EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Update of EudraVigilance Operational Plan

Pharmacovigilance platform meeting – 30 October 2020

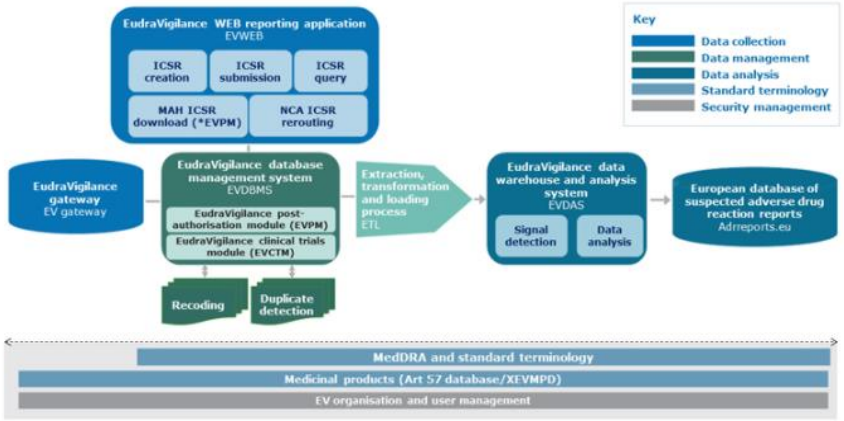
Presented by Rodrigo Postigo

Background

- 1st published following the launch of the new EV system in November 2017.
- Objective:
  - To outline technical as well as operational activities with anticipated timelines and to highlight how EV and stakeholders that interact with the system will be affected.
  - To ensure sustainability of EV in support of the EU pharmacovigilance activities and the protection of public health.
- The current operational plan covers the period 2020 to 2022.

Topics

- Agency's identity access
- Human and Veterinary EudraVigilance
- EV Gateway
- Brexit
- Mandatory use of ICH-E2B(R3)
- ISO IDMP standards
- EudraVigilance monitoring by MAHs
- ICSR data quality review
- Clinical trial regulation
- Medical Literature monitoring
- GVP VI
- EudraVigilance and operation in pharmacovigilance
- Training and support



Integration with the Agency's identity and access management (IAM2) project

- Integration of the EV Human XCOMP (external testing system) registration process with the IAM components completed successfully.
- Improvements of the IAM Human components and the EudraVigilance Human registration to include the self-management of virtual affiliates also completed.
- Revisions of the EV Human registration manual and online training in line with the updates are provided on the EudraVigilance training page.

EudraVigilance: how to register

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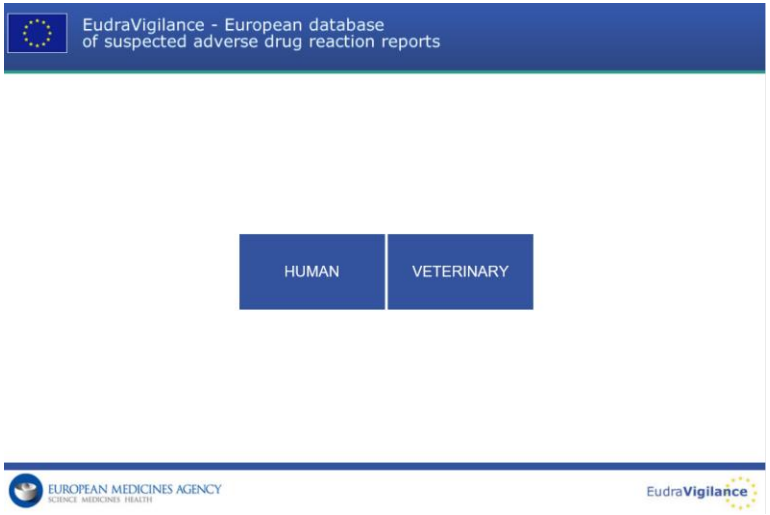
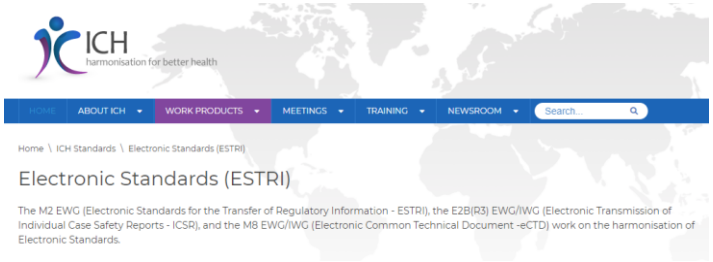
The integration of the Human and Veterinary EudraVigilance system component

