost
Spain	**€ 3 000**	
Germany	**€ 3 700**	€ 400 million
United-Kingdom		€ 706 million (72% preventable)
France		€ 636 million (38% preventable)

On this basis (summarised in Table 3), European health authorities should recognise the high incidence of preventable adverse drug events and the important increase of health care costs by patient harms.

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Chapter I - Learning from medication errors

Key points:

- Patient safety incidents should be considered as opportunities to learn which component has failed in a system for preventing worse repeating. Therefore, the World Health Organization, the Council of Europe and other authorities recommend health care organisations to implement patient safety incident reporting systems at both local and national level.
- Medication errors are an important component of patient safety incidents, so that medication error reporting systems (MERS) may be established as stand alone systems or integrated in comprehensive patient safety incident reporting systems. However, either alone or in a wider reporting system, MERS do not exist in all European countries.
- The characteristics of a culture of safety endorsed by the Council of Europe Recommendation Rec(2006)7 are necessary prerequisites of successful reporting systems, especially MERS, and include incident report analysis and trend monitoring, risk reduction initiatives, evaluation, dissemination of learning. MERS should be non-punitive, confidential, independent, based on expert analysis, timely, systems-oriented, and responding.
- In order to fully understand the (potential) health damages caused by medicines, European health authorities should establish patient safety incident reporting systems incident involving medicines. Such MERS must involve primary care as well as hospital settings, nursing homes and should comprise local, regional, national and European elements.
- Local MERS in both primary and secondary care should be managed by a safe medication practice committee that is authorised to deal with medication safety. This multidisciplinary committee should include pharmacists, physicians, nurses, quality managers and administrators.
- All Council of Europe member states should establish a recognised national focal point for safe medication practices which cooperates in a collaborative and complementary way with pharmacovigilance system. It should be based on a national system for reporting medication errors, analysing causes and disseminating information on risk reduction and prevention. Anonymisation of data should be ensured as well as confidentiality for reporting health care practitioners.
- Council of Europe member states should rapidly adopt and promote standardised operational definitions and a common taxonomy in order to establish efficient and standardised reporting systems in Europe.
- European health authorities invited to facilitate the sharing of information about medication errors and safe medication practices that have been found effective to minimise these risks. Therefore, they should
    - standardise requirements for national centres,
    - build a European network of national MERS whose representatives should meet formally periodically to exchange information and agree actions across European countries,
    - mandate the co-ordination between MERS as well as the management and the promotion of safe medication practices in Europe. It could be envisaged that this is co-ordinated supranationally through a permanent network;

- ensure that all medication error reports related to medicines' naming, labelling, packaging and advertising are shared with the European Medicines Agency and national drug regulatory agencies together with recommendations for the prevention of these type of errors (i.e. the introduction of important details for use into SmPCs or PILs);
- ensure that all medication error reports related to the recommended International Non-proprietary Names (INN) are shared with the World Health Organization (WHO Essential Medicines Department), in order to submit proposals for substitution to the WHO INN programme.

All medication errors should be considered as opportunities to learn which element of the medication use system has deficiencies in order to reduce the risk of similar errors recurring. When considering the ways to learn from errors and to share an in-depth analysis at European level, medication errors reporting systems (MERS) seem a necessary prerequisite as well as backbone to successfully preventing medication errors. The ultimate goal of MERS is to take action for improving the safety of the medication use system.

Since medication errors are a part of errors occurring in the course of medical treatment, contributing to patient injury through preventable adverse drug events, MERS should be considered as specific, specialised patient safety incident reporting systems. Their general features are presented with special references to the Council of Europe Recommendation Rec(2006)7 of the Committee of Ministers to member states on management of patient safety and prevention of adverse events in health care" (see Appendix 1) and to the "World Health Organization draft guidelines for adverse event reporting and learning systems". [1,2]

At present, only a few European countries have established MERS at national level or in hospitals, either alone or integrated in a patient safety incident reporting system (see Appendix 5). Moreover, MERS do not exist in all European countries.

One of the main difficulties encountered during the design of any MERS is the adoption of an appropriate terminology and taxonomy, allowing in particular further exchanges between MERS. From this point of view, the lack of standardisation is a major obstacle for co-operation between MERS especially at European level.

However, standardisation is not a sufficient condition for building successful MERS, since their processes and technology involve communication, analysis, dataset formatting, feedback, response and dissemination of lessons learnt from reported medication incidents.

This chapter presents
- objectives of and different levels of medication error reporting systems,
- requirements for reporting medication errors,
- concepts and methods needed for analysing reported medication errors,
- feedback management from reported medication errors,
- recommendations for a European co-ordination to share information on medication errors and safe medication practices.

I.1 Medication error reporting systems (MERS)

As a powerful way to learn from medication errors, MERS provide the basis to improve medication safety at different levels of the health care system. MERS help reviewing error reports collectively, avoiding individuals to feel guilty and isolated.[3]

I.1.1 Objectives of MERS

The primary objective of a MERS is the enhancement of patient safety by learning from adverse events, errors and near misses[i]. Reporting and collection of adverse drug events, near misses and medication errors are the first step to learn from patient safety incidents. However, a MERS is meaningful only if each report is subject to an in depth analysis and is evaluated and feedback is given to the involved professionals and to all other who could learn from this medication error[ii].[2,4,5]

Information on near misses and intercepted errors is as valuable as the events that resulted in errors.[6] Reports of rare types of medication errors offer the opportunity of detecting unknown risks and early modelling of innovative safety organisations.

Valuable insights into the medication process can be gained from medication error surveillance and tracking.[4] Beside the knowledge issued from epidemiological and observational studies, MERS enhance awareness on medication errors more quickly than case reports submitted due to publication delays. By identifying the types of the medication errors and at which stages they are involved, MERS provides specific knowledge on the medication use system. By evaluating the causes of medication errors, their contribution and environmental factors, MERS provide more accurate choices for corrective and preventive actions.

MERS allow that lessons can be shared that others can avoid the same mishaps.[4] Providing feedback increases the awareness of medication errors and involve health care practitioners in medication errors prevention due to both a better understanding and acceptance of solutions.

It is recommended that MERS involve both private and public sectors and facilitate the involvement of patients and their relatives in all aspects of patient safety activities[iii,iv]. Thus, MERS assist health care practitioners and patients to be proactively engaged in medication error prevention and furthermore, to reduce the risk of similar errors recurring.[3]

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[i] Council of Europe Recommendation Rec(2006)7 of the Committee of Ministers to member states on management of patient safety and prevention of adverse events in health care (see Appendix 1) para ii.d.
[ii] Recommendation Rec(2006)7 Appendix D1.1.
[iii] Recommendation Rec(2006)7 para iii.e,f.
[iv] Recommendation Rec(2006)7 Appendix D1.3.

I.1.2 Reporting at each level of the health care system

The Council of Europe Recommendation Rec(2006)7 recommends to promote the development of local reporting systems for collecting and analysing patient safety incidents and, further, to aggregate them at national level[v]. At all levels, actual and potential problems and errors should be reported when they occur[vi].

The efficiency of MERS in improving medication safety of the national European health care systems depends on the exchange of information and co-operation between these different levels.

Most of the concepts developed in this chapter are common to all MERS. However, sometimes differentiations have to be made between the different levels in which these concepts are implemented. Therefore, a brief description of these levels of MERS is provided in order to give a broader view on their interfaces.

I.1.2.1 Local medication error reporting systems

The greatest effect on patient safety is generated locally when the organisation uses patient safety incident reporting as part of a continuous system of safety and quality improvement. Local safety and quality initiatives should be promoted in all health care units and organisations, both in primary and secondary care. The follow-up assessment of the patient safety policy should start at the lowest possible level at the units[vii].

Each health care site has unique systems and circumstances that necessitate specific data. This can be accomplished only through an adequate incident reporting system within the facility.[6] In order to accomplish this objective, health care sites should establish a safe medication practice committee authorised to deal with medication safety. This multidisciplinary committee should include pharmacists, physicians, nurses, quality managers and administrators.

Besides, the chief executive, the board and administrative and clinical directors need to establish an environment in which the whole organisation learns from safety incidents and where staff is encouraged to both proactively assess and reactively report risks[viii]. Based on this knowledge, it becomes possible to amend these systems to reduce risk and improve patient safety.[5] Local policies should clearly describe how organisations manage staff involved in incidents, complaints and claims. Staff should be comprehensively trained in clinical and administrative procedures for responding to a serious error[ix].

Lessons learned from a medication error at one organisation can prevent the same or a similar error from recurring at another facility if the lesson learnt is disseminated to other organisations in the aftermath. Therefore, health care practitioners and providers should be encouraged to share anonymously reports on medication errors with others.

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[v] Recommendation Rec(2006)7 para iii.d.
[vi] Recommendation Rec(2006)7 Appendix B.3.f.
[vii] Recommendation Rec(2006)7 Appendix D1.5.
[viii] Recommendation Rec(2006)7 Appendix B.3.
[ix] Recommendation Rec(2006)7 Appendix B.3.f.

As a conclusion, local programmes for reporting errors and the dissemination of lesson-learnt points should be developed and all serious medication errors and near misses reported to a national focal point.[5]

I.1.2.2 National medication error reporting systems

A national MERS offers the additional benefit of sharing experience gained at the local level. It should be comprehensive, addressing all levels and areas of health care provision, including the private sector service[x]. In this way, it is possible to select those medication errors where national learning and action can prevent future recurrence[xi]. Aggregation of data will have greatest value in revealing systematic failures, accumulation of certain incidents or failures in new equipment that cannot be readily identified at local level, i.e. where a larger dataset is required to make such issues more apparent[xii].

A variety of MERS have been established at national level. In North America and in some European countries, medication errors may be reported to a specific MERS or to broader patient safety incident reporting systems. The presentation of some existing MERS is summarised in Appendix 5 demonstrating the variety of national systems.

Example of action by a national MERS

In the United Kingdom, the National Patient Safety Agency (NPSA) National Reporting and Learning System (NRLS) includes a MERS.[7] Between 2000 and 2005 there were seven published case reports of deaths due to the administration of high dose (30 mg or greater) diamorphine or morphine to patients who had not previously received doses of opiates. These case reports prompted the National Patient Safety Agency (NPSA) to review reports in the NRLS on the same subject. Between January and October 2005, the NPSA received 16 reports of similar patient safety incidents of which two had resulted in the death of the patients. Many of these incidents involved diamorphine and morphine 30mg ampoules being selected in error for lower strength ampoules and overdoses were administered as the appearance of these products was very similar. In May 2006, the NPSA issued "Safer Practice Notice 12" to identify this risk and recommend safer practice guidance concerning risk assessing the prescribing, supply, storage, preparation and administration of diamorphine and morphine ampoules to reduce patient harm.[8]

MERS contribute to a wide dissemination of recommendations for improving the patient safety and preventing medication errors.

[x] Recommendation Rec(2006)7 Appendix D1.7.
[xi] Recommendation Rec(2006)7 Appendix D1.6.
[xii] Recommendation Rec(2006)7 Appendix D1.8.

I.2 Providing conditions for reporting medication errors

As consequences of failures arising at a specific part of patient care, medication errors have to be analysed by taking account more in detail of the specificities of the medication use system. The more so as drug events are the most common single type of serious adverse events. The experience offered by the already established MERS, such as, in particular those operated by the Institutes for Safe Medication Practices or the British National Patient Safety Agency provide concepts and tools for developing such highly specialised specific reporting systems. Therefore, in line with the Recommendation Rec(2006)7, a focus will be put on the specific conditions needed for implementing MERS.

I.2.1 Characteristics of reporting systems

Reporting of medication errors is voluntary and depends on the willingness of frontline clinical staff. Appropriate policies should be designed to remove existing barriers to reporting[xiii]. In order to overcome many of these barriers and to enhance the effectiveness of error reporting, Leape summarised the following characteristics of successful reporting systems, also applicable to an optimal MERS which should be non-punitive, confidential, independent, based on expert analysis, timely, system-oriented, and responding.[2,4]

These principles are endorsed by the Recommendation Rec(2006)7 which stipulates that a patient safety incident reporting system, encompassing a MERS, should be [xiv]:
- non-punitive and fair in purpose,
- independent of other regulatory or accrediting processes,
- offer enabling conditions for the health care providers and health care personnel to report safety incidents (such as voluntarily, anonymity, confidentiality, where applicable).

The appendix to the Recommendation Rec(2006)7 gives additional indications on its features: a reporting system should[xv]:
- be objective with findings and recommendations;
- encourage unrestricted reporting by all working in the health care system;
- provide incentives for reporting.

These characteristics imply a set of safeguards which consider comprehensively the patient's rights and privacy, the needs of the reporting health care professional and the MERS itself. Additional considerations regarding these characteristics are provided by several parts of the Appendix to the Council of Europe Recommendation Rec(2006)7.[xvi]

[xiii] Recommendation Rec(2006)7 Appendix D2.5.
[xiv] Recommendation Rec(2006)7 para iii.
[xv] Recommendation Rec(2006)7 Appendix D1.4.
[xvi] Recommendation Rec(2006)7 Appendix B, Appendix D1, Appendix J1.

I.2.2 Facts to be reported to MERS

According to the Recommendation Rec(2006)7, reporting systems for patient safety incidents should receive reports of serious and fatal events caused by incidents, "near misses", and hazardous situations that could lead to safety incidents[xvii]. "Patient safety incident" means any unintended or unexpected incident(s) that could have or did lead to a health damage of one or more persons receiving health care (see Appendix 3). "Patient safety incident" is an umbrella term which is used to describe a single incident or a series of incidents that occur over time and to avoid the use of the word "error" considering its negative meaning.[3]

Since the analysis of medication errors is very specific, careful attention must be paid to the exact type of events reported to MERS. A correct understanding of this matter should allow a complementary design with the different patient safety incidents reporting systems and avoid any confusion with the pharmacovigilance systems specifically dedicated to adverse drug reactions. Thus, the positioning of MERS in the field of patient safety appears more clear as well as the relations between these programmes.

MERS are not only designed to receive medication errors that have caused health damages (preventable adverse drug events). They should also analyse medication errors that do not cause harm including "potential adverse drug events", "close calls" or "near misses" as well as circumstances or events that may lead to errors.

I.2.3 How to report to MERS

With regard to the variety of situations to be reported to MERS, some recommendations may be implemented, particularly at local level[4]:

- give clear and concise reporting guidelines: health care practitioners are more likely to report if reporting guidelines are established;
- develop criteria for what should be reported to identify not only errors that reach the patient, but also near misses;
- use standardised forms for reporting based on standardised error reporting taxonomy (see I.3.2);
- creating incentives or rewards for error reporting may encourage health care practitioners to report.

The medication error reporting forms should be as simple as possible, since detailed information for analysing the medication error may be obtained during a comprehensive interview. Staff should also be aware that when an incident does occur, they should keep relevant medicine and device packs, containers or any other material that may be important in analysing the cause of error.

Medication error reports should not highlight single individuals or departments for blame, neither speculate as to why an error may have occurred. Overall, such speculation should be not recorded in the patient's record, only specific facts about the administration of the medicine and subsequent therapeutic measures. The cause of an incident can only be determined after investigation even if involved care-givers are asked about what they think about the possible causes and how similar incidents may be prevented.

[xvii] Recommendation Rec(2006)7 Appendix D1.4.h.

The development of Internet-based reporting systems should make the establishment of national and European-wide medication error databases easier to maintain and less costly to operate[xviii]. The differences in the structure of information related to medication errors should be clearly made between reporting and analysing.

I.3 Analysing reported medication errors

However, each reporting system has its own terminology and taxonomy for the information related to the errors. In consequence, it is difficult to share and compare data across European countries and, indeed, within the same country. A critical key to establish efficient and standardised reporting systems in Europe is undoubtedly a common taxonomy. Besides, it is critical to do this without delay, considering that some countries are just starting working in this area. Otherwise, each country will develop its own system, and medication safety will become a Babel tower.

I.3.1 Requirements for analysing medication errors

Being able to analyse medication errors is a necessary prerequisite for understanding how medication errors are recurring. The collecting data of medication errors is an activity of value for improving patient safety only if these data are submitted to expert analysis and trend monitoring and further are taken into account in recommendations on how to prevent them.

I.3.1.1 Medication error analysis

I.3.1.1.1 Medication error analysis at local level

At the level of health care organisations, the chief executive, the board and administrative and clinical directors should establish an environment in which the entire organisation learns from safety incidents and where staff is encouraged to both proactively assess and reactively report risks. Medication errors should be reviewed and investigated thoroughly, thoughtfully, 'transparent' and fairly, free from hindsight bias[xix].

Medication incident reports and data obtained by other methods used to track and monitor the medication use system (see chapter II), can be analysed through a variety of techniques. Typically, the analysis focuses primarily on systems and processes not on individual performance.[9] The objective of the analysis is to reveal the underlying system failures aiming at redesigning systems to reduce the likelihood of patient injury.[2]

The process of categorising the data and developing solutions should be started by the classification of the incident and simple analytic schemes.[2] The classification by taxonomy constitutes the first step of analysis after a notification of an incident has been received. The classification facilitates the aggregation of the data (see I.3.1.2). Mostly, the classification of incidents together with further registration in a database at local level are sufficient to complete the analysis of the incident. However, when a serious adverse drug event has happened it is advisable to carry out in depth research by means of different techniques such as root cause analysis (RCA). An example of this approach is the Sentinel Events Monitoring Programme

[xviii] Recommendation Rec(2006)7 Appendix D1.9.
[xix] Recommendation Rec(2006)7 Appendix B.3.h.

required by the US Joint Commission on Accreditation on Health Care Organizations (see Appendix 5.1) and the tools for root cause analysis developed by the US Veterans Affairs National Center for Patient Safety (NCPS).

Root cause analysis is a systematic investigation technique looking beyond the affected individuals and seeing to understand the underlying causes and environmental context in which the incident happened.[5] The analysis focuses on identifying the hidden conditions that underlie variations in performance and on developing recommendations for improvements to decrease the likelihood of a recurrence.[10] It is not limited to the process of incident evaluation. It comprises design, implementation, evaluation and the follow-up of improved safety systems[xx].

Root cause analysis investigation techniques are usually applied to serious adverse events or critical incidents also known as sentinel events. There is a variety of methods for stratifying events for the purpose of deciding whether root cause analysis should be undertaken (i.e. see I.3.2.4 for the "severity assessment code" matrix).

I.3.1.1.2 Analysis of large datasets of medication errors

When medication error reports are aggregated in large datasets, they can be analysed to understand the frequency of type of errors, characteristics and contributing factors. Examples are provided in the National Reporting and Learning System (NRLS) of the NPSA or the MedMARx° programme overseen by the US Pharmacopoeia.

The calculation of events over time (trend analysis) permits to identify significant changes suggesting new problems. A cluster of particular types of suddenly arising medication errors suggest a need for further analysis and allows to recognise specific problems and develop research for improvement.

Under the condition of an appropriate set of data requested, MERS can provide valuable information about risk. The probability of the recurrence of a specific type of error can be calculated as well as the average severity of health damage caused by the error. A risk analysis of this specific type of error based on a decision tree considering severity and frequency may be provided (see I.3.2.4).

Causal analysis is facilitated by correlations established between a specific type of medication error and particular causes or contributing and environmental factors. Insights into the medication use system's vulnerabilities are provided and allow to understand the system failures that caused the medication error.

[xx] Recommendation Rec(2006)7 Appendix D.2.2.

I.3.1.2 Rationale underlying a common medication error taxonomy

Operational definitions and taxonomy are needed to permit an efficient use of medication error data and should be translated into analysis into action for preventing the recurrence of medication errors.

Therefore, the Recommendation Rec(2006)7 recommends to international co-operation in building a platform for mutual exchange of experience and learning on all aspects of health care safety, including the development of a standard nomenclature and/or taxonomy for patient safety and safety of processes of care[xxi].

A common medication safety taxonomy of medication errors is may allow the standardisation of detection, analysis, classification and recording of medication errors by providing a standardised language and a structured classification of medication error related data. These data can be used for the development of databases analysing medication error reports whatever the level of the health care system they come from.[11,12]

Its aim is to allow a complete analysis of medication errors in different situations. The availability of such a tool is necessary to promote the implementation of MERS in health care systems.

The outstanding efforts of the National Coordinating Council for Medication Error Reporting and Prevention (NCCMERP) established in the United States of America (USA) in 1995 have led to the first recognised taxonomy shared at national level by certain MERS (e.g. ISMP, USP, FDA and others (see Appendix 5.1)). Likewise, it has constituted a very important instrument in the USA to facilitate the development of internal MERS in hospitals.

In addition to an improved sharing of medication error analyses, information exchange between European MERS could be facilitated by the use of a recognised common language. This effort will provide a useful instrument for standardising the detection, analysis, classification and record of medication. The use of a common taxonomy will aim at contributing to the establishment of programmes of detection and analysis of medication errors at local, regional, and national levels. It will allow to compare the information proceeding from different MERS, particularly at national and European levels. Therefore, sharing data at European level on the basis of a common database is strongly recommended.

I.3.2 Elements of a medication error taxonomy

Starting from earlier proposals, the NCCMERP published in 1998 the first taxonomy classifying the different aspects of medication errors and provided an essential basis.[11,13]

Existing MERS in Europe have adapted the NCCMERP taxonomy to their context of work. Some of them have carried out modifications to the order of the main chapters aiming at increased coherence with the logical sequence guiding medication error analysis and facilitating the practical application of taxonomy. Other changes were introduced concerning the categories and subcategories of the different criteria in order to improve coherence with national practices. These efforts provide a common data set for medication error reporting and analysing.

[xxi] Recommendation Rec(2006)7 para vi.f.

A medication error taxonomy is a structured classification of medication error categories and subcategories allowing to document the different aspects of a medication error. A medication error category is a group or a class of medication errors presenting the same attribute (characteristics) according to a definite criterion, such as the degree of realisation (potential or achieved), the type of error, the stage of occurrence within the medication use process, the severity of the consequences and the cause.[14]

Existing medication error taxonomies use very similar categories and subcategories (see Table 4).

Table 4: Main categories and subcategories of existing medication error taxonomies

Main categories of a medication error taxonomy	NCCMERP	ISMP Spain	REEM	NPSA
Descriptive elements				
Patient information	10	1.3	X	PDXX
Details of the circumstances of the medication error				
Date & time	21-22	2.1-2.3	X	IN03
Setting (initial error, perpetuation)	23	2.4-2.5	X	RP02
Personnel involved (initial error, perpetuation, discovery)	60	2.6-2.7	X	STXX
Associated devices involved			X	DEXX
Description of the circumstances			X	IN07
Prevention, mitigation, recovery				PD12-4
Medicines involved (given, intended)	50	4.2-4.3	X	MDXX
Stage of the error in the medication use system (initial, secondary)		5.1	X	MD01
Patient outcome				
Gravity of patient outcome	30	3.1	X	PD09
Clinical symptomatology		3.2		PD10
Type of error	70	5.2	X	MD02
Causes of error				MD03
Communication	81	6.1	X	
Patient name confusion		6.2	X	
Drug name confusion	83	6.3	X	
Packaging and labelling problems	85	6.4	X	
Equipment & devices used in dispensing/preparing/administering	89	6.5	X	
Human factors	87	6.6	X	
Contributing and environmental factors (system related)	90	7	X	
Prevention, minimisation			X	PG04

However, a medication error taxonomy should remain sufficiently flexible to allow every health care site to adapt and select these fields and elements that match working processes and structures.

I.3.2.1 Description of a medication error

The identification of the case is intended to assign an internal code to identify the incident.

Information related to the patient must remain anonymous. The only information related to the patient used in a MERS includes age and sex in order to ensure the confidentiality of the information.

Generally, the circumstances of the medication error are described in a free text before structuring data using a taxonomy. The details of the circumstances of the medication error include, date, day of the week and time (hours) of the event, setting (initial error, perpetuation), health care practitioners and persons involved (initial error, perpetuation, discovery), associated medicines and devices involved, a description of the circumstances, information and proposal for prevention, treatment and recovery.[10]

The purpose is to describe when, where, who and how the medication error happened and/or has been prevented.

I.3.2.2 Medicines involved in a medication error

The information related to the medicine(s) involved in a medication error includes, names (both proprietary/trade name and generic name/INN), dosage or pharmaceutical form, strength, dosage, frequency and route of administration. Special attention should be paid when describing packaging and labelling in case they are involved in the medication error.

Other descriptive items are status, the manufacturer, distributor, batch number (if appropriate).
It is useful for further research in medication errors databases to refer to the pharmacologic-therapeutic classification to which the involved medicine belongs. In case of confusion of two medicines, information should be provided for the medicine used and for the intended medicine.

I.3.2.3 Level of the medication use system where the error occurred

It is impossible to analyse a medication error without knowing about the processes of the medication use system where it happened. Therefore, the description of a medication error needs to include the level where the medication error occurred, was detected as well as the personnel involved.[12]

A system is a set of interdependent elements interacting to achieve a common goal. These elements may be both human and non human (equipment, technologies, etc.).[15] A process is a series of related actions to achieve a defined outcome. Prescribing medication or administering medication are processes.[16]

The medication use system is a combination of interdependent processes that share the common goal of safe, effective, appropriate and efficient provision of medicine therapy to patients. Major processes in the medication use system are the selection and procurement, storage; prescription, transcription and verification, preparation and dispensation, administration and monitoring.[12,17,18,19]

The determination of the level of occurrence of a medication error in the medication use system takes into account of theses processes. By focusing on the organisation, more emphasis is given on the system than on personnel involved. Each process and corresponding errors are described in Table 5.

Table 5: Medication errors related to the stages in the medication use system

Stages in the medication use system	Description
Prescription all the activities insured by a doctor or an authorised health care practitioner, from the coverage of a patient : the patient and medication history, the clinical examination, the prescription of complementary explorations and tests (if needed), the therapeutic decision taking into account the benefits-risks balance, the information of the patient, and the writing of the medicine order.[14]	**prescribing error:** a medication error occurring during the prescription of a medicine that it is about writing the medicine order or taking the therapeutic decision, appreciated by any non- intentional deviation from standard references such as: the actual scientific knowledge, the appropriate practices usually recognised, the summary of the characteristics of the medicine product, or the mentions according to the regulations. A prescribing error notably can concern : the choice of the drug (according to the indications, the contraindications, the known allergies and patient characteristics, interactions whatever nature it is with the existing therapeutics, and the other factors), dose, concentration, drug regimen, pharmaceutical form, route of administration, duration of treatment, and instructions of use; but also the failure to prescribe a drug needed to treat an already diagnosed pathology, or to prevent the adverse effects of others medicines.[14,2020]
Transcription reproduction, handwritten or computerised, of all or any of the information relative to the medicine therapy and used by the health care practitioners or by the patient.[14]	**transcription error:** any deviation from the initial prescription or medication order, occuring during written or computer transcribing of the prescription.
Verifying and reviewing medicine orders the clinical relevant analysis and others pharmaceutical interventions related to the medicine order and to the patient's medicine therapy	
Preparation compounding of a medicine, that it is about its formulation, about its packaging or about its labelling.[14]	**preparation error:** whatever type of medication error, of omission or commission, that occurs in the preparation stage when the medication has to be compounded or prepared by a pharmacist, a nurse, or the own patient, or a caregiver.
Dispensing set of pharmaceutical activities including: - the preparation of the doses to be administered; - the information and the advices necessary for the safe use of medicines; - the delivery of ordered medicines.[14] *Delivery* set of distributive activities insured by a pharmacist or a pharmacy technician, according to the legal rules, and containing, from the reception of a demand, the collection, the distribution and the delivery of the medicine to the wards or to the patient.[14]	**dispensing error:** a deviation from an interpretable writen prescription or medication order, including written modification of the prescription made by a pharmacist following contact with the prescriber or in compliance with the pharmacy policy. Any deviation from professional or regulatory references, or guidelines affecting dispensing procedures is also considered as a dispensing error[21] **delivery error:** whatever type of medication error, of omission or commission, that occurs in the dispensing stage in the pharmacy when distributing medicines to nursing units or to patients in ambulatory settings
Administration self-administration, including compliance, or set of activities done by nurses and including, from the notification of the prescription: extemporaneous preparation of the doses to be administered (if necessary), preliminary controls (3P: prescription versus product versus patient), the administration itself of the medicine, information of the patient, recording of the administered doses.[14]	**administration error:** whatever type of medication error, of omission or commission, that occurs in the administration stage when the medication has to be given by a nurse, or the own patient, or a carer
Monitoring set of follow-up of the patient including the clinical and biological status, each caring activity, the compliance to the treatment, the therapeutic monitoring (drug dosages) in the aim of continuous reassessment of the benefits-risks balance.[14]	**monitoring error:** failure to review a prescribed regimen for appropriateness and detection of problems, or failure to use appropriate clinical or laboratory data for adequate assessment of patient response to prescribed therapy.

I.3.2.4 Consequences of the medication error

The consequences of a medication error (outcome) is a set of events, harmful or not, with or without different consequences (including health damage) following a medication error. According to the levels, distinction has to be done between:

- the individual clinical, biologic or psychological consequences for the patient.[11] They notably include the worsening of health resulting caused by ineffective treatment or omission errors or under dosage.[20]
- The consequences for health care practitioners and the health care sites, health care insurance and the insurance companies include

- financial and economic consequences (direct, indirect, intangible), in particular: costs for hospitalisation, medical certificate, incapacity, conditions of assurance, etc.,
- judicial consequences such as claims, law suits, penalties, compensation of the patient,
- consequences of media attention for the reputation of health care sites practitioners.[14]

The assessment of the clinical severity of the outcome of the patient allows staging the level of individual harm. Harm is defined as death or temporary or permanent impairment of body function/structure requiring intervention. Intervention may include monitoring the patient's condition, change in therapy or active medical or surgical treatment.[11]

The approaches to classifying the severity of possible damages for the patient are mainly based on the NCC MERP classification because this taxonomy provides the most details for the classification of severity. When this classification is not used, the relationship between related terms should be established as shown in Table 6, in order to permit exchange of information between medication error reporting systems.

Table 6: Severity of the consequences of medication errors

NCC MERP (ISMP Spain, REEM)		NPSA terms
No error	Category A Circumstances or events that have the capacity to cause error	No harm - Impact prevented Any patient safety incident that had the potential to cause harm but was prevented, resulting in no harm to people receiving care.
Error, no harm	Category B An error occurred but the medication did not reach the patient	
	Category C An error occurred that reaches the patient, but did not cause harm	No harm - Impact not prevented Any patient safety incident that ran to completion but no harm occurred to people receiving care.
	Category D An error occurred that resulted in the need for increased patient monitoring, but no patient harm	
Error, harm	Category E An error occurred that resulted in need for treatment or intervention and caused temporary patient harm	Low Any patient safety incident that required extra observation or minor treatment and caused minimal harm, to one or more persons receiving care.
	Category F An error occurred that resulted in initial or prolonged hospitalisation and caused temporary patient harm	Moderate Any patient safety incident that resulted in a moderate increase in treatment x and which caused significant but not permanent harm, to one or more persons receiving care.
	Category G An error occurred that resulted in permanent patient harm	Severe Any patient safety incident that appears to have resulted in permanent harm y to one or more persons receiving care.
	Category H An error occurred that resulted in a near-death event (e.g., anaphylaxis, cardiac arrest)	
Error, death	Category I An error occurred that resulted in patient death.	Death: Any patient safety incident that directly resulted in the death of one or more persons receiving care.

In case adverse drug events are caused by a medication error, (clinical) symptoms and affected organ systems should be reported as additional information in detail and in line with the terminology related to adverse drug reactions as established by the WHO.[12]

From a risk management perspective, consequences for the health care site should be also kept in mind: hospitalisation; medical intervention or corrective treatment, continuation of the hospitalisation, enhanced monitoring, transfer to intensive care, mediatisation/damaged reputation, law suits, claims, and compensations.[14]

In order to prioritise the required follow-up to medication errors (see I.3.1.1.1), scoring systems are used. They are based on specific scales using a "safety assessment code matrix" [2] which consider both the potential severity and the likelihood of occurrence of events. The degree of risk is then expressed as a **risk matrix** that plots the severity of the outcome against the likelihood of its recurrence.[5]

An example is the Severity Assessment Code (SAC) matrix used by the US Veterans Affairs NCPS.[22] The SAC matrix links the severity of the event with the probability of reoccurrence in order to determine whether or not further analysis is required. An event with a SAC score of 3 indicates that a root cause analysis is required. Events with SAC scores less than 3 may be analysed in a simple and aggregate way.

I.3.2.5 Types of medication error

The characteristics of each type of medication errors should be categorised for avoiding misclassification particularly with a view to the sharing of information across Europe. Therefore, it is important to define each error type to enable its classification.

On the basis of the NCC MERP taxonomy, some types of medication errors have been added or modified by European medication error reporting systems such as ISMP Spain (see Table 7). As an example, ISMP Spain added in line with NCC MERP taxonomy 15 types of medication errors "lack of patient compliance", "wrong frequency of administration" and replaced "wrong strength/concentration" by "wrong preparation, manipulation, and/or mixing".

Subcategories were added inside the types of "wrong/improper drug" and "drug or dosage omission" to describe different subtypes associated with prescribing errors, since the NCC MERP taxonomy focuses primarily on dispensing and administration errors occurring in hospital settings.[12]

Table 7: Principal types of medication error[12]

Types of medication error		Description
ISMP Spain	NCC MERP	
1. Wrong / improper drug *1.1. Inappropriate drug selection* 1.1.1. Medication not indicated/inappropriate for the condition being treated 1.1.2. Previous history of allergy or similar adverse effect with the same medication or with another similar one 1.1.3. Medication contraindicated 1.1.4. Medication inappropriate for the patient due to his age, clinical status, or underlying pathology 1.1.5. Therapeutic duplicity *1.2. Unnecessary medication* *1.3. Transcription/dispensing/administration of a medication other that the one prescribed*	70.4 12.3	The category of wrong medication includes the inappropriate choice of medication according to the recognised indications, contraindications, known allergic reactions, pre-existing pharmacological treatment, and other factors, such as prescribing a medication for which there no indication is found (unnecessary medication). Also included in this category are transcription/ dispensing/ administration of medicines not prescribed or different from the ones prescribed.
2. Drug or dosage omission *2.1. Failure to prescribe a necessary medication* *2.2. Transcription omission* *2.3. Dispensation omission* *2.4. Administration omission*	70.1	Drug omission is considered to be the failure to prescribe a necessary medication as, for example, lack of a established prophylaxis or forgetting to include a medication when writing medical orders. It also includes a failure to transcribe, dispense, or administer a prescribed medication. Dosage omission is considered to be not transcribing/dispensing/administering a prescribed dosage to a patient before the next programmed dosage, if there were a next. Cases in which a patient voluntarily refuses to take the medication are excluded, as are decisions to not administer the medication due to existing contraindications or cases where there are obvious reasons for the omission (for example, when a patient is absent from the nursing unit for tests).
3. Improper dose *3.1. Amount given greater than the correct dosage* *3.2. Amount given less than the correct dosage* *3.3. Extra dose given*	70.2	Prescribing/transcribing/dispensing a larger or smaller dosage than necessary for the patient. It excludes deviations accepted by a particular institution as per its established criteria for professionals in charge of administration and dosages administered according to accepted criteria when the prescription does not indicate amount to be administered (for example, topical dosage forms). Extra dosage includes re-administering a dosage that has already been given.
4. Wrong frequency of administration		Prescription/transcription/dispensation/administration of a medication at a different interval than that necessary for the patient.
5. Wrong dosage form	70.5	Prescribing a medication in a dosage form different from the one necessary for the patient, or transcription/dispensation/administration of a dosage form different from that prescribed (for example, administering a slow-release medication when a conventional one is prescribed. This category excludes accepted protocols (established by the Pharmacy and Therapeutic Committee, or its equivalent) that authorise the pharmacist to dispense alternative pharmacological presentations to patients with special needs (for example, liquid forms for patients with a nasogastric tube in place or those who have difficulty in swallowing).
6. Wrong preparation, manipulation, and/or mixing	70.3	Medications incorrectly mixed or manipulated before administration. These include, for example, incorrect dilution or reconstitution, mixing medicines that are physically or chemically incompatible and incorrect packaging of the product.
7. Wrong administration technique	70.6	Inappropriate procedures or techniques in administering a medication. This category includes, for example, incorrect activation of a dosage pump or inappropriate crushing of pills.
8. Wrong administration route	70.7	Administering a medication via an unaccepted route or a route different than the prescribed one, for example, giving a formula exclusively for intramuscular administration intravenously.
9. Wrong rate of administration	70.8	Administering an intravenous medication at a different rate than the correct one.
10. Wrong administration timing	70.10	Administering a medication at a different interval than the one programmed at the institution.

Types of medication error		Description
ISMP Spain	NCC MERP	
11. Wrong patient	70.11	Prescription/transcription/dispensation/administration of a medication to a patient other than the patient who should be receiving the treatment.
12. Wrong duration of treatment *12.1 Lasting longer than it should* *12.2 Lasting a shorter time than it should*	70.9	Duration of treatment longer or shorter than necessary. This also includes stopping treatment too early or administering the treatment after the prescription has been suspended.
13 Insufficient monitoring of treatment *13.1 Lack of clinical review* *13.2 Lack of analytic controls* *13.3 Drug-drug interaction* *13.4 Drug-food interaction*	70.12	Failure to review the prescribed treatment to verify the appropriateness of the treatment and to detect possible problems, or a failure to utilise pertinent clinical or analytical data to adequately evaluate patient response to the prescribed therapy.
14 Deteriorated drug error	70.13	Dispensation/administration of an expired medication or one whose physical or chemical integrity has been compromised, for example, by less than optimum storage conditions.
15 Lack of patient compliance		Inappropriate patient compliance with a prescribed medication regimen.
16 Others	70.14	Other medication errors not included in the categories described above.

The different types of errors are not mutually exclusive given the multi-disciplinary and multi-factorial reasons for medication errors.[12]

I.3.2.6 Causes of medication errors

A cause is an antecedent factor that contributes to an event, effect, result or outcome. A cause, e.g. an action, may be proximate in that it immediately precedes the outcome. 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.[10]

The subcategories of the causes of medication errors are derived from the NCC MERP taxonomy. However, in comparison with the NCC MERP taxonomy, the possible confusion of patient names or surnames is an additional cause of medication error to be taken in consideration. The European MERS have implemented modification to the categories of packaging and labelling problems and of equipment and devices involved in the preparation, dispensation and administration of medicines in order to reflect more closely the associated practices. The current main subcategories of causes of medication errors used by European MERS are:

- communication problems related to the order of medicines (verbal miscommunication, written miscommunication, misinterpretation of the order);
- patient name confusion,
- confusion of the name of the medicine (look-alike, sound-alike),
- labelling and packaging problems (dosage form confusion, immediate container and labels of the product, outer packaging): inaccurate or incomplete information, looks too similar to other products, appears to be misleading or confusing, disturbing symbols or logo,
- equipment and devices used for dispensing/preparing/administering [malfunction, wrong device or adapters selected, automated distribution and preparation systems, dosing devices, infusions (i.e. PCA, infusion pumps)],
- human factors.

The term "human factors" refers to the study of the interrelationships between humans, the tools they use, the environment in which they live and work, and the design of efficient, human-centred processes to improve reliability and safety.[10]

A lot of subcategories can be drawn up to describe the factors related to the working conditions inside of the medication use system. In consequence of the differences in the practices, procedures and working conditions in Europe, European MERS have adapted the NCC MERP taxonomy which is based on the "American way of life".[12] Here again, given its multifactor origin, several causes can be attributed to a medication error.[12]

I.3.2.7 Contributing and environmental factors (system-related)

Contributing or environmental factors are factors likely to generate, alone or combined, the risk of a medication error.

A contributing factor (interchangeable with contributory factor) is 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 hidden condition that played a role in the genesis of the outcome.[10]

Hidden errors are errors in the design, organisation, training or maintenance that lead to operator errors. They may not become evident for long periods of time.[15] They represent root causes of adverse events and arise from decisions made by designers, builders, procedure writers and top level management. Hidden conditions may not become evident for many years before they coincide with active failures and local triggers to create an accident opportunity.

Here also, as a consequence of the differences in the practices, procedures and working conditions in Europe, European MERS have adapted the NCC MERP taxonomy based on the American "way of life".[12]

I.3.3 Feedback from reported medication error

Analysing medication errors is an indispensable pre-requisite for learning from them. However, medication error analysis should not be an objective by itself. Identifying the frequency, the severity, the type and causes of medication errors helps finding ways to improve medication safety.

Reporting and collecting of patient safety data is only meaningful if analysed and extracted information is translated into preventive action. Feedback to health professionals, managers and patients allows learning from incidents and maintains motivation for further reporting[xxii].

Example of feedback from reported medication error

In the United Kingdom, the National Patient Safety Agency (NPSA) received a number of incident reports of problems involving Repevax® and Revaxis® vaccines (Aventis, Pasteur, MSD) between September 2005 and March 2005. Staff had mistakenly administered the wrong vaccine to patients because the medicines have similar names, labelling and packaging. In one report, 93 school children were vaccinated with Repevax instead of Revaxis.

[xxii] Recommendation Rec(2006)7 Appendix D2.1.

In April 2005. the NPSA issued the "Patient Safety Notice 07" to make health care practitioners aware of the risk and introduce additional safety measures to prevent misselection of these vaccines.[23] (www.npsa,nhs.uk).

The more errors are reported, the more data will be available to examine the failures that are inherent to the medication use system and, furthermore lead to improvement of the medication use system.[24] Reported and analysed medication errors can lead to learning how to improve safe medication practices by several ways.

I.3.3.1 Local approach - learning from errors within an organisation

At local level, analysis reports of medication errors should be prepared regularly by a safe medication practice committee authorised to deal with medication safety.[6] This multidisciplinary committee should be in charge of evaluating potential preventive actions and of prioritising measures to be adopted and implemented in the facility to prevent medication errors with the purpose of achieving the maximum benefit.[25] In fact, each organisation should choose, adapt and introduce the most suitable measures to correct concrete aspects of the different processes of the medication use system, such as prescription, dispensing, administration, etc.[24]

Decisions may be taken on the basis of some of the following criteria:
- high impact on the prevention of the most serious medication errors (for example, measures of prevention related to high-risk medicines of high-risk populations),
- high impact on the prevention of the most frequent medication errors,
- evidence about reduction of medication errors,
- contribution to training health care practitioners on prevention of medication errors,
- resolution of several medication error problems at the same time.

Once the safe medication practice committee has prepared the decision for adoption by the health care site, it is essential that it develops an action plan, assists the implementation of recommended measures and the evaluation of the results.

Through regular information, practitioners will feel committed to the programme and appreciate the value of medication errors reporting. A fundamental step of local medication error prevention programmes is to give practical feedback on the MERS, the implantation of measures of improvement and the surveillance of their results.

Medication errors of general interest should be communicated to the national MERS.

I.3.3.2 National focal points for safe medication practices

The Recommendation Rec(2006)7 recommends to develop MERS also at national level[xxiii]. Aggregation of data will be of greatest value in revealing systematic failures, accumulation of certain incidents or failures in new equipment that cannot be readily identified at local level, i.e. where a larger dataset is required to make rare incidents become evident. Strict methods should be used to ensure representativeness of the data and to minimise bias[xxiv].

[xxiii] Recommendation Rec(2006)7 para iii.d.
[xxiv] Recommendation Rec(2006)7 Appendix D1.6.

A national framework for medication errors management should be defined and implemented to identify those medication errors from local systems where national learning and action can prevent recurrence[xxv]. A nationally recognised focal point for safe medication practices should be set up in each country with a view to cooperating and complementing pharmacovigilance systems. They should be based on a national system for reporting medication errors, analysing causes and disseminating information on risk reduction and prevention[xxvi]. The centres need not be part of public administration, such a centre can be independent and needs at a minimum to be nationally recognised: reference is made to the role played by ISMP Canada when establishing the Canadian Medication Incident Reporting and Prevention System (CRIMPS) (see Appendix 5.1).

A small number of reports can provide sufficient data to recognise a significant risk, or a new risk associated with the use of a medication or a device and generate an alert. Therefore, the review of reports by medication errors specialists permit to identify new risks and to prioritise them. Recommendations are then disseminated by specific alerts, such as the National Patient Safety Agency "Patient Safety Alerts" and "Safer Practice Notices", or by a periodic newsletter, e.g. the "ISMP Medication Safety Alert!".

I.3.3.3 Disclosure and communication with patients

All patient safety incidents should be acknowledged as soon as they are identified. In cases where the patient or their relatives or carers inform health care staff about an incident, it must be taken seriously from the beginning. Any concerns should be treated with compassion and understanding by all health care staff. The National Patient Safety Agency in the United Kingdom has developed some guidance on disclosure and communication with patients.[5] This guidance has been summarised below:

Truthfulness, timeliness and clarity of communication
Information about a patient safety incident must be given to patients and their relatives or carers in a truthful and open manner by an appropriately nominated person. Communication should also be timely: patients and their relatives or carers should be provided with information about what happened as soon as practicable. It is also essential that any information given is based solely on the facts known at the time. New information may emerge as an investigation is undertaken, and patients and their relatives or carers should be kept up to date with the progress. They should receive clear, unambiguous information and be given a single point of contact for any further questions or requests. They should not receive conflicting information from different members of staff and medical jargon which they may not understand should be avoided.

Apology
All patients and their relatives or carers should receive a sincere expression of sorrow and regret for the harm that has resulted from a patient safety incident. This should be in the form of an appropriately worded and agreed manner of apology, as early as possible.

[xxv] Recommendation Rec(2006)7 Appendix D1.8.
[xxvi] Recommendation Rec(2006)7 Appendix E.5.

Recognising patient and carer expectations
Patients and their relatives or carers may reasonably expect to be fully informed of the issues surrounding patient safety incidents and their consequences. They should also be treated sympathetically, with respect and consideration. Confidentiality must be maintained at all times. Patients and their relatives or carers should also be provided with support in a manner appropriate to their needs.

Confidentiality
Full consideration and respect should be given to patients', relatives', carers' and staff privacy and confidentiality. Details of a patient safety incident should at all times be considered confidential. Communicating confidential patient data in an incident investigation may not require the consent of the individual to be lawful. However any discussions with parties outside the clinicians involved in treating the patient should be on a strictly need-to-know basis. In addition, it is good practice to inform the patient and their relatives or carers about who will be involved in the investigation before it takes place, and give them the opportunity to raise any objections.

Continuity of care
Patients who have been involved in a patient safety incident are entitled to expect they will continue to receive all usual treatment and continue to be treated with respect and compassion. If a patient expresses a preference for their health care needs to be taken over by another team, the appropriate arrangements should be made for them to receive treatment elsewhere.

I.4 Sharing information on analysed errors at a supranational European level

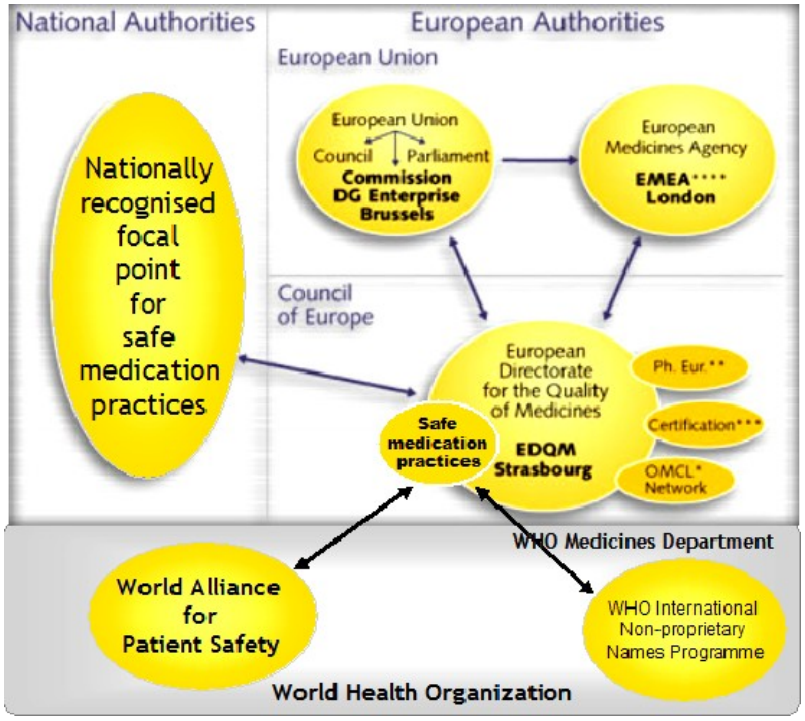
Regarding MERS, most measures have to be taken at local level, some at national level. Yet at international level, collaboration is needed for implementing some measures (i.e. regulations regarding medicinal products and medicine information) or to further improve and standardise best medication practices.

That is why information obtained by nationally recognised focal points for safe medication practices should be shared with patient safety organisations or government departments in other European countries[xxvii]. Moreover, the governments of member states are recommended to co-operate internationally to build a platform of mutual exchange of experience and learning on all aspects of health care safety[xxviii], including safe medication practices.

The need for co-ordination between MERS, as well as the management and the promotion of safe medication practices in Europe. It could be envisaged that this is co-ordinated supranationally through a permanent network. (see Figure 2).

[xxvii] Recommendation Rec(2006)7 Appendix D1.8.
[xxviii] Recommendation Rec(2006)7 para vi.

Figure 2: MERS Co-ordination at supranational European level



In this perspective, "European health authorities should recognise medication safety as a priority, and share and disseminate data between countries"[xxix].

Therefore, the Expert Group on safe medication practices recommends:

- to facilitate the sharing of information about medication errors and safe medication practices in European countries by standardising requirement asked to national centres;
- to build a European network of national MERS whose representative should meet formally periodically to exchange information and agree action across European countries;
- to mandate the co-ordination between MERS, as well as the management and the promotion of safe medication practices in Europe, possibly through supranational coordination through a permanent network;
- to ensure that all medication error reports related to its relevant missions, such as naming, labelling, packaging, advertising of medicinal products, are shared with the European Medicine Agency and national regulatory agencies, as well as corresponding recommendations for the prevention of these type of errors;
- to ensure that all medication error reports related to the recommended International Non-proprietary Names (INN) are shared with the World Health Organisation (WHO Essential Medicines Department), in order to submit and document proposals for substitution, if needed, to the WHO INN Programme.

[xxix] Recommendation Rec(2006)7 Appendix E.6.

References Chapter I

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Chapter II - Assessing safe medication practices

Key points:

- In order to improve medication practice it is necessary to have reliable methods for assessing its safety. Methods that can be used to assess medication safety include: spontaneous reporting, review of patient records, observation. Methods that can be used to detect and prevent adverse drug events are: interventions by pharmacists, adverse drug event trigger tools and computer monitoring.
- No single method offers a comprehensive measure of medication safety, which means that a combination of methods need to be used to estimate the system performance over time.
- Institutions should establish appropriate methods to detect medication incidents that are occurring and to evaluate the effect of medication safety practices and initiatives intended to minimise risks.
- There is no external audit system that exclusively reviews safe medication practices.
- The Institute for Safe Medication Practices in the United States has developed self-assessment tools for hospitals and ambulatory care designed to help assessing the safety of medication practices, identifying opportunities for improvement and enabling a comparison of individual scores with the aggregate experience of demographically similar sites.
- The production of an annual safe medication practice report enables health care organisations to summarise and prioritise their medication risks and provides a blueprint for action in the coming year. The report should be submitted and approved by a senior management board in the organisation and should be a key document for external audit and performance management organisations to review and assess medication safety.
- National Centres for Safe Medication Practices should publish annual reports to identify risks and methods that have been used effectively to manage these risks. The information should be collated at European level and should be used to inform the external assessment of health care organisations.

