8 June 2018
EMA/100194/2018
Inspections, Human Medicines, Pharmacovigilance and Committees Division

EudraVigilance Operational Plan

Milestones 2018 to 2020

Pharmacovigilance Business Team (agreement)	15 March 2018
Pharmacovigilance Risk Assessment Committee (PRAC) (agreement)	22 March 2018
EU Pharmacovigilance Oversight Group (agreement)	26 March 2018
IT Directors Executive Committee (for information)	12 April 2018
Telematics Forum (for information)	27 April 2018

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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 new 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 specifications[1]. The new EudraVigilance system was launched on 22 November 2017, providing enhanced functionalities to national Competent Authorities (NCAs), EMA 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. The operational plan describes key activities and developments that will impact on or relate to EudraVigilance and its stakeholders during the next three years from 2018 to 2020.

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 activities 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 will be updated regularly as regards timelines and new activities/developments.

A summary of the milestones from 2018 to 2020 is provided in Chart 1.

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

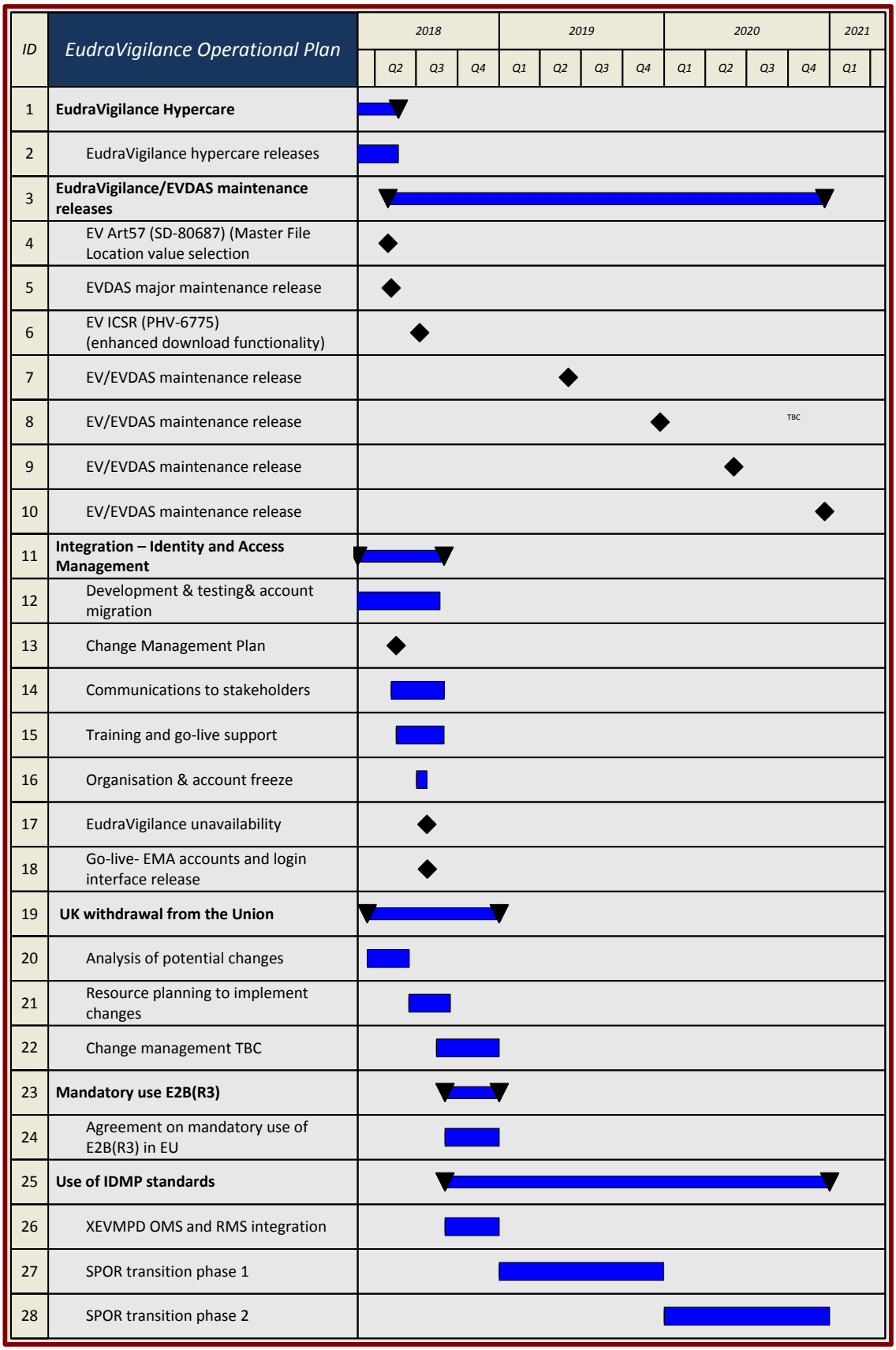

Chart 1 (part 1): EudraVigilance Operational Plan Milestones 2018 to 2020

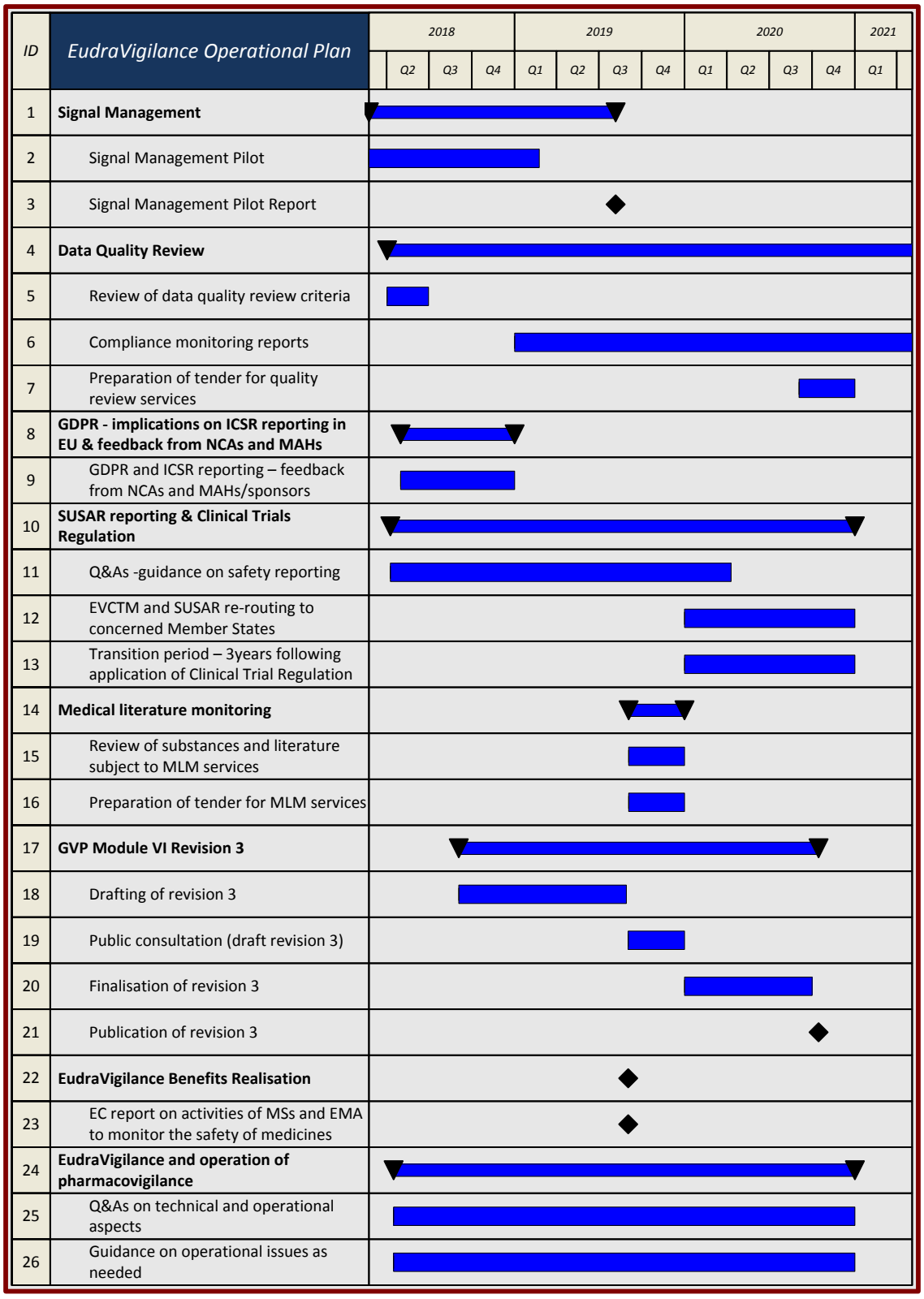

Chart 1 (part 2): EudraVigilance Operational Plan Milestones 2018 to 2020

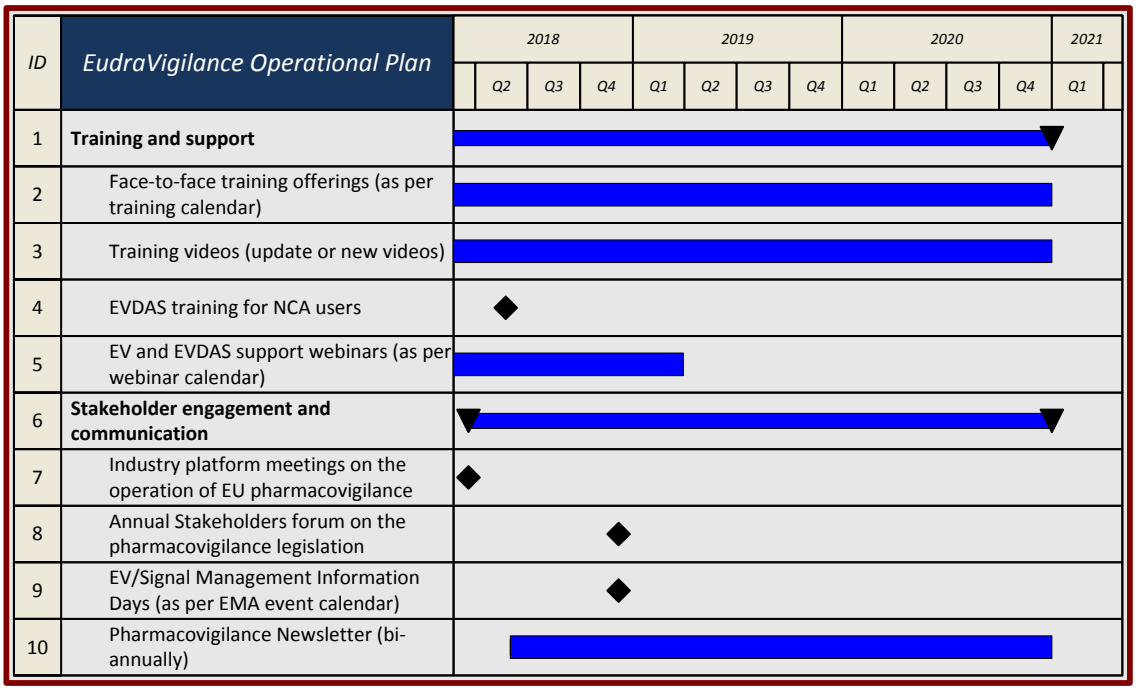

Chart 1 (part 3): EudraVigilance Operational Plan Milestones 2018 to 2020

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 specifications[2]. The new EudraVigilance system was launched on 22 November 2017, providing improved functionalities to national Competent Authorities (NCAs), EMA 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 facilities 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.