- Messaging components using a common platform completed.
- adrreports.eu portal upgraded to include veterinary ADR reports.



Gateway for the Electronic Standards for the Transfer of Regulatory Information (ESTRI)

- Software upgrades as required by the Agency's IT strategy, in particular the implementation of the EDIINT recommendations on the secure transfer of regulatory information which were updated in June 2018.
- The Agency has contacted all organisations that are currently still using AS1 for connecting to the EV gateway to inform them of stopping the use of AS1 towards the end of 2020.
- Survey launched on 20th March 2020 for completion by 3rd April 2020, to gather information from our industry end users to inform future planning of the development of the Gateway for the ESTRI. (The EV-EWG was consulted on the survey).



Brexit preparations

- Technical adaptations to implement the relevant changes at the end of the transitional period.
- Discussions about the impact of the Northern Ireland protocol.
- Communications will be issued.

EUROPEAN COMMISSION
DIRECTORATE-GENERAL FOR HEALTH AND FOOD SAFETY

EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Brussels, 13 March 2020
REV3 - replaces the notice (REV2) dated 1 February 2019 and the Q&A document (REV4) dated 1 February 2019

NOTICE TO STAKEHOLDERS

WITHDRAWAL OF THE UNITED KINGDOM AND EU RULES FOR MEDICINAL PRODUCTS FOR HUMAN USE AND VETERINARY MEDICINAL PRODUCTS

- Non-serious adverse events occurring in Northern Ireland have to be reported as if they have occurred in the EU;

Agreement on mandatory use of E2B(R3) in EEA

- Having considered the PRAC recommendation, the EMA Management Board announces that the use of:
  - the ISO Individual Case Safety Report standard as referred to in Article 26(2)(a) of the Commission Implementing Regulation (EU) No 520/2012 and the modalities on how to use this ISO ICSR standard defined in the ICH E2B(R3) documentation, and
  - the ISO terminology on pharmaceutical dose forms and routes of administration referred to in Article 25(1)(f) of Commission Implementing Regulation (EU) No 520/2012,
- shall become mandatory as of **30 June 2022** in relation to reporting obligations to EudraVigilance.
- EU Individual Case Safety Report (ICSR) Implementation Guide currently under revision.

EMA Management Board
EMA/561671/2019

Announcement of the EMA Management Board

Confirmation of the mandatory use of the ISO Individual Case Report standard based on ICH E2B(R3) modalities and related ISO standard terminology

ISO IDMP standards (Cont)

- **RMS** and **OMS** went live in June 2017. Any requests for new or updated referentials or organisations have now to be pre-registered via the Agency's SPOR portal.
- Further integration steps of **RMS** and **OMS** and the XEVMPD are planned to be implemented as part of the **PMS** project.
  - The submission process of XEVPRMs will remain unaffected although it will no longer be possible to create proposed terms and create/update organisations via XEVPRM.

SPOR data management services

- Substance Management Services (SMS)
- Product Management Services (PMS)
- Organisation Management Services (OMS)
- Referentials Management Services (RMS)

ISO IDMP standards (Cont)

- **SMS** Phase 1 went live in June 2019. Substances are no longer registered in the XEVMPD, instead, they are being registered in SMS and then synchronised with the XEVMPD through a feedback loop.

