

SCOPE Work Package 4 ADR Collection

**Medication
Errors**



SCOPE

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1. Introduction

1.1 Purpose of the document

The purpose of this document is to promote the importance of a uniform approach regarding coding of MEs during the assessment of an Individual Case Safety Report (ICSR), to raise awareness about the importance of inter-institutional collaboration and exchange of information regarding MEs. Also, the intention is to start a discussion regarding HCPs' liability in the context of ADR reporting of cases of MEs.

This document is not intended to be a duplicate of the European Medicines Agency's (EMA) guide regarding MEs, although some recommendations are the same.

1.2 Background

The Strengthening Collaboration for Operating Pharmacovigilance in Europe (SCOPE) Joint Action has been created to support operations of pharmacovigilance (PV) in the European Union (EU) following the requirements introduced by the 2010 European PV legislation^{1,2,3}, which came into force in June 2012. Information and expertise on how regulators in Member States (MSs) run their national PV systems was gained in order to develop and deliver guidance and training in key aspects of PV, with tools, templates and recommendations. The aim of the SCOPE Joint Action was to support consistent approach across the EU network for all PV operations, in order to benefit medicines safety monitoring and communications to safeguard public health.

SCOPE was divided into eight separate Work Packages (WPs), with five WPs focusing on PV topics to deliver specific and measurable objectives, ranging from improvements in Adverse Drug Reaction (ADR) reporting to assessment of quality management systems.

WP4 ADR Collection was focused on national schemes for the spontaneous reporting of ADRs and was aimed to provide National Competent Authorities (NCAs) with a full understanding of and good practices within national systems for collecting ADRs. Information was gathered from European MS institutions to understand their national ADR system, PV IT system capabilities, as well as implementation of patient reporting, types of reporting forms developed, and electronic reporting developments, including those from clinical healthcare systems. This information was used to create best practice guidelines, performance indicators and a media toolkit for raising awareness of ADR reporting systems which will be supported through delivery of a training course for institutions.

¹ Directive 2010/84/EU of the European Parliament and of the Council

² Regulation (EU) No 1235/2010 of the European Parliament and of the Council

³ Commission Implementing Regulation (EU) No 520/2012

1.3 Definitions and abbreviations

Terminology	Description
ADR	Adverse Drug Reaction
AEMPS	Spanish Agency of Medicines and Medical Devices
EU	European Union
CA	Competent Authority
EV	EudraVigilance
EMA	European Medicines Agency
FU	Follow-up
GVP	Guideline on Good Pharmacovigilance Practices
HCP	Healthcare Professional
ISMP	Instituto para el Uso Seguro de los Medicamentos (ES)
ICSR	Individual Case Safety Report
ICPS	International Classification for Patient Safety
MAH	Marketing Authorisation Holder
MedDRA	Medical Dictionary for Regulatory Activities
ME	Medication Error
MERS	Medication Error Reporting System
MS	Member State
MSO	Medication Safety Officer
MTS:PTC	MedDRA Term Selection: Points to Consider
NCA	National Competent Authority
NRLS	National Reporting and Learning System
PSO	Patient Safety Organisation
PSUR	Periodic Safety Update Report
PV	Pharmacovigilance
RMP	Risk Management Plan
PVC	Pharmacovigilance Centre
SCOPE	The Strengthening Collaboration for Operating Pharmacovigilance in Europe
SOP	Standard Operational Procedure
UK	United Kingdom

Terminology	Description
WHO	World Health Organisation
WP	Work Package

2. Medication errors

This document is intended to provide survey findings that were indicative of MSs' practice regarding management of medication errors (MEs), with special focus on coding of MEs, liability of Healthcare Professionals (HCPs) when reporting cases of ME, and collaboration between institutions dealing with MEs (together with examples of good practice).

The aim of the paper is to promote the importance of a uniform approach regarding coding of MEs during the assessment of an Individual Case Safety Report (ICSR), to raise awareness about the importance of inter-institutional collaboration and exchange of information regarding MEs. Also, the intention is to start a discussion regarding HCPs' liability in the context of ADR reporting of cases of MEs.

This document is not intended to be a duplicate of the European Medicines Agency's (EMA) guide regarding MEs, although some recommendations are the same.

Information on the topic of MEs was gathered from EU NCAs through a dedicated the SCOPE Joint Action WP4 ADR Collection survey, which was distributed in June 2014. Participants were asked to provide a description of their practices as they were at the end of 2013.

