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## EudraVigilance stakeholder change management plan

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Consultation of Eudravigilance Expert Working Group	23 September 2015
Consultation of Signal Management Review Technical Working Group (SMART WG) – Work Stream 1	7-10 September 2015
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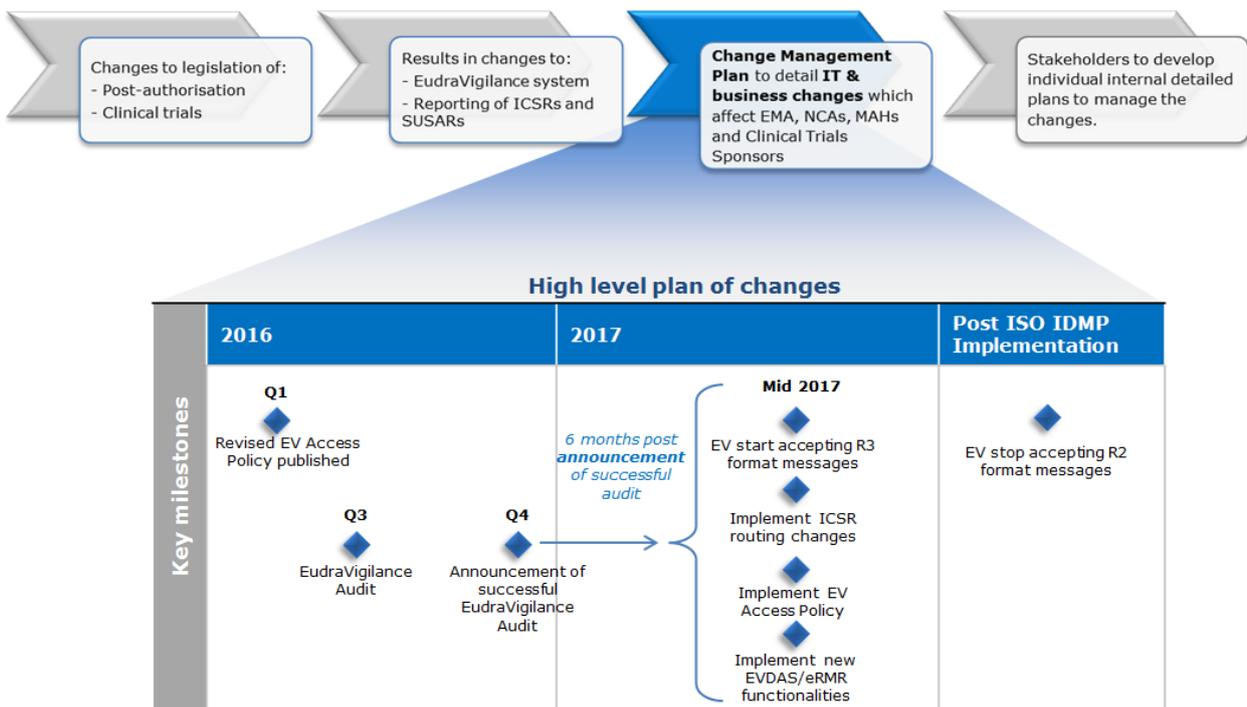
# 1. Executive summary

This document details the changes taking place in the EudraVigilance system and to the process of reporting Individual Case Safety Reports (ICSRs) and Suspected Unexpected Serious Adverse Reactions (SUSARs). These changes are being brought about by changes to the post-authorisation and clinical trials legislation.

The intended audience of this document are the National Competent Authorities (NCAs), Marketing Authorisation Holders (MAHs), sponsors of clinical trials and the EMA. This document details the IT & business changes being made at both European and stakeholder level.

Organisations are advised to use this document as a starting point to develop their own internal plans to manage the changes that will take place once the new EudraVigilance system is moved into production.

This document is not static and may be updated as the development of the new system progresses. Therefore EudraVigilance stakeholders should periodically ensure that they have the latest version of this document.



Context of Change Management Plan and key milestones

## 2. Changes to legislation

This section provides an overview of the main changes introduced through updates to the legislation concerning the EudraVigilance and associated systems.

### 2.1. Legal requirements

Regulation (EC) No 726/2004, Directive 2001/83/EC as amended, Directive 2001/20/EC, and Regulation (EU) No 536/2014 outline the electronic reporting requirements to EudraVigilance, the data processing network and management system for reporting and evaluating suspected adverse reactions during the development and following the marketing authorisation of medicinal products in the European Economic Area (EEA).

#### 2.1.1. Post authorisation legal requirement changes

In December 2010 the pharmacovigilance legislation was updated through amendments to Regulation (EC) No 726/2004 and Directive 2001/83/EC. This was followed by the addition of Commission Implementing Regulation (EU) No 520/2012<sup>1</sup> in June 2012.

The main changes to electronic reporting requirements that have been brought about by these amendments to the legislation are:

- Usage of ISO standards in the reporting of ICSRs, ISO ICSR standard 27953-2:2011
- Usage of ISO IDMP terminologies, once available, in the submission of ISO ICSR messages
- EMA medical literature monitoring service
- The audit of the EudraVigilance system
- Centralisation of reporting of ICSRs in the EU and forwarding of national cases to the relevant NCA.

There is currently no date from which E2B(R2) cannot be used in the EU, therefore organisations may continue receive and send E2B(R2) as well as E2B(R3) format messages after the new EudraVigilance system is implemented.

#### 2.1.2. Clinical trials

The new clinical trials regulation (Regulation (EU) No 536/2014) will apply as from six months after the publication of the Commission notice about the full functionality of the EU portal and database, and no earlier than 28<sup>th</sup> May 2016. According to Article 40 of the Regulation (EU) No 536/2014, the Agency shall set up and maintain an electronic database for the reporting of suspected unexpected serious adverse reactions (SUSARs) and annual safety reports. The database shall be a module of the EudraVigilance database.

The main changes to electronic reporting requirements that are planned in relation to clinical trials are:

- Usage of ISO standards in the reporting of SUSARs, ISO ICSR standard 27953-2:2011

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<sup>1</sup> <http://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2012:159:0005:0025:EN:PDF>

- Usage of ISO IDMP set of standards and terminologies, once available, in the submission of ISO ICSR messages
- Centralisation of reporting SUSARs in the EU
- Development of a standard web-based structured form for the SUSARs reporting by sponsors to EudraVigilance; This form would be ISO ICSR 27953-2:2011 (E2B(R3)) compliant.

This change management plan will be updated to include additional details on clinical trials as soon as amended guidance and more information becomes available.

### **3. Business Process Change management**

It is suggested that all impacted organisations should prepare plans concerning the implementation of the new EudraVigilance system and the resulting changes that will occur to reporting, downloading and analysis of data. This section highlights the main changes the new system will bring to business processes for all stakeholders. Section 5. provides more detailed guidance specific to each stakeholder group.

