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EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Pharmacovigilance Programme UPDATE

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IN THIS ISSUE

Enhanced Pharmacovigilance through effective implementation of information systems and services

This 4th update document captures the important progress made in the development of the pharmacovigilance information systems and services and describes how the Agency is preparing for the successful delivery of these changes, focusing on the most critical questions: what needs to be done by whom and by when.

Need more information?

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

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

Links to the National Competent Authorities can be found here.

Medical Literature Monitoring

Need more information?

Medical Literature Monitoring website

Scope:

- Legal requirement for EMA to monitor selected medical literature for reports of suspected adverse drug reactions containing certain active substances and to enter individual case safety reports into the EU adverse reaction database (EudraVigilance).

Benefits:

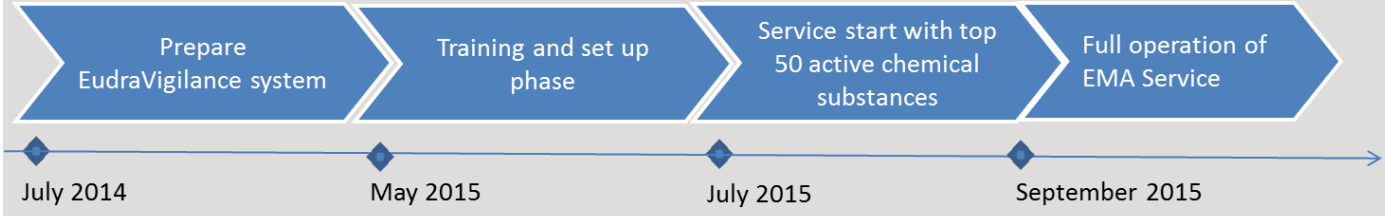
- This will improve safety monitoring of medicines through better quality of safety information;
- This will reduce the administrative burden on Marketing Authorisation Holders (MAHs) for the relevant substances;
- MAHs will have access to up-to-date results of MLM activities and ICSRs generated, allowing them to repost ISCRs to other regulatory bodies (outside EU) in a timely fashion;
- Supports signal detection activities by the EMA, National Competent Authorities (NCAs) in EEA and MAHs.

News:

- As of the 1st July 2015, the service will cover the top 50 active chemical substance groups and is expected to reach full operational levels by September 2015, covering 300 active substances and 100 herbals;
- Additional supporting documents including the duplicate management process and Questions and Answers document were published on 12 June 2015;
- Dedicated questions and answers sessions with NCAs and MAHs were held on 26 May, 2 June, 8 June and 15 June. The MLM support sessions are planned on a monthly basis until the end of the year (see Medical Literature Monitoring website for schedule);
- A dedicated service desk will be available as of 1st of July to assist in dealing with specific enquiries from MAHs and NCAs in EEA Member States;
- On 12 May 2015 the EMA published: a list of substances and a description of the literature reference database, a detailed guide regarding the monitoring of medical literature and a series of training videos.

What MAHs need to do:

- In accordance with Article 107, paragraph 3 of Directive 2001/83/EC, marketing-authorisation holders shall not be required to report to EudraVigilance suspected adverse reactions recorded in the listed medical literature monitored by EMA for products containing the active substances referred to in the list of substances being monitored by EMA;
- It is important to note that marketing-authorisation holders **shall monitor all other medical literature** and report any suspected adverse reactions;



Medical Literature Monitoring

What MAHs need to do:

- The concerned marketing-authorisation holders should note the following high-level technical environment requirements and pre-requisites below:
  - For EVWEB users: no changes apply.
  - For non-EVWEB users: the marketing-authorisation holder safety system should be configured to be able to upload ICSRs with the Sender identifier "MLMSERVICE". For MAHs to be able to access the EudraVigilance Download Area, at least one MAH user should be registered with EudraVigilance. Further information can be found at the EudraVigilance website.
  - **Adaptations of business processes** by concerned marketing-authorisation holders can be found at the dedicated Medical Literature Monitoring website.
- The business processes to be discontinued are summarised as follows:
  - Concerned marketing-authorisation holders should not re-submit the ICSRs resulting from the medical literature monitoring service to EudraVigilance.
  - *Unless otherwise specified by national legislation and guidance*, concerned marketing-authorisation holders should no longer submit the ICSRs resulting from the medical literature monitoring service to the concerned national competent authorities in the EEA.
  - NCAs in EEA Member States should not re-submit the ICSRs resulting from the medical literature monitoring service to EudraVigilance.
  - NCAs should no longer provide the ICSRs resulting from the medical literature monitoring service to the concerned marketing-authorisation holders, since they can download those ICSRs from the EudraVigilance download area.

