EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

6 May 2013
EMA/144458/2013
Patient Health Protection

Medication-errors workshop

Workshop report

28 February – 1 March 2013
European Medicines Agency, London, United Kingdom

7 Westferry Circus ● Canary Wharf ● London E14 4HB ● United Kingdom
Telephone +44 (0)20 7418 8400 **Facsimile** +44 (0)20 7418 8416
E-mail info@ema.europa.eu **Website** www.ema.europa.eu

An agency of the European Union

© European Medicines Agency, 2013. Reproduction is authorised provided the source is acknowledged.

Tackling medication errors: European Medicines Agency workshop calls for coordinated EU approach

Proposals to improve reporting and prevention of medication errors are made

Executive summary

Medication errors cause a large number of adverse drug reactions (ADR) with negative patient health outcomes each year and are a major public-health burden representing 18.7–56% of all adverse drug events among hospital patients[1]. A medication error as per Good Pharmacovigilance Practices (GVP) refers to any unintended error in the prescribing, dispensing or administration of a medicinal product while in the control of the healthcare professional, patient or consumer. Medication errors do not always lead to ADRs but if they do they may cause harm and are considered preventable.

Several activities are on-going or have recently been reported at European and international level to address medication errors[2,3]. In order to recognise medication errors as an important public health issue, the European Medicines Agency (EMA) organised a workshop on 28 February and 1 March 2013. 240 participants attended the workshop representing various stakeholder groups, including regulators, national patient safety agencies, patient and healthcare professional representatives, academia and the pharmaceutical industry. The primary objective was to raise awareness among the stakeholders involved in the reporting, evaluation and prevention of medication errors of the new legal provisions at EU level with the aim to facilitate their implementation. The workshop was broadcast live and a recording is available here.

The workshop was divided into six sessions covering the assessment of the potential for medication errors during drug development and in the post-authorisation phase by industry and regulators, experience with medication error reporting at the level of the regulators and national patient safety authorities and the regulatory tools for managing the risk of medication errors and the implementation of preventive measures by different stakeholders. In the last session a panel of experts representing the various stakeholders discussed and summarised the key findings and recommendations of the workshop.

The workshop highlighted that despite on-going efforts of various stakeholders in reporting, evaluating and preventing medication errors, medication errors can have serious impacts on patient safety especially in populations at risk such as older people and children. The systematic assessment of the potential for medication errors during the development of a medicine and after its authorisation is therefore critically important. Since July 2012, the EU pharmacovigilance legislation [Directive 2001/83/EC, Recital (5) and (17), Article 1(11) and 101(1)] explicitly includes medication errors in the definition of a reportable ADR and offers an opportunity for the surveillance of medicines. The workshop emphasised current preventive actions at the level of medicines regulators including routine risk minimisation measures addressing the risks of error associated with the invented name, labelling

[1] Creation of a better medication safety culture in Europe: Building up safe medication practices. Council of Europe Expert Group on Safe Medication Practices (2006).
[2] Reporting and learning systems for Medication Errors: detecting, analysing and preventing within Pharmacovigilance centres. Draft report of the FP7 funded project 'Monitoring Medicines'. WHO Monitoring Centre Uppsala, Sweden (2012).
[3] Pharmaceutical Care – Policies and Practices for a Safer, More Responsible and Cost-effective Health System. European Directorate for the Quality of Medicines & HealthCare of the Council of Europe (2012): http://www.edqm.eu/site/policies_and_practices_for_a_safer_more_responsiblpdf-en-31003-2.html

and packaging as well as additional risk minimisation measures such as educational programmes for patients and healthcare providers. Methods used by the pharmaceutical industry to assess the potential for errors were described which include failure mode and effects analysis (FMEA) and simulated user testing.

The workshop underlined several shortcomings in existing pharmacovigilance systems. The lack of an operational definition of a medication error makes a common approach to reporting, detection, classification and prevention of medication errors difficult. Shortcomings in coding terminologies to capture medication errors can lead to difficulties in identifying medication errors from spontaneously reported suspected adverse reaction reports through signal detection activities. The workshop highlighted the complexity of tackling medication errors since different organisations are involved in the collection of reports of adverse drug reactions and medication errors, and information on medication errors not resulting in harm (‘near misses') is currently not captured through pharmacovigilance systems. The value of reports of near misses was emphasised and there was consensus that the current systems need to be adapted to fully capture comprehensive information and to optimise the surveillance of medicines in respect of medication errors. In order to tackle medication errors earlier sharing and pooling of information with other stakeholders is important. This requires closer collaboration between national patient safety authorities, national competent authorities, the EMA, and the European Commission. Article 107a (5) of Directive 2001/83/EC explicitly foresees liaison between national authorities for medicines and national patient safety organisations to improve public health. In addition, experiences from national reporting systems show that there is a need to improve spontaneous reporting of medication errors by patients and healthcare professionals by further engaging them. In this respect legal implications of reporting systems will have to be addressed.

