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EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Pharmacovigilance Programme UPDATE

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IN THIS ISSUE

This Update

This third edition is aimed at providing marketing authorisation holders (MAHs) with information to help prepare for business change and give you full awareness of the projects, their scopes and timelines.

Enhanced Pharmacovigilance through effective implementation of information systems and services

New EU Pharmacovigilance legislation has been operational since July 2012. The legislation foresees various information systems to enhance pharmacovigilance, particularly to support the collection, management and analysis of data, information and knowledge. These systems will contribute to public health through optimisation of the safe and effective use of medicines.

We are at an important point in our projects with major deliverables scheduled throughout 2015 to support business activities of the revised pharmacovigilance legislation and to improve the relevant business functions to maximise the benefits for stakeholders.

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

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).
- This will improve safety monitoring of medicines through better quality of safety information. This will reduce the administrative burden on MAHs for the relevant substances.
- This service will carried be only by a contractor, selected following a recent tender process.

Benefits:

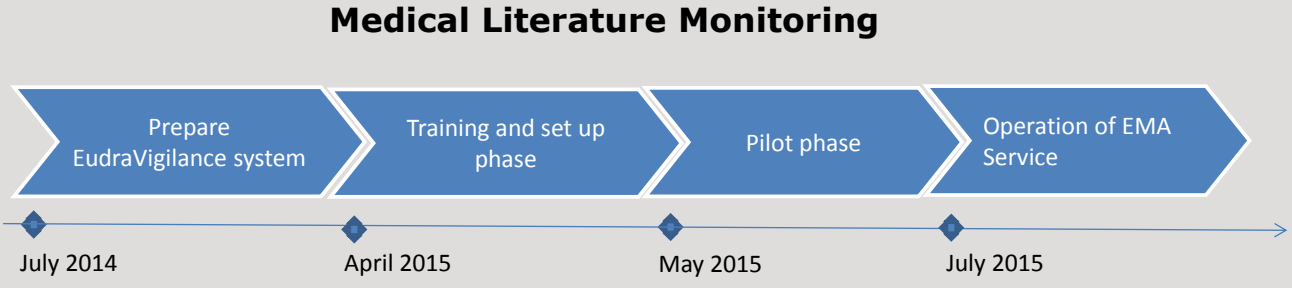
- MAHs will have access to up-to-date results of MLM activities and ICSRs generated for selected medicinal products, allowing them to repost to other regulatory bodies (outside EU) in a timely fashion;
- This service will be carried out by a contractor, selected following a recent tender process.

What MAHs need to do:

- Consider the potential impact of the EMA literature service on your business processes taking into account the provisions set out in Article 107 (3) of Directive 2001/83/EC i.e. for medicinal products containing the active substances referred to in the list of publications monitored by the Agency, MAHs shall not be required to report to the EudraVigilance database the suspected adverse reactions recorded in the listed medical literature.
- Review the detailed guidance and list of substances when published by EMA

Medical Literature Monitoring news:

- EMA is in the process of finalising:
  - A detailed guide regarding the monitoring of medical literature and the entry of relevant information into the EudraVigilance database by the European Medicines Agency
  - The scope of the service in terms of substances including herbals, to be monitored. The service will aim to benefit the maximum number of companies by focussing on established substances, i.e those substances in multiple medication products.



Pharmacovigilance Fees

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;

Need more information?

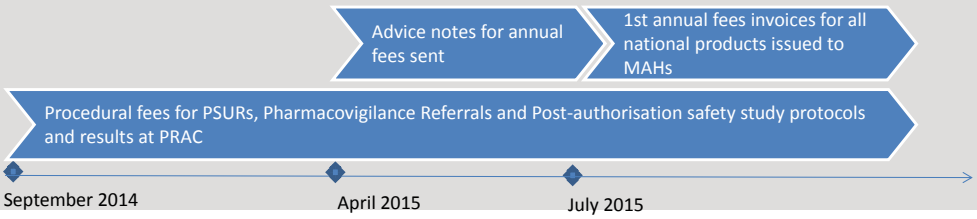
Pharmacovigilance fees payable to the European Medicines Agency

Explanatory note on pharmacovigilance fees payable to the European Medicines Agency: see here

What MAHs need to do:

- Read the Explanatory Note on pharmacovigilance fees payable to the European Medicines Agency.
- Keep the QPPV's addresses, emails and names up-to-date in the Article 57 product database in order to promptly receive the advice note , due in April 2015, that explains the annual fee (see under news) and any other relevant communication from the Agency.
- In the Article 57 product database, ensure the legal basis, medicinal product type and SME status is correct thereby allowing correct calculation of any fee reductions or fee exemptions.
- Ensure are up to date MAH names and addresses in the Article 57 product database (Organisation CV) to:
  - Avoid generation of duplicate Chargeable Units (due to different MAH name spelling)
  - Avoid duplication of invoices dispatched
- Upon receipt of the Annual Fee advice note in April 2015, check if the chargeable units line listing information 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 product database thus ensuring that a correct Invoice will follow in July 2015.**