#### ***3.1. Submission of ICSRs within the EEA***

Up until the implementation of the new EudraVigilance system there is no change to the current process for the submission of ICSRs for either authorised medicinal products or investigational medicinal products. Following the implementation of the new EudraVigilance system ICSR submissions in the EEA should only be made to the EudraVigilance in order to meet reporting compliance, this applies to NCAs and MAHs. Therefore, submissions from MAHs to NCAs and from NCAs to MAHs should stop from this point forward, for SUSAR submissions see section 3.2. below for details.

The EudraVigilance gateway will not however prevent stakeholders from sending ICSR to each other. This is because some organisations use the gateway for MAH to MAH, NCA to regional pharmacovigilance centres and sponsor to MAH transmissions. However, it should be noted that these types of exchanges are made outside of official support by the EMA.

With regards to the post-authorisation pharmacovigilance requirements, in addition to the centralised reporting of serious cases, EEA non-serious cases should also be reported to EudraVigilance within 90-days of receipt in order to meet reporting obligations. Non-serious non-EEA case should not be reported to EudraVigilance unless a case that was previously reported as serious is being amended to a non-serious case. It should also be noted that in E2B(R3), seriousness is reported at event level rather than at case level in E2B(R2), therefore if any event is considered serious then the whole case should be considered serious.

#### ***3.2. Clinical trial SUSAR reporting***

Until the clinical trials regulation is applicable there is no change to the current process for the submission of SUSARs for clinical trials.

The clinical trials regulation will become applicable six months after the European Commission publishes a notice in the Official Journal that the clinical trials EU portal and the EU clinical trials database have achieved full functionality and the systems meet the functional specifications. The clinical trials regulation will start to apply from this "Application Date".

Clinical trials already approved through the clinical trials directive 2001/20/EC will continue to have the same SUSAR reporting requirements as specified in the directive for a transition period of 3 years after the clinical trials regulation is applicable.

In addition, in the 12 months following the application date, a sponsor can choose to have their trial approved through the clinical trials Directive rather than through the Regulation. If so that trial and SUSAR reporting responsibilities will follow the clinical trials Directive for up to three years after the application date.

Sponsors that have a clinical trial approved through the clinical trials regulation are normally required to send SUSARs to EudraVigilance only. The EudraVigilance system will then automatically reroute the SUSARs to the concerned NCAs. However, the option remains for small organisations to report SUSARs directly to the NCA that has approved the trial through establishing an agreement between the sponsor and the NCA concerned. The NCA will then forward any SUSARs reported to them under such agreements to the EudraVigilance system.

### **3.3. EEA case submissions to the WHO UMC**

Until the implementation of the new EudraVigilance system there is no change to the current process for the submission of ICSRs from NCAs to the WHO-UMC. Following the implementation of the new EudraVigilance system, ICSR submissions for cases occurring in the EEA should only be made by the EudraVigilance system to WHO-UMC. Therefore, NCAs should plan to stop their own processes for submitting ICSRs to the WHO-UMC after the new EudraVigilance system goes live.

### **3.4. Signal Management**

Authorised users of the EudraVigilance Data Analysis System (EVDAS) will be expected to retrieve data and use the available predefined reports included in the newly implemented functionalities in order to meet their data analysis and signal detection obligations. User manuals and training materials will be made available to support all users of the system. A change in process is expected for Marketing Authorisation Holders as they will be granted access to the EudraVigilance data analysis system in order to support their obligation to monitor EudraVigilance, detect and validate safety signals for the products and substances for which they hold a marketing authorisation. In the event of identifying and validating a safety signal, these safety signals should be reported in accordance to the revised GVP Module IX on Signal Management. The current EU signal management process will be impacted and new roles and responsibilities will be further developed.

Indeed, the Guidance on statistical methods in signal detection is under revision and an updated version will start the public consultation process by the end of 2015. This, together with revised GVP signal module and guidelines the Agency is developing to support signal detection in special areas of interest, will support MAHs and NCAs when analysing the EudraVigilance data.

## **4. EudraVigilance system implementation plan**

The EudraVigilance system is being updated to be ISO ICSR 27953-2:2011 (E2B(R3)) compliant. As the use of ISO IDMP terminologies will only apply when they become available, the use of these terminologies will not be part of the initial implementation. In line with the ICH E2B(R3) implementation guidelines the E2B(R2) code lists or free text (where an E2B(R2) code list does not

exist) will be used in the interim period. Once the ISO IDMP standards are available, the EudraVigilance system will be amended accordingly to implement these new terminologies.

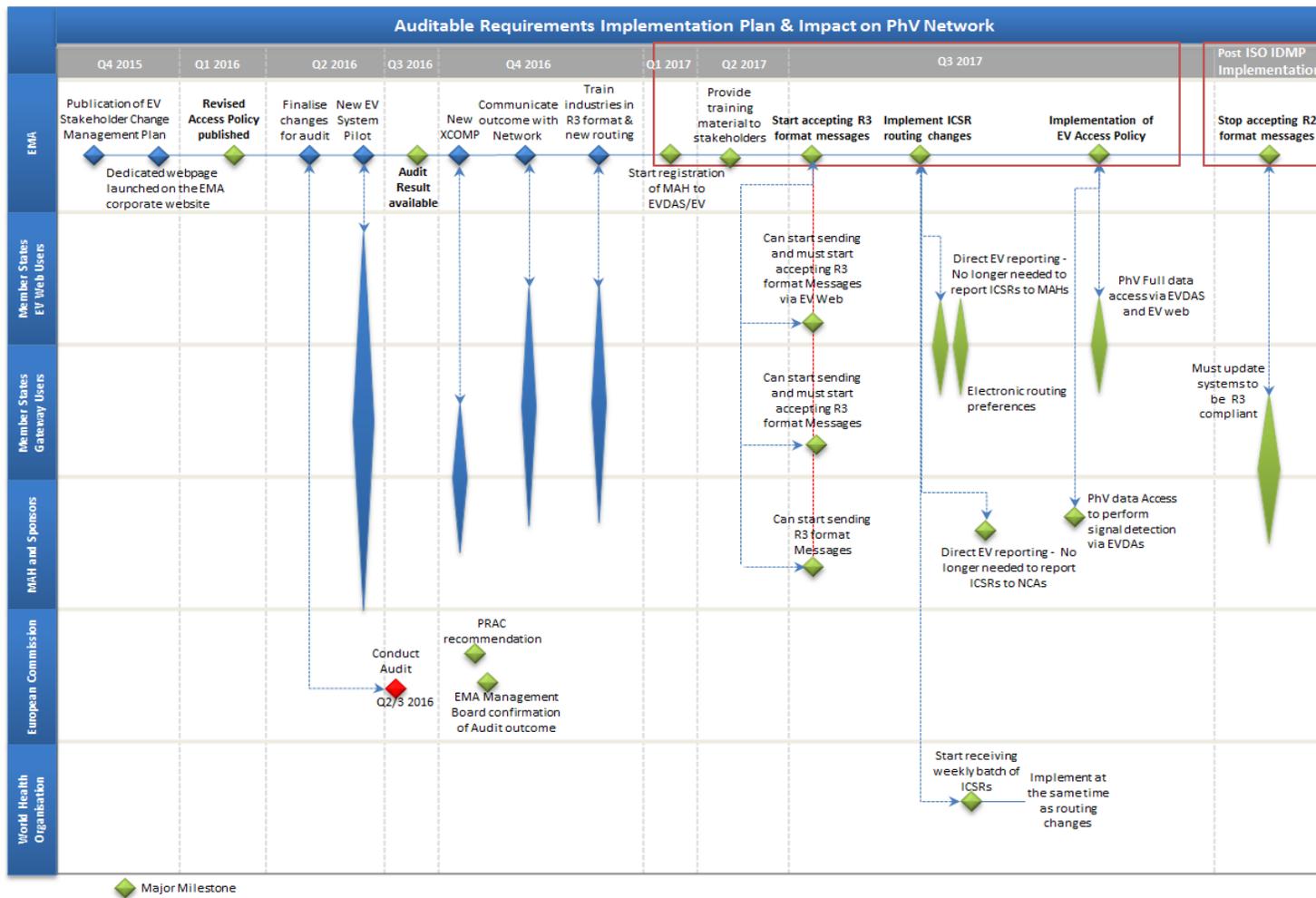
Before the move to centralised reporting, the new EudraVigilance system has to undergo an independent audit that will check that the required functionalities agreed with the Pharmacovigilance Risk Assessment Committee (PRAC) and the EMA Management Board in December 2013 have been implemented. The audit report along with a PRAC recommendation will be presented to the EMA Management Board, which will then announce if the EudraVigilance system has implemented the functionalities. Six months after the announcement of the EMA management board, the move to centralised reporting will be take effect.