This event which brought together the different stakeholders involved in healthcare offered an excellent opportunity to gather available expertise in the field and to take stock of current best practice. The workshop led to concrete recommendations which are detailed at the end of this report (page 13: The way forward). These include the development of best practices across the EU for the reporting, evaluation and prevention of medication errors, the need for sharing information between national patient safety authorities, national regulators and the EMA and the development of new methods to identify medication errors earlier. Active engagement and capacity building with patients and healthcare providers and research into safe medication practice should be priorities. The Agency in collaboration with the European Commission and the EU regulatory network will develop an implementation plan and carefully prioritise actions proposed during the workshop (see annex) taking into consideration the potential benefit for public health and the resource implications at Member States and EU level.

Good pharmacovigilance practices (GVP)

Adverse reaction definition in GVP Module VI: A response to a medicinal product which is noxious and unintended [Directive 2001/83/EC]. This includes adverse reactions which arise from:

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

Member States should operate a pharmacovigilance system to collect information that is useful for the monitoring of medicinal products, including information on suspected adverse reactions arising from use of a medicinal product within the terms of the marketing authorisation as well as from use outside the terms of the marketing authorisation, including overdose, misuse, abuse and medication errors, and suspected adverse reactions associated with occupational exposure [Directive 2010/84 (EC) Recital (17)].

For the purpose of risk-management and adverse-reaction reporting GVP Modules V and VI refer to medication error as "any unintentional error in the prescribing, dispensing, or administration of a medicinal product while in the control of the healthcare professional, patient or consumer".

The new legal provisions present the opportunity for national and European collaboration to reduce the burden of harm from medication errors.

Introduction

After the workshop was opened by Professor Guido Rasi, Executive Director of the EMA, Dr Peter Arlett, Head of Pharmacovigilance and Risk Management Sector, set out the goals of the meeting. The primary objective was to raise awareness among stakeholders involved in the reporting, evaluation and prevention of medication errors with the aim to facilitate the implementation of the new legal provisions at EU level through the following secondary objectives:

- Clarification and common understanding of what constitutes a medication error and the new legal requirements for reporting cases of medication error at EU level.
- Better understanding of how medication errors are managed at national level.
- Sharing best practice for the prevention of medication errors.
- Proposals to improve stakeholder co-operation at national and international level.

Opening Session: Public-health burden of medication errors and how this might be addressed through the EU pharmacovigilance system

Dr David Cousins, Associate Director of the NHS Commissioning Board, described the impact of medication errors on patient safety and the adverse events they may cause. In order to improve patient safety and prevent medication errors a complex system-wide effort is required, involving a range of actions to improve performance, environmental safety and risk management, including infection control, safe use of medicines, equipment safety, safe clinical practice and safe environment of care. Pharmacovigilance systems in the Member States and the EU can help to minimise harm from medicines by adopting lessons from the discipline of patient safety:

- Broader view of patient safety, not only focused on the medicinal product;
- Greater understanding how medicines are used in practice, including human factors;
- Categories and methods for reporting and learning systems that are wider and more widely applicable;
- New methods to identify and communicate risks and solutions, and to implement and sustain safer medication practice;
- Better use of risk-management planning;
- Better use of technology in prescribing and dispensing systems (e.g. bar codes).

Session: Medication errors in the product lifecycle and special populations

When considering medication errors a common understanding is paramount. Dr Jeffrey Aronson, University of Oxford, explained how the lack of a universally accepted definition has complicated the study of medication errors and their causes. A critical analysis of published definitions of medication error revealed several shortcomings. Definitions are for the most part either circular (e.g. defining a medication error as "an error in the medication process") or based on an assessment of preventability, despite the fact that not all errors are preventable and not all preventable events are errors. Dr Aronson proposed for further discussion a definition that overcomes the problems raised:

"A failure in the treatment process, whether through omission or commission, that leads to, or has the potential to lead to, harm to the patient."

This definition which has been adopted by the Australian Commission on Safety and Quality in Health Care implies that the treatment process has fallen below some attainable benchmark in relation to therapy, prevention, investigation of the condition and that the error does not have to result in harm. The definition has additional notes, intended to enable it to be used uniformly in identifying medication errors in practice. The definition should be tested, using large numbers of real cases.

