



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Preventing medication errors in the European Union

14 April 2015 – The European Medicines Agency (EMA), on behalf of the European Union (EU) Regulatory Network, has released two draft good practice guides that aim to improve the reporting, evaluation and prevention of medication errors by regulatory authorities and pharmaceutical industry throughout the EU. The deadline for stakeholders to send their comments to EMA was 14 June 2015.

Medication errors are unintended mistakes in the prescribing, dispensing and administration of a medicine that could cause harm to a patient. They are the most common preventable cause of undesired harmful effects (adverse events) in medication practice and present a major public health burden.

With the entry into force of the EU pharmacovigilance legislation in 2012, reporting of all suspected adverse reactions resulting from medication errors became mandatory. Pharmaceutical companies and national regulatory agencies in the EU Member States are obliged to enter these adverse events in EudraVigilance, the EU adverse reaction collection and management system. The primary purpose of the two guides released today is to support industry and regulators in the implementation of these legal requirements.

One of the two guides focuses on the prevention of medication errors. It describes the main sources and types of these errors and proposes measures to minimise the risk of medication errors throughout the life cycle of a medicine.

The other guide provides guidance on how suspected adverse reactions that are caused by

medication errors should be recorded, coded, reported and assessed. It also gives recommendations for marketing-authorisation holders on how to report information on medication errors that are brought to their attention but have not caused adverse reactions. This information must be provided in periodic safety update reports and in the risk management plans that are compulsory for all medicines. This allows a continuous evaluation of the benefits and risks of a medicine based on real life data by regulators.

The guidance released today is one of the key deliverables of the EMA/Heads of Medicines Agencies (HMA) joint action plan on medication errors agreed in 2013. It was developed in consultation with the European Commission's Patient Safety Quality of Care Working Group and takes into account recommendations from stakeholders that were gathered during a workshop held at EMA in February 2013.

Scientific advice leads to stronger applications from industry

17 April 2015 – The majority of clinical development plans submitted for scientific advice to the European Medicines Agency (EMA) prior to a marketing authorisation application were found not suitable for future benefit-risk assessment. Companies that changed their clinical development plans in accordance with the recommendation from EMA were more likely to be granted a marketing authorisation.

These are the main findings of an analysis of marketing authorisation application outcomes between 2008 and 2012 conducted by staff members of EMA and its Scientific Advice Working Party (SAWP) and published in *Nature Reviews Drug Discovery*.

EMA, through its SAWP, provides scientific advice to companies during the development of their medicines to help them design trials that are scientifically sound and generate adequate data for the benefit-risk assessment by EMA's Committee for Medicinal Products for Human Use (CHMP).

Scientific advice is the Agency's key instrument to support the development of high-quality, effective and safe medicines that meet the needs of patients. By providing scientific advice to developers of medicines, EMA also protects patients from

participating in clinical trials that are unlikely to lead to the approval of new medicines.

Detailed analysis of marketing authorisation applications received by EMA that had an opinion between 2008 and 2012 and of the scientific advice provided to these applicants shows that:

- Two out of three programmes submitted for scientific advice had poor clinical trial designs that were inadequate to generate data for the assessment of the benefits and risks of the medicine;¹
- An acceptable trial design at the time of scientific advice, or a change of a deficient trial design to conform with scientific advice recommendations, equally increased the likelihood of a positive outcome with success rates of 84% and 86% respectively, compared with only 41% when a deficient clinical trial design was not adapted according to scientific advice recommendations;¹
- Compliance with scientific advice on clinical trial design was associated with a reduction in major objections raised by CHMP during the assessment of the application, and a 61-day shorter assessment procedure on average, meaning that these medicines may be available to patients earlier.

A number of medicines fail to obtain a marketing authorisation due to deficiencies in the clinical trial design and the inability to demonstrate that the benefits of the medicine outweigh its risks. This not only deprives patients of new medicines but also means that patients may participate in clinical trials that are not suitable for generating data for regulatory assessment.