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

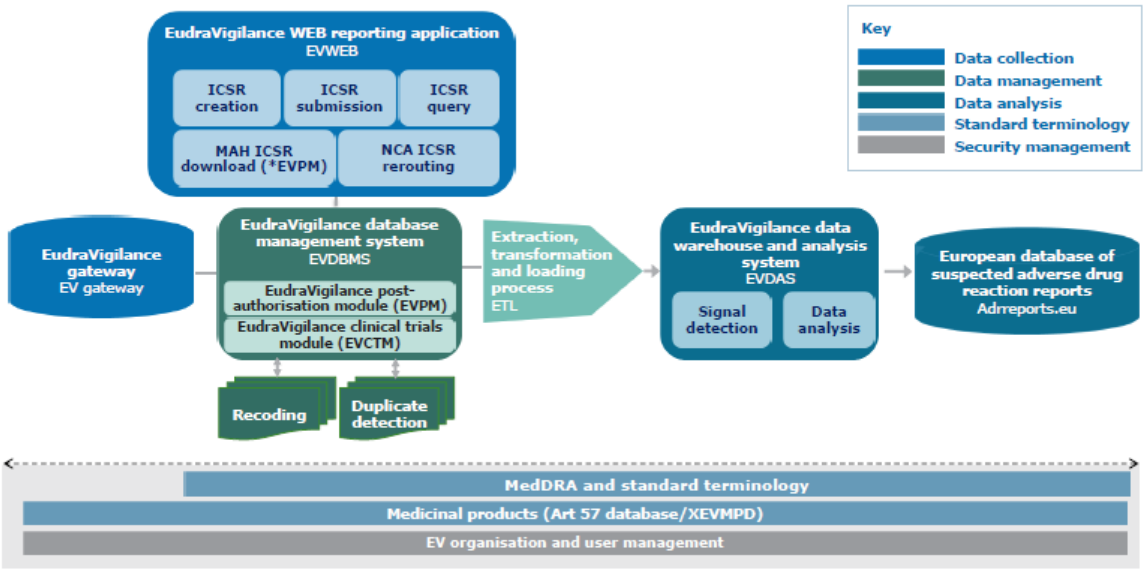

Figure 1: EudraVigilance system components

By the end of 2017, EudraVigilance held information on more than 12.45 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 regular 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 initiated 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.

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

- Collecting and processing of adverse drug reaction reports.
- Maintaining and updating the extended EudraVigilance Medicinal Product Dictionary (XEVMPD) 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 informatin.
- 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.

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.

The Pharmacovigilance News Letter provides regular updates on important pharmacovigilance topics including EudraVigilance related activities.

2. Objectives of the EudraVigilance Operational Plan

The 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 life-cycle.

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 2018 to 2020.

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 will be updated regularly as regards timelines and timelines or new activities/developments.

3. Key factors and activities that will impact EudraVigilance: 2018 to 2020

The following chapters outline key factors and activities that relate to or that will impact on EudraVigilance directly or indirectly from 2018 to 2020.

It should be noted that the activities outlined in this plan for 2018 onwards have been scheduled considering the respective business priorities, as well as the Agency's relocation as a result of the UK's exit from the EU and its impact on the Agency's business continuity, and may be subject to further review and reprioritisation in accordance with the business continuity plan of the Agency.

3.1. EudraVigilance: system maintenance

Following the delivery of the new and enhanced EudraVigilance system, EudraVigilance is currently subject to "hypercare", a stabilisation period focusing on user support, data integrity, and system stability. This stabilisation period will end in May 2018 after which the system will be subject to routine IT maintenance. Bug fixes and minor improvements will be subject to planned maintenance releases with minimal downtimes. Release notes will provide a summary for each maintenance release and will be published on the EudraVigilance training and support webpage.

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).

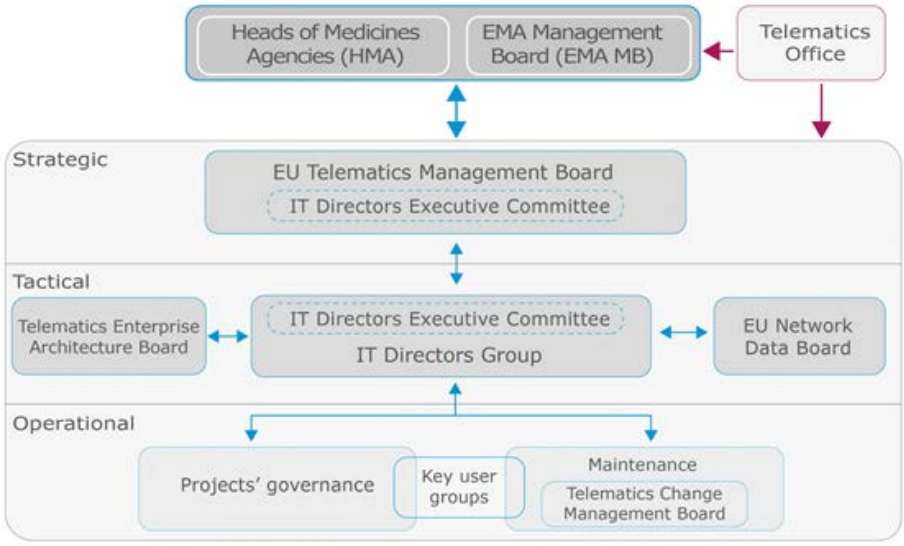

Figure 2: Telematics Governance Model

Given the Agency's preparation for its relocation to Amsterdam, there are several relocation-critical projects and initiatives that have been prioritised during 2018 and 2019. This will significantly reduce the implementation of changes to existing Telematics applications including EudraVigilance during the next 18 months focusing on those which are flagged as business critical. During 2019, development work on existing applications and implementation of change requests will resume taking into account planning, relative prioritisation and spare capacity.

For 2018 to 2020, the following releases and activities are scheduled:

- From March to May 2018 (hypercare period), two releases are scheduled per month to allow for final fixes of identified issues.
- In the 2nd quarter of 2018, a maintenance release is planned for the XEVMPD to allow for an update of the Master File Location (MFL) values. In addition, a maintenance release of EV is planned for to further improve the ICSR download functionality. For EVDAS, a major maintenance release is planned for May 2018.
- For 2019 to 2020, two maintenance releases for EudraVigilance/EVDAS are currently planned.
- The EudraVigilance Veterinary system, which is using certain components of EudraVigilance Human, will be subject to upgrades in 2019 following a design phase in 2018. These upgrades may

require downtimes, which could also impact on EudraVigilance Human. Users will be informed where this might impact the availability of the system components of EudraVigilance Human.