Professor Andrea Laslop, from the Austrian Agency for Health & Food Safety, gave an overview of the draft EMA CHMP position paper on medication errors in the context of benefit-risk balance[4]. The paper addresses the risk of medication errors that can arise where a newly introduced medicinal product could potentially be mistaken for an already established product containing the same active substance or similar in some other attributes such as appearance and/or name, but different in strength, dosing or route of administration. The position paper provides guidance on how the benefits of such products should be weighed against their risks and how the risk of medication errors can be adequately addressed. It is proposed that the assessment should include a comparison with existing products on the market with respect to the risk of medication errors and should focus on medicines with a narrow therapeutic index and/or use in special populations. Prior to authorisation the applicant should demonstrate that the benefits clearly outweigh the potential product-associated risk of medication error. This will be assessed and confirmed by the CHMP based on a comprehensive case-by-case benefit-risk evaluation. Applicants are advised to collaborate early with the competent authorities when considering the development and submission of an application involving a product that will lead to changes in already established clinical practice.

The industry perspective on the evaluation, classification and management of medication errors during the different stages of product development was explored by Ms Elizabeth Swain representing the European Federation of Pharmaceutical Industries and Associations (EFPIA). By conducting failure mode and effects analysis during the pre-authorisation phase, issues related to the invented name, presentation, labelling, users of the product, translation into Braille, accidental ingestion by children etc. may be detected. Any risks identified are then addressed with appropriate risk minimisation measures in the risk-management plan (RMP). In the post-authorisation period the potential for medication errors is monitored through the collection of spontaneous reports of medication errors which may or may not include details of clinical consequences. It was highlighted that the detection of safety signals is challenging due to problems of categorising medication errors appropriately in safety databases. Ms Swain recommended a number of initiatives to improve the way medication errors could be defined, detected and reported:

- Agreeing on a clear definition of what constitutes a medication error;
- Improving the granularity of the Medical Dictionary for Drug Regulatory Activities (MedDRA) terminology used for coding reports of medication error;
- Improving the rate of reporting of medication errors and collation of reports to a single database applying a non-punitive approach;
- Giving access to this database to stakeholders including industry to detect signals of medication errors earlier;

Professor Ian Wong of the University of Hong Kong described the incidence and nature of medication errors in the paediatric population. Similarly to what can be seen in adults, the incidence rate of medication errors in the medical literature is very variable in the paediatric population depending on the study design. Most studies show dosing errors as the most common type of error. The paediatric population is at an increased risk due to specific risk factors such as the need for individualised doses

4 Position Paper on potential medication errors in the context of benefit risk balance and risk minimisation measures (EMA/274183/2012), draft under consultation, CHMP (2012). http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2012/06/WC500128054.pdf

depending on age, weight and body surface area. Other factors include age-related weight increase over time, inadequate information in the Summary of Product Characteristics (SmPC) and the package leaflet and the lack of appropriate paediatric formulations. The risk of medication errors is particularly high in specific paediatric groups such as neonates, in circumstances where specific drug combinations and formulations are used, or where untrained healthcare workers are involved, and in transitions of care such as admission and discharge. There is an urgent need to reduce medication errors in children and in this respect the Global Research in Paediatrics (GRiP) Network of Excellence offers an opportunity to stimulate and facilitate the development and safe use of paediatric medicines.

Dr O'Mahony of Cork University Hospital, Ireland, gave an overview of common medication errors in older people and measures to reduce them. Older people are susceptible to a variety of medication errors including prescription errors, medication reconciliation problems, poor adherence and increased susceptibility to ADRs. Multiple morbidities in older people lead to an increased likelihood of polypharmacy which is a powerful predictor of inappropriate prescribing and ADRs in this patient group. Research is emerging which indicates that specific interventions focused on the detection and correction of inappropriate prescribing and ADRs such as the use of criteria to screen for older persons potentially receiving inappropriate prescriptions (STOPP) and to alert doctors to necessary treatments (START), as well as structured pharmacist-led medication review help to reduce the incidence of ADRs in older people. Dr O'Mahony concluded that strategies for minimising medication errors in older people require co-ordinated, integrated efforts of prescribers and pharmacists, and further research is needed on structured software-systems enabling effective and efficient pharmacotherapy optimisation.

Session: Reporting

In this session Mr Mick Foy from the UK Medicines and Healthcare products Regulatory Agency (MHRA) described how medication errors are reported at national level in the UK. With the new pharmacovigilance legislation the definition of an ADR has been broadened and now requires pharmacovigilance systems to capture new safety information including data from medication errors resulting in harm. National reporting systems can be complex with different organisations involved in the collection of ADR and medication error reports. This creates challenges for the assessment of reports by national competent authorities and for reporters sending reports to the appropriate organisation. It is therefore necessary that data sharing arrangements between these organisations are in place. National competent authorities should always receive reports of ADRs which may or may not involve medications errors and patient safety authorities should receive reports on medication errors including those where no harm was incurred (near misses). Mr Foy concluded that there is a need for national competent authorities to raise awareness among stakeholders for reporting of ADRs, including medication errors.

