02 **Issue 2 - 2017**
July 2017

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

What's new in Pharmacovigilance?

QPPV UPDATE

Published by the European Medicines Agency

An agency of the European Union

IN THIS ISSUE

QPPV Update

The second issue provides you with information on recent developments in EU Pharmacovigilance, relating to medicines for human use, and includes updates on the EU network activities and relevant projects.

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 to Jolanta.Palepsaitiene@ema.europa.eu.

Need more information?

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

For topics on implementation of the new Pharmacovigilance legislation – see here

Links to the National Competent Authorities can be found here

Pharmacovigilance IT Systems

EudraVigilance

What's new?

- On 22 May 2017 the EMA Management Board (MB) confirmed that the EudraVigilance (EV) database has achieved full functionality and the system meets the functional specifications that were adopted by the Pharmacovigilance Risk Assessment Committee (PRAC) and Board in December 2013. It is based on an independent audit and a subsequent favourable recommendation from the PRAC concluding that the updated EV system is fully functional. The new EV System will become operational on 22 November 2017.

  To allow the transition from the current EudraVigilance system to the new one, a 10 business day downtime is required. Therefore, from 8 to 21 November 2017, key functionalities of EudraVigilance will not be available or they will be only partially functional. A go-live plan is being set up in consultation with NCAs and will be published on EMA's website in September 2017. It will outline the impacted stakeholders the impacted technical and business processes and the alternative arrangements to be planned for stakeholders. The plan will also highlight the mechanisms in place to notify any emerging safety issues by MAHs or sponsors of clinical trials to NCAs and the EMA.

- The go-live of the external Eudravigilance test (XCOMP testing) system on 26 June 2017 allows organisations to become familiar with the new system and test their local pharmacovigilance/safety IT system and their interoperability with the enhanced EV system. Please note that the XCOMP environment is designed for testing purposes only and testers should only use test ("dummy") data for the purpose of the interoperability and functional testing with EudraVigilance. The use of fictitious, scrambled or anonymised information is the preference in any EudraVigilance system testing regime. To use the XCOMP environment, it is recommended to use Google Chrome or Mozilla Firefox as the preferred internet browser.

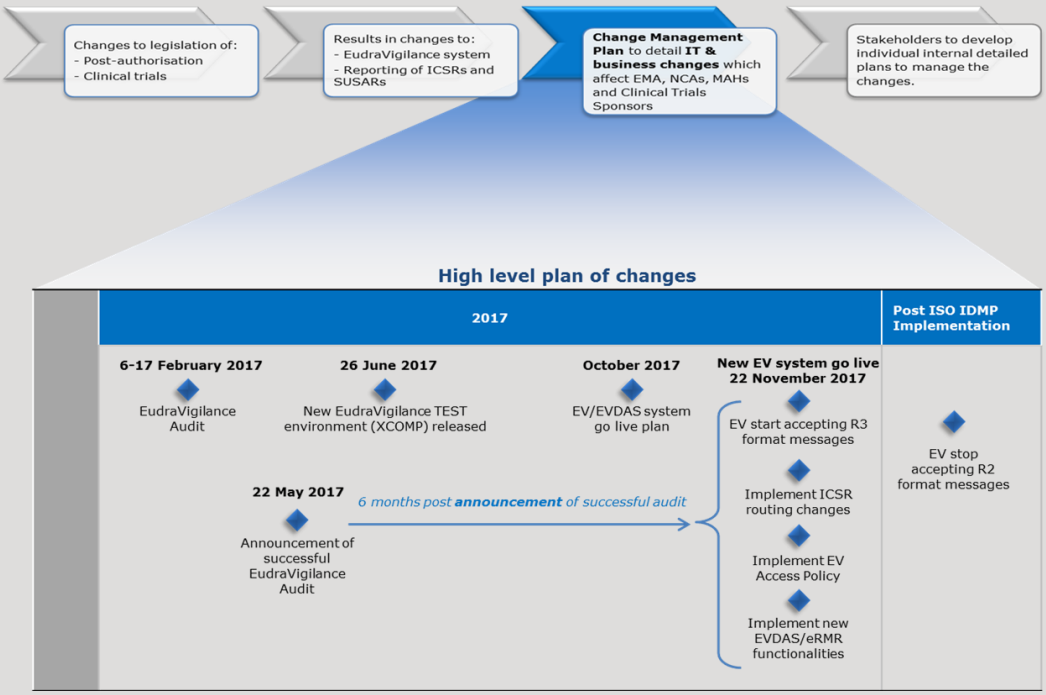
- To further assist MAHs and sponsors of clinical trials, the Agency has released a 'Checklist and testing instructions for MAHs and Sponsors of Clinical Trials in the EEA'. This document provides testing instructions and steps to follow in preparing for the technical and business process changes.

