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EudraVigilance Operational Plan Milestones 2020 to 2022



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Executive Summary

EudraVigilance is the central pillar for pharmacovigilance activities in the European Economic Area (EEA). In February and April 2017, the enhanced EudraVigilance system successfully passed an independent audit in accordance with Article 24 of Regulation (EC) 726/2004. The EMA Management Board confirmed on 22 May 2017 that the full functionality of the EudraVigilance database had been achieved and the system met the defined functional specifications¹. The new EudraVigilance system was launched on 22 November 2017, providing enhanced functionalities to national Competent Authorities (NCAs), the European Medicines Agency (EMA), the Commission and marketing authorisation holders (MAHs) for effective reporting and monitoring of suspected adverse reactions and detection of risks related to the safety of medicines, thus contributing to the protection and promotion of public health. Furthermore, EudraVigilance facilitates the safety reporting of suspected unexpected serious adverse reactions (SUSARs) to investigational medicinal products occurring during clinical trials.

This operational plan has been prepared upon request by the Pharmacovigilance Risk Assessment Committee (PRAC), which is overseeing the operation of EudraVigilance. This operational plan has been updated and describes key activities and developments that will impact on or relate to EudraVigilance and its stakeholders during the next three years from 2020 to 2022.

The plan's objective is to outline technical as well as operational activities with anticipated timelines and to highlight how EudraVigilance and the stakeholders that interact with the system will be affected. This should facilitate planning by the Agency, which is operating EudraVigilance on behalf of the network and ensure timely preparedness of NCAs, MAHs, commercial and non-commercial sponsors of clinical trials and the WHO Uppsala Monitoring Centre.

The goal is to ensure sustainability of EudraVigilance and associated actions in support of the EU pharmacovigilance activities and the protection of public health.

In addition, the interaction with stakeholders as part of training and support as well as communication and engagement are covered to ensure that a platform for learning, cooperation, dialogue and alignment throughout the evolution and operation of EudraVigilance system is provided for.

This plan is updated regularly as regards timelines and new activities/developments.

1. Introduction

EudraVigilance is the system for managing and analysing information on suspected adverse reactions to medicines which have been authorised or are being studied in clinical trials in the European Economic Area (EEA). The European Medicines Agency (EMA) operates the system on behalf of the European Union (EU) medicines regulatory network. The Pharmacovigilance Risk Assessment Committee (PRAC) as part of the pharmacovigilance governance provides oversight of the operation of the system and its functionalities.

In February and April 2017, the new and enhanced EudraVigilance system successfully passed an independent audit in accordance with Article 24 of Regulation (EC) 726/2004. The EMA Management Board confirmed on 22 May 2017 that the full functionality of the EudraVigilance database had been achieved and that the system met the defined functional specifications². The enhanced EudraVigilance system was launched on 22 November 2017, providing improved functionalities to national Competent Authorities (NCAs), EMA, the Commission and marketing authorisation holders (MAHs) for effective

¹ http://www.ema.europa.eu/docs/en_GB/document_library/Other/2017/05/WC500228158.pdf

² http://www.ema.europa.eu/docs/en_GB/document_library/Other/2017/05/WC500228158.pdf

reporting and monitoring of suspected adverse reactions and detection of risks related to the safety of medicines, thus contributing to the protection and promotion of public health. Furthermore, EudraVigilance facilitates the safety reporting of suspected unexpected serious adverse reactions (SUSARs) to investigational medicinal products occurring during clinical trials by commercial and non-commercial sponsors.

An overview of the EudraVigilance system components is provided in figure 1, with further information provided on the dedicated [EudraVigilance system overview](#) webpage.