In order to improve the medication use system it is useful to have reliable methods for assessing safety. Institutions should establish appropriate methods to detect medication incidents that are occurring with the aim of evaluating the effect of medication safety practices and initiatives intended to minimise risks. Besides, periodically carried out self-assessments should help institutions to evaluate their state of progress in improving safe medication practices.

This chapter will review methods to detect and measure medication errors and adverse drug events. The use of audit and self-assessment of the safety of medication practices will be discussed. Finally, the use of annual safe medication practice reports will be recommended where measurement and incident data are summarised each year, progress assessed and plans and targets for the next year are set out.

II.1. Methods to detect and measure medication errors and adverse drug events

Unfortunately, no single method offers a comprehensive measure of medication safety, which means that a combination of methods needs to be used to estimate system performance over time.[1] From the literature it is clear that the spontaneous incident reporting method is comparatively poor at identifying and measuring medication errors and adverse drug events and that other methods are more effective.

Considering the very large literature available on methodologies applied to medication errors, only six methods will be considered in this chapter: spontaneous reporting, review of patient records, observation, interventions by pharmacists, adverse drug event trigger tools and computer monitoring. This part only summarises some very basic information in order to clarify their impact on risk management for non specialised readers. For this reason, an artificial but didactic distinction has been made between the collection of medication errors and adverse drug events for assessing the safety of the medication use system (see II.1.1); and methods allowing the early detection of preventable adverse medicines events signs in order to mitigate the adverse effects of medication errors on patients (see II.1.2).

II.1.1. Assessing medication errors and adverse drug events

II.1.1.1. Spontaneous reporting programmes

The most frequently method used to identify medication errors is the use of spontaneous incident reporting (see I.1.2). The use of this method is quite common in hospital services and has also been used in some primary care settings because error reporting is a fundamental component of a safety culture. The importance of involving pharmacy staff to review and quality assure medication incidents submitted via spontaneous reporting programmes has been identified recently. [2]

The advantages of this method are that it is inexpensive and relatively easy to set up. However, the number of reports received is limited by the culture of the organisation so they will only represent a very small percentage of the total number of medication errors that are actually occurring, and the details submitted may be incomplete or inaccurate.[1]

This method does not produce quantitative data because medication errors and adverse drug events are underreported due to the fact that voluntary reporting schemes rely on error awareness and willingness to report. Low reporting rates reduce the chances of identifying trends and limit the opportunity to review processes and reduce risks to patients. In a study, of 54 adverse drug events identified, only 3 patients (6%) had a corresponding incident report submitted via the hospital spontaneous incident reporting programme.[3] For this reason, using incident reporting for quality improvement will lead to significant bias when assessing quality of care. However, the number of reports can be used as a measure of the safety culture.[1]

II.1.1.2. Patient record review

This method consists in the exhaustive revision of the information contained in the medical record of the patients (medical history, medication order sheets, medication administration records, etc.) by trained personnel (nurses, pharmacists, doctors).[1,4] The information can be collected in a prospective way and be completed by interviews with the health professionals and patients, themselves, or it can be collected in a retrospective way. This method can be used to detect all types of incidents, although it is more useful to detect adverse drug events and potential adverse drug events, mainly those generated in the prescription and monitoring processes. It is less effective to detect errors in the dispensing and administration processes, unless they cause damages.

Prospective revision of clinical histories is the only method that allows for valid information to be obtained about the frequency of adverse drug events in a specific setting. Since 1995, chart review has been used to study the nature and incidence of adverse drug events in adult patients[2], paediatric patients[5] and patients in critical care units[6] (see results reviewed in Appendix 4.1 and summarized in the introduction). It has the disadvantage that it is time consuming and requires important human resources, making it too expensive to be carried out on a routine basis. Other inconveniences are that it depends on the training of the reviewers and that often medication incidents are not documented in the clinical history and consequently can not be detected. However, with defined methodology and an experienced reviewer, detailed information can be obtained.

The prospective chart review has been compared with other methods (computer monitoring and stimulated voluntary reporting).[7] Chart review allowed for detecting the biggest number of adverse drug events (n=398) in comparison with computer monitoring (n=275) and stimulated voluntary reporting (n=23). However, it was less useful for detecting medication errors and potential adverse drug events, with 23 potential adverse drug events detected by chart review, 2 by computer monitoring and 61 by voluntary reporting.

As prospective chart review performed at the intensity required for research studies is not sustainable, other more efficient alternatives have been proposed, such as the use of the adverse drug events trigger tool developed by the Institute for Health care Improvement (IHI) (see II.1.2.2) to identify adverse drug events and to follow the monthly evolution of their incidence in the hospital.

II.1.1.3. Observation method

This method consists of direct observation of the administration of medicines by nurses or other properly trained external observers, such as pharmacists or technicians. Each observation is registered and it is compared with the prescribers' order, considering as an error any difference among what the patient receives and the medical prescription.[8]

Observation is the most valid and effective method to detect and to quantify the administration errors and is also valuable for the detection of dispensing errors,[9] but it is not useful to detect errors in the prescription and monitoring processes. It is a very quantitative method that can be used to track and trend performance and the impact of changes at the drug administering and dispensing processes.[1] With this method it may be possible also to compare performance among

different institutions.[1] Unfortunately this method is comparatively labour intensive and mostly measures actual errors, but not adverse drug events.

The guidelines established for observational studies of medication errors states that the observer should follow the subject to the patient's bedside, the observer should witness patient consumption of each dose, the observer should not be familiar with patient drug regimens before observation, operational definitions must be used, and having an error validation committee can be advantageous.[8,10]

II.1.1.4. Validity and reliability concerns related to assessment methods

The validity and cost-effectiveness of the observation method compared with chart review and spontaneous reporting were examined (see Table 8).[11] Direct observation was more efficient and accurate than reviewing charts and incident reports in detecting medication errors.

Table 8: Comparison on 2556 doses of 3 methods for detecting medication errors

Methods	No of errors detected	Error rates	Potentially clinically significant	Mean cost of error detection per dose
direct observation	373	14.6%	25	$4.82
chart review	24	0.9%	3	$0.63
incident report review	1	0.04%	0	-
Total errors confirmed	457	17.8%	35 (8.0%)	

The technician was the least expensive observer at $2.87 per dose evaluated. Nurses were the least expensive chart reviewers at $0.50 per dose. Pharmacy technicians were more efficient and accurate than nurses in collecting data about medication errors. The authors of the study concluded that this technique was the most efficient and accurate for the detection of administration errors.

The validity and reliability of observational methods for studying medication administration errors has been studied. There was no difference between the observation and non observation periods in the percentage of omitted doses for which a reason was documented, and there was no change in the error rate with repeated observations. There was no difference in error rates before and after the first intervention for each nurse. There was also no difference in error detection between the two observers and no change with increasing duration of observation. Observation of nurses during drug administration at a UK hospital did not significantly affect the medication administration error rate; nor did tactful interventions by the observers. Observer reliability was high.[12]

II.1.2. Preventable adverse drug event early detection

II.1.2.1. Pharmacy intervention-reporting systems

Pharmacists, working in both hospital and in the community, review the safety of prescriptions and the use of medicines as part of their core responsibilities. They also interact with health professionals, patients and carers who administer medicines, when undertaking these duties within the pharmacy or when the visit clinical areas. Pharmacists frequently encounter prescriptions and medicine use that are unsafe and intervene to eliminate or minimise these risks often by contacting the prescriber with suggestions to change the medication (see IV.9.3).

Numerous studies demonstrate that hospital pharmacists play a large part in monitoring and improving 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.[13,14,15]

Recording and collecting information concerning these interventions can help identify and measure medication risks and track changes over time. This method is efficient for detecting medication errors at the prescription process. It also has the advantage of not only detecting errors, but also intercepting errors before they reach the patient.[1,16] In this sense, it can be used mainly to detect medication errors and potential adverse drug events.

Intervention reporting can also be used to measure the effectiveness of automation. For instance, the effectiveness of a computerised order-entry system can be evaluated by measuring by changes in how often and what types of interventions pharmacists make, or in terms of error reduction.[16]

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

II.1.2.2. Adverse drug event trigger tools

A major barrier to progress in patient safety has been the difficulty in detecting and measuring medicine related harm easily, effectively and consistently and thus develop targeted strategies to prevent occurrence.[17] The Institute of Healthcare Improvement in the USA has developed an adverse drug event trigger tool requiring little additional resources to help identify and measure adverse drug events occurring in individual health care environments.[18,19]

An adverse drug event chart review sheet is used by reviewers to identify various triggers that may appear in the medical record. There are three types of trigger:

i) Use of specific drug antidotes used to treat ADEs,
ii) Results from laboratory tests that may indicate an ADE
iii) Clinical events that may indicate a ADE. (see Table 9).

Table 9: The Institute of Healthcare improvement trigger tool

Trigger No	Name	Process identified
	Use of following medicines:	
T1	Diphenhydramine	Hypersensitivity reaction or drug effect
T2	Vitamin K	Over-anticoagulation with warfarin
T3	Flumazenil	Oversedation with benzodiazepines
T4	Antiemetics: droperidol, ondansantron, promethazine, hydroxyzine, trimethobenzamide; prochlorperazine, metoclopramide	Nausea/emesis related to drug use
T5	Naloxone	Oversedation with narcotic
T6	Diphenoxylate, loperamide, kaopectate	Medicine induced diarrhoea
T7	Sodium polystyrene	Hyperkalaemia related to renal impairment or effect of medicine
	Laboratory test results:	
T8	Prothrombin (PTT)>100	Over anticoagulation with heparin
T9	INN>6	Over anticoagulation with warfarin
T10	White blood count <3000 x 10^6 microlitres	Neutropenia related to medicine or disease
T11	Serum glucose <50 mg/dl	Hypoglycaemia due to insulin use
T12	Rising serum creatinine	Renal insufficiency related to medicine use
T13	Clostridium difficile positive stool test	Exposure to antibiotics
T14	Digoxin level >2 nanog/ml	Toxic digoxin level
T15	Lidocaine level >5nanog/ml	Toxic lidocaine level
T16	Gentamicin or tobramycin peak >10 micrograms/ml; trough >10 micrograms/ml	Toxic levels of aminoglycosides
T17	Amikacin levels > 30 micrograms/ml; trough >10micrograms/ml	Toxic level of amikacin
T18	Vancomycin levels > 26 micrograms/ml	Toxic level of vancomycin
T19	Theophylline levels > 20 micrograms/ml	Toxic level of Theophylline
	Clinical events	
T20	Oversedation, lethargy	Related to overuse of medication
T21	Rash	Medicine related
T22	Abrupt medication stop	Adverse drug event
T23	Transfer to a higher level of care	Adverse drug event
T24	Locally selected trigger Customised to individual institution	Adverse drug event

Once any of the triggers are found in the medical record, the reviewer must then review the use of the trigger in the context of the care document. A review of the record will enable the reviewer to determine whether the trigger identifies a true ADE.

A random sample of charts (e.g., 10 per week) is reviewed. A trigger review takes no longer than one hour per trainee. With little experience, the review of 10 charts takes 2–3 hours. By using such sampling, hospitals can obtain monthly estimates of their adverse drug event rates. The pilot study of the tool examined 2,837 charts, involving 268,796 doses and found an overall adverse drug event rate of 2.68/1000 medicine doses administered. Of the 274 adverse drug events found using the trigger tool, only 5 (1.8%) were found using the more established or traditional methodologies.

Trigger tools may be also used for the intensive care environment, for process specific tool e.g. for warfarin, and for the ambulatory care setting.[19] When the trigger tools are integrated in a computerized hospital information system, they allow for the detection of adverse drug events occurring in hospital patients using similar triggers as used in the manual trigger system (see II.1.2.4).

II.1.2.3. Preventable drug related morbidity (PDRM) indicators

A series of validated indicators for preventable drug related morbidity (PDRM) have been described for primary care:[20]

Table 10: Indicators to prevent drug related morbidity

No	Pattern of Care	Outcome
1	Addition of amiodarone to the treatment of a patient already prescribed digoxin without reducing the digoxin dosage by initially one third to one half and subsequent monitoring of the digoxin level	Anorexia or nausea and vomiting or diarrhoea or visual disturbance or fatigue or drowsiness or confusion or arrhythmias or delirium or hallucinations
2	Regular use of strong opiod analgesia without concurrent administration of a stimulant laxative	Chronic constipation
3	Concurrent use of a ACE inhibitor and either a 1) a potassium sparing diuretic or potassium supplement without monitoring the potassium level at least annually	Hyperkalaemia – Potassium level > 5.5 mmol/l
4	Use of metoclopramide in a patient with Parkinsons Disease	Worsening of Parkinsons Disease symptoms e.g., attacks of rigidity or tremor
5	Use of an inhaled steroid by high dose mtered aerosol without usage of a spacer device	Oral thrush/dysphonia
6	Use of a statin without monitoring liver function before starting therapy, within 3 months of commencement and then a 6 month intervals therafter	Serum transaminase concentrations elevated to three times the upper limit of the reference range or clinical jaundice
7	Prescribing beta blocker eye drops to a patient with a history of asthma or chronic obstructive airways disease	GP or hospital contact because of deterioration in symptoms or acute exacerbation of asthma or COPD
8	Use of long term steroids at a dose of >7.5mg of prednisolone per day without osteoporosis prophylaxis	Osteoporosis or broken bone
9	Addition of amiodarone to the treatment of a patient already prescribed warfarin without reducing the warfarin dose and closely monitoring the INR	A minor or major haemorrhagic event
10	Use of a ACE inhibitor without monitoring the potassium level before starting therapy withjn six weeks of commencement and at least annually thereafter	Hyperkalaemia – Potassium level > 5.5 mmol/l
11	Use of ACE inhibitor without monitoring the creatinine level before starting therapy, within six weeks of commencement and at least annually thereafter	Raised serum creatinine > 150 micromols/L
12	Use of a potassium wasting diuretic without 1) concurrent use of a potassium supplement 2) concurrent use of a potassium sparing diuretic 3) monitoring the potassium level annually	Hypokalaemia – Potassium level < 3mmol/l
13	Use of an oral or topical nonsteroidal anti-inflammatory drug for one week or more in a patient with a history of peptic ulcer or GI bleeding	Dyspepsia or upper GI bleed or GI perforation or GI ulcer or anaemia
14	Dispensing or issuing a prescription by a pharmacist for a beta blocker eye drop to a patient with a known history of asthma or COAD without advising them to contact their GP in the event of any deterioration of their respiratory symptoms	GP or hospital contact because of deterioration in symptoms or acute exacerbation of asthma or COPD
15	Dispensing or issuing a prescription by a pharmacist for an oral NSAID without advising the patient to consult their GP if they experience indigestion or heartburn	Upper GI bleed or GI perforation or GI ulcer or anaemia
16	Prescribing for the first time an oral or topical NSAID to a patient with a known history of asthma or COAD without advising them to return in the event of any deterioration in their respiratory symptoms	GP or hospital contact due to either deterioration in symptoms or an acute exacerbation of asthma or COAD
17	Dispensing and issuing a prescription by a pharmacist for an oral or topical NSAID to a patient with a known history of asthma or COAD without advising them to contact their GP in the event of any deterioration in their respiratory symptoms	Hospital admission because of an acute exacerbation of asthma or COAD
18	Continued use of a previously established dose of digoxin without assessing the digoxin level in a patient presenting with any of the following symptoms: anorexia, nausea and vomiting, diarrhoea, visual disturbances or fatigue.	Drowsiness, confusion, arrhythmias, delirium, or hallucinations
19	Continued use of a previously established dose of phenytoin without assessing the phenytoin level in a patient experiencing an altered seizure pattern	Hospital admission because of a loss of seizure control
20	Prescribing for the first time carbimazole without advising the patient to return should they experience any of the following symptoms: sore throat, mouth ulcers, brusing, fever, malaise	Agranulocytosis or pancytopenia
21	Dispensing and issuing a prescription by a pharmacist for carbimazole without advising the patient to contact their GP if they experience any of the following symptoms: sore throat, mouth ulcers, brusing, fever, malaise	Agranulocytosis or pancytopenia
22	In the absence of any contraindication, failing to prescribe aspirin in a patient with a history of MI	A second myocardial infarction

Table 10 (cont'd)

No	Pattern of Care	Outcome
23	In the absence of any contraindication, failing to prescribe a beta blocker for 2 to 3 years following an myocardial infarction	A second myocardial infarction
24	In the absence of a contraindication failing to prescribe an ACE inhibitor to a patient with known congestive heart failure	GP contact or hospital admission because of worsening symptoms of congestive heart failure

II.1.2.4. Computerised monitoring method

Computerised monitoring consists of the incorporation in the pharmacy computer system of specific applications for detecting adverse drug events. The requirement is to have patient medication profiles. These applications look for certain triggers or markers that trigger suspicions that an adverse drug event has happened. The most common are: names of specific drug antidotes used to treat adverse drug events, abnormal laboratory values associated with adverse drug events, abnormal values of drug serum concentrations, and combinations of names of medicines and of laboratory tests.[21,22] The most advanced applications also include a search for combinations of texts of clinical symptoms that may indicate adverse drug events and medicines or pharmacological groups frequently implied in their appearance.[18,23]

This method allows for the detection of adverse drug events, but it is not valid for detecting medication errors and potential adverse drug events.[1] The great advantage consists in that permit early detection adverse drug events, which enables prompt treatment.

These systems have been demonstrated to be quite efficient for detecting and preventing adverse drug events, and with a smaller cost than chart review, [24] so that in time they are almost certain to be incorporated into hospital practice and will constitute a fundamental tool for detecting adverse drug events.

II.1.3. Selecting methods to detect and measure medication safety

A major barrier to progress in patient safety has been the difficulty to detect and measure medication incidents easily, effectively and consistently and thus develop targeted strategies to prevent occurrence.[17] The following table helps selecting methods regarding the aims and resources of health care organisations:

Table 11: Summary of the scopes, strengths and limitations of considered methods

Methods	Strengths	Limitations
Methods to measure medication errors and adverse drug events		
Spontaneous reporting programmes	- identifiy medication errors and adverse drug events - inexpensive - relatively easy to set up, enhanced by computerised reporting - stimulate health care profesionals to understand the causes of errors - anonymity might remove some barriers to reporting errors, - number of reports can be used as indicator of the safety culture	- lack of epidemiological significance. Reported data have only qualitative value and represent a very small percentage of the real number of medication errors and adverse drug events (underreporting). - voluntary reporting schemes rely on error awareness and willingness to report - number of reports received is limited by the culture of the organization -details reported may be incomplete or inaccurate
Patient record review	- can be used to detect all types of incidents, but more useful to detect adverse drug events - identifies more adverse drug events than spontaneous reporting - allows to detect mainly adverse events generated in the prescription and monitoring processes - enhanced by automatic research on computerised medical records - only research method that allows to obtain valid information about the frequency of adverse drug events in a specific setting	- less useful for detecting medication errors and potential adverse drug events - depends on quality of documentation of medication incidents in the clinical history - depends on the formation of the reviewers - less effective for detecting errors in the dispensing and administration processes, unless they harm the patient - too time consuming for routine use if automatic research on computerised medical records is not available
Observation method	- most effective method to detect and to quantify administration errors, dispensing errors and transcribing errors - documents the type of errors - quantitative method that can be used to track and trend performances and the impact of changes - allows to compare performances among different institutions. - possible documentation by barcode bedside documentation systems	- measures errors, but not adverse drug events - not useful for detecting prescribing errors and monitoring errors - labour intensive, needing trained observers
Methods to detect preventable adverse drug events		
Pharmacy intervention-reporting systems	- effective to detect prescribing, transcribing and monitoring errors, - improve prescribing performance and safety - allows to detect near misses, medication errors and potential adverse drug events before they reach the patient - allows to compare performances among different institutions.	- less effective to detect dispensing, and administration errors, - computerised documentation system needed - record time needed
Adverse drug event trigger tools	- allows to identify adverse drug events - allows to obtain monthly estimates of their adverse drug event rates in the hospital. - requires little additional resources: a trigger review takes no longer than one hour per trainee - integrated in a computerized hospital information system, allows the automatic detection of adverse drug events occurring in hospital patients	- computerised documentation system needed - detection bias depending upon triggers used: only some particular ADEs are detected
Preventable drug related morbidity (PDRM) indicators		
Computerised monitoring method	- effective to detect prescribing and monitoring errors, if corresponding triggers are available - quite efficient for detecting and reducing the severity of adverse drug events - allows to compare performances among different institutions. - less expensive than chart review	- computerised medical records needed in an integrated computer network, at minimum: diagnosis, prescriptions and laboratory information - more effective with numeric values (such as laboratory results) - not valid for detecting medication errors and potential adverse drug events - limited availability of commercial softwares

The following must be considered when one or more methods are to be chosen:[25]

- none of the available methods are able to detect all the medication incidents that occur, given the big complexity of the 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 to detect administration errors.
- some methods only capture incidents that cause damage to the patients, as with the methods using adverse event triggers, while others usually detect errors without damage, such as is the case of the observation methods.
- the results that are obtained should be interpreted keeping in mind the limitations and characteristics of each method. For example, the rates of error estimated using an observational method can never be applied in a broad sense nor generalized for a system as a whole.

In conclusion, keeping in mind that the different methods constitute complementary options, each institution, depending on its characteristics and resources, should select and adapt appropriate methods that it considers more likely to be effective for its use and that allow the institution to identify its problems, to evaluate the performance of its medication-use system and to test the effect of the medication safety initiatives implemented.

II.2. Evaluating safe medication practice initiatives

II.2.1. Auditing the safety of medication practices

II.2.1.1. The different ways for external assessing

Many countries have voluntary and statutory mechanisms for periodic external assessment of health care organisations against defined standards:[26]

There are no external assessments that only review safe medication practices. Either these practices are assessed as part of a more comprehensive quality assessment, or this topic is not included in the assessment process.

They are designed to assure or improve some elements of quality, but they are usually run by different organisations without national co-ordination to make them consistent, mutually supportive, economical, and effective. Broadly, these mechanisms include variants on five approaches described in following table.

Table 12: Common models of external assessment in health care

International Organization for Standardization		www.iso.ch/
	Origin and focus	European manufacturing industry 1946; quality systems (often within individual department or function)
	Standards	ISO 9000 series (quality systems); also specific for radiology and laboratory systems
	Products	Certification
Malcolm Baldrige "excellence" model		www.asq.org/abtquality/awards/baldrige.html
	Origin and focus	U.S. industry 1987; management systems and results
	Standards	European and national variants published with criteria
	Products	Self-assessment, national awards
Peer review		
	Origin and focus	Health care; specialty-based professional training, clinical practice, and organisation
	Standards	Variable detail, limited access
	Products	Accreditation (of specialty training)
Accreditation		
	Origin and focus	U.S. health care 1919; service organisation, performance
	Standards	Published with criteria such as acute care, long term care, primary care, networks
	Products	Accreditation (of organisation or service)
Inspection		
	Origin and focus	National or regional statutes; competence, safety
	Standards	Published regulations such as for fire safety, radiation exposure, hygiene
	Products	Registration, licensing

Countries have good reasons to be able to show that health care standards are not only consistent within their own territory but also that they are comparable with those of their neighbours, suppliers, and competitors.

Schemes for inspection, registration, revalidation, and review are proliferating with little international, national coordination or regard for the evidence of what has worked or not worked for health care. This leads to uncertainty among service providers about which standards to adopt, inefficiency in developing new inspection and development programmes, duplication and inconsistency of external assessments, and an excessive burden on the services under scrutiny.

II.2.1.2. Involved bodies

Several recent European and international initiatives are making traditional assessment methods more accessible, convergent, and relevant to health care.

International Organization for Standardization

The ISO 9000 series of standards were designed for manufacturing industries. European initiatives are under way to develop ISO guidelines specific to health care.

European Foundation for Quality Management

The original "business excellence" model has given way to "excellence" in the 1999 version and has shifted emphasis from "enabling processes" to results of concern to patients, staff, and society

Accreditation

The international arm of the US Joint Commission on Accreditation of Healthcare Organisations has developed a set of multinational accreditation standards (www.jcrinc.com/internat.htm).

In addition the International Society for Quality in Health Care has developed ("ALPHA") standards and criteria (available from the society's website www.isqua.org.au) against which an accreditation programme may apply to have its standards and process assessed and internationally accredited. These also offer a template for standardisation and self-assessment to any external assessment programme.

II.2.2. Self-assessment of the safety of medication practices

The Institute for Safe Medication Practices (ISMP) in the USA published a medication safety self-assessment (MSSA) tool for hospitals first in 2000 and it was revised and issued again in 2004.[27,28] The tool was designed to help organisations assess the safety of their medication practices, identify opportunities for improvement and enable a comparison of individual scores with the aggregate experience of demographically similar hospitals. It was endorsed by 22 health care organisations in the USA.

The MSSA was adapted for use in Canada and in Australia and it is now in process of adaptation in Spain and in other countries.[29]

The tool has 194 self-assessment items grouped in the following ten key elements:
- Patient information,
- Medicines information,
- Communication of drug orders and other information,
- Drug labelling, packaging and nomenclature,
- Drug standardisation, storage and distribution,
- Medication device acquisition, use and monitoring,
- Environmental factors, workflow and staffing patterns,
- Staff competency and education,
- Patient education,
- Quality processes and risk management.

The items address safe medication practices identified by the ISMP from analysis of incident reports submitted to the USP – ISMP Medications Errors Reporting Programme, and from problems and practices identified by the ISMP during on-site consultations with health care organisations. Hospitals are asked to rate their compliance with each individual item according to the following scale:

A – There has been no activity to implement this item.
B – Discussed and considered, but has not been implemented.
C – Partially implemented in some or all areas of the organisation.
D – Fully implemented in some areas of the organisation.
E – Implemented in all areas of the organisation.

Each response is assigned a weighted score. The weight for each self-assessment item was developed by ISMP on the impact of that item on patient safety and its ability to sustain improvement. The self-assessment items with the highest weight were those that:

- target the system, not the workforce.
- do not rely heavily on human memory and vigilance.
- demonstrate through scientific evidence that they are effective in reducing serious medication errors.
- solve several medication–error related problems at the same time.
- prevent errors with high alert medicines that have the greatest potential to cause patients harm.
- simplify complex and error prone processes.
- safeguard high risk patient populations and
- make it hard for health care practitioners to do their job wrong and easy for them to do it right.

ISMP recommends the self-assessment exercise to be undertaken by a multidisciplinary team. The value and accuracy of the self-assessment is significantly reduced if completed by a single discipline involved in medication use, because the medication use is a complex, interdisciplinary process.

The results of the use of the ISMP MSSA tool published in 2000 have been reported.[30] A summary of the scores from the 2004 survey are available on the ISMP web site (www.ismp.org). The ISMP MSSA has been used by health care organisations as a tool to increase understanding of their medication use process and to guide and prioritise the implementation of the best improvement safety practices. A collaborative group of 21 hospital in New England showed an important progress when they used the ISMP MSSA in this way, increasing their self-assessment scores by approximately 20% from their baseline scores when the self-assessment was repeated during the second quarter of 2002.[31]

ISMP have developed similar self-assessment tools for community/ambulatory practice and antithrombotic therapy in hospitals. Details of these tools are available on the ISMP web site (www.ismp.org).

II.3. Annual safe medication practice reports

In the same way as European health care organisations track infection rates, identify targets and the plan and execute initiatives to reduce these infections, adverse drug events and medication errors should be reduced.

At local level, health care organisations should summarise the medication incident reports and other data that have been collected each year in an annual safe medication practice report. They should describe the improvement targets and actions and summarise what progress has been made and what progress they have still to make. In doing so, health care organisations can identify and measure the effectiveness of a planned series of interventions to decrease the incidence of patient harm. [32]

The production of an annual safe medication practice report is considered essential for health care organisations to take stock of medication safety. The report should summarise and prioritises the medication risks in an organisation and provide a blueprint for action in the

coming year. The report should be submitted and approved by a senior management board in the organisation and should be a key document for external audit and performance management organisations to review and assess medication safety.

At national level, the national focal point for safe medication practices should publish annual reports to identify risks and methods that have been used effectively to manage these risks.

At European level, the information should be collated from these reports and be used to inform the external assessment of health care organisations.

References Chapter II

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Chapter III - Improving the safety of naming, labelling and packaging of medicines marketed in Europe

Key points:

- Current European medicines regulations and guidelines concerning naming, packaging and labelling of medicinal products do not consider adequately all aspects pertaining to patient safety.
- Medication errors frequently occur because of sound-alike or look-alike names, similarities in the lay-out of packaging and labelling and unclear, ambiguous or incomplete label information.
- There is little recognition of the importance of incorporating human factor principles in the selection and design of medicines names, labels and packaging in order to minimise the potential for error and enhance medication safety, neither within the pharmaceutical companies or representative offices nor drug regulatory agencies.
- Medicines regulations should be updated to require the systematic evaluation of the risks of the proposed proprietary names by the manufacturer. The evaluation should use a standardised procedure to identify possible sound-alike or look-alike confusion with the names of already approved medicines and should include user testing. The evaluation should be submitted to the drug regulatory agencies as part of the application for marketing authorisation. Proposed names should be modified or rejected if systematic review and user testing have identified a high risk of confusion of the proposed name with other products.
- The use of international non-proprietary names (INNs) instead of invented names in medication practice should be promoted with a view to improving medication safety. In addition, MERS and national centres on safe medication practices should be encouraged to comment on proposed INNs during the 4-month objection period. The steps followed by the WHO INN selection procedure should address all available means to select INNs with a focus on safety.
- The WHO International Non-proprietary Names Programme and national nomenclature committees should apply adequate assessment techniques including review by health care practitioners and patients with a view to ensuring that new INNs are safe in use. If a potential for confusion of INNs is identified, a proposal for substitution should be submitted to the WHO INN programme. The use of both the INN and the invented name in the medication use system should be promoted as an additional safeguard.
- The current design for labelling and packaging puts first priorities of industry, such as “trade dress”, instead of considering adequately the context in which medicinal product will be used. It is not patient-centred, but rather relies on an assumption of perfect performance by health professionals and by patients.
- It is recommended that European health authorities take steps to implement widely and to further update as applicable European medicines regulations on design features for packaging and labelling of medicinal products taking account of human factors and favouring in-use safety. The above-mentioned features include
    - large font sizes,
    - the use of Braille on medicines’ packaging,

  - use of clear descriptions for the strength of a medicinal product to minimise errors in dosage,
  - prominent positioning of the INN,
  - adequacy of the package design for the delivery and administration of the medicine,
  - appropriate use of colour and design to minimise errors caused by mis-selection,
  - clear presentation of "essential information" on at least three surfaces of the medicine pack,
  - as regards multi-language packs, all information should be presented in a clear and legible manner.

- Medicines should be provided in unit dose presentations, ready for use and administration, in order to help minimising the occurrence of errors. Medicines regulations should be updated to require complete and unambiguous labelling of every single unit of all licensed medicines (e.g. tablet, ampoule, vial, nebules), including the INN, trade name, strength, expiry date and batch number and a data matrix bar code.
- The data matrix bar code should contain a GS1 Global Trading Index Number (GTIN) identifier. A unique identifier may also be included in data matrix bar codes for medicines as part of more general patient safety measures to minimise the risk of counterfeit medicines and health care products entering the supply chain.
- Medicines regulations should be updated to include a requirement that packaging and labelling should be subject to human factor assessment and user testing which should be undertaken by the manufacturer. At present this is only mandatory for patient information leaflets (PIL). Safety assessment of packaging and labelling should be submitted to the regulatory agencies as part of the marketing application together with reports concerning other issues identified during product development. Risks identified by such assessment should be either controlled or minimised by a specific risk management plan which should be implemented with respect to the European Union regulations and considered in the marketing authorisation.
- The label of medicines intended for use in ambulatory setting in Europe should have a space for a dispensing label. Medicines regulations should be updated to include a requirement for pharmacists and other health care personnel dispensing medicines for ambulatory patients to put a typewritten label on the medicine package when it is dispensed. The dispensing label is intended to assist patients, carers and other health professionals to use medicines as intended and to minimise errors.
- National centres for safe medication practices should identify problems related to poor naming, labelling and packaging that occur with medicines already in use through post-marketing monitoring and work closely with national drug regulatory agencies and manufacturers to respond appropriately and timely to all detected problems. Co-ordination at European level is desired involving for example national centres for safe medication practices, drug regulatory agencies, the European Medicines Agency, the European Directorate for the Quality of Medicines and the WHO INN programme.

III. 1. Tackling medication errors related to the naming, labelling and packaging of medicines

III.1.1. Primacy of safety in design and assessment of naming, label information and packaging

Confusing naming, labelling and packaging of medicinal products is widely recognised as one of the main causes of medication errors.[1] These errors frequently occur because of sound-alike or look-alike medicines names, similarities in the appearance of packaging and labelling, unclear, ambiguous or incomplete label information. However, labelling, packaging and naming of medicines should have a preventive and not a causal role in the genesis of medication errors and overall contribute to patient safety.

The recent EU legislation[1a] , includes requirements for medicines names, labelling and packaging and the European Medicines Agency (EMEA) and national drug regulatory agencies issued provisions concerning this matter. However, in spite of existing regulations and guidelines, reports from cases in Europe have revealed numerous cases of errors attributable to poor naming, labelling and packaging which have resulted in patient injury or even death.

There are several approaches to reduce medication errors associated with nomenclature, labelling and packaging.

Design
The first approach is to improve the design of new medicines as regards their in-use safety targeting the risk of confusion and ensuring legibility and comprehensibility of essential information and instructions (see III.2.3 and III.3.2).

It is essential that pharmaceutical companies apply human factor principles in selection and design of medicines names, labelling and packaging already in drug development in order to minimise the potential for errors and enhance medication safety. Other industry branches working with hazardous materials have recognised the effectiveness of applying these principles for risk reduction. However, there is little recognition of the importance of these principles neither within pharmaceutical industry nor drug regulatory agencies.

Pre-marketing evaluation
The second approach is to proactively evaluate medicine naming, label information and packaging before the marketing authorisation procedure is started (see III.2.3.2, III.3.3 and Appendix 6).

It is essential to assess medicine naming, label information and packaging in the pre-marketing phase with a view to ensuring in-use safety of new medicines. Testing the in-use safety should follow the same principles as clinical trials for safety and efficacy.

Every step of the medication use system has to be taken into account in the evaluation of potential risks: storage, dispensation, preparation and administration by health professionals or carers and patients in the ambulatory setting. Drug Regulatory Agencies should require for new medicines in-use testing in the frame of applications for marketing authorisation. Interestingly, European directives on other types of health care products require in use testing. Regrettably, in–use testing is required by the respective EU legislation only for patient information leaflets (see V.2.2.1).

Information
Furthermore, it is important to ensure that users of medicines (patients, carers and health professionals) have all required information for the safe and effective use of the medicine. Essential information is provided on commercial medicine packs, patient information leaflets and datasheets (SmPC's). These aspects, in particular relevant for injectable medicines, will be dealt with in further sections of this chapter.

It is important that information concerning the specific directions for use together with the patient´s name, dispensing, and name and address of the dispensing pharmacist is supplied in the form of a dispensing label. This specific information about the patient is essential for ensuring the safe use of medicines and should be implemented all over Europe. Pharmaceutical industry should foresee sufficient space for the dispensing label on the packaging. Otherwise, the dispensing label may hide important information on the package.

Monitoring
Finally, a further approach to improving safety is to detect errors involving medicines already on the market through post-marketing monitoring: This responds to the fact that not all safety issues can be predicted before a medicine is marketed (see III.4).

Therefore, it is necessary to establish adequate procedures to identify problems caused by poor naming, label information or packaging and to respond appropriately and timely to prevent their recurrence by resolving the causes. Every country should operate a national centre for medication error reporting in order to accomplish the above goal. But, at the same time, there should be a co-ordination of these centres at supranational, European level, since many medication issues affect most or all European countries and require solutions at European level.

This chapter contains a section on machine readable codes which are promoted to reduce medication errors (see III.5 and Appendix 8). Use of this technology is a possibility to ensure that identity and dosage strength of the medicine correspond to the prescription, that the medicine is administered to the right patient and that timeliness and accuracy of all stages of dispensing and administration processes may be monitored. [2] Since most manufacturers do not yet use machine readable codes for every dispensing unit, it is important to promote the standardisation and general use of machine readable codes, which must allow to trace products.

For safer medicine information practices concerning **package leaflets and Summary of Products Characteristics based information**, please see chapter V. Safer medicine information practices, in particular V.2.2. Medicines information sources for patients and V. 3. Safe medicine information for health professionals.

III.1.2. Background to the recommendations

The aim of the Council of Europe Expert Group on Safe Medication Practices is to provide recommendations for naming, labelling and packaging based on the above-mentioned principles in order to enhance the safe use of medicines by patients and health professionals in Europe. In addition, recommendations aimed specifically at the inclusion and standardisation of machine readable codes on all medicinal products marketed in Europe have been included.

These recommendations are in no way intended to contradict current European legal requirements, such as those established in Title V of Directive 2001/83/EC[3] amended by Directive 2004/27/EC of 31 March 2004[4], and the *Guideline on the acceptability of invented*

names for human products processed through the centralised procedure[5] and other guidelines contained in the Quality Review of Documents (QRD) templates [1a] but, rather, to complement those requirements by addressing safety concerns not sufficiently covered by existing legislation.

The Medicines and Healthcare products Regulatory Agency (MHRA), United Kingdom, has published *Best practice guidance on the labelling and packaging of medicines*[6]. The document has been used by the Expert Group on Safe Medication Practices as a basis for their recommendations. The MHRA and the National Health Service have cooperated with pharmaceutical industry in the implementation process of the guidance into practice. As a consequence, notable progress has been made towards safer design of labelling and packaging of medicinal products.[7]

The authors of this chapter considered newsletters and relevant documents published by the Institute for Safe Medication Practices (ISMP)[8], the draft *General Requirements for the Labelling Medicines*[9], under discussion by the Australia-New Zealand Joint Therapeutic Products Agency, the *Guidelines for the Labels of Prescribed Medicines*[10] issued by the International Pharmaceutical Federation (FIP), the revised guidance *Drug Name Review: Look-alike Sound-alike (LA/SA) Health Product Names*[11] published by Health Canada and a number of medication error reports associated with confusing labelling, packaging and nomenclature by the *Revue Prescrire* [12] in France and by the Spanish ISMP[13] in Spain in the preparation of this chapter. In addition, recent FDA regulations requiring pharmaceutical manufacturers to include bar codes on medicines were considered.[14]

III.2. Improving the safety of medicines names

III.2.1. Medicines names and medication errors

Similar medicines names are a frequent cause of medication errors.[15] Many medicines names may look or sound like other medicines names, which may lead to confusion and threaten patient safety. The United States Pharmacopoeia (USP) and the ISMP publish a periodically updated list with more than 700 pairs of similar medicines names which caused mix-ups.[16,17] Likewise, ISMP-Spain edited a list of several thousands of registered pairs of potentially confusing medicines names. This was done in co-operation with the General Spanish Council of Pharmacists which launched campaigns to prevent medication errors caused by similar medicines names in Spain.[18] Comprehensive lists of medicines with similar names were also published in the United Kingdom and in other countries.

There are no cumulative studies available on the incidence of errors resulting from confusing names. A report on errors communicated to the USP-ISMP medication error reporting system (MERS) indicates that look-alike and sound-alike medicines names account for at least 15% of errors.[19] Approximately 12% of the errors reported to the ISMP-Spain MERS are also related to name confusion.[13.20]

Medication errors related to name confusion occur with [15,21]
- look and/or sound-alike invented names,
- look and/or sound-alike trademarks of medicines with different non-proprietary names,
- look and/or sound-alike names and trademarks of medicines with similar non-proprietary names,
- umbrella names for different presentations of medicinal products.

The risk of confusion of two medicinal products with similar names increases substantially if they have the same dosage strength, form, administration route and dosing schedule. In addition, other factors may increase the potential for confusion, including similar packaging and labelling, recent placing on the market, storage in close vicinity on pharmacy shelves, dispensing cabinets, on the ward or in the patient's home.

The prevention of medication errors related to similar medicines names requires both pre- and post-marketing strategies and involves drug regulatory agencies, pharmaceutical manufacturers, medication error reporting programmes, health care practitioners and patients.[22] Pre-marketing strategies should aim at designing new drug names which do not pose a risk for confusion with existing names and assess new names in a systematic and standardised approach for a potential to be confused with existing names. By this, medicines with a high risk of confusion would not be placed on the market. Post-marketing strategies should aim at minimising errors occurring with medicines that are already on the market and comprise the implementation of specific practices that prevent errors due to name confusion and reporting and dissemination of experiences the aim of changing practices and thus reducing the risks of recurrence.

III.2.2. How is the name of a medicinal product established?

Medicines names are composed of the invented name, strength, pharmaceutical form. Alternatively, the INN or usual common name or scientific name of the active pharmaceutical substance followed by a trademark or name of the manufacturer may be used if there is no invented name. In case of a medicinal product with an invented name which contains one active pharmaceutical substance, the name must be followed by the INN or usual common name of the active pharmaceutical substance (see also III.3.2.1.1. Name of the medicinal product and of active pharmaceutical substances). Different organisations and procedures are used to assign non-proprietary names and to protect proposed invented names.

All information pertaining to the name of the medicinal product, non-proprietary and proprietary elements, are important for the identification of the medicine in all communication between health professionals and patients. Any new name, proprietary or non-proprietary, should not look nor sound similar to any other existing non-proprietary or proprietary names. This will ensure in-use safety.

III.2.2.1 Non-proprietary names

The World Health Organization (WHO) system for International Non-proprietary Names (INNs) of medicines was established in 1950. Since 1953 it has selected scientifically appropriate and accurate names for active pharmaceutical substances used in medicines.[23,24] Each INN is a unique name that is globally recognised and is public property. The non-proprietary name of the active pharmaceutical substance is part of the name of a generic medicine.

The use of INNs based on international nomenclature for active pharmaceutical substances brings forward the standardisation of medicines naming at international level, allows the identification of medicines and facilitates communication and exchange of information among health professionals and scientists worldwide.[25] INN standards recommend that medicines names should be different in sound and spelling and not cause confusion with other medicines.

INNs aim at improving the in-use safety of medicines through several principles involving well-established human and cognitive factors: standardisation, simplification, use of terms well-established in medicine, improved communication, etc.

National Drug Regulatory Agencies' nomenclature committees are involved in the WHO INN Programme for the selection of a unique, worldwide accepted name for every active pharmaceutical substance which is used in a medicinal product.[26]

Every WHO INN disposes of a syllable ("stem") differentiating the name from other INNs and providing certain information: it is possible to identify active pharmaceutical substances that share similar therapeutic activity, a specific mode of action or a chemical or biochemical feature from a common stem.[25] Examples of stems include prefixes, such as "cef" for cefalosporins, infixes such as "erg" for ergot alkaloid derivatives and suffixes, such as "pril" for angiotensine converting enzyme inhibitors.[27] In addition, INNs aim at facilitating pronunciation in as many as possible languages, for example, the letters "h" and "k" are avoided, the letter "e" is used instead of "ae" or "oe", the letter "f" is used instead of "ph", etc.

III.2.2.2. Invented names

Proprietary names (or invented names) are owned by the manufacturers and their selection is driven by marketing concepts. Medicines with the same composition may be marketed even in the same country with several invented names and may have different invented names in different countries.

In Europe, national drug regulatory agencies and the European Medicines Agency (EMEA) are responsible for granting the marketing authorisation for medicines including their names. In most countries the drug regulatory agency approves the name of the medicine as a part of the marketing authorisation. Medicines may have the same invented name but may contain different active pharmaceutical substances in different countries across the world.[28,29] Also with a view to international tourism, it is necessary to achieve an international agreement so as to prevent errors.

Rules for the design of new proprietary names established by EMEA require industry to consider the following criteria in order to minimise the potential risks:[5]

- The use of abbreviations or suffixes is discouraged. Therefore, an invented name should preferably consist of only one word and should avoid the use of additional letters or numbers (both Arabic and Roman). In addition, it should be followed by the indication of strength and pharmaceutical form.
- Descriptive abbreviations may be acceptable if there is a need to distinguish different routes of administration for the same medicinal product, e.g. iv. (for. Intravenous), im.(for intramuscular), sc. (for subcutaneous).
- Invented names should not
    - convey any promotional message with respect to the use of the medicinal product, e.g. "plus";
    - appear offensive or have a "bad" connotation in any of the official EU languages;
    - convey misleading therapeutic or pharmaceutical connotations;
    - be misleading with respect to the composition of the product;
    - cause confusion in print, handwriting or speech with the proprietary name of an existing medicinal product;
    - cause confusion in print, handwriting or speech with an established INN.

  - be derived from INNs and in particular from names that include an established INN stem. It is especially important to avoid that the proposed invented name includes an INN stem from a different pharmacological group.[25]
- The use of superscript capitals together with invented names should indicate that the trade mark registration was approved or is pending. It should be kept in mind that many local software registers do not distinguish between capitals and small letters.
- For medicinal products containing a pro-drug, an invented name different from the invented name of the medicinal product containing the related active substance is required. Prefixes like “pro-“ and “neo-“ should be avoided.

Product line extensions and umbrella brands

Product line extensions are new dosage forms or strengths of already authorised medicinal products. Naming of medicines belonging to a product line deserves special attention, particularly if the initial invented name is modified by a prefix or suffix.

In the case of a switch from "prescription" to "non-prescription" status of an already authorised medicinal product it is up to the applicant the switch to chose whether to retain the same invented name or to chose a new invented name: application for a marketing authorisation of an OTC medicine which has the same umbrella name but different active pharmaceutical substances should be discouraged.

Umbrella brands for a different combination of medicines with several active pharmaceutical ingredients may lead to confusion. Patients and professionals may not be aware of the difference, which may give rise to errors that can lead to unexpected consequences. [30,31]

III.2.3. Recommendations to improve the safety of medicines names

III.2.3.1. Verification of the safety of International Non-proprietary Names (INN)

The WHO INN Programme and the national nomenclature committees have established a procedure to verify the safety of INNs as regards confusing similarities between new INN and existing INNs or trademarks worldwide. Although it is assumed that the name proposed by the applicant has been checked for the absence of potential confusion, the INN Secretariat and experts will verify safety by consulting appropriate national databases. Such access is easy for INN, but more difficult for trademark databases.

Since INN stems allow to identify generic medicines that share a similar therapeutic activity, medication errors related to the use of INNs have been reported.[32] However, the building-up principles of INNs appear to be a mitigating factors of such medication errors: the confusion occurring between identical stems of INN names (such as “cef-” for cephalosporins, “–olol” for beta-adrenergic blocking agents), might reduce the clinical consequences of confusions between INNs, more often related to inadequate dosage than to different and unexpected pharmacological effects.[27]

Considering their interest in the safety of medicines names, medication errors reporting systems (MERS), as well as national focal points on safe medication practices, should be strongly invited to systematically comment on the proposed INN published in *WHO Medicines information* during the four month deadline for objections. Under the sole condition of (free)

membership, MERS and national centres may easily provide comments by the INN Mednet, a secure electronic WHO information exchange service. The comments of all interested parties will be taken into consideration by the WHO INN Programme.

However, the steps followed by the WHO INN procedure do not yet address all available measures to select the INN names from the perspective of in-use safety. In addition to currently used methods, the WHO INN Programme and national nomenclature committee should apply methods to assess medicines trade names to ensure in-use safety. This implies the review of the proposed INN by health care users and patients to ensure in-use safety (see III.2.3.2).

III.2.3.2. Pre-marketing safety assessment of proprietary medicines names

National drug regulatory agencies and EMEA should require manufacturers to assess systematically and with a focus on in-use safety the risk of possible sound- or look-alike confusion with existing medicines before new medicines are approved. The results of the risk assessment should be submitted to the drug regulatory agency together with other evidence included in the marketing authorisation application.

National drug regulatory agencies and EMEA should review the risks of proposed proprietary names as a part of regular marketing authorisation procedures.

There is a variety of assessment methods that may be applied to identify if there are look- or sound-alike invented or non-proprietary medicines names already registered which could be confused with the new proprietary name, such as:[22,33]

- computerised searching using objective measures of linguistic similarity (orthographic/phonetic),
- frontline health professionals /expert judgement,
- testing of prescription in oral and written communication.

Once the potential risk for medication errors in relation to existing medicines names with similarities to the new proposed drug name has been identified, it should be systematically assessed by “failure mode and effect” analysis.[33] It will consider the closeness either in speech or in writing, and possible contributing factors according to the use of the new medicine (i.e. Who will it purchase? Where will it be stored? Who will prescribe it and how? Where will it be used? Who will administer it? etc.). The following contributing factors should be taken in consideration during this assessment of the likelihood of confusion due to the similarity between new and existing medicines names:
- pharmaceutical forms and routes of administration;
- dosage strengths;
- proposed dosage and dosing intervals;
- clinical settings for dispensing or use;
- conditions of use of the concerned medicinal products, i.e. restricted to hospital, specialists, over-the-counter, etc.;
- storage;
- therapeutic category and indications;
- patient populations.

When comparing the proposed name with other existing medicines names the potential risk of health damage either due to the inadvertent administration of the medicine or the lack of administration of the intended medicine to a patient has to be considered.

The above-mentioned methods are not scientifically validated and it is unclear which assessment method or which combination of methods will be the most relevant to predicting risks of look-alike and sound-alike medicines names.[34,35] On the other hand, medicines regulators may chose adequate criteria to assess proposed proprietary names.

EMEA and national drug regulatory agencies should establish standardised procedures for carrying out a systematic assessment of medicines names with a view to consistent results and a focus on in-use safety. In addition, medicines name review procedures should be updated once a validated, reproducible, and objective methodology is available. With a view to transparency and as a reference for auditing, publication of assessment criteria for proprietary names would be important.

III.2.4. Safe practices related to medicines names

III.2.4.1. Promotion of the wide-spread use of non-proprietary names

The use of non-proprietary names instead of invented names in medication practice should be promoted to improve medication safety. Some observations indicate that the alternate use of both generic and invented names for the same medicinal product leads to medication errors, particularly overdosing, due to the use of several medicines with different names but containing the same active pharmaceutical substance.[36]

By standardising the identification of active pharmaceutical substances worldwide, the INN system facilitates communication between patients and health professionals both nationally and internationally. [37]

INNs decrease the number of names to keep in mind, since a unique name corresponds to several invented names for the medicines which contain the active pharmaceutical substance. In this way, the INN system is useful for those who prescribe, dispense and administer medicines, helping them to be better informed, avoiding overdosing by the repeated dosing of the active pharmaceutical substances in medicines with different invented names and reducing interactions resulting from lack of awareness of all active pharmaceutical substances contained in a branded medicine.

Patients should be informed on where to find the description of the INN on the medicines' labelling: if they recognise the active pharmaceutical substances in their treatment, their health literacy and active involvement in treatment plans will increase. Knowing the INNs of their medicines, patients may recognise a dispensing or administration error and be able to inform health professionals if they have suffered previously some adverse effect or allergies related to a medicine. They will be better prepared to avoid the risk of taking the same medicine with different invented names.