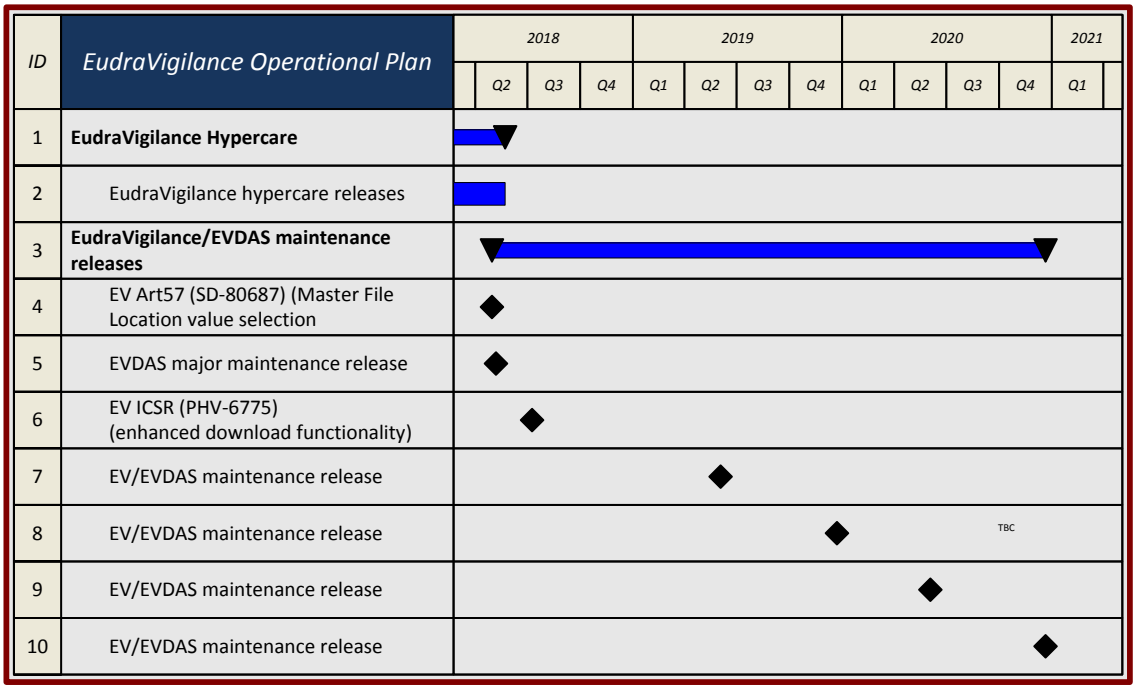

Chart 2: EudraVigilance system maintenance - milestones 2018-2020

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

The Agency's Identity and Access Management (IAM2) project aims 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, the EudraVigilance platform will be 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 will be on-boarded in OMS. This will have no impact on the organisation identifiers currently in use by sender organisations.

In addition, the EudraVigilance applications (EVWEB, EVDAS, XEVMPD) will be updated to use the EMA Account already in use by other EU Telematics applications, such as EudraLink and EudraGMDP. New workflows will be put in place to enable EudraVigilance users to self-manage their access through the EMA Account Management Portal.

A change management plan will provide organisations and users with an overview of the timelines for the switch and explain the transition and data migration approach. Testing will be scheduled with volunteers from different stakeholder groups. Online training on the use of the new registration interface will also be offered.

For 2018 the following activities and milestones are scheduled:

- Development and testing of the new functionalities integrated with EudraVigilance including account management.

- Publication of Change Management Plan.
- Communication with stakeholders and provision of training and support.
- Go-Live (EV downtime as part of the deployment of new system functionality planned for 25 July 2018) with EMA accounts and the login interface to be made available to the EV users planned for 26 July 2018.

Currently, there are no further activities planned for 2019 and 2020 as regards the identity and access management integration with EudraVigilance.

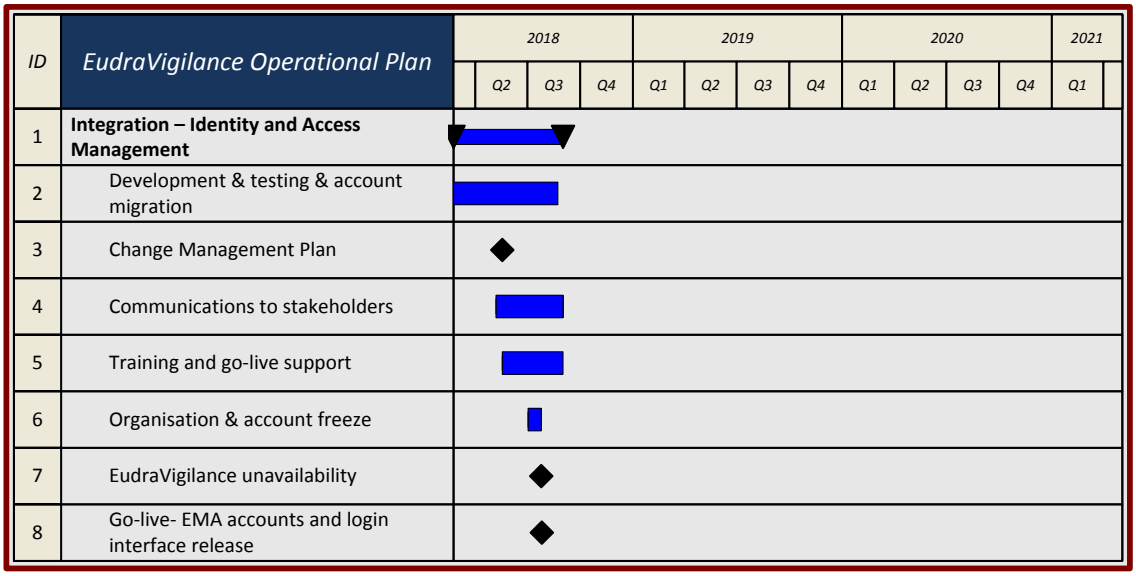

Chart 3: EudraVigilance and integration with IAM2 project deliverables- milestones 2018

3.3. United Kingdom withdrawal from the Union

EMA and the European Commission are working on the assumption that the UK will leave the European Union as of 30 March 2019 and will become a 'third country' thereafter. Therefore as of 30 March 2019 the UK will no longer participate in the work of the Agency. This means that access to a number of systems and applications supporting the approval and safety monitoring of medicines across the EU would have to be closed to the UK as of that date.

The Agency is currently working on a plan that identifies possible changes and proposes consistent solutions across all concerned IT systems.