In general, 28 MSs responded to the questionnaire, which consisted of 16 questions⁴, with the ability to give a positive answer to more than one option for certain questions.

2.1 Coding of medication errors

According to the available literature definitions, code is a series of letters, numbers or symbols assigned to something for the purposes of classification or identification. The same principle is followed when coding the data contained in an ICSR. Through coding of data contained in an ICSR, a uniform approach, understandable to all involved parties, is achieved in order to retrieve, present, analyse and communicate the contained information.

As laid down in the Directive 2010/84/EU amending, as regards PV, Directive 2001/83/EC of the Community code, relating to medicinal products for human use, the term 'adverse reaction' covers noxious and unintended effects resulting not only from authorised use of a medicinal product at normal doses, but also from medication errors and uses outside the terms of the marketing authorisation, including overdose, abuse and misuse and suspected adverse reactions associated with occupational exposure.

⁴ It should be noted that introductory text or section headers appeared as questions in the questionnaire due to the functionality of the survey tool used, although they were not questions as such.

Ferner defined a ME as “*unintended failure in the drug treatment process that leads to, or has the potential to lead to, harm to the patient*”⁵. The Guideline on Good Pharmacovigilance Practices (GVP) Module VI⁶ refers to a ME as any unintentional error in the prescribing, dispensing, or administration of a medicinal product while in the control of the healthcare professional or consumer.

Also, the GVP Module VI addresses legal requirements detailed in the Directive⁷ and Regulation⁸ that are applicable to NCAs, marketing authorisation holders (MAHs) and the EMA with regard to the collection, data management and reporting of suspected ADRs to EudraVigilance (EV)⁹.

Taking all of the above into account, 2010 PV legislation introduced the need for procedures to be put in place by MAHs and NCAs in order to collect and record relevant information regarding MEs.

2.1.1 SCOPE results

Included in the 16 questions in the SCOPE Joint Action WP4 ADR Collection survey was a question asking NCAs when they code ME(s). It was possible to choose multiple answers among the following:

- If specified in ADR report
- When the ADR is reviewed/assessed
- We do not code ME(s)
- Other, please specify
- Our institution is not responsible for this activity (if applicable).

Analysis of gathered results showed that:

- Eighteen out of 28 (18/28) MSs code MEs if specified in the ADR report, as well as during the assessment/review of ADR; in addition, two MSs stated that they are coding only when the ADR is reviewed/assessed (20 MSs in total)
- Seven out of 28 (7/28) MSs code only when it is specified in the report (25 MSs in total)
- One out of 28 (1/28) MSs does not code MEs.

⁵ Ferner RE, Aronson JK (2006). Clarification of terminology in medication errors: definitions and classification. *Drug Saf.*29:1011–22.

⁶ Guideline on good pharmacovigilance practices (GVP) Module VI – Management and reporting of adverse reactions to medicinal products (Rev 1) 6 June 2013 EMA/873138/2011 Rev 1*

⁷ Title IX of Directive 2001/83/EC [DIR]

⁸ Chapter 3 of Regulation (EC) No 726/2004 [REG]

⁹ EudraVigilance (EV) is a data processing network and management system for reporting and evaluating suspected adverse drug reactions (ADRs) during the development, and following the marketing authorisation of medicinal products in the European Economic Area (EEA)

Additionally, three MSs provided some descriptive answers supporting their chosen response.

In order to gain a deeper insight into coding practice, a follow-up (FU) question was sent to nineteen MSs¹⁰ that responded that they code ME(s) during the assessment/review of the ICSR. The FU question aimed to clarify whether they code ME(s) by using one of the Medical Dictionary for Regulatory Activities (MedDRA) terms during the assessment of the ICSR, even if it was not explicitly regarded as a ME by the reporter.

Answers to the FU question were received from 18 MSs, while an answer was not obtained from one (1) MS. Among 18 MSs:

- Eleven (11) stated that they code ME(s) even if it is not specified in the report
- Five (5) stated that they code ME(s) only if it is specified in the report
- Two (2) stated that they code ME(s) into section 'Sender's comment' of the ICSR.

It should be noted that although an explanation for this practice was not gathered through the questionnaire, a possible cause can be assumed based on other received responses, as discussed below.