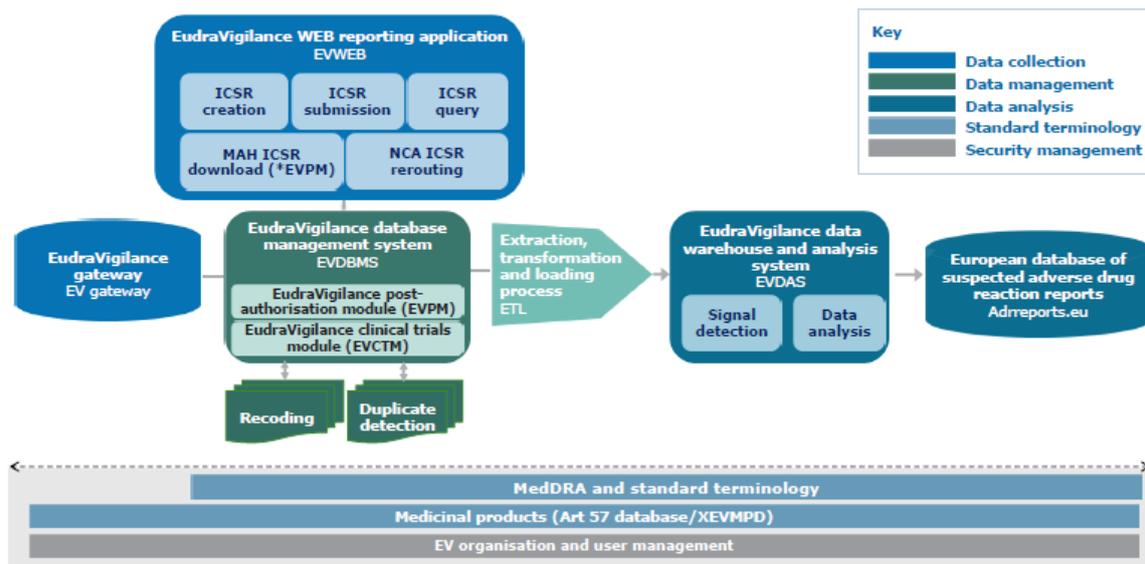


Figure 1: EudraVigilance system components

By the end of 2019, EudraVigilance held information on more than 16.5 million safety reports, referring to 7.95 million cases, as well as information on 744,219 medicinal products on the EU market. EudraVigilance is being used for signal detection by EMA and NCAs and in support of other pharmacovigilance procedures in terms of data analysis. Furthermore, making all ICSRs from the EEA available to the World Health Organisation (WHO) Uppsala Monitoring Centre (UMC) directly from EudraVigilance facilitates global pharmacovigilance activities.

Access to EudraVigilance for MAHs was extended at the end of 2017, to allow MAHs to comply with their safety monitoring obligations. Improved access to EudraVigilance data is also being provided for healthcare professionals, the public and academia. With the simplifications in reporting of suspected adverse reactions and improvements in the tools for their analysis and monitoring, EudraVigilance is contributing to optimising the benefit-risk balance of medicines and thus to the protection and promotion of public health. For further details, please refer to the EudraVigilance Annual Reports published at the dedicated EudraVigilance webpage³.

The key areas supported by EudraVigilance can be summarised as follows:

- Collecting and processing of adverse drug reaction reports.

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- Maintaining and updating the extended EudraVigilance Medicinal Product Dictionary (XEVMPPD) based on information on all medicinal products authorised in the EU.
- Ongoing data quality activities, detecting and managing duplicate reports and classification of reported medicinal product information.
- Production and provision of data analysis reports on medicines safety to the EU network (electronic reaction monitoring reports - eRMRs) and provision of data analyses to support assessments in pharmacovigilance procedures.
- Supporting the central role of the PRAC in assessing and monitoring the safety of human medicines in the EU, including prioritising and assessing safety signals.
- Signal management and monitoring of the data available in EudraVigilance by MAHs.
- Continued public access to aggregated EudraVigilance data (www.adrreports.eu).
- Making available ADR reports originating from the EEA to the WHO-UMC.

EMA is also delivering training courses on EudraVigilance to support users of NCAs, MAHs and sponsors of clinical trials. Training includes targeted e-learning and face-to-face trainings, webinars and information days.

The Pharmacovigilance News Letter What's new in Pharmacovigilance? provides regular updates to QPPVs on important pharmacovigilance topics including EudraVigilance related activities.

2. Objectives of the EudraVigilance Operational Plan

This EudraVigilance operational plan has been prepared upon request by the PRAC, which is overseeing the operation of EudraVigilance in the context of the overall monitoring of the safety of medicines throughout their lifecycle.

The plan is designed to describe key factors that will impact on EudraVigilance and its stakeholders from a technical and operative perspective during the next three years from 2020 to 2022.