SPOR data management services

Substance Management Services (SMS)

Product Management Services (PMS)

Organisation Management Services (OMS)

Referentials Management Services (RMS)

ISO IDMP standards (Cont)

- As future steps, EMA plans to further deliver **SMS** and **PMS** releases to support EU-wide regulatory activities building upon the data foundations of **RMS** and **OMS**.
- As regards ICSR submissions, EudraVigilance and EVDAS, the main impact expected in relation to the implementation of the ISO IDMP standards during 2020 to 2022 will refer to the implementation of the ISO IDMP standard 11239 on pharmaceutical dose form, units of presentation and routes of administration.

SPOR data management services

- Substance Management Services (SMS)
- Product Management Services (PMS)
- Organisation Management Services (OMS)
- Referentials Management Services (RMS)

EudraVigilance Monitoring and signal management

- In Dec 2019, EMA and the Commission agreed to extend the pilot until the end of 2021 to generate more robust data, after reviewing the experience gained in the first year of the pilot.
- In April 2020, a new availability of eRMRs was launched in the EVDAS MAHs' Dashboard to increase the quality of the data and minimise the number of technical issues.
- The MAHs EVDAS Manual was updated to reflect the changes.
- Currently reviewing the possibility to increase the number of users per MAH from 5 to 10.

20 April 2020
EMA/167839/2016

EudraVigilance User Manual

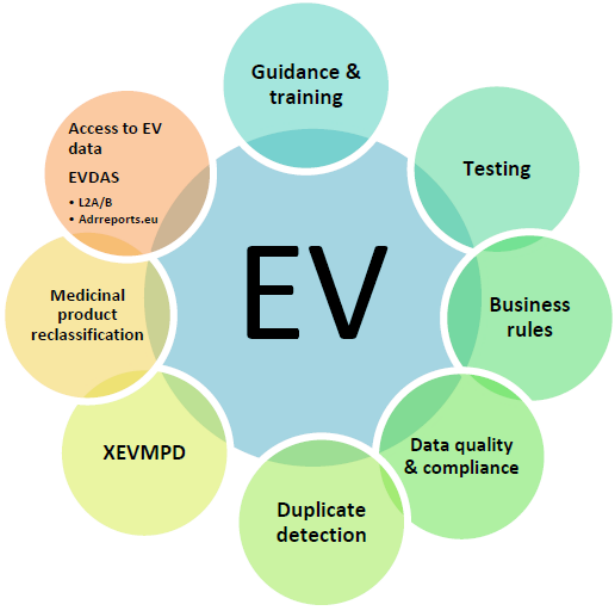
Marketing Authorisation Holders - EudraVigilance access via the EudraVigilance Data Analysis System

electronic Reaction Monitoring Reports, Line Listings and Active Substance Grouping reports

Version 2

EudraVigilance and ICSR data quality review

- Detailed guide regarding the EV data management activities by the EMA – published in January 2020 – currently under revision to update Section 8 'Roles and responsibilities of different stakeholders'.
- A monthly publication of spreadsheets providing information on nullified ICSRs and master cases with associated duplicates to facilitate case reconciliation by NCAs and MAHs is planned to start in **Q4 2020**.
- The monthly provision of compliance reports for the purpose of the monitoring of ICSR submission time frames to all EudraVigilance registered organisations is planned to start in the **first half of 2021**.
- The ICSR data quality review activities will be continued. A new tender for an EMA service provider will conclude in 2020 and the activity will continue uninterrupted.



Clinical Trial Regulation

Simplifies the safety reporting by sponsors by facilitating the submission of:

- Annual Safety Reports (ASRs) directly to the ASR EudraVigilance Module in the European Clinical Trials Information System (CTIS).
- SUSARs sent directly to the EV Clinical Trial Module (EVCTM), from where these reports are forwarded to the Member States concerned. In this context, functionalities that facilitate the forwarding of SUSARs from EVCTM to the Member States concerned have already been put in place so they can be "switched on" when the regulation becomes applicable.
- It is proposed to fix the Go-Live date of CTIS to **December 2021**, which means the Clinical Trial Regulation would also enter in application at that time.

01 Issue 1 June 2020

EUROPEAN MEDICINES AGENCY
SCIENCE · MEDICINES · HEALTH

CTIS HIGHLIGHTS

News, views and interviews for the Clinical Trials Information System (CTIS). Published twice a year by the European Medicines Agency.