The current road map foresees the audit taking place during Q3 2016 followed by a Management Board decision at the end of 2016. Therefore, the likely start of centralised reporting will be mid-2017.

The requirements for centralised SUSARs reporting and the development of the standard web-based structured form mentioned above are part of the provisions of the new clinical trials regulation and are not subject to the independent audit.

## 4.1. Implementation roadmap

The diagram below illustrates the sequence of planned IT and business process changes to the EudraVigilance (transactional system and EVDAS) and the impact of these on the EudraVigilance stakeholders.



## **4.2. EudraVigilance system changes**

The current Eudravigilance system is made of the following components that will be amended in order to fulfil the auditable requirements:

- EV organisation and user management;
- EV gateway;
- EV database management system;
- EVWEB reporting application;
- EV data analysis system, including the European database of suspected adverse drug reaction reports (<http://www.adrreports.eu/>);
- EudraVigilance duplicate detection and management system;
- EudraVigilance medicinal product recoding application.

Two new components will be added to the system:

- EV rerouting rules engine;
- ICSR download functionality for MAHs.

The eXtended EV Medicinal Product Dictionary (XEVMPPD) component will no longer be an integral part of the EudraVigilance system and instead will become an independent system that the EudraVigilance system and XEVMPPD users will access for information on medicinal products.

### **4.2.1. EV organisation and user management**

The EudraVigilance registration process will not change with the implementation of the new system and all existing organisation and user registrations will be transferred to the new system. However, it should be noted that a different registration process exists for access to the EudraVigilance data analyses system which is described below in section 5.1.2.3. A new registration process for MAH users in EVDAS will be implemented.

### **4.2.2. EV gateway**

The EudraVigilance gateway will not have any significant changes other than being configured to accept E2B(R3) files. When centralised reporting becomes effective, the transmission of ICSRs by MAHs through the gateway to National Competent Authorities (NCAs) will no longer be supported by the EMA. Gateway users will not be prevented from sending ICSRs through the gateway to other registered organisations that are connected to the gateway. However, organisations performing such transmissions will not be able to contact the gateway helpdesk for support if issues occur with these transmissions. At the time of implementation, organisations should be aware that only submissions of ICSRs to the EudraVigilance system will be considered as fulfilling the legal obligations of the sender. Therefore, organisations should ensure that the transition to centralised reporting is coordinated with the new system implementation.

### 4.2.3. EV database management system

The EudraVigilance database management system will have the most significant changes as the database will be updated to support the E2B(R3) structure and fields. All existing E2B(R2) data will be migrated into this new database.

The XML parser<sup>2</sup> will be replaced and will be able to process both E2B(R2) and E2B(R3) messages. If an E2B(R2) message is sent to the EudraVigilance system, an E2B(R2) acknowledgement message will be returned. Likewise, an E2B(R3) acknowledgment will be returned for E2B(R3) ICSR messages.

EudraVigilance applications for Medicinal Product Recoding and Duplicate Detection and management will also be amended to support E2B(R3). Master cases that are produced by the EMA in response to identifying duplicated ICSR in the EudraVigilance system will be produced in E2B(R3) format only.

### 4.2.4. EVWEB reporting application

The EVWEB application will be rewritten using a different technology which will enable the application to work in additional browsers rather than being restricted to specific versions of Internet Explorer. The planned supported browsers will be Firefox, Chrome and Internet Explorer; other browsers may work with the application but will not be supported by the Agency.

The functionalities of the application will be changed to only support E2B(R3) ICSR data entry. Although the application will have the same ICSR functionalities, the user interface will have a different appearance and the E2B(R3) standard will itself introduce additional fields and different ways of structuring the data. These changes will require users of the current system to undertake some training in order to become familiar with these changes. This training will not be mandatory for access to the new system for existing registered users, however it will be strongly recommended.

### 4.2.5. EV data analysis system (EVDAS)

The EudraVigilance data analysis system (EVDAS) will be updated to the new E2B(R3) data structure. In addition, a new set of functionalities and predefined reports (as per level of access defined in the revised EV access policy) will be implemented. The subsequent sections provide details on what functionality will be available for specific stakeholder groups.

#### 4.2.5.1. *Healthcare professionals and general public*

The current European database of suspected adverse drug reaction reports (<http://www.adrreports.eu/>) will be updated and improved to include:

- Weekly refresh of published data;
- Publication of data for non-serious cases received in EudraVigilance;
- Publication of 'country' data (in aggregated dashboard);
- Publication of additional data elements via Line listing reports and the new ICSR form (replacing the existing CIOMS I form).

Please note that several safeguards will be put in place in order to ensure full compliance with personal data protection i.e. to prevent patient identification.

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<sup>2</sup>An application that processes and loads the data held within an XML file into the database

#### **4.2.5.2. Marketing Authorisation Holders**

Access will be granted to the EudraVigilance data analysis system to marketing authorisation holders to use signal detection and analytical/reporting functions to the extent necessary to comply with their pharmacovigilance obligations. Such functions will include:

- The electronic Reaction Monitoring Report (eRMR) based on the eRMR used within the EU network and the EMA for signal detection activities;
- The individual case line listing and ICSR form.