When confusion errors between INNs occur, the use of both the INN and the invented name should be promoted in medication practice as an additional safeguard to differentiate between medicinal products, thus providing a redundancy control.[38] In such cases of error-prone INNs,

national focal points on safe medication practices should liaise at European level and submit to the WHO INN Programme a well documented proposal for substitution (see III.4).[25]

III.2.4.2. Safety practices for health professionals

Medication errors resulting from the confusion of medicines names may occur at any stage of the medication use system: procurement, prescribing, dispensing and administration. There are some safety practices that practitioners may use to minimise errors with medicinal products that have sound-alike/look-alike names:[39]

- Considering the possibility of name confusion when new medicinal products are added to the medicines formulary;
- Avoiding, as far as possible, the inclusion of medicinal products with similar pronunciation or spelling in the formulary. If look-alike or sound-alike medicines remain in the formulary, taking measures to avoid errors as listed below;
- Implementing electronic prescribing systems that will help to eliminate handwritten prescriptions. Until this technology is more widely available, prescribers should be encouraged to write prescriptions legibly and carefully, specifying the pharmaceutical form and dosage strength. It is important that prescribers add the indication to the prescription. The use of both the brand and generic names on prescriptions is recommended in case of medicines with a high risk of confusion errors;
- Verbal orders should be avoided. If verbal orders are absolutely necessary, the nurse or pharmacist taking the order should verify it by repeating back to the doctor all elements. Confirmation of the generic name together with the invented name would also help to avoid mistakes;
- Implementation of computerised reminders for most serious confusing names in hospital and community pharmacy administration programmes. So an alert is generated when prescriptions for error-prone medicines are issued;
- Changing the appearance of look-alike medicines on computer screens, pharmacy and nursing unit shelf labels and bins (including automated dispensing cabinets), pharmacy product labels and medication administration records by highlighting the parts of the names that are different in bold, colour, and/or capital letters, (e.g. hydrOXYzine, hydrLAzine);
- Separation of medicinal products with look-alike or sound-alike names in storage areas in the pharmacy as well as in patient care areas. Application of stickers to the location of look or sound-alike medicinal products in order to warn professionals of the risk of confusion;
- Verification of the prescription medicine in front of the patient to confirm the expected appearance and review of the indication;
- Cautioning of patients about the risk of errors when taking medicinal products that have look-alike or sound-alike. Taking time for assessment if a patient states he is taking a medicine about which the professional lacks information;
- Encouraging the reporting of errors and potential look and sound-alike medicinal product names and use of the information to implement measures such as those mentioned above. Communication of the errors to the national medication errors reporting systems MERS (see chapter I).

III.3. Improving the safety of label information and packaging of medicines

Safety and effectiveness of medicinal products depend on health professionals and patients selection of the adequate medicine and their ability to understand the information pertaining to its adequate use. Medicines' labelling and packaging should be designed to ensure the unambiguous identification and safe use. It is important recall the purpose of good medicine packaging:[40]

- Medicine integrity: the primary function of packaging is to preserve the basic properties of the medicine (e.g. sterility, concentration, etc.) during its shelf-life from a variety of chemical and physical factors, such as temperature, humidity, shock and light;
- In-use safety: another essential function is to make the medicine clearly and immediately distinguishable by sight from other medicines or from different dosage forms of the same medicinal product;
- Prevention of accidental poisoning, particularly of children.

The aim of good medicine labelling is:[10,41]

- Correct description of the medicinal product;
- Clear product identification, ensuring that the appropriate medicine is selected leaving no room for doubt or error;
- Provision of information to ensure appropriate and safe storage, preparation, dispensing and administration;
- Tracing of the medicinal product in case of problems with either the manufacturing, prescribing or dispensing process.

III.3.1. Label information and packaging as sources of medication errors

Inappropriate labelling and similarities in packaging and labelling are frequent sources of dispensing and administration errors.[1]

The incidence of medication errors and adverse drug events caused by packaging and labelling is unknown and difficult to estimate, since there are no studies on this problem are available. Information is available from case reports and from reports forwarded by health professionals to national medication error reporting systems (MERS) (see Chapter I).

In the United States, the Institute for Safe Medication Practices (ISMP) receives 1200-1500 reports of serious medication errors per year.[8] Approximately 25% of these reports are related to labelling and packaging.

In Spain, confusing, unclear or incomplete labelling and packaging are associated to 28% of the actual or potential errors reported to the ISMP-Spain MERS.[13] One third of the reports communicated via the French medication errors reporting system (REEM) involves labelling and packaging.[42]

Causes of frequent errors may be categorised as follows:

- Similarities in the packaging and labelling of different dosage strengths of the same medicinal product or of different medicines marketed by the same pharmaceutical company;
- Unclear or inappropriate labelling, particular poor display of dosage strength/contents leading to dosage errors;

- Poor packaging design that leads to incorrect preparation and administration of medicines.

Analysis of the causes and contributing factors of medication errors communicated to the various national medication error reporting systems over the past few years, has led to the identification of labelling and packaging issues frequently associated to incidents and to the improvement of labelling and packaging design. The following issues causing errors are particularly noteworthy:[1,43]

- The design of packaging and labelling often supports a common "trade dress" ("corporate dress") serving as an identifying mark ("corporate identity") for the manufacturer which may make the differentiation of one medicnal product from another sometimes difficult;
- look-alike medicines names, same dosage strengths and labelling with medicines names printed in small size with very little contrast are factors that increase more the potential of confusion of medicinal products with otherwise similar packaging;
- less important information for the correct use of the product, such as the company name and logo, is sometimes much too prominent, interfering with the readability of essential labelling information. Essential label information, such as the medicine name and the strength, may be displayed on the label much less prominent or in very small letter size;
- colour coding may help to differentiate between therapeutical classes, but may increase the possibility of intra-class medication errors, because different medicines and dosage strengths belonging to the same class would be labelled in the same colour;
- blister packs for oral medicines do not generally permit to identify each unit dose individually, so that cutting the blisters increases the risk of confusion;
- expression of the dosage strength by concentration (quantity of active pharmaceutical substance per unit of volume) rather than total amount per total volume in injectable products and liquid preparations frequently leads to overdosing, since the concentration per millilitre may be mistaken for the total amount in each container;
- dosing errors may occur if dosage strength is expressed as a percentage of weight to volume (% w/v) which is commonly not well understood and which requires calculation to determine the quantity of active pharmaceutical substance per dosage unit;
- many dosing tools (dispensers) supplied together with multi-dose oral solutions are inexact and/or difficult to use and lead to dose errors.

An in-depth analysis of medication errors reveals that the current design for labelling and packaging is not patient-centred, but, rather, relies on perfect performance by health professionals and by patients, as well as the utilisation of medicines under ideal conditions.[44]

Emergency situations and common environmental factors, such as noise, frequent interruptions or insufficient light, are not considered when labelling and packaging are designed, thus increases the risk of medication errors. Often, information is not developed for the patients' needs, so that patients may not fully understand warnings or other information on the label.

The current design for labelling and packaging considers insufficiently the context in which the medicinal product will be used: health professionals are handling many different medicines and patients may also be taking several medicines and might easily confuse medicines having similar packaging.

The "real-life" medication use stages and possible risk situations are not systematically analysed and taken into consideration when product packaging and labelling is designed.[45] For example, it is not considered that medicines are often removed from the original package in hospitals and that every presentation (ampoules, vials, etc.) must be completely and correctly identifiable and

distinguishable from other medicinal products. The lack of original unit doses drives hospital pharmacies to repack poorly packed medicines, opening up opportunities for errors as well as an economic burden. Likewise, patients may remove blister strips from their original containers at home. Occasionally, they may cut blister strips leaving them with insufficient labelling information for identification.

Post-marketing surveillance of the medication errors and measures taken when potentially harmful problems are identified, are not sufficiently protecting patients from health damages related to medicine packaging. More proactive approaches are required: improvement of design as regards labelling and packaging safety for new medicines and the evaluation of the safety of labelling and packaging to be carried out by the pharmaceutical industry systematically and with a focus on in-use safety before a medicine is marketed.

III.3.2. Recommendations to improve the design of label information and packaging with a view to medication safety

In the following reference is made to the recommendations on labelling and packaging design of the Council of Europe Expert Group on Safe Medication Practices. Pharmaceutical industry is encouraged to consider the recommendations in the pre-marketing phase in order to reduce the number of medication errors stemming from labelling and packaging. In addition, Appendix 6 includes a checklist based on the above-mentioned recommendations which the Expert Group on Safe Medication Practices considers as helpful for drug regulatory authorities, pharmaceutical industry, and health professionals in assessing the label information and packaging safety.

Human error is unavoidable and must be anticipated. Experience from other industry branches has shown that the natural tendency of human beings to make mistakes can be significantly reduced by designing products which are difficult to use improperly.[46] The afore-mentioned "safety by design" concept needs to be applied to the design of packaging and labelling of medicinal products to make it easy to use them correctly and difficult to use them incorrectly.

Effective solutions require the application of human factor principles to the design of medicine labels and packaging and an in-depth understanding of the range of potential users and how they will use them under different conditions.[47] Simplicity, distinctive features, standardisation and unambiguous information are some of these principles that are important for the improvement of medicine labelling.[43] If applied to health care, effective design concepts will bring forward medicinal products that are simple and convenient to use and consequently, less likely to lead to accidental misuse, error and harm. If applied to packaging and labelling of medicinal products, effective design will improve the in-use safety of medicines by enhancing visual distinction of medicinal products, clarifying presentation and readability and improving the legibility of essential information.

The following recommendations apply these principles to the improvement of labelling and packaging safety by design. They are based on the *Best practice guidance on the labelling and packaging of medicines*[6] published by the Medication and Health Care Product Regulatory Agency (MHRA) and complementary design research[7] conducted in the United Kingdom, numerous newsletters and other documents published by the Institute for Safe Medication Practices (ISMP)[8] and the draft *General Requirements for the Labelling Medicines* [9], under discussion by the Australia-New Zealand Joint Therapeutic Products Agency. These sources will not be cited below. Instead, other references used for some specific aspects will be quoted.

III.3.2.1. Essential information

Certain information is essential for the in-use safety of a medicine and should be presented clearly and in sufficiently prominent manner on the label of the outer packaging (see respective European and national legal provisions) . These items are:

- name of the medicinal product;
- international non-proprietary name(s) of active pharmaceutical substances;
- dosage strength/concentration;
- route of administration;
- dosage instructions (for over-the-counter medicines);
- specific warnings including pictograms/symbols.

This essential information should be always presented on the main face(s) and should be grouped together on the same face, where practicable. These items should not be separated by additional information, logos or graphics.

In line with article 54 of Council Directive 2004/27/EC[4], other obligatory information on the packaging must appear in less prominent position or be printed elsewhere. For example, marketing authorisation number, batch number and expiry date could be positioned on the back or side panels of the package. Additional less safety-relevant information should be presented less prominently, e.g. in the package leaflet, to avoid impaired legibility.

Preferably, labelling information should appear only in the official language (or languages) of the country where the product is marketed. In case of multi-language packs, special attention should be drawn to the need to present labels in a clear and legible manner in order to avoid diminishing the visual appeal and the ease in locating and understanding essential information.

A clearly designated space should be provided on the outer packaging to include patient-specific information in the form of a dispensing label (see III.3.4.1). Dimensions may vary (i.e. 80 x 45 mm in Australia)., A minimal 70 x 35 mm space should be foreseen as this is the most common size of a dispensing label.[7]

III.3.2.1.1. Name of the medicinal product and of active pharmaceutical substances

The name of the medicinal product has to comprise the trade name (or generic name with indication of manufacturer), dosage strength and pharmaceutical form and must include all labelling and packaging components where the name is required to appear.

The international nonproprietary name (INN) or, if none exists, the usual common names, should immediately follow the name of the medicinal product on the front face of the packaging.

The full name of the medicinal product should appear prominently on at least three non-opposing faces of the outer packaging to allow clear identification of the medicinal product: the front face, one of the two side panels and one of the two end panels. The Europea Pharmacopoeia (Ph. Eur.) List of Standard Terms[i] should be used for the pharmaceutical form. The List of Standard Terms contains short terms for some pharmaceutical forms, but these short terms should be only used if there is insufficient space on the label to print the full standard in 7

[i] published by the European Directorate for the Quality of Medicines and Health care, Council of Europe

points Didot on small labels. Other abbreviations and different expression of dosage strength may be unsafe and should be avoided.

III.3.2.1.2. Expression of dosage strength[1a]

The quantity of the active pharmaceutical substance should be expressed in one of the following ways:
- per dosage unit,
- per unit of volume, if appropriate for the dose form,
- per unit of weight, if appropriate for the dose form.

Dosage strength of single dose injectables and single dose liquid preparations should be stated as the total quantity of the active pharmaceutical substance per total volume and per ml: if the volume in the container exceeds 1 ml, the concentration (quantity of active pharmaceutical substance per one ml) should be indicated immediately below, either between brackets or in less prominent letters. For large volume and multi-dose parenterals the quantity of active pharmaceutical substances should be stated per ml, per 100 ml etc. as appropriate.

The dosage strength of solutions and suspensions for oral administration should preferably be expressed as concentration (i.e. mg/ml).

With a view to in-use safety, it should be generally avoided to indicate strength in percentages. An exception may be justified in certain cases where the name of the medicine includes the indication of strength as percentage (e.g. in medicines for cutaneous use).

The dosage strength for a medicinal product should be expressed in an appropriate metric system unit, except in situations where other units of measure are accepted and required, e.g. the use of I.U. (international units) of potency for biological medicinal products.

Different strengths of the same medicinal product should be stated in the same way, for example tablets 250 mg and 500 mg (mg should be used from 1 mg to 900 mg). The simultaneous use of milligrams and international units for the same medicinal product should be avoided. The use of decimal points should be avoided where they can be easily removed (i.e. 250 mg is acceptable whereas 0.25 g is not).

The expression “microgram” should always be spelled out in full rather than abbreviated in order to minimise the possibility of confusion with “milligram”.

Trailing zeros should not appear (2.5 mg and NOT 2.50 mg). The decimal point need not be centred, provided that any full stop used is clearly visible.

The strength of medicinal products with up to three active pharmaceutical substances should be indicated in the name with the numerical quantity for each active pharmaceutical substance separated by a dash (for example “INVENTED NAME 20/10”). In such cases, units of measure (e.g. mg, units) may be omitted.

The dosage strength of medicinal products with four or more active pharmaceutical substances may be omitted, but on the front face of the package a term such as “combination product” or “multi-ingredient” should be added.

III.3.2.1.3. Route of administration

Positive messages should be used; for example "give by ..." and only the European Pharmacopoeia (Ph. Eur.) List of Standard Terms[ii] for the route of administration should be used. Non-standard routes of administration should be spelled out in full to avoid confusion.

Some routes of administration will be unfamiliar to patients and may need careful explanation. This is particularly important for medicines which are available for self-medication. However, additional information on the route of administration in standard terms may be given on a dispensing label.

III.3.2.1.4. Dosage instructions

General dosage instructions are required on the outer package of medicinal products for self-medication. Medicines that are supplied on prescription should have individual dosage instructions added at the time of dispensing. General dosage instructions and other essential information about the medicinal product are supplied with the mandatory package leaflet.

III.3.2.1.5. Special warnings

The marketing authorisation of certain medicinal products may require that specific, warnings essential for in-use safety are stated on the front face of the package. Examples of warnings appearing on the front face and which should be considered before use are mentioned in the following:

Warnings	Product
To be given intravenously only - fatal if given by other routes	**Vinca alkaloids**
Usually taken once a week	**Oral methotrexate**
Dilute before use	**Potassium chloride concentrate injection**
Contains penicillin	**All penicillin products**

Only positive statements should appear on medicines' labelling to avoid ambiguous messages. Negative statements should not be used.

III.3.2.2. Format, design and use of colour

The information on the label must be clearly visible and presented in legible characters that are easily understood by all those involved in supplying and using the medicine.

Essential information should appear in the order stated (see III.3.2.1) and in a font size as large as possible to maximise legibility, at least, on the front face of the packaging. It should not be mixed with less essential information. The minimum letter size recommended for use on the outer packaging is 12 point, although 14 point would be more adequate for patients with visual impairment.

[ii] published by the European Directorate for the Quality of Medicines and Health care, Council of Europe

Although the use of a large font may be appropriate, other factors are equally important in making the information legible. The fonts should be clear and legible, in a colour or colours contrasting strongly with the background. Clear and legible *sans serif* fonts, such as Arial, Helvetica or Univers, in bold or semi-bold should be used. It is recommended to avoid the use of capital letters and to spell sentences in upper case. Attention should be given to letter and line spacing and condensing the text should be avoided in such a way that the legibility of the information may be compromised. At the same time, some areas should be left blank in order to highlight information essential for safe identification and administration, e.g. the medicine's name and strength.

Text should be presented with the same orientation on every face of the outer packaging excluding the ends. This will facilitate reading information on adjacent panels without having to turn the pack.

Innovative labelling can be used to highlight the difference between medicinal products with look-alike and sound-alike names. *Tall man* (capital) letters may be used for example to highlight those letters that help to distinguish medicines names such as chlorproPAMIDE and chlorproMAZINE. The use of colours for highlighting these letters may help to differentiate between medicinal products with similar names.[48]Effective use of colour and other elements such as colour bands, boxed text, reversed out printing in the design of the packaging should be used to ensure correct identification of the medicinal product. It is necessary to consider for the assessment of a particular packaging design distinguishing features from other packages. Different strengths and presentations of the same medicine or different medicines from the same manufacturer should always be clearly distinct.

Colour differentiation for better identification may be useful when properly used.[49] Colours may be used to differentiate between concentrations or dosage strengths of the same medicine and to draw attention to specific information on the label or to enhance recognition of individual letters (see Figure 3).[7]

Figure 3: Use of colours to facilitate differentiation or to highlight information[7]

The association of colours with information on the label should not reduce attention needed for identifying the name and the dosage strength of the medicinal product.[7]

The use of colour coding on a general basis is not recommended.[7] Although colour coding may help to differentiate between medicines from different therapeutic classes, it may increase intra-

class medication errors. Colour coding of syringe or ampoule labels for anaesthetics are promoted at national level and have inspired national standards[50] for instance in Canada.[51,52] In the United Kingdom, the Association of Anaesthetists, the Royal College of Anaesthetists, the Intensive Care Society and the Faculty of Accident and Emergency Medicine have published a colour code chart for syringe labelling in a joint initiative.[53]

However, even if colour coding appears as an obvious solution to many authors and professional organisations, there is no clear evidence on the impact of coloured syringe labels in reducing medication errors.[54] Moreover, "blind" trust in colour labels may add new risks of medication errors. Under these circumstances, colour coding should be restricted to few situations for specific medicines that are used by a small number of individuals in closed settings and only after testing by practitioners.

If the medicine cannot be seen without breaking the seal of the packaging, consideration should be given to include on the outer packaging diagrams, other visual description or picture of the product, such as tablets or capsules.

III.3.2.3. Small containers

A container with a nominal volume of 10 ml or less is generally considered a small container.

The requirements of article 55 of Council Directive 2004/27/EC, should be applied to a container if the requirements of article 54 cannot be legibly applied.[4] However, other factors such as the amount of information which needs to appear on the label and the font size necessary to achieve legibility of the information may be considered.

In case of limited space, consideration needs to be given to innovative solutions for ensuring that all relevant information is provided and is legible. It should be avoided that logos dominate over essential in-use information.

Medicinal products in small containers may carry space for a dispensing label with individualised information on a cardboard back.

III.3.2.4. Blister packs

Each individual pocket of a blister strip of a medicine in blister packs should preferably include both the trade name of the medicine and non-proprietary name of the active pharmaceutical substance, dosage strength of the product, batch number, expiry date and bar code. Firstly, single blister pockets are regularly cut from the strip being left without adequate labelling information and secondly, labelling information may be damaged as the medicine is removed for use. It is important that information for identification remains available to the user from the first to the last dose (see Figure 4).[7]

Figure 4: Clear presentation of the name and strength of medicines in blister packs on each individual pocket and the use of non-reflective foil may enhance the safe use of medicines[7]

High-risk medicines such as opioids should always be packed in blister pockets with individual information on the label for identification.

It is recommended to use coloured, non-reflective foils to enhance the readability of the information presented and to allow correct identification of the medicine. Blister foils should be printed with a sufficiently large, legible, bold or semi-bold *sans serif* fonts, such as Arial, Helvetica or Univers in order to ensure maximum legibility of the information. Text colours should be chosen carefully in order to contrast text from foil background taking into account that foils are usually reflecting. The text colour should be different for every dosage strength.

III.3.2.5. Adequacy of the package design to medicine delivery and administration

Manufacturers should pay particular attention to the design of the package of a medicinal product: this is to take account sufficiently of the usual conditions for preparation and administration of the medicine by health professionals or patients and to reduce the risk of errors to a minimum.

Medicines should be supplied in ready-to-use and ready-to-administer unit dose presentations in order to help minimising errors.[55,56,57] Thus, possible preparation and administration errors may be prevented as much as possible. The supply of unit dose presentations by industry is also important for avoiding errors from re-packaging medicines into unit dose presentations by personnel in hospitals and institutions.[41]

Pharmaceutical manufacturers should ensure that the presentation of the medicine on labelling and packaging does not lead to the incorrect administration of the medicine, e.g. by an inadequate route. For example, packaging of a concentrate which requires dilution prior to intravenous administration in a syringe bears a risk of injection without proper dilution which puts the patient at an unacceptable risk.[58] The packaging design should also not trigger unsafe use. Design misleading the patient as regards the inherent benefits and risks of the medicine may encourage overdosing.

Strength and content of the medicinal product should be adapted to the usually prescribed dosage. For example, the presentation of an injectable medicinal product in an amount exceeding the amount required for administration might lead to overdosing since the entire volume could be easily administered by error.

The devices used to administer or deliver the medicinal product should also be designed so as to avoid dosage errors. Their graduation should be adapted to the usual dosage.

III.3.3. Pre-marketing safety assessment of label information and packaging

Packaging and labelling of a medicinal product may be a key factor for its safety and efficacy and should be assessed as scrupulously as the medicine.[41] In line with European and national medicine regulations, the quality of a medicinal product must be as such as to ensure safe use as set out in the marketing authorisation and the summary of characteristics (SmPC).

Drug regulatory agencies should require that labelling and packaging are assessed by the manufacturers systematically and with a focus on in-use safety before granting a marketing authorisation. Results of the safety assessment of labelling and packaging should be submitted by the applicant to the drug regulatory agencies in the application for marketing authorisation together with other issues observed during development.

In addition, drug regulatory agencies must also review labelling and packaging before approval and they should require the submission of all different packaging components with a view to comprehensive evaluation. At present, it is required to submit mock-ups at the time of submitting an application for marketing authorisation.

Manufacturers may minimise the potential for medication errors by carrying out a pre-marketing risk assessment including both (potential) medication errors and near misses (incidents) during product development in clinical trials and the results of a systematic risk analysis of all proposed labelling and packaging components.

Some medication errors have been detected during clinical trials, particularly involving medicinal products for parenteral use. If errors or near misses (incidents) such as inadequate dilution or administration methods occur, they should be documented, reported and analysed and appropriate measures should be taken to improve in-use safety.[58,59]

Systematic risk analysis should consider every possible way in which the new medicine may be handled and used in all contexts including both community and hospital settings. Every stage of the medication use system such as storage, dispensing, preparation and administration must be considered to ensure safety of labelling and packaging. In addition, all possible device failures that could result in improper administration should be examined when developing a medicinal product that is going to be administered or delivered by a device.[58]

This analysis must include testing by practitioners and patients under real-life conditions of use of the medicinal product to ensure the maximum clarity and convenience of use of labelling, packaging and any device used to administer or deliver the medicinal product. In addition, these data should be examined by expert panels who will carry out their own assessment.

Care should be taken to ensure that the test conditions are applicable to all practitioners and patients because potential users have different needs as regards the same in relation to the same medicine package. Testing must therefore be tailored to the needs and settings of the different user groups.

Appendix 6 presents a template that has been developed by the Council of Europe Expert Group on Safe Medication Practices to assess in the pre-marketing phase the potential risk of label information. The template comprises four groups of questions that cover the following items: outer packaging, immediate packaging, delivery devices, diluents or other (secondary) containers and packaging design. Drug regulatory authorities and pharmaceutical industry are invited to use this template. In addition, it may be of use to purchasing groups and panels to evaluate the current label information of medicinal products already marketed.

III.3.4. Safety practices to minimise errors related to label information and packaging

III.3.4.1. Optimising patient information with dispensing labels

In Nordic countries, the Netherlands and the United Kingdom, pharmacies are required to put a typewritten label on the medicine packaging when it is dispensed. The dispensing label is required to contain

- identification of the medicine supplied (trade name, non-proprietary name, dosage strength and pharmaceutical form),
- name of the patient,
- date of dispensation,
- indication for use for this particular patient,
- dosage instructions,
- route and method of administration, if appropriate,
- name of the prescriber,
- name of the dispensing pharmacy.

The Council of Europe Expert Group on Safe Medication Practices recommends that the use of a dispensing label containing the above information should be a mandatory requirement in all European countries. It is acknowledged that medicinal products produced by industry and marketed in Europe contain patient information leaflets. However, a medicine may be authorised for a range of indications for which administration route, dosage, frequency of administration etc. may vary. In those instances, the patient information leaflet may provide general information but instructions for the safe use of the medicine need to be individualised.

It is also important to note that patients and carers may have difficulties to remember the exact instructions provided by the prescriber for all their medicines and may easily recall them from the information on the dispensing label.

In many European households several members of the family regularly use medicines and these medicines are often stored at the same place. It is helpful to identify the medicines prescribed for different members of the household in order to prevent medicines from being used by individuals for whom they were not intended.

Information concerning the dispensing date is helpful to patients, carers and health professionals to assess when the medicine has been supplied to the patient. This information, together with the remaining quantity of medicine provides an indication of whether the medicine is being used as directed.

Finally, the name of the dispensing pharmacy provides the contact details of the health professional who knows the patient and may provide further information concerning the prescribed medicines.

For the above reasons, the information on the dispensing label is considered essential. This information must be displayed together with other essential information on the medicine package. It is important that the application of the label does not hide other essential information on the medicine package.

Manufacturers need to recognise that this important information will be added before a medicine is given to the patient. They should develop medicine packages with a specific space of sufficient size to carry a dispensing label (see Figure 5). If current pack sizes are too small in order to do this, the size of the medicine packaging should be adapted or increased to allow the application of a dispensing label without hiding other essential information.

Figure 5: Secondary packaging should have a clearly marked space of at least 70 x 35 mm for the dispensing label[7]

It is recommended that the dimensions, design of a dispensing label have a standardised size and font size standadised across Europe to ensure that the information on the dispensing label can be

easily read by patients and other users. It is also very important to avoid the use of unsafe abbreviations and dosage expressions.

Dispensing labels should contain machine readable identification in order to ensure use on the correct medicine packaging.

III.3.4.2. Safety practices for health professionals

Medication errors resulting from inadequate labelling and packaging and similarities between medicines may occur at any stage of the medication use system: procurement, prescribing, dispensing and administration. There are some safety practices that practitioners may use to minimise this type of errors:[1]

- Analysing labelling and packaging when new medicinal products are added to the medicines formulary in order to avoid look-alike or error-prone medicinal products. It is advisable to purchase medicinal products from different manufacturers so that appearances may be different. If medicinal products with potential problems as regards labelling or packaging remain on the formulary measures should be taken to avoid errors (see chapter IV);
- It is always advisable to limit the number of medicines with different concentrations and strengths of the same active pharmaceutical substance in the hospital setting in order to avoid confusion. Such precaution is even more important in the case of medicinal products with similar or ambiguous labelling which are more likely to be confused among their various dosage strengths;
- Separation of medicinal products with look-alike or sound-alike names in storage areas in the pharmacy as well as in patient care areas. Application of stickers to the location of look or sound-alike medicinal products in order to warn professionals of the risk of confusion;
- Application of additional labels to medicinal products in order to facilitate their differentiation or to compensate for other risk situations (e.g. inadequate expression of the strength);
- Specific cautioning of professionals who use products with problematic labelling or packaging;
- Verification of the prescription medicine in front of the patient to confirm the expected appearance and review of the indication. Encouraging of patients to question health professionals if the medicine look different than expected;
- Cautioning of patients about the risk of errors when taking medicinal products that have look-alike or sound-alike. Taking time for assessment if a patient states he is taking a medicine about which the professional lacks information;
- Encouraging the reporting of errors and near misses due to packaging and labelling and use the information to implement appropriate preventives measures as those mentioned above. Communication of these errors to the national medication errors reporting systems MERS (see chapter I).

III.4. Post-marketing monitoring: sharing medicinal product safety concerns at European level

In spite of the implementation of safety recommendations and specific evaluation in the pre-marketing phase, confusion about labelling, packaging and medicines names may occasionally occur when a medicine is marketed. For this reason, it is necessary to establish adequate procedures to identify problems with marketed medicines due to poor naming, labelling or packaging and to respond appropriately and timely to resolve the problems detected.

In order to accomplish this goal, every country should establish a national centre in charge of monitoring reported medication errors and of making recommendations. At the same time and perhaps even more important for the specific topic of labelling, packaging and nomenclature should be co-ordinated in Europe at supranational level, since many of the same issues affect all or most European countries and cannot be solved at national level.

III.4.1. National medication error reporting centres and drug regulatory authorities

Drug regulatory authorities and manufacturers should establish adequate procedures to monitor problems due to poor labelling and packaging and should be prepared to act appropriately and timely to resolve detected problems.

Every country should establish a national centre for reporting medication errors. This centre should appropriately collect and analyse reports on problems due to medicines labelling and packaging submitted by local centres, health professionals and patients (see I.4.).

Once the reports have been analysed, the national centres should work together with the drug regulatory agencies and pharmaceutical manufacturers to implement appropriate changes in medicines labelling and packaging. In addition, national centres collaborating with the drug regulatory agencies should publish information to advise institutions, health professionals and patients of problems identified and to provide effective solutions for the different processes of medicine procurement, storage, preparation, dispensing and administering, in order to avoid recurrence of the same errors until changes in medicines labelling and packaging have been implemented.

It is also important that national medication error reporting systems provide summaries on medication errors concerning confusion about medicines names. Drug regulatory agencies will be able to assess the effectiveness of safety screening procedures and to request, if necessary, the adaptation of the naming, labelling and packaging of medicines giving rise to significant public health patient safety concerns.

Pharmaceutical manufacturers should solve the identified problems and should inform health care providers about changes in the presentation, labelling and packaging of medicinal products.

III.4.2. Need for co-ordination at supranational European level

In the context of a continuing globalisation of pharmaceutical industry, medicine labelling and packaging have to speak a "universally" comprehensible language[1]: So should be the communication about medication errors. Supranational co-ordination is required for learning and finding solutions.

III.4.2.1. Role of the European Commission (EC): European Medicines Agency (EMEA) Heads of Member States competent Authorities (HoA)

It is necessary to establish clear communication between the national centres for reporting medication errors, the national drug regulatory agencies and the EMEA, other competent bodies in order to analyse problems related to labelling, packaging and naming of all marketed medicines and requiring solutions at European level. Problems that may be improved through revision or modification of current legislation by the European Commission or national competent authorities or through the development of new guidelines to complement existing EMEA guidelines should be given priority: the EC Directorate-General Enterprise and Industry is mandated to maintain, update and give guidance on EU pharmaceutical legislation, draft new legislation and ensure appropriate standards of consumer protection in respect of pharmaceuticals.

EMEA and its subordinate working groups should further intensify their efforts to improve information for patients and professionals on the correct use of medicinal products as embraced by the mission statement of EMEA. In this context, reference is made to the EMEA working party on the quality review of documents and their guidance documents.

It should also be borne in mind that more and more medicines are registered through the centralised marketing authorisation procedure in the EU. In such cases, both the name of the medicinal product and the labelling texts are part of the marketing authorisation issued as a Community decision.[5,60] In consequence, all proposed changes of naming or any aspect of labelling or packaging must be submitted to the EMEA and a possible variation of the marketing authorisation will have an impact on the medicinal product in all EU countries where it is marketed.

As regards communicating the views of member states' drug regulatory authorities with the Commission and with the EMEA, particularly relevant for national marketing authorisations and products registered via the mutual recognition procedure, the heads of member states competent authorities provide an important platform: they would be also available to support and deliver solutions to emerging with the Community system of Medicines Regulation.

The above structures should give adequate follow-up to relevant findings of national centres for medication errors reporting and take them into account for all marketed medicines and all types of labelling which were identified to pose a risk to medication safety.

III.4.2.2. Role of the Council of Europe: European Directorate for the Quality of Medicines and HealthCare (EDQM & HC)

Reference is made to the contribution of the EDQM & HC to the in-use safety of medicines in particular through the general chapters of the Pharmacopoeia Europaea and its List of Standard Terms for pharmaceutical forms and administration routes.

III.4.2.3. Role of the WHO INN Programme

The WHO INN Programme procedure offers the possibility to revise an INN when it appears to cause medication errors:

> "In the extraordinary circumstance that a previously recommended international non-proprietary name gives rise to errors in medication, prescription or distribution, or a demonstrable risk thereof, because of similarity with another name in pharmaceutical and/or prescription practices, and it appears that such errors or potential errors cannot readily be resolved through other interventions than a possible substitution of a previously recommended international non-proprietary name, (…) proposals to that effect may be filed by any interested person."[25]

However, such substitution proposals should be approved by a significant number of member States to support them and to avoid jeopardising the basic principles of the WHO INN Programme. Therefore, a European co-ordination of national centres on safe medication practices is necessary to prepare a well documented proposal for substitution to be submitted to the WHO INN Programme.

III.5. Electronic identification of medicines to improve medication safety

III.5.1. Reducing medication errors with machine readable codes across the medication use system

Machine readable codes are included in bar codes and radiofrequency tags (RFID) incorporated into products. Machine readable codes can be read automatically and can be used for the identification of medicinal products and other encoded information.

Electronic prescribing allows electronic ordering of medicines. It is effective in preventing errors at the start (ordering) of the medication use system (see IV.3.3). However, electronic prescribing offers only a weak control over the following stages of dispensing, distributing and administration of medicines, even if information technology applied to the prescription stage has an impact on the whole medication use system.

Bar code based scanning of medicines offers an important advantage for the identification of medicines during medicines procurement, inventory, storage, preparation, dispensing and administration. Medication safety is supported by the above technology through a close connection of information with the medicinal product: Barcodes are printed on medicine packages or more sophisticated electronic devices such as radiofrequency tags (RFID) are attached to medicine packagings. Machine readable codes on medicinal products permit the

accurate identification during the supply chain and at the stages of dispensing, preparing and administration.[61]

The use of above technology may not only improve the efficiency of the medication use system, reduce delays, lowering costs, but also to assist in the dispensing of patient packs and, where appropriate, unit dose medicines distribution systems (see IV.6.1). This technology offers a method to confirm the origin of a medicine before it is dispensed and to identify counterfeit medicines.

Particularly in acute care setting, the use of bar code scanning of the health care provider, of the medicine, of the patient's medical record and of the patient himself helps ensuring safety in the administration of medicines. Patient safety is improved because this technology allows real-time confirmation of patient identification, medication, dose, time and route of administration and offers a unique opportunity to safety checks before the administration of the medicine (see IV.8.2).

By "closing the loop" the continuous identification of medicines during the medication use system reduces medication errors, prevents costs for the treatment of health damage due to medication errors and provides other benefits for a health care site such as a traceability and better identification of medicine-related costs.

Recommendations for machine readable code son medicinal products

Continuing the current non-standardised and unregulated use of machine readable code son medicinal products is likely to increase risks for patients in Europe. These codes are expected to be used more frequently in clinical practice in the future. Inaccurate, confusing or unreadable codes or codes not included in health care databases may pose risks.

Machine readable codes need to be standardised and considered together with other labelling information in the course of the marketing authorisation procedure of medicinal products in order to ensure patient safety and to prevent new risks.

European medicine regulations should include requirements for machine readable codes. As an important element, the medicine regulations should require that pharmaceutical companies provide unit dose medicines with a bar code.

With a view to full benefit for patient safety by this technology, it is recommended that the following changes are made to European medicines regulations: all medicinal products marketed in Europe should

- have an EAN-13 code bar containing the GTIN on the primary medicine container as a minimum requirement with an implementation period of two years (see Appendix 8);
- have a data matrix bar code or RFID chip on both the primary container and unit dose with an implementation period of five years. The GTIN, batch number and expiry date should be encoded;
- include a unique serial number for each packaging or container in addition to the data matrix and RFID chip with an implementation period of five years, if the medicine is at risk of being counterfeit.

Pharmaceutical manufacturers should be allowed to market medicinal products with higher level technology and patient safety features, such as EAN-13 code bar containing GTIN, data matrix

and RFID chip as soon as they wish but at the latest five years after the revision of the respective European regulations.

The use of a machine readable code at dispensation should be recommended as a new professional standard by professional pharmacist associations across Europe.

Bar code enabled point-of-care (BPOC) as well as RFID enabled point-of-care technology holds should be strongly promoted since these technologies are designed to prevent errors at those stages of the administration of medicines where errors occur most frequently. Only point-of-care systems can ensure the "five patients' rights" at the bedside: right medicine, right patient, right dose, right route of administration and right time.

III.5.2. Standardising the 'name field' in databases

The description of a medicinal product in databases deserves attention: The field is called 'name field' although it is usually a combination of 3 or more fields.

Name fields must be readable on computer screens and order forms and, at the same time, should give all relevant characteristics or properties of every medicine for accurate identification and differentiation from other medicines. However, usually, there are less than 50 characters available, which create a need for abbreviations.

The database owner is responsible for creating the 'name field'. Different systems may use different abbreviations and dose designations which may result in different name fields for the same medicinal product and, thus, contribute to medication errors. Research in this area is needed in order to establish a set of standards for the electronic description of medicines.

National drug regulatory authorities should take the initiative to ensure that name fields comply with safety requirements as regards abbreviations and dosage strength information as well as to promote harmonisation of name fields for the same language.

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Chapter IV - Improving the safety of the medication use system

Key points:

- Increasing experience and research on safe medication practices have been effective in managing medication related risks to patients. These practices have been developed in other health care sites, frequently in other countries, and are unlikely to meet the exact needs of individual sites without modifications. However, with local modification these methods are likely to be effective in minimising medication risks to patients. The effectiveness of these methods should always be evaluated to ensure the intended benefits are being delivered and to identify any new risks that will also need to be managed.
- Multidisciplinary medication practice procedures must be included in undergraduate, induction and refresher training for all health care staff that have responsibility for medicine use.
- Risk assessment of the safety of naming, labelling and packaging of medicinal products should be carried out and considered alongside clinical and cost effectiveness issues when organisations are selecting for purchase and procuring new medicinal products.
- In hospital settings, the storage of ward stock medicines on the nursing units or in patient care areas should be controlled and set at a minimum. High-risk medicines should be restricted, not stored in general patient care areas and procedures should be in place to ensure that there are adequate controls to ensure the safe use of these products e.g. special storage and documentation procedures in clinical areas and dispensed for individual patients from the pharmacy.
- Prescribers should evaluate the patient's total status and review all existing medicine therapy before prescribing new or additional medicines to ascertain possible preventable adverse drug events. Prescription information should be printed legibly. At a minimum, prescriptions should include patient name, patient allergies, non proprietary name (INN), route of administration, pharmaceutical form, dose, dosage strength, quantity, frequency of administration, indication, prescriber's name and date. Abbreviations should be avoided.
- There is some evidence that electronic prescribing systems with decision support and electronic alerts reduces prescribing, dispensing and administration errors. These same systems may also introduce new risks and such systems need to be evaluated in each health care institution as part of the implementation plan.
- There is evidence that enabling pharmacists to screen prescriptions and the patient health record before medication are dispensed and/or used can help identify and correct medication errors. Health care institutions should determine what percentage of prescriptions are not screened by pharmacists in this way and areas of high risk where there would be benefits in enabling pharmacists to provide this service.
- The preparation of complex and high risk injectable medicines in the hospital setting should be minimised. Presentation of ready-to-use ready or ready-to-administer injectable products preferably as licensed products but where necessary prepared in the hospital pharmacy.
- Pharmacists should ensure that medicines are delivered to the patient care area in a timely fashion after receipt of prescriptions, according to the method of unit dose drug distribution and a control system that brings a real and appreciable safety to hospitalised patients.

- - One-stop dispensing systems should be used to assist with the reconciliation of medicines on admission and discharge from hospitals, both own medicines and these dispensed during hospitalisation. This could ensure that hospital patients have ready access to a patient information leaflet for all medicines and could support further compliance as the same medicines are used in both hospital and ambulatory settings.
- Use of patients' own medicines and one-stop dispensing systems assist with the reconciliation of medicines on admission and discharge from hospitals, ensures that hospital patients have ready access to a patient information leaflet for all their medicines and aids patient compliance as the same medicine packs are used in both hospital and ambulatory settings.
- Health care practitioners should review the patient's list of medicines with the patient at every encounter. The reconciliation of medication histories should be done at every transition of care in which new medicines are ordered or existing orders are rewritten.
- Ongoing patient profiles, including medicine therapy records as well as demographic and clinical information, should be maintained by prescribers. Pharmacists can collaborate proactively with prescribers and patients, reviewing the patient's medication profile and involving patients in their treatment, to ensure that the goals of pharmacological therapy are being met.
- Prior to each medication administration: patient identity is verified/double-checked (e.g., via wristband), and medication to be administered is verified against the patient's prescription at the point of administration.
- Improving the safety of the medication use system is feasible: multiple solutions are ready to be implemented, mainly based on changes for better medication use practices. National authorities and health care organisations should impose the measures and resources necessary for putting these practices into effect.

Introduction: making use of medicines safer

Ensuring medication safety is a challenge for each dose to be administered or to be taken. However, we know that it really is possible to improve the safety of the medication use system and to avoid unnecessary injuries to the patients. Numerous strategies, practical solutions and effective measures allow to reduce and to prevent medication errors and, therefore, preventable adverse drug events. This chapter briefly describes shortly various safety practices proposed to prevent medication errors in the medication use system both in the hospital environment and in the ambulatory setting.

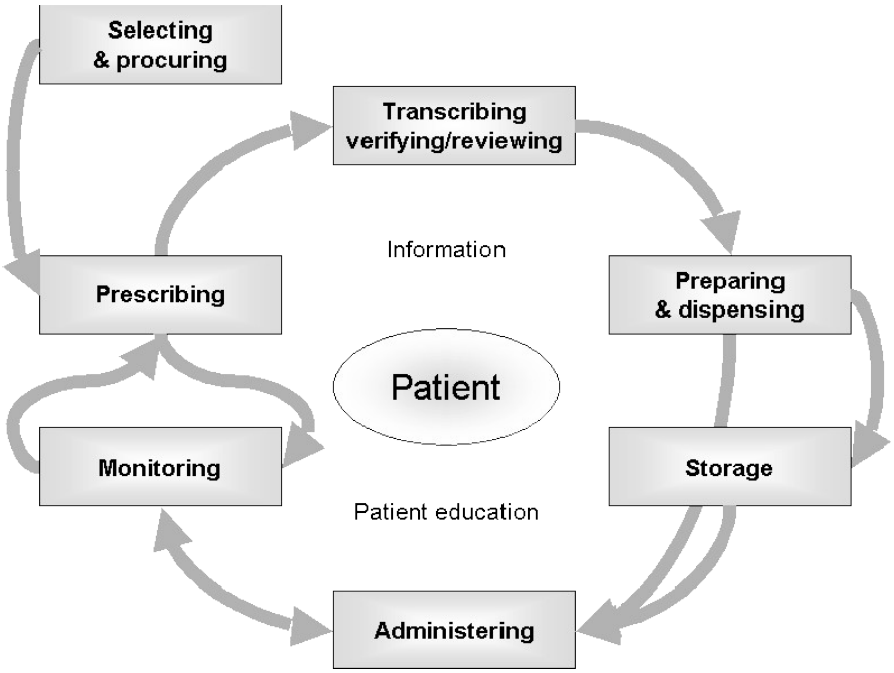
Safety improvement in health care is based on the application of principles and techniques grounded on the "sciences of the safety", as the analysis of systems, the cognitive psychology and the engineering of human factors.[1] Besides these concepts, when it is sought to approach a programme of reduction and prevention of medication errors, it is necessary to keep in mind the following principles.[2]

Understanding the use of medicines as a complex system

The provision of medicines to patients, regardless of the setting, hospital and health care sites, but also ambulatory care, depends on a set of processes, inputs (patient and medicine therapy information), and outputs (effective, efficient, and safe treatment). Therefore, medication use can be viewed as a system.[3,4]

The medication use system is a patient centered combination of interdependent processes that share the common goal of safe, effective, appropriate, and efficient provision of medicine therapy to patients (see Figure 6). Major processes in the medication use system are selection, procurement, storage, prescribing, transcribing and verifying/reviewing, preparation and dispensing; administration and monitoring (should a table describe the different activities undertaken in each process and professionals involved).[5,6]

Figure 6: A general view of the medication use system



The safety of a particular system is a property of the whole system that depends on the operation of all its components and processes, to the professionals that intervene and of the interactions among them. In consequence, improving only one component of the system or preventing a particular failure does not drive to integral improvements of the overall system.

The medication use system is very complex with numerous components and processes. "*Each major process in the medication system - ordering, dispensing, and administration - has its own unique opportunities for error*".[7]

In consequence, any practice or strategy will not in itself solve the medication error problem neither guarantee the safety of the medication use system. Rather, it is necessary to introduce a set of measures or changes in each of the stages of the medicines use system which involves all health professionals and procedures.

Any medication error prevention programme implies the application of a broad array of changes in procedures, teams, organisation and training in order to improve the safety of the whole system. As Leape et al. say: "*Safety is doing a lot of little things that, in the aggregate, make a big difference*".[8]

Using the knowledge of human factors engineering
To err is human, this we know. No error-free system involving human intervention is possible.[9] However, it is possible to design fail-safe systems in order to avoid that the errors cause injury to the patients (adverse drug events). As well as for aviation, such safety systems are based on the introduction of different types of measures not only directed to prevent the errors, but also to make them visible, allowing to detect them on time, in case they occur, and to intercept them before reaching the patient. Based on the knowledge of the engineering of human factors, these measures attempt: [10]

- to reduce the complexity, simplifying and standardising the procedures;
- to optimise the procedures of information;
- to automate the processes;
- to incorporate barriers or restrictions that limit or force to carry out the processes in a certain way and
- to be proactive and to analyse the possible risks coming from the introduction of changes in the system, to prevent the errors before and not after they happen.

It is also necessary to introduce measures mitigating the possible consequences of the errors, in case of the previous safety measures are failing and of the errors reaching the patient.[10]

Establishing a strategic plan for medication safety
Institutions should establish a well-organised strategic plan for medication safety that will include those practices that best fit each particular situation.[11] Such a plan should be integrated into a global multidisciplinary programme of medication risk management and should have the support and commitment of leaders to provide the necessary infrastructure and resources, and to adopt a culture of safety that includes the training of the health professionals.[11,12] Therefore, multidisciplinary medication practice procedures must be included in undergraduate, induction and refresher training for all health care staff who have responsibility for medicine use. It is also important to assess whether the practices applied to improving medication safety have been successful, measuring the reduction of medication errors and adverse drug events seen as a result of using these procedures (see Chapter II).

Creating a culture of safety
The prevention of errors is a long term objective, since the necessary changes needed to improve the patient safety are more cultural than technical.[13] In this sense, it is necessary to always have present that there are no quick solutions because the creation of a culture of safety, with characteristics similar to the one that have the organisations of high reliability, it is the long term more effective measure to prevent medication errors. Since it is a matter of the values and beliefs of the health care organisations, the setting-up of an institutional culture of safety is a long and difficult process.

The primary goal of the Council of Europe Expert Group on Safe Medication Practices was to establish a feasible list of recommended best practices, more than an exhaustive, but dissuasive list of proposed practices. Since more important is to put them into practice, means should be provided for implementing safe medication practices and strategies should be expressed to help for their application.

IV.1. Best practices for preventing medication errors

The seminal publication in the United-States of America of the first report of the Institute of Medicine (IOM) on patient safety 'To Err is Human'[14], led to the publication of numerous documents and reports with recommendations seeking to reduce medical errors in general and medication errors in particular.

Critical reviews of the existing evidence on interventions aimed at reducing medication errors in the health care delivery have been conducted, some of them focused on preventable adverse drug events, such as pharmacist participation in rounds, unit dose distribution systems, electronic prescribing with clinical decision support, etc.[15,16] In the USA, the United States Agency for Healthcare Research and Quality (AHRQ) commissioned the University of California San Francisco (UCSF)-Stanford University Evidence-based Practice Centre (EPC) to produce a report summarising the literature concerning practices relevant to improving patient safety.[17] The report contains summaries of evidence supporting 83 safety practices. Only seven of these practices concern the medication use process and the prevention of adverse drug events:

- computerised physician order entry (CPOE; computer physician order entry) with clinical decision support systems;[18]
- the clinical pharmacist's role in preventing adverse drug events;[19]
- computer adverse drug event detection and alerts;[20]
- protocols for high risk medicines: reducing adverse events related to anticoagulants;[21]
- unit dose drug distribution systems;[22]
- automated medication dispensing devices;[23]
- information transfer.[24]

However, this report of the Agency for Healthcare Research and Quality has been a matter of controversies, appearing "neither a complete nor necessarily an appropriate inventory of practices for priority action to improve patient safety".[8,,25]

Outside the USA, other agencies have also proposed practices, recommendations or standards to prevent medication errors, accessible many of them through their respective websites (see Table 13).

The Council of Europe Expert Group on Safe Medication Practices was committed to recommend the practices having the biggest impact on medication safety and has adopted the following criteria for their selection, which have been adapted from those of the National Quality Forum (NQF):

- Benefit: If the safe medication practices were more widely implemented, it would save lives endangered by the medicine use process, reduce disability or other morbidity, or reduce the likelihood of adverse drug events.
- Evidence of effectiveness: There must be clear evidence that the practice would be effective in reducing the risk of harm resulting from the medicine use process, systems or environment of care.
- Generalisability: The safe medication practice must be able to be implemented in multiple applicable care settings (i.e., inpatient or outpatient settings) and/or for multiple conditions.
- Feasibility: The necessary technology and appropriately skilled staff must be available to most health care sites. Most are widely applicable regardless of size of settings or financial capabilities.[26]
- Cost: Cost might to be considered as a component of the feasibility criterion.

The relative cost of "safe practices" is a matter of prioritisation within each institution because the costs to an individual provider of full implementation of a practice almost entirely depend on whether the provider has already improved medication practices.