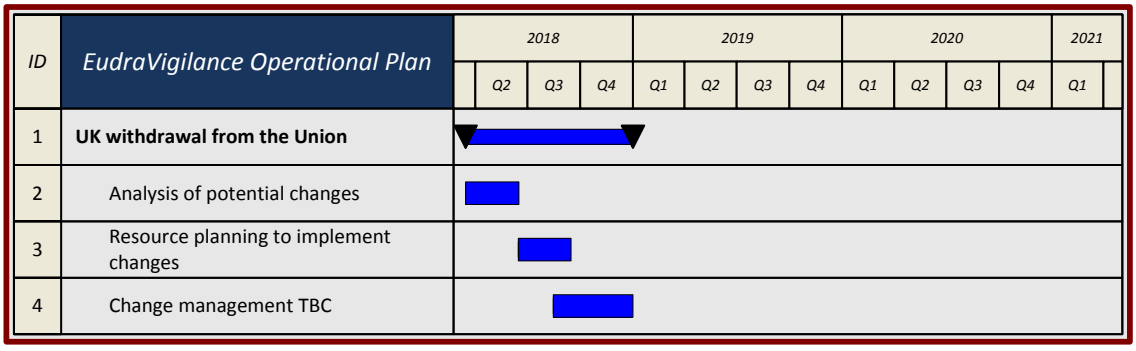

Chart 4: EudraVigilance and UK withdrawal from the EU - milestones 2018

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 it will be important for the EU medicines regulatory network to agree on a date for the mandatory use of the E2B(R3) format. This will need to take into account the readiness of NCAs in EEA Member States as well as sufficient time for marketing authorisation holders and sponsor of clinical trials to upgrade their system to become fully E2B(R3) complaint.

As a milestone for 2018, the agreement on a date for the mandatory use of the E2B(R3) ICSR format in the EU is planned for the 4th quarter 2018.

In this context, the EU medicines regulatory network will also need to agree on the implementation timeline of the use of ISO IDMP EDQM terms for routes of administration and dosage forms, for which a first publication by ICH is planned for in the 2nd or 3rd quarter of 2018. The aim is to link the use of the EDQM terms in the EEA to the mandatory use of E2B(R3) in the EEA. An update of the EU ICSR Implementation Guide will be planned for with the application of the ISO IDMP EDQM terms.

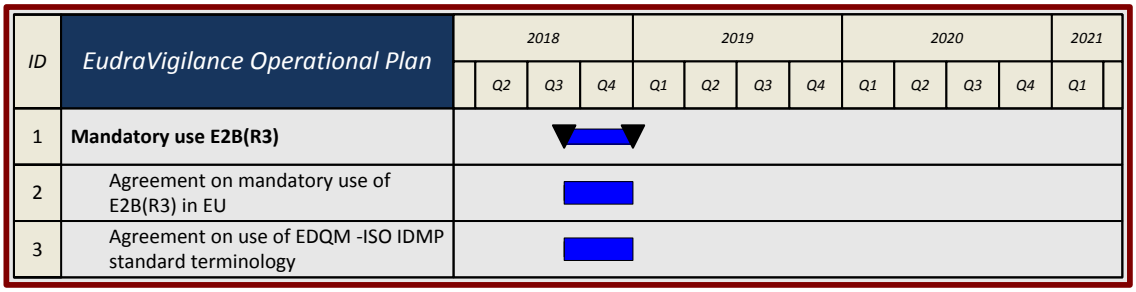

Chart 5: EudraVigilance and agreement on date for mandatory use of ICH E2B(R3) format in the EU – milestones 2018

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 product, substances, pharmaceutical forms, units of presentations, routes of administration and units of measurements. 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 projects 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 & OMS were delivered in June 2017. As a next step, EMA plans to deliver SMS and PMS to support EU-wide regulatory activities building upon the data foundations of RMS and OMS.
During 2018, this will have no impact on the submission of information on medicinal products (Article 57 XEVPRM submissions) by MAHs or the registration of Investigational Medicinal Products (IMPs) by sponsors of clinical trials. XEVPRM submissions allow MAHs and sponsors to create proposed terms and create/update organisations.

For the 4th quarter of 2018 the integration of RMS and OMS is planned for the XEVMPD.
In 2019, SPOR transition phase 1 is scheduled to start, which implies that new referentials (with the exception of substances) and new organisations will need to be pre-registered via the Agency's SPOR portal. 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.
In 2020, transition phase 2 is planned for where also substances, as well as referentials and organisations will need to be pre-registered via the Agency's SPOR portal. The submission of XEVPRMs will again remain unaffected.

As regards ICSR submissions, EudraVigilance and EVDAS there is no impact expected in relation to the implementation of the ISO IDMP standards during 2018 to 2020.

Further information on SMS and PMS is available at the dedicated Substance and product data management services webpage.

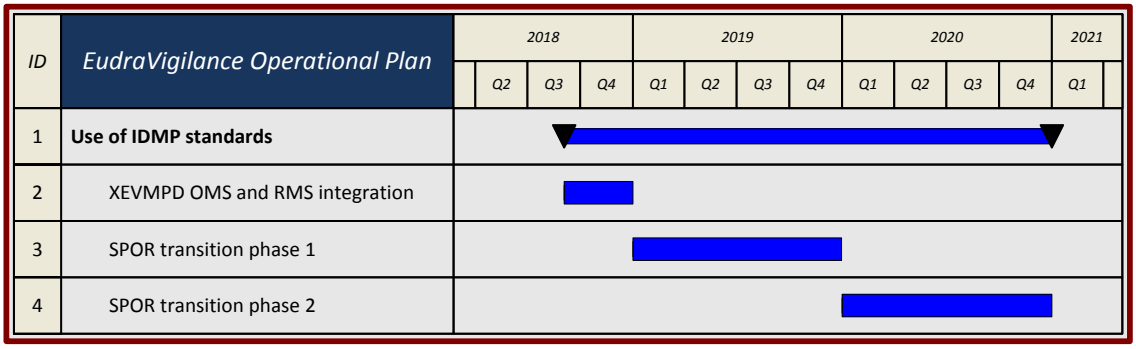

Chart 6: EudraVigilance and use of IDMP standards milestones 2018 to 2020

3.6. EudraVigilance: Monitoring and signal management

Commission Implementing Regulation (EU) No 520/2012 (Article 18) requires EMA, national competent authorities 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 on signal management.

EMA has also published scientific guidance on routine signal detection methods in EudraVigilance for use by the Agency, national competent authorities and MAHs.

Guidance on the notification of emerging safety issues can be found on the EMA's contact page.

EMA and the European Commission have agreed transitional arrangements to streamline the monitoring of EudraVigilance by MAHs. During a pilot period of one year (February 2018 to 2019), MAHs of the active substances included in the "List of active substances involved in the pilot on signal detection in EudraVigilance by marketing authorisation holders" will have to monitor them in EudraVigilance and inform EMA and NCAs of validated signals with their medicines. After one year, EMA will base the next phase of implementation on experience gained through the pilot and summarise the results in the form of a report.