The level of access to each ICSR and data elements will be implemented as defined in the revised EudraVigilance access policy. Several safeguards will be put in place in order to ensure compliance with personal data protection i.e. to prevent patient identification.

#### **4.2.5.3. Commission, Medicines Regulatory Agencies in the EEA and the EMA**

New functionalities and predefined reports will be implemented in the EudraVigilance data analysis system to support:

- Signal detection and management activities;
- ICSR Data quality monitoring;
- Publication of Article 57 data;
- The electronic Reaction Monitoring Report (eRMR).

#### **4.2.6. EV rerouting rules engine**

The EudraVigilance rerouting rules engine is a new component that will forward ICSRs to the relevant NCAs depending on a set of conditions agreed with the NCAs. This functionality will not be available for other stakeholders. As per the EU ISO ICSR implementation guide, the EV system will reroute ICSRs in the format received i.e. no conversions will be applied. The rerouting of recoded ICSRs will be put in place as part of the implementation of the ISO IDMP terminologies, in a future upgrade of the EudraVigilance system.

#### **4.2.7. ICSR download function for MAHs**

After the switch to centralised reporting, MAHs will no longer receive ICSRs directly from NCAs. In order for MAHs to receive ICSRs concerning their products download functionality will be made available.

MAHs will be able to request ICSRs for any substance and product that has been indicated as a suspect or interacting drug. However, the data fields that will be provided for the ICSRs will be restricted to the fields as defined in the revised EudraVigilance access policy. The higher levels of access foreseen for MAHs of a particular substance will be determined based on the Article 57 substance and product information submitted to the xEVMPD or future ISO IDMP system.

It should be noted that the ICSRs that will be provided via this download functionality will only be available in E2B(R3) format.

Access to the download tool will be through the secure area of the EudraVigilance website and will therefore require users to be registered.

#### **4.2.8. EudraVigilance duplicate detection and management system**

The change to ICH E2B(R3) does not affect the logic of the duplicate detection algorithm as the fields used do not change between ICH E2B(R2) and E2B(R3). The duplicate detection client will be amended in order to handle duplicates existing in both ICH E2B(R2) and E2B(R3) formats and will need to be amended in order to produce valid E2B(R3) messages. The duplicate detection client will only produce valid E2B(R3) master messages including the cluster information.

The management of duplicates will require the training of EMA staff and its contractors in the new ICH E2B(R3) fields and structures along with changes to the duplicate management interface.

NCA's and MAHs will not be affected by changes to the system apart from having access to Master cases in EudraVigilance created by the EMA in ICH E2B(R3) format.

#### **4.2.9. EudraVigilance medicinal product recoding application**

The change to ICH E2B(R3) does not affect the recoding process as the xEVMPD will continue to be used until ISO IDMP terminologies are available and implemented. The fields used to describe product and substances do not change between ICH E2B(R2) and E2B(R3), however, an additional field for capturing device components of advanced therapies will be implemented. The recoding application will need to be amended in order to handle both ICH E2B(R2) and E2B(R3) formats and the interface will be updated to the new software technology.

These updates to the recoding application will require the training of EMA staff and its contractors in the new ICH E2B(R3) fields, structures and the new interface.

The automated recoding will also require updates to the new EudraVigilance database structure in order to reflect the changes to fields and data structures.

NCA's and MAHs will not be affected by these changes to the system.

#### **4.2.10. Nullification requests**

When an organisation submits a nullification report, EudraVigilance will automatically mark an ICSR as nullified if the pre-existing case has been submitted by the same organisation or one of its affiliates. These nullification reports will have the report classification "Nullified report".

If a nullification request is received for a case that was previously sent by another organisation the following processes apply:

- If the nullification concerns an EEA case, the nullification report will be stored and the nullification retransmitted to the concerned NCA. The concerned NCA should then review the nullification, if the nullification is for a valid reason, the NCA should submit a nullification for the case they have previously submitted to EudraVigilance. The nullification reports from the sending organisation will have the report classification "EEA Nullification request";
- If the case is from outside the EEA, the case ID must match a case ID that already exists in the EudraVigilance database. If no matching case ID exists, the nullification report will be rejected. If a matching case ID is found, the nullification will be accepted and stored with the report classification "Nullification request". The EMA will then review the nullification request and if the nullification is for a valid reason, the EMA will mark the associated ICSRs as nullified through changing the report classification of the appropriate ICSRs to "Nullified report".

The first of these two processes does not require any EMA involvement unless the concerned NCA has requested not to receive rerouted ICSRs. In such situations the EMA will periodically provide those NCAs with details of the nullification requests so that the NCA can submit nullifications if appropriate.

The second process does require EMA involvement in order to approve nullifications of cases held in EudraVigilance. Some limited training will be required at the level of the EMA in order to support this process however the number of these types of nullification requests is expected to be low.

### 4.3. Supporting documentation for stakeholders

ICH E2B(R3) documentation provides the basis for the implementation of the ISO ICSR standard with two main documents downloadable from the ICH ESTRI website <http://estri.ich.org>.

In addition to the ICH Implementation guide, an EU implementation guide has been developed and published. Associated supporting documents, including user guides, training material and guidelines have also been developed or updated and are described below. Together these documents provide additional information on specific regional requirements that are not provided in the ICH documentation and will be published as soon as they are finalised on a dedicated webpage.

Documentation	Description	Date available
ICH Implementation guide package	A set of documents including the ICH ICSR implementation guide, backwards and forwards compatibility recommendations and element mapping	Available now - <a href="#">ICH Implementation guide package</a>
ICH E2B(R3) Questions & Answers (Q&As)	A question and answer document relevant for technical E2B questions	Available now - <a href="#">ICH E2B(R3) Questions &amp; Answers (Q&amp;As)</a>
EU Individual Case Safety Report (ICSR) implementation guide	A guide which describes the additional EU specific requirements to generate a valid ICSR and Message acknowledgment to implement EN ISO ICSR in accordance with ICH E2B(R3)	Available now - <a href="#">EU Individual Case Safety Report (ICSR) implementation guide</a>
EU ICSR implementation guide business rules spreadsheet	This spreadsheet includes all the ICH E2B(R3) and EU specific business rules in a format to help system developers	Will be made available in October 2015
EU backwards forwards conversion element mapping spreadsheet	This document describes the relationship between EU specific data elements in E2B(R3) and E2B(R2). This document is an addition to the ICH backwards forward conversion rules. It covers additional EU specific rules for the conversion back and forth between E2B(R2) and E2B(R3).	Will be made available in October 2015
EU backwards forwards conversion tool	Based on the ICH BFC tool it includes the additional EU specific data fields	Draft will be made available in