2.1.3 Discussion

As a part of the Monitoring Medicines project funded by the EU, which was completed in 2012, the World Health Organisation (WHO) published guidance Reporting and learning systems for medication errors: the role of pharmacovigilance centres. This publication intended to strengthen the capacity of national Pharmacovigilance Centres (PVCs) to identify, analyse and issue guidance to prevent or minimise MEs that harm patients and to stimulate cooperation between national PVCs and Patient Safety Organisations (PSOs).

Three years later, in October 2015, the EMA published the Good practice guide on recording, coding, reporting and assessment of medication errors (EMA/762563/2014). The EMA's guide addresses the recording, coding, reporting and assessment of MEs with medicinal products associated with suspected ADR(s) in everyday medicinal practice, but also gives a recommendation regarding cases of ME(s) not associated with an ADR. The guide clearly states that if a NCA or MAH disagrees with the diagnosis reported by the primary source, an alternative diagnosis can be provided in the ICH E2B (R2) data element B.5.3 'Sender's diagnosis/syndrome and/or re-classification of reaction/event' in addition to the reported diagnosis provided in the ICH E2B (R2) section B.2 'Reaction(s)/event(s)'.

¹⁰ Follow-up question was sent to 19 MSs, instead of 20, since one country did not fully participate in SCOPE project

With the introduction of ICH E2B (R3), if a ME is not explicitly reported by the reporter, but information and assessment of case leads to a suspicion that a ME has occurred, the sender may choose to 'flag' the event by populating data element 'Additional information on the drug' (G.k.10.r) at their discretion and/or populate data element 'Sender's diagnosis' (H.3.r.1b).

Both publications provide background and technical guidance on methods for identification and management of ICSRs reporting ME(s) in order to harmonise the process between PV assessors, regardless of whether they belong to NCAs, PVCs or MAHs.

Although the use of MedDRA is embedded in EU PV reporting requirements, in accordance with Directive 2001/83/EC and Regulation (EC) No 726/2004, from gathered data it is clear that the ICH-endorsed guide for MedDRA Users 'MedDRA Term Selection: Points to Consider' (MTS: PTC) was not completely followed by all MSs.

The MTS: PTC document provides guidance on term selection, along with practical examples for ensuring an accurate and consistent approach. Section 3.15.1.4 of the MTS: PTC document clearly states: *"Do not infer that a medication error has occurred unless specific information is provided. This includes inferring that extra dosing, overdose, or underdose has occurred"*. The same principle is supported and emphasised both in the WHO publication and the EMA's guide. It is acknowledged that the EMA's guide was not available to support coding practice in MSs at the time the SCOPE survey was conducted, however, the MTS:PTC document was already in place.

The different practices observed could also be caused by the lack of standard operational procedures (SOPs) in NCAs regarding management of ME cases. When asked whether they have a system in place, i.e. SOPs to support coding, reporting, analysis and prevention of cases of MEs, 18 out of 28 (18/28) MSs responded that they do not have specific SOP(s) in place. Interestingly, when comparing data, there is high overlap between MSs that code ME(s) even if not specified in the ICSR by the reporter and MSs that do not have SOP(s) in place (around 80%).

Different approaches that MSs take are probably in relation to the basic PV principle, 'do not infer an ADR', on one side, and the striving to fulfil the requirements laid down by 2010 PV legislation with regards to MEs on the other side. However, not every MS has put operational procedures in place to support the transition of legislation into everyday practice.

The different coding practices observed could lead to the difference among countries in the number of MEs; it could create additional workload for PV staff, impact the signal detection process and potentially lead to forming an incorrect picture of routine clinical practice. Also, it could lead to potentially unnecessary development of minimisation measures and impact risk communication. It is important to bear in mind that, without the reporter clearly specifying an occurrence of ME and/or performed FU in certain cases, it is hard to distinguish whether a ME has indeed occurred or whether an HCP has intentionally decided to prescribe the medicinal product in an unapproved indication (off-label use) or in a higher/lower dose for example.

2.2 Exemption from liability for HCPs when reporting cases of medication errors (MEs)

MEs are most common single preventable cause of adverse events in medication practice associated with significant public-health burden¹¹. However, reporting cases of MEs is inextricably linked with the question of liability for the error that has been made.

In this section we present data gathered through a questionnaire and discuss only the issue of exemption from liability with the respect to the fulfilment of PV obligations, as described in Title IX of Directive 2001/83/EC. The guidance clearly states that the reporting of MEs by HCPs is not intended, nor should it be interpreted or construed by a MAH, NCA or any other third party as an admission, allegation or claim for potential liability, but for the sole purpose of the PV tasks.