Table 13: Organisations providing standards or recommendations for improvement of safe medicines practices

Patient Safety Agencies	
	Australian Council for Safety and Quality in Healthcare[27] (ACSQHC)- http://www.safetyandquality.org
	Canadian Patient Safety Institute (CPSI) - http://www.hc-sc.gc.ca/english/care/cpsi.html
	National Patient Safety Agency[28] (England and Wales) (NPSA) - http://www.npsa.nhs.uk
Health care official bodies	
	Agency for Healthcare Research and Quality (AHRQ) - - www.ahrq.gov
	Joint Commission on the Accreditation of Healthcare Organizations (JCAHO) - http://www.jcaho.org
	United States Pharmacopeial Convention (USP) - http://www.usp.org
Institutes for safe medication practices	
	Institute for Safe Medication Practices (ISMP USA) – http://www.ismp.org
	Institute of Safe Medication Practices Canada (ISMP Canada) - http://www.ismp-canada.org
	Instituto para el Uso Seguro de los Medicamentos (ISMP Spain) - http://www3.usal.es/ismp
Other independent organisations	
	Aktionsbündnis für Patiententensicherheit - www.aktionsbuendnis-patientensicherheit.de
	California Institute for Health Systems Performance - www.cihsp.org
	Emergency Care Research Institute (ECRI) - http://www.ecri.org
	Institute for Healthcare Improvement (IHI) - http://www.ihi.org/ihi
	National Coordinating Council for Medication Error Reporting and Prevention - www.nccmerp.org
	National Quality Forum (NQF) - http://www.qualityforum.org/
	Wisconsin Patient Safety Institute (WPSI) - http://www.wpsi.org
Professional organisations	
	American Hospital Association (AHA) - www.aha.org
	American Society of Health-System Pharmacists (ASHP) - www.ashp.org
	Arbeitsgemeinschaft Deutscher Krankenhausapotheker (ADKA) – www.adka.de
	Florida Society of Health-System Pharmacist - www.fha.org
	Massachusetts Coalition for the Prevention of Medical Errors (MHA) - www.macoalition.org
	Pharmacy Society of Wisconsin – www.pswi.org

There is controversy concerning the evidence base and whether or not practices and recommendations can be generalised to all health care settings and countries. A review of international perspectives on medication safety has identified significant differences in the systems of medicines management between the USA and European countries and the need for safe medication practices developed in one country to be evaluated in another country before these practices are implemented on a wider scale.[29]

A document listing standard and best practices for preventing medication errors and improving medication safety already proposed by several organisations, with indication of their sources, has been established by the Council of Europe Expert Group on Safe Medication Practices (see Appendix 9). This chapter focuses briefly on some practices according to the different processes of the medication use system. It not only recommends best practices selected as described, but

also indicates when practices or equipments fail to evidence their claimed prevention of medication errors, therefore being not recommended.

IV.2. Safer selection and procurement of medicines

Objective: "selecting and purchasing for safety"
Particular care should be taken by assessing potential risks associated with labelling, packaging and naming when selecting new medicines in health care organisations formularies or during the purchase of medicinal products.

Background:
Naming, labelling and packaging of medicinal products is a cause of medication errors (see chapter III). Therefore, potential associated risks should be taken in consideration at earlier stages when selecting and purchasing medicines. When medicines are included in the formulary through a systematic procedure, it is possible to assess the medication error risk involved in the use of each new medicine and, if necessary, to establish safety measures designed to prevent medication errors before rather than after the medicine is ever used. Methods to assess the safety of labelling and packaging are available for helping health care organisations[28,30,31] as well as own practitioners[32] in their choices for building safer formularies (see III.3.3 and Appendix 6).

Safe practices
At all levels of the health care system, health care organisations as well as own practitioners, all formulary and purchasing decisions should critically assess the potential risk involved in the use of new medicines.

Additional specifications

- for hospital and health care organisations:
Establish a systematic procedure for evaluating the addition of new medicines to the hospital formulary as well as the acquisition of new medicinal products with regard to the likelihood of them being involved in serious errors because of similarity in labelling, packaging, or nomenclature, or others causes.

If medicines with potential for error must be purchased, appropriate preventive measures should be adopted prior to the use of the medicinal product.

Purchase of unit dose and ready-to-use medicines should be maximised within the scope of practice needs.

When pharmaceutical manufacturer, packaging or formulations change, medical and nursing staff should be alerted before the medicine becomes routinely available in the wards and the operating theatre.

All decisions for the purchase of medication delivery devices should consider medication safety, including the appropriate level of human factors evaluation, keeping in mind the need for standardisation, and involve physicians, biomedical engineering staff, risk management staff, pharmacists, and nurses in purchasing decisions.

- for ambulatory care
The own preferred medicine prescription list of each general practitioner is established on the basis of safety and practical criteria of use by the patients.

Applicable clinical care setting
Mainly hospital and health care organisations, but also ambulatory care.

IV.3 Safer prescribing of medicines

Prescribing errors can concern: the choice of the medicine[33] (according to the indications, contraindications, known allergies and patient characteristics, interactions, and other factors), dose[34], concentration, posology, pharmaceutical form, route of administration, duration of treatment, and instructions of use but also the failure to prescribe a medicine needed to treat an already diagnosed – or to be prevented - pathology, or to prevent the adverse effects of other medicines (see Appendix 3).

Therefore, prescription errors involve not only the failures related to writing the medicine order but also the failures associated with taking a wrong therapeutic decision, appreciated by any non intentional deviation from standard references such as: the actual scientific evidence, the appropriate practices usually recognised, the summary of the characteristics of the medicine product, or the mentions according to the regulations.

IV.3.1. Adapting safer therapeutic decisions to individual patient needs

Objective
Prescribers should be aware of all patient characteristics that may affect the choice of a medicine or dosage regimen, and adjust the treatment plan accordingly.

Safe practices
Prescribers should take time enough to evaluate the patient's total health status and review all existing medicine therapy before prescribing new or additional medicines to ascertain possible preventable adverse drug events. Prior to prescribing, they should review relevant information related to medicine therapy and check the patient's medical record. They should also take time enough to discuss with the patient.

Additional specifications

Relevant patient-specific information is readily available to prescribers, nurses, pharmacists and other health care providers caring for the patient.
Such information may include:

- medication history
- patient assessment findings
- health screening results
- laboratory results and reports
- medicine therapy notes
- adverse drug events (past allergy information)
- complications
- other patient-specific findings, including those discovered by other health care providers
- best ways to contact the patient (e.g., phone, e-mail, fax, care manager, case worker).

Prescribers should have ready access to relevant medicine information and therapeutic guidelines. Appropriate dosage adjustments are made for children, the elderly and anyone with impaired renal or hepatic function, on the basis of readily available information on dosing medicines in special populations.
A written standard should be established for the documentation of allergies to medicines, including roles and responsibilities of different health professionals involved in the medication process.

When possible, medicines should be prescribed for administration by the oral route rather than by injection.

Applicable clinical care setting
All care settings.

IV.3.2. Safer writing of prescriptions

Objective
Medicine orders should be complete, unambiguous and legible.

Safe practices
Prescription information should be printed legibly. Medicine orders should include patient name, patient allergies, non-proprietary name (INN), invented name (if a specific medicinal product is required), route and site of administration, dosage form, dose, strength, quantity, frequency of administration, prescriber's name and date. In some cases, a dilution, rate, and time of administration should be specified. Abbreviations should be avoided.

Prescribers should review all medicine orders for accuracy and legibility immediately after they have prescribed them.

Methods of communicating medicine orders and other medicine information are standardised and automated to minimise the risk for error.

Additional specifications

The INNs should be provided on all medication orders/prescriptions (see also III.2.4.1). Invented names are optional on all orders and are only an alternative to INNs for combination trademark products. An active programme of education should ensure the widespread use of recommended INNs.

No ambiguous orders which require additional interpretation or clarification are used. Prescriptions should always carry patient directions and never be issued with vague instructions such as: "take as directed," "resume all pre-op medicines," "continue home medicines," or "fill as before".

Explicit organisational policies and procedures should be in place regarding the use of only standardised abbreviations and dose designations.

Weight and date of birth are provided with all paediatric (e.g., neonate, infant, toddler) prescriptions and, where the dose is weight dependent, and the intended dose in mg/kg. Calculated dose and the mg/kg dose are recorded on pediatric prescriptions.

The same method for calculating body/face area should be used by all staff involved in calculating or checking doses which are based on body/face area.

Exact dosage strengths (such as milligrams) should be specified rather than dosage form units (such as one tablet or one vial). An exception would be combination drug products, for which the number of dosage form units should be specified. Leading zeros are used before decimal expressions of less than one (0.1 mg not .1 mg).Trailing zeros are not used after a decimal (2 mg not 2.0 mg).

Standard medicine concentrations and dosage charts should be developed to minimise the need for dosage calculations by staff. Solutions, medicine concentrations, doses, and administration times should bee standardised whenever possible.

Explicit organisational policies and procedures should be in place regarding verbal orders. Policies and procedures limit the use of verbal and telephone orders to emergency situations or situations when the prescriber is physically unable to write the order him/herself; they should not be used as a routine method of order communication. When receiving verbal orders, practitioners repeat the entire order back to the prescriber for verification.

Applicable clinical care setting
All care settings.

IV.3.3. Electronic prescribing and alerts

Objective
Electronic prescribing systems should be implemented and carefully used with awareness of their limitations.

Background: benefits and risks of electronic prescribing
More than two third of prescribing errors, some of them causing adverse drug events, are likely to be prevented with electronic prescribing (also called computerised physician order entry (CPOE; computer physician order entry) in the USA).[35] Several European studies have evidenced the improvement in patient safety (reduction of prescribing errors as well as administration errors) related to the implementation of computerised medication charts compared with handwritten prescriptions [36,37,38,39,40,41].The evidence of electronic prescribing impact on patient safety is clearer when clinical decision support provides timely alerts[15,18,42,43,44,45,46.]

However, it depends on electronic prescribing system characteristics. High rates of adverse drug events may continue to occur after implementation of electronic prescribing and related computerised medication systems that lack decision support for drug selection, dosing, and monitoring.[47] An electronic prescribing system has been found to facilitate 22 types of medication error risks.[48] An increased mortality rate from 2.8% before to 6.57% after electronic prescribing implementation occurred in a American children's hospital.[49] Such a lack of expected performance results from error risks still present in electronic prescribing system and from the poor efficacy of commercially available systems to detect medication errors.[50] Moreover, safety alerts both in hospitals and in general practice may fail to warn in a situation when a warning is expected, thus potentially creating a health hazard to patients.[51,52]

Safe practice
Prescribers should enter prescription using an information management system that
- is linked to prescribing error prevention software, including dose range checks, maximum dose alerts, pediatric dosing based on weight, medicine interactions and checks of compatibility;
- distinguishes between different doses of the same medication used for multiple indications, including off-label uses;
- requires prescribers to document the reasons for any override of an error prevention notice;
- permits the notation in one place of all pertinent clinical information about the patient, including allergies, pertinent laboratory values reviewed prior to proceeding with select medication orders, proposing specific laboratory tests related to specific drug therapies;
- transfers prescriptions directly to pharmacies and enables the review of all new orders by a pharmacist before the administration of the first dose and internally and automatically checks the performance of the information system.

Applicable clinical care setting
All care settings.

IV.4. Safer validation of the prescriptions

IV.4.1. Pharmacists review of prescriptions

Objective
The clinical appropriateness of prescriptions should be reviewed prior to dispensing, and any ambiguity or potential risk clarified with the prescriber.

Safe practices
Pharmacists should review all prescriptions and the complete patient medication profile before medication are dispensed or made available for administration except in those instances when review would cause a medically unacceptable delay. Therefore, pharmacists should have access to the electronic patient's medical record.

All necessary clarifications or changes in a prescription must be resolved with the prescriber before a medication is administered to the patient or taken by himself.

Additional specifications

Relevant patient-specific information as well as medicine information are readily available to pharmacist (see IV.3.1)

Pharmacists should compare each new prescription against the patient profile to detect dosage problems, potential contraindications, drug-drug interactions, drug-disease interactions, and therapeutic duplication before dispensing.

Prescription problems should be resolved directly between the prescriber and the pharmacist. In institutions such as hospitals and nursing homes, written documentation of such consultations should be made in the patient's medical record or other appropriate record. If applicable, nursing staff should be informed of any changes made in the prescription.

Applicable clinical care setting
All care settings.

IV.4.2. Use of pharmacy software for checking

Objective
Pharmacy system software should incorporate an adequate standardised set of checks (e.g. screening for duplicate drug therapies, allergies, drug interactions, dose ranges, alert for look-alike names, etc.) in order to help pharmacists to validate the prescriptions.

Safe practices
Pharmacy should validate medication orders using a pharmacy management computer system that:
- reviews each new medication order/prescription to detect dosage problems, potential contraindications, allergies, drug-drug interactions, drug-disease interactions, and therapeutic duplication;
- automatically checks dose ranges and warns about potential underdoses and overdoses;
- alerts about high-risk medicines, look-alike and sound-alike drug names, packaging, or labelling;
- incorporate triggers and markers to detect ADE and to intervene (see Chapter II).

Additional specifications
Pharmacists review all clinically significant warnings generated by a pharmacy computer system during order entry. Sensitivity of drug-drug interaction warning flags in the pharmacy computer system can be set to minimise non-clinically relevant warnings.

Applicable clinical care setting
All care settings.

IV.5. Safer preparation of injectable medicines

Objective
The amount of injectable dose preparation on nursing units should be minimised by centralising aseptic dose preparation within pharmacy-based IV admixture systems.

Background
Injectable medicines are used to a greater extent than ever before and are commonly being prepared in near-patient areas in European hospitals due to insufficient resources (see Appendix 4.2). In the United States the majority of intravenous doses are prepared in the pharmacy department.

The key problems identified during the preparation of intravenous doses are: poor aseptic technique, complex or multiple manipulations, inaccuracies during calculation and dose preparation, use of wrong diluent, unlabelled products, temporary storage of unlabelled products before use, etc.

Prioritised targeting has been suggested as a practical solution where identified high risk products are prepared in the pharmacy and risk reduction initiatives are used to control the ward based preparation of low risk products[53,54,55]; not enough however to control the high risk

inherent to injectable medicines. Initiatives to improve safe preparation of intravenous medicines and parenteral medicines should be a high priority.

Safe practices
The intravenous dose preparation on nursing units should be minimised by centralising aseptic dose preparation within pharmacy-based IV admixture systems.

Additional specifications (hospital and health care organisations)

Injectable products should be distributed from the hospital pharmacy in a ready-to-administer form e.g. pre-filled syringes, infusion bags, etc.

Medications are not compounded if a suitable and similar commercially available product exists. The range of strengths and formulations of intravenous products should be standardised and simplified.

All injectable chemotherapy should be prepared centrally within the pharmacy and be labelled according to agreed protocols. All calculations should be double-checked as part of this process.

Applicable clinical care setting
Hospital settings.

IV.6. Safer dispensing of medicines

IV.6.1. Safer hospital drug distribution systems

In the hospital setting, the pharmacy department is responsible for the procurement, distribution, and control of all medicines used within the organisation. Pharmacists should ensure that medicines are delivered to patient care areas in a safe and secure manner and are available for administration within a time frame that meets essential patient needs.

Methods in which medicines are dispensed within European hospitals differ. In some hospitals patient packs are supplied; in other hospitals unit dose drug packages are supplied. According to the needed investments, the economic analysis of the costs and the benefits associated with the different medication use systems should be conducted. Strong support for this research and appropriate funding should be provided by the European member states in order to improve simultaneously patient safety, health care workforce employment and health care investments.

IV.6.1.1. Unit dose drug dispensing

Objective
To reduce the opportunities for error for each dose to be administered to hospitalised patients.

Background: individualising drug distribution systems for safety
Unit dose drug dispensing significantly reduces the incidence of medication errors. The evidence issued from comparative studies conducted during the 1960's and the 1970s led to establish unit dose dispensing of medication as a standard of practice in the hospitals in United States of America since it supports nurses in medication administration, reduces the waste of expensive medicines and enable patients to be more easily charged for inpatient doses.[15,22,56]

Although some studies undertaken in Europe, mainly since the 1990s, have also demonstrated comparable results, unit dose dispensing systems are less widely used in Europe than in USA. According to the first European survey of hospital-based pharmacy services conducted in 1995 by the European Association of Hospital Pharmacy, unit dose drug dispensing is not widespread throughout Europe: only 6.5% of the hospitals, except some more advanced countries regarding this organisation such as Spain,[57,58] the Netherlands and Portugal. When comparing USA and Europe, demographic data demonstrate that the difference comes from the lack of staff and equipment devoted to European hospital pharmacies mainly for economic considerations (see Appendix 4.2 for more details).[29,59]

Safe practices
For patient safety, the recommended method of distribution within the organised health care setting is the unit dose drug distribution and control system. Except in emergency situations, all oral and injectable medicines should be dispensed from the pharmacy department for individual patients in unit dose and in ready-to-administer dosage forms whenever possible.

Medicines should be contained in unit dose (single-unit) packagings and unit-of-use ready-to-administer products utilised to the greatest extent possible (see IV.5 and III.3.2.5).

Additional specifications

In the aim to reduce the number of opportunities for error, and for most medicines, not more than a 24-hour supply of doses should be delivered to or be available at the patient care area at any time.

If there are apparent missing doses, it is important that the pharmacy contact for explanation or correction. There may be an important reason why the dose was not sent to the patient care area (e.g., allergy, contraindication, and questionable dose), and resolution of the potential question or problem may be pending.

Medicines should be provided to health care organisations in unit dose, unit of use and ready-to-use packagings (see III.3).

Guidance for repackaging safely medicines in unit dose and unit-of-use packagings should be provided at European and national level.[60,61]

Applicable clinical care setting
Hospitals and health care institutions.

IV.6.1.2. Use of patients own medicines and patient packs in hospital

Background
In the United Kingdom, patients are encouraged to bring in their own medicines, frequently in patient packs, on admission to hospital.[62] The patients own medicines are used during their inpatient episode and the same pack is discharged with the patient. If new medicines or supplies are required during the hospital stay, a patient pack is dispensed and used for the remainder of the inpatient stay and again where the treatment is to be continued, taken away by the patient on discharge from the hospital.

This system of medicines distribution is intended to reduce patients' confusion over their medicines, minimises unintended omission, duplication, variation and wastage of medicines, as well as ensuring the patient has the patient information leaflets for each medicine that they are taking. As well as reducing waste, the use of patients' own medicines and, where appropriate, self-administration can reduce administration errors and help patients prepare for self-care after leaving hospital. This principle has been incorporated into the National Service Framework for Older People.[63]

Safe practices
The use of patients' own medicines and, where appropriate, legal, and self-administration by hospital inpatients could be an option to minimise errors in the transitions of care.

Applicable clinical care setting
Hospitals and health care institutions.

IV.6.1.3. Automated unit dose point of care dispensing devices

Objective
Automated dispensing devices are used in an attempt to improve medication availability, increase the efficiency of drug dispensing, and claim to be able to reduce medication errors.

Background
Point-of-care dispensing devices are also described as automated ward stock dispensing machines (ADM) or unit-based cabinets. These computer-controlled cabinets enable clinical staff access to unit doses of medicines provided that there is a valid electronic prescription entered into the computer control system. Automated dispensing devices have become increasingly common either to supplement or replace unit dose distribution systems. The evidence provided by the limited number of available, generally poor quality studies does not suggest that automated dispensing devices reduce medication errors.[22]

These devices may have the potential to harm since pharmacists and nurses can override some of the patient safety features. When the turn around time for order entry into the automated system is prolonged, nurses may override the system thereby defeating its purpose. Furthermore, the automated dispensing systems must be refilled intermittently to replenish exhausted supplies. Errors can occur during the course of refilling these units or medicines may shift from one drawer or compartment to another causing medication mix-ups.[64] Several studies have found a greater medication administration error or discrepancies prevalence for medicines dispensed using unit-based cabinets compared with those dispensed using unit dose drug dispensing systems.[65,66,67,68]

Safe practices: "wait evidence before implementing"
The conditions of using unit-based cabinets should still be evaluated. Since their contribution to patient safety is still unclear, distribution of these devices is not recommended.

Applicable clinical care setting
Hospitals and health care institutions.

IV.6.2. Safer dispensing in ambulatory care

Objective
To prevent preventable adverse event resulting from dispensing errors in ambulatory care.

Background
Although their extent in community pharmacy is unclear, dispensing errors may harm patients.

Safe practices
During the dispensing process, in addition to the validation of prescriptions (see IV.4), pharmacists:
- reconcile prescription(s) and confirm indication(s) of medicine therapy with the patient or agent;
- show the medication to the patient or agent and ensure that the colour, shape and size of the medication are consistent with what the patient has received in the past; if not consistent, the pharmacist confirms medication identity with the patient prior to dispensing;
- perform counselling and document refusal;
- ask open-ended questions to assess patient and caregiver level of understanding;
- encourage patients and caregivers to ask questions or raise concerns about their medicines.

Additional specifications

A dispensing label should be provided on the medicine package (see III.3.4.1), containing: identification of the medicine supplied, name of the patient, date of dispensing, indication for use for this particular patient, dosage instructions, if appropriate, route and method of administration, name of the prescriber, and the name of the pharmacy.

Particular care needs to be taken when dispensing medicines to children when adult formulations are prescribed.

All supplies of oral cytotoxic medicines should be double-checked before being issued to patients. For short courses or intermittent therapy, dispensing labels should always specify the course length.

Oral anticoagulants dispensing should be double-checked whenever possible. Pharmacy staff should confirm that the dosage strength of tablets and the total amount supplied corresponds to the patient's current dose.

Applicable clinical care setting
Community pharmacies.

IV.7. Safer storage of medicines

IV.7.1. Storing medicines safely

Objective: 'storing useful medicines, not errors waiting to happen'.
In health care sites or at home, medicines should be available only if necessary, in reduced amounts, stored safely and in such a way that the risk of medication errors occurrence is minimised.

Background
The risk of selecting an incorrect medicine increases with the number of available medicine doses, particularly when medicines are poorly stored either at home or in busy, cluttered nursing units. Moreover, in health care sites, floor stock (also called 'ward stock') bypass pharmaceutical safety controls, by allowing nurses to borrow different patient's medicines and hidden medicine supplies. In response, the unit dose drug distribution system (see IV.6.1.1) has been designed to withdrawn unneeded medicine doses as a constraint function[69], evidenced by a reduction of medication errors rates in comparative studies.[70]

Safe practices
The storage of non-emergency medicines should be controlled and set at a minimum on nursing units, in patient care areas or at patient home.

Additional specifications (hospital and health care organisations)

Unit floor stock supplies are customised to the unit needs depending on patient population.

Appropriate storage conditions exist for all medicines at all times (e.g., well designed cupboards, shelves and other storage facilities, refrigerated storage conditions during power outages).

Pharmacists should regularly control all medication storage areas, including operating theatres and anaesthetic rooms, to make sure medicines are stored properly.

Applicable clinical care setting
All care settings.

IV.7.2. Restricting storage of high risk medicines

Objective
To reduce the risk associated with the storage of high risk medicines.

Background
High alert medicines, mainly injectables, are medicines that bear a heightened risk of causing significant patient harm when they are used in error (see Table 14).[71] Although mistakes may or may not be more frequent with these medicines, the consequences of an error with these medicines are clearly more devastating to patients.

Table 14: ISMPs List of High-Alert Medications

Classes/ Categories of medicines		
Adrenergic agonists,IV	Epidural or intrathecal medicines	Moderate sedation agents oral for children
Adrenergic antagonists,IV	Glycoprotein Iib/IIIa inhibitors	Narcotics / opiates
Anesthetic agents, general, inhaled and IV	Hypoglycaemic oral agents	Neuromuscular blocking agents
Cardiplegic solutions	Inotropic medicines (e.g. digoxin)	Radiocontrast agents, IV
Chemotherapeutic agents	Liposomals forms of medicines	Thrombolytics/ fibrinolytics, IV
Dextrose, hypertonic, 20% or greater	Moderate sedation agents, IV	Total parenteral nutrition solutions
Dialysis solutions, peritoneal and hemodialysis		
Specific medicines		
Amiodarone, IV	Magnesium,IV	Potassium Chloride
Heparin	Methotrexate oral	Potasium phosphate injection
Insulin	Nesiritide	Sodium chloride injection, hypertonic
Lidocaine	Nitropusside sodium	Warfarin, acenocumarol

Concentrated potassium chloride requires special consideration since it has led to numerous fatal incidents which could be prevented by safer practices.[72] In 2002, the newly formed NHS National Patient Safety Agency made its first directive recommending the withdrawal of potassium products from ward stock and replacing them with ready-to-use infusion products.[73] The implementation in NHS trust has been fully effective (90% to 98% compliance[74]) since there have been no further incident report to the NPSA of death or serious harm in England or Wales involving potassium chloride concentrate.[75] The cost of the reduction in risk has been estimated £0.50 per opportunity for error.[76]

Safe practices

High-risk injectable medicines should be dispensed to clinical areas only in ready-to-administer or ready-to-use presentations to minimise the requirement for complex calculations and manipulations (see IV.5 and III.3.2.5).

High-risk medicines should be restricted, not stored in patient care areas, withdrawn from ward stock where appropriate and dispensed from pharmacy against individual prescriptions. Explicit organisational policies and procedures should be in place for the management of high alert medicines, particularly when these conditions cannot be achieved.

Additional specifications (hospital and health care organisations)

Safer to use products should be supplied by the pharmaceutical industry as authorised medicinal products. When these medicinal products are not available, they should be prepared in the hospital pharmacy (see IV.5).

High-risk medicines stocked as unit floor stock are only available if a profile-dispense function exists and only if the medicines are packaged and stored in a way that minimises the likelihood of a dispensing error.

High-risk medicines are differentiated from other medicines using flags, highlighting, or some other effective system.

Applicable clinical care setting

Mainly hospital and health care institutions, but also ambulatory care.

IV.8. Safer administering medicines

IV.8.1 Safety checking before administration

Objective
There should be clear procedures to ensure that the right patient receives the right medicine, in the right dose, by the right route at the right time. All medicine orders should be verified before medicine administration. All doses should be administered at scheduled times unless there are questions or problems to be resolved.

Safe practices
Any patient counselling needed should be provided before the first dose is administered, when possible. Prior to each medicine administration: patient identity is verified/double-checked (e.g. via wristband); medicines to be administered are verified against the patient's prescription at the point of administration process. The label should be read and reread at each stage.

Additional specifications

Nurses should talk with patients or carers to ascertain that they understand the use of their medicines and any special precautions or observations that might be indicated.

When a patient objects to or questions whether a particular medicine should be administered, the nurse should listen, answer questions, and (if appropriate) double check the medicine order and medicinal product dispensed before administering it to ensure that no preventable error is made (e.g. wrong patient, wrong route, and dose already administered).

The first dose of each new routine (non-emergency) medicine order is administered only after the order has been reviewed and approved by a pharmacist, a nurse has reconciled the medicine order against the medication administration record (MAR) and compared them with medicines dispensed. Doses should not be administered unless the meaning of the original order is clear and unambiguous and there are no questions with respect to the correctness of the prescribed regimen.

When standard medicine concentrations or dosage charts are not available, dosage calculations, flow rates, and other mathematical calculations should be checked by a second individual (e.g. another nurse or a pharmacist). Staff should only administer medicines that are properly labelled. Medicine doses should not be removed from packaging or labelling until immediately before administration. Nurses should check the identity and integrity (e.g. expiration date and general appearance) of the medicines dispensed before administering them.

If there are questions when a large volume or number of dosage units (e.g., more than two tablets, capsules, vials or ampoules) is needed for a single patient dose, the medicine order should be verified. If an unusually large number of dose units appears to be needed this should alert staff to a potential error.

When administering medicines to seriously ill patients with multiple lines, particular attention should be made to confirming the route of administration. The distal ends of all lines should be labelled to ensure that the site of access for medicine administration can be positively identified.

Medicines to be given by the oral route and medicines to be given by the intravenous route should not be taken to the patient's bedside together. Intravenous syringes should not be used to prepare or administer oral medicines. Oral syringes, whose tips are designed to be incompatible with Luer connectors, should always be used. The use of Luer connectors should be restricted.

Applicable clinical care setting
Hospitals and health care institutions.

IV.8.2. Electronic systems to assist medicine administration

Objective
To encourage the use of computer-generated or electronic medicine administration records (MAR) and consider the use of machine readable coding (i.e. bar coding) in the medicine administration process.

Background
Computerised prescriptions and medicine administration record including a bar code reader was found to help reduce administration errors.[77,78,79,80]

Safe practices
Pharmacy-generated medicine administration records or labels are recommended to assist nurses in interpreting and documenting activities involving medicines.
Point-of-care barcode scanning technology is used to verify and chart medicine administration and

- verifies nurse, patient, and medication identity prior to medicine administration;
- warns staff when a medicine is about to be given in error;
- alerts nurses to missed doses;
- makes available at the point of administration pertinent patient- and medication specific information and instructions entered into the pharmacy/hospital computer system;
- prompts the nurse to record pertinent information before administration may be documented;
- includes real-time systems integration from the point of medicine order entry through patient administration;
- interfaces with the pharmacy computer system, allowing the nurse to view and access only those medicines which have been ordered for the specific patient;
- forces the user to confirm his or her intention whenever medicines are accessed or administration is attempted outside of the scheduled administration time. Such events are signalled visibly or audibly for the user, and all such events are documented electronically and reported daily for follow-up.

Applicable clinical care setting
Hospitals and health care institutions.

IV.8.3. Documenting drug administration

Safe practices
Appropriate documentation/charting is completed during or immediately following medicine administration. If a medicine cannot be administered for any reason the prescriber should be notified.

Additional specifications

If a patient refuses to take a prescribed medicine, that decision should be documented in the appropriate patient records.All discontinued or unused medicines should be returned to the department of pharmacy promptly on discontinuation or at patient discharge. Pharmacy staff should review medicines that are returned to the department in order to seek system breakdowns or problems that may have resulted in medication errors (e.g. omitted doses and unauthorised medicines).

Applicable clinical care setting
All care settings.

IV.9. Safer monitoring of medicine therapy

IV.9.1. Reconciliation of medicine histories

Objective
The reconciliation of medicine histories should be done at every transition of care in which new medicines are ordered or existing orders are rewritten.

Background
Medication errors related to medication reconciliation typically occur at the "interfaces of care" - when a patient is admitted to, transferred within, or discharged from a health care site.[81,82,83,84,85]

Medicine reconciliation is the process of comparing a patient's medicine orders to all of the medicines that the patient has been taking. This reconciliation is done to avoid medication errors such as omissions, duplications, dosing errors, or drug interactions at every transition of care including changes in setting, service, practitioner or level of care. This process comprises five stages : 1) develop a list of current medicines; 2) develop a list of medicines to be prescribed; 3) compare the medicines on the two lists; 4) make clinical decisions based on the comparison; and 5) communicate the new list to appropriate carer and to the patient.

Potential adverse drug events can be reduced by pharmacists or pharmacy technicians by obtaining medicine histories of patients.[86,87]

Safe practices
A complete and accurate list of medicines is compiled at admission and discharge to assure proper continuity of care.

Adopt a systematic approach to reconciling medicines at admission.

1. Assign primary responsibility for reconciling to someone with sufficient expertise, within a context of shared accountability (the ordering physician, nurses, and pharmacist work together to achieve accuracy);
2. Reconcile patient medicines within specified time frames;
3. Develop clear policies and procedures for the steps in the reconciling process.

Additional specifications

Health professionals should request that the patient bring the full names, addresses, and phone numbers of all other physicians or other providers that he is seeing as well as pharmacy(ies) being used prior to commencing treatment.

Communications with general practitioners, patients, carers and community pharmacists about discharge medication should be timely and comprehensive. Community pharmacies maintain a reference list of contact people at area hospitals (e.g. nursing stations, pharmacy satellites, care managers, case workers) to facilitate the resolution of problems with recently discharged patients.

A practitioner reviews and compares all discharge medication orders with the patient's inpatient and pre-admission medication regimens.

Applicable clinical care setting
All care settings.

IV.9.2. Monitoring of medicine therapy

Objective
To evaluate and optimise patient response to prescribed medicine therapy, appropriate monitoring of clinical signs and symptoms and of relevant laboratory data is necessary.

Safe practices
Ongoing patient profiles, including medicine therapy records as well as demographic and clinical information, are maintained.

At periodic intervals, prescribers and pharmacists assess efficacy, tolerance, and patient adherence with the prescribed medicine regimen.

Additional specifications

When appropriate, the patient should be observed after administration of the medicine to ensure that the doses were administered as prescribed and have the intended effect.

Toxicity and efficacy of the prescribed regimen are assessed and documented at appropriate intervals (e.g., symptoms, blood pressure, cholesterol, liver enzymes).

Wherever possible, prescribers should use computer decision support systems that have been designed to standardise anticoagulant control. Such systems can reduce the risks associated with anticoagulation by standardising dosage recommendations, providing information on clinic attendance, and alerting the prescriber to potential drug interactions.

When anticoagulants are prescribed on a shared care basis, the responsibilities of primary and secondary care professionals should be clearly defined. When prescribing other medicines for a patient on oral anticoagulants, a no interacting drug should be chosen whenever possible. After any medicine therapy changes the need for adjustment of the anticoagulant dose should be carefully evaluated.

Applicable clinical care setting
All care settings.

IV.9.3. Using pharmacists to minimise adverse drug events and medication errors

Objective
Pharmacists should collaborate proactively with patients and prescribers to ensure that the goals of therapies are being met.

Background
Pharmacists give a valuable contribution by providing clinical pharmacy services.[88] They work in direct collaboration with prescribers and nurses, monitor medicine therapy and provide medicine information. In hospitals, they are "decentralised" to patient care areas participating in patient care rounds.[89]

Safe practices
On a regular basis, the pharmacist reviews the patient's profile, assesses potential preventable adverse drug events and discusses problems with the prescriber, if needed. Such review includes an assessment of the following, untreated indications, medication use without an indication, contraindications, improper medicine selection, overdose or sub-therapeutic dose, therapeutic duplication, efficacy, adverse drug reactions/toxicity, potential medicine interactions, weight changes, appropriate duration of therapy, and compliance with prescribed regimen.

Additional specifications

Relevant patient specific information as well as medicine information and therapeutic guidelines are readily available to pharmacists.

Pharmacists should maintain medicine profiles for all patients, both inpatients and ambulatory patients. This profile should include adequate information to allow monitoring of medication histories, allergies, diagnoses, potential drug interactions and adverse drug reactions, duplicate drug therapies, pertinent laboratory data, and other information; problem lists, goals, assessments, and recommendations in the patient's profile or some other readily retrievable format.

The review of medication orders by pharmacists should be documented in the patient's record.

Pharmacists assess patient adherence with the prescribed medicine regimen at every patient encounter. When a pharmacist determines that a patient is not adhering to the prescribed regimen, the pharmacist discusses the situation with the patient then, if necessary, notifies the patient's prescriber.

Applicable clinical care setting
All care settings.

IV.9.4. Computer adverse drug events detection and alerts

(see Chapter II)

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Chapter V - Safer medicine information practices

Key points

- The aim of good medicine information practices is to enable an optimum benefit-risk balance of medicine therapy in the interest of the patient. By analogy, the aim of safe medicine information practices is to prevent medication errors and adverse drug events related to medicine information and education of patients and health practitioners.
- The main problems with medicine information are: the lack of awareness about the importance of medicine information; the purposes of medicine information and the control over its production; the idea of medicine information laid down in Summaries of Product Characteristics (SmPCs) as a simple communication tool between manufacturers and prescribers; the imbalance between commercial and independent medicine information; the insufficient use of non-proprietary names (INNs); the lack of independence of drug regulatory agencies in charge of medicine information quality control from pharmaceutical companies; the felt dependence of continuous education of health care practitioners from companies; the few user tests of the medicine information concerning patient information leaflets (PILs) and the missing user tests of the SmPCs, the lack of infovigilance; the poor quality of patient education and the recent expansion of public (Internet-based) information sources beyond control.
- The impact of quality of medicine information practices on medication safety is evident, even if not yet well documented by specific studies. For this reason, information should be considered as an integral part of medicines, from research to vigilance. The quality of medicine information should be considered as important as the technical quality of medicine therapy and treated accordingly: all authorised medicine information supports (SmPCs, PILs IT based supports) and medicine (information) flow should be part of the clinical development (Phase III) and be user tested before approval.
- European states should ensure that the concept of concordance is put into practice wherever possible. Patients should be encouraged to take an active role in their treatment as a way to safeguard themselves. Health professionals should be educated to communicate about medicines with patients in an empowering way to involve them in self-management of the treatment as active partners and experts of their disease/symptoms.
- All health professionals involved in patient counselling should have a good basic and continuing education that covers medicine therapies, therapeutic guidelines, communication skills, including human relationships and safe medication practices. The competency of health professionals involved in patient education should be regularly evaluated as regards clinical knowledge and communication skills.
- Medicine information practices must meet patients' and health care practitioners' needs. Information needs of different populations and special groups should be taken into account, such as the elderly, children, people with disabilities, immigrants, people of (low) health literacy: e.g. adequate use of Braille on medicines packages to assist blind people.
- Patients' medicine information needs to include the choice of the most appropriate treatment for their health problem, including "non-drug" options; comprehensive and understandable information about the expected therapeutic effects, potential adverse drug reactions and instructions for the use of the medicine.

- Authorised medicine information should be considered as a communication tool between public health authorities and different health professionals or patients:
  - European regulations on authorised information for health professionals and patients should be adapted accordingly.
  - European states should allocate parts of health care budgets to clinical trials meeting defined public health needs, to the conception of balanced information based on these trials and for guaranteeing commitment of drug regulatory agencies or medicine information centres to defined public health needs.
  - Drug regulatory authorities should become more reliable sources of medicine information for health professionals as well as for patients.
  - Essential and up-to-date medicine information and therapeutic guidelines should be available at the point of care for health professionals who prescribe, dispense, prepare and administer medicinal products. The use of sources of objective and comparative medicine information should be widely promoted and easily accessible, using the most appropriate information technology. These sources should provide authoritative and practical information on the selection and clinical use of medicines in a clear and concise manner.
  - Health professionals and patients need to be educated to distinguish between commercial and balanced information and to think in terms of international non-proprietary names (INNs). Health professionals should be trained to use the basics of evidence-based medicine as well as handling benefit/risk and cost/benefit ratios.
  - Essential, comparative and up-to-date official medicine information for prescription and non-prescription medicines should also be available for patients. To assure quality of published information, content and dissemination of medicine information to patients should be officially regulated and supervised. Direct-to-consumer advertising for prescription medicines, even indirectly, should be forbidden.

The aim of this chapter is

- to outline the needs of patients and health professionals as regards medicine information with a focus on medication safety;
- to recommend changes in the medicine information flow in order to improve safety of medicine information practices.

Other important issues related to information for patients and health professionals are discussed in other chapters of this report: for more details on drug labelling see Chapter III of this report, and patient information is also discussed in Chapter IV (see IV.3.1, IV.3.3, IV.8.2, IV.9).

For safer medicine information practices concerning label information and packaging please see chapter III. 1. Tackling medication errors related to the naming, labelling and packaging of medicines.

V.1. Medicines information and medication safety

V.1.1. Medication errors caused by poor medicine information practices

The aim of good medicine information practices is to ensure the best possible use of medicines including an optimum benefit-risk balance of medicine therapy in the interest of the patient. By analogy, the aim of safe medicine information practices is to prevent medication errors and adverse drug events caused by medicine information.

Even if not yet well documented by large-scale specific studies, numerous case reports suggest a close relationship between the quality of medicine information practices and medication safety: lack or mistaken medicine information and lack of education on medicine therapy, both of patients and health care practitioners, can cause medication errors and harm.

Poor communication between patient and health professional is one of the most commonly cited causes of medication errors, particularly in the community setting.[1,2] In hospitals, a classical study identified the lack of medicine knowledge as the most common proximal cause of medication errors, accounting for 22% of adverse drug events.[3] In fact, the most common medication use system failure concerns the dissemination of medicine knowledge and the making accessible of medicine information at the time it is needed.[4] For this matter, the Institute for Safe Medication Practices (ISMP) considers that medicine information and patient education are key elements of medication safety.[5,6]

Today, there is a wide consensus that information should be considered as an integral part of medicines from research to vigilance.[7] That means that - with regard to medication safety - the quality of medicine information ("software") should be considered as important as the technical quality of medicines ("hardware") and treated accordingly.

Nevertheless, little action has been taken so far to ensure easy access of patients and health professionals to balanced and ready-to-use information.[7] Much information is still marred by poor content and format and more product-centred rather than patient-centred. Some of the reasons are:

- the purposes of medicine information and the control over its production,[7,8]
- the idea of authorised medicine information as a simple communication tool between manufacturers and prescribers,
- imbalance between commercial and independent medicine information,
- extensive use of trade names of medicinal products instead of international non-proprietary names (INNs) of the active pharmaceutical substances,
- felt dependence of drug regulatory agencies in charge of medicine information quality control from drug companies,[8]
- lack of balanced continuous education of health care practitioners in pharmacotherapy due to its felt financial dependency from companies,
- few user tests of the authorised medicine information concerning PILs[9] and no user tests of the SmPCs in the context of use,

- as regards medication errors, lack of follow-up and quality assurance of these official medicine information sources, leading to discrepancies and errors in official medicine information. Particularly the lack of 'infovigilance' systems based on the reporting of errors or inaccuracies in information sources may be responsible for medication errors,
- poor quality of patient education caused by insufficient involvement of health care professionals in provision of written and oral information about prescription and non-prescription medicines to patients,[e.g.10,11]
- recent expansion of public (internet-based) sources beyond control operating as a disguised direct to consumers advertising (DTCA).

In summary, numerous sources of medication errors remain in place. This is mainly the consequence of a lack of awareness of the value and importance of good medicine information practices.

V.1.2. Assessing the safety of medicine information practices

When evaluating the quality of medicine information practices, aspects like the needs of patients and professionals; official balanced, comparative and commercial information; content and format of information should be considered.

The most comprehensive tool available to evaluate medicine information practices has been developed by the U.S. Institute for Safe Medication Practices[5,6,12] (ISMP, see II.2.2).
ISMP medication self-assessment tools for hospitals and community/ambulatory pharmacies consist of 194 and 198 assessment items, respectively, that address safe medication practices.[5,6] These items are grouped in ten key elements covering 20 core distinguishing characteristics to be evaluated. Four of the ten key elements are related to medicine information and communication practices, patient information, datasheets (medicine information), patient education, staff competency and education (Table 15).

Table 15: ISMP key elements related to safe information practices[5,6]

ISMP Key Element	Number of items	Core distinguishing characteristics	
		Hospitals (H)	Community Pharmacies (CP)
Patient Information	23 (H) 15 (CP)	Goal 1: Essential patient information is obtained, readily available in useful form, and considered when prescribing, dispensing, and administering medicines.	Goal 1: Essential patient information is obtained, readily available in useful form, and considered when dispensing medicines.
Medicines information	31 (H) 23 (CP)	Goal 1: Essential medicine information is readily available in useful form, and considered when ordering, dispensing, and administering medicines. Goal 2: A controlled medicine formulary system is established to limit choice to essential medicines, minimize the number of medicines with which practitioners must be familiar, and provide adequate time for designing safe processes for the use of new medicines added to the formulary.	Goal 1: Essential medicine information is readily available in useful form, and considered when dispensing medicines. Goal 2: The inventory system promotes safe use of new medicines added to the inventory and limits choice to minimize the variety of brands and dosage forms with which practitioners must by familiar.
Patient Education	11 (H) 24 (CP)	Goal 1: Patients are included as active partners in their care through education about their medicines and ways avert errors.	Goal 1: Patients are included as active partners in their care through education about their medicines and ways to avert errors. Goal 2: Pharmacists establish and participate in community-based disease prevention and monitoring programmes to promote health and ensure appropriate therapy and outcomes of medication use.
Staff Competency and Education	21 (H) 13 (CP)	Goal 1: Practitioners receive sufficient orientation to medication use and undergo baseline and annual competency evaluation of knowledge and skills related to safe medication practices. Goal 2: Practitioners involved in medication use are provided with ongoing education about medication error prevention and the safe use of medicines that have the greatest potential to cause harm if misused.	Goal 1: Practitioners and support staff receive sufficient training and orientation to the dispensing process and undergo baseline and annual evaluation of knowledge and skills related to safe medication practices. Goal 2: Practitioners are provided with ongoing education about medication error prevention and the safe use of medicines and devices that have the greatest potential to cause harm if misused.

V.1.2.1. Information about the patient

The concept of the information about the patient covers information practices related to access to patient-specific information and clinical data that are needed in different stages of care to avoid safety incidents caused by patient-related factors.[5,6] These include contraindications, allergic reactions, and conditions of co-morbidity that may influence the treatment (e.g., hypertension, diabetes, renal or liver impairment, pregnancy and lactation).

According to ISMP recommendations[5,6], the patient file including medicine history should be available at the point of care and should be detailed. In addition to prescription and non-prescription medicines, it should include a history of use of vitamins, herbal products, dietary supplements, homeopathic medicines and alternative medicines.

The ISMP recommendations consider it as a standard that prescribers, nurses and pharmacists are able to access electronically inpatient and outpatient laboratory values while working in their respective inpatient locations.[5,6] It is also assumed that community pharmacies have computer-based databases on medicine history, allergies, conditions of co-morbidity and/or chronic diseases and recent patient-specific clinical data such as blood glucose levels, liver enzymes, renal function, blood pressure and cholesterol levels to support clinical drug monitoring.

Even if computerised systems do not exist, these aspects of care are crucial in preventing medication errors. Therefore, a lot of efforts need to be put on them to assure easy access to patient information at all levels of care.

V.1.2.2. Medicines information

Essential, up-to-date medicine information should be readily available in a useful form and consulted when medicines are prescribed/ordered, dispensed, and administered.[5,6] There should be easy access to evidence-based, computerised medicine information systems which include information on herbal and alternative medicines in all patient care areas and in dispensing areas in community pharmacies.

Community pharmacy computers that are used for order entry should also allow seamless, easy access to the Internet to search for information about disease processes, posology, availability, and off-label uses of medicines and other medicine information.[6] Furthermore, community pharmacies should have easy access to a medicine information centre (DIC) staffed with a clinical pharmacist (see also V.3.1.4. and V.3.2.3).

The recommendations require that medicine information resources are electronically linked to patient data to facilitate automatic screening of potential medication errors.[5,6] The recommendations pay quite a lot of attention to creating quality improvement procedures for assuring that medicine information systems are routinely used in clinical practice, that the systems work accurately, and that they are regularly updated. These principles apply both to hospitals and community pharmacies.

V.1.2.3. Patient education

The fundamental principle for planning patient education services to promote medication safety is to include patients as active partners in their care.[5,6] All health professionals involved in the care should contribute to patient education. With a view to involving patients, they should be encouraged to ask questions about the medicines they are receiving. In addition to oral information, patients should be provided with up-to-date, useful written information at an 8th grade reading level or lower. Cultural issues that may effect compliance with the prescribed therapy should be considered when counselling patients about their medicines, as well as information needs of the patients in the community who do not speak the major language of the country (e.g. migrants).

According to ISMP recommendations, community pharmacy management should budget adequate time for patient counselling activities and provide for this purpose a suitable private area with minimal distractions.[6] Community pharmacies should also establish and contribute to

community-based disease prevention and monitoring programmes to promote health and ensure appropriate therapy and outcomes of medication use.

V.1.2.4. Staff competency and education

This part of the ISMP recommendations gives guidelines on assuring that all health professionals dealing with medicines of patients have competency and practical skills needed in medication use and dispensing process.[5,6] This concerns particularly new staff members that should have baseline competency evaluation and necessary interdisciplinary induction before participating independently in patient care activities. Practitioners should have ongoing education about medication error prevention and the safe use of medicines after induction. These recommendations apply both to hospitals and community pharmacies.

Special attention should be paid to the competency of pharmacy technicians in community pharmacies.[6] As pharmacy technicians are responsible for most of the dispensing activities and selling non-prescription medicines in many European countries, it is crucial to ensure that their education and induction is adequate for meeting the requirements of the actual work.

V.2. Safe medicine information for patients

Medicines information is an integral part of health care. Easy access to high quality medicine information is crucial to those involved in the medication use process regardless of whether they were health professionals or laymen. However, patients' needs must be in the centre of good medicine information practices.

A patient well informed on his medicine therapy remains one of the best (and the latest!) safeguards against medication errors. Therefore, all those involved in the medication use process, notably medicine manufacturers, drug regulatory agencies, universities, professional and patient organisations, and health care professionals must undertake all effort to meet patients' needs at best.

V.2.1. Patients' needs

V.2.1.1. Needs of patients as regards medicines information

Even though patients' right to know about their medicines and access to quality medicine information is widely acknowledged in principle, little is really *known* about information needs of patients.[13] Medicine information has traditionally been disseminated to patients "top down" in an authoritarian way leading often to a monologue by the health care practitioner.[13,14-17] This authoritarian approach also is reflected in the structure for contents of PILs in the European Union[9]. Typically, the research about medicine information rarely takes into account the patients' perspective.

The existing evidence shows also that the public and health professionals have different opinions on the desired content of medicine information.[13,18] The main difference concerns the disclosure of information about the therapeutic effects of medicines: in fact, the information

needs of the public are mainly focused on effects, adverse effects and interactions of the medicines[19-22], whereas professionals prioritise information on dose regimen and proper storage.[13,18]

Furthermore, the information needs of the patients depend on the medical condition and the phase of the disease (e.g. severity of the disease, recently diagnosed/early phase/advanced phase); the length of the medicine therapy (a short course vs. long-term therapy)[10,23]; the special features of the medicine therapy (e.g. high alert medicines, different therapy groups[24]); number of concomitantly used medicines and the special characteristics of the patient.

Therefore, it is a common misunderstanding, reflecting current communication behaviours in health care that medicine users need information only at the beginning of medicine therapy[e.g.10.] Worse: it is simply impossible for a patient to learn all facts related to his/her condition during one single appointment with a doctor or another health professional. It is often a long learning process that needs to be supported by the professionals by dialogue-based communication that enhances problem solving skills of the patient and assist with proper management of medical condition and the effective use of medicine.[16,25] This kind of communication should be based on interactive and collaborative discussion and learning between patient and provider.

Patients' needs related to medicine information can be summarised on the basis of existing evidence with a view to ensuring the safe use of medicines:

- Information about the most appropriate treatment for their health problem considering the risk/benefit- and cost/benefit-ratio of treatment options, including the awareness of "non drug" options;
- comprehensive and understandable information about expected therapeutic effects and potential adverse drug reactions of medicines to use;
- comprehensive and understandable information about how the medicine should be used.

Whereas the first of the above items is closely related to the quality of medicine information for health care professionals (see V.3), the necessary conditions to meet the other needs are outlined hereafter.

V.2.1.2. Needs of special population groups of medicine information

Most of written patient medicine information is created by and addresses to adult "standard" consumers.[9,13] But the need of information sufficiently ensuring the safe use of medicines may vary between special groups, such as the elderly, children[26], disabled, immigrants, low literacy people: e.g. blind people cannot read normal letters, elderly people are much more likely to have multiple disorders requiring multiple medication (polypharmacy) and need comprehensive medicine review and counselling.[9,13] Thus, it is important to take into account the specific needs of these population groups also in verbal counselling across the health care system.

As information technologies become more widely available, patients may accede services in formats better tailored to their needs[13] and become more independent from health professionals in their search for information.

V.2.2. Medicines information sources for patients

V.2.2.1. Authorised medicine information: Patient Information Leaflets (PILs)

Patient information leaflets (PILs) present authorised medicine information for patients in the European Union.[27] Therefore, it should be written in a simple language understandable by any layman.[28] The content of a PIL should provide up-to-date medicine information and reflect the summary of product characteristics (SmPC) of the medicinal product for which it has been prepared.[27] PILs are the primary and often only written source of information about their medicine for patients.[9,13] Therefore, quality of content, format and access to PILs are of fundamental importance to guarantee the correct use of the medicine use by patients.

V.2.2.1.1. European regulation

PILs must be submitted as a part of marketing authorisation applications in the EU.[27] The information which has to be provided in the PIL is set out in European and national legislation.[28] Since 1999, PILs have to be supplied with all medicines marketed in the EU.[27] In October 2005, a new requirement was implemented that medicinal products authorised in several member states through the European mutual recognition and decentralised procedures must have a harmonised PIL.[29]

a. Content and format

The Directive on the labelling of medicinal products and package leaflets, issued by the European Commission in 1992, had patient safety as key concern.[27] Seven PIL sections are required:

- identification of the medicine,
- therapeutic indications for the product,
- information which patients need to be aware of prior to taking the medicine,
- dosage and usual instructions for use,
- description of possible side effects,
- how to store the product,
- date on which the leaflet was prepared.

