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What's new in Pharmacovigilance?

QPPV UPDATE

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QPPV Update

This QPPV Update provides Qualified Persons responsible for Pharmacovigilance (QPPVs) and all other people working in pharmacovigilance with an update on EU Pharmacovigilance, relating to medicines for human use.

We would welcome your feedback as well as any suggestions on topics you think would be of interest to colleagues. Your feedback should be sent via ASK EMA online form.

Guidance for pharmaceutical companies to prepare for UK withdrawal from the EU

On 19 June 2018 the European Medicines Agency (EMA) and the European Commission updated their guidance to help pharmaceutical companies prepare for the United Kingdom's (UK) withdrawal from the European Union (EU).

Updates to the questions-and-answers document are marked 'NEW' and include new information on back-up arrangements for QPPVs. The Agency has also published an updated version of its practical guidance for industry which outlines the steps that companies should follow to make sure that necessary changes to their marketing authorisation are made by the end of March 2019. The document should be read in conjunction with the updated Q+A document. Further information can be found here .

Need more information?

Further information about the work of the European Medicines Agency is available on our website

For topics on Pharmacovigilance legislation – see here

Links to the National Competent Authorities can be found here

Pharmacovigilance IT Systems

Article 57 database

What's new?

On 30 July 2018, the Agency published a subset of information contained in the Article 57 database of medicinal products. The data was published in accordance with Article 26 (1) e of Regulation (EC) No 726/2004, which creates a legal requirement to publish the contact details for pharmacovigilance enquiries and of the locations in European Union where the pharmacovigilance system master files are kept.

In addition, several other data fields are included in the publication to provide context to the data, making the full list of data fields published as follows:

- Product short name (brand name or the combination of the generic name and the company name)
- Active substance
- Route of administration
- Authorisation country
- Name of the Marketing Authorisation Holder
- Country of location in the EU where the Pharmacovigilance System master file is kept
- Pharmacovigilance enquiries contact email address
- Pharmacovigilance enquiries contact telephone number

The data are accessible on the EMA external website in the form of an Excel file and will be updated periodically.

What do you need to know about this data release?

- Lists the medicinal products (at product short name level) authorised in the EU submitted by marketing authorisation holders (MAHs) to the Article 57 database. Only information on products that have a valid marketing authorisation status is included in the publication.
- Provides the public with a dedicated point of contact within the MAH regarding any safety concerns related to individual medicinal products listed in the Article 57 database.
- Allows EU citizens to know what products are authorised.
- Facilitates the activities of the (Invented) Name Review Group (NRG)– whose main role is to consider whether the (invented) name proposed by a product's manufacturer could create a public health concern or potential safety risk.
- Enables pharmaceutical industry to provide a better assessment of potential invented names.

What MAHs need to do?

- MAHs have already been informed regarding the publication of Article 57 data and were given an opportunity to check their entries.
- MAHs must submit information to the EMA on authorised medicines and keep this information up-to-date in accordance with EU pharmaceutical regulation.
- Documentation related to the submission of medicinal product information under the Article 57(2) requirements can be found on the guidance documents webpage.

EudraVigilance

The new EudraVigilance (EV) system was launched on 22 November 2017. EudraVigilance now holds information on more than 12.45 million safety reports, referring to 7.95 million cases, as well as information on 744,219 medicinal products on the EU market. EudraVigilance provides enhanced functionalities to National Competent Authorities (NCAs), and marketing authorisation holders for effective reporting as well as an extensive data set for monitoring of adverse drug reactions and detection of risks related to the safety of medicines.

Major achievements in 2018

- On 26 July 2018, the European Medicines Agency integrated the services of EudraVigilance (human) with EMA's Account Management portal and the Organisation Management Service (OMS). The new platform simplifies the registration and management of organisations and users interacting with EudraVigilance. Further details on the integration process are available in the EudraVigilance stakeholder change management plan: integration with the Identity and Access Management (IAM2) project deliverables.

- Following the launch, the user management takes place through the EMA Account Management Platform. Organisations and users already registered with EudraVigilance are being automatically migrated to OMS and the EMA Account Management Platform.

  Further information is available on the updated EudraVigilance: how to register webpage.

- On 23 July 2018 the Agency released a note for clarification for MAHs on the recording of ICSRs accessed in EV. It provides clarification on the obligations of MAHs on how to record information on suspected adverse reactions accessed in EudraVigilance.
- The EudraVigilance Operational plan was published on 8 June 2018. This operational plan describes key activities and developments that will impact on or relate to EudraVigilance and its stakeholders from 2018 to 2020. The plan will be updated regularly as regards timelines and new activities and developments.
- Following the launch of the new and enhanced EudraVigilance, access to the system has been enabled for MAHs. The legislation requires MAHs to inform EMA and NCAs of validated signals detected when monitoring the database. To streamline the involvement of MAHs in the monitoring of EV data, a phased implementation was agreed with the European Commission. On 22 February 2018 a pilot started. From that day MAHs are required to monitor EudraVigilance data for active substances included in the 'List of active substances involved in the pilot on signal detection in EudraVigilance by marketing authorisation holders'. During this pilot period, MAH signal detection in EudraVigilance is not required for other products.

  The Agency will use the results and experiences from this pilot for the next signal management implementation step. More information on the 'phased implementation' requirements to monitor EudraVigilance data can be found on the signal management webpage.

- In accordance with the EudraVigilance Auditable Requirements project plan, the EudraVigilance release 5.0 was launched on 14 February 2018. It delivered improvements based on the initial implementation experience and addressed minor issues identified since the go-live on 22 November 2017. EudraVigilance is now in maintenance mode and regular system upgrades are planned to address feedback from users.

