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EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Pharmacovigilance Programme UPDATE

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IN THIS ISSUE

In this update

This 5th Update captures the important progress made in the development of the pharmacovigilance information systems and services. These systems will contribute to public health through optimisation of the safe and effective use of medicines. They should also facilitate pharmacovigilance, delivering rationalisation and efficiency gains, involving the processes and systems of European Medicines Agency, National Competent Authorities and Marketing Authorisation Holders.

Enhanced Pharmacovigilance through effective implementation of information systems and services

- On 6 August 2015 the EU Telematics strategy and implementation roadmap 2015-2017 was published.
- This describes the vision and strategy, and includes the implementation of Pharmacovigilance systems and services as a priority.

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:

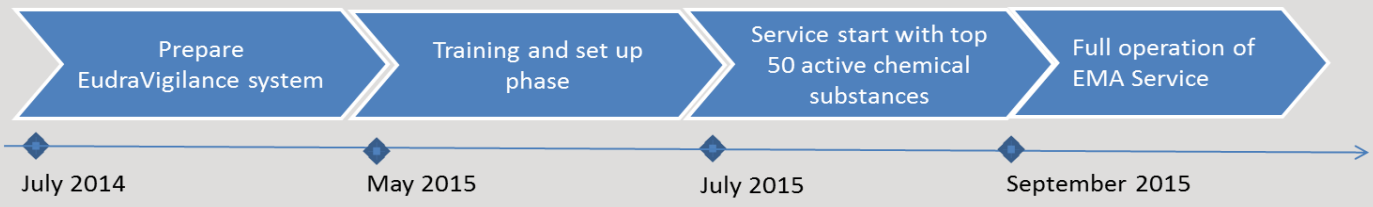
- Improved safety monitoring of medicines through better quality of safety information;
- Reduced administrative burden on Marketing Authorisation Holders (MAHs) for the relevant substances;
- MAHs will have access to up-to-date results of medical literature monitoring (MLM) activities and ICSRs generated,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

News:

- The full operation of the European Medicines Agency's medical literature monitoring service was launched on 1st September 2015. The service covers 300 chemical active substance groups and 100 herbal active substance groups;
- The 2 month launch phase was completed on 31st August 2015. The service covered the 50 most common chemical active substance groups during this period. The MLM launch phase closure report will be published on 14 October 2015;
- Support webinars for stakeholders have been organised until the end of 2015 (see Medical Literature Monitoring website for schedule);
- An independent audit of the service provider's internal quality management and control systems and of the output of the service will be conducted at the end of 2015 (and 2-yearly thereafter);
- Additional supporting documents including the EMA contractor Standard Operating Procedures (SOPs) for conducting MLM service were published on 1 October 2015.

What MAHs need to do:

- The list of active substance groups and a reference to the journals covered by EMA's medical literature monitoring service are available on the Medical Literature Monitoring page. Companies are advised to consult the list to check whether their products are covered by the service;
- For products containing active substances covered by Agency's MLM service, marketing authorisation holders shall not be required to report to EudraVigilance the suspected adverse reactions from the medical literature monitored by EMA. It is important to note that marketing-authorisation holders need to continue to monitor all other medical literature not covered by the literature reference databases applied for the service by the Agency (e.g. monitor scientific and medical publications in local journals in countries where medicinal products have a marketing authorisation);
- Further information on the adaptations of business processes can be found at the dedicated Medical Literature Monitoring website;
- Please send all enquiries to mlm@ema.europa.eu.



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:

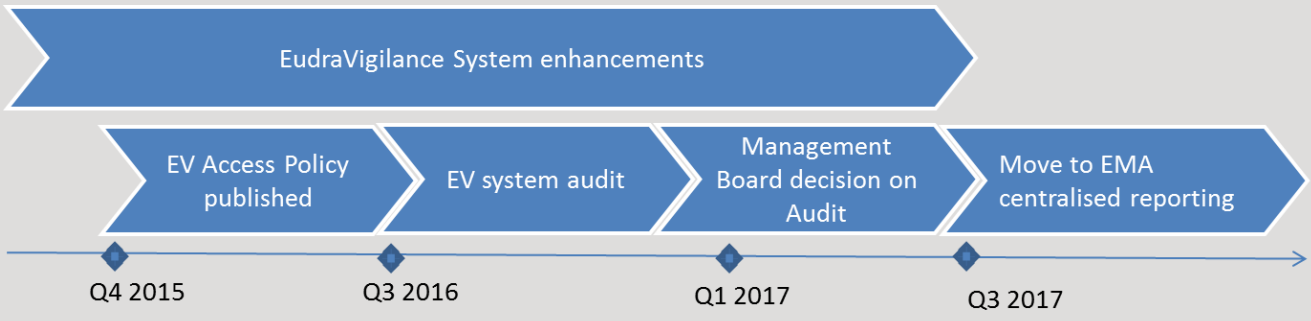
- Compliance with international data standards (and future compatibility with ISO IDMP standards based on Article 57 data) including backwards and forwards conversion tools for E2B(R2)/(R3) messages;
- Improved performance and scalability of new system to cope with foreseen increase in users and volume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