Adverse drug reaction reporting and Signal management

Further information can be found at: EudraVigilance website

Scope:

- Legal requirement for an enhanced adverse reaction collection and management system (EudraVigilance) that delivers better health protection through simplified reporting, better quality data and better searching, analysis and tracking functionalities. Enhanced detection of new or changing safety issues allows more rapid action to protect public health;
- Legal requirement for MAHs to monitor the EudraVigilance data to the extent to which they have access.

Benefits:

- Compliance with international data standards (and future compatibility with ISO IDMP standards based on Article 57 data) including backwards and forwards conversion tools for E2B(R2)/(R3) messages;
- Improved performance and scalability of new system to cope with foreseen increase in users and volume of data;
- Simplified reporting delivered for MAHs.

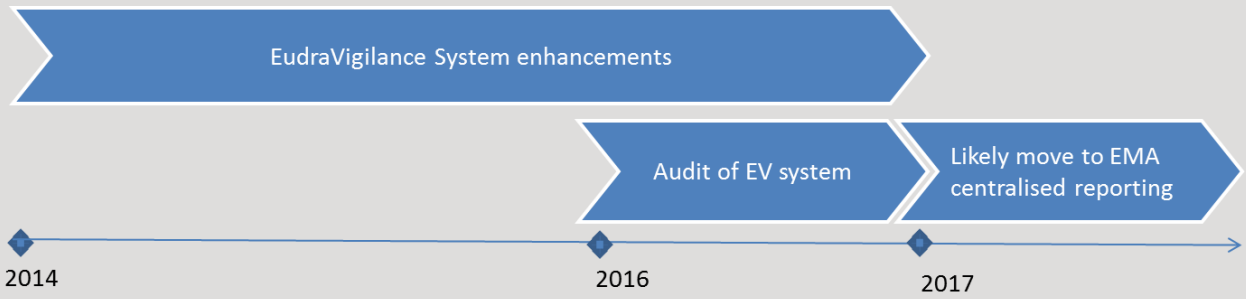
Adverse drug reaction reporting and Signal management

News:

- The transition to using the new international standard will be actively managed by the Agency in collaboration with NCAs and MAHs. The Stakeholder business change management plan will be launched in Autumn 2015;
- The EudraVigilance functionalities audit is scheduled to take place in 2016, with the move to centralised reporting in 2017.

What MAHs need to do:

- Plan for the implementation of the revised EudraVigilance Access Policy, which will lead to increased access to adverse reactions reports and responsibilities for signal detection in 2017 (see Art.18 of Commission Implementing Regulation (EU) No 520/2012);
- Engage with information and training events.



Database of Products (Article 57)

Scope:

- To deliver structured and quality assured information on medicinal products authorised in the EU that can support EU terminologies of products, substances, and organisations used to power pharmacovigilance and regulatory systems.

Benefits:

- Facilitate the coordination of regulatory decisions and actions to safeguard public health and to fulfil regulatory actions and legal obligations including:
  - identification of products and substances in reports of suspected adverse drug reactions;
  - literature monitoring service;
  - repository of Periodic Safety Update Reports (PSURs);
  - referral procedures;
  - collection of pharmacovigilance fees.
- Strengthen communication with stakeholders by granting access to safety data, efficiently exchanging data within the EU Network and international partners, and supporting communication between the Agency's Committees and the pharmaceutical industry;
- Support the reduction of duplication of encoding and maintenance of the same information on medicines, thus reducing costs (e.g. Implement a single database and set of terminologies for multiple business cases).

Database of Products (Article 57)

Need more information?

Data submission for authorised medicines

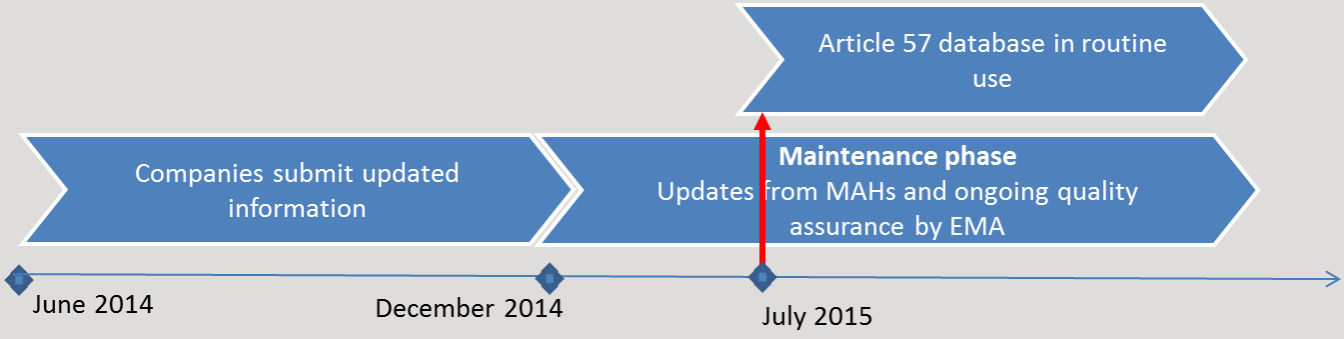
A new webpage dedicated to ISO IDMP standards implementation is now available