What MAHs need to know and do:

- All EudraVigilance users, including organisations, **need an active EMA account** created through the EMA Account Management portal. To ensure a smooth transition, the EMA has published a Registration manual for companies and users wishing to register with, access or manage their account for the EudraVigilance (human) production environment.

- Following the EudraVigilance platform integration with the EMA Account Management Portal and OMS, the Agency has reinforced its support to EudraVigilance users. For support on access and registration related questions, the stakeholders should contact eudravigilanceregistration@ema.europa.eu

- In addition, the training material for the EudraVigilance face-to-face training course has been updated. Online eLearning videos are available on the EudraVigilance change management and the EudraVigilance: electronic reporting webpages.

Pharmacovigilance Processes

Public hearing on quinolone and fluoroquinolone antibiotics

What's new?

On 13 June 2018 the EMA held a public hearing on Quinolone- and fluoroquinolone-containing medicinal products. Quinolones and fluoroquinolones are a class of antibiotics which are widely prescribed in the EU and are important for treating serious, life threatening bacterial infections.
The summary report of EMA's public hearing on quinolone and fluoroquinolone antibiotics is now available.
The public hearing was held as part of a safety review by the PRAC, investigating the persistence of serious side effects with quinolone and fluoroquinolone antibiotics mainly affecting muscles, joints and the nervous system.
In particular, the PRAC was interested to hear the public's view on acceptability of risks associated with quinolones and fluoroquinolones in both mild and severe infections, and to explore what further measures could be taken to ensure that these antibiotics are used as safely as possible. The hearing was broadcast live and the video recording can be found here.
Patients, carers, doctors, pharmacists shared their experience, which will complement the available scientific evidence and will enrich the PRAC's deliberations and will be used to finalise its assessment.

What's coming?

After the public hearing, the PRAC will continue its review according to the published timetable. Once the assessment is finalised, the PRAC report on the safety of quinolones and fluoroquinolones will be published. This will set out its conclusions and will clearly explain how the information gathered during the public hearing has informed the Committee's recommendations.

EU-funded initiatives for real-world evidence

A review of EU-funded initiatives linked to 'Real World Evidence' (RWE) was performed by the EMA to determine whether their outputs could be used for the generation of real-world data able to support regulatory decision making on medicines.

The full article can be accessed here.

Enhancing independence and transparency in observational medical research

What's new?

In March 2018 the European Network of Centres for Pharmacoepidemiology and Pharmacovigilance (ENCePP) adopted the 4th revision of its Code of Conduct that sets out the principles to be applied to ensure scientific independence and transparency in pharmacoepidemiology and pharmacovigilance research.
The fourth revision provides a clear definition of scientific independence and transparency, and further clarifies the roles of the study lead investigator and the funder to ensure scientific independence throughout the research process. A summary of the main changes introduced with the current 4th revision of the Code can be found here.

How is it relevant for you?

The provisions of the Code apply to medical research that is fully or partially financed from external sources, e.g. studies commissioned by pharmaceutical companies, research grants etc. where researchers, study funders and other involved parties agree to adhere to the Code.

Following its first release in 2010, the Code has been regularly revised based on feedback and experience of various stakeholders, such as pharmaceutical industry, contract research organisations, learned societies and regulatory authorities conducting collaborative research. Feedback should be provided by email to: encepp_secretariat@ema.europa.eu

Crisis simulation exercise

In October 2017 a crisis simulation exercise was coordinated by EMA on behalf of the EU Regulatory Network. The exercise aimed to test the EU Regulatory Network Incident Management Plan for Human Medicines (EU-IMP) in the case of a potential crisis situation. This was considered a very useful exercise which demonstrated that overall the EU-IMP process functions correctly. Further details are available in the released public note.

Pharmacovigilance guidance

Recently published guidance

The ENCePP Guide on Methodological Standards in Pharmacoepidemiology offers a single web resource for methodological English language guidance in pharmacoepidemiology**.** For each topic covered, direct electronic access is given to internationally agreed recommendations, and key points from important guidelines, published articles and textbooks are highlighted. Where relevant, gaps in existing guidance are addressed with what ENCePP considers good practice.

The current version of the Guide is Revision 7, dated July 2018. It includes revisions, amendments and new references in all the chapters. Revisions were performed by the authors in collaboration with the editorial group. External comments received were also considered.

Due to developments in some areas or need for restructuring and clarification, the ENCePP Guide has been more significantly revised in the following chapters:

- 4.3. Patient registries
- 4.5. Social media and electronic devices
- 4.6. Research networks
- 5.1. Definition and validation of drug exposure, outcomes and covariates
- 5.3. Methods to address bias
- 5.9 Methods for pharmacovigilance impact research – **NEW CHAPTER**

Chapter 5.9 is complemented by Annex 2 which provides more detailed guidance on methods for pharmacovigilance impact research developed by an ENCePP Special Interest Group.

The Guide is updated regularly by structured review to maintain its dynamic nature. It may also be amended as necessary in response to comments received. For this purpose, any comment and additional relevant guidance document may be forwarded to encepp_comments@ema.europa.eu

Pharmacovigilance dialogue

Reports from meetings and events

A report from the (CAR) T-cell therapy registries workshop, which was held on 9 February 2018, has now been published. The report summarises observations made by the participants on the use of registry data to support regulatory benefit-risk evaluations of CAR T-cell therapies and, in particular, post-authorisation follow-up. It makes recommendations for actions that aim to facilitate and improve registry data use including the systematic collection of a set of core commonly-defined data elements.

Upcoming EMA meetings and events

Industry stakeholders are invited to follow the Agency's news and events calendar for upcoming events taking place in 2018.

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