News:

- Following public consultation the revised EudraVigilance Access Policy is being finalised and will be considered by EMA Management Board in December 2015. This foresees enhanced access to adverse reactions reports in mid-2017;
- The EudraVigilance webpage will be updated from November 2015 with the publication of several key documents for the future of EudraVigilance, such as the EudraVigilance Stakeholder Change Management Plan, which outlines the IT & business changes to be made by stakeholders;
- The EudraVigilance functionalities audit is scheduled to take place in 3rd quarter 2016, with the move to centralised reporting in mid-2017.

What MAHs need to do:

- Review the EudraVigilance Stakeholder Change Management Plan and develop a change management plan for use within each company.



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.

News:

- An annual fee is charged for nationally authorised medicines only, with respect to the monitoring of literature cases and the improved use of information technology tools. The 1st annual pharmacovigilance fee invoices were issued in July 2015;
- On 21 July 2015 the Agency published a document which outlines how 'chargeable units' for Pharmacovigilance fees are calculated: Guidance on how chargeable units are derived from medicinal product information held within the Article 57 database;
- The EMA invoicing portal has been launched (enables customers to get instant access to their account, view and print invoices, raise invoice queries and make payments via SEPA direct debit) https://fees.ema.europa.eu/bd/public/zindex.jsp.

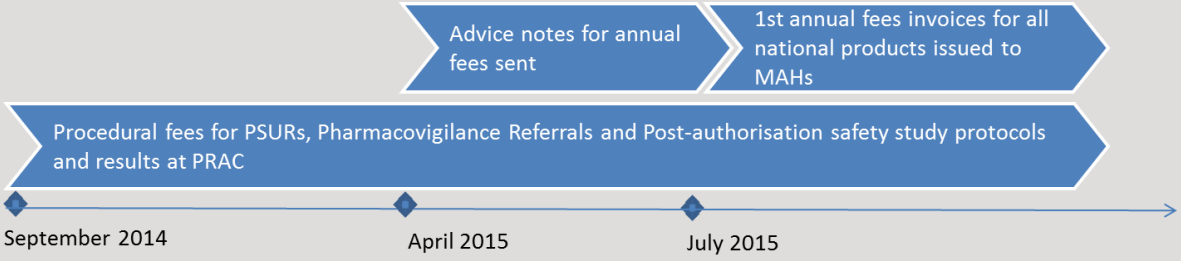
What MAHs need to do:

- Register with the EMA invoicing portal by selecting "Register Now…" from the portal log-in page.

  NOTE: Your Customer Account Number will be required and an Invoice Number will be required in order to register for the portal. Therefore, only existing customers of the EMA will be able to register at this stage.

  If you are not an existing customer of EMA request a Customer Account Number by contacting 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 within 30 calendar days from the date of the invoice from the Agency. If a marketing authorisation holder already holds a valid SME status with the Agency, you are not required to re-submit this information.



Database of Medicinal Products (Article 57)

Need more information?

Data submission for authorised medicines

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

Scope:

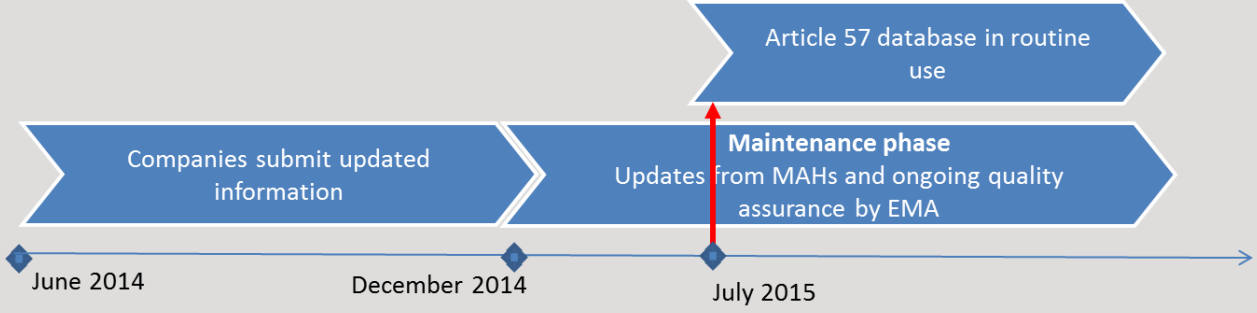
- To deliver structured and quality assured information on medicinal products authorised in the EU that can support EU terminologies of products, substances, and organisations used to power pharmacovigilance and regulatory systems.