The plan's objective is to outline important activities and developments with anticipated timelines and to highlight how EudraVigilance and the stakeholders that interact with the system will be affected. This should facilitate adequate planning by the Agency, which is operating EudraVigilance on behalf of the EU medicines regulatory network and ensure timely preparedness of NCAs, MAHs, commercial and non-commercial sponsors of clinical trials and the WHO Uppsala Monitoring Centre.

The goal is to ensure sustainability of EudraVigilance in support of the EU pharmacovigilance activities and the protection of public health taking into account the evolving environment in which the system is operated.

In addition, the interaction with stakeholders as part of training and support as well as communication and engagement are covered to ensure that a platform for learning, cooperation, dialogue and alignment throughout the evolution of the EudraVigilance system is provided for.

This plan is updated regularly as regards timelines and timelines or new activities/developments.

3. Key factors and activities that will impact EudraVigilance: 2020 to 2022

The following chapters outline key factors and activities that relate to or that will impact on EudraVigilance directly or indirectly from 2020 to 2022.

It should be noted that the activities outlined in this plan for 2020 onwards have been scheduled considering the respective business priorities and may be subject to further review in accordance with EMA's priorities.

3.1. EudraVigilance: system maintenance

Following the delivery of the enhanced EudraVigilance system, EudraVigilance is subject to routine IT maintenance. Bug fixes and minor improvements are part of planned maintenance releases with downtimes kept to a minimum where possible. Downtimes which impact business processes are communicated in advance to registered users.

Release notes are updated regularly thus providing a summary of improvements for each maintenance release and are published on the [EudraVigilance training and support webpage](#). For EVDAS, updated release notes are published in the respective EVDAS dashboards.

Requests for improvements in relation to EudraVigilance system functionalities are being dealt in accordance with the change requests management process for Telematics systems overseen by the [Telematics Change Management Board](#) as part of the [EU Telematics governance](#) (Figure 2).

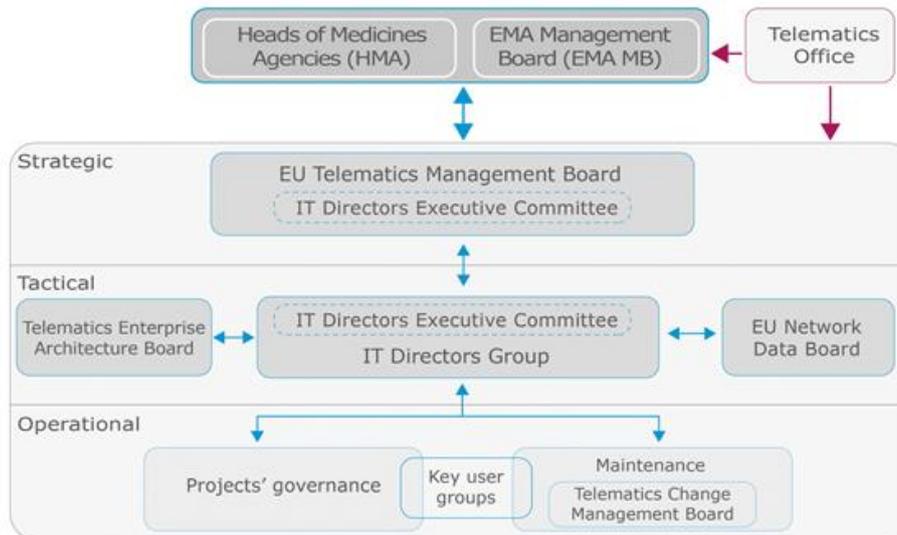


Figure 2: Telematics Governance Model

For 2020 to 2022, the following releases and activities are scheduled:

- Maintenance releases for EudraVigilance are being planned for on a monthly basis to address feedback reported daily by users;
- Maintenance releases for EVDAS to address any problems identified in the production system and to implement business requests for change (e.g. additional fixed-eRMRs for signal detection, compliance reports for MAHs, sponsors of clinical trials and NCAs);
- EV and EVDAS bi-annual MedDRA upgrades, as per the [international agreed dates](#);
- The integration of the Human and Veterinary EudraVigilance messaging component into a common platform;
- The integration of the Human and Veterinary EudraVigilance public website into the [adrreports.eu](#) web portal;