		October 2015
EU E2B(R3) code lists	Provides the list of codes for EU specific data fields	Will be made available in October 2015
EU reference instance	An amended ICH reference instance that includes the EU specific data fields	Will be made available in October 2015
EU example instances	Additional example instances that should be used for testing E2B(R3) transmission to the EudraVigilance system	Will be made available in October 2015
Revised EudraVigilance access policy	This Policy follows the approach that information related to safety signals of medicinal products will be disclosed on a systematic basis proactively with adherence to the requirements of personal data protection.	Will be made available early 2016
EVWEB training material	In addition to the automated message generation and processing, the EudraVigilance database management system also provides interactive tools to allow for a 'manual' safety and acknowledgement message as well as medicinal product report generation and administration by a user via a web interface, called EVWEB.	Will be made available in 2017
Download tool training material		Will be made available in 2017
EVDAS training material	Training material on how to use EVDAS	Will be made available in 2017
Revised EudraVigilance Website	EudraVigilance Website	Will be made available in 2017
Revised GVP Module VI	This module addresses the management and reporting of adverse reactions to medicinal products	Will be made available in 2016
Revised GVP Module IX	This module describes the general guidance and requirements on structures and processes involved in signal management and how they are applied in the setting of the EU pharmacovigilance and regulatory network	Will be made available in 2016

#### **4.4. E2B(R3) Stakeholder implementation considerations**

Once an organisation submits an E2B(R3) version of an ICSR, it will not be permitted for that organisation to submit a follow-up to that ICSR in the previous E2B(R2) format. This is in order to prevent inconsistencies that would occur between the two submission formats.

Once the new EudraVigilance system is implemented, organisations can submit data in both E2B(R2) and E2B(R3) formats. However, access to ICSR XML data held within EudraVigilance will be in the E2B(R3) format only. Organisations should therefore make sure that they have systems in place that can process E2B(R3) files. This can be done either by implementing native E2B(R3) support in their own pharmacovigilance system or by implementing the published Backwards/Forwards conversion (BFC) tool to convert E2B(R3) files into E2B(R2) files. An extended version of the ICH E2B(R3) BFC tool that includes the additional EU specific data fields specified in the EU implementation guide will be made available in the EU.

#### **4.5. Testing with the new EudraVigilance system and user training**

During Q2/3 2016 an external testing pilot for the new EudraVigilance system is planned. Following this and the Audit, the Test EudraVigilance system (XCOMP) will be migrated to the new system. Once the Audit has been completed, all organisations with a registered Test EudraVigilance account can start sending E2B(R3) Test files and will also be able to download E2B(R3) files based on test data. In addition, EVWEB users will be able to view and use the new EVWEB interface in the Test EudraVigilance system.

If organisations wish to train internal users on the older (E2B(R2)) version of the EVWEB tool without using the production environment, they will need to contact the EMA through the EudraVigilance helpdesk one month in advance of their planned training in order to obtain user credentials for the EudraVigilance Training system.

The go-live of the external testing system in mid-2016 will allow around a one year period for organisations to become familiar with the new system before it is implemented into production.

##### **4.5.1. Testing process for E2B(R3) & E2B(R2) submissions**

A set of E2B(R3) example test files will be made available as described in the EU implementation guide. Testing organisations are expected to upload these files into their own Pharmacovigilance system and then resubmit these cases to the EudraVigilance system. The EMA will then check that the original file and resubmitted file are identical in all the fields apart from those that can be changed by a re-transmitter e.g. administrative field.

Organisations wishing to test E2B(R2) submissions from a new pharmacovigilance system will also be provided with example test files and should follow the same approach as described above.

##### **4.5.2. New EVWEB application user training**

As described in section 4.5. above, the new EVWEB application will be made available for from mid-2016. Therefore, organisations currently using EVWEB and intending to use EVWEB in the future will have a period of around one year in order to become familiar with the updated application. Users and organisations that have already attended and passed the EVWEB training course do not need to re-attend the course. The EMA will publish a user guide, online eLearning training materials and provide Webinars. The training materials will explain the new E2B(R3) format including the new data fields and

the new EVWEB tool. Some face-to-face short training courses will also be available for users that have previously attended an EVWEB training course; however, the number of places will be limited.

For users that have never used EVWEB a more comprehensive training course to provide a more in depth training of the EVWEB tool will be made available in the continuation of what is currently being done for the current EudraVigilance system. The user manual, training materials and courses will be made available from mid-2016.

Some limited training for the old EVWEB application will be available during the period Q2 2016 to Q1 2017. However, organisations should be aware that these new users will also need to follow the online training or other courses in order to be ready to use the new EVWEB application.

### **4.5.3. EVDAS user training**

The EVDAS user manual for Pharmacovigilance reports will be updated and new user manuals for new reports (e.g. Art.57 data and data quality reports) will be created.

eLearning courses will be created for existing EVDAS users to highlight new functionalities/reports or changes to the existing reports in EVDAS that the users might already be familiar with.

New users will be trained as part of the standard EVDAS training provided every year to NCAs by the EMA and training materials will be updated accordingly.

EVDAS stakeholders should be aware that these users will need to familiarise with user manuals, training materials and e-learning in order to be ready to use the new EVDAS. These materials will be made available from 2017.

### **4.6. Art 57 – xEVMPD**

The new EVWEB application will not include a component for creating and sending xEVPRM messages to the Art 57 database. The current version of the EVWEB version 7 tool will be kept in place for the submission of Art 57 data. The ICSR related functionalities will be removed from the EVWEB version 7 tool at the time of implementation of the new EudraVigilance system. A separate project to replace the xEVMPD data format with the ISO IDMP format is being considered and would lead to the future replacement of the EVWEB 7 tool.

No changes to the business process or resource requirements are expected until the ISO IDMP format is implemented.

### **4.7. What to do in case of system failure**

The process to follow in case of a failure of submission of ICSRs occurring at the sending organisation side or at the level of the EMA will change once the new system is implemented. If the failure occurs at the sender's side, the process of submission of CIOMS forms via fax or other methods is no longer permitted, and the organisation must submit the cases electronically to EudraVigilance as soon as their system is available again. Manual recoding of the official receipt dates by the EMA to the data of the fax CIOMS form will no longer continue.

If the failure is occurring at the level of EudraVigilance, organisations will need to submit cases within two business days after the system failure has been resolved. Cases received late due to the system failure at the level of the EudraVigilance system will be excluded from reporting compliance by setting the official receive date of the cases submitted in this period within EudraVigilance to the date the

system became non-available or the Receipt date (A.1.7 E2B(R2) or C.1.5 E2B(R3)), whichever is greater.

#### **4.8. Production go-live planning**

In order to put the new system in the production environment it is foreseen that the previous production systems will be shut down as described in section 5.1.1. below. During this period, all the data in the old EudraVigilance production environment will be migrated to the new EudraVigilance database. Once this has been completed, the new EudraVigilance system components will be installed to the production environment and configuration changes will be implemented on the EudraVigilance gateway. The new functionalities of the EudraVigilance data analysis system will also be made available.

During this period, organisations will not be able to send ICSR electronically via the Eudravigilance gateway; organisations should therefore plan to submit any cases that are coming up for the 7/15 day compliance limits before the system is taken offline. If ICSRs need to be submitted during this period, organisations should follow the process described in the section "I.C.2.1.6 What to do in case of system failure" of the EU Individual Case Safety Report (ICSR) implementation guide.