The marketing authorisation holder is responsible for providing for the blind and partially sighted on request from patient's organisations, the package leaflet in an appropriate format and to ensure that the current version is supplied.[30]

- for partially sighted people, the package leaflet should be provided on request in a suitable print, taking into consideration all aspects determining the readability (e.g. Font size: Sans serif typefaces, 16 - 20 point, contrast: black letters on white paper).
- for blind people the text has to be provided in an appropriate format, it is recommended to provide the text in a format perceptible by hearing (CD-ROM, audiocassette, etc.). In certain cases the appropriate format may be the package leaflet available in Braille.

b. User testing

In March 2004, the European Union introduced a new legal obligation (directive D2004/27/EC)[29] for all marketing authorisation holders to ensure that PILs reflect the results of

consultations with "target patient groups" in order to guarantee readability, clarity and ease of use.[30,31] A separate amendment to the order of leaflet information ensures that important safety messages are presented in a more logical manner.[32]

Several countries have already implemented these new amendments. For instance, the British authorities have set up a working group on patient information that has published a practical guide to assist in producing information for patients about medicines.[9] This guidance has special focus on principles and methods in user testing, communicating risk and meeting the needs of special groups of patients. Patients can also report to the MHRA any PILs that they do not understand via a link to the British Medicine Agency's website.[33]

This MHRA working group has been working with other European drug regulatory authorities to promote a common interpretation of the new legislation and to learn from experience of other member states.[9] This working group has been set up as the Commission on Human Medicine's Expert Advisory Group on Patient Information (PIEAG) to give the MHRA independent expert advice on how PILs can be improved. Work is in progress also to revise the European readability guideline (European Commission 1998) and to develop guidance on user testing.[9]

V.2.2.1.2. Patients' unmet needs

Unfortunately, whilst basic regulatory requirements are met, in general variable quality of the information, failing meeting patients' needs has been observed [e.g. 9].

- Differences between the SmPCs for medicines containing the same active pharmaceutical substance available from different manufacturers have led to inconsistent information in the PILs.[8] There is still no follow-up of such discrepancies (infovigilance) through national or international programmes;
- Patients need balanced information. It is not desirable to stress in PILs a medicine's expected benefit at the detriment of its risks.[34] As PILs contain no data from comparisons with other treatments, stressing the expected benefits would be equivalent to surreptitious advertising and would divert patient's attention away from possible adverse drug reactions.
- Perhaps the most significant criticism concerned poor communication of risk, often in form of a long and intimidating list of potential adverse drug reactions. Published studies indicate that patients' understanding of terms commonly used by health professionals generally exaggerated the likelihood of risk.[35]
- Nevertheless, as the content of PILs is focused on benefits and risks, they do not provide precise information on how the medicine should be used.[36]
- Many patients fail completely to take note of the PIL and only a part of those who recall receiving a leaflet read some or all of it.[37]
- Often, PILs are lengthy, complex and very poorly laid out. Currently, PILs are full of administrative jargon, their contents do not appear in prioritised order, and they are poorly suited to the situations that patients most often encounter.[9] Patients quickly lose interest in the document, failing to read or to understand information essential for the safe use of the drug.[9,38]
- Access to PILs has been improved by publishing them on the websites of the national drug regulatory agencies (e.g. in Finland). They are also available on the EMEA website. But the fundamental problems with European PILs is that they still cannot be individualised like computer generated leaflets which are used in the US and Australasia.[36]

- Although *voluntary* user testing has been part of the EU guidance available for manufacturers[28] since some time, few companies actually sought the views of patients on the information they provide and even less have voluntarily undertaken user testing before it became obligatory.[29,32]

These deficits of PILs create confusion and reduce trust of patients in authorised medicine information.

V.2.2.2. Medicine information by health care professionals

Written authorised medicine information of good quality is essential, but rarely sufficient to guarantee therapeutic success. That is why good medicine information practices are very important to ensure medication safety. In fact, available medicine information has to be interpreted and/or adapted by health professionals to the particular situation of patients and all relevant information has to be communicated in an understandable way.

One critical point is the marketing of an active pharmaceutical substance in medicines under different trade names. This hinders thinking in terms of "best pharmacological choice"[39], confuses health professionals and patients, and is responsible for overdosing by the concurrent use of the same medicine under different trade names as well as for interactions resulting from a lack of awareness of the active pharmaceutical substance contained in branded medicinal products.

V.2.2.2.1. Patients' empowerment and concordance

Patients demand and need comprehensive and understandable medicine information, the underlying concepts of which are patient empowerment and concordance. Although the concepts of empowerment and concordance have become popular, particularly "empowerment" is often inadequately conceptualised and vaguely defined. Furthermore, the concept of concordance is mixed with the concepts of compliance and adherence and looked upon as a synonym.[14,40]

Empowerment means a process of building knowledge, skills and competencies which leads ultimately to more willingness to participate in wider social settings.[26,41,42] It means also that active involvement and personal experiences are essential.[43,44]

In 1997, a new concept, called "concordance" was introduced in the United Kingdom[14] "Concordance" means that the health care professional needs to elicit and understand the patient's view of the treatment and agree about the treatment plan with the patient considering him as an equal partner.[45-47] Thus, the core of "concordance" is the recognition that patient's views and beliefs need to be openly discussed.[48] The patient needs skills to take responsibility for his/her own medication to be able to be involved and actively participate in decision making.[26] Thus, the underlying approach in concordance is empowerment.

It is obvious that empowerment and patient's active involvement in decision making and management of care will require new kind of communication skills of health professionals [17].

The Ljubljana Charter stressed in 1996 that the voice and choice of citizen's should be as important as of economic, managerial and professional decision makers when shaping health care services.[49] This goal can only be achieved if effective mechanisms for involving and seeking the views of patients/citizens are established. Several tools may be used to empower patients [e.g. 31,50].

- recognising patients' needs and expertise;
- training of health professionals in shared decision-making;
- wherever possible, offering informed choice, not passive consent;
- public access to comparative data on quality and outcomes;
- public awareness campaigns to encourage the public to seek information before starting treatment with medicines;[51,52]
- patients' and consumers' training to ask their health professionals more questions;[53]
- patients' training to use a medicines real name: the INN;
- patient access to electronic health records;
- openness and empathy with patients (or parents) when medical errors are disclosed (see I.3.3.3), and surveys of patients' experience in order to prioritise quality improvements.

The concepts of empowerment and concordance are adapted to adult "standard" patients and maybe to children and adolescents at a certain age.[26] In reality, many but not all patients are able to take over responsibility for themselves. Although the concept of concordance should be put into practice wherever possible, it is evident that this concept has to be adapted for special groups and to particular situations, e.g. intensive care units.

V.2.2.2.2. Patient counselling for safe use of medicines

Patient counselling appears to be a valuable tool for intercepting medication errors, e.g. before patients leave the pharmacy since it takes place after the pharmacist's accuracy check and before the patient leaves the pharmacy. A review of errors showed that 286 (89%) of 323 reported medication errors were detected during patient counselling and successively corrected.[54] The interactive environment created during the patient encounter is likely to increase concentration and facilitates the detection of previously overlooked prescribing or dispensing errors.

a. Encouraging patients to ask questions about their medicines

Patients want medicine information, particularly from physicians and pharmacists [13,55], and this makes the dissemination of information an important part of their work.

According to the concepts of empowerment and concordance, counselling should be a two-way interactive communication process: the role of the health professional is to support the patient in constructing his/her own knowledge and attitudes about the use of the medicine[14,17,25,47,56,57]. A two-way interactive communication process requires communication techniques that encourage people to ask questions about their medicines.[e.g. 17,51,52]

b. Principles of patient counselling

In spite of interesting experiences in the hospital setting, patient counselling or advice-giving has only been studied in some European countries and mostly in community pharmacies.[10,11,13] Nevertheless, many findings are of general interest and should be applied by all health professionals involved in managing medicine therapies of patients and their counselling.

As minimum requirement, health professionals should have a good basic and continuing education covering medicine therapies, therapeutic guidelines, communication skills and safe medication practices. [17] In any setting, patients' needs, appropriateness of health care sites and professional competence of the professionals should be taken into account in the development of safe medication counselling practices.[10, 58] The principles of patient-cantered counselling should be known and put to practice by all health professionals. Interdisciplinary guidelines about patient counselling practices – agreed with other health professionals - should be established. Self-evaluation and peer-evaluation of performance may be used to evaluate and improve patient counselling practices.[e.g. 5,6,10,59]

Patients' disease profiles and medicine use patterns should be systematically assessed. Both electronic and printed medicine information sources should be accessible during patient counselling and health professionals should be able to use them.

Patients need to be informed about the potential for confusion between generic and invented names of medicines. The INNs should be systematically used to avoid confusion and improve compliance.

c. Oral and written patient counselling

Specific guidelines on patient counselling are scarce.[e.g. 10,60] The United States Pharmacopeia (USP) established one of the most comprehensive definitions of patient counselling which is based on the concept of concordance (see Table 16).[10,17, 25, 59]

According to the USP, patient counselling is an approach that focuses on enhancing individual problem-solving skills for the purpose of improving or maintaining quality of health and quality of life.[16,25] With a view to achieving the above goal, the approach builds on the health professional providing and discussing medicine information with the appropriate person. The physical, psychological, socio-cultural, emotional, and intellectual perspective as well as the health beliefs and values of the individual must be respected.

Table 16: Counselling items of the USP Medication Counselling Behaviour Guidelines[25]

Needs assessment
1. Obtains pertinent initial drug related information (e.g. allergies, other medicines, age)
2. Responds with understanding/empathic responses
3. Reviews patient record prior to counselling
4. Explains the purpose of the counselling session
5. Presents facts and concepts in a logical order
6. Uses appropriate counselling aids to support counselling
7. Assesses any actual and/or potential concerns or problems of importance to the patient
8. Determines if the patient has any other medical conditions which could influence the effects of this drug or influence the likelihood of an adverse reaction
9. Conducts appropriate counselling introduction by identifying self and the patient or patient`s agent
Management of the Treatment
10. Discusses storage recommendations, ancillary instructions (e.g. shake well, refrigerate, etc.)
11. Explains how long it will take for the drug to show an effect
12. Tells patient when he/she is due back for a refill
13. Summarises by acknowledging and/or emphasizing key points of information
14. Emphasises the benefits of completing the medication as prescribed
15. Helps patient to plan follow-up and next steps
16. Provides an opportunity for final concerns or questions
17. Verifies patient's understanding via feedback
18. Maintains control and direction of the counselling session
19. Assists the patient in developing a plan to incorporate the medication regimen into his/her daily routine
20. Uses open-ended questions
21. Explains the dosage regimen, including scheduling and duration of therapy when appropriate
22. Probes for additional information
Precautions and Warnings
23. Explores with the patient potential problems in taking the medication as prescribed (e.g. cost, access,etc.)
24. Discusses potential (significant) side effects
25. Warns patient about taking other medicines, including OTCs (e.g. herbals/botanicals) and alcohol, which could inhibit or interact with the prescribed medication
26. Discusses significant drug-drug, drug-food, and drug-disease interactions
27. Discusses precautions (activities to avoid, etc)
28. Explains in precise terms what to do if the patient misses a dose .
29. Discusses how to prevent or manage the side effects of the drug if they do occur
30. Helps patient generate solutions to potential problems
Communication
31. Uses language the patient is likely to understand
32. Provides accurate information
33. Discusses the name and indication of the medication
34. Displays effective nonverbal behaviours: a. Appropriate eye contact b. Voice is audible; tone and pace are good c. Body language, postures and gestures support the spoken message d. Distance between the health care professional and patient is appropriate
35. Assesses the patient`s understanding of the reason(s) for the therapy

The aim of the USP Medication Counselling Behaviour Guidelines is to support the person's efforts to develop medicine management skills and to move towards responsibility for their treatment with empathy, sincerity and patience.[17,25,59] The relationship between the patient and health care providers is interactive and offers a collaborative learning process for both parties[16].

Furthermore, there exist some specific guidelines for the pharmacist-patient interaction, mostly developed in the United States (see Table 17).

Table 17: Recommended topics for the pharmacist-patient interaction according to selected patient counselling guidelines (modified from [60])

Prescription medicine information	Reeder 1989[61]	OBRA` 1990[62]	American Society of Health-System Pharmacists 1997 [63]	American Society of Consultant Pharmacists 1998 [64]
Medication name, description and/or purpose	X	X	X	X
Route, dosage, dosage form, and administration schedule	X	X	X	X
Directions for preparation and administration		X	X	X
Precautions to be observed			X	X
How to identify and manage adverse reactions	X	X	X	X
Techniques for self-monitoring		X	X	X
Proper storage	X	X	X	X
Potential drug-drug, drug-food interactions	X	X	X	X
Radiology and laboratory procedure issues			X	X
Prescription refill information	X	X	X	X
Action to be taken in the event of a missed dose	X	X	X	X

It appears that number and content of items have remained almost the same over more than a decade.[60]

However, studies assessing implementation and actual use of these guidelines in daily practice have not been conducted or published in peer-reviewed literature with the exception of OBRA'90 legislation the implementation of which has been widely assessed in the US.[e.g. 65,66] The conclusion of the study was that the counseling performance of community pharmacists does not change if the legal requirement for counseling is not supported by implementation and enforcement systems.[67, 68] The same has been observed in Finland.[10,11]

Additionally, pharmacists have been encouraged to use counselling strategies developed for US pharmacists working in the Indian Health Service (IHS) and to ask patients following questions:[69]

1. What did your doctor tell you the medicine is for?
2. How did the doctor tell you to take the medicine?
3. What did the doctor tell you to expect?
4. Just to make sure I didn't leave anything out, please tell me how you are going to take your medicine?
5. What kind of problems have you had with medicines in the past? (optional)

Summarising these recommended topics, 12 basic questions concerning safe medication use have been listed by the ISMP:[70]

1. What are the brand and the generic names of the medicine?
2. What is the purpose of the medicine?
3. What is the strength and the dosage?
4. What are the possible side effects? What should I do if they occur?

5. Are there any other medicines I should avoid while using this product?
6. How long should I take the medication? What outcome should I expect?
7. When is the best time to take the medication?
8. How should I store the medication?
9. What do I do if I miss a dose?
10. Should I avoid any foods while taking this medicine?
11. Is this medicine meant to replace any other medicine that I am already taking?
12. May I have written information about this medicine?

Studies assessing the implementation and actual use of such guidelines in daily practice should be conducted and published in the peer-reviewed literature. In fact, daily practice seems to be far from to be optimal [e.g. 10,11]. In France for instance, unsuitable conditions such as lack of time, lack of training, patient's resistance to education and lack of confidentiality limit the frequency and length of communication with patients.[71] Assessments should also involve counselling practices of other health professionals than pharmacists who are involved in managing medicine therapy of patients.

V.2.2.2.3. Medicine (drug) information Centres (DICs)

A medicine information centre (DIC) is a service unit where patients can make a call or establish contact by other appropriate means in order to obtain unbiased medicine information.[13,72]

Nowadays, these services exist practically all over Europe.[72] Nevertheless, the motivation of patients for contacting a DIC differs considerably across countries. A call centre operated by the Helsinki University Pharmacy, Finland, received for example more than 230,000 calls from patients in 2003.[73] Some patients prefer to discuss their medicine treatment with a professional but anonymous information service. The availability of a DIC to discuss harm related to medicines or to prevent medication errors may be important in some cases. [74]

As more than half of the information services provided by DICs are intended for health professionals[72, 75], the missions and needs of DICs will be explained in the chapter about medicine information for health professionals (see V.3.1.4.).

V.2.2.2.4. Patients' unmet needs

In traditional health care concepts, the patient has been expected to passively obey the "advice" of the health professional.[14,40] If this "advice" is not followed, the patient is considered "non-compliant". This is just one of the reasons why the nature of patient-practitioner relationship is often perceived as authoritarian and little patient-centred. In consequence, this approach prevents often the full benefits of medicines.[76]

If applied with deliberation, checklists of items that should be asked or told to patients might be helpful, even if the included specific counselling items seem often to be focused more on the medicine than on the patients' needs. But when applied routinely to every patient regardless of his/her individual needs, counselling check-lists become prejudicial. The USP Medication Counselling Guidelines should be used as a tool for self- and peer-evaluation of counselling skills and as a tool for understanding medicine counselling as a process.[25,59]

V.2.2.3. Public sources beyond control: Internet and direct-to-consumer advertising

In line with the concept of patient empowerment, patients, considered as consumers, should have easy access to medicine information. Virtual medicine information sources, e.g. available on the Internet, may meet that demand.
Unfortunately, not all of them are reliable, comparative and user-friendly. Although the scope of medicine information and the ease of its access to patients and consumers has to be increased in some parts of Europe e.g. by new information technologies, uncontrolled medicine information may pose new problems:

- the lack of quality control of medicine information which is free available on the Internet to health care professionals - and even more to laymen, is most important;
- not every consumer and patient has the opportunity to use of information technology which may increase inequality [e.g. 13].

Pharmaceutical companies are very interested in managing the dissemination of medicine information to consumers with the aim of increasing the sales of medicinal products, even of prescription medicines, through consumer demand.[77]

Direct-to-consumer advertising (DTCA) bypasses competent health professionals, such as physicians and pharmacists, is considered as a potential vehicle to increasing the sales of medicines. Direct-to-consumer advertising, disease awareness campaigns, disguised as public health campaigns, and more recently, disease mongering increase consumption, sales, and inappropriate use of prescription medicines. Regulation of these activities is vague and not proactive.

Nevertheless, three types of DTCA for prescription medicines are permitted in the United States: 1) product claim advertisements, which include both the product name and specific therapeutic claims; 2) reminder advertisements, which provide the name of a product without stating its use; and 3) help-seeking advertisements, which inform consumers of new but unspecified treatment options for diseases or conditions.[78]

In the European Union, due to citizen pressure, DTCA for medicines is still forbidden despite pressure from pharmaceutical companies.[43,79] Recently, the European Commission has *recommended* authorising advertising for the public, disguised as information what may open the door for abuse: e.g. in France, pharmaceutical companies have already tried to introduce DTCA as “compliance support programmes” - which are not mentioned in the European directive[80]; similar DTCA methods are also used in other European countries.

The European Commission has recently opened a web portal dedicated to health care[81] and EMEA has been mandated to develop an information website on medicinal products authorised in the EU.[82] The EMEA search engine should allow medicine information searches based on INNs.[83]

Nevertheless, the patients should not be given the impression that medicines are the only solution for their health problems. They should have access to balanced information on existing treatments including information on added therapeutic value of treatment alternatives mentioning also non-drug interventions. They should be educated on how to find such information and to understand the difference between promotional (commercial) information and objective medicine information. Ideally, this kind of systematic consumer education starts already in elementary schools.[26, 53]

V.2.3. Recommendations for safer medicine information for patients

- European states must ensure that the current EU and national legislation and guidelines concerning the contents and format of PILs are applied. The contents of the PILs must reflect the SmPC of the medicinal product for which it has been created. They must ensure that PILs contain up-to-date and essential information about expected therapeutic effects, potential adverse drug reactions and correct use in understandable language and format. The information should be given in the order of the importance of the expected benefits and possible dangers, and should clearly distinguish facts from assumptions. More detailed recommendations for improving the readability of PILs needs to be set.
- The changes in the quality of PILs as a result of recent amendments in EU and national legislation should be monitored and their clinical consequences assessed; the supporting guidelines should be periodically reviewed in the light of experience and evidence.
- European states should take measures to promote wide public awareness of PILs. Options should be explored for improved access to PILs, including availability at or before the prescription or purchase of a medicine, and in other situations where a PIL is not currently available (e.g., via the websites of national drug authorities).
- European states should ensure that official medicine information is also available in alternative formats, adapted to special groups, e.g. information leaflets and posters; simplified leaflets; use of pictograms and signposts; information in other languages and/or translation services; intermediates to facilitate the provision of information to people with special access needs (infomediaries); help lines; patient organisations; navigators, pointers to information sources; videos/CDs, digital TV, Internet/websites; booklets, magazines.
- European states should ensure that the concept of concordance is put into practice wherever possible. Health education about medicines should start at school. Health professionals should encourage patients to take a bigger responsibility for their own treatment and to make evidence-based choices.
- European states should ensure that all health professionals involved in patient counselling have a good basic and continuing education that covers medicine therapies, therapeutic guidelines, communication skills including human relationship and safe medication practices.
- The basic advice given to patients about medicines should be increased. In case of polypharmacy, health professionals must particularly be aware to deliver sufficient information to patients and other professionals (e.g. INN-names, treatment changes and reasons).
- Information available on the Internet should be transparent regarding: origin, authorship, funding and date of preparation of information. Patients and consumers should be instructed and empowered to use interactive Internet tools to critically assess the relevance and the quality of information. Regarding their natural conflict of interest, pharmaceutical companies should be forbidden to provide any information or recommendations directly to consumers.

V.3. Safe medicine information for health care professionals

V.3.1. Health professionals' needs to meet patients' needs

Clinical practice may vary in the different European countries. Everywhere, the provision of information to the patients is a shared activity of different health professionals, e.g. physicians, nurses and pharmacists. Therefore, patient education should be set up as a shared responsibility of all health professionals and the role of every professional involved in medicine information must to be clearly defined.

V.3.1.1. Physicians

V.3.1.1.1. Clinical situation and mission

In ambulatory care and in the hospital setting, the relationship between the patient and his/her physician is confidential and based on a nearly unlimited trust. The physician has the overall responsibility for the well being of his/her patient and the primary responsibility for establishing and discussing with the patient the diagnosis and the therapeutic plan. Furthermore, he is the one who involves other health professionals in the treatment by medical prescription.

With regard to patients' needs in medicine treatment (see V.2.1.), physicians have key responsibility in proposing the most appropriate treatment for the diagnosed health problem and in giving comprehensive and understandable information about the expected therapeutic effects, potential adverse drug reactions and the correct use of medicines. Adequate information has been considered as necessary for compliance with the therapy although the mechanism of association between these two parameters has not yet been clearly shown.[40]

Information about the diagnosis and the therapeutic plan should be given to the patient well in time before start of treatment because the patient is motivated at the time of diagnosis to receive information and has the possibility to ask complementary questions about the treatment. Patient counselling and education is an ongoing task: it should not be limited to the first encounter with the doctor but should continuously support the patient in his self-management of the treatment.

V.3.1.1.2. Physicians' needs

a. Content

First of all, physicians need a solid basic education in pharmacology, principles of evidence based medicine (EBM) and patient counselling, financially independent continuing education and access to comparative medicine information.

At the point of care in hospitals and ambulatory care, physicians need easy access to patient information records, medicine information sources of high quality and therapeutic guidelines. These different information tools have to be considered in the decision making process by the prescribers.[5,6]

Patient information (see also chapter V.1.1.): The prescriber must have as much as possible detailed information about the patient, his clinical condition, and a comprehensive history of previous and current medicine treatment (e.g. laboratory values, co-morbid conditions that may influence the treatment, contraindications, allergic reactions). As it is the prescriber's responsibility to communicate necessary patient information to all concerned health professionals (see IV.3.3), he needs the information from others (see IV.4.1 and IV.9). This

information is crucial to making rational and safe decisions about the care and in preventing medication errors (see IV.3.1).

Medicines information: The professional medicine information available at the point of care should cover the following topics:
- clinical indication;
- dose for adults/children/geriatric/renal and hepatic impaired patients;
- management of therapy;
- follow-up, e.g. laboratory tests required during the treatment;
- contraindications and cautions;
- potential/significant adverse drug reactions and instructions about how to avoid/minimise/manage them;
- interactions between medicines with the class of severity (including also non-prescription medicines);
- warnings related to taking food, herbals/botanicals, and alcohol which could inhibit or interact with the medicine;
- details of both branded and generic medicines.

Therapeutic guidelines (see V.3.2.2.): The implementation of EBM in practice means "integrating the best evidence established by research in clinical expertise and patient values"[84]. "Disease-oriented", therapeutic guidelines, derived from qualified scientific evidence should be available to prescribers to standardise their knowledge and information about medicine therapy. Medical students should be trained to select reliable sources and to avoid using biased information.

b. Format

Ready-to-use format: It is not sufficient to have easy access to patient and medicine information sources and therapeutic guidelines. The information must also be presented in a ready-to-use and standardised format in order to avoid long and error-prone interpretation. Authorised medicine information should already meet these needs.

Networks: Electronic prescribing systems increase the possibility to have simultaneously access to patient and medicine information sources and to therapeutic guidelines which increase patient safety[2,5,6].

Last but not least, physicians must have enough time to inform patients correctly.

V.3.1.2. Nurses

V.3.1.2.1. Clinical situation and mission

Particularly in hospitals, nurses are usually the professionals who are closest to the patients' bedside. Thus, they have the primary responsibility for the handling of medicine handling on the wards. Their performance is crucial to medication safety on the wards and for the patients at discharge.

In some countries, nurses are also allowed to prescribe certain medicines, but mostly they are responsible for carrying out correctly medical treatment as prescribed by the physician e.g. preparation, administration and monitoring.

With regard to patients' needs concerning medicine treatment (see V.2.1.), particularly in the hospital setting, nurses are in charge of medicine delivery, mostly under time pressure, and they are often the easiest accessible information source for patients. Nurses should therefore be able to give at least most essential information about the expected therapeutic effects, potential adverse drug reactions and the correct use of prescribed medicines.

V.3.1.2.2. Nurses' needs

a. Content

First of all, nurses need a good education in pharmacology and patient counselling. Then they need the necessary knowledge to carry out correctly the medical treatment prescribed by the physician, e.g. calculation of dilution and to use authorised and additional medicine information.

At the point of care in hospitals and ambulatory care, nurses need easy access to official up-to-date medicine information, patient information, and to therapeutic guidelines.[5,6]

b. Format

Ready-to-use format: It is not sufficient to have easy access to up-to-date medicine information sources. The information must also be presented in a ready-to-use and standardised format in order to avoid long and error prone interpretation, e.g. presentation of essential information for medicine handling in form of tables, use of pictograms. The authorised medicine information should already respond to these needs.

Last but not least, nurses must have enough time to inform patients correctly.

V.3.1.3. Pharmacists

V.3.1.3.1. Clinical situation and mission

Throughout Europe, pharmacists have different roles and responsibilities in the medicine management process depending upon national legislation, regulations and traditions, as well as settings, education and training. The pharmacist's role has evolved step-wise, from officinal preparation to pharmaceutical care, which constitutes an activity relying to a great extent to information.[85,86] Today, in most European countries, pharmacists working in hospitals and community pharmacies have a multifaceted role in medicines management that goes far beyond dispensing and patient counselling.

Pharmacists are everywhere and in all settings the pivotal link in the medication use process and the only health professionals focusing on medicine treatment. Thus, they have the primary responsibility for the reliability of the medication use process and for recognising medicine use problems that other disciplines may have overlooked.[87] It has been found that "the provision of medicine information is among the fundamental professional responsibilities of pharmacists in health systems".[75] Therefore, they have to dialogue with other practitioners, e.g. physicians and nurses.

With regard to patients' needs in medicines treatment (see V.2.1.), pharmacists are responsible for double-checking that the dosage regimen is correct, for screening for interactions, for validating prescribed medicine treatments as well as for the preparation and dispensing of medicines. Finally, they assist in the follow-up of treatment.

Furthermore, pharmacists have an important role in providing comprehensive and understandable information about the expected therapeutic effects, potential adverse drug

reactions, correct use of prescribed medicines and alternative treatment, if necessary. They reinforce patient education by the physician and translate professional medicine information into information understandable by the patient. Pharmacists' role is also to help consumers in planning rational and safe self-medication practices.

Finally, pharmacists are well placed to assist the physician by carrying out a comprehensive medication review for those patients who have problems with their medicines; their observation is documented and reported to the physician for clinical decision making.[88]

V.3.1.3.3. Pharmacists' needs

a. Content

First of all, pharmacists need a solid basic education in pharmacology, applied clinical pharmacotherapy, and in pharmaceutical technology, principles of evidence based medicine (EBM), patient counselling and safe medication practices, financially independent continuing education; and access to balanced medicine information.

At the point of care in hospitals and ambulatory care, pharmacists need easy access to quality medicine information sources, therapeutic guidelines and patient information records.[5,6] This is required to validate the prescription and to give medicine advice to patients, physicians, nurses and other health professionals.

Medicines information: The professional medicine information available at the point of care should not only cover the same topics as for physicians but also provide technical information concerning the preparation and the administration.

Therapeutic guidelines (see V.3.2.2.): The therapeutic guidelines available at the point of care should cover the same topics as for physicians and nurses.

Patient information (see IV.4): The pharmacist should have as much detailed information as possible about the patient and his clinical condition and a comprehensive history of previous and current medicine treatments, e.g. laboratory values, co-morbid conditions that may influence the treatment, contraindications, allergic reactions. This information is crucial for making rational and safe decisions about care and in preventing medication errors.[5,6]

b. Format

Ready-to-use format: It is not sufficient to have easy access to medicine information, therapeutic guidelines and patient information. The information must also be presented in a ready-to-use and standardised format in order to avoid long and error prone interpretation. The official medicine information should already respond to these needs.

Networks: Electronic prescribing systems increase the possibility to have simultaneously access to medicine information and patient sources and to therapeutic guidelines.

And last but not least, pharmacists must have enough time to adequately validate prescriptions and to provide information to the patients and to other carers.

V.3.1.4. Medicines (drug) information centres (DICs)

V.3.1.4.1. Clinical situation and mission

Most DICs are established in teaching hospitals (e.g. USA, Germany, France, Italy, Czech Republic, in Russia, Moldova, Romania) and some DICs are located in universities e.g., in Medical/Pharmacy schools or university pharmacies (e.g. Czech Republic, Russia, Moldova, Romania and Finland).

Originally, DICs were designed to assist health professionals, and even in the end of 1990s, more than half (56%) of the information services of DICs were intended for health professionals and only 43% for patients.[72]

With regard to patients' needs in drug treatment (see chapter V.2.1.), DICs may provide important counselling services directly to patients and indirectly to health professionals. DICs may help to find the most appropriate treatment for a diagnosed health problem, for giving balanced, comprehensive and understandable information about observed or expected therapeutic effects, observed or potential adverse drug reactions and the correct use of prescription and non-prescription medicines.

Furthermore, DICs may give information about pharmacoeconomics, conduct drug use reviews and medicine research and may be implicated in pharmacovigilance and medication error reporting programmes.

Finally, DICs may contribute to undergraduate and continuing education of physicians and pharmacists by offering training possibilities in applied pharmacology.

V.3.1.4.2. DICs' needs

a. Content

First of all, physicians and pharmacists working in a DIC need - beyond a solid basic education - a specialisation in clinical pharmacology or clinical pharmacy. Furthermore, they need education in patient counseling skills, and financially independent continuing education.

DICs need easy access to medicine information sources of high quality and balanced medicine information, therapeutic guidelines and patient information. These different information tools are needed to give medicine advice to patients and health professionals who are in charge of providing advice.

Medicines information is the cornerstone of a DIC. Professional medicine information available in a DIC should cover the same topics as for physicians and pharmacists. It is fundamental to have easy access to standard textbooks, commonly used medical and clinical pharmacology journals, and databases e.g. Martindale®, Micromedex®, local data bases of authorised medicines, Cochran database. These sources allow to answer more than 50% of requests of medicine information.

Therapeutic guidelines (see chapter V.3.2.2.): The therapeutic guidelines available in a DIC should cover the same topics as for physicians, nurses and pharmacists.

Patient information (see chapter V.2.2.): DICs should have as much detailed information as possible about the patient and his/her clinical condition. Unfortunately, there exist some geographical, technical and psychological barriers to get comprehensive patient information, which are particular barriers for DIC-located in universities.

b. Format

Ready-to-use format: It is not sufficient to have easy access to medicine information, therapeutic guidelines and patient information. Particularly for urgent patients' requests, it may be vital that the information is presented in a ready-to-use format in order to avoid error-prone interpretation. The authorised medicine information should already meet these needs.

V.3.2. Medicine information sources for health professionals

V.3.2.1. Authorised medicine information: Summary of Product Characteristics (SmPC)

V.3.2.1.1. European Union regulations

The European Public Assessment Report (EPAR) is an essential source of information for health professionals on medicinal products approved via the centralised authorisation and contains the essential scientific evidence on the quality, efficacy and safety of the medicinal product. The current EU medicines legislation requires that national public assessment reports (NPARs) are made available: some EU member states like the Netherlands, the United Kingdom and Sweden have already published NPARs. The Summary of Product Characteristics (SmPC) is appended to the public assessment report and should provide up-to-date medicine information. Therefore, SmPCs are the most important public documents emanating from the medicines authorisation process in European Union member states.

The SmPC in its current format became obligatory for all new medicinal products marketed in the European Union in 1986 (Directive 83/570/EEC on the approximation of provisions laid down by law, regulation, or administrative action relating to proprietary medicinal products[89]) superseding earlier requirements to provide scientific information to health professionals on medicinal products (Directive 75/319/EEC on the approximation of provisions laid down by law, regulation, or administrative action relating to medicinal products[90]). The key intention of these directives was to define and harmonise all data required for approval of marketing authorisation applications of medicinal products in EU member states. Successively, harmonisation and access to medicine information were facilitated.

Harmonised dossier requirements as regards quality, safety and efficacy and the inclusion of SmPCs and PILs into marketing authorisation applications and actual authorisations of medicinal products have helped to make the European Union's pharmaceutical legislation more public-health oriented.[8]

From the very beginning, the SmPC has been considered a communication tool between manufacturers and prescribers and influenced the development of guidelines on establishing SmPCs.

All scientific information and promotional material developed by the company should be in compliance with the contents of the SmPC.

a. Contents

The contents of SmPC should be structured as follows (Notice to Applicants: A Guideline on Summary of Product Characteristics; current version of October 2005):

1. name of the medicinal product;
2. composition (active pharmaceutical substances and other ingredients used);
3. dosage form/formulation;
4. clinical information: therapeutic indications, posology and method of administration, contraindications, special warnings and precautions for use, interactions, pregnancy and lactation, effects on ability to drive and use machines, undesirable effects (frequency and severity), overdose;
5. pharmacological properties; pharmacodynamics, pharmacokinetics, pre-clinical safety data;
6. pharmaceutical information: excipients, significant incompatibilities, shelf life; storage instructions; packaging and packaging materials; name and address of the marketing authorisation holder;
7. marketing authorisation holder.

The SmPC may also include information about the number and date of marketing authorisation, prescription status of the medicinal product, date of drafting/updating the SmPC.

b. Format

There are strictly harmonised format and requirements in SmPCs both for national and centralised marketing authorisations, however wording may be different.

V.3.2.1.2. Professionals' unmet needs

Although the SmPC has improved access to standardised medicine information within EU countries with a view to promoting medication safety, several problems still remain[ing. 8] :

- SPCs are product specific, the information conveyed for both branded and generic medicinal products with the same composition and formulation may vary substantially. In general, marketing authorisation of generic medicinal products requires that their SmPC is harmonised with the SmPC of the originator: in some instances, if there is more than one branded medicinal product with the same active pharmaceutical substance the SmPC may differ e.g. if different indications are authorised.
- SmPCs comprise up to 20 pages. It is obvious that length and complexity of the text will reduce usefulness and readability. Problem awareness increased with the implementation of the centralised marketing authorisation procedure in 1995. Since then, EMEA has developed templates for drafting SmPCs (QRD templates). Amongst other information, the MedDRA system is recommended for information on undesirable effects, to improve the accuracy of information about the frequency, seriousness and severity of undesirable effects and much more guidance is available.
- Medicine information for injectables may be not adequate. Although, manufacturers are required to supply the medicine with a patient information leaflet and additional information for the health professional, users may find it sometimes difficult to locate at a glance information on administration and handling of the particular medicinal product.
- Sometimes, pharmacovigilance issues may dramatically change the therapeutic value of product (e.g. Rofecoxib®). In these instances, it is crucial to medication safety that the contents of an authorised SmPC are adapted without delay. Beyond the urgent safety

restriction mechanism which allows manufacturers to implement the labelling restriction immediately, there may be some doubt about the efficiency of longer decision ways.[91]

V.3.2.2. Standardised medicine information: therapeutic guidelines

Therapeutic guidelines are disease-oriented guidelines for prescribing. They are prepared for national or local use and give clear, practical and succinct recommendations for therapy. Alternative, "non-drug" options are indicated when appropriate. The guidance is derived from qualified scientific evidence.[92] Therapeutic guidelines should be available to all health professionals involved in patient care to standardise their knowledge and information about medicine therapy.

The ideal information source should be valid (contains data of high quality), relevant (clinically applicable), comprehensive (offers information on benefits and risks of all possible interventions), and user-friendly (is quick and easy to access and use).

The recent growth of EBM has fuelled more useful information sources (see

Table 18).

Table 18: **Types of research evidence and usefulness for decision-making**[92]

Type of evidence	Advantages	Disadvantages
Evidence-based guideline	Very comprehensive-summarises all relevant research information about all possible interventions for a common clinical problem-improved power to detect small and important differences Very useful applicability information - explores the trade-off of benefit and harm according to the level of risk in different patient subgroups	Can be difficult to use if not formatted with the end-user in mind May quickly become out of date
Systematic review	Moderately comprehensive - summarises all relevant research information about a common intervention Less random error - improved power to detect small and important differences Useful applicability information - analyse variability of effects among different patient subgroups	Generally only one of many possible interventions considered Often insufficient data about potential harms Generally provides little information from cohort studies for estimating disease risk to individual patients
Primary study	Very specific information available	Not comprehensive - only one of (usually) many studies available · Insufficient for clinical application

Primary research data may be compiled in systematic reviews and evidence-based guidelines. In general, systematic reviews summarise and analyse data from randomised controlled trials of a single intervention, which may be used for deciding on treatment. Mostly, there are more treatment options for the same clinical problem: systematic reviews of these treatment options may be further expanded and used as a basis for the development of evidence-based guidelines.

With a view to their usefulness in the clinical setting, guidelines should also consider diagnostic and prognostic research to assist in individualising therapy taking account of disease severity. Guidelines and systematic reviews may be stand-alone documents, or, more usefully, summarised in compendia.

V.3.2.3. Customer-specific medicine information: medicine information centres (DICs)

Clinical situation, mission and needs: see chapter V.3.1.4.

V.3.2.3.1. Quality assurance

Biased or irrelevant information, wrong or misleading information, supplying patients with medicine information without recommending to contact their general practitioner or knowing the treatment plan may seriously jeopardise patient safety.

In order to provide high quality information to health professionals and patients, DICs must ensure quality of their services. At least the following aspects should be evaluated when establishing good DIC practices:

- Staff,
- Databases,
- Equipment,
- Process documentation,
- Standard Operating Procedures (SOPs).

In principle, DICs should have easy access to standard textbooks, common medical and clinical pharmacology journals and databases (e.g. Martindale Extra Pharmacopoeia®, Micromedex®, local databases of authorised medicines, Cochrane Library database, etc.). This suffices to answer half of all questions, more questions could be answered by using bibliographic databases.

Standard operating procedures should describe:

- how to accept questions by e-mail, via web, by phone, by fax,
- how to prepare replies in standardised form,
- how to verify the reply by a senior staff member,
- how to reply by fax, phone (in case of urgency) or mail,
- how to request the returning of an evaluation form,
- how to enter the query (answer-reply) into an electronic register (database),
- how to carry out peer review of staff by clinical pharmacists and clinical pharmacologists.

It is necessary to collaborate at European level to help to identify best practices in order to standardise DIC activities and to harmonise programmes of common interest.

V.3.2.3.2. Funding

Adequate funding of DICs is crucial. There are different ways of funding DICs based on services rendered: fee for every query, fee depending on the level of difficulty of the query, fee for services. Although funding by the Public Health Care Authority would be by far most appropriate taking account of the public health mission of DICs and the fundamental importance of unbiased medicine information to patient safety.

V.3.3. Medicines information flow: an example of a system failure

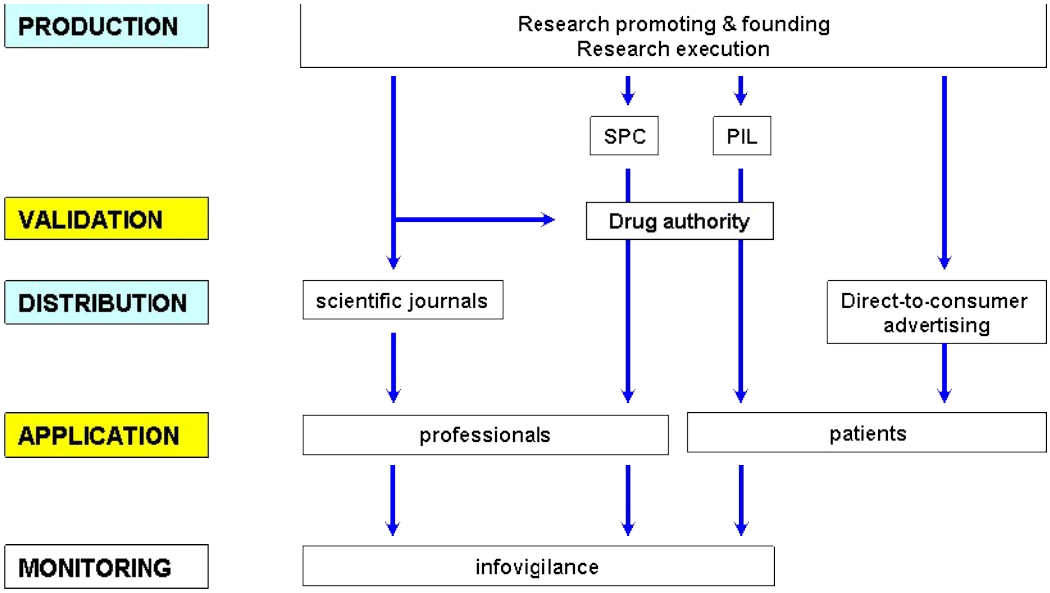
The usual media for authorised medicine information in European Union are the SmPCs (see V.3.2.1) intended for health professionals and the PILs (see V.2.2.1) for patients. Both are product-specific and are approved by drug regulatory authorities as a part of the marketing authorisation of a medicinal product.

The SmPC is the most important public document produced by the marketing authorisation process of a medicine in the EU. Nevertheless, it has been always considered as a communication tool between manufacturers and - only! – prescribers, not for communication between public health authorities and different health professionals and patients.

Unfortunately, this approach to authorised medicine information does not take into account the dual role of pharmaceutical companies: on one hand, they are developing medicinal products that are intended to treat diseases for the benefit of individual and public health; but on the other hand they are doing business in a commercially competitive environment. The conflict of interests between fighting disease and business is evident.[e.g. 8]

In consequence, numerous biases have been introduced at all levels of medicine information processes, starting with the creation of medicine information and validation of information (see Figure 7). [93]

Figure 7: Current medicine information flow



- Medicine research, information validation and distribution channels are widely controlled by pharmaceutical companies without systematic indication of sponsorship and conflict of interests;
- a strong majority of clinical drug trials is promoted and funded by manufacturers themselves instead of public authorities, health insurances or health care providers;
- clinical drug trials are designed to arrive at results favourable for the marketing of the developed medicine instead of producing answers to pressing health questions;
- information about ongoing clinical drug trials and results are not comprehensively published, biasing the availability of information and undermining evidence based medicine practice;
- lack of transparency of regulatory activities, and the fact that marketing application fees represent often more than half of the drug regulatory authorities' budget may increase the dependence on pharmaceutical companies and may weaken consideration of public health needs;
- quality and transparency of decisions of drug regulatory authorities are often considered less important than the rapid granting of marketing authorisations limiting the possibilities for critical review and quality control of medicine information;
- pharmaceutical companies have entered many spheres of medical practice. initial and continuing medical education depend very often from financial support by manufacturers, influencing in that way strongly prescribing habits;
- post-marketing studies on the efficiency of medicines compared to other therapies including alternative treatments may not be carried out or delayed;
- vigilance of medicine information (infovigilance) is still unstructured although errors or inaccuracies in information sources may cause medication errors;[9.27]
- direct-to-consumer advertising (DTCA) by-passes competent health professionals as physicians and pharmacists, and is considered by industry as potential barriers to increasing medicine sales.

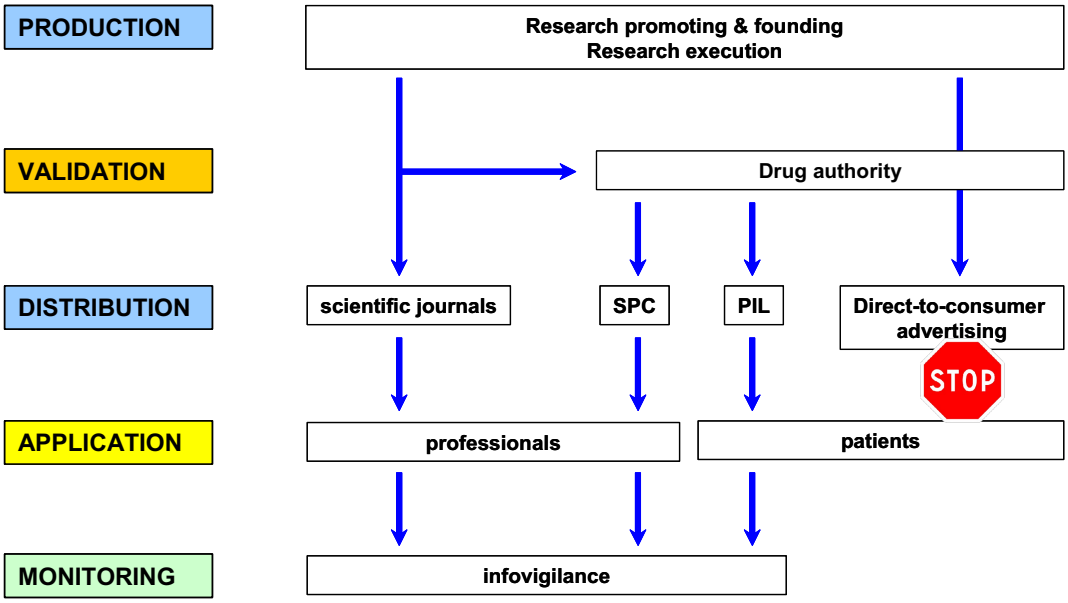
In general, safe use of medicines and rational selection of medicines in particular, depend on unbiased, comparative information which is ready-to-use. Independent medicine information is essential for the development of therapeutic guidelines and for putting EBM to practice. That is why the perception of the role of medicine information should be fundamentally changed and different measures taken.[61]

V.3.4. Recommendations for safer medicine information for health professionals

Research

- At national and international level, health professionals and patient organisations should identify research needs for diseases and pathologic conditions requiring improved therapy options, e.g., improved safety compared to existing options.
- International organisations and governments should allocate parts of health care and research budgets to large-scale clinical trials and post marketing studies meeting public health needs, based on proposals coming from professionals and the public. In particular, adequate public funding is needed for trials the subject is of no commercial interest to pharmaceutical manufacturers. This engagement should be maintained at long term.
- The benefits, risks, burden and effectiveness of a new method should be tested against those of the best current prophylactic, diagnostic, and therapeutic methods. The added therapeutic value of medicinal products should be defined and medicinal products belonging to the same therapeutic group should be critically compared.
- Ethic committees should not approve a study unless it is stated in writing that the full results will be made publicly available whether or not the medicinal product will finally be granted a marketing authorisation.
- Information support (labelling on primary, secondary packaging, patient leaflet as well as IT based supports) and user testing should be part of the clinical development (Phase III) and be adequately designed both for hospital and ambulatory care.

Figure 8: Improved medicine information flow



Validation

- Drug regulatory authorities should be managed and primarily accountable to the public. Governments should use parts of health care budgets for guaranteeing commitments of drug regulatory agencies to public health needs.
- Policy makers should actively improve the legal framework for public health so as to enable drug regulatory agencies to facilitate access to relevant information to health professionals and the public: all information on medicines safety and pharmacovigilance signals should be made public as soon as the medicine is marketed.
- Validation of medicine information in an information society should also cover IT end products e.g. CPOE (computer physician order entry), CDSS (computerised decision support systems), PDA (personal digital assistant) and evolving technologies based on the labelling in standardised format approved by the drug regulatory authority as well as strict requirements for internet based information (see Figure 1).
- No medicine should be authorised without testing all information (SmPCs, PILS, etc.) under real life conditions carried out by patient representatives independent from industry funding, in order to ensure that medicine information is as well tested as the technical quality of medicines.

Distribution

- Drug regulatory authorities should become a reliable source of medicine information for health professionals as well as for patients (e.g. access to SmPCs and PILs on their websites). Health professionals as well as for patients should be better informed about the role of the authorities in medicine information (see Figure 1).
- Sources of independent comparative medicine information and their providers, such as medicine information centres (DICs) and therapeutic bulletins of the International Society of Drug Bulletins (ISDB), should be widely promoted for use. Independent medicine information comprises both data and analyses of the highest possible degree of objectivity and is provided by bodies having no commercial or other interest in the promotion of particular patterns of medicine treatment. Their sole aim is to optimise treatment in the interest of the patient and society at large.
- Initial and continuing education on medicines should be carried out independently from manufacturers.
- Journalists, editors and publishers should be encouraged to check their sources through impartial and informed experts in order to avoid being simply unwitting agents of commercial campaigns.

Application

- Health professionals should be trained to use the basics of evidence-based medicine as well as handling benefit/risk and cost/benefit relations.
- When a newly marketed treatment is offered, health professionals should have all information to explain risks and benefits in comparison to established treatment options in order to make informed choice.

Infovigilance

- Infovigilance should be expanded and structured in analogy to pharmacovigilance based on standardised procedures concerning nomenclature and information collection, e.g. supported by WHO. In this context, the performance of the pharmacovigilance system and how the accumulating information on unexpected adverse drug reactions is included in the authorised sources of medicine information are crucial.
- Professional societies should be involved in the collection and analysis of reports (notifications) e.g. physicians, pharmacists, nurses.

V.4. Safer medicine information practices: need for further research

More research is needed to understand information needs of patients and health professionals with a view to preventing medication errors. Inventories should be made of:

- existing evidence on the usefulness of medicine information for preventing medication errors; in fact, although there is evolving literature on medication errors and related factors, little is still known about the exact relation between medicine information practices and medication safety and the same applies to communication behaviours in health care;
- mandates, standards and professional agreements facilitating quality information practices to promote medication safety;
- medicine information sources and therapeutic guidelines with emphasis on comparative medicine information routinely available to physicians, nurses, pharmacists and patients;
- existing guidelines on the evaluation of medicine information sources of high quality and medicine information practices;
- training health professionals to use medicine information sources and to communicate about medicines to colleagues and patients;
- critical steps in the medicines use process where medicine information is needed e.g. criteria for using parenterals to avoid confusion among nurses; alert cards for therapeutic areas; computerised alert systems for identifying medicines interactions, easy to use pocket information to implement therapeutic guidelines;
- applying information technology to safe medicine information practices.