An agency of the European Union

Welcome to CTIS

Fergus Sweeney, Accountable executive for delivery of the Clinical Trials Information System (CTIS), European Medicines Agency

"Welcome to the first edition of CTIS Highlights, the newsletter for the Clinical Trials Information System (CTIS) Programme. It is an exciting time for the system as we progress to the audit and then to Go-Live. Future editions will give insight into the functionality that is being made available and information on the rollout of training and user support."

INSIDE THIS ISSUE

CTIS Overview

The implementation of the Clinical Trial Regulation (Regulation (EU) No 536/2014) (CTR) will bring a major change in the authorisation, conduct, supervision and reporting of clinical trials in the European Union (EU). The Regulation harmonises the submission, assessment and supervision processes for clinical trials throughout the EU via CTIS. Articles 80 and 81 assign the European Medicines Agency (EMA) to set up and maintain the information system, in collaboration with the Member States and the European Commission. CTIS will enable the implementation of the Regulation.

CTIS will be the single-entry point for submitting, assessing, authorising, supervising and reporting a clinical trial in all Member States of the EU. The system is currently under development and will have collaboration and communication tools, workflow and document management capabilities. It will include a user

clinical trials information. CTIS will centralise the submission process for clinical trial applications and the assessment and authorisation by Member States in a single unique platform.

It will facilitate day-to-day business processes of Member States and sponsors of clinical trials throughout the lifecycle of a clinical trial harmonising submission and maintenance of trial applications, assessment and supervision of trials and promoting patient safety and transparency.

More information ...

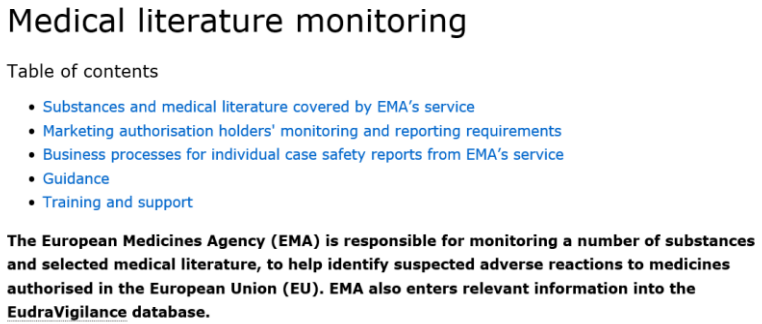
The CTIS user community will consist of clinical trials sponsors including academia, commercial and non-commercial organisations, marketing authorisation applicants, Member States' national competent authorities and ethics committees, the EMA, the European Commission and the general public. Except for the general public, all users will access the CTIS functionalities via the two restricted dedicated workspaces: the sponsor workspace and the authority workspace. The

Clinical Trial Regulation (cont)

- Revision of a number of documents in Eudralex Volume 10.
- New documents were prepared to cover new aspects introduced by the same Regulation.
- Until the Clinical Trial Regulation becomes applicable, sponsors should follow the documents relevant to the Clinical Trials Directive.
- Reference is made to the "Questions & Answers" Document on the Clinical Trial Regulation, which is routinely being updated and for which a publication is planned for in a staggered approach.

Medical Literature Monitoring (MLM) service

- In June 2020, EMA added nine additional active substances which are being investigated as potential treatments for COVID-19, and for which there are multiple MAHs.
- COVID-19-related search terms were added to the regular literature searches for six active substance groups (azithromycin, ciclosporin, dexamethasone, hydrocortisone, ribavirin and prednisolone) that were already included in the service.
- COVID-19-related literature searches started on 1st June 2020 in EMBASE, and on 1st July 2020 in EBSCO.
- New tender for an EMA service provider to be launched in 2020.



Medical literature monitoring

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- Substances and medical literature covered by EMA's service
- Marketing authorisation holders' monitoring and reporting requirements
- Business processes for individual case safety reports from EMA's service
- Guidance
- Training and support

The European Medicines Agency (EMA) is responsible for monitoring a number of substances and selected medical literature, to help identify suspected adverse reactions to medicines authorised in the European Union (EU). EMA also enters relevant information into the EudraVigilance database.