Scientific advice offers an opportunity to initiate a scientific dialogue on all aspects of the development of a medicine including clinical trial design. Scientific advice should be sought sufficiently early in the development of a medicine to ensure that appropriate changes can be implemented where necessary.

A request for scientific advice is voluntary and sponsors are not obliged to comply with it.

Provision of scientific advice is not a guarantee for pharmaceutical companies to obtain a marketing authorisation.

The assessment of the data that have been generated through a company's development programme is independent from scientific advice.

A positive recommendation on marketing authorisation by EMA's CHMP is based on an assessment concluding an overall positive benefit-risk balance.

Reference

1. Hofer MP, Jakobsson C, Zafiroopoulos N, Vamvakas S, Vetter T, Regnstrom J, *et al.* Regulatory watch: Impact of scientific advice from the European Medicines Agency. *Nat Rev Drug Discov.* 2015;14(5):302-3.

Progress in science, medicines, health

30 April 2015 – The annual report published by the European Medicines Agency (EMA) today focuses on the Agency's key priorities, including the evaluation of medicines and the support to research and development of new and innovative medicines. In 2014, the Agency recommended 102 new medicines for marketing authorisation, both for human (82) and animal (20) use. The number of applications for orphan designation increased by 63% and requests for scientific advice for human medicines by 16% compared to 2013. Developers of medicines are making more and better use of EMA's tools aimed at helping patients to get access to effective and safe medicines more quickly.

The capacity for safety monitoring has been strengthened as patients, healthcare professionals and companies followed up on their commitment to report side effects to the Agency. This is reflected in the increase in the number of suspected side effects reported in EudraVigilance, the EU adverse drug reaction collection and management system. For human medicines, the number of side effects reported rose by 6.5% and for veterinary medicines by 27% compared to 2013. A range of new pharmacovigilance activities has become part of the Agency's core business as a consequence of the implementation of the EU pharmacovigilance legislation. For example, the periodic safety update reports for centrally and nationally authorised medicines that contain the same active substance are now routinely assessed together.

The annual report also highlights some of the main projects, initiatives and achievements in 2014 that had and still have a profound impact on the Agency and the way it operates. Among these are: the adoption of EMA's policy on the publication of clinical data which sets a new standard for transparency in public health and pharmaceutical research and development; the launch of a pilot project on adaptive pathways to accelerate access to new medicines for patients; the involvement of patients in the discussions on benefits and risks of medicines assessed by the Committee for Medicinal Products for Human Use (CHMP); the implementation of various new pieces of legislation; and EMA's move to its new office building.

European Medicines Agency agrees policy on publication of clinical trial data with more user-friendly amendments

6 June 2015 - The European Medicines Agency Management Board on 12 June 2014 agreed the policy on publication of clinical trial data, together with more user-friendly amendments proposed by EMA Executive Director Guido Rasi, that will not only allow the Agency to proactively publish clinical trial data that are submitted as part of marketing authorisation applications, but also give the possibility to download, save and print the trial data for academic and non-commercial research purposes.

In light of discussions at the Board, the wording of the policy, including practical arrangements for academic and non-commercial research users, will now be finalised with a view to its adoption by the Board through written procedure by mid-July 2014, and will be effective from 1 October 2014.

Importantly, the Agency will ensure that the policy will not prejudice citizens' rights under existing access to documents legislation and the new clinical trials regulation.

Since embarking on its plans for the proactive publication of clinical trial data, the Agency has aimed to achieve the broadest possible consensus among its stakeholders and their often competing views and interests. After an extensive consultation phase that took place between June and September 2013, the Agency carried out a second round of targeted consultation in May 2014 that showed broad support for the policy, but highlighted concerns over the proposed view-on-screen-only access.

The Agency's policy is an important step forward towards achieving increased transparency in the regulation of medicines in Europe. It takes the Agency beyond its legal obligations and provides an unprecedented level of access to clinical trial data that are used as part of decision-making for new medicines.