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Appendices

Appendix 1

Recommendation Rec(2006)7 by the Committee of Ministers to member states on management of patient safety and prevention of adverse events in health care

(Adopted by the Committee of Ministers on 24 May 2006
at the 965th meeting of the Ministers' Deputies)

The Committee of Ministers, under the terms of Article 15.*b* of the Statute of the Council of Europe,

Considering that the aim of the Council of Europe is to achieve a greater unity between its members and that this aim may be pursued in particular by the adoption of common rules in the health field;

Considering that access to safe health care is the basic right of every citizen in all member states;

Recognising that although error is inherent in all fields of human activity, it is however possible to learn from mistakes and to prevent their reoccurrence and that health care providers and organisations that have achieved a high level of safety have the capacity to acknowledge errors and learn from them;

Considering that patients should participate in decisions about their health care, and recognising that those working in health care systems should provide them with adequate and clear information about potential risks and their consequences, in order to obtain their informed consent to treatment;

Recalling that Article 2 of the Council of Europe's Convention on Human Rights and Biomedicine (ETS No. 164) establishes the primacy of the human being over the sole interest of society or science, and recalling its Article 3 on the equitable access to health care of appropriate quality;

Considering that the methodology for the development and implementation of patient safety policies crosses national boundaries and that their evaluation requires substantial resources and expertise and should be shared;

Recalling its Recommendations Nos. R (97) 5 on the protection of medical data, R (97) 17 on the development and implementation of quality improvement systems (QIS) in health care, and R (2000) 5 on the development of structures for citizen and patient participation in the decision-making process affecting health care, and its Resolution ResAP(2001)2 concerning the pharmacist's role in the framework of health security, which explicitly suggests working in partnership with other health professionals;

Noting the relevance of the World Health Organisation (WHO) "Health for All" targets for the European Region (target 2) and of its policy documents on improving health and quality of life and having regard to its Health Assembly Resolution 55.18 (2002) on "Quality of care: patient safety", which recognises the need to promote patient safety as a fundamental principle of all health systems;

Considering that patient safety is the underpinning philosophy of quality improvement and that all possible measures should therefore be taken to organise and promote patient safety education and quality of health care education;

Considering that the same principles of patient safety apply equally to primary, secondary and tertiary care and to all health professions as well as to health promotion, prevention, diagnosis, treatment, rehabilitation, and other aspects of health care;

Recognising the need to promote open co-ordination of national and international regulations concerning research on patient safety,

Recommends that governments of member states, according to their competencies:

i. ensure that patient safety is the cornerstone of all relevant health policies, in particular policies to improve quality;

ii. develop a coherent and comprehensive patient safety policy framework which:

- *a.* promotes a culture of safety at all levels of health care;
- *b.* takes a proactive and preventive approach in designing health systems for patient safety;
- *c.* makes patient safety a leadership and management priority;
- *d.* emphasises the importance of learning from patient safety incidents;

iii. promote the development of a reporting system for patient safety incidents in order to enhance patient safety by learning from such incidents; this system should:

- *a.* be non-punitive and fair in purpose;
- *b.* be independent of other regulatory processes;
- *c.* be designed in such a way as to encourage health care providers and health care personnel to report safety incidents (for instance, wherever possible, reporting should be voluntary, anonymous and confidential);
- *d.* set out a system for collecting and analysing reports of adverse events locally and, when the need arises, aggregated at a regional or national level, with the aim of improving patient safety; for this purpose, resources must be specifically allocated;
- *e.* involve both private and public sectors;
- *f.* facilitate the involvement of patients, their relatives and all other informal caregivers in all aspects of activities relating to patient safety, including reporting of patient safety incidents;

iv. review the role of other existing data sources, such as patient complaints and compensation systems, clinical databases and monitoring systems as a complementary source of information on patient safety;

v. promote the development of educational programmes for all relevant health care personnel, including managers, to improve the understanding of clinical decision making, safety, risk management and appropriate approaches in the case of a patient safety incident;

vi. develop reliable and valid indicators of patient safety for various health care settings that can be used to identify safety problems, evaluate the effectiveness of interventions aimed at improving safety, and facilitate international comparisons;

vii. co-operate internationally to build a platform for the mutual exchange of experience and knowledge of all aspects of health care safety, including:

a. the proactive design of safe health care systems;
b. the reporting of patient safety incidents, and learning from the incidents and from the reporting;
c. methods to standardise health care processes;
d. methods of risk identification and management;
e. the development of standardised patient safety indicators;
f. the development of a standard nomenclature/taxonomy for patient safety and safety of care processes;
g. methods of involving patients and caregivers in order to improve safety;
h. the content of training programmes and methods to implement a safety culture to influence people's attitudes (both patients and personnel);

viii. promote research on patient safety;

ix. produce regular reports on actions taken nationally to improve patient safety;

x. to this end, whenever feasible, carry out the measures presented in the appendix to this recommendation;

xi. translate this document and develop adequate local implementation strategies; health care organisations, professional bodies and educational institutions should be made aware of the existence of this recommendation and be encouraged to follow the methods suggested so that the key elements can be put into everyday practice.

* * *

Appendix to Recommendation Rec(2006)7

A. Prerequisites

1. In developing patient safety strategies, governments should take a proactive, preventive and systematic attitude: to admit that errors happen, to identify and manage risk points in processes, to learn from errors and minimise their effects, to prevent further occurrences of patient safety incidents and to encourage both patients and health care personnel to report those patient safety incidents they are confronted with. This could be achieved by proactive management and systematic design of safe structures and processes.

2. Patient safety should be recognised as the necessary foundation of quality health care, and should be based on a preventive attitude and systematic analysis and feedback from different reporting systems: patients' reports, complaints and claims as well as systematic reporting of incidents, including complications, by health care personnel. The patient safety strategy should become an integral component of the overall continuing quality-improvement programme (Recommendation No. R (97) 17 on the development and implementation of quality improvement systems (QIS) in health care). Investment in patient safety, as in quality improvement, should be considered as economically sound and good value for money.

3. A system-based approach presupposes the systematic design of safe structures, procedures and processes, together with corrective reactions in response to safety incidents. It is accepted that errors are a consequence of normal human fallibility and/or deficiencies of the system; these could be prevented by improving the conditions in which humans work. The aim is a system designed with built-in defences.

4. Patient safety programmes should use the same language, consistent terminology and be focused around similar concepts. "Patient safety incident" is understood as any unintended and/or unexpected incident that could have led, or did lead, to harm for one or more patients receiving health care. In this document it is covered by various expressions, including "adverse event", "medical/clinical error" and "near miss".

5. Patient safety is dependent on many factors, including: an adequate level of resources; sufficient financing; an appropriate number of well-trained staff; appropriate buildings; use of high-quality material, technical equipment and medicines; the establishment of standard diagnostic and therapeutic procedures (clinical practice guidelines); a clear division of tasks and responsibilities; appropriate and smooth connections between processes; proper information systems; accurate documentation and good communication between health care professionals and teams, patients and informal caregivers. The creation of suitable working conditions and atmosphere through: correct work organisation, the reduction of stress and tension; the provision of good, safe, social and health conditions for health-service workers; and increased motivation reduces the role of the "human-factor" issues in patient safety incidents. It includes prevention of causes contributing to (near) incidents and errors, such as: time-pressure on health care providers (leading to insufficient time to communicate properly among professionals and with patients and other informal caregivers); frequent "handing over" of patients from one health care professional to another (which leads to poor communication and errors related to poor transfer of information); shortage of staff; pressure on health care professionals to quickly discharge a patient from hospital; intrusion of commercial elements in health care and side-effects of competing commercial insurance companies.

B. Cultures of safety/environment

1. Credibility at the highest level of a health care system is the key factor for developing a safety culture. Government and other decision makers' policy and action should support measures to allow health care organisations to be open and fair in all they do:

a. the first stage in developing a safety culture is to define the existing culture of a system and organisation. A safety culture is essentially a culture where everyone has a constant and active awareness of her/his role and contribution to the organisation, and of the

potential for things to go wrong. It is an open and fair culture, where people are able to learn about what is going wrong and then put things right;

b. developing a safety culture in an organisation needs strong leadership and careful planning and monitoring. It also requires changes and commitment to safety at all levels of the system, from government to clinical teams and supporting staff;

c. a clear and strong focus on patient safety should be established through the health care system and organisations: safety should be valued as the primary priority of health care, even at the expense of productivity or "efficiency";

d. the commitment to quality and safety should be articulated at the highest level of the health care system and translated into policies and political support of public health and patient safety issues;

e. necessary financial and logistical resources, incentives and rewards should be provided by the health care system to make this commitment possible:
- risk management in health care organisations should be obligatory and controlled;
- individual incentives and rewards should be completed by team incentives and rewards;
- individuals should be rewarded for taking safety-oriented initiatives, even if they turn out to be wrong;

f. quality and risk management concepts and activities should be included in the under- and postgraduate educational programmes of all health care professions;

g. recognised national focal points for patient safety, with relevant health care professionals, should be created and supported;

h. the government should ensure that no legal action is taken in case of self-reported incidents.

2. A system-based approach is the proven way to improve patient safety. Risk management is based on, and integrated in, quality management and also takes into account human-factor engineering in structures and human-factor principles in processes.

a. Effective risk management requires understanding of human behaviour, the varieties of human error, and the conditions likely to cause such error.

b. It must be accepted that people will make mistakes and that processes and equipment will sometimes fail. It must be accepted that in specific instances and for various reasons individuals can make errors.

c. The systems-based approach takes into account many components recognised as contributing to an incident or to the events leading up to it (see figure 1, Explanatory Memorandum). This moves the investigator away from focusing blame on individuals and looks at what was wrong with the system in which the individuals were working.

d. Systems should therefore be designed and maintained to reduce as far as possible the likelihood of patient harm caused by mistakes. By accepting this approach, organisations can focus on change and develop defences and contingency plans to cope with these failures, and can learn lessons and potentially stop the same incident reoccurring or harming patients and providers of care.

3. At the level of health care organisations, the chief executive, the board and administrative and clinical directors need to establish an environment in which the whole organisation learns from safety incidents and where staff are encouraged to both proactively assess and immediately report risks.

These should be consistent with already established quality-management systems, of which it should be an integral part (Committee of Ministers' Recommendation No. R (97) 17 on the development and implementation of quality improvement systems (QIS) in health care).

a. Quality and risk management should be led by the highest level of the organisation and translated into shared values, norms and behaviour at all levels.

b. Health care organisations should introduce systems allowing them to regularly conduct safety-culture assessments and learn from them. Safety should be expressed by quality indicators and followed up.

c. At all levels, from top management to frontline, staff should be educated in human-behaviour (human factor) and risk management principles. Potential accidents should be proactively identified and assessed (for example by Failure Modes Effects and Criticality Analysis (FMECA)). Systems and processes should be developed to manage the risks.

d. Health care professionals should interact and communicate openly with and listen to patients. Communication with the public should be transparent.

e. Communication between individuals and teams and across organisational levels should be frequent, cordial, constructive and problem-oriented. Organisational management is kept informed about and involved in the improvement of patient safety.

f. At all levels, actual patient safety incidents, problems and errors should be properly reported when they occur. Local policies describe clearly how organisations will

manage staff involved in incidents, complaints and claims. Staff should be comprehensively trained in clinical and administrative procedures for responding to a serious error. Reporting of incidents should be promoted, locally and nationally.

g. At all levels, problems and errors should be treated openly and fairly in a non-punitive atmosphere. The response to a problem must not exclude individual responsibility, but should focus on improving organisational performance rather than on individual blame.

h. Incidents should be reviewed and investigated thoroughly, transparently and fairly, free from hindsight bias. Problem analysis should focus on organisational performance. All staff should be trained in teamwork-based problem solving and encouraged to use root-cause analysis to learn how and why incidents happen.

i. Solutions to prevent incidents should be implemented through changes in structure and processes. Safety lessons should be communicated to frontline staff and other relevant professional health care groups and integrated into training curricula. Ongoing interdisciplinary educational programmes allow for discussions about causes and prevention of errors and adverse events. Incidents should be shared with other organisations to broaden learning as much as possible.

j. Best-practice examples and "success stories" should be collected and disseminated.

C. Assessment of patient safety – The role of indicators

1. There is a major need to assess patient safety on an ongoing basis, implement a learning organisation, demonstrate ongoing safety improvement and determine when lapses in patient safety occur.

2. Systematic collection and analysis of patient safety indicators should help prevent future "unsafe" methods of care and, in the long term, their adverse effect on treatment.

3. Patient safety is an outcome of many factors, especially safe practices within the framework of a safe system. While patient safety is the ultimate goal, belonging to "good outcomes", what ultimately determines safety is a safer care environment during the patients' whole "journey of care".

4. Prior to embarking on actual patient safety assessment activities, a systematic strategy should be established at an institutional or regional level to measure, report, and use information about the most common services associated with a high probability of error.

5. The assessment of process safety should be carried out through both qualitative and quantitative methods.

6. The qualitative methods map the various activities that exist in the routine delivery of services, for example using methods used in pathways analysis without, however, recommending one pathway as more appropriate than another. The purpose of the descriptive phase is to "map the genome of safety" in the delivery of care and services.

7. The quantitative approach uses indicators and epidemiological methods of analysis to systematically quantify distinct aspects of processes and their immediate outputs in relation to:

- adverse events;
- adverse events causing harm to patients;
- adverse events causing harm to providers; and
- for the risk of adverse events.

8. In 2004, the Organisation for Economic Co-operation and Development (OECD) produced a report on patient safety indicators that would best allow the assessment of patient safety in an ongoing way, given current available knowledge. A total of 21 patient safety indicators were selected (OECD health technical paper DELSA/ELSA/WD/HTP(2004)18, www.oecd.org/els/health/technicalpapers), which address hospital patient safety incidents and include only measures that focus on specific clinical outcomes. Another approach is to use indicators that apply at an organisational level, for example whether a hospital or practice uses electronic prescribing, or has implemented practices that have been shown to reduce the rate of ventilator-associated pneumonia.

9. Quality and safety indicators should be determined and reasonably applied to the entire treatment process (both outpatient and hospital treatment).

D. Data sources – Reporting systems

D.1. Patient afety incident reporting

1. The primary objective of an incident reporting system is the enhancement of patient safety, by learning from adverse events and mistakes made. Reporting and collection of incident data is meaningful only if the data is analysed and evaluated and if feedback is given to the professionals involved in the incident, and to all others who could learn from the incident.

2. Incident reporting systems are not intended to identify and punish the individual staff members involved in patient safety incidents.

3. Incidents may be reported by health professionals, patients and relatives, or by other informal caregivers and suppliers.

4. An incident reporting system should:

a. preferably be voluntary in nature; in most instances the professional in question is the only one who knows about a near miss or an adverse event (alternatively: the system may be mandatory on the part of the institution, giving the controlling bodies an opportunity to measure the institution against a standard or an obligation). A mandatory system for individual health care personnel could completely demotivate those directly involved in the provision of health care and who are invited to participate in such reporting systems);

b. be at least confidential; however, if the event is to be analysed in order to learn from it, the names of the personnel involved may need to be known locally (that is, inside the actual institution);

c. be anonymous, at least at regional and national levels;

d. be non-punitive with respect to those who report, but provide no immunity if supervisory bodies or legal authorities need to be informed of the event in some way, because of its consequences for the patient;

e. be objective with findings and recommendations;

f. encourage unrestricted reporting by all working in the health care system;

g. provide incentives (for example, express recognition) for reporting;

h. receive reports of serious and fatal events caused by incidents, near misses, and hazardous situations that could have led to safety incidents;

i. be independent of regulatory or accrediting processes;

j. use a single format for the reporting of all incidents, preferably including discrete categories for onward reporting to public authorities or for separate analysis. Where a variety of reporting formats already exists, the definition of a standard set of minimal data should be agreed upon, to be used in every subsequent reporting system.

5. The greatest effect on safety and quality improvement is generated locally when the institution uses patient safety incident reporting as part of a continuous system of safety and quality improvement:

a. local safety and quality initiatives should be promoted in all health care units and organisations;

b. ongoing assessment of the patient safety policy should start at the lowest level possible within the service.

6. A national framework for incident management should be defined and implemented, to capture from local systems those patient safety incidents where national learning and action can prevent future reoccurrence. Where appropriate this information could then be shared with patient safety organisations or government departments in the other European countries.

7. As a final goal to be reached after gaining experience at local level, a national incident reporting system should be considered: comprehensive, which should be covering all levels and areas of health care provision, including the private sector.

8. Aggregation of data regionally, nationally or internationally will be particularly useful for uncovering systematic failures and the accumulation of certain incidents or failures in new equipment that cannot be readily identified at the local level, in other words, those which can only be revealed by a larger dataset. Rigorous methods should be used in order to guarantee representativeness of the data and to minimise any possible bias. Institutions have to be equipped with appropriate resources to achieve this purpose.

9. The development of Internet based reporting systems should make the establishment of national and European-wide safety incident databases easier to maintain and less costly to operate.

10. Experience from different countries varies as to whether there is a need to make reporting and analysis of patient safety incidents a legal obligation.

11. When designing patient safety incident reporting systems it may be an advantage to have in place a complaints system, a patient compensation system and a supervisory body for health professionals. These should complement the patient safety incident reporting system, and together these systems would form an overall integrated system for managing risks, both "clinical" and "non-clinical".

D.2. Use of data

1. Reporting and collection of patient safety data is meaningful only if the data is intelligently analysed and information is, where appropriate, fed back to health care professionals, managers and patients.

2. The Root Cause Analysis process is a systematic and comprehensive means of collecting and analysing data following a patient safety incident. It does not end at the investigative process. It also includes the design, implementation, evaluation and follow-up of improved safety systems.

3. There needs to be a clear understanding and agreement with health care institutions and professionals on how the data collected will be put to use.

4. The collection and use of data will also need to comply with domestic and European data-protection legislation.

5. Effective data collection depends on the willingness of frontline clinical staff. The following barriers to reporting exist, which should be removed through appropriate policies:
a. fear of blame, resulting from a lack of open and fair culture;
b fear of the reports being used out of context by the media and others;
c. lack of feedback as to what has changed as a result of the report;
d. lack of time to report;
e. lack of support from the management of the organisation;
f. lack of legal protection against using the information for purposes other than learning;
g. breaches of confidentiality or anonymity leading to ineffective separation of incident reporting systems from disciplinary and regulatory bodies.

D.3. Other sources of information on patient safety

1. Patient safety incident reporting systems can be established as "stand-alone" systems or can be integrated with systems for recording complaints and compensation claims or applications for benefits (the different sources of information will depend on the situation in each country). Each organisation should develop systems to analyse this information and to learn from it.

2. A patient-complaints system should be regarded as an instrument ensuring patient rights, but representing a minor part of reported data on patient safety:

a. complaints, criticism or suggestions, whether oral or written, made by patients or their representatives, should be taken seriously, and handled appropriately and sensitively;

b. patients should feel able to approach the staff who provided the service, and professionals should make every attempt to resolve complaints locally at an early stage;

c. the primary objective of any system is to provide the fullest possible opportunity for investigation and resolution of the complaint, as quickly as circumstances allow.

3. Clear procedures for recording and analysing patient complaints should be defined, which should be simple and integrated by all stakeholders:

a. the process should be fair, transparent, flexible and conciliatory and should be easy to access for all service users;

b. rigid, bureaucratic and legalistic approaches must be avoided.

4. In addition to patient safety incident reporting, all other reporting systems and channels should be used to collect data. There should be a register of such sources, such as those for medical device failures, complaints, legal claims, applications for disability benefits, death inquests, and reports of adverse drug reactions: mechanisms should be introduced at regional or national level to collect this information and share the lessons learned from these systems with those able to take action.

E. Medication safety – A specific strategy to promote patient safety

1. The use of medicines represents the most frequent health care intervention in developed countries. Medication errors are the most common single preventable cause of adverse events and European health authorities should consider them as an important public health issue.

2. Medication safety comprises both adverse drug reactions and medication errors. A clear distinction has to be made between them. In a recent World Health Organization (WHO) report adverse drug reactions (pharmacovigilance) were linked to product safety, whereas medication errors were linked to the safety of health care services.[i]

3. A medication error is defined as follows: "Any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. Such events may be related to professional practice, health care products, procedures, and systems, including prescribing; order communication; product labelling, packaging, and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use."[ii]

4. The following key dimensions in the provision of care should be taken into account in order to prevent medication errors:

[i] WHO Quality of care: patient safety Report EB113/37 by the Secretariat to the Executive Board, 4 December 2003, 6p.
http://policy.who.int/cgi-bin/om_isapi.dll?hitsperheading=on&infobase=ebdoc-en&record={809}&softpage=Document42

[ii] National Co-ordinating Council for Medication Errors Reporting and Prevention NCC MERP Taxonomy of Medication Errors. 1998 http://www.nccmerp.org/pdf/taxo2001-07-31.pdf

a. the organisation and structures used within health care that govern the prescription, dispensing, administration, and monitoring of medication use;

b. the patient safety culture in health care that promotes the understanding of activities that may have a high risk of undesirable outcomes with the use of medication, in the overall care process;

c. the use of indicators that can establish a baseline for the actual incidence of undesirable events;

d. the level of understanding among staff of the necessary and ongoing observations that need to be made to prevent or minimise the likelihood of errors in medication use.

5. A recognised national focal point for safe medication practices should be designated in each country in a collaborative and complementary way with pharmacovigilance systems for reporting medication errors, analysing causes and disseminating information on risk reduction and prevention.

6. European health authorities should recognise medication safety as a priority, promoting Europe-wide standards for safe medication practices and share and disseminate data and strategies for prevention and risk reduction between countries.

7. The nature, causes, frequency and clinical consequences of medication errors in hospitals and home-care settings in Europe should be assessed.

8. The improvement of the system of medication use requires the prevention of medication errors at every stage, including:

a. improvement of packaging and labelling of medicines as well as proprietary and non-proprietary nomenclature, in co-operation with European regulators and the industry;

b. safer selection and procurement of medicines, including a medication-error-risk assessment of medicines and medical devices during formulary and purchasing decisions;

c. safer storage of medicines in clinical areas in hospitals, where unit-based floor stock should be restricted, and home-care settings;

d. safer prescribing of medicines, helped by the availability of complete patient records, electronic prescribing, decision support and clinical pharmacy services;

e. safer medicine preparation, by minimising the preparation in clinical areas and supplying ready-to-use medicines;

f. safer dispensing of medicines, enhancing the ability to intercept medication errors, and reducing dispensing errors by the use of automated dispensing systems;

g. safer administration of medicines, through clear and legible labelling of medicines up to the point of care, bar-coding, minimising the storage of high-risk medicines and the use of standardised procedures;

h. safer monitoring of medicines based on regular medication reviews and the proactive detection of adverse drug events;

i. independent, updated and accessible information on medicines must be available to health care providers and patients, and considered with patient information when prescribing, dispensing, and administering medication;

j. patients' and citizens' education for safer medicine use, considering patients as active partners in their care;

k. safer communication about medicines for individual patients between health care providers.

9. In this context, reference is made to an ongoing project of the Committee of experts on pharmaceutical questions (P-SP-PH) on safe medication practices.

F. Human factors

1. In order to reduce and prevent patient safety incidents, health professionals must understand their own behaviour patterns, their decision-making process and their ability to cope with challenging situations in daily activities.

2. Health professionals should be given the opportunity to learn how to handle guilt and be supported to avoid becoming "the second victim" of the safety incident.

3. Support from the organisation to the health professionals is crucial to make disclosure of the incident possible and to enable continuation of work in health care, where risks will always exist and adverse events happen.

4. Decision-making supports such as reference works and reminders cannot replace sound human and clinical reasoning.

5. Sharing decision-making with patients should be learned and applied in practice when appropriate.

6. All measures that increase patients' compliance with their treatment should be implemented in order to avoid both poor outcomes and safety incidents.

7. Education and training curricula for all health professions should include basic knowledge on: the principles of clinical decision making, risk awareness, risk communication, risk prevention, individual and collective attitudes and behaviour in the case of adverse events (medical, legal, financial and ethical aspects).

8. Continuous education should contribute towards building a safety culture in health care by changing attitudes, from an illusion of infallibility to acceptance of human error and to the ability to learn from mistakes.

9. Interdisciplinary co-operation, a non-hierarchical structure and open communication in healthcare organisations are necessary for building a safety culture. In some specialities systematic training in team work is indispensable.

G. Patients' empowerment and citizens' participation

1. Policy makers, planners and organisations delivering health care must place patients and the public at the centre of delivering safe health care:

2. Citizens should be able to rely on the safety of their health services. Information should be available to the public about the safety of their health services, together with safety improvement measures.

3. Patients using health services must have adequate information available, allowing them to include safety considerations when making decisions:

a. this information should allow patients to balance the risks and benefits of different treatment options;

b. when asking for the patient's informed consent, a clinician must explain the risks and benefits of the treatment in terms that the patient can understand;

c. patients, along with health care staff, should be involved at an early stage in the design and testing of medical procedures, devices and equipment;

d. patients should receive information about who is responsible for their treatment, especially when this involves interdisciplinary co-operation, and learn how to establish a positive relationship with health professionals;

e. patients and relatives should be made aware of their own "risky" behaviour and encouraged to adopted more appropriate habits.

4. People who have been harmed because of their treatment must be taken care of openly, honestly and with compassion – a transparent communication policy should be followed:

a. patients must feel able to speak up when they feel that something could go, or has gone, wrong during the course of their treatment;

b. organisations should have mechanisms to allow patients to report safety incidents to health care organisations, so that these organisations can learn from what has gone wrong;

c. these reporting systems should be in addition to the organisations' complaints procedures;

d. patients who have been harmed because of their treatment should have the possibility of receiving financial compensation without lengthy legal action.

H. Patient safety education

1. Education for patient safety should be introduced at all levels within health care systems, including individual public and private health care organisations. The main focus should be on educating health care professionals, including managers and senior figures involved in health care governance, in patient safety issues relevant to their function. In order to promote a change in attitudes towards greater patient safety, informing and educating to this end should begin for future doctors, nurses and other health professionals, and for administrators, as part of their training.

2. Education for patient safety should also be introduced for patients and their families, the general public, the media, consumer organisations, health purchasers and insurers, corporate organisations, government bodies and other relevant organisations. The main focus should be on raising awareness of patient safety issues.

3. Patient Safety Education Programmes (PSEPs) should be developed and implemented by all educational institutions providing health-related curricula; professional accrediting bodies; certifying and licensing boards; and diploma appraisal and revalidation bodies.

4. Issues or topics for consideration in developing PSEPs should include, as a minimum:

a. the essence of a good patient safety culture;

b. risk assessment, decision making and proactive management of safe health care processes;

c. moral, legal and technical considerations;

d. human factor considerations;

e. patients' perspective of safety and their values together with the point of view of health professionals;

f. essential communication and interaction considerations for health care professionals and teams;

g. informed consent – scope and content;

h. reporting and analysing patient safety incidents;

i. root cause analysis and learning from patient safety incidents;

j. open disclosure of patient safety incidents;

k. shared decision-making.

I. Research agenda

The development and implementation of an effective patient safety policy requires sound evidence (as opposed to mere opinion). Therefore, applied research on patient safety is a vital component of a comprehensive strategy to address this problem. Areas that should be considered for inclusion in research programmes include:

a. descriptive, qualitative studies of patient safety incidents in all health care settings, including outpatient care, home care, acute hospital care and rehabilitation;

b. analytical, quantitative epidemiological, preferably prospective, studies to identify risk factors for patient safety incidents and iatrogenic complications;

c. experimental research on human factors and human error, and on modifiable factors that decrease the likelihood of error. The studies on human-technology interaction should be included;

d evaluation of the most effective ways of involving patients in the prevention and management of incidents;

e. development and validation of patient safety indicators;

f. simulation studies and small scale pre-tests to identify potentially effective interventions to improve patient safety;

g. evaluations of the real life effectiveness of interventions to improve patient safety, and of unintended side effects of such interventions;

h. studying the processes of care and safer practices;

i development and introduction of instruments promoting the prevention of adverse events. The Failure Mode and Effects Analysis (FMEA) is one example of tools to prevent a failure before any harm is done. Less known in health care organisations, they should be adapted, tested and, where appropriate, implemented;

j. appropriate procedures to ensure safety of experimental diagnostic and therapeutic procedures;

k. methods (including e-learning and other innovative approaches) to educate health professionals in a safety culture and in safe practice.

J. Legal framework

1. Legislation constitutes one of the most important regulatory mechanisms in health care, but the diversity of existing legal traditions and practices in Europe calls for a country-specific approach.

2. Member states shall consider the following elements:

a. Legal approaches regarding a patient safety reporting system should:

i put in place national and local policies and mechanisms enabling a timely and explicit assessment of the nature of the incident:
– what must be reported and to whom;
– what can be reported;
– what kind of incidents should be reported in the context of the reporting system;

ii. oblige all providers of health care services – both public and private – to receive, record and analyse reports on patient safety incidents for use in the improvement of patient safety and treatment;

iii. ensure that reports on patient safety incidents, which may be attributed to specific individuals, can be exchanged within the group of people who locally handle tasks pursuant to paragraph ii. above;

iv. ensure that reports on patient safety incidents can be passed on to clinical databases and other registers where health information is recorded with a view to increasing documentation and improving quality in the area of patient safety;

v. comply, as regards approaches under paragraphs iii. and iv., with professional secrecy and data-protection rules, for example by providing the information in a register in an anonymous form;

vi. ensure the confidentiality of the reporting procedure, that is, ensure the identity of the reporting health care professional or patient shall not be disclosed to patients or to the public; if the event is to be analysed and learned from, the names of the personnel involved may need to be known locally (that is, inside the actual institution);

vii. ensure the legal protection of the reporting health care professional, that is, ensure that a health care professional reporting to the system shall not, as a sole result of such reporting, be subjected to disciplinary investigation or measures by the employing authority, or reprisals such as supervision or criminal sanctions by the courts;

viii. not, as regards the questions of when, by whom and how the reporting is to be done, be a matter of free choice or open to random decision making but must follow an established, well-justified policy.

3. Legal approaches regarding patients' rights should:

a. ensure that complaints, criticism or suggestions made by patients or their representatives are taken seriously and handled appropriately;

b. ensure that patients are immediately informed of an adverse event and of any events entered into the patient's medical file;

c. ensure that patients who have been harmed by a patient safety incident are entitled to receive financial compensation;

d. ensure the presence of an efficient and sufficient supervisory system to identify and manage cases of malpractice;

e. take into consideration the fact that any incident can have multiple legal consequences, depending on the nature and severity of the incident and on the causal relationship between the process of care and an adverse event.

4. It may appear difficult to establish a patient safety reporting system without compromising patients' rights. However, if the public is ready to accept the presence of a confidential, anonymous, non-punitive reporting system the public must be assured that its legal and financial rights will be protected. The existence of a fair and open complaints system, a just and adequate compensation system and an efficient and reliable supervisory system will certainly make the process easier and politically more acceptable. Promoting a "no blame" culture is not intended to diminish the effective legal protection of patients.

K. Implementation of the patient safety policy

A successful implementation of the patient safety policy requires concerted activities of all stakeholders, and in particular:

a. health care staff involvement from the very beginning, starting with the development of a patient safety strategy;

b. prompt feedback to all health professionals and patients involved in a patient safety incident at the local level;

c. putting emphasis on the development of a simple, non-bureaucratic safety enhancement system;

d in corporate health care organisations, patient safety starts at the top; therefore management should offer leadership and support and implement a learning organisation, to assess the contribution of professionals;

e. raising citizens' awareness through information for, and involvement of, citizens in patient safety issues;

f. informing the public of results achieved by patient safety actions (transparency);

g. obligation for health care units to report on the implementation of patient safety measures;

h. adjusting, if necessary, existing systems of care by medical, economic, legal and political measures to improve patient safety;

i. continuous quantitative assessment of the patient safety policy at national and, where available, international level. It should be reported back in due time to enable the future updating of the policies inspired by the recommendation as well as the text of the recommendation itself;

j. the implementation of patient safety policies should not be conditioned or inhibited by financial considerations. The safety of medication and interventions is the essential feature of health care provision and its cost should be included in the general budget, instead of being covered by special tariffs and reimbursement schemes. Health care providers should receive an adequate payment through normal channels, for their quality services;

k. member states can decide upon financing of research projects according to their perceived needs and established priorities.

Appendix 2

Council of Europe Committee of Experts on Pharmaceutical Questions Expert Group on Safe Medication Practices – Vision statement

Having regard to World Health Assembly Resolution 55.18 (2002) recognising the need to promote patient safety as a fundamental principle of all health systems and to all Resolutions of the Council of Europe's Committee of Ministers dealing with health protection of the consumer in its widest acceptation,

- in particular to Resolution ResAP(2001)2 concerning the pharmacist's role in the framework of health security, in partnership with others health professionals, participants at the Expert Meeting on Medication Safety co-sponsored by the Council of Europe (Partial Agreement in the Social and Public Health Field) and the World Health Organization/Regional Office for Europe, agree that

1. all European Health Authorities should recognise medication safety as a priority,

2. medication safety comprises both adverse drug reactions and medication errors and that a clear distinction has to be made between them,

3. medication errors, responsible of preventable events, be recognised as an important system-based public health issue,

4. the approach to safe medication practices should be multidisciplinary and should include patients, professionals and their organisations and all other stakeholders involved in the medication use system,

5. medication safety should be considered as an essential element in the development and design of medicinal products, technology and medical devices including nomenclature, packaging and labelling,

6. medication safety should proactively focus on prescribing, dispensing, administration, monitoring and information in outpatient and inpatient settings and their interfaces,

7. a recognised national focal point for safe medication practices be designated in each country in a collaborative and complementary way with pharmacovigilance systems based on a national system for reporting medication errors, analysing causes and disseminating information on risk reduction and prevention,

8. an assessment at national level and funding of research of the frequency, nature and causes of medication errors and preventable adverse events is needed,

9. there should be Europe-wide standards for safe medication practices,

10. local targets are valuable in implementing safe medication practices and sharing and disseminating of data and strategies for prevention and risk reduction between countries,

11. medication safety culture should be a part of under and post graduate and continuous education of health professionals,

12. the public should be integrated in safe medication practice.

Strasbourg, 13 November 2003

Appendix 3

Glossary of terms related to patient and medication safety

Confusion and misunderstandings occur very easily because the different terms used for medication safety are not carefully defined. For a correct use of evidence-based data on medication errors as much as for avoiding any confusion with already well-established health care control organisations, such as pharmacovigilance, an accurate use of the specifics terms of this field is needed.

Some definitions have already been proposed in the United States of America by health care practitioners and academic organisations such as the Institute of Medicine, the National Coordination Council for Medication Error Reporting and Prevention, the American Society of Health-System Pharmacists and the Institute for Healthcare Improvement. At international level, some of these definitions have been adopted by the World Health Organisation and the International Pharmaceutical Federation.

At national level, the clarification work has been done in some European countries, such as in France, as the result of the collaboration between the Medication Errors Epidemiological Network (Réseau épidémiologique de l'erreur médicamenteuse) and the French Society of Clinical Pharmacy, and in Spain as initiative of the Instituto para el Uso Seguro de los Medicamentos (ISMP Spain) with the support of the Spanish Society of Hospital Pharmacy.

On the basis of the different available definitions of terms related to medication errors and adverse events in seminal publications and public reports, and in co-operation with the Council of Europe SP-SQS Committee, the Expert Group on Safe Medication Practices has established a glossary aiming at permitting to use terms having the same signification, allowing, as far as possible, lesser confusing debates.

Terms and translations	A	R	P	B	Definitions and references	Comments and synonyms
accident French : accident Spanish : accidente German : Unfall Italiano : incidente Slovene : nesreča				X	**accident :** an unplanned, unexpected, and undesired event, usually with adverse consequences.[55]	*"For many years safety officials and public health authorities have discouraged use of the word "accident" when it refers to injuries or the events that produce them. An accident is often understood to be unpredictable -a chance occurrence or an "act of God"- and therefore unavoidable. However, most injuries and their precipitating events are predictable and preventable. That is why the BMJ has decided to ban the word accident. (...) Purging a common term from our lexicon will not be easy. "Accident" remains entrenched in lay and medical discourse and will no doubt continue to appear in manuscripts submitted to the BMJ. We are asking our editors to be vigilant in detecting and rejecting inappropriate use of the "A" word, and we trust that our readers will keep us on our toes by alerting us to instances when "accidents" slip through."*[17]
active error French : erreur active Spanish : error activo German : aktiver Fehler Italiano : errore attivo Slovene : neposredna napaka see also : *error*	X		X		**active error :** an error associated with the performance of the 'front-line' operator of a complex system and whose effects are felt almost immediately.[46]	Synonym : *sharp-end error* This definition has been slightly modified by the Institute of Medicine : "*an error that occurs at the level of the frontline operator and whose effects are felt almost immediately.*"[26]
active failure French : défaillance active Spanish : fallo activo German : aktives Versagen Italiano : fallimento attivo Slovene : aktivna napaka see also : *active error*				X	**active failures :** actions or processes during the provision of direct patient care that fail to achieve their expected aims, for example, errors of omission or commission. While some active failures may contribute to patient injury, not all do.[15,57]	Since failure is a term not defined in the glossary, its use is not recommended. A different meaning exists for active failure : "*an error which is precipitated by the commission of errors and violations. These are difficult to anticipate and have an immediate adverse impact on safety by breaching, bypassing, or disabling existing defenses.*"[23]
administration error French : erreur d'admnistration Spanish : error de administración German : Anwendungsfehler Italiano : errore di somministrazione Slovene : napaka pri dajanju see also : *medication error*	X				**administration error :** whatever type of medication error, of omission or commission, that occurs in the administration stage when the medication has to be given by a nurse, or the own patient, or a caregiver.	A process error taking place in the medication use system: definition and type to be refined with the taxonomy of medication errors.

Terms : **A** – approved term ; **R** – regulatory term ; **P** – patient safety term ; **B** - term to be banned : not to be used

Terms and translations	A	R	P	B	Definitions and references	Comments and synonyms
adverse drug event French : événement indésirable médicamenteux Spanish : acontecimiento adverso por medicamentos German : unerwünschtes Arzneimittelereignis Italiano : evento avverso legato all'uso di farmaci Slovene : neželeni dogodek pri uporabi zdravila see also : *adverse drug event trigger, potential adverse drug event, preventable adverse drug event, unpreventable adverse drug event*	X				**adverse drug event :** any injury occurring during the patient's medicine therapy and resulting either from appropriate care, or from unsuitable or suboptimal care. Adverse drug events include: the adverse drug reactions during normal use of the medicine, and any harm secondary to a medication error, both errors of omission or commission. An adverse drug event can result in different outcomes, notably: in the worsening of an existing pathology, in the lack of any expected health status improvement, in the outbreak of a new - or to be prevented - pathology, in the change of an organic function, or in a noxious response due to the medicine taken.[22]	"*Adverse drug events may have resulted from medication errors or from adverse drug reactions in which no error was involved.*" [24] "*An injury, large or small, caused by the use (including non-use) of a drug. There are two types of adverse drug events (ADEs) : those caused by errors and those that occur despite proper usage. If an adverse drug event is caused by an error it is, by definition, preventable. Nonpreventable adverse drug events (injury, but no error) are called adverse drug reactions (ADRs)* "[31]
adverse drug reaction French : effet indésirable d'un médicament Spanish : reacción adversa a medicamentos German : unerwünschte Arzneimittelwirkung Italiano : reazioni avverse da farmaci Slovene : stranski učinek zdravila see also : *mandatory reporting, voluntary reporting*		X			**adverse drug reaction** means a response to a medicinal product 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 restoration, correction or modification of physiological function ; **serious adverse drug reaction** means an adverse action which results in death, is life-threatening, requires inpatient hospitalisation or prolongation of existing hospitalisation, results in persistent or significant disability or incapacity, or is a congential anomaly/birth defect ; **unexpected adverse drug reaction** means an adverse reaction, the nature, severity or outcome of which is not consistent with the summary of product characteristics.	Chapter Va (Pharmacovigilance) of Directive 75/319/EEC (Article 29b) amended by Commission Directive 2000/38/EC of 5 June 2000 : similar to the WHO's definition : "*a response to a drug 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 physiological function.*" [WHO Technical Report No 498 (1972)] To be used where there is a causal relationship with the use of the "medicinal product" (medicine)[20] Synonyms (not recommended by EMEA) : *adverse effect, side effect, undesirable effect* *" Unfortunately, many have used the term ADR as synonymous with ADE, which blurs an important distinction. "*[31]
adverse event French : événement indésirable Spanish : acontecimiento adverso German : unerwünschtes Ereignis Italiano : evento avverso Slovene : varnostni incident see also : *adverse event trigger, harm, iatrogenic, incident, injury*			X		**adverse event :** an unintended injury caused by medical management rather than by a disease process.[33,59] **patient safety incident:** any unintended or unexpected incident(s) that could have or did lead to harm for one or more persons receiving NHS-funded health care. 'Patient safety incident' is an umbrella term which is used to describe a single incident or a series of incidents that occur over time.[38]	"*An adverse event results in unintended harm to the patient by an act of commission or omission rather than by the underlying disease or condition of the patient.*"[7] In the UK, the terms 'patient safety incident' and 'patient safety incident (prevented)' are preferred (by patients and the public) to the terms 'adverse events', 'clinical errors' and 'near misses'. Terms such as adverse, error or mistake suggest individual causality and blame. Medical error in particular suggests the main cause is the medical profession. (NPSA Terminology)
adverse event trigger, marker French : événement traceur Spanish : señal alertante de acontecimiento adverso, marcador German : Auslöser eines unerwünschten Ereignisses Italiano : trigger di eventi avversi Slovene : kazalnik verjetnega varnostnega incidenta see also : *adverse event, adverse drug event*	X		X		**adverse event triggers :** clinical data related to patient care indicating a reasonable probability that an adverse event has occurred or is occuring. An exemple of **trigger data for an adverse drug event** is a physician order for an antidote, a medication stop, or a dose decrease.[7] **adverse drug event triggers and markers :** a medication, laboratory value, or other indicator that prompts further review of patient care for the purpose of uncovering adverse drug events that may otherwise go undetected or unreported. Examples of triggers and markers include diphenhydramine, naloxone, aPTT greater than 100 seconds, serum glucose less than 50, falls, rash, and death.[3]	

Terms : **A** – approved term ; **R** – regulatory term ; **P** – patient safety term ; **B** - term to be banned : not to be used

Terms and translations	A	R	P	B	Definitions and references	Comments and synonyms
cause French : cause Spanish : causa German : Ursache Italiano : causa Slovene : vzrok see also : *root cause analysis*			X		**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.[57]	
causation French : causalité Spanish : causalidad, inferencia causal German : Kausalität Italiano : causazione Slovene : vzročnost see also : *root cause analysis*			X		**causation :** the act by which an effect is produced ; the causal relationship between the act and the effect.	Synonym: *causality.* In epidemiology, the doctrine of causation is used to relate certain factors (predisposing, enabling, precipitating, or reinforcing factors) to disease occurrence. The doctrine of causation is also important in the fields of negligence and criminal law.[23]
computer prescribing, computer physician order entry (CPOE) French : prescription informatisée *Spanish : prescripción informatizada asistida* German : elektronische Verordnung *Slovene : elektronsko predpisovanje*	X		X		**computer physician order entry (CPOE)** : clinical systems that utilize data from pharmacy, laboratory, radiology, and patient monitoring systems to relay the physician's or nurse practitioner's diagnostic and therapeutic plans, and alert the provider to any allergy or contraindication that the patient may have so that the order may be immediately revised at the point of entry prior to being forwarded electronically for the targeted medical action.[7]	Prefered synonym: *electronic prescribing*
constraint French : contrainte Spanish : restricción German : Beschränkung Italiano : limitazione Slovene : omejitev see also : *forcing function*	X		X		**constraint :** a limitation of the options available to keep behavior in a "safe" zone.[31]	
continuous safety improvement of the medication use system French : sécurisation du circuit du médicament Spanish : German :					**continuous safety improvement of the medication use system :** implementation of a set of measures allowing: to prevent and to intercept medication errors; to recover hazardous situations, to mitigate occurring adverse events; and to protect the patient from occurring errors.[22]	

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Terms and translations	A	R	P	B	Definitions and references	Comments and synonyms
contributing factor French : facteur contributif, facteur favorisant Spanish : factor contribuyente German : begünstigender/mitverursachender Faktor Italiano : fattori contribuenti Slovene : prispevajoči dejavnik see also : *root cause analysis*			X		**contributing factor (interchangeable with contributory factor) :** 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.[57]	
criticality French : criticité Spanish : criticidad German : Gefährlichkeit Italiano : indice di priorità di rischio Slovene : kritičnost see also : *failure mode and effect analysis*			X		**risk priority number (RPN) :** determines the criticality of the failure mode and helps determine whether the risk of failure should be accepted (do nothing about the potential failure), controlled (take action to enhance detection or reduce the risk of the potential failure), or eliminated (prevent the potential failure). This number plays a role in the failure mode and effects analysis process.[3]	
culture of safety French : culture de la sécurité Spanish : cultura de seguridad German : Sicherheitskultur Italiano : cultura della sicurezza Slovene : varnostna kultura see also : *just culture*			X		**culture of safety:** an integrated pattern of individual and organizational behavior, based upon shared beliefs and values, that continuously seeks to minimize patient harm which may result from the processes of care delivery.[7]	"*There isn't a universally accepted definition of a safety culture in health care but it is essentially a culture where staff have a constant and active awareness of the potential for things to go wrong. It is also a culture that is open and fair and one that encourages people to speak up about mistakes. In organisations with a safety culture people are able to learn about what is going wrong and then put things right.*"[38]
dispensing error French : erreur de dispensation Spanish : error de dispensación German : Abgabefehler Italiano : errori legati alla distribuzione del farmaco Slovene : napaka pri izdajanju see also : *medication error*	X				**dispensing error :** a deviation from an interpretable writen prescription or medication order, including written modification of the prescription made by a pharmacist following contact with the prescriber or in compliance with the pharmacy policy. Any deviation from professional or regulatory references, or guidelines affecting dispensing procedures is also considered as a dispensing error.[12]	Whatever type of medication error, of omission or commission, that occurs in the dispensing stage in the pharmacy when distributing medicines to nursing units or to patients in ambulatory settings A process error taking place in the medication use system: definition and type to be refined with the taxonomy of medication errors. Since they can be detected by this way, dispensing errors are also defined as deviations from the prescriber's order.[3]
drug-related problem French : problème lié la prise en charge médicamenteuse Spanish : problema relacionado con medicamentos German : Arzneimittelproblem Italiano : problemi legati al processo terapeutico Slovene : problem povezan z zdravili					**drug-related problem :** an event or circumstance involving medicine therapy that actually or potentially interferes with desired health outcomes.[44]	This working definition is designed for *pharmaceutical care*, that is to mean "*the responsible provision of medicine therapy for the pupose of achieving definite outcomes that improve a patient's quality of life*",[25] in fact optimizing the individual benefit/risk balance for each individual patient. Even if the diagnosis of DRPs overlaps with the detection of medication errors threatening the patient, these definitions are not applicable to medication safety, focused on a system approach. For preventing any risk of confusion, the proposed recommandation is to strictly avoid the use of "medication or drug -related problems" when the matter is medication safety.