- The activation of the SUSARs re-routing to NCAs and the submission of Annual Safety Reports (ASRs) (timeline to be confirmed by the Agency);
- Potential technical adaptations of the EudraVigilance system, including EVDAS due to Brexit;
- Maintenance release(s) in preparation of the mandatory use of the ISO Individual Case Safety Report standard^[3] as referred to in Article 26(2)(a) of the Commission Implementing Regulation (EU) No 520/2012^[4] together with the implementation of the ISO terminology on pharmaceutical dose forms and routes of administration^[9] referred to in Article 25(1)(f) of Commission Implementing Regulation (EU) No 520/2012^[4];
- 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. This will result in the retiring of the AS1 secure transfer protocol which is no longer being supported by most of the ICH regions and is considered as a deprecated specification for ICH use. The Agency will therefore start the process to phase out the support of AS1 (e-mail) and solely use AS2 (HTTP). The Agency will be contacting all organisations that are currently still using AS1 for connecting to the EudraVigilance gateway to inform them of stopping the use of AS1 towards the end of 2020.

3.2. EudraVigilance: integration with the Agency's identity and access management (IAM2) project

The Agency's Identity and Access Management (IAM2) project aimed to simplify the registration and management of EudraVigilance organisations and users from a business process and technology point of view. As part of the project, in 2019 the EudraVigilance platform was integrated with two services/platforms already put in place by the Agency: the [EMA Account Management Portal](#) and the [Organisation Management Services](#) (OMS).

Existing EudraVigilance organisations were on-boarded in OMS. In addition, the EudraVigilance applications (EVWEB, EVDAS, XEVMPD) were updated to use the EMA Account already in use by other EU Telematics applications, such as EudraLink and EudraGMDP. As a result, new workflows have been put in place to enable EudraVigilance users to self-manage their access through the [EMA Account Management Portal](#).

A new [registration manual](#) has been created to provide instructions on using the new interface and the new process for registration.

In addition, updated online training was published on the [EudraVigilance training page](#).

For 2020 to 2022 the following activities and milestones are scheduled:

- Integration of the EudraVigilance Human XCOMP (external testing system) registration process with the IAM components;
- Improvements of the IAM Human components and the EudraVigilance Human registration to include the self-management of virtual affiliates;
- Further revisions of the EudraVigilance Human registration manual and supporting training materials in line with planned updates.

3.3. United Kingdom's withdrawal from the Union

As of 1.2.2020, the UK is no longer an EU Member State. However, EU law still applies to the UK during the transition period. This means that during the transition period reporting and access to EudraVigilance continues as if UK was an EU Member State.

Without prejudice to the future EU-UK relationship, the Agency will implement any changes that will be required to all its concerned IT systems at the end of the transition period. EudraVigilance stakeholders and partners will be informed of the technical adaptations to be implemented for EudraVigilance including EVDAS and the website on adverse drug reaction reports in due time. Training materials and user guides will be updated and published as needed.

3.4. Agreement on mandatory use of E2B(R3) in EEA

Article 26 of the Commission Implementing Regulation (EC) 520/2012 outlines the use of internationally agreed formats and standards in the context of pharmacovigilance. As part of the launch of the new and enhanced EudraVigilance system, the new ICH E2B(R3) ICSR format based on the ISO standard 27953-2:2011 "Health Informatics, Individual case safety reports (ICSRs) in pharmacovigilance — Part 2: Human pharmaceutical reporting requirements for ICSR (ISO 27953-2:2011)" has been fully implemented.

Whilst EudraVigilance can process ICSRs received from sender organisations in both formats - the ICH E2B(R2) format and the new ISO format - a conversion of the file formats is necessary, which often results in loss of granularity of the data and thus impacts on the analysis of the data for the purpose of safety monitoring.

To fully benefit from the improved ISO ICSR format, the EU medicines regulatory network agreed on a date for the mandatory use and related standard terminology. Based on a readiness survey directed to Member States and pharmaceutical industry associations and following consultation of the pharmacovigilance, clinical trials and IT governance of the EU Medicines Regulatory Network, the Pharmacovigilance Risk Assessment Committee (PRAC) considered the matter.