Dr María José Otero from the Institute for Safe Medication Practices (ISMP), Spain, gave a brief overview of the experience from national patient safety organisations, in particular the National Medication Error Reporting and Learning System that ISMP-Spain which operates with the support of the Spanish Ministry of Health. It was highlighted that as most errors collected by the medication error reporting systems are practice related, it is important that the analysis is performed by experts aware of the procedures and practices related to the medication-use system, in order to properly understand the reports and develop adequate solutions. The presentation outlined how ISMP-Spain collaborates with the Spanish Agency of Medicines and Health Products and the Spanish Pharmacovigilance System by sharing reports of medication errors and allowing for appropriate and timely resolution of safety issues as soon as they are detected. Collaborative efforts are also made at international level with the International Medication Safety Network (IMSN). Hence, the new EU pharmacovigilance legislation should reinforce existing collaborative work to make medication use systems safer for patients. This collaboration should be extended to include the development and implementation of practical solutions.

In addition, there is a need to establish homogeneous criteria for the process of sharing information between medication safety and pharmacovigilance systems.

From a patient and consumer perspective Ms Kaisa Immonen-Charalambous, Senior Policy Adviser at the European Patients' Forum, took stock of patient medication error reporting and guidance issued to patients to stimulate reporting. The added value of spontaneous reporting by patients and consumers for pharmacovigilance was highlighted. Although patient reporting is an expression of patient empowerment, patient involvement in the implementation of EU rules at national level has been so far limited. A number of critical success factors to stimulate patient reporting were highlighted: clarity about what to report and how; accessibility of the reporting system through various media; existence of a feedback mechanism to encourage further engagement; achieving wide public awareness of the importance of patient reporting through media attention, ensuring that information to patients is tailored to their needs and health literacy levels; engaging patient organisations at national level in awareness campaigns and evaluating reporting systems. Ms Immonen-Charalambous also recommended user testing the existing tools and carrying out an EU wide study of the implementation of patient reporting.

Professor Carlos Maria Romeo-Casabona of the University of Deusto and the University of the Basque Country, Spain, explored the legal consequences healthcare professionals may expect when engaging with reporting systems. Cultural biases and corporate culture could prevent successful implementation of ADR reporting systems at national level. Directive 2001/83/EC provides the essential legal framework for reporting medication errors, but is silent on liability aspects. Any reporting system should be linked to improvement in the quality of healthcare services and should be separate from legal proceedings. Reporting systems should be non-punitive, voluntary and confidential and set up with the aim to promote learning and to prevent harm. The role of anonymity in some medication error reporting systems was noted. There are challenges in terms of separating the process of reporting incidents from disciplinary procedures and legal provisions should be introduced to guarantee the indemnity of the reporter.

Dr Thomas Goedecke of the European Medicines Agency provided an operational definition of medication errors in the context of the reporting requirements to EudraVigilance, the EU system for monitoring the safety of medicines through suspected ADR reports. As required by the new pharmacovigilance legislation and described in GVP Module VI on management and reporting of adverse reactions to medicinal products, for reports of medication errors associated with ADRs the normal reporting rules for individual case safety reports (ICRSs) apply. For serious cases a 15 day reporting timeline and for non-serious cases a 90 day reporting timeline applies to national competent authorities and the pharmaceutical industry. Besides an identifiable reporter and patient the criteria for a valid ICSR include at least one MedDRA term describing the medication error, at least one suspected adverse reaction with a possible causal relationship and a suspected medicinal product (or substance). Medication errors not associated with an adverse reaction should be considered in the Periodic Safety Update Reports (PSUR) prepared by pharmaceutical companies and in addition notified as an emerging safety issue if there is an impact on the benefit-risk balance of the product concerned.

Dr Sabine Brosch of the European Medicines Agency introduced MedDRA for coding case reports resulting in harm with a focus on the latest guidance and examples elaborated by the MedDRA Points to Consider Working Group in relation to medication errors. The guidance recommends that for medication errors with clinical consequences MedDRA terms for both the medication error and the clinical consequences should be selected. Although medication errors without clinical consequences are not considered ADRs, it is important to record their occurrence. The MedDRA term which is closest to the description of the medication error reported should be used for coding. Dr Brosch also addressed the coding of medication errors in the context of labelled interactions and highlighted that a medication error should never be inferred and that it is important to distinguish between product quality issues

and medication errors. Finally Dr Brosch gave an overview of medication errors reported to EudraVigilance since 1995. The data grouped in accordance with the proposed World Health Organisation (WHO) classification showed that medication errors affect all stages of medication practice, and are especially frequent during the drug administration phase and mostly related to wrong drug administration, wrong technique, drug omissions and treatment non-compliance.