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error French : erreur humaine Spanish : error German : Fehler Italiano : errore Slovene : napaka see also : *mistake, slip, lapse*	X		X		**error :** a generic term to encompass all those occasions in wich a planned sequence of mental or physical activities fails to achieve its intended outcome, and when these failures cannot attributed to the intervention of some change agency;[46] failure of planned actions to achieve their desired ends-whithout the intervention of some unforeseeable event.[48]	"*The failure of a planned action to be completed as intended (i.e., error of execution) or the use of a wrong plan to achieve an aim (i.e., an error of planning)*";[26,59] "*and also the failure of an unplanned action that should have been completed*".[7] "*Errors can include problems in practice, products, procedures, and systems.*"[45]
error of commission French : erreur par commission Spanish : error de comisión German : Ausführungsfehler Italiano : errore di esecuzione Slovene :napaka izvršitve see also : *error, mistake, slip, lapse*	X		X		**error of commission :** an error which occurs as a result of an action taken.[23]	Examples include when a drug is administered at the wrong time, in the wrong dosage, or using the wrong route;
error of omission French : erreur par omission Spanish : error por omisión German : Unterlassungsfehler Italiano : errore di omissione Slovene : napaka opustitve	X		X		**error of omission :** an error which occurs as a result of an action not taken.[23]	For example, when a nurse omits a dose of a medication that should be administered;[23] failing to prescribe a medication from which the patient would likely have benefited.[7]
evidence-based guidelines French : recommandations fondées sur des preuves Spanish : recomendaciones basadas en la evidencia German : Evidenz-basierte Leitlinien Italiano : linee guida basate sull' evidence-based Slovene : na dokazih temelječe smernice					**evidence-based guidelines :** consensus approaches for handling recurring health management problems aimed at reducing practice variability and improving health outcomes. Guideline development emphasizes using clear evidence from the existing literature, rather than expert opinion alone, as the basis for advisory materials.[7]	

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failure mode and effects analysis French : analyse des modes de défaillance et de leurs effets (AMDE) Spanish : análisis modal de fallos y efectos (AMFE) German : Fehlermöglichkeits- und Wirkungsanalyse Italiano : analisi delle modalità e degli effetti del fallimento Slovene : analiza možnih napak in njihovih posledic (AMNP) see also : *error, mistake, slip, lapse, number*			X		**failure mode and effects analysis (FMEA)** : a risk assessment method based on the simultaneous analysis of failures modes, their consequences and their associated factors. This systematic method is used to identify and prevent product and process problems before they occur.	Others risk assessment methods using the failure mode (that is : "*different ways that a process or subprocess can fail to provide the anticipated result*"[3]) exist, like: - failure mode analysis (FMA) "examining a product or system to identify all the ways in which it might fail";[3] - failure mode, effect, and criticality analysis (FMECA) "a systematic way of examining a design prospectively for possible ways in which failure can occur. It assumes that no matter how knowledgeable or careful people are, errors will occur in some situations and may even be likely to occur." [23]
forcing function French : fonction de contrainte Spanish : función de restricción German : erzwingende Funktion Italiano : limitazioni al comportamento Slovene : prisilna omejitev see also : *constraint*	X		X		**forcing function :** something that prevent the behaviour from continuing until the problem has been corrected;[46] design features that make it impossible to perform a specific erroneous act.	e.g. using oral syringes, for oral liquid doses, that will not fit with IV tubing and to which needles cannot be attached; and computer order entry which can be used to 'force' the physician to order standardized products.[3]
harm French : dommage Spanish : daño German : Schaden Italiano : danno Slovene : škodlji vost see also : *adverse event, adverse drug event, iatrogenic*			X		**harm :** temporary or permanent impairment of the physical, emotional, or psychological function or structure of the body and/or pain resulting therefrom requiring intervention.[37]	Synonyms: *iatrogenic illness*, *iatrogenic injury*
high-alert medicines French : médicaments à haut risque Spanish : medicamentos de alto riesgo German : Hochrisiko-Arzneimittel Italiano : farmaco ad alto rischio	X				**high-alert medicines :** medicines that bear a heightened risk of causing significant patient harm when they are used in error. Although mistakes may or may not be more common with these medicines, the consequences of an error with these medicines are clearly more devastating to patients.[13]	ISMP's list of high-alert medicines available at: http://www.ismp.org/MSAarticles/highalert.htm
human factors French : facteur humain Spanish : factores humanos German : menschliche Faktoren Italiano : fattore umano Slovene : človeški dejavniki	X		X		**human factors :** the study of the interrelationships between humans, the tools they use, the environment in which they live and work, and the design of efficient, human centred processes to improve reliability and safety.[51,57]	

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iatrogenic French : iatrogène Spanish : iatrogénico German : Iatrogen Italiano : iatrogena (malattia) Slovene : iatrogen see also : *adverse event, harm*			X		**iatrogenic 1**. any undesirable condition in a patient occurring as the result of treatment by a physician (or other health professional). **2.** Pertaining to an illness or injury resulting from a procedure, therapy, or other element of care.[23]	iatrogenic illness : "*any illness that resulted from a diagnostic procedure or from anyform of therapy.*" [56] iatrogenic injury : "*injury originating from or caused by a physician (ιατρος: for "physician"), including unintended or unnecessary harm or suffering araising from any form of health care management, including problems arising from acts of commission or omission.*"[7]
incident French : incident Spanish : incidente German : Zwischenfall Italiano : incidente Slovene : incident see also : *adverse event*			X		**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.[8,59] In the UK, the NHS National Patient Safety Agency defines 'patient safety incident' as "*any unintended or unexpected incident that could have or did lead to harm for one or more patients receiving NHS funded health care*".[38]	"*An incident includes any irregularity in the process of medication use. It might represent an ADE, potential ADE, medication error, or none of these-it is essentially a "catch all" term for what to call something before it has been classified.*"[34]
just culture French : culture de la responsabilité Spanish : cultura de responsabilidad German : Gerechtigkeitskultur Italiano : cultura giusta Slovene : kultura pravičnosti see also : *culture of safety*			X		**just culture :** is a key element of a safe culture.[7]. A just culture reconciles professional accountability and the need to create a safe environment to report medication errors; seeks to balance the need to learn from mistakes and the need to take disciplinary action.[32]	Reason was the first to coin the term "just culture" which provides a fair and productive alternative to the two extremes of punitive or blame-free cultures. "*Creating a just culture –it could be just as well be called a trust culture- is the critical first step in socially engineering a safe culture. (...) A just culture hinges critically on a collectively agreed and clearly understood distinction being drawn between acceptable and unacceptable behaviour.*"[50] Marx has expanded the concept further and provided guidance for health care organizations.[32]
lapse French : raté, erreur de mémoire Spanish : lapsus, error de memoria German : Aussetzer Italiano : lapsus Slovene : lapsus see also : *error, mistake, slip*	X		X		**lapses :** errors which result from some failure in the execution and/or storage stage of an action sequence, (…) largely involving failures of memory, that do not necessarily manifest themselves in actual behaviour and may be only apparent to the person who experience them;[46] internal events [that] generally involve failures of memory.[48]	

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latent (error, conditions) French : défaillance latente Spanish : error latente German : latente Fehler, Systemfehler Italiano : errori latenti Slovene : latentna napaka see also : *root cause analysis, human factor*	X		X		**latent errors :** errors in the design, organization, training, or maintenance that lead to operator errors. They may lie dormant in the system for lengthy periods of time.[26,59] They represent root causes of adverse events. **latent conditions :** arise from decisions made by designers, builders, procedure writers, and top level management. Latent conditions may lie dormant within the system for many years before they combine with active failures and local triggers to create an accident opportunity. Unlike active failures, latent conditions can be identified and remedied before an adverse event occurs. Understanding this leads to proactive rather than reactive risk management.[49]	Synonym : *latent failures* Latent errors have been described as "*accidents waiting to happen*".[29] "*Latent conditions are the inevitable "resident pathogens" within the system. They arise from decisions made by designers, builders, procedure writers, and top level management. Such decisions may be mistaken, but they need not be. All such strategic decisions have the potential for introducing pathogens into the system. Latent conditions have two kinds of adverse effect: they can translate into error provoking conditions within the local workplace (for example, time pressure, understaffing, inadequate equipment, fatigue, and inexperience) and they can create longlasting holes or weaknesses in the defences (untrustworthy alarms and indicators, unworkable procedures, design and construction deficiencies, etc). Latent conditions - as the term suggests- may lie dormant within the system for many years before they combine with active failures and local triggers to create an accident opportunity. Unlike active failures, whose specific forms are often hard to foresee, latent conditions can be identified and remedied before an adverse event occurs. Understanding this leads to proactive rather than reactive risk management.*" [49]
mandatory reporting French : système de déclaration obligatoire Spanish : notificación obligatoria German : obligatorische Meldung, Meldepflicht Italiano : reporting obbligatorio Slovene : obvezno poročanje		X			**mandatory reporting :** those patient safety reporting systems that by legislation and/or regulation require the reporting of specified adverse events.[7]	
medication error French : erreur médicamenteuse Spanish : error de medicación German : Arzneimittelfehler, Medikationsfehler Italiano : errori legati ai farmaci Slovene : napaka pri ravnanju z zdravili	X				**medication error :** any deviation from ordinary standards of care appropriate for the time of the medicine therapy of a patient. A medication error is a non intentional omission or failed activity related to the medication use system, which can be the cause of a risk or of an adverse event reaching the patient. By definition, a medication error is preventable because it evidences what should have been done and what was not it during the medicine therapy of a patient. A medication error can concern one or several stages of the medication use system, such as: formulary selection, prescription, dispensing, orders validation, preparation, storage, delivery, administration, therapeutic monitoring, and information; but also its interfaces, such as communications and transcriptions.[22]	**medication error :** "*any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the health care professional, patient, or consumer. Such events may be related to professional practice, health care products, procedures, and systems, including prescribing; order communication; product labelling, packaging, and nomenclature; compounding; dispensing; distribution; administration; education; monitoring; and use*".[37] "*Obviously, nonpreventable drug-related problems (DRPs) are not included.*"[21]
medication safety French : sécurité des soins médicamenteux Spanish : seguridad en el uso de los medicamentos German : Arzneimittelsicherheit Italiano : sicurezza dei farmaci Slovene : varnost pri ravnanju z zdravili see also : *patient safety, pharmacovigilance*	X				**medication safety :** freedom from accidental injury during the course of medication use; activities to avoid, prevent, or correct adverse drug events which may result from the use of medicines.[3]	

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medication use system French : circuit du médicament Spanish : sistema de utilización de los medicamentos German : Arzneimittelanwendungssystem Italiano : sistema di utilizzo dei farmaci Slovene : sistem ravnanja z zdravili see also : *process, system*	X				**medication use system :** a combination of interdependent processes that share the common goal of safe, effective, appropriate, and efficient provision of medicine therapy to patients. Major processes in the medication use system are : selecting and procuring; storage; prescribing; transcribing and verifying/reviewing; preparing and dispensing; administering and monitoring.[3,13,23,42]	"*Medication use within a healtcare organisation can be viewed as a system, with several components and processes, inputs (patient and medicine therapy information, and outputs (effective, efficient, and safe treatment). The provision of medicines to patients, regardless of the setting, depends on a set of processes…*" [35] "*Each major process in the medication system- ordering, dispensing, and administration – has its own unique opportunities for error.*"[31] For flowcharts describing the medication use system, see these references.
mistake French : erreur de jugement Spanish : equivocación German : Beurteilungsfehler, Irrtum Italiano : mistake Slovene : zmota see also : *error, slip, lapse*	X		X		**mistake :** deficiency or failure in the judgemental and/or inferential processes involved in the selection of an objective or in the specification of the means to achieve it, irrespective whether or not the actions directed by this decision-scheme run according to plan;[46] errors of concious though including *rule-based errors* that occur during problem solving when a wrong rule is chosen, and *knowledge-based errors* that arise because of lack of knowledge or misinpretation of the problem.[28]	"*The actions may conform exactly to the plan, but the plan is inadequate to achieve its intended outcome.*"[48]
monitoring error French : erreur de suvi thérapeutique Spanish : error de seguimiento German : Überwachungsfehler Italiano : monitoraggio degli errori Slovene : napaka pri sledenju	X				**monitoring error :** failure to review a prescribed regimen for appropriateness and detection of problems, or failure to use appropriate clinical or laboratory data for adequate assessment of patient response to prescribed therapy.[31]	A process error taking place in the medication use system: definition and type to be refined with the taxonomy of medication errors.
negligence French : faute, négligence Spanish : negligencia German : Fahrlässigkeit, Vernachlâssigung Italiano : negligenza Slovene : malomarnost			X		**negligence :** care provided failed to meet the standard of care reasonably expected of an average practitioner qualified to care for the patient in question.[3]	
nosocomial French : nosocomial Spanish : nosocomial German : nosokomial Italiano : nosognomico Slovene : nosokomialen			X		**nosocomial :** pertaining to or originating in a health care sitey.[8]	Synonym : *health care acquired*
observation method French : méthode d'observation directe Spanish : método de observación German : Beobachtungsmethode Italiano : metodo di osservazione Slovene : opazovalna metoda	X				**observation method :** an active method of error surveillance in which a trained observer observes medication administration during peak workload periods and compares the observations to the original order on the patient's chart for the purpose of uncovering medication errors and clues as to why they happen.[1,23]	

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opportunity for error French : opportunité d'erreur Spanish : oportunidad de error German : Fehlermöglichkeit Italiano : opportunità di errore Slovene : priložnost za napako	X				**opportunity for error :** any dose dose given plus any dose ordered but omitted. It is a basic unit of data in medication error studies preventing the error rate from exceeding 100%.[1,9]	
patient safety French : sécurité des patients Spanish : seguridad clínica German : Patientensicherheit Italiano : sicurezza del paziente Slovene : varnost bolnikov see also : *medication safety*			X		**patient safety :** freedom from accidental injuries during the course of medical care; activities to avoid, prevent, or correct adverse outcomes which may result from the delivery of health care.[3,26,59] **patient safety :** the identification, analysis and management of patient-related risks and incidents, in order to make patient care safer and minimise harm to patients.[7,38]	"*Safety, the first domain of quality, refers to "freedom from accidental injury." This definition is stated from the patient's perspective*." (Kohn, 2000)
pharmacovigilance French : pharmacovigilance Spanish : farmacovigilancia German : Pharmakovigilanz, Artzneimittelüberwachung Italiano : farmacovigilanza Slovene : farmakovigilanca see also : *adverse drug reaction*		X			**pharmacovigilance :** the science and activities relating to the detection, assessment, understanding and prevention of the adverse effects of medicinal products. (WHO, 2002)	
potential adverse drug event French : événement indésirable médicamenteux potentiel Spanish : acontecimiento adverso por medicamentos potencial German : mögliches unerwünschtes Arzneimittelereignis Italiano : eventi avversi potenziali legati ai farmaci Slovene : možen neželeni dogodek pri uporabi zdravila see also : *recovery*	X				**potential adverse drug event** : a serious medication error-one that has the potential to cause an adverse drug event, but did not, either by luck or because it was intercepted and corrected. Examining potential adverse drug events helps to identify both where the system is failing (the error) and where it is working (the interception).[31,34]	Synonyms : *near miss, close call,*[59] *prevented patient safety incident* close call : "*an event or situation that could have resulted in an adverse event but did not, either by chance or through timely intervention*."[7] near miss : "*an act of commission or omission that could have harmed the patient, but did not so as a result of chance (e.g., the patient received a contrraindicated drug, but did not experienced an adverse drug reaction), prevention (e.g., a potentially lethal overdose was prescribed, but a nurse identified the error before administering the medication), or mitigation e.g., a lethal overdose was administered but discovered early, and countered with an antidote).*"[7]
potential error French : erreur potentielle Spanish : error potencial German : möglicher Fehler, beinahe Fehler Italiano : errore potenziale Slovene : možna napaka see also : *latent error*	X		X		**potential error:** circumstances or events that have the capacity (potentiality) to cause error	

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preparation error French : erreur de préparation Spanish : error de preparación German : Zubereitungsfehler Italiano : errore di preparazione Slovene : napaka pri pripravi see also : *medication error*	X				**preparation error :** whatever type of medication error, of omission or commission, that occurs in the preparation stage when the medication has to be compounded or prepared by a pharmacist, a nurse, or the own patient, or a caregiver.	Synonym : *compounding error* A process error taking place in the medication use system: definition and type to be refined with the taxonomy of medication errors. For example, an IV compounding error is "*a deviation of the actual compounding process from specifications in the pharmacy's patient-specific IV label or the hospital's policies and procedures for IV Compounding.*" [2]
prescribing error French : erreur de prescription Spanish : error de prescripción German : Verschreibungsfehler Italiano : errore di prescrizione Slovene : napaka pri predpisovanju see also : *medication error*	X		X		**prescribing error :** a medication error occurring during the prescription of a medicine that it is about writing the medicine orders or taking the therapeutic decision, appreciated by any non intentional deviation from standard references such as: the actual scientific knowledges, the appropriate practices usually recognized, the summary of the characteristics of the medicine product, or the mentions according to the regulations. A prescribing error notably can concern : the choice of the drug (according to the indications, the contraindications, the known allergies and patient characteristics, interactions whatever nature it is with the existing therapeutics, and the other factors), dose, concentration, drug regimen, pharmaceutical form, route of administration, duration of treatment, and instructions of use; but also the failure to prescribe a drug needed to treat an already diagnosed – or to be prevented - pathology, or to prevent the adverse effects of others medicines.[22]	A process error taking place in the medication use system: definition and type to be refined with the taxonomy of medication errors. "*A clinically meaningful prescribing error occurs when, as a result of a prescribing decision or prescribing writing process, there is an unintentional significant (1) reduction in the probability of treatment being timely and effective or (2) increase in the risk of harm when compared with generally accepted practice.*" [18]
preventable adverse event French : événement indésirable évitable Spanish : acontecimiento adverso prevenible German : Vermeidbares unerwünschtes Ereignis Italiano : evento avverso prevenibile see also : *adverse drug event, unpreventable adverse drug event*	X		X		**preventable** : potentially avoidable in the relevant circumstances.[8] **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;[33] caused by an error or other type of systems or equipment failure.[59]	
preventable adverse drug event French : événement indésirable médicamenteux évitable Spanish : acontecimiento adverso por medicamento prevenible German : Vermeidbares unerwünschtes Arzneimittelereignis Italiano : evento avverso da farmaco prevenibile Slovene : preprečeni neželeni dogodek pri uporabi zdravila see also : *adverse drug event, unpreventable adverse drug event*	X				**preventable adverse drug event :** any adverse drug event that would not have occurred if the patient had received ordinary standards of care appropriate for the time when this event occurred, so that, associated to a medication error.[22] **preventable adverse drug event :** an adverse drug event associated with a medication error.[52]	"*any adverse drug event due to an error or preventable by any means currently available*" [10]

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preventability French : évitabilité Spanish : evitabilidad German : Vermeidbarkeit Italiano : prevenibilità Slovene : preprečevanje	X		X		**preventability** : implies that methods for averting a given injury are known and that an adverse event results from failure to apply that knowledge.[27] **prevention** : modification of the system or its exploitation in order to decrease the probability of adverse events and to return to an acceptable risk level ; any means aiming at reducing the frequency and the severity of the risks.[22]	« *Some adverse events are unavoidable. Patients and their caregivers are sometimes forced to kowingly accept adverse secondary consequences to achieve a more important primary treatment goal. The concept of* ***preventability*** *separates care delivery errors from such recognized but unavoidable treatment consequences* » (Aspden, 2004, 195)
process French : processus Spanish : proceso German : Prozess Italiano : processo Slovene : proces see also : *medication use system, system*	X				**process :** a series of related actions to achieved a defined outcome. Prescribing medication or administering medication are processes.[31]	
recklessness French : imprudence Spanish : imprudencia German : Unvorsichtigkeit, Sorglosigkeit Italiano : spericolatezza Slovene : neodgovornost see also : *just culture, violation*			X		**recklessness :** 1) The individual knows that there is a risk, is willing to take that risk, and takes it deliberately. 2) The individual performs an act that creates an obvious risk, and when performing that act has either given no thought to the possibility of such a risk, and having recognised that such a risk existed, goes on to take it.[38]	NPSA'*Incident Decision Tree* (IDT), based on a model developed by Professor J Reason for the aviation industry, is an interactive web-based tool for NHS managers and organisations dealing with staff who have been involved in an incident. It helps to identify whether the action(s) of individuals were due to systems failures or whether the individual knowingly committed a *reckless*, *intentional unsafe* or *criminal act*. The tool changes the focus from asking 'Who was to blame' to 'Why did the individual act in this way?' [38]
recovery French : récupération Spanish : restablecimiento German : Erholung, Genesung Italiano : recupero Slovene : poprava see also : *close call, near miss, potential adverse drug event*	X		X		**recovery :** an informal set of human factors that lead to a risky situation being detected, understood, and corrected in time, thus limiting the sequence to a near-miss outcome, instead of it developping further into possibly an adverse event.[7] **mitigating factors :** some factors, whether actions or inaction such as chance or luck, may have mitigated or minimised a more serious outcome.[38]	Synonym : *mitigating factors*
risk assessment French : évaluation des risques Spanish : evaluación de riesgos German : Risikobewertung Italiano : valutazione del rischio Slovene : ocena tveganja			X		**risk assessment :** the process that helps organisations understand the range or risks that they face both internally and externally, the level of ability to control those risks, the likelihood of occurrence and their potential impacts. It involves a mixture of quantifying risks and using judgement, assessing and balancing risks and benefits and weighing them for example against cost.[38]	

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Terms and translations	A	R	P	B	Definitions and references	Comments and synonyms
risk management French : gestion des risques Spanish : gestión de riesgos German : Risikomanagement Italiano : gestione del rischio Slovene : upravljanje s tveganji			X		**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.[23] **risk management :** identifying, assessing, analysing, understanding, and acting on risk issues in order to reach an optimal balance of risk, benefits and costs'.[38]	
root cause analysis French : analyse des causes profondes Spanish : análisis de causas raíz German : Ursachenanalyse Slovene : analiza porekla vzrokov see also : *cause, latent conditions*	X		X		**root cause analysis :** a systematic investigation technique that looks beyond the individuals concerned and seeks to understand the underlying causes and environmental context in which the incident happened.[38] The analysis focuses on identifying the latent conditions that underlie variations in performance and on developing recommendations for improvements to decrease the likelihood of a recurrence.[15,57]	Typically, the analysis focuses primarily on systems and processes, not individual performance.[7]
sentinel event French : événement sentinelle Spanish : acontecimiento o suceso centinela German : Sentinel-Ereignis, Signal-Ereignis Italiano : evento sentinella Slovene : opozorilni nevarni dogodek	X		X		**sentinel event** : an unexpected occurrence involving death or serious physical or psychological injury, or the risk thereof. Serious injury specifically includes loss of limb or function. The phrase, "or the risk thereof" includes any process variation for which a recurrence would carry a significant chance of a serious adverse outcome. Such events are called "sentinel" because they signal the need for immediate investigation and response.[23]	
slip French : lapsus, erreur d'attention Spanish : distracción, desliz, error de atención German : Ausrutscher Slovene : spodrsljaj see also : *error, mistake, lapse*	X				**slip :** error which result from some failure in the execution and/or storage stage of an action sequence, (…) potentially observable as actions-not-as-planned (slips of the tongue, slips of the pen, slips of action).[46] Slips relate to observable actions and are commonly associated with attentional or perceptual failures.[48]	"*They are errors of execution that occurs when there is a break in the routine while attention is diverted.*" [28]
system French : système Spanish : sistema German : System Italiano : sistema Slovene : sistem see also : *medication use system, process*	X				**system :** a set of interdependent elements interacting to achieve a common aim. These elements may be both human and non-human (equipment, technologies, etc.).[26,59]	

Terms : **A** – approved term ; **R** – regulatory term ; **P** – patient safety term ; **B** - term to be banned : not to be used

Terms and translations	A	R	P	B	Definitions and references	Comments and synonyms
unpreventable adverse drug event French : événement indésirable médicamenteux inévitable Spanish : acontecimiento adverso por medicamento inevitable German : unvermeidbares unerwünschtes Arzneimittelereignis Italiano : eventi avversi da farmaci non prevenibili Slovene : neželeni dogodek pri uporabi zdravila, ki ga ni moč preprečiti see also : *preventability*	X				**unpreventable adverse event:** an adverse event resulting from a complication that cannot be prevented given the current state of knowledge.[45] **unpreventable adverse drug event :** an adverse drug event that do not result from an error but reflect the inherent risk of medicines and cannot be prevented given the current state of knowledge.[41]	"*Nonpreventable adverse drug events (ADEs) are called adverse drug reactions (ADRs)*".[31]
violation French : non respect des règles ou procédures Spanish : transgresión German : Regelverletzung Italiano : violazione Slovene : kršitev		X			**violation :** a deliberate -but not necessarily reprehensible- deviation from those practices deemed necessary (by designers, managers and regulatory agencies) to maintain the safe operation of a potentially hazardous system;[46] appreciated by the individual as being required by regulation, or necessary or advisable to achieve an appropriate objective while maintaining safety and the ongoing operation of a device or system.[53]	
voluntary reporting French : notification spontanée Spanish : notificación voluntaria German : freiwilliges Meldesystem Italiano : reporting volontario Slovene: prostovoljno poročanje	X		X		**voluntary reporting :** those reporting systems for which the reporting of patient safety events is voluntary (not mandatory). Generally, reports on all types of events are accepted.[7]	

Terms : **A** – approved term ; **R** – regulatory term ; **P** – patient safety term ; **B** - term to be banned : not to be used

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Appendix 4

European evidence on medication errors

1. European studies on adverse drug events

Table 19: Studies on adverse drug events in medicine and intensive care

Studies	Admissions caused by ADEs		ADEs occurring during the hospital stay		Comments
	overall	preventable ADEs (part of admissions caused by ADEs)	overall	preventable ADEs	Incidence expressed in % of hospitalized patients or admissions * recalculated values
Medicine					
Schmitt et al, 1983[1]	0.2% *		0.9% *		9,055 admissions – ADR reporting
Auloge et al,1980[2]	0.5% *		5.8%		1,903 admissions – ADR
Jamaa et al, 1993[3]	1.0% *		1.4% *		2,598 admissions cardiology - ADR
Hess et al, 1979[4]	1.5%				1,325 admissions
van der Hooft et al,2006[5]	1.8%				12,249 admissions - ADR
Huic et al, 1994[6]	2.5%				5,227 admissions - ADR
Ghose, 1980[7]	2.6%				569 admissions
Curien-Chevrier et al, 1997[8]	2.7% *		2,1% *		810 admissions cardiology
Barneoud, 1981[9]	2.9% *		2,2%		964 admissions
Moore et al, 1995[10]	3.0%		6.4%		329 admissions
Baune et al, 2003[11]	3.6% *	0.9% *(25.0%)	6.3%	1.6% *	902 admissions
Fattinger et al, 2000[12]	3.3%		8.2%		4,331 admissions
Hallas et al, 1992[13]	3.5%				313 admissions resp. medicine
Dormann et al,2003[14]	3.8%				915 admissions - ADR
Bricard-Pacaud et al, 1999[15]	4.0%		19.8%		248 admissions
Hallas et al, 1990[16]	4.1%	1.4% * (33.3%)			366 admissions cardiology
Hardmeier et al, 2004[17]	4.1%	1.2% * (30.1%)	7.2%	0.4%	6,383 admissions
Lepori et al, 1999[18]	4,1%				2,168 admissions - ADR
Girardot, 1978[19]	4.6% *		1.4%		765 admissions
Allain et al, 1983[20]	5.5%				550 admissions
Ponge et al, 1989[21]	5.5%		7.7%		505 admissions
Roux-Jegou et al, 1999[22]	5.7%				3536 admissions
Lawson & Hutcheon, 1979[23]	5.8%				2,580 admissions
Black & Somers, 1984[24]	6.2%				481 admissions
Howard et al, 2003[25]	6.5%	4.3% * (67.0%)			4,093 admissions
Otero et al, 2006[26],[27]	6.7%	4.7% (70.6%)	7.2%	1.4%	2,643 admissions
Lagnaoui, 1997[28]	7.2%		5.9%		444 admissions
Green et al, 2000[29]	7.5%				200 admissions
Martin et al, 2002[30]	7.7%				1,633 admissions
Hallas et al, 1992[31]	7.8%	3.0% (46.9%)			1,999 admissions
Hallas et al, 1991[32]	7.9%	1.8% * (23.1%)			366 admissions gastroenterology
Peyrière et al, 2003[33]	9.6%	(57.9%)			156 admissions
Hallas et al, 1990[34]	10.8%	2.7% (58.3%)			333 admissions
von Euler et al, 2006[35]	11.0%				168 admissions - ADR
Davidsen et al, 1988[36]	11.5%				426 admissions cardiology - ADR
Bergman et al, 1981[37]	12.6%				285 admissions
Mjôrndal et al, 2002[38]	13.8%				681 admissions
Klein et al, 1976[39]			18.7%		914 admissions - ADR
Emerson et al, 2001[40]			7.0%		303 admissions - ADR

Studies	Admissions caused by ADEs		ADEs occurring during the hospital stay		Comments
	overall	preventable ADEs (part of admissions caused by ADEs)	overall	preventable ADEs	Incidence expressed in % of hospitalized patients or admissions * recalculated values
Piquet et al, 1999[41]			8.7% *	7.3% *	240 admissions
Lecointre et al, 2003[42]			11.9%	4.3% *	1,598 admissions
Intensive care					
Faccioli et al, 1987[43]	3.4%				cardiology
Trunet et al, 1986	5.9%	(44.3%)			1651 admissions
Darchy et al, 1999[44]	6.6%	(73.2%)			623 admissions
Trunet et al, 1980[45]	7.1%	5.8% * (60.9%)			325 admissions

Table 20: National multi-centre adverse drug events studies

Studies	Admissions caused by ADEs		ADEs occurring during the hospital stay		Comments
	overall	preventable ADEs part of admissions caused by ADEs	overall	preventable ADEs	Incidence expressed in % of hospitalized patients or admissions * recalculated values
Hurwitz & Wade, 1969[46]	0.5%				1,160 admissions - ADR
Imbs et al, 1997-1999[47]	1.1% *		5.6% *		2,132 admissions – ADR
Schneeweiss et al,2002[48]	2.4%				41,375 admissions * - ADR
Pouyanne et al, 2000[49]	3.2%	48.0%			3137 admissions - ADR
Queneau et al, 1992[50]	3.3% *			1,6% *	1,733 admissions - ADE
Michel et al. (ENEIS) 2005[51]	4.0%	47.0%	6.6‰		8,574 admissions – ADE ‰ ADE incidence per 1000 days
Pirmohamed et al, 2004[52]	6.5%	72.0%			18,820 admissions - ADR

Table 21: Studies on adverse drug events in emergency units or admissions

Studies	Admissions caused by ADEs		ADEs occurring during the hospital stay		Comments
	overall	preventable ADEs part of admissions caused by ADEs	overall	preventable ADEs	Incidence expressed in % of hospitalized patients or admissions * recalculated values
Visits to emergency units					
Dumas, 1978[53]	0.3%				44,662 visits
Munoz et al, 1998[54]	1.0% 1.0%				47,107 pediatric visits (0,01% adm) 68,431 visits (0,2% admissions)
Otèro et al, 1999[55]	2.3%	43.3%			33,975 visits (0,5% admissions)
Ayani et al, 1999[56]	2.6%				5,209 visits (0,3% admissions)
Trifiro et al, 2005[57]	3.3%				18,854 visits
Raschetti et al,1999[58]	4.3%				5497 visits
Queneau et al, 2003[59]	16.9%	37.9%			1,937 visits
Queneau et al, 2005[60]	20.2%	46.8%			1,826 visits
Emergency admissions					
Rostin et al, 1987[61]	1.1%				2,017 emergency admissions
Ibanez et al, 1991[62]	1.1%				48,678 emergency admissions
Ayani et al, 1999[56]	1.6%				1,033 emergency admissions
Raschetti et al,1999[58]	2.4%	55.6%			1,833 emergency admissions
Demange et al, 1999[63]	2.5%				4,951 emergency admissions
Perault et al,1999[64]	2.5%				1,235 emergency admissions

	Admissions caused by ADEs		ADEs occurring during the hospital stay		Comments
Studies	**overall**	**preventable ADEs** part of admissions caused by ADEs	**overall**	**preventable ADEs**	Incidence expressed in % of hospitalized patients or admissions * recalculated values
Otèro et al, 1999[55]	3.3%	66.9%			5,466 emergency admissions
Trifiro et al, 2005[57]	4.3%				4,467 emergency admissions
Zenut et al, 2001[65]	4.4%				2,162 emergency admissions
Chassany et al, 1995[66]	4.8%				147 emergency admissions
Olivier et al, 2001[67]	6.1%	54.5%			671 emergency admissions
Saviuc, 1985[68]	6.7%				4,056 emergency admissions
Wasserfallen et al, 2001[69]	7.0%	32.0%			
Cretin-Maitenaz, 1988[70]	7.1%				2,906 emergency admissions
Jean-Pastor et al, 1998[71]	8.6%				163 emergency admissions
Guemes et al,1999[72]	9.6%				1,097 emergency admissions

Table 22: Studies on geriatrics adverse drug events

	Admissions caused by ADEs		ADEs occurring during the hospital stay		Comments
Studies	**overall**	**preventable ADEs** part of admissions caused by ADEs	**overall**	**preventable ADEs**	Incidence expressed in % of hospitalized patients or admissions * recalculated values
Cunningham et al, 1997[73]	5.3%				1011 medicine admissions patients >65
Dubos et al, 1987[74]	6.1% *		2.3%		611 admissions
Lindley et al, 1992[75]	6.3%	50.0%			416 medicine admissions patients >65
Fradet et al, 1996[76]	7.7%				medicine admissions patients >65
Gillespie et al, 2005[77]	9.4%				214 admissions - DRP
Dupont, 1996[78]	10.4%		5.2%		498 admissions - ADR
Williamson,1980[79]	10.5%				1,998 admissions – multicentre study
Michel et al. (ENEIS) 2005[51]	11.4%		7.0‰		8,574 admissions – ADE ‰ ADE incidence per 1000 days
Mannesse et al, 2000[80]	12.0%				106 medicine admissions patients >65
Véronèse et al, 1999[81]	12.9%				1,550 admissions
Hallas et al, 1991[82]	13.1%	30.1%			294 admissions
van Kraaij et al, 1994[83]	13.3%				105 medicine admissions patients >65
Somers et al,2003[84]	18.4%				76 admissions - ADR

Table 23: Studies on paediatrics adverse drug events

	Admissions caused by ADEs		ADEs occurring during the hospital stay		Comments
Studies	**overall**	**preventable ADEs** part of admissions caused by ADEs	**overall**	**preventable ADEs**	Incidence expressed in % of hospitalized patients or admissions * recalculated values
Jonville-Béra et al, 2002[85]	1.5% 0.9%		2.6%		260 admissions – ADR 428 visits to emergency unit
Pouyanne et al, 2000	1.9%				
Haffner et al, 2005[86]	2.7%		14.1%		703 admissions - ADR
Martinez-Mir et al, 1996[87]	4.1%				512 admissions - ADR
Whyte et Greenan, 1977[88]			6.0%		1,000 admissions - ADR
Gill et al, 1995[89]			7.0%		899 admissions - ADR
Martinez-Mir et al, 1999[90]			11.5%		512 admissions ADR
Gonzalez-Martin & al, 1998[91]			13.7%		219 admissions - ADR
Weiss et al, 2002[92]			21.5%		214 admissions - ADR

Table 24: Preventability of adverse drug events occurring during the hospital stay

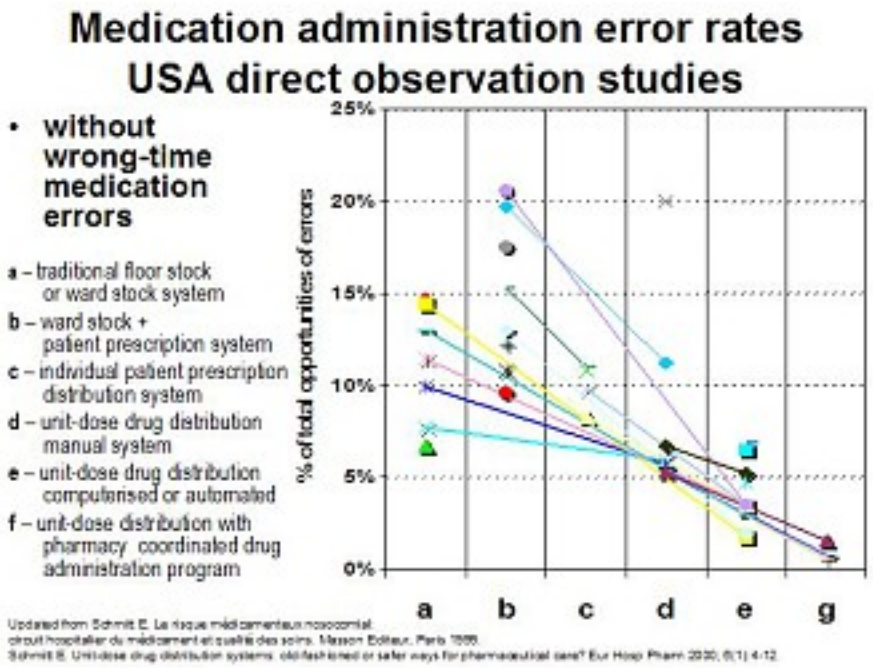
Studies	Part of preventable ADEs in overall ADEs		
	in traditional distribution systems	in unit dose distribution systems	Comments * recalculated values
Hardmeier et al, 2004[17]	6.0%		
Baune et al, 2003[11]	25.0%		
Queneau et al, 1992[50]	30.3%		
Michel et al. (ENEIS) 2005[51]	31.0%		
Lecointre et al, 2003[42]	35.8%		
Piquet et al, 1999[41]	77.4%		
Leape et al, 1991		17.7%	$p < 0.001$
Otèro et al, 2006[26]		19.9%	
Bates et al, 1995		20.0% *	
Bates et al, 1995		28.3%	

2. Medication administration errors observation studies

Various assessment methods of medication errors and adverse drug events have evidenced differences between the various organisations of the medicine use process (se II.1).[93,94,95,96] The observation technique, originally developed in 1962, is the more accurate for detecting errors occurring with medicines administration and has since been used in more than 50 studies (see II.I.I.4).[97,98]

The evidence issued from comparative studies conducted during the 1960s and the 1970s led to establish unit dose dispensing of medicines as a standard of practice in the hospitals in United States since it support nurses in medication administration, reduces the waste of expensive medicines and enable patients to be more easily charged for inpatient doses.[99,100,101] In a unit dose dispensing system, all oral and injectable medicines are dispensed from the pharmacy department for individual patients in ready-to-administer dosage forms. Figure 9 summarises the results of these studies, according to the main organisations of drug distribution systems.

Figure 9: Medication administration error rates in United States according to the medication use system



Research studies with the same direct observation technique have also been undertaken in Europe, mainly since the 1990's, confirming that unit dose drug distribution systems bring a real and appreciable safety to hospitalised patients (see
).

Table 25: European direct observation studies on medication administration errors

			Medication administration errors rates* according to the type of medication use system					
Studies	**Year**	**Country**	**a**	**b**	**c**	**d**	**E**	**F**
Hill & Wigmore[102]	1967	UK	12.9%		9.1%			
Hill & Wigmore[102]	1967	UK	12.9%	2.4%				
Hill & Wigmore[102]	1967	UK	12.9%	7.4%				
Hill & Wigmore[102]	1967	UK	12.9%	3.1%				
Dean et al.[103]	1995	UK		3.0%				
Ridge at al.[104]	1995	UK		2.9%				
Gerthins[105]	1996	UK		3.0%				
Cavell[106]	1997	UK		5.7%				
Cavell[106]	1997	UK		5.6%				
Ho et al.[107]	1997	UK		5.5%				
Odgen et al.[108]	1997	UK		5.5%				
Hartley et Dhillon[109]	1998	UK		26.6%				
Lacasa et al.[110]	1998	Spain						4.9%
Lacasa et al. [1]1[0]	1998	Spain						2.9%
Schneider at al.[111]	1998	Swisserland	18.2%					

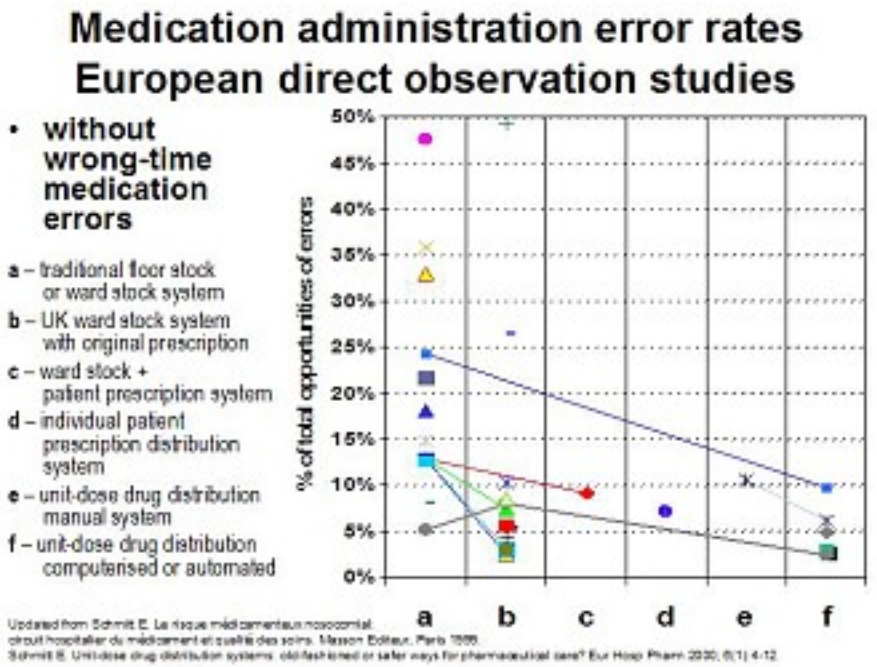
Studies	Year	Country	Medication administration errors rates* according to the type of medication use system					
			a	b	c	d	E	F
Tissot et al.[112]	1999	France	21.6%					
Taxis et al.[113]	1999	Germany	5.1%					2.4%
		UK		8.0%				
Dean et al.[114]	2001	UK		4.2%				
Bruce et al.[115]	2002	UK	10.3%					
van der Bemt et al.[116]	2002	Netherlands	33.0%					
Colen et al.[117]	2002	Netherlands				7.2%		
Tissot et al.[118]	2003	France	8.1%					
Tissot et al. [118]	2003	France	13.5%					
Fontan et al.[119]	2003	France	24.3%					9.7%
Taxis & Barber [120]	2003	UK		49.3%				
Taxis & Barber [121]	2004	Germany	47.5%					
Franklin et al.[122]	2005	UK		8.6%				
Lisby et al.[123]	2005	Denmark	35.9%					
van Gijssel-Wiersma et al.[124]	2005	Netherlands					10.5%	6.1%
Le Grognec et al[125]	2005	France	34.5%					

* Medication administration error rates without wrong-time medication errors
a – traditional floor stock or ward stock system
b – UK ward stock system with original prescription and daily ward visits by pharmacists
c – ward stock + patient prescription system
d – individual patient prescription distribution system
e – unit dose drug distribution manual system
f – unit dose drug distribution computerised or automated

Some of these European studies indicate that the rate of intravenous medicine errors in hospitals are considerably higher than those involving oral medicines.[126,127,128,129,130,131] In one study at least one error occurred in 49.3% of intravenous medicine doses prepared on hospital wards; 1% were judged to be potentially severe errors, and 29% potentially moderate errors.[132] This particular risk is mainly due to the lack of ready-to-use unit dose packages of injectable pharmaceutical forms on the European market and to inadequate manpower in hospital pharmacies, and other resources.

Figure 10 summarises the results of these studies, according to the main organisations of drug distribution systems.

Figure 10: Medication administration error rates in Europe according to the medication use system



In the Australian health care system also, errors occur in 15-20% of drug administrations when ward stock systems are used, and only 5-8% when individual patient systems are used.[133]

Whatever assessment methods used, unit dose medicines dispensing significantly reduces the incidence of medication errors. Strong presumptions exist that individualisation of medicines distribution systems reduces nosocomial adverse drug events.[134]

Since unit dose dispensing systems are less widely used in Europe than in USA, this picture evidences the high risk level of traditional ward stock drug distribution systems for European hospitalised patients. According to the first European survey of hospital-based pharmacy services conducted in 1995 by the European Association of Hospital Pharmacy, unit dose medicine dispensing is not widespread throughout Europe: only 6.5% of the hospitals[135]. The most advanced countries were Spain (57%, at the end of the 90's),[136,137] the Netherlands (43.5%) and Portugal (27.3%). Except for Sweden (6.7%), the implementation rate of unit dose drug distribution is lower than 5% of the hospitals in the other European states.

These values can be compared with the results of a survey on professional practices conducted in USA at the same moment: there were remaining fewer than 3% of responding hospitals without any bed served by unit dose drug dispensing.[138] When comparing USA and Europe, demographic data demonstrate that the difference comes from the lack of means and supportive personnel devoted to European hospital pharmacies (see Table 26). [139,140]

Table 26: Comparison of demographic data in USA and in Europe

	Europe in 2000	USA in 2001
Unit dose drug distribution system expressed as percentage of beds covered by the system	**< 10% (except Sp, NL)**	**> 90%**
Nunber of pharmacists per 100 occupied beds	**1.14**	**8** (6.5 in 1989)
No of pharmacy technicians per 100 occupied beds	**1.6**	**7.6** (5.3 in 1989)
No of registered nurses per 100 occupied beds	**96.8**	**196.6** (124.5 in 1989)
Ratio of registered nurses to pharmacists	**103 : 1**	**21.1 : 1**
Ratio of registered nurses to pharmacy technicians	**74 : 1**	**21.6 : 1**
Ratio of pharmacy technicians to pharmacists	**1.4 : 1** (0.66 : 1 in Spain)	**0.97 : 1**

The main reasons for the lack of penetration of the unit dose medicine distribution system in Europe are the high cost of staff and equipment required to operate this system and the absence of convincing evidence regarding its benefits on patient safety, since the observation method is not designed to detect adverse drug events (see II.1.3). According to the needed investments, it still remains necessary to conduct the economic analysis of the costs and the benefits associated with the different medication use systems, in particular by updating the results obtained abroad in the seventies.[141,142] A strong support and appropriate funding to this research should be provided by the European Union in order to improve simultaneously patient safety, health care workforce employment and health care investments.

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Appendix 5

Existing Medication Error Reporting Systems

A variety of medication error reporting systems have been established at national level. In North America and in some European countries, medication errors may be reported to specific reporting programme or to broader patient safety reporting programmes. These systems often co-operate, contributing by this way to a better dissemination of recommendations for improving the patient safety and preventing medication errors.

The following presentation of some existing systems has been summarised in order to allow to understand the variety of situations encountered in different countries. This may foster an open-minded design of medication errors reporting systems in co-operation with, sometimes being integrated in patient safety incident reporting systems. Specific medication error reporting systems (see table 23) are presented prior to systems integrated in patient safety incident reporting systems.

1. MERS Outside Europe

Institute for Safe Medication Practices (ISMP) & US Pharmacopeia (USP)
http://www.ismp.org/
http://www.usp.org/patientSafety/mer/
The medication error reporting programme of the Institute for Safe Medication Practices (ISMP) collects reports from health care practitioners since 1975. In 1991, ISMP merged its MERP with the US Pharmacopoeia. In 1992, the Food and Drug Administration (FDA) started monitoring these medication error reports. Health care practitioners and consumers can submit reports and associated material confidentially. The information is anonymously forwarded to the Food and Drug Administration (FDA) and to the manufacturer after removal of name and contact information to inform them about pharmaceutical labelling, packaging and nomenclature issues that may foster errors by their design. ISMP analyses the medication error reports and addresses recommendations to health care practitioners, community pharmacists, nurses, consumers, pharmaceutical companies and authorities.

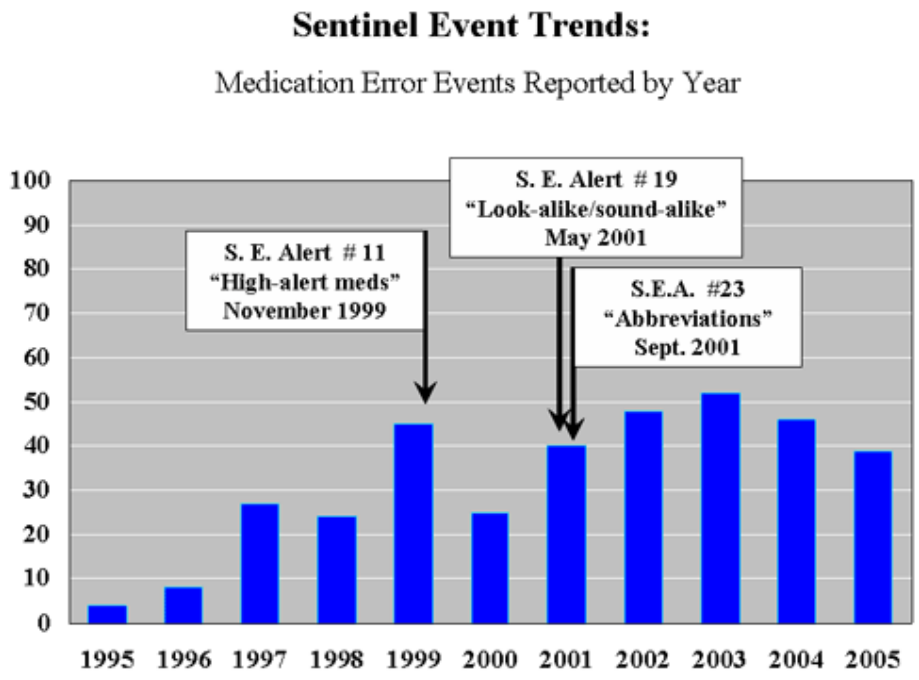
Since the establishment of the ISMP MERP, feedback information has been provided in the columns “Hospital pharmacy”. The feedback information is also available in many other health care journals, on the ISMP website. Several dedicated newsletters, formerly “ISMP Medication Safety Alerts!”, are published monthly or biweekly with a specific format for target audience: Acute Care Edition, Community/Ambulatory Care Edition, Consumer Edition, Nursing Edition. Tools for improvement of medication safety practices, such as IMSP Medication Safety Self-assessment, educational services, and others consulting services are also provided.

US Pharmacopoeia (USP)
http://www.usp.org/patientSafety/medmarx/
Since 1998, the US Pharmacopoeia operates in addition to MERP, MedMARx° programme, a national, anonymous, Internet-accessible reporting database that hospitals and health care systems use to identify and prioritise adverse drug reactions and medication errors. They participate voluntarily by subscribing to it on an annual basis, and have then access to data from the USP national database. This allows comparisons with data and solutions from other sites, trend analyses and assist in the development of best practices.

An annual report and feedback information are prepared from analyses and published together with an estimation of global trends in several journals, such as "Drug Topics" or "US Pharmacist", or in several newsletters: "Practitioner's Reporting News", "USP Quality Review", "CAPSLink" available on the USP Website.

Joint Commission on accreditation of Healthcare Organization (JCAHO)
http://www.jcaho.org/accredited+organizations/sentinel+event/se_index.htm
Serious adverse events appearing as consequences of medication errors should be reported by health care organisations to the Joint Commission on accreditation of Healthcare Organization (JCAHO) Sentinel Events Reporting Programme. If hospitals fail to report an event and JCAHO learns about it from a third party, it requires the hospital to conduct an analysis of the root cause or it risks loosing its accreditation.

Figure 11: Medication errors reported as sentinel events to JCAHO 1995-2005



Recommendations are published in "Sentinel Event Alerts", some of them dealing with medication errors such as vincristine intrathecal administration. Feedback is provided on the

JACHO website and more specifically through the newsletter "Sentinel Event Alert", issued as needed.

The Commonwealth of Pennsylvania Patient Safety Reporting System (PA-PSRS)
http://www.psa.state.pa.us/psa/site/default.asp
With reference to the recommendations of the "To err is human" report of the Institute of Medicine, Pennsylvania has enacted under Act 13 of 2002 a web-based, mandatory reporting system to which all hospitals, birthing centres and ambulatory surgical facilities licensed in Pennsylvania must submit reports of "serious events" and "incidents" including those related to medication errors. The programme provides individual facilities with detailed reports analysing their specific data so as to enable managers to use these reports for quality and patient safety improvement. ECRI (formerly the Emergency Care Research Institute, a WHO Collaborating Center) and the ISMP, both Pennsylvania based, nonprofit organisations, have been commissioned to develop this programme. On the basis of analyses and trends, an annual data report is provided and also feedback information in a newsletter "Patient Safety Advisory".

Because of strong confidentiality and protection of whistleblowers, all information submitted to PA-PSRS is confidential and no information about individual facilities or providers is made public. The principles of a protected mandatory patient safety reporting system are now enacted in the United States of America at federal level through the Patient Safety and Quality Improvement Act of 2005 signed into law by President Bush on July 29th 2005.

Efforts made in other countries evidence similar trends in enabling close co-operation between patient safety reporting systems and medication errors reporting systems.

Institute for Safe Medication Practices Canada (ISMP-Canada)
http://www.ismp-canada.org/
Since 2000, ISMP-Canada has received information on medication errors from individual health practitioners and institutions on a voluntarily basis. In addition, hospitals may report anonymous information on medication errors through ISMP-Canada's "Analyze-ERR", a software documentation tool designed to track and analyse medication errors. Feedback information is provided in the "ISMP Canada Safety Bulletin", available on ISMP-Canada website and through several journals, such as the "Canadian Journal of Hospital Pharmacy", "Canadian Association of Critical Care Nurses Dynamics" and the "Hospital News".

ISMP-Canada participates in co-operation programmes with professional organisations and universities in Canada not only by the way of educational programmes about medication errors and their prevention. A coalition of stakeholders including the Canadian Society of Hospital Pharmacists (CSHP), Health Canada's Marketed Health Products Directorate, the Canadian Institute for Health Information (CIHI) and further the Canadian Association of Chain Drug Store, the Canadian Healthcare Association, the Canadian Medical Association, the Canadian Nurses Association, the Canadian Pharmacists Association, the Canadian's Research Based Pharmaceutical Companies, the College of Family Physicians of Canada, the Consumer Association of Canada and the Royal College of Physicians and Surgeons of Canada, formerly the Canadian Coalition on Medication Incident Reporting and Prevention (CCMIRP) led to the creation of a national Canadian MERS (CCMIRP 2002) in 2004. Operated by ISMP-Canada, it is closely aligned to the work and the objectives of the Canadian Patient Safety Institute (CPSI).

Australian medication errors reporting services

Australian Incident Monitoring System (AIMS)
http://www.apsf.net.au
The Australian Incident Monitoring System (AIMS) is operated by the Australia Patient Safety Foundation (APSF) since 1993, as an extension of the Anesthesia AIMS formed in 1987. This reporting system was declared a Quality Assurance Activity under the law on Health Insurance by the Commonwealth Health Minister in June 2001. This status confers protection from legal disclosure. Reports are accepted from all sources including hospitals, outpatient facilities, health care professionals, patients and related, and anonymous sources. Reports are submitted by mail, electronically or by phone.

Australian Council for Safety and Quality in Health Care
http://www.safetyandquality.org/
The Adverse Medicine Events Line is operated on behalf of the Australian Council for Safety and Quality in Health Care by clinical and medicine information pharmacists from Mater Misericordiae Health Services, South Brisbane. The AME Line is an interactive service through which consumers may seek information about or report adverse events associated with medicines. Australians may report to experienced medicine information pharmacists by phone suspected adverse drug reactions, medicine errors or "near misses".

2. Existing national MERS in Europe

NHS National Patient Safety Agency (NPSA)
http://www.npsa.nhs.uk
The National Patient Safety Agency is a Special Health Authority created in July 2001 to co-ordinate reporting, analysing and learning from "adverse incidents" and "near misses" involving NHS patients.