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 will have no obligation to continuously monitor EudraVigilance and inform the regulatory authorities of validated signals.

In support of a fully integrated signal management process and taking into account the outcome of the one year signal management pilot, EMA will further consider the need of enhancing the tracking of signals through the signal management lifecycle up to and including completion of required action, including non-validated signals. This is to ensure a sustainable signal management system in line with the EU legislative requirements and the guidance provided in the GVP Module IX for the provision of data and tools to EMA, NCAs and MAHs to perform signal detection, validation, confirmation, analysis, prioritisation and evaluation as applicable including a tracking system for signals that covers different needs and levels within the signal management process. This should include PRAC support and should be linked with document management and transparency aspects. The aim is to gain efficiency in view of the significant increase in workload volumes, to improve systems integration across the signal life cycle for a robust and automated signal detection and management process.

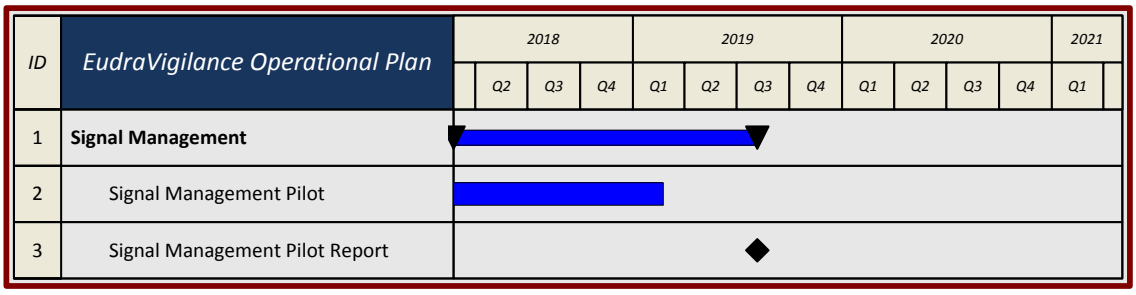

Chart 7: EudraVigilance and signal management - milestones 2018 to 2019

3.7. EudraVigilance and ICSR data quality review

The Agency in collaboration with stakeholders that submit ICSRs, are responsible to contribute to the quality and integrity of the data. 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 as well 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 on the basis 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 will continue 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.

As part of the milestones for 2018, the Agency plans to review the quality review parameters taking into account frequently identified issues that emerged 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.

By the end of 2018, the Agency will provide organisations registered with EudraVigilance monthly compliance reports for the purpose of the monitoring of the submission time frames of suspected adverse reactions related to medicines, which will apply to both initial and follow-up ICSRs.

The data quality review activities will be continued with a new tender for an EMA service provider planned for in 2020.

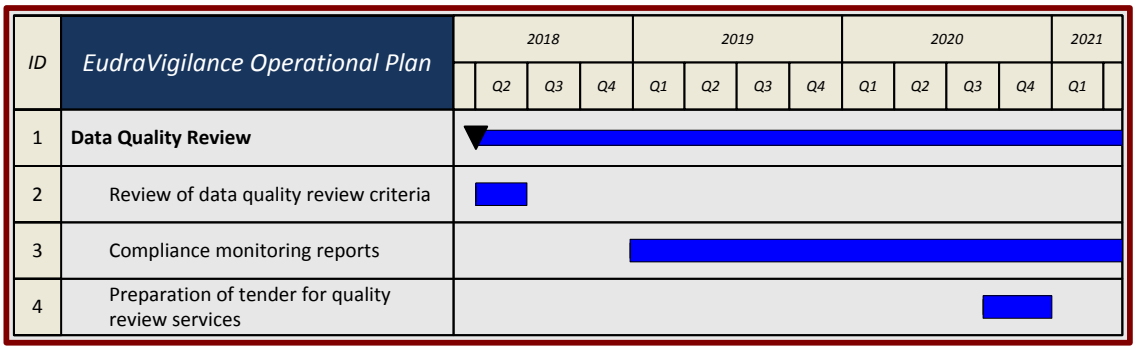

Chart 8: EudraVigilance and data quality activities - milestones 2018 to 2020

3.8. EudraVigilance and the General Data Protection Regulation (GDPR)

Regulation (EU) 2016/679 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 will apply from 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. The Regulation, albeit not directly applicable to EMA in virtue of its Article 2(3), will lay down new obligations and rules for all organizations including NCAs and MAHs which submit data to EudraVigilance.

In accordance with data protection legislation, national supervisory authorities are established in order to oversee the implementation of the legislation in an independent manner. As of 25 May 2018, the national data protection supervisory authorities will be 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.

A specific legal framework on data protection applies to EMA. Regulation 45/2001 sets forth the rules applicable to the processing of personal data by EU institutions and bodies, including EMA. On 10 January 2017, the Commission put forward a proposal to amend those rules to bring them in line with the General Data Protection Regulation (GDPR).

In accordance with Regulation (EC) No 45/2001, a supervisory authority, the European data protection supervisor (EDPS) is established as an independent body responsible for monitoring the application of data protection rules within European Institutions and for investigating complaints.

Personal data are processed in full compliance with the applicable data protection legislation (Regulation (EC) No 45/2001 of the European Parliament and of the Council of 18 December 2000 on the protection of individuals with regard to the processing of personal data by the Community institutions and bodies and on the free movement of such data). In accordance with Article 27 of this Regulation, EMA 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). As soon as the new legislation adopted in accordance with Article 2 (3) of the GDPR will be adopted, EMA will assess its impact to its processing operations including EudraVigilance, this is expected in 2019.

EMA will collect input from NCAs and MAHs and reflect on how to proceed.

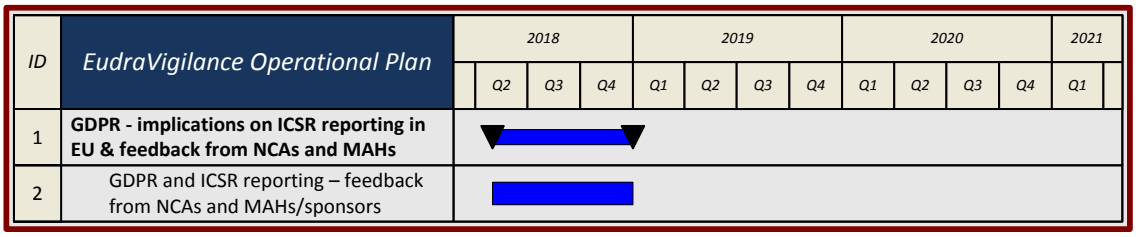

Chart 9: EudraVigilance and GDPR- milestones 2018

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 comes into application in 2019. The Regulation enables the harmonisation of the assessment and supervision processes for clinical trials throughout the EU, via an EU portal and database. It also simplifies the safety reporting by sponsors of SUSARs which are submitted 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 simplified reporting rules become applicable.