Session: Analysis of medication errors resulting in harm

Mr Phil Tregunno, from the UK MHRA, opened the session on the analysis of medication errors with an overview of the experience at the MHRA of reporting medication errors in the pharmacovigilance database. The presentation highlighted that automated methods are often employed for the analysis of large datasets, making accurate coding essential. Medication errors are identified from spontaneous data through signal detection using disproportionality analysis of MedDRA terms and through the analysis of individual 'alert terms'. However, often medication errors are identified outside the scope of these routine monitoring tools through case reviews based on different criteria. The presentation highlighted the difficulties in coding certain medication error events, the need for consistent coding conventions and involving multidisciplinary teams with experience in healthcare delivery in the safety signal management process.

Dr Almath Spooner, from the Irish Medicines Board, provided a regulatory perspective on the identification of preventable ADRs. She focused on the efforts made to ensure that risks are promptly detected and minimised in order to prevent harm from ADRs. The new pharmacovigilance legislation foresees a regulatory evolution that seeks to go beyond a narrow paradigm of 'product regulation' and towards the more inclusive concept of supporting safe and effective use of medicines in practice. This requires a lifecycle approach to monitoring the benefits and risks of medicines in everyday clinical practice. In her view, efforts need to be collective and all stakeholders must strive to minimise the burden of adverse reactions. There is an increased recognition of the need to engage patients and healthcare professionals in the various aspects of pharmacovigilance and risk-management processes ranging from data collection to the implementation of risk minimisation measures. Dr Spooner underlined that risk-management planning through the EU-RMP currently provides the framework for adequate risk characterisation and effective risk minimisation. The new pharmacovigilance legislation additionally seeks to strengthen the link between safety assessment and informed regulatory action. Dr Spooner concluded that the effectiveness of risk minimisation strategies in real life situations needs to be measured and strategies adapted accordingly to ensure that measures are effective, sustainable and proportionate. This also includes assessing how risk minimisation strategies are communicated and disseminated to healthcare providers and patients.

Dr David Cousins, from the NHS Commissioning Board, gave an overview of how patient safety incidents are assessed in healthcare settings. He discussed how incidents have to be considered in the context of the clinical setting where they occurred and in the wider context of patient care. Individual practitioners should not only report incidents to the regulatory authorities but also have a duty to report these locally as part of clinical governance in order to allow for local actions and learning within the healthcare provider organisation, via its governance structures. Root-cause analysis (RCA), a method used to identify the root causes and key learning from serious incidents can help to significantly reduce the likelihood of future incidents. All contributing factors including those associated with patients, staff, environment, organisation and external factors should be identified when conducting RCA. The basic elements of RCA include the assessment of what happened, how it happened and why it happened. Dr Cousins also referred to the conceptual framework for International Classification For Patient Safety (ICPS)[5], one of the key initiatives of the WHO World

5 Conceptual Framework for the International Classification for Patient Safety, Technical Report Version 1.1, WHO World Alliance for Patient Safety (2009) http://www.who.int/patientsafety/implementation/taxonomy/icps_technical_report_en.pdf

Alliance for Patient Safety, designed to provide a method of organising patient safety data and information so that it can be aggregated and analysed in order to:

- Compare patient safety data across disciplines, between organisations, and across time and borders;
- Examine the roles of system and human factors in patient safety;
- Identify potential patient safety issues;
- Develop priorities and safety solutions.

He argued that RCA and inclusion of some ICPS terms in pharmacovigilance classification systems will assist to broaden the role of EU pharmacovigilance to include medication error reporting and learning.

Session: Regulatory tools for managing the risk of medication errors

Speaking on behalf of the Danish Society for Patient Safety, Dr Annemarie Hellebek shared her experience on medication errors resulting from medicine name confusion. This type of error can be classified into phonetic (sound-alike), orthographic (look-alike) and cognitive errors. The risk of errors may be increased by similarity in sounds or letters. Common sources of errors are long names, suffixes, the inclusion of tall letters in names and the existence of national and centralised procedures for approval of invented names and suffixes. Dr Hellebek also explained the difficulties in differentiating strengths and forms of medicines through variation of specific suffixes indicating prolonged effects or strengths referring either to the pro-drug or active ingredient. She highlighted the work undertaken by the EMA Name Review Group and the EMA guideline for invented names and pointed out that generic product names using common stems may also cause name confusion. Dr Hellebek concluded her presentation by explaining a national initiative to improve medication safety by changing the layout and design of medicines' labels.