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 with 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).

News:

- The current Article 57 initial data re-submission produced over 500k medicinal products (EV Codes) updated in the Art57 database;
- Following discussions with Industry Associations at the Article 57 Implementation Working Group (IWG), from 4th November 2015, the Agency will start to communicate the outcome of the quality control process via an additional XEVPRM XML Acknowledgement message (so called "3rd Acknowledgement") to the MAH sender's organisation ID;
- The Agency is currently rolling out permanent access to Art57 data to the National Competent Authorities. This includes information on the QPPVs contact details, the contact information for pharmacovigilance enquiries and the locations in the Union where pharmacovigilance system master files are kept;
- In October 2015 the Agency published a document, which details the measures taken by the European Medicines Agency at the pre-submission, submission, and post-submission phases of data entry into the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD) to improve data quality in the Article 57 database.



Database of Medicinal Products (Article 57)

What MAHs need to do:

- Using the electronic XEVPRM format, 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 changes to the terms of the existing 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.
- MAH organisations using in-house solutions (i.e. Gateway Users), should enhance their system to allow the receipt of the 3rd Acknowledgement as of 4th November 2015.

PSUR repository

Need more information?

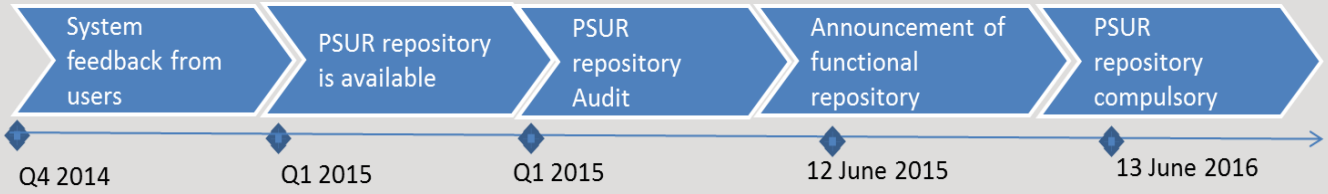
http://esubmission.ema.europa.eu/index.htm

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.



PSUR repository

News:

- On 12 June 2015 the EMA Management Board announced that PSUR Repository has achieved its full functionality and the use of the repository in the European Union will become mandatory on 13 June 2016;
- From 1 September 2015, the use of the XML delivery file for all PSUR submissions to the EMA via the eSubmission Gateway and/or the Web Client is mandatory. It is no longer possible to submit PSURs using the existing filenaming convention;
- The release of the new PSUR Repository version is scheduled in October 2015. The NCA and Industry user acceptance testing has taken place between 28 September – 02 October. This release will provide amongst others, linking of the PSUSA procedure number with products which are in scope of the procedure allowing more direct searches and improved validation functionality;
- The development of the four post-audit functionalities started 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. The most important feature of this release will be the API allowing an automated 2-way exchange between the NCAs' IT systems and the PSUR repository.

What MAHs need to do:

- The use of the PSUR repository in the European Union will become mandatory on 13 June 2016.
- It is important for MAHs to consider the following points when planning a submission to the repository:
  - Consider which business processes will have to be adapted to use the repository;
  - Access the available guidance on the use of the PSUR Repository and the eSubmissions Gateway/ Web Client well in advance of any planned submission to the repository;
  - Check that product data in the Article 57 database is correct prior to a planned submission.
- In addition to any submission to the PSUR Repository, MAHs for nationally authorised products (NAPs) are reminded that submissions to the relevant NCAs must continue until the use of the system becomes mandatory. Submission requirements for NAPs can be found here: Requirements on Submissions for Periodic safety update reports (PSUR) to National Competent Authorities (NCAs) for products authorised via National Procedures, MRP and DCP (NAPs)
- Follow the PSUR Repository bulletins published regularly on the eSubmission web page (http://esubmission.ema.europa.eu/psur/psur_repository.html)
- Users should report any issues they have with the system through the PSUR Repository mailbox: PSURrepository@ema.europa.eu

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