In addition, a number of documents in 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 currently being updated and for which a publication is planned for in a staggered approach.

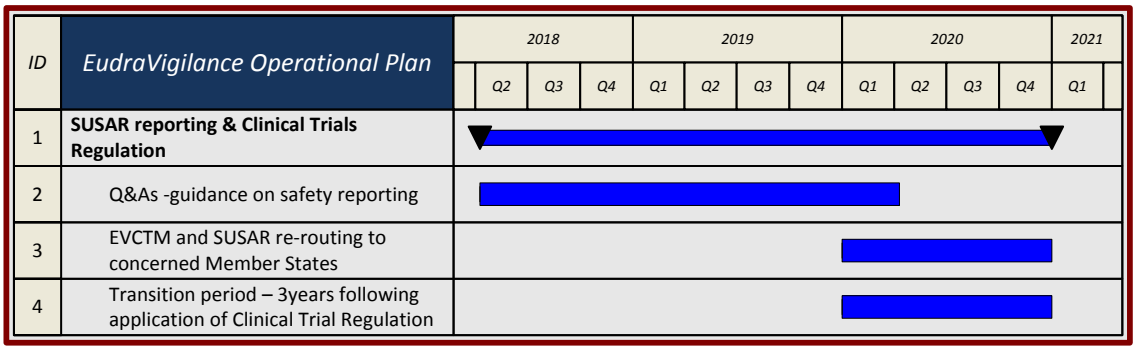

Chart 10: EudraVigilance and SUSAR reporting – milestones 2018 to 2020

3.10. EudraVigilance: Medical Literature Monitoring (MLM) service

The European Medicines Agency (EMA) is responsible for monitoring a number of substances and selected medical literature to identify suspected adverse reactions with medicines authorised in the European 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 and tender specifications prepared.

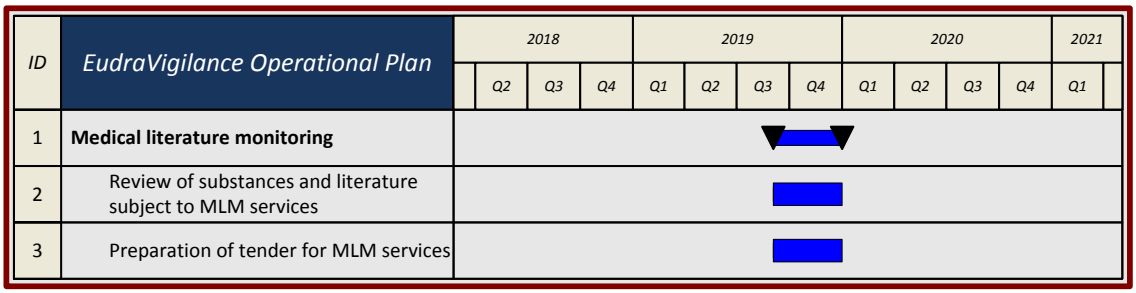

Chart 11: EudraVigilance and MLM service - milestones 2018 to 2020

3.11. GVP Module VI (revision 3)

The Guideline on good pharmacovigilance practices (GVP) - Module VI – Collection, management and submission of reports of suspected adverse reactions to medicinal products (Rev. 2) is planned to be updated with a public consultation scheduled for the 4th quarter of 2019 and the publication of a final version scheduled for 4th quarter of 2020.

The main areas 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.

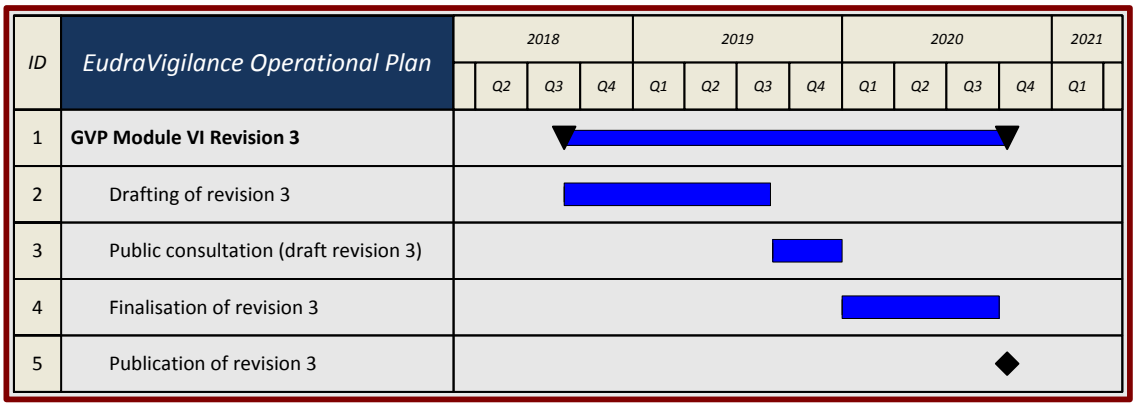

Chart12: EudraVigilance and revision 3 of GVP Module VI – milestones 2018 to 2020

3.12. EudraVigilance and benefits realisation

The Commission publishes at defined intervals a report on activities by Member States and the European Medicines Agency (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 covered the period 2012 to 2014 and concluded that the European pharmacovigilance network is an example of successful cooperation at EU level which directly benefits patients.
Taking into account 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 the 3rd quarter of 2019, which will cover the period 2015 to 2018.

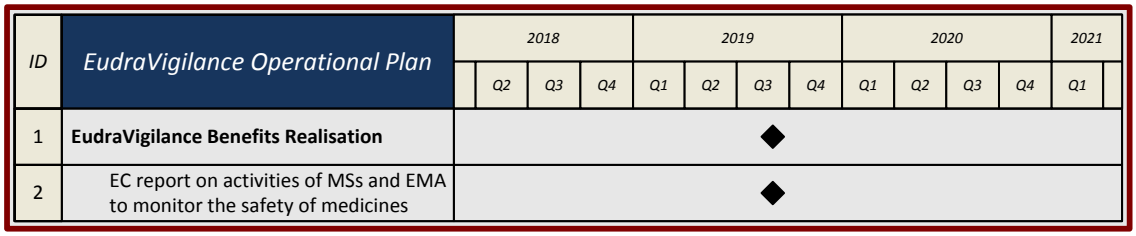

Chart 13: EudraVigilance benefits realisation- milestones 2019

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 monthly basis, the EudraVigilance Expert Working Group, which also includes members of industry associations at European level, is meeting three times per year.