Mrs Jan MacDonald from the UK MHRA provided the regulatory perspective of how labelling and packaging of medicines could contribute to medication errors. The primary purpose of labelling is the clear and unambiguous identification of the medicine and the conditions for safe use. There is no substitute for reading the label, but certain pieces of information on the label are critical to ensure the safe use of a medicine. These include the name of the medicinal product (followed by common name), strength, route of administration, and occasionally the posology and warnings. All information must be presented in a legible manner that is easily understood by all users. Innovative pack design and the judicious use of colour can improve patient safety and reduce the likelihood of error. Mrs MacDonald discussed initiatives using these principles which have been taken in the UK to improve pack design and to reduce the likelihood of medication errors. She concluded by suggesting that labelling and packaging are global issues and that different organisations should work together to ensure packaging addresses patient safety concerns.

Mr Tony West, from the European Association of Hospital Pharmacists, shared his experience of minimising risk through education of healthcare professionals and patients using a case study from his hospital, where a medication error involving the failure to recognize penicillin allergy resulted in death. He illustrated which questions should be raised during the investigation of medication errors, and which actions should be taken including recommendations to regulators and industry for specific risk minimisation measures. Existing procedures in clinical practice should be reinforced and medicines not prescribed, dispensed or administered without prior checking of patients' medical records and accurate and consistent documentation and follow-up. The primary focus of the presentation was the role of healthcare professionals and how future changes within the EU relating to medicines may help minimise the risk of future incidents. The revision of package information leaflets, risk-management

plans, the mandate of the PRAC, the new falsified medicines directive and the cross-border healthcare directive are all opportunities that need to be further explored to improve the prevention of medication errors.

Dr Laurent Auclert, from Sanofi-Aventis gave an overview of the strategies used by manufacturers during the design of a medicine in particular if combined with a medical device to prevent the risk of medication errors associated with its use. The strategies are based on the observation that medication errors with medical devices mostly result from the interaction between the medical device and the end user. The goal is to design products with minimal risk of error, to decrease the burden on healthcare providers and the need for patient education. Dr Auclert highlighted the initiatives by the FDA in this field with the draft guidance for industry on safety considerations for product design to minimise medication errors. The FDA is recommending proactive risk assessment methods such as failure mode and effects analysis (FMEA) and simulated user testing. Industry suggests using other methods of human factor engineering that test how the actual product is used, such as the perception-cognition-action (PCA) analysis which should be carried out early in development. This should be followed by risk mitigation measures which should be re-tested to ensure their effectiveness.

Dr Sabine Strauss, from the Dutch Medicines Evaluation Board, gave an overview of how health outcomes and patient compliance can be monitored to measure the effectiveness of risk minimisation. She elaborated on the tools available to regulatory authorities to minimise and prevent medication errors in the post-authorisation phase, including for example, amendments to the SmPC, labelling, and communications to health care professionals and patients. She described tools that are used as routine risk minimisation measures and the situations where additional measures are needed. She focused on how the effectiveness of risk minimisation activities can be measured using process and health outcome indicators. Process indicators measure how successful the implementing steps of risk minimisation activities are (e.g. the percentage of healthcare professionals or patients with sufficient knowledge of the risk and the ways to minimise it) and health outcome indicator measure how effective the risk minimisation activities are in accomplishing their intended results under real life conditions (e.g. by directly measuring the occurrence or severity of ADRs).

Session: Implementation of preventive measures

Dr Angeles Alonso, speaking on behalf of the European Society of Cardiology, used her clinical experience in an acute care setting to analyse how medication errors occur and to reinforce the importance of effective communication between healthcare professionals and patients. Factors that influence medication errors are related to the clinical practice setting, patient profile, unclear prescriptions, complex packaging and the poor functioning of the individual or the clinical team. The clinical setting is crucial and the reasons for medication errors usually differ depending on where and why a patient is treated (e.g. emergency department, ward or outpatient clinic). Regarding patient characteristics, age and functional state are important factors influencing medication errors which should be borne in mind by healthcare professionals. The elderly are at high risk of medication errors, as they account for 34% of all written prescriptions. In cardiology, giving information after an acute event can be time-consuming but it is important to communicate effectively with patients and relatives. Around 30% of individuals admitted with an acute cardiac event were otherwise healthy but on discharge from hospital many will leave with at least 5-6 medicines that they need to learn how to use. For patients with chronic conditions particular consideration should be paid to co-morbidities and poly-medication and how this increases the potential for medication errors.

The European Commission's report on Patient Safety was presented by Ms Agnieszka Daval-Cichon. The report was published in November 2012 and analyses patient safety measures implemented by EU Member States further to the Council Recommendation 2009/C 151/01. It shows that patient safety is

being prioritised in public health policies, and sets out areas for future development including greater involvement of patients in patient safety, improved training of healthcare professionals and further development of reporting and learning systems on adverse events. Finally, the report highlighted differences in the number of implemented measures across the EU Member States. The next report is planned for June 2014, and in the meantime EU health ministers will be discussing the development of a guideline on patient safety standards and the European Commission's Working Group on Patient Safety and Quality of Care (PSQCWG) will be focusing its attention on learning and reporting systems.