Pursuant to Article 24(2) third subparagraph of Regulation (EC) No 726/2004, PRAC recommended on 2 October 2019 that the use of the ISO ICSR standard based on the ICH E2B(R3) modalities and the related ISO standard terminology is to become mandatory as of 30 June 2022 as regards reporting obligations to EudraVigilance.

Having considered the PRAC recommendation, the EMA Management Board announced on 19 December 2019 that the use of:

- the ISO Individual Case Safety Report standard^[3] as referred to in Article 26(2)(a) of the Commission Implementing Regulation (EU) No 520/2012^[4] and the modalities on how to use this ISO ICSR standard defined in the ICH E2B(R3) documentation^[5, 6], and
- the ISO terminology on pharmaceutical dose forms and routes of administration^[9] referred to in Article 25(1)(f) of Commission Implementing Regulation (EU) No 520/2012^[4],

shall become mandatory as of 30 June 2022 in relation to reporting obligations to EudraVigilance.

For further details please refer to the [Announcement of the EMA Management Board](#) on the "Confirmation of the mandatory use of the ISO Individual Case Report standard based on ICH E2B(R3) modalities and related ISO standard terminology".

3.5. EudraVigilance: use of ISO IDMP standards

The set of five ISO Identification of Medicinal Products (IDMP) standards define the rules and data elements that uniquely identify medicinal products and related concepts such as the pharmaceutical products, substances, pharmaceutical forms, units of presentation, routes of administration and units of measurement. The Commission Implementing Regulation (EU) No 520/2012 (Articles 25 and 26) defines the use of the ISO IDMP standards in the context of pharmacovigilance.

To aid the implementation of the ISO IDMP standards, the EMA launched the SPOR programme and is establishing the processes and services to manage four domains of data (master data):

- [Substance Management Services](#) (SMS) (corresponding to the ISO 11238 substance standard).
- [Product Management Services](#) (PMS) – (corresponding to the ISO 11615 medicinal product standard, and the 11616 pharmaceutical product standard).
- [Organisation Management Services](#) (OMS) – stores master data on organisations, comprising organisation name and location address, for organisations such as MAHs, sponsors, regulatory authorities and manufacturers.
- [Referentials Management Services](#) (RMS) – (corresponding to the ISO 11239 pharmaceutical dose form, units of presentation and routes of administration standard and the 11240 units of measurement standard).

RMS and OMS went live in June 2017. Any requests for new or updated referentials (with the exception of substances) or organisations have now to be pre-registered via the Agency's SPOR portal (<http://spor.ema.europa.eu/>). 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.

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. Whereas currently requests for substance creations/updates have to be submitted through the EMA Service Desk, an SMS portal, which will include change request functionality for the pre-registration of substances, will be implemented. The submission of XEVPRMs will again remain unaffected. 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.

In relation to the implementation of the ISO IDMP standards and EudraVigilance and EVDAS, the main impact expected during 2020 to 2022 will refer to the implementation of the ISO standard on pharmaceutical dose forms, units of presentation and routes of administration.

Further information on SMS and PMS is available at the dedicated [Substance Management Services and product data management services](#) webpage.

3.6. EudraVigilance: Monitoring and signal management

The [Commission Implementing Regulation \(EU\) No 520/2012](#) (Article 18) requires EMA, NCAs and MAHs to continuously monitor the data available in EudraVigilance. It also requires MAHs to inform EMA and NCAs of validated signals detected when monitoring the database.

Guidance on regulatory requirements and on the monitoring and reporting processes for signals is available in [good pharmacovigilance practices \(GVP\) Module IX](#) Rev 1 on signal management.

EMA has also published [scientific guidance on routine signal detection methods](#) in EudraVigilance for use by the Agency, NCAs and MAHs.

Guidance on the notification of emerging safety issues can be found on the [EMA's contact page](#).

The EMA and the European Commission agreed transitional arrangements to streamline the monitoring of EudraVigilance by MAHs. A pilot on signal detection by MAHs started on 22nd February 2018 for a period of one year which was subsequently extended beyond February 2019.

Based on the experience during the pilot and the feedback collected from two surveys addressed to MAHs, the EMA prepared a report addressed to the Commission to consult, discuss and determine the next steps in the MAHs obligation to monitor EudraVigilance. Following consideration of the report by the Commission, in December 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.