During the period that the new system is being implemented, organisations should reconfigure their systems to ensure that future post-authorisation submissions are made to the EudraVigilance system only as it will become the central reporting system for the EEA. Once the system becomes available again, any reports that should have been submitted during this period of non-availability should be transmitted electronically to EudraVigilance only.

#### **4.9. Planned future updates to the new EudraVigilance system**

The ISO IDMP set of standards and their resulting terminologies will not be fully available at the time of implementation of the new EudraVigilance system. However, ISO IDMP integration is being planned for and will be implemented through a subsequent project. In addition, the Agency will also change the way organisations and users are registered to access IT systems and services which will replace the current EudraVigilance registration process. Further details on these updates will be discussed with stakeholders in the future.

## **5. Stakeholder Implementation planning**

This section provides specific detailed guidance to each stakeholder group on what activities need to be planned between now and the time when the new EudraVigilance system goes live.

### **5.1. EMA change management planning**

This section of the change management plan focuses on the IT and business process changes that have been considered by the EMA for the period of time leading up to and after implementation of the new EudraVigilance system.

#### **5.1.1. EMA IT implementation plan**

##### **5.1.1.1. EudraVigilance Testing**

In addition to the internal testing performed at the level of the EMA, external testing is planned for mid-2016 with a limited number of stakeholders. This testing will be performed in advance of the Audit

of the system. Once this testing has been completed, the external testing system (XCOMP) will be made available to all stakeholders. The organisations selected to participate in the external testing will be contacted several months in advance of the planned testing period.

#### **5.1.1.2. System Implementation**

Before the go live, the data from the current system will all be migrated to the new E2B(R3) compliant database. Due to the large amount of data to be migrated, this will require the system to be unavailable for up-to a week. The exact times will be confirmed and communicated around one month before the go live date.

All registered users at the time of the go live will be automatically granted access to the new EV system and therefore there will be no action required by existing users. New users will need to go through the registration process in place at the time of the go live.

The information held on the EudraVigilance website will be moved as part of an ongoing process to the EMA corporate website.

The currently implemented gateway will also be used for the new E2B(R3) compliant system. The E2B(R2) gateway community will also remain the same. For the submission of E2B(R3) messages the gateway configuration at the EMA will be updated; these updates may require organisations wishing to submit E2B(R3) messages to also update their own gateway configuration. Further details on these requirements will be provided in advance of the testing and production systems becoming available.

The EudraVigilance helpdesk contact details will remain the same:

#### **EudraVigilance Registration**

Email - [eudravigilanceregistration@ema.europa.eu](mailto:eudravigilanceregistration@ema.europa.eu)

Tel - 44 (0) 20 3660 7523

#### **EudraVigilance Helpdesk**

Email - [EudraVigilance@ema.europa.eu](mailto:EudraVigilance@ema.europa.eu)

Tel - 44 (0) 20 3660 7523

#### **Gateway Helpdesk**

Email - [gatewaysupport@ema.europa.eu](mailto:gatewaysupport@ema.europa.eu)

Tel - 44 (0) 20 3660 7523

Additional helpdesk contact details may be established to specifically support EVDAS users and for the process of reporting pharmacovigilance signals.

No changes will be made to the existing xEVMPD tool and therefore the functionalities and interface will remain the same.

### **5.1.2. Business process changes and resourcing requirements**

The changes relating to business process that will occur after the implementation of the new EudraVigilance system are described in section 3. above. The following sections describe these changes in relation to the EMA and the potential changes in work load and internal process ownership.

In addition, during the period of six months before the new system goes live, all relevant SOPs and working guides associated with the business process described in this section will need to be reviewed and amended as needed.

#### **5.1.2.1. Centralised reporting of ICSRs & SUSARs to EudraVigilance**

The configuration of rerouting rules is likely to be maintained by the NCAs directly in the system through an interface. If the interface is not accessible to the NCAs at the time when the new system is put in place the EMA will need to maintain these rules on behalf the NCAs. It is unlikely that these rules will be changed on regular basis and therefore, after the initial configuration setting are entered in the system a month before the system is put live, little additional work is expected from this activity. This activity will be performed by the Data Standardisation and Analytics (DSA) service.

#### **5.1.2.2. Access to data held in EudraVigilance by MAHs**

MAHs will be provided with tools to download and analyse data held within EudraVigilance, training materials and user manuals are planned to be provided in advance of system going live. It is therefore expected that external organisations will prepare themselves using these published materials and through regular communications sent out by the EMA. However, an increase in helpdesk queries is very likely leading up to the new system implementation and for a period of several months after implementation.

#### **5.1.2.3. EudraVigilance Registration requests**

The currently registered users for EudraVigilance will be migrated to the new EudraVigilance system with the same configuration settings for accessing EVWEB and the secure area of EudraVigilance.

As per updates to the EudraVigilance access policy, MAHs will be granted access to the EudraVigilance Data Analysis System (EVDAS). MAHs will therefore need to assign specific users the permission to access the EVDAS system in addition to EVWEB and the secure area of EudraVigilance. The person responsible for EudraVigilance from each organisation will be contacted six months in advance of the new system implementation in order to start making changes to the registration details and to inform the EMA of users that need to be granted access to EVDAS. It is likely that there will be a significant increase in registration requests during the six month period before the system goes live (potentially 25,000 users to be registered in EV and EVDAS). The effect of this additional work on EMA resources will need to be planned for, taking into account planned improvements to the functionalities to user and organisation management.

Additional registrations for the new XCOMP (EVTEST) system are also likely to occur once the new test system goes live after completion of the audit.

EV training environment will also be updated and the process for providing training accounts to the training courses will need to take into account the changes to the system.

It should be noted that, as the xEVMPD (Art57) system will remain based on the older EudraVigilance system implementation; the registration process for the submission of xEVMPD data will require the continued registration of users in this legacy system.

The registration process will be performed by the Data and Information Lifecycle Management service.

#### **5.1.2.4. Access to data requests**

Access to data requests received from the public, healthcare professionals, research organisations and other international regulatory authorities will be handled in the same way as the current process. The new access policy will be used to identify the fields that can be provided for such requests.

A significant increase in volume of requests is not expected once the new system is implemented. The answering of these requests will be performed by the Signal Management service.

#### **5.1.2.5. MAH Signal validation and management process**

Once MAHs are granted access to the EV database, MAHs will have a legal obligation to monitor the data available in the system and to inform the Agency and National Competent Authorities (NCAs) about validated signals. Those signals validated by MAHs should be incorporated into the signal management process for confirmation and further analysis when relevant.

The Signal Management service, in collaboration with the Member States (MSs), will establish the new process for signals validated by MAHs and should determine the criteria for validation and the different steps to be followed by the different stakeholders (i.e. MAHs, EMA, NCAs, PRAC) during the signal management process. Although it is not possible to estimate the amount of validated signals that will be submitted by MAHs, it is anticipated that there will be an increase in the volume of signals that will have to be tracked, confirmed, prioritised and evaluated and therefore resources implications for the EMA, MSs and PRAC should be considered.