2.2.1 SCOPE results

From the provided responses it was observed that twelve (12) MSs have a system in place, while 10 do not make any exemption from liability for HCPs.

A FU question was sent to these 10 MSs in order to re-examine whether the initial question was properly understood and, if possible, to investigate their understanding of liability. Unfortunately, the responses were received from only five countries and based on their responses it was seen that liability is understood differently. In one MS, liability is understood as overall legal responsibility of making the report available in EV and to other authorities while, in other MSs, HCPs can in some cases be liable for MEs they are responsible for and reporting does not make them exempt from liability.

¹¹ World Alliance for Patient Safety 2010, Creation of a better medication safety culture in Europe: Building up safe medication practices. Council of Europe Expert Group on Safe Medication Practices (2006)

2.2.2 Discussion

The EMA's guide also tackles the issue of the liability of HCPs. The guide suggests inclusion of a 'disclaimer' in the sender's comment data element or the narrative of an ICSR submitted by a MAH to the NCA or to the Agency. A disclaimer is one of possible ways to prevent possible claims that the classification of a suspected adverse reaction as a ME by the MAH implies that the HCP has contributed to the occurrence of ME.

The Malta Medicines Authority took a different approach regarding HCPs' liability. A statement is included in the reporting form indicating that reporters' details will be destroyed following transmission of the ICSR to the EV. Of note, the Malta Medicines Authority decided to collect ME reports that are not associated with an ADR; therefore, a single form was specifically developed to capture information related to ADRs, ADRs caused by ME(s) and MEs related to medicinal products not associated with an ADR, to the highest quality of documentation where the basic elements of a case report are fulfilled¹².

Another approach is that of MERS (Medication Error Reporting System) of the Ministry of Health of Malaysia, which emphasises the importance of learning from reported cases by inclusion of a statement in the online form:

"Dear healthcare providers,

*You can report near misses and actual medication errors here. Please include as much details as possible. Thank you for sharing information so that others can learn from the experience."*¹³

Although the proposed approaches can be endorsed, we are of the opinion that more needs to be done in order to achieve a more harmonised approach that protects HCPs from potential liability claims in relation to reporting MEs for PV purposes throughout the EU. The approach should take into account the organisational environment and culture in which the HCP operates – healthcare systems and the way errors are handled in general. This is particularly important given that MSs have different understandings of HCPs' liability in the context of ADR reporting.

¹² A. Tanti, A. Serracino-Inglott and J.J. Borg Designing a national combined reporting form for adverse drug reactions and medication errors, Eastern Mediterranean Health Journal Vol. 21 No. 4, 2015

¹³ <http://mers.moh.gov.my/MERS/>

2.2.3 Safety culture and medication errors

When it comes to healthcare systems and their response to MEs and errors in general, they underwent major transformation throughout the world – from being a punitive culture, where the prevailing understanding was that individual workers were fully, and sometimes solely, accountable for the outcomes of patients under their care, even if the underlying processes for achieving those outcomes were not under their direct control¹⁴, to the culture of safety characterised by leadership commitment to safety, open communication founded on trust, organisational learning, a non-punitive approach to event reporting and analysis, teamwork and shared belief in the importance of safety.¹⁵

Organisations with an established safety culture are creating blame-free environments where individuals are able to report errors or near misses without fear of reprimand or punishment.

Based on available data, examples of such systems can be found in Netherlands, France and the United Kingdom (UK). But, perhaps the clearest example of such a system can be found in Denmark. The Danish ‘Act on Patient Safety’ states that *“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). It should be noted that, although the SCOPE survey wasn’t designed to capture data about the number of ADR reports caused by MEs, it was interesting to observe that in fact Denmark has the highest number of ADR reports in general per million inhabitants for the period between 2009 and 2013.

Recognition that a blame-free environment leads to more reporting of MEs, improved patient safety and even reduced health expenditures¹⁶, received broad political backing. A statement from the Council of the European Union on patient safety (Recommendation 2009/C 151/01, 9 June 2009) stipulates that healthcare workers should be encouraged to actively report through the establishment of a reporting environment that is open, fair and non-punitive, and which is differentiated from MSs’ disciplinary systems and procedures for healthcare workers; moreover, where necessary, the legal issues surrounding the healthcare workers’ liability should be clarified.