After testing in 2003, the National Reporting and Learning System (NRLS), has been launched in 2004 to collect information on "patient safety incidents", including medication errors reports, from all 607 NHS organisations in England and Wales. The NRLS is the only national reporting system covering all health care settings, i.e. primary care, acute care, learning disabilities, mental health and ambulance care. Designed to complement local reporting systems, the information is stored anonymously by the NRLS. All reports related to patient safety are entered into the organisation's own risk management system and then sent automatically direct to the NPSA, where the information relating to individuals (staff or patients) is removed. An electronic web-based reporting form is also available. Patients and carers may report by telephoning to a free phone number to speak with a member of the Patient Advice and Liaison Service (PALS) team.

The information provided by the NRLS is a key component of the Patient Safety Observatory (PSO) and assists in the identification and understanding of error, and the development of solutions. In 2005, according to the first report of the NRLS and the PSA, medication errors represented 20.8% of patient safety incidents reported in general practice, 8.6% in acute hospitals, 3.4% in mental health trusts, 5.7% in learning disabilities services, 8.8% in ambulance services (NPSA, 2005).

The NPSA uses three distinct formats for communicating patient safety information to the NHS. The formats are: "Patient safety alert" requiring prompt action to address high risk safety

problems; ”Safer practice notice”, which strongly advises implementing recommendations or solutions; and “Patient safety information” which suggests issues or effective techniques that health care staff can consider to enhance safety.

The NPSA produces also number of publications, videos and tools, including e-learning, to assist the NHS. In partnership with the NPSA, BMJ Publishing Group, the Institute for Healthcare Improvement (IHI) “safer health care” (www.saferhealthcare.org.uk) is a website being both a patient safety information resource and a communication channel for sharing experiences.

Instituto par el Uso Seguro de los Medicamentos (ISMP-Spain)
http://www.usal.es/ismp
Since its creation in October 1999, ISMP-Spain has maintained a national medication error reporting programme. This programme is voluntary, confidential and independent. It collects observations and experiences concerning those potential or actual medication errors that health professionals voluntarily report. The information is independently analysed, with neither conflicts of interest nor administrative pressure, and all information is treated confidentially. Health professionals may either complete a report form or contact the ISMP-Spain either by e-mail, fax or telephone to report medication errors in complete confidentiality.
ISMP-Spain carefully reviews and analyses all reported errors, and depending on the characteristics sends a copy of the report to the Spanish Medicine Agency (AEM) and to the pharmaceutical companies whose products are mentioned in the reports. The information is also shared with the ISMP-USA.

Feedback information is provided by ISMP-Spain on its website and in Spanish health care journals.

Réseau Épidémiologique de l'Erreur Médicamenteuse
(French Epidemiologic network for reporting medication errors)
The Réseau REEM is the only French medication error reporting system proposed by AAQTE, a non-profit organisation promoting the quality assurance and evaluation of medicine therapy in 1998. Since 1999, the Réseau REEM has received medication error reports from individual health care practitioners at national level. This programme is voluntary, confidential and independent. Health professionals may either complete a report form or contact the Réseau REEM either by e-mail, fax or telephone to report medication errors in complete confidentiality. Feedback information is provided in French health care journals like the “revue Prescrire” or “Le pharmacien hospitalier”.

The small-sized AAQTE is currently merging its medication error reporting programme within the "Association Mieux Prescrire" (AMP), the “revue Prescrire” and “Prescrire International” Editor, extending the voluntary reporting programme to several disciplines of health care practitioners, in particular doctors and nurses, from hospital setting to ambulatory care, and expanding the reporting system from medication errors to overall patient safety. The name of the reporting system remains the same: REEM (“Réseau pour Éviter l’Évitable en Médecine” - Preventing what is preventable in medicine).

Dansk Patient Sikkerheds Database
http://www.dpsd.dk/
The Danish Act on Patient Safety passed the Parliament June 2003 and was put into force January 1, 2004. The Act obliges practitioners to report adverse events to a national reporting system. The Hospital owner is obliged to take follow-up actions on the reports and the National Board of Health is obliged to communicate the experiences at national scale. The aim of the reporting system is to learn, not to punish. Therefore the act contains a paragraph protecting the health care personnel from sanctions: "A practitioner who reports an adverse event cannot be subjected to investigation or disciplinary action by the employer, the Board of Health or the Court of Justice as a result of that report." (§6 of Danish Act on Patient Safety)Reports are accepted from all sources including hospitals, outpatient facilities, health professionals, patients and relatives and anonymous sources. Reports may be submitted by mail, electronically or by phone. Feedback information on medication errors is provided on the Dansk Patient Sikkerheds Database website and in the bulletin "Nyhedsbrev".The Danish Society for Patient Safety (http://www.patientsikkerhed.dk) is engaged in the reduction of medication errors in primary care in co-operation with the Danish Pharmaceutical Association and the Danish College of Pharmacy Practice (Pharmakon).

Swedish patient safety reporting system
http://www.socialstyrelsen.se/Patientsakerhet/
Since 1936, a reporting system has existed in Sweden under a law called Lex Maria. If a patient suffers serious injury during care or is exposed to a serious risk, all health care staff must report the incident to the National Board of Health and Welfare (Socialstyrelsen). If a staff member has made a great mistake, the National Board of Health and Welfare will report the event to the National Disciplinary Board (HSAN). This board can decide about disciplinary measures, i.e. warning. If a patient or a relative considers the given health care as incorrect he or she may also report the incident to the National Disciplinary Board.

In the 1990s the National Board of Health and Welfare issued a set of regulations on quality issues. The Board had decided on a system for continuous quality improvement. The aim is to create a better safety climate. Patients' injuries often depend on failures of the entire system. If the injury is not serious, all health care staff is obliged to report the incident to their management through an incident reporting system. The aim is to discuss the failure and change routines in order to prevent a recurrence of the incidence in a proactive way.

There are 40 national quality registers in Sweden. These registers constitute a very important knowledge base for continuous improvement. There has been much discussion in Sweden about these systems. Many staff members would not report because of the risk of punishment. In 2006, the National Board of Health and Welfare (Socialstyrelsen) proposed changes to the incident reporting system and the Lex Maria aiming at increasing and stimulating health care staff to report incidents. The National Board of Health and Welfare sent the proposal to the Government. It has been referred for consideration to several authorities and organisations. In this new proposal the importance of a proactive system is emphasised. Patient safety is a very important issue in the Swedish health care.

The Netherlands
A non-punitive, voluntary reporting system for adverse events, in use in most hospitals and health care organisations, is complemented by a mandatory reporting system of serious adverse events managed by the Dutch Health Care Inspectorate.

Table 27: Summary of the characteristics of MERS

Characteristics of MERS	ISMP-USP MERP	USP MedMarx°	ISMP Canada	ISMP Spain	NPSA	REEM
	USA	USA	Canada	Spain	UK	France
Characteristics of the reporting system						
Voluntary	X	X	X	X	X	X
Non-punitive	X	X	X	X	X	X
Confidential	X		X	X	X	X
Anonymous	No	Yes	If NI	No	Yes	No
Accessible						
Phone, e-mail, mail, fax	X		X	X		X
Secure online form	X	only	X	No	X	X
Data transmission from local level					X	
Free access	X		X	X		X
On subscription		only			NHS	
For risk management by users	No	Yes	Analyse-ERR°	No	Yes	No
For patients / consumers	Yes	No	CMIRPS	No	PALS	No
Independent						
Governmental body	No	Yes	No	No	Yes	No
Authority on standards	No	USP-NF	No	No	Yes	No
Disciplinary competence	No	No	No	No	No	No
Nonprofit organisation	Yes	Yes	Yes	Yes	Agency	Yes
Funding by pharmaceutical industry	No	No	No	No	No	No
Advertising	No	No	No	No	No	No
Grounded on expert-analysis						
Health care professionnals	X	X	X	X	X	X
Human factor and safety experts	X		X	X	X	X
Provision of recommendations (Timely, System-oriented, Responsive)						
Newsletter						
Health care practitionners	3	3	X	X	X	
Public / consumers	1					
Website						
On-line alerts	X	X	X	X	X	
Mail delivery service	X	X				
Message board / discussion forum	X					
Other educational tools	X	X	X	X	X	X
Co-operation						
With pharmacovigilance systems	FDA	FDA		AEM	MHRA	
With patient safety reporting systems						
at state or national level	PSA				NPSA	
under autohority of accrediting bodies		JCAHO				
With others MERPs						
at national level	NCC MERP	NCC MERP				
at international level	X		X	X	X	X
Additional quality improvement services						
Risk-assessment						
of the medication use sytem (on-site)	X					
of the drug packaging and labelling	?					X
of drug naming safety	X					

Table 27 (cont'd)

	ISMP-USP MERP	USP MedMarx°	ISMP Canada	ISMP Spain	NPSA	REEM
Surveys	X					
Education						
Educational programmes	X	X	X	X	X	X
e-learning					X	
Research				X		X

Appendix 6

Safety assessment template on label information and packaging

The Council of Europe Expert Group on Safe Medication Practices has developed a template that may be used to assess the potential risk of labelling and packaging of medicinal products.

The template is offered to drug regulatory authorities and pharmaceutical companies during drug development to assist in the marketing authorisation process. It may be also useful for purchasing groups or hospitals wishing to evaluate the safety of the labelling and packaging of medicines that they purchase or to select medicines for inclusion in the hospital formulary.

This template has been developed to specifically evaluate the potential risk of errors associated with labelling and packaging. It does not deal with the risk of errors caused by other aspects of the medicinal product. It permits the systematic assessment of the different components of the medication packaging: outer packaging, immediate packaging, delivery devices, diluents or secondary containers, and package design.

It takes account of relevant provisions of the EU regulations with a focus on in-use safety.

This template was developed taking into consideration the *Grille du conditionnement de la Revue Prescrire*, the MHRA *Best practice guidance on labelling and packaging of medicines*, the Directives 2001/83/EC and 2004/27/EC, the EC *Guideline on the readability of the label and package leaflet*, and the draft *General Requirements for the Labelling Medicines*, under discussion by the Australia-New Zealand Joint Therapeutic Products Agency.

Additionally, medication errors and problems associated with labelling and packaging published by the ISMP in the United States and by ISMP-Spain and the *Revue Prescrire* in Europe were reviewed.

Safety assessment template of medication labelling and packaging

Proprietary name:		
International non-proprietary name of active pharmaceutical substance(s):		
Manufacturer:		
Dosage form	**Dosage units**	**Presentation**
Therapeutic class (ATC):		
Approved indication **(or intended indication if not yet approved):**		
Clinical setting where it is expected to be used and prescribing considerations:		
Potential for harm [1]:		

Safety assessment template of medication labelling and packaging

1. Safety assessment of the outer packaging				
1.1. Identification & readability of the outer packaging label.	**Present** (Yes/No)	**Legibility** [2] (Yes/No)	**Comments** [3]	**Potential for error** [4] (L/S/M/H)
*** Name of the medicinal product [5].**				
*** International non-proprietary name (s) of APS.**				
*** Expression of strength/concentration [6].**				
*** Route of administration.**				
*** Special warnings (if necessary) [7].**				
Indications for use and dosage instructions (Posology) [8]				
Number of doses				
Excipients of obligatory declaration				
Special storage information (if any)				
Expiry date				
Lot number				
Bar codes				

*. Special attention should be given to the critical items of information (name of medicine, expression of strength/concentration, route of administration, posology and special warnings) in the design of the packaging label. These should be located together in a prominent position on the front label and appear in the same field of view. These items should not be broken up by non-critical information, logos or graphics.

1. With respect to narrow therapeutic range; overdose (accidental or self-poisoning) and clinical consequences of under dosing or omission. **See Appendix A.**

2. The size and font type should be adequate to ensured maximum legibility. The critical information should appear in as large a font as possible. According to the EC guideline on label readability, all the characters should be of at least 7 points (1.4 mm). However, minimum font size recommended is 12 points. A clear and legible sans serif typeface, such Arial or Helvetica, in bold or semi-bold type should be used. It is recommended the use of sentence case. Lettering should be printed in one or several colours that allow them to be clearly distinguished from the background.

3. Related to visual perception (inadequate placement, prominence or visibility); comprehension (ambiguous, confusing or incomplete terms), and usefulness (accordance with the purpose).

4. Potential for error: (L) Little or no error; (S) Slight; (M) Moderate or (H) High. **See Appendix 1.**

5. The name of the medicine is defined as comprising the name, strength and pharmaceutical form. It should appear on at least three non-opposing faces of the package.

6. For single dose injectable and liquid preparations it is particularly important to express the strength of the active substance as total quantity per total volume, and the concentration as amount per ml placed immediately below, either in parentheses or less prominently. For medicines in solution or suspension the strength should be expressed preferably as amount per mL. In addition, it is also important not to use percentages, not to abbreviate the word *micrograms* and to differentiate clearly base and salt strengths if needed.

7. The use of special warnings (expressed in positive terms) known to reduce the potential for error is encouraged, but not the use of non-important instructions that can occupied valuable space.

8. This is only required for over-the-counter medicines.

Safety assessment template of medication labelling and packaging

1.2. Other communication features related to the outer packaging label	Yes	No	Comments	Potential for error [4]
Does the label have distracting logos, symbols or icons?				
Does the label have a colour scheme prone to error [9]?				
Is the label written in more languages of the official ones in the country?				
Does the package provide enough space for the positioning of a patient- specific information in the form of a dispensing label [10]?				
1.3. Potential for similarities with the outer packaging of other medicinal product	**Yes**	**No**	**Comments**	**Potential for error [4]**
Is there a possible risk of confusion with another presentation of the same medicine with a different strength or form, or for another route of administration?				
Similar size/ shape				
Similar design (manufacturer trade dress)				
Similar colour schemes				
Is there a possible risk of confusion with another medicinal product from the same company [11]?				
Similar size/ shape				
Similar design (manufacturer trade dress)				
Similar colour schemes				
Is there a possible risk of confusion with another medicinal product from a different company [11]?				
Similar size/ shape				
Similar design (manufacturer trade dress)				
Similar colour schemes				

9. Colour differentiation is useful for preventing medication errors. However, the application of a colour coding system is not encouraged and must be considered cautiously and on an individual basis, because, although such a system might help to differentiate drug classes, it might also increase the chances of mix-ups among individual strengths and concentrations within a drug class.

10. Items especially important for medicines for use by the patient.. 11. With a particular attention to the proximity of storage and in alphabetic order.

Safety assessment template of medication labelling and packaging

2. Safety assessment of the immediate packaging				
2.1. Identification & readability of the immediate packaging label	**Present** (Yes/No)	**Legibility** [2, 12] (Yes/No)	**Comments** [3]	**Potential for error** [4] (L/S/M/H)
*** Name of the medicinal product [5].**				
*** International non-proprietary name (s) of APS**				
*** Expression of drug strength/concentration [6].**				
*** Route of administration.**				
Expiry date				
Lot number				
Bar codes				

*. Special attention should be given to the essential items of information (name of medicine, expression of strength/concentration and route of administration) in the design of the label. These should be located together in a prominent position and appear in the same field of view. These items should not be separated by information less relevant for safety, logos or graphics. In the case of small containers (less than 10 ml), the design is specially important and requires a particular attention.

2. The font type and size should be adequate and maximum legibility must be ensured. The critical information should appear in as large a font as possible. All the characters should be of at least 7 points (1.4 mm) according to the EU guideline on the readability of the label and package leaflet of medicinal products for human use. A clear and legible sans serif typeface, such Arial or Helvetica, in bold or semi-bold type should be used. It is recommended the use of sentence case. Lettering should be printed in one or several colours that allow them to be clearly distinguished from the background.

3. Related to visual perception (inadequate placement, prominence or visibility); comprehension (ambiguous, confusing or incomplete terms), and usefulness (accordance with the purpose).

4. Potential for error: (L) Little or no error; (S) Slight; (M) Moderate or (H) High. **See Appendix A.**

5. The name of the medicine is defined as comprising the name, strength and pharmaceutical form.

6. For single dose injectable products it is particularly important to express the strength of the active substance as total amount per total volume, and the concentration as amount per ml placed immediately below, either in parenthesis or less prominently. For medicines in solution or suspension the strength should be expressed preferably as amount per ml. For safety reasons it is also important not to use percentages and not to abbreviate the word *micrograms.*

12. In the case of embossed items on glass ampoules or vials, the font size, the font type and the colours should assure contrasting background and adequate legibility.

Safety assessment template of medication labelling and packaging

2.2. Specific safety considerations related to blister packs	Yes	No	Comments	Potential for error [4]
Is each blister pocket individually identified as a unit dose [13]?				
Does the label on each unit dose contain all necessary information (see 2.1) [14]?				
Do the type of film and the colours used ensure adequate legibility [15]?				
Are the contents of each unit dose easily removed from the blister?				

4. Potential for error: (L) Little or no error; (S) Slight; (M) Moderate or (H) High. **See Appendix A.**

13. In safety terms it is desirable for each blister pocket to be completely identified, and to avoid non-unit dose blister strips, which lead to errors due to a lack of information to identify the drug after some blisters have been cut off or torn apart to remove medication. It is also important to avoid two-unit blister on which one label is used for two dosage units which may lead to dosage errors.

14. The items of information that each blister should contain in order to ensure a correct identification of each unit dose are: trade name, non-proprietary name, strength, expiry date, lot number and bar code.

15. For blister packs, film brilliance, font type, font size and label colors should assure adequate label legibility. Where possible non-reflective material or colored foils should be considered to enhance readability.

Safety assessment template of medication labelling and packaging

2.3. Other communication features related to the immediate packaging label.	Yes	No	Comments	Potential for error [4]
Does the label have distracting logos, symbols or icons?				
Is the label written in more languages of the official ones in the country?				
Does the label have a colour scheme prone to error [9]?				
2.4. Potential for similarities with the immediate packaging of other products.	**Yes**	**No**	**Comments**	**Potential for error** [4]
Is there a possible risk of confusion with another presentation of the same medicine with a different strength, form or for another route of administration?				
Similar size/ shape				
Similar design (manufacturer trade dress)				
Similar colour schemes				
Is there a possible risk of confusion with another medicnal product from the same company [11]?				
Similar size/ shape				
Similar design (manufacturer trade dress)				
Similar colour schemes				
Is there a possible risk of confusion with another medicinal product from a different company [11]?				
Similar size/ shape				
Similar design (manufacturer trade dress)				
Similar colour schemes				

4. Potential for error: (L) Little or no error; (S) Slight; (M) Moderate or (H) High. **See Appendix 1.**
9. Colour differentiation is useful for preventing medication errors. However, the application of a colour coding system is not encouraged and must be considered cautiously and on an individual basis, because, although such a system might help to differentiate therapeutic classes, it might also increase the chances of mix-ups among individual strengths and concentrations within a therapeutic class.
11. With a particular attention to the proximity of storage and in alphabetic order.

Safety assessment template of medication labelling and packaging

3. Safety assessment of associated devices, diluents or critical secondary containers to be used with the medication				
3.1. Risks related to specific delivery devices to be used with the medicine	**Yes**	**No**	**Comments**	**Potential for error** [4]
Is the delivery device identified with the name of the medicine, in order to avoid risks of confusion with the delivery devices of other medicines ?				
Is there any risk of error in handling the delivery device?				
In the case of a dosing dispenser, does it allow for measuring precisely the dose ?				
If there is a dosing dispenser, is the graduation clearly readable?				
If there is a dosing dispenser, is the graduation adapted to the posology?				
3.2. Risks related to diluents to be used with injectable or oral medicines	**Yes**	**No**	**Comments**	**Potential for error** [4]
Does the diluent label ensure the correct identification of the diluent? (no medicines name)				
Does the diluent label ensure correct medicine preparation and administration ?				
Is confusion possible between the medicine and the diluent?				
3.3. Risks related to critical secondary containers [16]	**Yes**	**No**	**Comments**	**Potential for error** [4]
In the case of IV bags with protective foil containers, is there any risk of confusion because of this secondary container reducing medicine label visibility?				
Does the secondary container list the contents, ensuring correct identification and good differentiation of the medication from other products with similar protection?				

4. Potential for error: (L) Little or no error; (S) Slight; (M) Moderate or (H) High. **See Appendix A.**
16. This includes an over-pack, over-wrap or pouch to provide product stability protection.

Safety assessment template of medication labelling and packaging

4. Global safety assessment of the package with focusing on correct medicine use				
4.1. Adequacy of the package design to medicine use	**Yes**	**No**	**Comments**	**Potential for error** [4]
Is the package design adequate for storage in community pharmacies and in hospitals?				
Does the primary container provide enough protection from the environnement during storage until the medicine is completely used?				
Could the package design lead to incorrect preparation of the medicine?				
Could the package design lead to the medicine being administered incorrectly or by another route?				
Does the packaging present a design that might mislead the patient about inherent risks of the medicine and encourage overdosing?				
For oral formulations presented in bulk bottles or containers, are safety caps provided to prevent children from opening them?				
4.2. Adaptation of the medicine package to patient needs.	**Yes**	**No**	**Comments**	**Potential for error** [4]
Are the strengh and the content (unit quantity) adapted to usual posology and length of treatment?				
May the total amount of medcine contained in the package cause overdose or an intoxication?				
Is the medicine dosage form adequate for the intended route of administration?				
Is there any risk involved in the disposal of the unused or expired medicine ?				

4. Potential for error: (L) Little or no error; (S) Slight; (M) Moderate or (H) High. **See Appendix A.**

Suggestions for improving safety:

Are there risks not addressed by this assessment template?

How do you consider overall safety of this medicinal product?

AppendixA. Hazard scoring of the medication labelling and packaging

The risk related to the medication labelling and packaging can be evaluated by its criticality, measuring the exposure of the drug users.
The criticality is a three-dimensional weighted score taking in account:

- the potential of error of the drug packaging and labelling (E),
- the potential for harm of the drug and of the route of administration (H),
- and the frequency of use (U).

C = E * H * U

E - Potential for error: (L) Little or no error; (S) Slight; (M) Moderate or (H) High. Scoring from 1 to 4.
H - Potential for harm: (N) No harm, (T) Temporary harm, (P) Permanent harm, (V) Vital or death . Scoring from 1 to 9 according to NCC MERP taxonomy.
U - Use frequency: (R) Rare, (O) Occasional; (F) Frequent; (V) Very frequent. Scoring from 1 to 4.

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Appendix 7

Information on dispensing labels

1. Information elements

Dispensing labels are also called pharmacy labels.
The information elements of pharmacy labels can be classified into three groups.

1.1. Identification elements

Essential identification elements:
- Name of the patient,
- Identification of the medicine (active substances): machine readable and conventional (readable by humans). The conventional elements may be in the form of bar code digits (or parts) provided they are readable humans in the same format on the package;
- Date of dispensing.

Supportive identification elements:
- Name of the dispensing pharmacy;
- Name of dispenser;
- Dispensing (transaction) number;
- Item number (finished medicinal product);
- Operator ID.

1.2. Usage elements (posology)

In principle, the dispensing label needs only to state information for use specific for the individual patient:
- Indication for use: must not be included if the prescriber has not indicated it on the prescription;
- Dosage instructions. Must not be included if the prescriber has not indicated it on the prescription;
- Route of administration: important, if different from or not clearly indicated on the package. Examples: injectable solution taken orally, or combined eye/ear drops;
- Other elements which are considered important for the individual patient: some elements may need highlighting e.g. “stir before use”, “take with food”, “may cause drowsiness” and some may be needed because they are hidden by the dispensing label.

1.3. Other elements

- Price;
- Graphical elements like lines and frames;
- Logos.

2. Examples of European dispensing labels

Dispensing labels are produced with dispensing software systems. The complexity of these systems may vary, but they are often combined with modules for reimbursement claims and for stock control. They can also be used for patient information and for interaction control. Norway and Sweden are unique in that each has only one system platform being used in the entire country.

Dispensing software systems usually have registers containing sensitive patient data. Adequate procedures have to be put in place to protect sensitive patient data. In some European countries, pharmacies are not allowed to keep sensitive patient data. Restrictions for patient data registers may be a hinder the establishment of effective dispensing systems with dispensing labels.

The following is not intended to present an up-to-date description of the situation in every country but rather an overview. Some of the labels shown date back a few years ago and are from countries with several dispensing software systems.

In Nordic countries traditionally fixed size patient packs are supplied with a Nordic identification number system ("varenummer"). In Great Britain and the Netherlands, traditionally packs are split or the medicine is dispensed from bulk. This has lead to the development of numeric package identifiers on dispensing labels in Nordic countries and to generic package identifiers in Great Britain and the Netherlands.

2.1. The Netherlands

Typical size: 30x70mm. Three major software systems.
First line: date and name of prescriber, prescription number and operator ID.
Second line: name and address of patient.

zuidlaarder apotheek Kerkstraat 2, 9471 GB Zuidlaren
J.W.F. VAN MIL, A. RAMBHAROS, APOTHEKERS Tel. 050-4094333
02-08-2002 MEES PM HZ00405/1VM
Mw. H. Proef KERKS 2
3 X DAAGS (7-15-23 UUR) 1 TABLET
EERST OPLOSSEN IN -OF MENGEN MET- WATER.
KUUR AFMAKEN
* * BACTERIE INFECTIE * *
20 ST AMOXI DISP T 500MG

zuidlaarder apotheek Kerkstraat 2, 9471 GB Zuidlaren
J.W.F. VAN MIL, A. RAMBHAROS, APOTHEKERS Tel. 050-4094333
02-08-2002 MEES PM HZ00405/2VM
Mw. H. Proef KERKS 2
S MORGENS 1 TABLET
STIPT VOLGENS DIT VOORSCHRIFT GEBRUIKEN
IN OORSPRONKELIJKE VERPAKKING BEWAREN
1 ST ENALAPRIL T 10MG = RENITEC

2.2. Norway

Size: 30x75mm

Software system: Farmapro, 100% market share. Only thermo printers. The barcode is EAN-code for the Nordic varenummer (6-digit) which is printed on all packages and is an unique package identifier . On small containers, the label can be folded along the right edge of the red frame.

2.3. Sweden

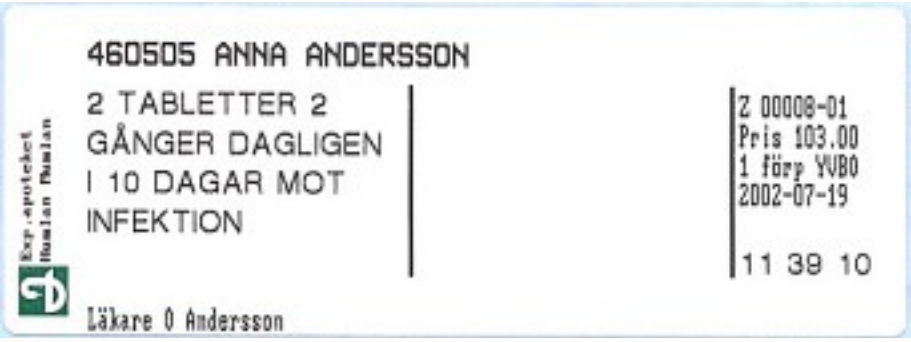
Size: 33x93mm.

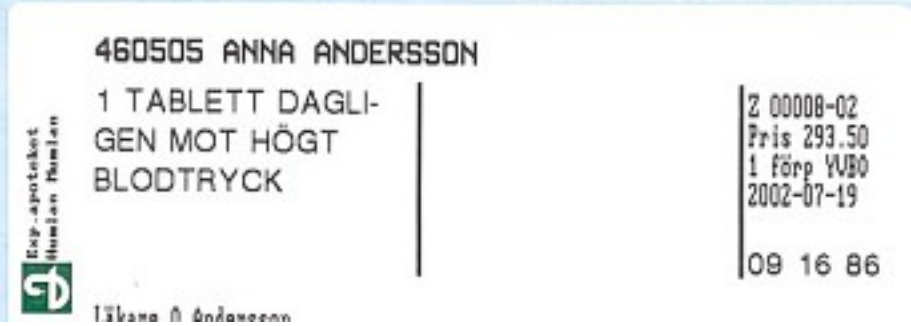
The software system is developed and owned by Apoteket AB, which is a state controlled company running all the pharmacies in Sweden.

First line: date of birth and name of patient.

First (and if necessary, second) column: dosage instructions and intended use of the medicine.

Third column: prescription number and item number, price, number of packages, operator ID. Date of dispensing. 6-digit Nordic vnr (unique package identifier).





Appendix 8

Machine readable codes

The industrial use of barcodes have been in use since the 1960s. Common barcodes started appearing on grocery shelves in the early 1970s as UPC codes which automated the process of identifying grocery items. Today, barcodes are just about everywhere and are used for identification in almost all types of business. When barcodes are implemented in business processes, procedures can be automated to increase productivity and reduce human error. Barcodes are extremely cheap, but their stumbling block is their low storage capacity and the fact that they cannot be reprogrammed.

The technically optimal solution would be the storage of data in a silicone chip. The most common form of electronic data carrying device in use in everyday life is the chip card based upon a contact field (telephone chip card, bank cards). However, the mechanical contact used in the chip card is often impractical. A contactless transfer of data between the data carrying device and its reader is far more flexible. In the ideal case, the power required to operate the electronic data carrying device would also be transferred from the reader using contactless technology. Because of the procedures used for the transfer of power and data, contactless ID systems are called RFID systems (Radio Frequency Identification).

Machine readable codes comprise bar codes and radiofrequency tags incorporated into products that can be read automatically that can identify the product and other encoded information.

A high percentage of medicinal products in Europe already have these codes. There are significant patient safety benefits if these codes are used as part of the dispensing and medicine administration processes to accurately match patients with their treatment. These codes also offer additional benefits including a reduced risk of expired medicines being used and easing medicine recall procedures.

Advanced uses of these codes include the use of unique serialised numbers on each medicine pack that can be used to authenticate the product at the point of dispensing and minimise the risks of patients' receiving counterfeit medicines.

1. The GS1Global Trade Item Number (GTIN)

The GS1Global Trade Item Number (GTIN) is a unique identification number that may be used for a product or service. (see details: www.GS1.com). The GTIN numbers are formatted and include a packing level and manufactures number.

2. Barcodes

A barcode is an assembly of black and white lines, usually vertical, that is symbolic or code, representing numbers and letters. The relative widths of both the bars and spaces code the data stored in the barcode. The barcode reader detects these relative widths and decodes the data from the barcode. A barcode is read by either scanning a spot of laser light across the entire barcode or taking a digital picture of the barcode with a digital camera.

Different versions of the EAN global coding standard are available for use with different types of bar codes on medicine product.

2.1. EAN 13 linear bar codes

Simple linear bar code called EAN 13 are the bar codes most commonly encountered in daily life outside of health care and over 80% of medicine products in the UK already include these bar codes. An EAN-13 barcode is divided into four areas:

1) the number system,
2) the manufacturer code,
3) the product code,
4) the check digit.

A GTIN can be encoded in a simple linear bar code called a EAN 13.

2.2. EAN 128 linear bar codes

The EAN 128 linear bar code is larger in size than the EAN 13 bar code, and used on pallets and cases of medicine products. It is usually too big to be applied to most individual medicine packs.

2.3. EAN 128 Reduced Space Symbology (RSS) bar codes

The size of the bar code used for EAN 128 can be reduced using Reduced Space Symbology (RSS). The smaller bar code size will allow the application of these bar codes on many individual medicine packs.

2.4. Data matrix bar codes

Expiry date and batch number information can be incorporated into a 2D data matrix bar code. The smaller bar code size will allow the application of these bar codes on individual medicine packs and unit of use packs e.g. 1ml ampoules or nebules or other small containers. GTIN, expiry date, batch number information and other information such as a unique serial number for each medicine pack or container can be incorporated into a 2D data matrix bar code.

3. Radio Frequency Identification (RFID)

A radio frequency identification system has three parts:
- a scanning antenna,
- a transceiver with a decoder to interpret data,
- a transponder that has been programmed with information.

The scanning antenna broadcasts a radio frequency (RF) signal in a relatively short range. The RF radiation provides a means of communication with the transponder tag and secondly provides the energy to transmit back the programmed information. The RFID tags do not contain batteries and are therefore small and relatively low cost.

The scanning antennas can be permanently fixed to a surface, doorway or may be hand-held. When a RFID tag passes through the radio frequency field of the scanning antenna it detects the activation signal from the antenna. This activates the tag that transmits the programmed information.

Small RFID Tags can be incorporated into unit of use packs. GTIN, expiry date and batch number and other information such as a unique serial number for each medicine pack or container can be encoded into a RFID chip. The advantages of RFID technology is that it does not require line of sight to operate.

Appendix 9

Key list of standard and best practices for preventing medicines errors and improving medication safety

A list of standard and best practices for preventing medication errors in each area of drug-related care has been established from each health professional point of view (doctors, pharmacists, nurses) on the basis of available recommendations. In order to rank their relevance for patient safety, a set of criteria has been adopted by the Council of Europe Expert Group on Safe Medication Practices such as potential benefit for the patients and ability of the practice to be easily utilised in different settings and types of patients.

Then these practices have been prioritised, using the Delphi method, based on these criteria leading to the selection of the list of standard and best practices for preventing medicines errors and improving medication safety.

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Safety objectives	Safe practices	Settings		Classes	
		Amb	Hosp	Std	Best
Raising awareness of medication errors and creating a health care culture of safety Practitioners are stimulated to detect and report errors, and interdisciplinary teams regularly analyse errors that have occurred within the organisation and proactively review external error reports for the purpose of redesigning systems to best support safe practitioner performance.					
Culture of safety A non-punitive, systems-based approach to error reduction	In a health care culture of safety, at a minimum, standardised policies and procedures are in place to : - Ensure that organisational leadership is kept knowledgeable about patient safety issues present in the organisation and continuously involved in processes to assure that the issues are appropriately addressed and that patient safety is improved. - Assess proactively the potential for error, before a new drug is added to the formulary or a new procedure or technique using new devices is incorporated to the organisation - Promote reporting : to ensure the staff can easily report incidents locally and nationally. - Learn and share safety lessons : to encourage staff to use root cause analysis to learn how and why incidents happen. - Implement solutions to prevent harm : to embed lessons through changes to practice, processes or systems. - Involve and communicate with patients and the public: to develop ways to communicate openly with and listen to patients. - Provide feedback to frontline heathcare providers about lessons learned. - Train all staff in techniques of teamwork-based problem solving and management.[11,12]	X	X	X	X
Staff competency and education	Practitioners receive sufficient orientation to medication use and undergo baseline and regular competency evaluation of knowledge and skills related to safe medication practices. Practitioners involved in medication use are provided with ongoing education about medication error prevention and the safe use of medicines that have the greatest potential to cause harm if misused.	X	X	X	X
Improving the safety of the medication use system by preventing medication errors "*Each major process in the medication system- ordering, dispensing, and administration – has its own unique opportunities for error.*"[8]					
Safer selection and procurement of medicines	Purchase of unit dose packaged medicines is maximised within the scope of practice needs.[14] Assessment of potential risks associated with labelling and packaging should be incorporated into the procurement process. All organisations should take particular care when new medicines, formulations or drug names are introduced to assess whether these present new risks.[13] All formulary and purchasing decisions critically consider medication safety.[3,14] If medicines with more potential for error must be purchased, safety enhancement strategies are adopted prior to the use of the product.[14] When drug manufacturer, packaging or formulations change, medical and nursing staff should be alerted before the drug becomes routinely available in the wards and the operating theatre.[13]	X	X	X	
Safer storage of medicines on wards and at home Medicine home and based floor stock is restricted or, at least, minimised.	All medicines should be stored safely and in such a way that the risk of drug confusions are minimised.[13] The storage of nonemergency floor stock medicines on the nursing units or in patient care areas should be minimised and high risk medicines, such as concentrated electrolytes, should not be included.[1,14] Unit floor stock supplies and unit based stocks are customised to the unit depending on patient population.[14] Pharmacists should regularly control all medication storage areas to make sure medicines are stored properly.[5] High-risk medicines should be restricted, not stored in patient care areas, withdrawn from ward stock where appropriate and dispensed from pharmacy against individual prescriptions.[13,14] High-risk medicines stocked as unit floor stock or unit based stocks are only available if a profile-dispense function exists and only if the medicines are packaged and stored in a way that minimises the likelihood of a dispensing error.[14]	X	X	X	
Safer prescribing of medicines	Prescribers should evaluate the patient's total status and review all existing medicine therapy before prescribing new or additional medicines to ascertain possible drug-related problems.[1] The patient's medical record should always be checked before a new prescription is written.[13] Appropriate dosage adjustments are made for children, the elderly and anyone with impaired renal or hepatic function on the basis of readily available information on dosing medicines in special populations.[14] When possible, medicines should be prescribed for administration by the oral route rather than by injection.[1]	X	X	X	

Safety objectives	Safe practices	Settings		Classes	
		Amb	Hosp	Std	Best
Safer doses preparation	Medications should be contained in unit dose packages and ready-to-use medicines utilised to the greatest extent possible.[12,14] Medications are not compounded if a suitable and similar commercially available product exists, in particular premixed intravenous solutions.[13,14] The intravenous dose preparation on nursing units should be minimised by centralising aseptic dose preparation within the hospital (pharmacy-based IV admixture systems).[9,13,14]		X	X	
Safer dispensing of medicines	Pharmacists should review all medication orders and the complete patient medication profile before medication are dispensed or made available for administration except in those instances when review would cause a medically unacceptable delay.[12] Pharmacists routinely review medication orders before the first dose is administered to a patient.[14] All systems should provide for review and verification of the prescriber's original order (except in emergency situations) before a drug product is dispensed by a pharmacist.[1] Prescriptions should be checked for clinical appropriateness by suitably qualified staff prior to dispensing.[13] All ambiguities or potential risks should be identified, and clarified with the prescriber before dispensing.[13] Pharmacists should never assume or guess the intent of confusing medication orders. If there are any questions, the prescriber should be contacted prior to dispensing.[1] Any necessary clarifications or changes in a medication order must be resolved with the prescriber before a medication is administered to the patient. Written documentation of such consultations should be made in the patient's medical record or other appropriate record. Nursing staff should be informed of any changes made in the medication order. Changes required to correct incorrect orders should be regarded as potential errors, assuming the changes occurred in time to prevent the error from reaching the patient.[1] Prescription problems/questions are resolved directly between the prescriber and pharmacist in a time frame and manner that meet the patient's needs.[14]	X	X		X
	During the dispensing process, pharmacists: reconcile prescription(s) and confirm indication(s) of medicine therapy with the patient or agent; show the medication to the patient or agent and ensure that the colour, shape and size of the medication are consistent with what the patient has received in the past; if not consistent, the pharmacist confirms medication identity with the patient prior to dispensing; verify allergy and adverse drug reaction history.; perform counseling and document refusal; ask open-ended questions to assess patient and caregiver level of understanding; encourage patients and caregivers to ask questions or raise concerns about their medicines.[14] Particular care needs to be taken when dispensing medicines to children when adult formulations are used to prepare doses.[13]	X		X	
	The pharmacy department must be responsible for the procurement, distribution, and control of all medicines used within the organisation. For safety, the strongly recommended method of distribution within the organized health care setting is the unit dose drug distribution and control system. Except in emergency situations, all sterile and nonsterile drug products should be dispensed from the pharmacy department for individual patients and in ready-to-administer dosage forms whenever possible.[1,9,12] In the aim to reduce the number of opportunities for error, and for most medicines, not more than a 24-hour supply of doses should be delivered to or be available at the patient care area at any time.[12]		X	X	
Safer administration of medicines	All medicine orders should be verified before medication administration. Doses should not be administered unless the meaning of the original order is clear and unambiguous and there are no questions with respect to the correctness of the prescribed regimen.[1] The first dose of each new routine (non-emergency) medication order is administered only after: the order has been reviewed and approved by a pharmacist ; a nurse has reconciled the medication order against the medication administration record (MAR) and compared them with medicines dispensed.[1,14] All doses should be administered at scheduled times unless there are questions or problems to be resolved. Medication doses should not be removed from packaging or labelling until immediately before administration.[1] Staff should only administer medicines that are properly labelled.[13] Nurses should check the identity and integrity (e.g., expiration date and general appearance) of the medicines dispensed before administering them. If a person administering a drug is unsure of the drug, dose or regimen it should be confirmed with a second individual, preferably the prescriber or a pharmacist, prior to administration.[1] If a drug cannot be administered for any reason the prescriber should be notified.[13] Prior to each medication administration: patient identity is verified/double-checked (e.g., via wristband); medication to be administered is verified against the patient's prescription at the point of administration process. The label should be read and reread at each stage.[1,13;14]		X	X	
	Clear, written protocols of the dose ranges of medicines commonly prescribed for seriously ill patients in critical care situations should be in place. These protocols should include standardised dilutions for use in infusion devices.[13] Infusion rate charts or validated computer programmes to aid calculation should be available for use in paediatric units, particularly for potent medicines such as digoxin or opiates.[13] When standard drug concentrations or dosage charts are not available, dosage calculations, flow rates, and other mathematical calculations should be checked by a second individual (e.g., another nurse or a pharmacist).[1] Particular attention should be paid to confirming the accuracy of complex dose calculations.[13]	X	X		X

Safety objectives	Safe practices	Settings		Classes	
		Amb	Hosp	Std	Best
Safer monitoring of medicine therapy	Pharmacists give a valuable contribution by participating in the medication ordering process and provide clinical pharmacy services. They collaborate with prescribers in clinic and office settings to maximise safe medication use; work in direct collaboration with prescribers and nurses; are "decentralised" to patient care areas in order to participate in patient care rounds, monitor medicine therapy and provide medicine information.[14] Pharmacists collaborate proactively with patients and prescribers to ensure that the goals of therapies are being met.[14] On a regular basis, the pharmacist reviews the patient's profile, assesses potential drug-related problems and discusses problems with the prescriber, if needed. Such review includes an assessment of the following: untreated indications, medication use without an indication, contraindications, improper drug selection, overdose or sub-therapeutic dose, therapeutic duplication, efficacy, adverse drug reactions/toxicity, potential drug interactions, weight changes, appropriate duration of therapy, medication adherence with prescribed regimen, need to contact prescriber before patient's next appointment.[14]	X	X		X
Patient education for a safer medicine therapy Patients are active partners in their care through education about their medicines and ways to avert errors.	Patients must receive ongoing education from physicians, pharmacists and the nursing staff about the brand and generic names of medicines they are receiving, their indications, usual and actual doses, expected and possible adverse effects, drug or food interactions, and how to protect themselves from errors. Patients can play a vital role in preventing medication errors when they have been encouraged to ask questions and seek answers about their medicines before medicines are dispensed at a pharmacy or administered in a hospital. Providers/professionals should encourage patients to maintain a list of current medicines and their intended purpose as well as a list of any medicines to which the patient is allergie or has had idiosyncratic or other untoward reactions.[12]	X	X	X	
Improving medication safety by reducing the risks Change concepts: reduce reliance on memory; simplify; standardise; use constraints and forcing functions; use protocols and checklists wisely; access to information; decrease reliance on vigilance; reduce hand-offs; decrease multiple entry; differentiate: eliminate look-alike and sound alike; automate carefully.[8]					
Improve the safety of drug naming, labelling and packaging	To minimise the possibility of errors with drug products that have similar or confusing manufacturer labelling/packaging and/or drug names that look and/or sound alike, drug manufacturers, the European and the national Drug Agencies are urged to involve pharmacists, nurses, and physicians in decisions about drug names, labelling, and packaging.[1] Drug manufacturers are encouraged to make dosage forms available commercially in unit dose and unit of dispensing containers, ready-to-use or ready-to-administer, to facilitate their appropriate use in all practice settings and their purchasing maximized within the scope of practice needs.[1,13,14]	X	X	X	
Standardise the methods for labelling, packaging, and storing medicines Medicines remain clearly and legibly labelled up to the point of actual drug administration.	Standardise the methods for labelling, packaging, and storing medicines in the institution. They should include, at a minimum, requirements for : labelling of all medicines until they are administered to the patient; storing medicines with similar names, labels or packages in separates locations, and ensuring compliance with policies and procedures for medication labelling, packaging, and storage.[12,13] To the greatest extent possible, all products should be available in single unit or unit dose packages, with following labelling requirements on each dose: nonproprietary name (and proprietary name if to be shown); dosage form (if special or other than oral); strength; strength of dose; expiration date; control of lot number.[1,2,12,14]		X	X	
Standardise the use of high alert medicines	Explicit organisational policies and procedures should be in place for the management of "high alert" medicines, products that have commonly been involved in serious medication errors or whose margin of safety is narrow, such as concentrated forms of drug products that are intended to be diluted into larger volumes (e.g., intravenous adrenergic agonists and antagonists, chemotherapy agents, anticoagulants and anti-thrombotics, concentrated parenteral electrolytes, general anesthetics, neuromuscular blockers, insulin and oral hypoglycemics, narcotics and opiates).[12,14] Develop special procedures for high-risk medicines using a multi-disciplinary approach. These include written protocols, guidelines, dosing scales, checklists, pre-printed orders, double-checks, special packaging, special labelling, and education.[10,12] Infusions of 'high risk' medicines should, where possible, not be prepared at ward level, i.e., they should be purchased or prepared centrally by pharmacy.[13,14]		X	X	
Standardise medication device acquisition, use and monitoring	The potential for human error is mitigated through careful procurement, maintenance, use, and standardisation of devices used to prepare and deliver medicines.		X	X	

Safety objectives	Safe practices	Settings		Classes	
		Amb	Hosp	Std	Best
Minimise the risk for errors in communicating medication orders Methods of communicating medicine orders and other medicine information are standardised and automated to minimise the risk for error.	Drug orders should be complete, unambiguous and legible. They should include patient name, patient allergies, generic drug name, trademarked name (if a specific product is required), route and site of administration, dosage form, dose, strength, quantity, frequency of administration, prescriber's name and date. In some cases, a dilution, rate, and time of administration should be specified. Specify exact dosage strengths (such as milligrams) rather than dosage form units (such as one tablet or one vial). An exception would be combination drug products, for which the number of dosage form units should be specified.[1,14] Weight and date of birth are provided with all pediatric (e.g., neonate, infant, toddler) prescriptions[14] and, where the dose is weight dependent, the child's weight and the intended dose in mg/kg.[13] Expected duration of therapy is included on all antimicrobial orders.[14]	X	X	X	
	Transcriptions of drug or prescription orders should be avoided to the extend possible and should be recognised as prime opportunities of errors. The original source documents (e.g., laboratory reports or medication administration records) should be in the transcriber's immediate possession and be visible when it is necessary to transcribe information from one document to another.[12] Patient care summaries or other similar records should not be prepared from memory.[12]	X	X	X	
Minimise the risk for errors in communicating at the interfaces between health care levels	There should be a structured process for review of patients' medication on admission and discharge from hospital: pharmacists should be available to participate in reviews.[13] A complete an accurate list of medicines is compiled by the inpatient facility at admission and discharge to assure proper continuity of care.[14] A systematic approach to reconciling medicines at admission is adopted[10], and a pharmacist gathers a medication history from each new patient and documents this information in the patient profile.[14] Pharmacists are involved in planning for transitions in level of care (e.g., hospital or nursing home admission and discharge).[14]		X		X
Manage patient information Essential patient information is obtained, readily available in useful form, and considered when prescribing, dispensing, and administering medicines.	Relevant patient-specific information is readily available to prescribers, nurses, pharmacists and other health care providers caring for the patient, including[14]: • medication history and patient's list of medicines reviewed with the patient at every encounter.[12]; • adverse drug events (allergy status information)[13]; • laboratory results and reports, patient assessment findings, health screening results ; • medicine therapy notes, complications, other patient-specific findings, including those discovered by other health care providers ; • the best way to contact the patient (e.g., phone, e-mail, fax, care manager, case worker) Critical patient information such as allergies (including description of reaction), height and weight, kidney function, are prominently displayed on every patient medical record/profile.[13,14]	X	X	X	
Manage medicine information Essential medicine information is readily available in useful form and considered when ordering, dispensing, and administering medicines.	Adequate, complete and up to-date medicine information resources are available for all health care providers involved in the drug use process[1,3,13], who should have ready access : - to therapeutic guidelines and pathways, especially for complex or potentially toxic treatments, for prescribers ; - to appropriate reference sources to support safe administration, including local medicine information departments, for nurses. Medicines information services provided by pharmacy departments, ensure that sufficient, easily accessible information is available for nurses and doctors[13] and maintain the most recent drug reference information; regularly removing from use outdated references.[14]	X	X	X	
	Information on new medicines, infrequently used medicines, and non-formulary medicines should be made easily accessible to clinicians prior to ordering, dispensing, and administering medicines (e.g., have pharmacist round with doctors and nurses; distribute newsletters and drug summary sheets; use computer aids, and access to the physician desk reference, formularies, and other resources).[10]	X	X		X

Safety objectives	Safe practices	Settings		Classes	
		Amb	Hosp	Std	Best
Implement computer prescribing or computer physician order entry (CPOE) Electronic prescribing systems, linked to the patient record, may reduce the risk of many prescribing errors.	Electronic prescribing systems or computerised prescriber order entry (CPOE) systems should always be used[6,12,13] or implemented when technically and financially feasible in light of a hospital's existing resources and technological development.[10] Prescribers should enter medication orders using an information management system that:[12,14] - is linked to prescribing error prevention software, including dose range checks, maximum dose alerts, pediatric dosing based on weight, drug interactions and compatibilities checks; - distinguishes between different doses of the same medication used for multiple indications, including off-label uses; - requires prescribers to document the reasons for any override of an error prevention notice; - permits the notation in one place of all pertinent clinical information about the patient, including allergies, pertinent laboratory values rewieved prior to proceeding with select medication orders, proposing specific laboratory tests related to specific drug therapies; - transfers prescription orders directly to pharmacies and enables the review of all new orders by a pharmacist before admlnlstratlon of the first dose of the medlcatlon; and - internally and automatically checks the performance of the information system.	X	X		X
Use machine readablecoding technology	Bar-coding technology and a standard bar-coding system for medicines should be developed.[12,13,14]		X		X
	Use of automated ward cabinets systems only where appropriate (e.g. narcotics). Their conditions of use must be defined in accordance with patient safety. Cabinets utilise a profile-dispense function with predetermined override capabilities.[14]		X		X
	Consider the use of machine readablecoding (i.e. bar coding) in the medication administration process.[10,14] Making available at the point of administration pertinent patient- and medication specific information and instructions entered into the pharmacy/hospital computer system, point-of-care barcode scanning technology is used to: include real-time systems integration from the point of medication order entry through patient administration; interface with the pharmacy computer system, allowing the nurse to view and access only those medicines which have been ordered for the specific patient; verifiy nurse, patient, and medication identity prior to medication administration; prompt the nurse to record pertinent information before administration may be documented; alert nurses to missed doses; warn staff when a medication is about to be given in error; force the user to confirm his or her intention whenever medicines are accessed or administration is attempted outside of the scheduled administration time. Such events are signaled visibly or audibly for the user, and all such events are documented electronically and reported daily for follow-up.[14]		X		X
Consider environmental factors	Medications are stored, prescribed, transcribed, prepared, dispensed, and administered in a physical environment reflecting careful consideration of the principles of human factors engineering so that space, airflow, moisture, temperature, and lighting are appropriate; fatigue distractions and noise are minimized; and infection control is provided.[3,14] The environment for prescribing and dispensing should take the factors that predispose to error into account and minimise distractions. Resources, both facilities and staff, should be appropriate for the workload.[13]	X	X		X

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