In addition, the following updates have been carried out on the dedicated EudraVigilance webpages:

- EudraVigilance Training and Support webpage: an updated version of the training plan, the EVWEB user manual, the Individual Case Safety Report (ICSR) Form user manual and three additional e-learning videos have been published.

- EudraVigilance Change management: an updated communication plan, an update of the change management plan and the EU ICSR Implementation Guide as well as a Questions and Answers document on the launch of the new EudraVigilance system have been published.

- EudraVigilance: electronic reporting: test instructions for organisations reporting electronically ICSRs to EudraVigilance for the first time ("new organisations") or introducing major changes to their local safety/pharmacovigilance database, which might impact the electronic reporting of ICSRs have been further elaborated. Additionally, instructions have now been added for initial testing of software/system solutions by IT vendors and third party service providers.



EudraVigilance

What MAHs need to know and do?

- Users of EudraVigilance have to make final preparations to ensure that their processes and local IT infrastructure are compatible with the new system and the internationally agreed format.
- MAHs should plan to complete any testing of their existing systems well in advance to the new system going live to give time for any issues to be addressed. A specific testing time slot can be booked from 26 June 2017 by contacting EMA at qattesting@ema.europa.eu. This **applies only where the testing refers to a new ICH E2B(R3) complaint system** or a **major update of an existing E2B(R2) complaint system** that would require retesting with EudraVigilance. Instructions published on the webpage EudraVigilance: electronic reporting should be followed.
- MAH users should check the validity of their EVWEB user-IDs and passwords and contact the EudraVigilance Registration team if user credentials need to be updated. Further details are outlined at the dedicated webpage EudraVigilance: how to register.
- MAHs should progress with the registration of their EVDAS users in accordance with their **allocated time slots** to allow the Agency to process the expected high volume of new registrations.
- Engage with information and training events. As of June 2017 support webinars are being organised for MAHs to address implementation questions.

Pharmacovigilance processes

Transitional arrangements for the monitoring of EudraVigilance by marketing authorisation holders

What's new?

From 22 November 2017 (go-live of the new EudraVigilance system), marketing authorisation holders will have extended access to the EudraVigilance database to support the fulfilment of their pharmacovigilance obligations. These obligations include the continuous monitoring of EudraVigilance data and the communication of validated signals to the Agency and national competent authorities, as outlined in Commission Implementing Regulation (EU) No 520/2012[1].

In order to streamline this new process, the Agency and the European Commission have agreed on a phased implementation of the requirements for marketing authorisation holders to monitor EudraVigilance data, as follows:

- For an initial 'pilot' period of one year, marketing authorisation holders will only be required to monitor EudraVigilance data for active substances included in the 'List of medicinal products under additional monitoring' that will be in force on 22 November 2017.
- This pilot period will start on 22 February 2018.

What do you need to know?

For a 'pilot' period of one year commencing on 22 February 2018, marketing authorisation holders will be required to monitor EudraVigilance data and inform the Agency and national competent authorities of validated signals, only for active substances included in the 'List of medicinal products under additional monitoring' that will be in force on 22 November 2017.

For other active substances, marketing authorisation holders would still have access to EudraVigilance database which they could use as an additional data source for their signal detection activities; however, they would not be required to continuously monitor the Eudravigilance database and inform forthwith EMA/NCAs of validated signals.

In order to provide marketing authorisation holders involved in the 'pilot' with adequate time to prepare, the requirement to monitor EudraVigilance data will only start on 22 February 2018. Between 22 November 2017 and 22 February 2018, marketing authorisation holders that will be involved in the 'pilot' will be expected to familiarise themselves with the tools developed to support the monitoring of EudraVigilance data.

Marketing authorisation holders should also use these three months to finalise their internal processes with a view to comply with the guidance outlined in GVP Module IX on Signal Management, whose revision is being finalised for a planned publication in advance of the go-live of the new EudraVigilance system.

This information has been reflected on the Agency's signal management webpage. Further information on practical aspects of the phased implementation will be communicated by the Agency closer to the time.

The experience gained through the 'pilot' will be analysed by the Agency and will inform any decision as to the next stage of the implementation. Information on the next stage will be communicated in due course.

The Agency is supporting marketing authorisation holders through targeted e-learning and face-to-face trainings, webinars and information days. Further information is available on the EudraVigilance training and support webpage.