News:

- The current Article 57 initial data re-submission produced over 500k medicinal products (EV Codes) updated in the Art57 database.
- EMA continues its co-operation with Industry to ensure Article 57 correctness. As of the end of May approximately 220k medicinal products (EV Codes) had been quality reviewed against the provided SmPCs.
- Further to the suggestions received from the Industry, EMA is now providing Industry with enhanced, individual detailed feedback on findings of the quality review.
- To further support with submission of the high quality data Agency and Industry have agreed to implement an additional XEVPRM XML Acknowledgement message (the 3rd Acknowledgement) to the sender's organisation ID. The roll-out of this notification is scheduled for November 2015.
- In Autumn 2015 the Agency will launch a service for the National Competent Authorities to make available the relevant information from the Article 57 database such as the QPPVs contact details, the contact information for pharmacovigilance enquiries and the locations in the Union where pharmacovigilance system master files are kept.

What MAHs need to do:

- Since 1 January 2015, using the electronic XEVPRM format as amended on 31 January 2014, marketing-authorisation holders need to:
    - Notify the Agency of any **new marketing authorisations** within **15 calendar days** from the date of authorisation (i.e. 15 calendar days from the date of notification of the granting of the marketing authorisation by the competent authority);
    - notify to the Agency any subsequent changes to the terms of the marketing authorisations following variation, transfer, renewal, suspension, revocation or withdrawal of the marketing authorisation as soon as possible and no later than **30 calendar days** from the date of which the changes have been authorised.
- Since the 3rd Acknowledgement notification has been endorsed at the level of the Article 57 Implementation Working Group (IWG), MAH organisations using in-house solutions (i.e. **Gateway Users**), should enhance their system to allow the receipt of the 3rd Acknowledgement as of November 2015. Further information will be communicated in the near future.



PSUR repository

Need more information?

http://esubmission.ema.europa.eu/index.htm

Scope:

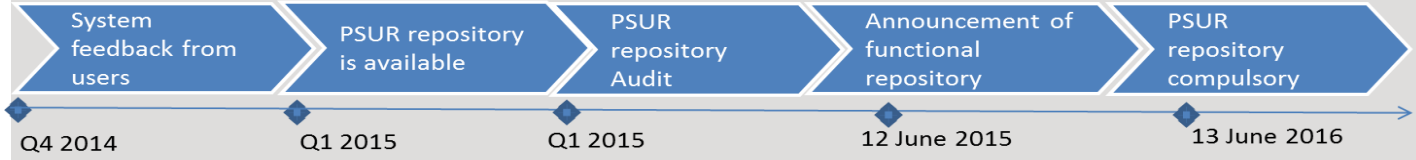
- Legal requirement for EMA to set up a repository for periodic safety update reports (PSURs) and their assessment reports;
- To allow centralised PSUR reporting and to enhance access to data and information, thereby supporting benefit risk assessments of medicines.

Benefits:

- Provides a simplification of PSUR submissions benefiting pharmaceutical industry (PSURs submitted electronically to the Repository, submissions accessible to regulators);
- Once the use of the Repository is mandatory, it will include all PSURs, including those that follow the PSUR Single Assessment (PSUSA) and those PSURs which are not part of a Single Assessment;
- Delivers a user interface to regulators to query and retrieve documents by use of metadata based on fields present in the list of EU reference dates (EURD list) for each active substance/combination of active substances;
- Delivers a user interface to National Competent Authorities to upload and retrieve assessment reports and comments to the repository.

News:

- Based on a positive PRAC Recommendation and the independent audit report on 11 June 2015 the EMA Management Board announced that the PSUR repository meets the functional specifications as agreed in the 'PSUR Repository functionalities to be audited' document and therefore concluded that it has achieved its full functionality. **The legislation foresees that 12 months after the EMA Management Board announcement, the use of the repository in the European Union will become mandatory (13 June 2016);**
- The detailed business requirements for the 4 non-auditable requirements have been finalised and the planning for the post-audit functionalities has successfully passed the audit. The development of the post-audit functionalities will likely start in July 2015 to deliver enhancements to the system in terms of usability and support to the work of the regulatory network. The delivery of the 4 non-auditable requirements, as agreed by the EMA Management Board in December 2013, is planned for Q4 2015;
- From 1 September 2015, the use of the XML delivery file for all (CAPs and NAPs) PSUR submissions to the EMA via the eSubmission Gateway and/or the Web Client will also become mandatory. After this date, it will no longer be possible to submit PSURs using the existing filenaming convention. The mandatory use of the PSUR XML delivery file is introduced to harmonise the submission mechanism for all PSURs submitted to EMA and it will apply to all types of PSUR and PSUR supplementary information submissions.