GVP Module VI (revision 3)

- On 20 November 2019, the Assembly of the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) endorsed the "Concept Paper Post Approval Safety Data Management: Definition and Standards for Expedited Reporting E2D (Revision 1)".
- Taking into account that the revision of the E2D guideline will impact on the provisions set out in the Guideline on good pharmacovigilance practices (GVP) - Module VI – Collection, management and submission of reports of suspected adverse reactions to medicinal products (Rev. 2), a revision of GVP Module VI will be scheduled following adoption of the harmonised ICH E2D(R1) guideline (step 4 of the ICH process)

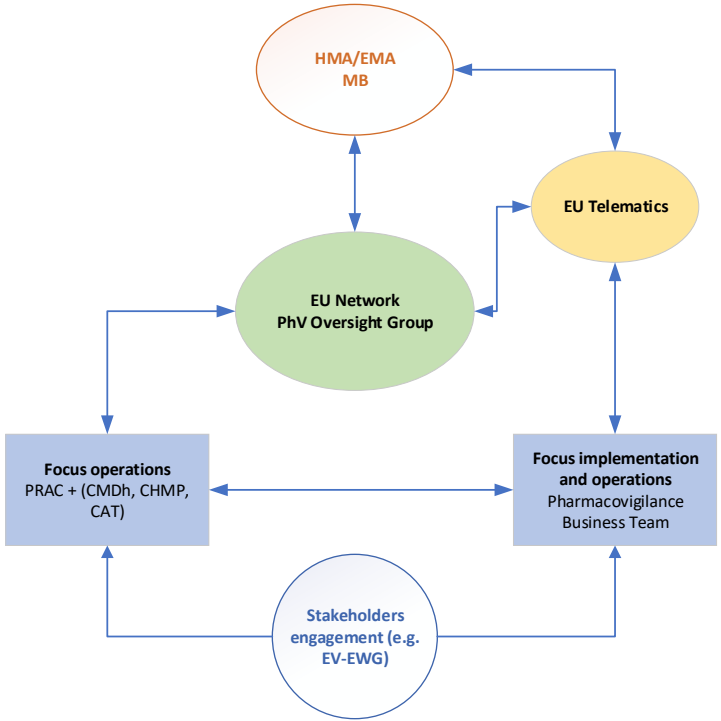
28 July 2017
EMA/873138/2011 Rev 2*

Guideline on good pharmacovigilance practices (GVP)

Module VI – Collection, management and submission of reports of suspected adverse reactions to medicinal products (Rev 2)

EudraVigilance and operation of pharmacovigilance

- In the context of the operation of EV, technical and procedural aspects are raised by NCAs, MAHs and sponsors of clinical trials, which require further discussion and clarification to ensure a coordinated approach across the EEA.
- The pharmacovigilance governance in the EEA provides a forum to discuss and address emerging issues.
- The **Pharmacovigilance Business Team** which is composed of pharmacovigilance experts of NCAs and the EMA is meeting on a regular basis.
- Guidance and communications will be issued as needed.



EudraVigilance Expert Working Group

- Includes members from the NCAs and representatives of Industry associations.
- During the EMA BCP for relocation the meetings were significantly reduced.
- Members were consulted via written procedure on different issues.
- Virtual meetings were restarted 22nd October 2020.
- The updated work-programme and new membership list will be published by end of 2020.

PDCO | Working parties and other groups

EudraVigilance Expert Working Group

Share

The EudraVigilance Expert Working Group (EV-EWG) advises the pharmacovigilance governance structure of the European Union (EU) regulatory network on aspects of the EudraVigilance system.

EV-EWG meetings take place at the European Medicines Agency's (EMA) offices. The Agency also provides secretariat support for the group.