Pharmacovigilance Fees



Pharmacovigilance Fees news:

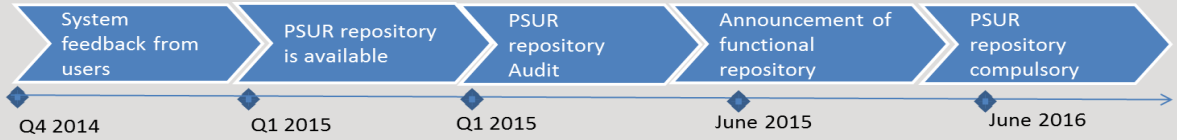
- In March 2015, the EMA published an Explanatory Note on pharmacovigilance fees payable to the Agency and launched a dedicated Pharmacovigilance Fees webpage; see here
- As specified in the Regulation (EU) No 658/2014, on fees, two types of Pharmacovigilance fees are payable to EMA for the conduct of pharmacovigilance activities:
  - The **procedure-based fees** which apply to pharmacovigilance referrals, PSURs and PASS procedures. The EMA began charging and collecting for these procedure-based in August 2014.
  - The **annual fee** which is applicable to Nationally Authorised Products only. Invoices will be calculated based on Article 57 product data and will be sent out in July 2015.
- MAHs subject to a pharmacovigilance annual fee will be issued with an electronic invoice in July 2015.
- Prior to issuing an invoice, the Agency will provide MAHs with an opportunity to review their product information as recorded in the Article 57 database by supplying the qualified person for pharmacovigilance with an advice note. The advice note contains the chargeable units line listing and a reference to the related products. For procedure-based fees, the advice note also contains regulatory background and electronic submission guidance. Please note that an advice note is supplied for the Annual Fee, PSURs and Referrals only – it is not applicable for PASS procedures (where the fee amount levied is not based on the number of 'chargeable units').
- The Advice note will include:
  - Information on Pharmacovigilance procedure type, number where applicable (PSUSA, Annual Fee, Referrals)
  - Information on procedural regulatory background (where applicable)
  - General information on Fees payable to the European Medicines Agency
  - Determination of the number of 'chargeable units'
  - Possible fee reductions and fee exemptions
  - Invoicing and payment formalities
  - Reference to the data submission obligations for MAHs as laid out in Article 57(2) of Regulation EC

PSUR repository

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.

PSUR Repository



PSUR Repository 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:

- The Repository for PSURs and their assessment reports was launched by the European Medicines Agency on 26th January 2015;
- The PSUR Repository audit is ongoing; the finalised audit report is expected be submitted to the PRAC in April 2015. Based on the audit report, the PRAC is expected to adopt a recommendation as regards the PSUR repository. The PRAC recommendation is expected be provided to the EMA Management Board in June 2015;
- The initial pilot phase started in February with nine centrally authorised product (CAP) PSUSA procedures run in the repository. In March, 10 CAP PSUSA procedures will run in the system. Standard business processes at NCAs and EMA will run in parallel to repository activity. Submission requirements to NCAs remain unchanged for MAHs, (until twelve months after the EMA Management Board decision, that the repository is functional);
- NCAs and industry trainings were held regularly in February and March;
- The extended pilot phase will begin in May and will include nationally authorised products (NAP) in addition to CAPs. CAP MAH contacts and NAP QPPV contacts have been invited to participate for procedures starting in May; all NAP MAHs are encouraged to submit their PSURs not only to the relevant NCA, but additionally to the repository;
- The detailed business requirements for post-audit deliverables have been finalised and the planning for the post-audit functionalities is part of the ongoing audit. The development of the post-audit functionalities will likely start in July 2015.

What MAHs need to do:

- Follow announcements on the EMA website on the PSUR repository phased implementation process and mandatory use in 2016;
- Follow the regular news bulletins on the dedicated PSUR Repository section of the eSubmission webpage for information on project activities and upcoming trainings, see here;
- Enrol for interactive Q&A sessions where a short demo of the system will be presented after which questions about the repository can be discussed. Previously recorded webinar training sessions on how to submit to the PSUR Repository, together with presentations and user guidance documents are also available (see eSubmission Gateway/Web Client website for details);
- Companies, who have not previously used the eSubmission Gateway/Web Client should register as soon as possible. More information on the eSubmission Gateway/Web Client can be found on the eSubmission Gateway/Web Client website.