PSUR repository

What MAHs need to do:

- Prepare for the mandatory use of the PSUR Repository in June 2016:
  - Consider which business processes will have to be adapted to use the repository;
- The Agency will be making the use of the XML delivery file mandatory from 1 September 2015 for all PSUR submissions to the EMA via the Gateway or Web Client. The Agency strongly recommends users to switch to the XML deliver file option at the soonest opportunity. Further information is available at Statement of intent for use of xml delivery file.

Pharmacovigilance Fees

Need more information?

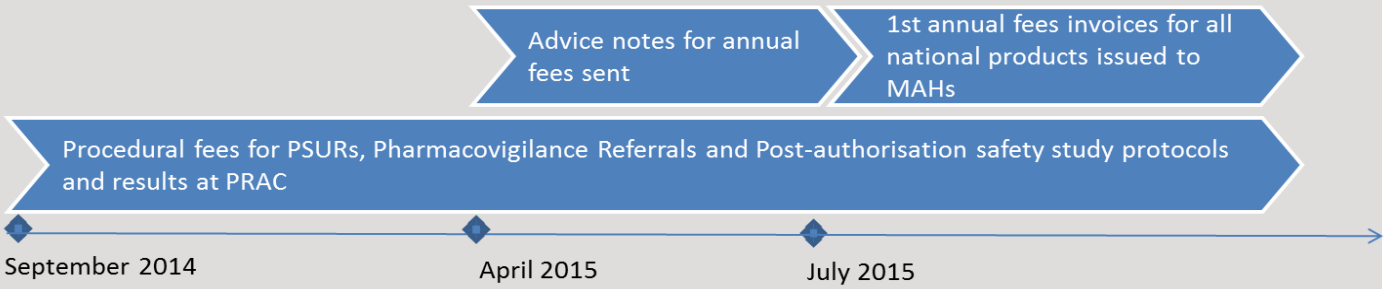
Pharmacovigilance fees payable to the European Medicines Agency

Scope:

- The pharmacovigilance legislation foresees that pharmacovigilance activities conducted at EU level for medicinal products for human use should be financed by fees paid by MAHs. The pharmacovigilance fees regulation adopted in 2014 allows the EMA to collect these fees;
- The income will be used to remunerate national competent authorities (NCAs) of the EU for the scientific assessment carried out by the rapporteurs and to contribute to the pharmacovigilance-related costs of the Agency.
- Delivers functionality for online payment of fees and updating of account details.

Benefits:

- In addition to remunerating procedures, fees support the implementation and maintenance of measures from the 2010 pharmacovigilance legislation including: medical literature monitoring, enhanced functionalities for EudraVigilance and the PSUR repository which ultimately provides public health benefits across Europe;



Pharmacovigilance Fees

News:

- Pharmacovigilance annual fee advice notes were sent to QPPVs on the 20th April 2015 and the Agency will send the Pharmacovigilance annual fee invoices early July 2015;
- Following feedback received from Industry, the Agency is currently producing a document which will outline how 'chargeable units' for Pharmacovigilance fees are calculated;
- Pharmacovigilance fees Questions and Answers page published and dedicated pharmacovigilance fees query management system launched;
- A series of training videos to provide further information on the pharmacovigilance fees payable to the Agency was released.
- The European Medicines Agency launched the EMA invoicing portal: https://fees.ema.europa.eu/bd/public/zindex.jsp

What MAHs need to do:

- As already instructed, check that the chargeable units line listing information found within the annual fee advice notes is correct:
  - If chargeable units line listing is **correct** - **No further action required.**
  - If chargeable units line listing is **incorrect - Amend the relevant data in the Article 57 database no later than by the 30th June.**
  - NOTE**:** Failure to comply with these instructions will lead to the rejection of any subsequent dispute on fees payable where the claim is relating to the incorrectness of any element relevant to the determination of a chargeable unit.
- Register with the EMA invoicing portal by selecting "Register Now…" from the portal log-in page.
  NOTE: You will require your **Customer Account Number** and an **Invoice Number** in order to register for the portal. Therefore, only existing customers of the EMA will be able to register at this stage.
  To request a **Customer Account Number**, please contact the EMA via the following email address: accountsreceivable@ema.europa.eu.
- In order to benefit from a fee reduction or fee exemption, any marketing authorisation holder claiming to be a micro-, small- or medium-sized enterprise must complete the SME declaration form, found on the SME Office's "How to apply" page, and send it to sme@ema.europa.eu. If a marketing authorisation holder already holds a valid SME status with the Agency, you are not required to re-submit this information.

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