Dr Dolores Montero, from the Spanish Agency of Medicines and Medical Devices presented the regulatory perspective on the implementation of preventive measures. She described the involvement of PRAC in the assessment of medication errors. This includes the prioritisation and assessment of signals emerging from reported medication errors, the assessment of RMPs where medication errors are identified as a safety concern together with proposed risk minimisation activities and impact assessment, as well as the assessment of PSURs which also reflect data on medication errors from spontaneous reporting and other sources. Dr Montero showed the results of a ten-year retrospective review of safety issues related to medication errors discussed at the EU level. The safety issues were classified according to their root causes, the most frequent cause being the introduction of new strengths, formulations and/or devices of an already marketed medicinal product. Dr Montero concluded by emphasising the need for shared learning by patient safety organisations and regulatory authorities as their work is complementary.

Mr François Houÿez, from the European Organisation for Rare Diseases, discussed in his presentation strategies patients can use to minimise medication errors. As the last person in the medication use cycle the patient can either detect a medication error and take appropriate preventive measures before taking the medicine or make a medication error and potentially suffer harm. He provided several recommendations such as the use of separate medicines cabinets for different household members and introduced sophisticated tools that can help to prevent medication errors (e.g. smart phone applications and websites to identify medicines). Mr Houÿez suggested that their efficacy and convenience should be further explored and guidance provided. He also highlighted the need to improve package design and labelling, to make better use of colour-coding and of shapes of medicines. Working groups comprising regulators, industry, healthcare professionals and patients should discuss medication error issues and propose remedies that have proved to be useful.

Carol Holquist, from the U.S. Food and Drug Administration, shared the trans-Atlantic experience and FDA's current work in developing a set of guidance covering safety considerations for product design[6] and for container labels and carton labelling design as well as best practices in developing proprietary names to minimise medication errors. She also explained how human factors (the end user), the environment of use and the interface for the medicine are taken into consideration in FDA's risk assessment before granting marketing authorisation.

6 Safety Considerations for Product Design to Minimize Medication Errors. Draft guidance under consultation, FDA (2012). http://www.fda.gov/downloads/Drugs/GuidanceComplianceRegulatoryInformation/Guidances/UCM331810.pdf

The way forward – key recommendations

The workshop's objectives to raise awareness amongst stakeholders involved in the reporting, evaluation and prevention of medication errors, and to facilitate the implementation of the new reporting requirements for adverse reactions resulting from medication errors, was achieved. In a panel discussion at the end of the workshop there was broad consensus that medication errors are a global concern and need to be addressed in the broader context of patient safety. Such a vision requires the need for collaboration and synergies to be leveraged with different stakeholders and also calls for action at different levels (international, national, local and individual).

The European Medicines Agency in collaboration with the European Commission has a key role in facilitating the coordination between medicines regulatory authorities in Member States, national pharmacovigilance centres and national patient-safety authorities. The workshop revealed many opportunities to be explored and further developed, and concluded with the following six key recommendations.

Recommendations

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

The annex to this meeting report presents the considerations and suggestions for action raised during the workshop for each of the aforementioned recommendations. These will be carefully considered by the EMA in collaboration with the European Commission and the EU regulatory network. It is envisaged for a prioritised action plan to be made public in Q4 2013.

Abbreviations

ADR	adverse drug reaction
CHMP	Committee for Medicinal Products for Human Use
EC	European Commission
EDQM	European Directorate for the Quality of Medicines & HealthCare
EFPIA	European Federation of Pharmaceutical Industries and Associations
EMA	European Medicines Agency
FDA	United States Food and Drug Administration
FMEA	failure mode effect analysispaediatric
FP7	European Commission's Seventh Framework Programme
GRiP	Global Research in Paediatrics
GVP	good pharmacovigilance practices
ICPS	International Classification for Patient Safety
ICSR	individual case safety report
IMI	Innovative Medicines Initiative, a joint undertaking between the European Union and the pharmaceutical industry association EFPIA
IMSN	International Medication Safety Network
ISMP	Institute for Safe Medication Practices
MedDRA	Medical Dictionary for Drug Regulatory Activities
MedDRA MSSO	MedDRA Maintenance and Support Services Organisation
MHRA	United Kingdom Medicines and Healthcare products Regulatory Agency
PCA	perception-cognition-action analysis
PRAC	Pharmacovigilance Risk Assessment Committee
PSQCWP	European Commission's Patient Safety & Quality of Care Working Group
PSUR	periodic safety update reports
RCA	root-cause analysis
RMP	risk-management plan
SmPC	summary of product characteristics

Annex – proposed actions

The following table presents the considerations and suggestions made during the workshop of how the six key recommendations of the workshop could be taken further. The Agency in collaboration with the European Commission and the EU regulatory network will carefully consider these proposed actions taking into consideration the potential benefit for public health and the resource implications for the EU regulatory network. It is envisaged for a prioritised implementation plan to be made public in Q4 2013.