The new process for signals validated by MAHs will be designed, discussed and consulted during the 1st revision of the GVP Module IX on signal management. Other guidance documents including training materials will be created and provided as needed.

EPITT is the current system for tracking signals at the EU level and MAHs have no access to the system. It is therefore anticipated that signals validated by MAHs should be manually entered in EPITT according to the process established in GVP module IX. Future approaches for the submission of signals by MAHs and the tracking system through the implementation of new tools are being considered.

As this is a new process, the Signal management service will need to provide additional resource to support it.

#### **5.1.2.6. Recoding application**

The recoding process does not change significantly with the system updates; this will however need to be reviewed when ISO IDMP is implemented. The new E2B(R3) structure does however introduce new fields such as Device ID for Advanced therapies and therefore the application will be changed. As this process is carried out by a contractor, training needs to be planned for the contractor. This can be carried out through Train the Trainer sessions and webinars. This training should be started six months before the system go live date followed by refresher training three months and two weeks before.

The activities of monitoring the contractor and providing their training will be performed by the Data Standardisation and Analytics service. Apart from the set-up phase, no change to resource requirements is foreseen.

#### **5.1.2.7. Duplicate detection tool**

The duplicate detection process does not change with the system updates. The new E2B(R3) structure and new fields and the subsequent changes to the duplicate detection tool do need to be appropriately managed. As this process is carried out by a contractor, training needs to be planned for the contractor. This can be carried out through Train the Trainer sessions and webinars. This training should be started six months before the system go live date followed by refresher training three months and two weeks before.

The activities of monitoring the contractor and providing their training will be performed by the Data Standardisation and Analytics service. Apart from the set-up phase, no change to resource requirements is foreseen.

#### **5.1.2.8. Data quality review**

The data quality review process does not change with the system updates. The new E2B(R3) structure and new fields and the subsequent changes to the EVWEB tool do need to be appropriately managed. As this process is carried out by a contractor training needs to be planned for the contractor on both EVWEB and the changes brought in through the implementation of E2B(R3). In addition, as data will continue to be submitted in E2B(R2) format and the EVWEB tool will display the content in E2B(R3) format the data quality reviewers will need specific training. This training should provide a detailed understanding on how to assess these two different submission formats in a review tool. The training can be carried out through Train the Trainer sessions and followed up with webinars. This training should be started six months before the system go live date followed by refresher training three months and two weeks before.

The activities of monitoring the contractor and providing their training will be performed by the Data Standardisation and Analytics service. Apart from the set-up phase, no change to resource requirements is foreseen.

#### **5.1.2.9. EudraVigilance testing with organisations**

The method for testing of submission of ICSR to the new EudraVigilance system has now changed. The EMA will now provide a set of sample ICSR files to be uploaded and transmitted to the EudraVigilance external testing system along with a testing script to be followed by the EDI partner.

In addition, for organisations that have not implemented importing functionality the data for submission will be made available in a human readable format for manual data entry and submission. The set of sample files will cover a range of different reporting scenarios in order to ensure that the sending system has been correctly implemented, including the additional EU specific requirements. This applies to organisations testing updates to systems using the E2B(R2) specification or for systems that have implemented the ISO ICSR 27953-2:2011 (E2B(R3)) standard.

The organisation performing the testing is expected to upload these sample files into their pharmacovigilance system and follow the test script. Once uploaded, these test files should be transmitted to the EudraVigilance external testing system for review by the EMA. Unexpected differences between the sample set of ICSR files and the information received by the EudraVigilance external testing system will be communicated to the EDI partner. Any issues identified will need to be addressed before allowing the EDI partner into the production phase.

These testing activities will be performed by the Data Standardisation and Analytics service. This new testing process should lead to a reduction of work compared to the current process. However, it is expected that in the period of time leading up to the new EudraVigilance system implementation and for a period of several months after, there will be a significant rise in testing as new pharmacovigilance systems are implemented by MAHs and NCAs.

#### **5.1.2.10. Medical Literature Monitoring Service**

The Medical Literature Monitoring Service does not change with the system updates. The new E2B(R3) structure and new fields and the subsequent changes to the EVWEB application do need to be appropriately managed. As this process is carried out by a contractor using EVWEB, training will need to be planned for the contractor. This can be carried out through Train the Trainer sessions, webinars and planned stakeholder training courses. This training should be started six months before the system go live date followed by refresher training three months and two weeks before.

The activities of monitoring the contractor and providing their training will be performed by the Data Standardisation and Analytics service. Apart from the set-up phase, no change to resource requirements is foreseen.

#### **5.1.2.11. WHO-UMC reporting**

The reporting of EEA ICSRs to the WHO-UMC will be a new process for the EMA, the new EudraVigilance system will forward relevant ICSRs automatically using a set of predefined rules. Apart from the set-up phase, the automation put in place should mean that only limited resources are required to support this process. Some checking and monitoring will be needed to ensure the successful forwarding of ICSRs to the WHO-UMC; in addition, some helpdesk support for WHO-UMC queries will be planned although the expected workload is very low.

This process will be performed by the Data Standardisation and Analytics service. Apart from the set-up phase, no significant increase in resource requirements is foreseen.

#### **5.1.2.12. Helpdesk - business support**

No changes are expected to the helpdesk process for EudraVigilance business support. However, an increase in queries leading up to the new EudraVigilance system implementation and for several months after the new system is implemented is expected. The following query topics are likely:

- Submission of ICSRs in E2B(R3) format;
- Testing E2B(R3) submissions;
- Centralised reporting;
- MAH downloading of ICSRs;
- MAH Signal reporting;
- MAH & NCA EudraVigilance data analysis (Including eRMR & Art 57);
- EudraVigilance system Registration;
- New EVWEB interface;
- ADR website.

More EMA resources will need to be planned for the support of helpdesk activities, first line support and will need training on standard answers. Data Standardisation and Analytics service will need to provide standard answers and links to documents to first line support in order to support the handling of helpdesk queries.

#### **5.1.2.13. Helpdesk Second-line (IT operations) Support**

No changes are expected to the helpdesk process for EudraVigilance (including EVDAS and ADR website) second-line support. However, an increase in queries relating to potential system issues at the level of the users and the EMA can be expected. This increase is likely to occur as soon as the new test EV system (XCOMP) is implemented and again in the period after the production system goes live.

More EMA resources may need to be planned for the support of helpdesk second-line support activities.