The pilot involves 288 active substances and combinations included in the "[List of active substances involved in the pilot on signal detection in EudraVigilance by marketing authorisation holders](#)". The concerned MAHs should continue to monitor the relevant substances in EudraVigilance and inform EMA and NCAs of validated signals with their medicines.

All other MAHs also have access to EudraVigilance data and can integrate the data into their own signal management processes. However, during the pilot period, they do not have obligation to continuously monitor EudraVigilance and inform the regulatory authorities of validated signals.

The following key activities should be noted:

- EMA will also introduce changes in the availability to the eRMRs in 2020 (see chapter 3.1.) based on the feedback obtained from MAHs. The change will include the retiring of the ad-hoc reference period eRMR and a replacement by five fixed reference periods eRMRs. This will allow for a better quality and availability of the eRMR outputs. The changes are expected to be implemented during the 1st half of 2020.
EMA will communicate the changes in due course and with sufficient time for the stakeholders to prepare for relevant changes to their current processes.
- EMA will investigate the technical feasibility of increasing the number of EVDAS users for MAHs. This is taking into account that MAHs expressed the need to increase the number of EVDAS user accounts to better accommodate their signal detection practices. Based on initial feedback from MAHs to increase the current number of users from 5 to 10, EMA will assess the impact on system scalability, performance and security.
- An update of the EVDAS user manual for MAHs is planned for 2020 to reflect changes within the MAHs EVDAS dashboard and Brexit related changes (see chapter 3.3.).

3.7. EudraVigilance and ICSR data quality review

EMA, in collaboration with stakeholders that submit ICSRs, are responsible to contribute to the quality and integrity of the information held in EudraVigilance.

This is reflected in the legislation as follows:

- The Agency shall, in collaboration with the marketing authorisation holder or with the competent authority in Member State that submitted an ICSR to the EudraVigilance database, be responsible

for operating procedures that ensure the highest quality and full integrity of the information collected in the EudraVigilance database [REG Art 24(3)].

- This includes the monitoring of use of the terminologies referred to in Chapter IV of the Commission Implementing Regulation (EU) No 520/2012, either systematically or by regular random evaluation [IR Art 25(3)].

Specific quality system procedures and processes shall be in place in order to ensure the:

- Submission of accurate and verifiable data on serious and non-serious suspected adverse reactions to the EudraVigilance database within the 15 or 90-day time frame [IR Art 11 (1) (c).];
- Quality, integrity and completeness of the ICSRs submitted, which should also be entire and undiminished in their structure, format and content [IR Art 11 (1) (d) and Art 15 (1) (a)];
- Detection of duplicates of suspected adverse reactions reports in collaboration with the Agency [DIR Art 107(5) and Art 107a (3)].

A review of the ICSRs quality, integrity and compliance with the submission time frames is performed by the Agency at regular intervals for organisations submitting ICSRs to EudraVigilance in line with the Agency's Standard Operating Procedures (SOPs). Parameters upon which the review of organisations may be initiated, refer for example to the volume of reports being submitted to the EudraVigilance database, major changes to pharmacovigilance databases, quality issues identified as part of the signal management, requests from pharmacovigilance inspectors, or the time interval since the last review. The outcome of the review of the ICSRs quality and integrity is provided to the organisations in the form of a report, which includes the need for corrective measures where applicable and the time frames for these measures to be applied. The time frames and the method for corrective measures depend on the quality issues identified (e.g. corrections of the MedDRA coding of ICSRs to be performed by means of amendment reports).

The Agency continues to conduct the classification of reported medicinal product information in ICSRs against the XEVMPD and operates duplicate detection and management procedures in line with the [Guideline on good pharmacovigilance practices \(GVP\) - Module VI Addendum I – Duplicate management of suspected adverse reaction reports](#).

The Agency applies quality review parameters taking into account frequently identified issues that emerge as part of the simplified reporting rules, the use of the new ICH E2B(R3) format and the backwards and forwards conversion rules applied by organisations not yet E2B(3) compliant. This is to ensure that these are identified and addressed adequately by the sender organisations with the goal that EudraVigilance is based on the highest possible data quality standards.

The following key activities should be noted:

- A [detailed guide on the EudraVigilance data quality management performed by the Agency](#) has been published in Q1 2020.
- 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 Q2 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 2020.
- The ICSR data quality review activities will be continued with a new tender for an EMA service provider planned for in 2020.