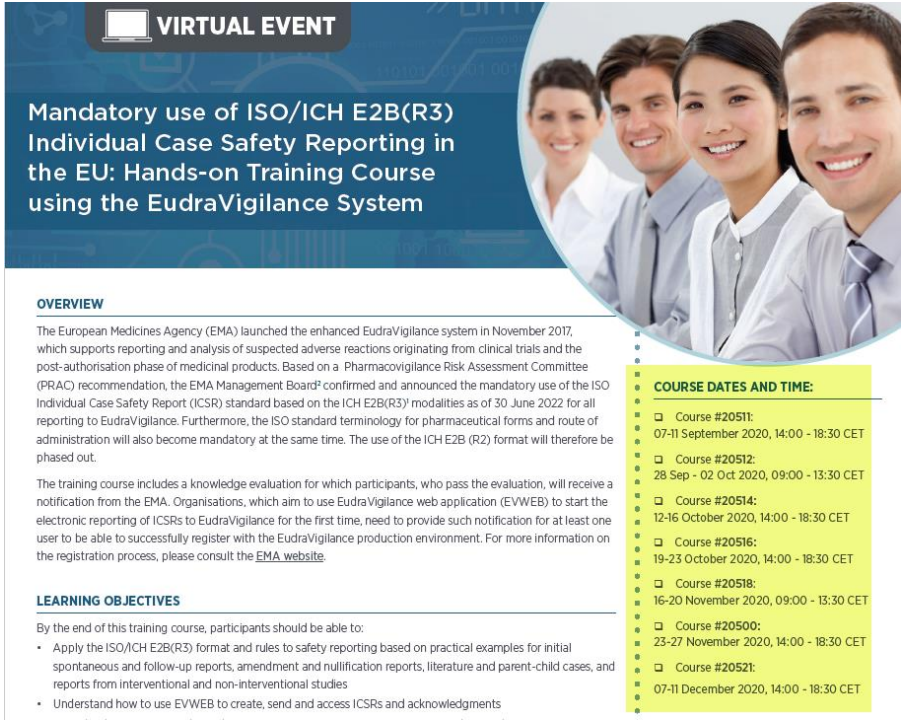
Mandate

The working group's mandate includes:

- developing policies and business requirements, drafting guidance and co-ordinating aspects related to implementing, operating and accessing EudraVigilance;
- co-ordinating personal data protection activities in relation to pharmacovigilance in accordance with EU data protection legislation;
- providing input into the international standardisation work in pharmacovigilance and facilitating a harmonised implementation in the EU and at international level, including support for the maintenance of the EU important medical events list ;

Training and support

- Face-to-face training courses on the enhanced EV system were cancelled.
- Replaced by virtual events, calendar published from Sep to Dec 2020.
- EVDAS training for Member States scheduled for Nov 2020 also virtually.
- Support webinars have been discontinued.
- The e-learning modules remain available.



VIRTUAL EVENT

Mandatory use of ISO/ICH E2B(R3) Individual Case Safety Reporting in the EU: Hands-on Training Course using the EudraVigilance System

OVERVIEW

The European Medicines Agency (EMA) launched the enhanced EudraVigilance system in November 2017, which supports reporting and analysis of suspected adverse reactions originating from clinical trials and the post-authorisation phase of medicinal products. Based on a Pharmacovigilance Risk Assessment Committee (PRAC) recommendation, the EMA Management Board[2] confirmed and announced the mandatory use of the ISO Individual Case Safety Report (ICSR) standard based on the ICH E2B(R3)[1] modalities as of 30 June 2022 for all reporting to EudraVigilance. Furthermore, the ISO standard terminology for pharmaceutical forms and route of administration will also become mandatory at the same time. The use of the ICH E2B (R2) format will therefore be phased out.

The training course includes a knowledge evaluation for which participants, who pass the evaluation, will receive a notification from the EMA. Organisations, which aim to use EudraVigilance web application (EVWEB) to start the electronic reporting of ICSRs to EudraVigilance for the first time, need to provide such notification for at least one user to be able to successfully register with the EudraVigilance production environment. For more information on the registration process, please consult the EMA website.