¹⁴ Our long journey towards a safety-minded Just Culture, Part I: Where we’ve been, From the September 7, 2006 issue, ISMP Medication Safety Alert

¹⁵ Safety Culture in Healthcare: A review of concepts, dimensions, measures and progress; Michelle Halligan, MSc

¹⁶ Health Policy. 2015 Mar;119(3):367-74. doi: 10.1016/j.healthpol.2014.09.010. Epub 2014 Sep 28. The impact of no-fault compensation on health care expenditures: an empirical study of OECD countries. Vandersteegen T, Marneffe W, Cleemput I, Vereeck L.

The Council of Europe Recommendation Rec(2006)7 of the Committee of Ministers to MSs on the management of patient safety and prevention of adverse events in health care states that, although error is inherent in all fields of human activity, it is possible to learn from mistakes and to prevent their reoccurrence. As a means of building a culture of safety, the government should ensure that no legal action is taken on the basis of self-reported incidents. 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.

Nevertheless, despite a clearly demonstrated political will to establish such systems throughout the EU, the Commission's Second Report to the Council on the implementation of Council Recommendation 2009/C 151/01 of June 2014 stated that the implemented recommendation *"had less of an impact in increasing patient safety culture at healthcare setting level, i.e. encouraging health professionals to learn from errors in a blame-free environment."*

On the basis of the above facts, the implementation of exemption from liability for reporting cases of MEs in national legislation should be considered, in order to promote a blame-free environment for reporting purposes and to strengthen safety culture. We use this opportunity to call on decision-makers throughout the EU to make an effort to set up such systems, in which a change is encouraged in *"the attitudes and behaviour of health care providers: from fear and defensiveness about things that go wrong in health care, to an attitude of openness and a readiness to learn and make changes."*¹⁷

¹⁷ Wallis K. Developing a culture of safety: regulation or education? PhD dissertation. University of Otago, Dunedin, 2013. Available from:
<http://otago.ourarchive.ac.nz/bitstream/handle/10523/4195/WallisKatharineA2013PhD.pdf?sequence=1>.

2.3 Collaboration with other institutions which deal with medication errors (MEs)

A subsection of the questionnaire was dedicated to investigating the collaboration between NCAs and other institutions that deal with MEs, if applicable, especially to investigate whether they exchange information.

2.3.1 SCOPE results

All 28 MSs selected at least one option when asked which institution deals with cases of MEs. Responses obtained revealed that, in 24 out of 28 (24/28) MSs, the same institution which populated the questionnaire is responsible for collection of MEs (NCAs in most MSs), while in 15 out of 28 (15/28) MSs some other institution is responsible besides the NCA.

In eight (8) MSs other organisations are responsible for collection of MEs in relation to quality improvement work, although rarely systematically. Examples of such organisations include professional organisations, health general directorate, regional programmes, physicians chamber, pharmaceutical chamber, nurses chamber, poisoning centres, regional PVCs, regional health agencies, or hospitals.

When asked whether they exchange information of ADRs that resulted from MEs with other responsible institutions or organisations, only 14 out of 28 (14/28) MSs responded positively. Three stated that they exchange it as E2B (R2) ICSR, two as some other standard and nine in more informal way.

Unfortunately, 14 MSs do not exchange information with other national institutions about ADR(s) resulting from MEs, which clearly shows that there is room for improvement. Therefore, good practices for inter-institutional collaboration identified through the SCOPE survey and found in the literature are briefly described below.

Example 1. UK



In the UK, reports of ME (with and without harm) are reported through the National Reporting and Learning System (NRLS), which is monitored by the NHS Improvement Agency (formally part of the remit of NHS England) and also, where harm has occurred, reported directly to the MHRA as ADR reports.

In 2014, the MHRA, together with NHS England, established a National Medication Safety Network as a forum for discussing potential and recognised safety issues, identifying trends and implementing actions to improve the safe use of medicines¹⁸. The MHRA has been working with this network to simplify and increase ME reporting, improve data quality, maximise learning and guide practice to minimise harm from MEs by sharing incident data. The initiative reduces the need for duplicate data entry by frontline staff in the healthcare system.

NHS Improvement and the MHRA share incidents relating to medication errors in the form of Excel spreadsheets. NRLS reports are received by the MHRA on a weekly basis and the MHRA sends ADR reports to NHS Improvement on a monthly basis. This process is currently being updated to a daily sharing of data through an automatic file transfer process.