	Proposed action
1. Harmonisation and further development of terminologies and definitions at EU and international level	
1.1	Propose a common operational definition of medication error to support reporting, classification, analysis and prevention through existing patient safety and pharmacovigilance systems and a testing protocol for that definition.
1.2	Further develop and align MedDRA with International Classification for Patient Safety (ICPS) and WHO Adverse Reaction Terminology (WHO-ART) standards.
1.3	Develop best practice guidance for regulators, patient safety authorities and industry in using terminologies for coding and analysis of cases of medication error.
2. Establishment of collaborative relationships between national patient safety authorities, national regulators, the EMA and the European Commission	
2.1	Launch awareness campaign of the new legal requirement for Member States and industry to report adverse reactions resulting from medication errors including to EudraVigilance.
2.2	Establish standardised criteria for data sharing agreements and operational rules between national patient safety authorities and national pharmacovigilance centres based on good practice examples.
2.3	Foster collaborative work between national patient safety authorities and national pharmacovigilance centres and the EMA to develop and implement preventive measures.
2.4	Propose how information on medication errors not resulting in harm (near misses) could be voluntarily collected, collated and made available (e.g. through EudraVigilance) at EU level for the benefit of public health.
2.5	Develop best practice guidance for anonymisation of patient and health care practitioner data and compliance with EU data protection laws in reporting systems.
2.6	Build trust and encourage reporting at healthcare professional and patient level by communicating to stakeholders how the data is used to minimise medication errors.
2.7	Consider revision of format, content and accessibility of ADR reporting forms to routinely address medication errors in pharmacovigilance reporting systems.
3. Development of new methods to identify medication errors from a patient safety and pharmacovigilance perspective through data pooling and analysis	
3.1	Review how disproportionality analysis and criteria-based methods (alert terms, high risk population groups etc.) could improve the identification of medication errors in pharmacovigilance and patient safety reporting systems.
3.2	Develop a standard MedDRA query to support the detection of medication errors resulting in harm.
3.3	Develop best practice guidance for industry and regulators for pooling and analysis of EudraVigilance data for early detection of adverse reactions that could be preventable (i.e. ADR caused through medication error).

Proposed action	
3.4	Consider medication errors as part of the Agency's transparency measures implemented with the new pharmacovigilance legislation.
3.5	Provide patient safety authorities and regulators with access to key findings from industry's assessment of failure mode and effects analysis (FMEA).
3.6	Develop guidance for industry on how to follow-up reports of medication errors.
4. Systematic assessment and prevention of the risk of medication errors during the product life-cycle including prior the granting of marketing authorisation through the EU risk-management planning process	
4.1	Develop guidance for industry on methods for testing and understanding the risk of medication errors during product development and design.
4.2	Provide patient safety authorities and regulators with access to key findings from industry's assessment including, where appropriate, results of failure mode and effects analysis.
4.3	Review the existing EMA guideline on product name review to minimise name confusions.
4.4	Provide the EMA recommendations about safety considerations in labelling, packaging, product design, devices design, healthcare professional information, etc.
4.5	Expand the scope of scientific guidance for industry on studies monitoring the risk of medication error and measuring the effectiveness of risk minimisation strategies.
4.6	EU risk-management plans to include data on the risk of medication errors pre- and post-authorisation (e.g. in high risk groups, -formulations and -situations) both for medicines and application devices.
4.7	Develop methods to measure the effectiveness of the risk minimisation tools for medication errors, seeking feed-back from patient safety organisations and other stakeholders.
4.8	Develop best practice guidance for industry and regulators on effective medication error prevention based on shared national experience with existing regulatory tools.
4.9	Monitor opportunities from new technologies in prescribing and dispensing systems (smart phone apps, bar–coding, pill identifiers, dispensing labels etc.) to improve safe medication practice.
4.10	Strengthen the link between safety issue detection and effective risk-management building on the role of PRAC.
5. Active engagement and capacity building with patient consumer groups and healthcare professionals to improve safe medication practices	
5.1	Develop ways to better communicate risks and risk-management strategies to healthcare providers, patients and caregivers taking into account root causes and context of healthcare delivery systems.
5.2	Improve education and training of healthcare professionals and patients/caregivers with respect to medication error reporting and prevention (e.g. user testing tools, web based education, etc.).
5.3	Conduct a survey on the implementation of patient reporting systems at national level, and how medication errors are captured. Provide recommendations based on the survey.
6. Support to research into safe medication practices	
6.1	Consider research into safe naming, packaging and labelling, safe medication practices, effectiveness of medication error prevention and the role of new technologies.