Questions and Answers (Q&A) addressing technical and operational aspects are planned to be published quarterly. Guidance on operational aspects will be issued as needed. Guidance on the obligations of MAHs as regards the recording of ICSRs accessed through EudraVigilance is planned to be published in the 2nd quarter of 2018.

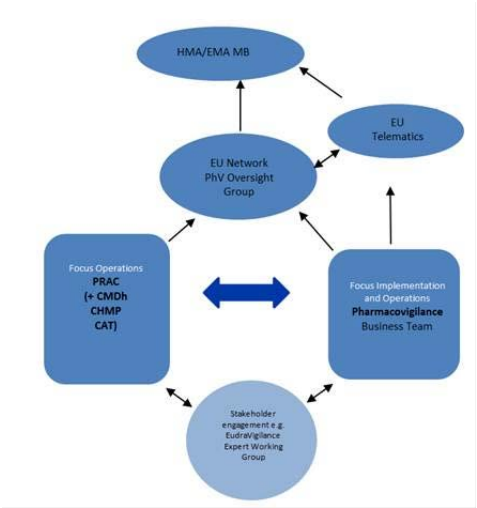

Figure 3: Pharmacovigilance governance in the EU

ID	EudraVigilance Operational Plan	2018				2019				2020				2021
		Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	
1	**EudraVigilance and operation of pharmacovigilance**													
2	Q&As on technical and operational aspects													
3	Guidance on operational issues as needed													

Chart 14: EudraVigilance operational aspects – 2018 to 2020

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 will be continued during 2018.
- The e-learning modules will remain available throughout 2018 to 2020 with updates provides as necessary.
- EVDAS training for Member States will be offered on 24 and 25 May 2018.

Training offerings for 2019 are subject to further planning taking into account that training facilities in the temporary building in Amsterdam will not be available. Following the Agency's move to the permanent building, training dates for 2020 will subsequently be defined.

Support webinars dedicated to EudraVigilance and signal management will be continued during 2018 and the 1st quarter of 2019. The need for the continuation of the support webinars thereafter will be determined and planned for accordingly.

The EudraVigilance training and support webpage will be updated regularly with training and webinar dates.

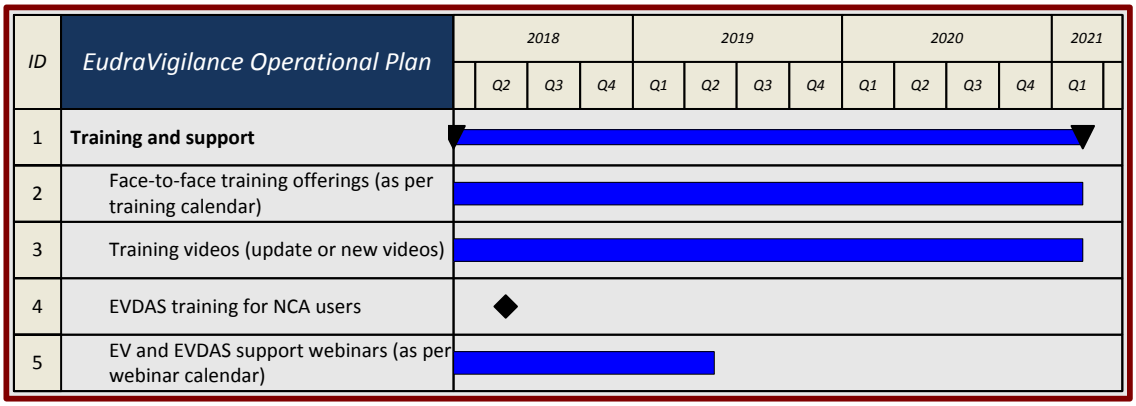

Chart 15: EudraVigilance training and support – milestones 2018 to 2020

3.15. Stakeholder engagement and communication

The Agency will continue its engagement with stakeholders in relation to EudraVigilance. This will include the:

- Annual Stakeholders forum on the pharmacovigilance legislation scheduled for 24 September in 2018;
- Industry stakeholder platform meetings on the operation of EU pharmacovigilance usually organised three times per year: 1st meeting in 2018 scheduled for 20 March;
- EudraVigilance and Signal Management Information Days scheduled for 7 December 2018.

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

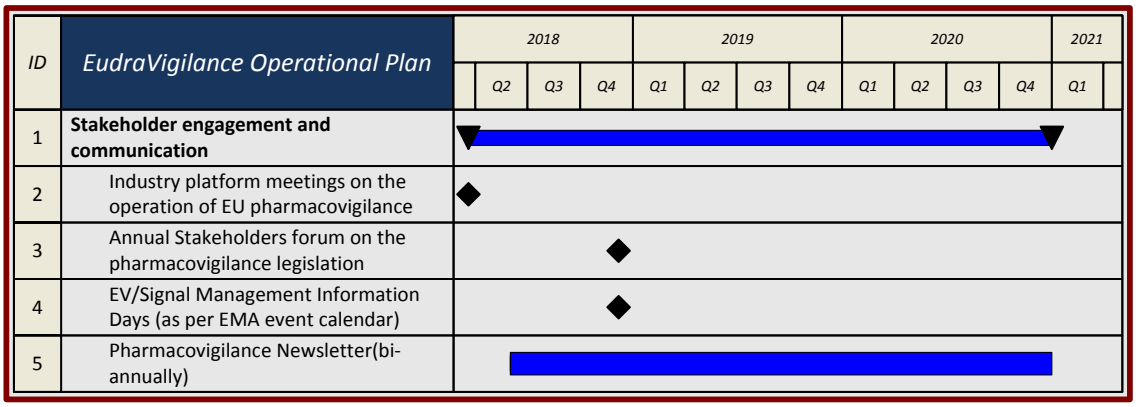

Chart 16: EudraVigilance stakeholder engagement and communication – milestones 2018 to 2020