Adverse drug reaction reporting and Signal management

Scope:

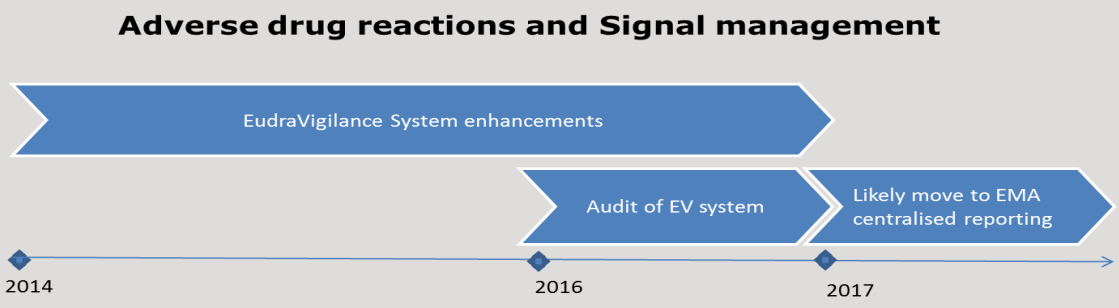
- Legal requirement for an enhanced adverse reaction collection and management system (EudraVigilance) that delivers better health protection through simplified reporting, better quality data and better searching, analysis and tracking functionalities. Enhanced detection of new or changing safety issues 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:

- On 21st January 2015 the EMA published a guide to support the implementation of a new international standard for the safety monitoring of medicines in the EU. The so-called ISO ICSR standard improves the reporting of suspected side effects of medicines in Individual Case Safety Reports (ICSRs).
- The transition to using the new international standard will be actively managed by the Agency in collaboration with NCAs and MAHs. This transition will be the subject of future communications;
- The testing of the ICSR backwards and forwards conversion rules for EU specific data fields is ongoing with the plan to complete the work by the end of April 2015;
- Following the closure of the public consultation in September 2014, the revised EudraVigilance Access Policy is being finalised and is expected to be published in Q3 2015. This foresees enhanced access to data to conduct product monitoring;
- As a service to industry and to increase efficiency the Agency has started to translate its recommended changes to product information based on the assessment of safety signals into all official languages of the European Union. The translations should be used by MAHs to update the product information of their medicines.



Adverse drug reaction reporting and Signal management

What MAHs need to do:

- Prepare for use of the new data format – ISO/ICH ICSR E2B(R3) – and simplified reporting to EV;
- 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 (see Art.18 of Commission Implementing Regulation (EU) No 520/2012);
- Engage with information and training events.

Further information can be found at: https://eudravigilance.ema.europa.eu/human/index.asp

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.

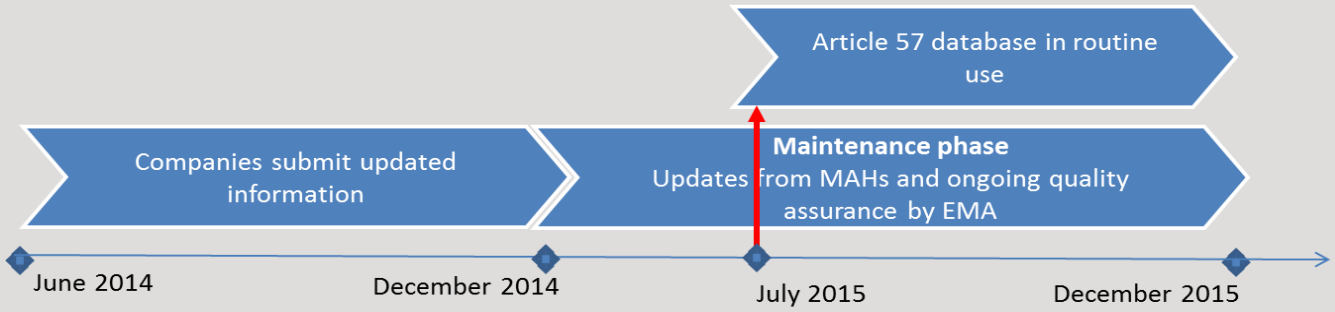
What MAHs need to do:

- From 1 January 2015, 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 the Agency of any subsequent changes to the terms of already granted 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.
- The Agency is planning services for the National Competent Authorities to make available 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.

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).

Article 57 database on medicinal products



Database of Medicinal Products (Article 57) news:

- The Article 57 data re-submission led to approximately 490k products updated in the Article 57 database (March 2015). The EMA is continuing to support industry in the submission of medicinal product data under the Article 57 legal requirements.
- The EMA will follow-up on submissions from MAHs that informed of a delay in their plans for submission.
- EMA continues its co-operation with MAHs to ensure Article 57 data correctness. As of the end of February approximately 97k Products (EVCodes) were quality reviewed against the provided SmPCs. When errors are found, and there is information available to correct it in the MAH submitted product information, amendments are made by the Agency in the Article 57 database. A quality control report is provided to the sender organisation's QPPV, outlining the quality findings and the required actions to be taken by the concerned MAH. Should the MAH wish to query any of the changes/corrections made by the EMA, or would like to receive further clarification on the performed amendments, an email should be submitted to the Article 57 Quality Control Inbox (Art57-QC@ema.europa.eu);
- On 17th February 2015, the Agency published Outlines on Article 57(2) of Regulation (EC) No 726/2004, which provides a general overview on the Article 57 data work-flow, data management and governance aspects and future use and evolution of the data.

Need more information?

Data submission for authorised medicines

List of guidance documents related to the data submission for authorised medicines

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