3.8. EudraVigilance and Union Data Protection Legislation

The EudraVigilance database and data processing network is operated by the Agency and is designed to collate and analyse pharmacovigilance information. Article 24(2) of Regulation (EC) 726/2004 and the EudraVigilance Access Policy set out the level of access to information held in EudraVigilance.

The Agency submitted a notification for a prior check Opinion to the European Data Protection Supervisor (EDPS). The EDPS issued the Opinion regarding the EudraVigilance database on 7 September 2009 ([Case 2008-402](#)).

The General Data Protection (GDPR) i.e., Regulation (EU) 2016/679⁴ on the protection of natural persons with regard to the processing of personal data and on the free movement of such data came into force on 24 May 2016 and is applicable since 25 May 2018. The GDPR is applicable, among others, to NCAs and MAHs since 25 May 2018. The regulation is an essential step to strengthen citizens' fundamental rights in the digital age and facilitate business by simplifying rules for companies in the digital single market. It lays down new obligations and rules for all organisations including NCAs and MAHs which submit data to EudraVigilance.

The main contact point for questions on data protection is the Data Protection Authority (DPA) in the Union Member State where the NCA's or MAH's controller is based. The DPAs of the Member States are competent for monitoring and enforcing the application of the GDPR. For EU institutions and bodies, the EDPS is responsible for ensuring compliance with data protection law when personal data are being processed.

The DPAs and the EDPS are part of the European Data Protection Board (EDPB). The EDPB has the status of an EU body with legal personality and is provided with an independent secretariat. The EDPB has extensive powers to determine disputes between national supervisory authorities and to give advice and guidance on key concepts of the GDPR.

The Agency as the operator of EudraVigilance does not operate under the GDPR, but it is subject to the EU DPR, i.e. Regulation (EU) 2018/1725⁵ which entered into force on 11 December 2018 and is applicable to Union institutions, bodies, offices and agencies. Both, the GDPR and EU DPR align the standard of data protection in the Union.

The Agency is continuing to assess its impact to its processing operations including EudraVigilance and will collect input from NCAs and MAHs.

3.9. EudraVigilance Clinical Trial Module (EVCTM) and SUSAR reporting in accordance with the Clinical Trial Regulation

The way clinical trials are conducted in the European Union (EU) will undergo a major change when the [Clinical Trial Regulation \(EU\) No. 536/2014](#) will become applicable. The Regulation enables the harmonisation of the assessment and supervision processes for clinical trials throughout the EU, via a Clinical Trials Information System (CTIS), formerly the EU clinical trial portal and database. The Regulation simplifies the rules on safety reporting introducing the possibility of risk proportionate approach, in particular, but not limited to, low intervention clinical trials.

⁴ [Regulation \(EU\) 2016/679](#) of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation).

⁵ [Regulation \(EU\) 2018/1725](#) of the European Parliament and the Council of 23 October 2018 on the protection of natural persons with regard to the processing of personal data by the Union institutions, bodies, offices and agencies and on the free movement of such data, and repealing Regulation (EC) No 45/2001 and Decision No 1247/2002/EC.

It also simplifies the safety reporting by sponsors, in accordance with article 40 of the Regulation, 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 EudraVigilance 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 become applicable.

In addition, a number of documents in [EudraLex Volume 10](#) are being revised and updated to bring them in line with the changes required by the Clinical Trials Regulation (EU) No 536/2014. Furthermore, 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. During the transitional period, which will last for a period of 3 years starting from when the Regulation becomes applicable, both sets of documents will apply accordingly and should be referred to respectively according to the legislation under which the clinical trial is conducted. At the end of the transitional period all clinical trials shall be conducted under the Regulation and should follow only the set of documents applicable to the Regulation.

Although it is not mandatory, stakeholders are encouraged to take already into consideration a number of aspects that are outlined in the new or updated documents published in the page dedicated to the [Clinical Trial Regulation](#) and apply them to those clinical trials authorised under the Directive, to the extent possible and in compatibility with the legal framework of the Directive.

For more guidance on safety reporting, reference should be 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.

3.10. EudraVigilance: Medical Literature Monitoring (MLM) Service

The Agency is responsible for monitoring [a number of substances and selected medical literature](#) to identify suspected adverse reactions with medicines authorised in the Union, and for entering the relevant information into the EudraVigilance database. The service is fully operational as of 1 September 2015.