LEARNING OBJECTIVES

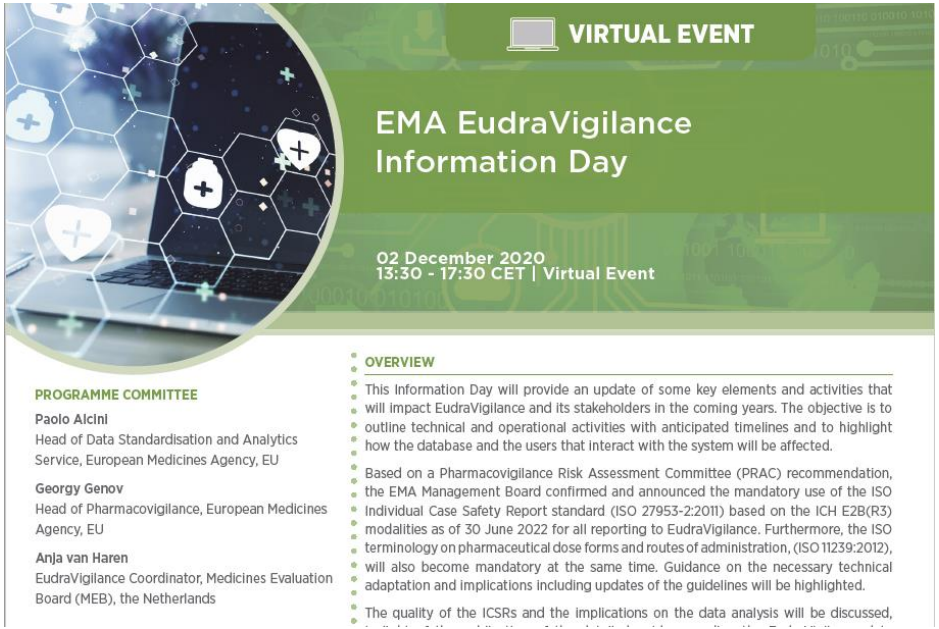
By the end of this training course, participants should be able to:

- Apply the ISO/ICH E2B(R3) format and rules to safety reporting based on practical examples for initial spontaneous and follow-up reports, amendment and nullification reports, literature and parent-child cases, and reports from interventional and non-interventional studies
- Understand how to use EVWEB to create, send and access ICSRs and acknowledgments

COURSE DATES AND TIME:

- Course #20511: 07-11 September 2020, 14:00 - 18:30 CET
- Course #20512: 28 Sep - 02 Oct 2020, 09:00 - 13:30 CET
- Course #20514: 12-16 October 2020, 14:00 - 18:30 CET
- Course #20516: 19-23 October 2020, 14:00 - 18:30 CET
- Course #20518: 16-20 November 2020, 09:00 - 13:30 CET
- Course #20500: 23-27 November 2020, 14:00 - 18:30 CET
- Course #20521: 07-11 December 2020, 14:00 - 18:30 CET

Training and support



VIRTUAL EVENT

EMA EudraVigilance Information Day

02 December 2020
13:30 - 17:30 CET | Virtual Event

PROGRAMME COMMITTEE

Paolo Alcini
Head of Data Standardisation and Analytics Service, European Medicines Agency, EU

Georgy Genov
Head of Pharmacovigilance, European Medicines Agency, EU

Anja van Haren
EudraVigilance Coordinator, Medicines Evaluation Board (MEB), the Netherlands

OVERVIEW

This Information Day will provide an update of some key elements and activities that will impact EudraVigilance and its stakeholders in the coming years. The objective is to outline technical and operational activities with anticipated timelines and to highlight how the database and the users that interact with the system will be affected.

Based on a Pharmacovigilance Risk Assessment Committee (PRAC) recommendation, the EMA Management Board confirmed and announced the mandatory use of the ISO Individual Case Safety Report standard (ISO 27953-2:2011) based on the ICH E2B(R3) modalities as of 30 June 2022 for all reporting to EudraVigilance. Furthermore, the ISO terminology on pharmaceutical dose forms and routes of administration, (ISO 11239:2012), will also become mandatory at the same time. Guidance on the necessary technical adaptation and implications including updates of the guidelines will be highlighted.

The quality of the ICSRs and the implications on the data analysis will be discussed,

Any questions?

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