[1]COMMISSION IMPLEMENTING REGULATION (EU) No 520/2012 of 19 June 2012 on the performance of pharmacovigilance activities provided for in Regulation (EC) No 726/2004 of the European Parliament and of the Council and Directive 2001/83/EC of the European Parliament and of the Council

Pharmacovigilance in the product lifecycle

EU PAS Register: RMP category for studies imposed or required by a regulatory authority

For all post-authorisation studies (PAS) imposed or required by a regulatory authority in the EU, a new field has been added in July 2016 in the EU PAS Register to request information on the EU RMP category (1, 2 or 3)*. For PAS not requested by a EU regulator, the field should be populated by one of the following options: 'Not applicable' (if the PAS has not been requested by any regulatory authority) or 'Non-EU RMP only' (if the PAS has been only requested by a regulator from outside the EU).

For PAS registered in the EU PAS Register before July 2016, the primary lead investigator has been requested to populate retrospectively this new EU RMP category field. QPPVs are reminded that they should ensure that the EU PAS Register has been updated accordingly for all PAS involving their company.

*Category 1: imposed as condition of the marketing authorisation; Category 2: specific obligation of the marketing authorisation; Category 3: required in the RMP.

PSUR training

A webinar training on PSUR led by a joint panel of industry and regulator authorities will take place **on 22 September 2017** in the morning. the 2-hour Q&A session will cover topics including signals and close monitoring, safety specification, product information / reference safety information and use of summary tabulations, as described **in the explanatory note to GVP module VII and the PSUR Q&A for assessors**.

Participants are invited to send questions for all topics to both the assessors and industry speakers before the joint training via email to PSURtraining@ema.europa.eu as well as during the training using the aforementioned email address.

The session will be broadcast from EMA and widely accessible to participants. The agenda of the joint training as well as the details to participate will be made available by the end of August on the EMA website.

Related information: Explanatory Note to GVP Module VII | Q & A on PSUSA: Guidance document for assessors

Pharmacovigilance guidance

The ENCePP Guide on Methodological Standards in Pharmacoepidemiology offers a single web resource for methodological 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 6, dated July 2017. 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, there have been more important changes in the following chapters:

- 3. Development of the study protocol
- 4.6. Research networks
- 5.2. Bias and confounding
- 5.6. Pragmatic trials and large simple trials
- 7. Quality management
- 9.2. Scientific integrity and ethical conduct

The following chapters were newly added:

- 1. Introduction
- 4.3. Patient registries
- 4.1.1. Surveys

Annex 1. to the Guide provides methodological guidance addressing the conduct of systematic reviews and meta-analyses of drug safety endpoints generated in completed (published or unpublished) comparative pharmacoepidemiological studies.

The Guide is updated annually 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.

- GVP Module VI – Collection, management and submission of reports of suspected adverse reactions to medicinal products (Rev 2), following the public consultation in 2016, was released as final on 2 August 2017.

Guidance under public consultation

- GVP chapter Product- or Population-Specific Considerations IV: Paediatric population was released for 2-months public consultation (until 13 October 2017) on 2 August 2017.

Updated guidance to be released as final in 2017

- GVP - Annex I - Definitions (Rev 4) is anticipated to be released in Q3 2017.
- GVP Module XV – Safety communication (Rev 1) and related templates in Annex II is expected in Q3 2017.
- GVP Module IX – Signal management (Rev 1) and revised guidance on statistical methods (addendum I), following the public consultation in 2016, will be released as final in Q3 2017.

Pharmacovigilance guidance

Guidance under revision or development

- The pharmacovigilance guideline regarding use of medicines in pregnancy is under development to become a chapter of GVP.
- The pharmacovigilance guideline for medicines used by older populations is under development to become a chapter of GVP and is planned to be released for public consultation in 2017.
- GVP Module VI Addendum I on ICSR Duplicate Management is under development.
- GVP Module VII – Periodic Safety Update Reports (Rev 2) drafting is ongoing.

Administrative guidance

Information for companies

- On 31 May 2017, EMA and the European Commission published a questions-and-answers (Q&A) document concerning the location of establishment of a company in the context of centralised procedures and certain activities, including the location of orphan designation holders, qualified persons for pharmacovigilance (QPPVs) and companies' manufacturing and batch release sites: Questions and Answers related to the United Kingdom's withdrawal from the European Union with regard to the medicinal products for human and veterinary use within the framework of the centralised procedure
- The Q&A provides further details following the European Commission/EMA notice of 2 May 2017 intended to remind marketing authorisation holders of centrally authorised medicines of their legal obligations in preparation for Brexit:

  Notice to marketing authorisation holders of centrally authorised medicinal products for human and veterinary use

Pharmacovigilance dialogue

Upcoming EMA meetings

- 11th Stakeholders forum on the pharmacovigilance legislation – 21 September 2017.
- 12th Industry stakeholder platform-operation of EU pharmacovigilance - 24 November 2017.

Training

- For EudraVigilance training courses, please visit the EudraVigilance training page.

PSUR training

- Joint industry and regulatory authority partners - 22 September 2017.