The activities will be continued until 2021 with a new tender for an EMA service provider to be launched in 2020. In this context a review of the substances and the medical literature currently included as part of the service will be initiated in Q2 2020 and tender specifications prepared in Q2 2020.

3.11. 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).

The main areas expected to be addressed as part of the revision refer to the management of reports from patient support programmes and market research programmes, the integration of the Innovative Medicines Initiative (IMI) WEB-RADR regulatory recommendations as regards the social media monitoring activities, alignment of definitions and processes in the context of the Clinical Trial Regulation (EU) No. 536/2014 and the reporting of non-related events in the context of non-interventional studies. An assessment of the impact of changes as regards the EudraVigilance functionalities will be also conducted in parallel to ensure that business rules correspond to new requirements accordingly.

3.12. EudraVigilance and benefits realisation

The Commission publishes at defined intervals a report on activities by Member States and the EMA, to monitor the safety of medicines throughout their life cycle as foreseen by the pharmacovigilance legislation. The report describes the activities of the collaborative EU system for monitoring and controlling the safety of human medicines.

The aim of EU rules on pharmacovigilance is to monitor the safety of medicines so that regulators can take action to reduce the risks and increase the benefits of medicines for human use. The role of individual EU countries is to monitor medicine safety data, assess signals of possible emerging side effects, and analyse the data when a safety issue is identified at European level. EMA has a central role in the EU system of pharmacovigilance – it coordinates the activities of an EU regulatory network of over 30 national competent authorities, and provides technical, regulatory and scientific support.

The last [Commission report](#) focused on the national and European Medicines Agency experience regarding the list of medicines for human use subject to additional monitoring.

Considering the important role of EudraVigilance in the monitoring of the safety of medicines and the assessment of signals of possible emerging side effects the benefits of the system will be reflected in the context of the overall EU pharmacovigilance activities addressed in the next report expected for 2022.

3.13. EudraVigilance and operation of pharmacovigilance

In the context of the operation of EudraVigilance in support of pharmacovigilance 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 (figure 3) 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, the [EudraVigilance Expert Working Group](#), which also includes members of industry associations at European level, is meeting three times per year.

Guidance on operational aspects will be issued as needed.

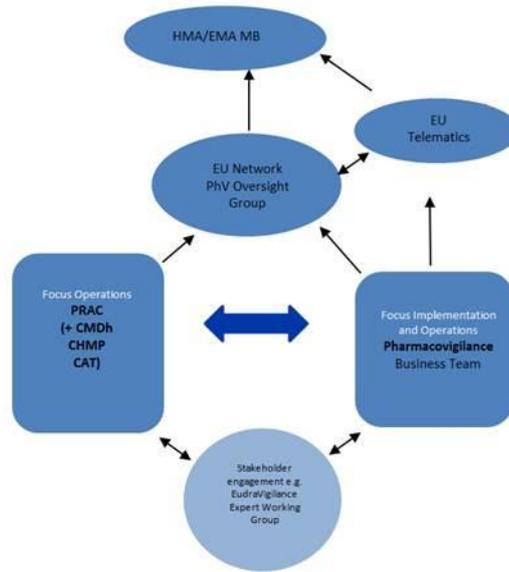


Figure 3: Pharmacovigilance governance in the EU

3.14. Training and support

The Agency is also delivering training courses on EudraVigilance to support users of NCAs, MAHs and sponsors of clinical trials. Training includes targeted e-learning and face-to-face trainings, webinars and information days.

- Face-to-face training courses on the enhanced EudraVigilance system are continuing and dates are published on the EudraVigilance webpage.
- The e-learning modules remain available throughout 2020 to 2022 with updates provided as necessary.
- Face-to-face EVDAS trainings for Member States are continuing twice yearly. In 2020 trainings will be offered for June and November. The [EudraVigilance training and support webpage](#) will be updated regularly with training and webinar dates.

3.15. Stakeholder engagement and communication

The Agency will continue its engagement with stakeholders in relation to EudraVigilance.

The Agency will continue to issue half yearly Pharmacovigilance News Letters providing updates on important pharmacovigilance topics including EudraVigilance related activities.