ADR reports received directly by the MHRA concerning a ME are handled in the same way as all other ADR reports, including case processing and signal detection procedures. NRLS reports received from NHS Improvement are separately reviewed on a weekly basis before being added to the MHRA's ADR database as necessary to identify potential safety signals.

As with other types of ADR reports, ADRs arising from medication errors are followed up with the original reporter according to defined SOPs. Factors affecting the decision to carry out FU include clarity of understanding of the root cause of the error, the severity of the reaction, whether it is a recognised ADR in the product information and whether important information for assessment of the case is missing.

The MHRA and NHS Improvement also frequently liaise when potential safety issues are identified by either party that may require analysis of both databases to evaluate all available data and determine possible safety actions for both agencies.

By the end of 2015, the National Medication Safety Network had a total of 380 registered Medication Safety Officers (MSOs) in England. The MSOs are nearly all hospital pharmacists who continue to report themselves as well as encourage reporting within their trusts. This initiative has improved learning at local level, clarifying medication safety roles and identifying key safety contacts to allow better communication between local and national levels. As a result, the MSO network is now well established, with monthly web conferences taking place with approximately 100 attendees.

¹⁸ NHS England and MHRA. Patient Safety Alert; Stage 3 Directive. Improving medication error incident reporting and learning. 20th March 2014. Available: www.england.nhs.uk/2014/03/20/med-devices.

Example 2. Denmark (DK)



In Denmark there is a clear distinction between adverse events and ADRs and, therefore, the initial reports are received by two different organisations – adverse events must be reported to the National Agency for Patients' Rights and Complaints (Danish Patient Safety Database) while ADRs are reported to the Danish Medicines Agency.

The Law defines an adverse event as: *"... an event that results from treatment at or stay in a hospital, and which is not caused by the patient' illness, and which is concomitantly either harmful or could have been harmful, but was prevented from occurring or did not occur for other reasons. Adverse events include both previously known and unknown events and errors."*

The reporting of adverse events was embedded in the Patient safety law from 2003 and, since 1 January 2004, reports about patient safety incidents occurring in public and private hospitals in Denmark have been reported to a National Patient Safety Reporting System. The National Patient Safety Reporting System is a learning system that is kept separate from the putative system, and no information reported to the learning system can be used in the putative system. In an amendment to the Health Act, the reporting system was extended (September 2010) to include incidents occurring at private practices, pharmacy sector, pre-hospital area, municipal health service and to allow patients and relatives to report safety incidents.

It is mandatory for HCPs to report adverse events and incidents with medical devices and other healthcare products.

As an ADR can result from a ME, there is a close coordination between the two institutions, sharing relevant reports and sometimes making joint statements.

The legislation states that reporting of adverse events to the National Agency for Patients' Rights and Complaints shall be anonymised with regard to the patient concerned, as well as the reporting individual, and the information on the identity of the person that has submitted a given report may only be shared with the individuals in the same region or municipality who are responsible for following up on the report.

The person reporting may not be, as a consequence of reporting, subjected to disciplinary investigations and measures by his or her employer or supervisor.

The central authority's main role is to disseminate learning nationwide through newsletters, alerts, reports on specific subjects (e.g. MEs), quarterly and annual reports, theme days and presentations.

Denmark is using their own classification for adverse events in relation to MEs, originating from WHO International Classification for Patient Safety (ICPS).

2.3.2 Literature examples

Besides the examples of good practice already identified by the survey, a review of available literature provides additional examples of collaboration between institutions, such as the National Patient Safety Agency in the UK and the Institute for Safe Use of Medicines (Instituto para el Uso Seguro de los Medicamentos, ISMP) of Spain¹⁹. ISMP-Spain carefully reviews and analyses all reported errors and, depending on the characteristics, sends a copy of the report to the Spanish Agency of Medicines and Medical Devices (AEMPS) and to the pharmaceutical companies whose products are mentioned in the reports. The information is also shared with the ISMP from USA, while feedback information is provided by ISMP-Spain on its website, through bulletins, alerts and publications in Spanish healthcare journals.

2.3.4 Discussion

Gathered data shows that in most MSs the same institution that collects data from spontaneous reporting is also responsible for collecting data about MEs. Unfortunately, it was also seen that if some other institution is responsible for collection of ME reports besides the NCA, in as many as 14 MSs there is no respective exchange of information between the NCA and the responsible institution (or organisation).

The EU PV legislation provides a framework for all involved stakeholders (NCAs, MAHs, patients/patient organisations and HCPs) to share available information and stimulates collaboration in order to minimise (preventable) harm from MEs.

Although, there is no requirement to submit ICSR of ME(s) if not linked to suspected ADR(s), they should be captured by MAHs in order to conduct signal detection, to monitor or to inform the competent authority (CA) of any changes to the benefit-risk balance of the medicinal product. Relevant data should be presented in periodic safety update reports (PSURs), if applicable, and according to the GVP Module V²⁰, MAHs are also requested to discuss a potential for ME(s) in a risk management plan (RMP) of the medicinal product, if this exists; especially if during the post-marketing period there have been cases of ADRs occurring as a result of MEs.

Similarly, NCAs need to take into account all cases referring to MEs, whether or not ADR(s) occurred, to be able to decide if a risk minimisation measure needs to be put in place. On the other hand, HCPs and patients have the opportunity to learn from gathered experience about the proper and safe use of the medicine.

One should remember that neither potential causes of, nor reasons for, MEs can be identified or risk minimisation/mitigating actions can be proposed or introduced, if there is no knowledge that ME(s) occurred. Therefore, all involved parties need to stimulate exchange of all available data regarding MEs.

¹⁹ <http://www.usal.es/ismp>

²⁰ Guideline on good pharmacovigilance practices (GVP) Module V – Risk management systems (Rev 1) 15 April 2014 EMA/838713/2011 Rev 1*

3. Conclusions

The SCOPE Joint Action provided the opportunity to look into the PV practices of EU MSs and to investigate the management of ME reports.

A difference between MSs' practices regarding coding of MEs during ICSR management was observed, e.g. all MSs do not follow the same principle when coding ME during an ICSR assessment. Some MSs (11 out of 19 that do code MEs), code it in the case report, even if it is not specified as such by the reporter.

The observed difference in the coding practice of MEs confirmed that the development of an EU-wide guide was much needed, even though the MTS: PTC document was available at that time. MTS: PTC clearly states that only what can be read should be coded (i.e. what is stated by the reporter), without adding or subtracting any information. A ME should not be inferred unless the information provided by the primary source clearly describes it. It is unknown to which extent the lack of SOPs in NCAs contributed to the formation of different practices, although it is interesting to note that among the abovementioned eleven MSs, eight of them did not have SOP(s) in place supporting the coding, reporting, analysis and prevention of ME cases. Also, we can only speculate on other possible causes, for example, the absence of dedicated ME guidelines, a lack of training or a lack of customisable option for flagging events of interest in national ADR databases, etc.

Since the questionnaire showed the practice before the introduction of the 2015 EMA's guide, to see whether the practice in MSs has indeed changed, additional research ought to be performed. Different coding practices between MSs can lead to a falsely interpreted rise in the number of MEs and possibly cause interference in the signal detection process, which impedes evidence-based decision-making. Also, it can create a distorted picture of clinical practice in some or in all EU MSs.

Therefore, a practice of performing FU for cases reporting a possible ME is highly recommended, although then a problem of creating the right FU question without prejudicing or accusing the reporter could emerge. The uniform approach to coding of cases of MEs impacts the overall ICSR management and enables the identification of true cases without creating additional workload to PV staff.

The significance of identifying cases of medication errors lays in the possibility of discovering causes and preventing them for future instances. It should be noted that although each case is unique, patterns can often be recognised that could lead to the prevention of future cases. As stated by Michael R. Cohen²¹ *“Reporting is absolutely essential. If errors go unreported, no one benefits. If we learn about errors, we are a giant step closer to preventing them.”*

MSs should be encouraged to develop and strengthen collaboration between different stakeholders, especially those involved in ME management. Sharing data between different stakeholders and subsequently raising awareness about identified ME(s) can contribute to overall transparency and education. The exchange of information is of the utmost importance in order to develop effective prevention strategies, especially given that approximately half of ADRs are preventable, whilst their treatment constitutes a significant burden on healthcare systems. Furthermore, blame free systems for reporting MEs is of critical importance for increasing transparency and improving patient safety, and efforts should be made to establish these kinds of systems across the EU.

²¹ Michael Richard Cohen ‘Medication errors: Causes, Prevention, and Risk Management’, Jones & Bartlett Learning, 1999