### 5.1.2.14. EudraVigilance data analysis system

The main change for EMA users will be the implementation of several new functionalities and predefined reports in the EudraVigilance data analysis system to support:

- Pharmacovigilance activities, including the implementation of a new measure of disproportionality (reporting odds ratio), new functionalities for sub-group analyses and new data elements;
- Data quality monitoring, including reports on organisation reporting to EudraVigilance, safety report monitoring, expedited reporting timelines compliance monitoring, safety reports data quality;
- Publication of Article 57 data, including reports on authorised medicinal products, legal entity (MAH) and QPPV details, approved substances, pharmacovigilance system master file and listings on authorised medicinal products;
- The electronic reaction monitoring report (eRMR), including the integration with EVDAS, the improvement of data visualization and the clarification on methodology

Support to the users will also be performed by the Data Standardisation and Analytics (DSA).

### 5.1.3. EMA training

The EVDAS user manual for Pharmacovigilance reports will be updated and new user manuals for Article 57 reports and data quality reports will be created.

eLearning courses will be created for existing EMA users in EVDAS that will highlight new functionalities/reports or changes that have been made to pre-existing reports..

New EMA users will be trained as part of the standard EVDAS training provided every year to NCAs by the signal management service. Training materials will be updated accordingly.

	Training type	Training goal	Timeline	
			2016	2017
<b>Key Training Milestones</b>	<b>User Manual</b> <ul style="list-style-type: none"> <li>• Update of existing EV and EVDAS user manuals</li> <li>• Creation of new user manuals: ROR reports, Art.57 reports Data quality reports, Duplicate Detection user guide</li> </ul>	Detailed guides to support all EVDAS and EV users	<i>Under Development</i> 	Available Online
	<b>E-Learning</b> <ul style="list-style-type: none"> <li>• New functionalities/ reports in EVDAS (including changes to the existing reports)</li> <li>• The move from R2 to R3</li> <li>• EudraVigilance R3 Format</li> </ul>	Support existing EVDAS and EV users	<i>Under Development</i> 	Available Online
	<b>Face to Face</b> <ul style="list-style-type: none"> <li>• Standard EVDAS training by the Signal Management Service</li> <li>• Regulatory and procedural aspects</li> <li>• EudraVigilance Access Policy</li> <li>• Electronic reporting principles based on new ISO ICSR standard</li> </ul>	Support new and existing EVDAS and EV users	Standard EVDAS Training Available on Demand <i>EV Training Under Development</i> 	Standard EVDAS Training Available on Demand Available On Demand

#### **5.1.4. EMA communications plan**

A communication plan has been developed to ensure that the necessary information is circulated to relevant stakeholders at the appropriate time and to ensure that impacted parties are aware of the modifications to the EudraVigilance system. This is to ensure that they are prepared for the IT and business changes that they will need to make. Communications will be undertaken through both general update communications and targeted communications based on key project milestones.

##### **5.1.4.1. General update communications**

Quarterly updates on the development and progress of the changes to the EudraVigilance system will be communicated via the Pharmacovigilance Update Bulletin. This document is distributed to both Industry and Member State stakeholders on a quarterly basis to Industry Associations, Qualified Persons for Pharmacovigilance (QPPVs), Heads of Medicines Agency (HMA), Programme Maintenance Groups (PMGs), EU Commission, international partners, ENCePP and the Implementation Working Group (IWG). The Pharmacovigilance Programme Update Bulletin issues 01, 02, 03 and 04 can be accessed through the following link:

[http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general\\_content\\_000520.jsp&mid=WC0b01ac05804fa031](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000520.jsp&mid=WC0b01ac05804fa031)

The EudraVigilance website contains a wealth of information regarding recent news, information days, helpdesk information, training information and EudraVigilance system information. This website will be maintained on a regular basis to ensure that the content is relevant and up-to-date. The EudraVigilance Website can be accessed through the following link:

<https://eudravigilance.ema.europa.eu/human/index.asp>

##### **5.1.4.2. Targeted communications based on key milestones**

Information on key milestones will be disseminated to relevant parties through the following channels:

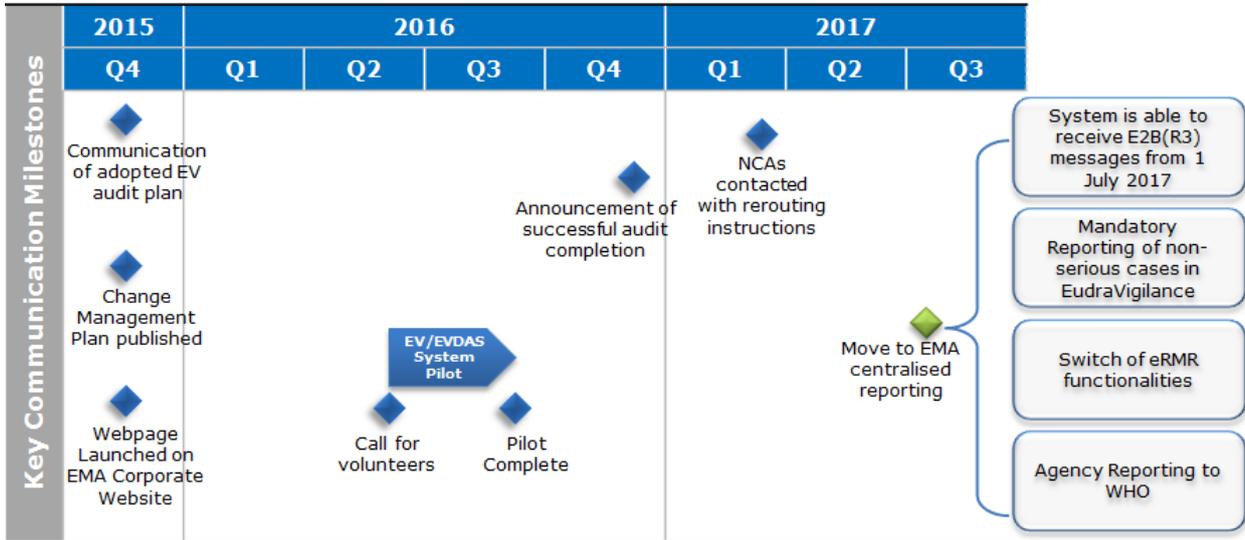
- Publication of EMA News Items on the Agency corporate website;
- Tailored emails to the registered EudraVigilance users;
- Presentations and teleconferences with PMG1, the Pharmacovigilance Risk Assessment Committee (PRAC), the EudraVigilance Expert Working Group (EV-EWG), the Implementation Group (IG), the European Risk Management Facilitation Group (ERMS-FG) and the HMA.

The key project milestones around which our communications will be anchored are:

- The audit of EudraVigilance system;
- The availability of the conversion tool for E2B(R2)/(R3);
- The Management Board announcement of results of audit of EudraVigilance system;
- The availability of the new EudraVigilance test system;
- The move to ICSR centralised reporting;
- The availability of the new EVDAS functionalities
- The mandatory reporting requirement of non-serious cases in EudraVigilance;
- The commencement of Agency reporting to WHO;

- The ability of the EudraVigilance system to receive E2B(R3) messages;
- The enabling of the EudraVigilance ICSR re-routing.
- Stop accepting E2B(R2) messages

Additionally, targeted information announcing the available training dates and information days will be communicated to relevant stakeholders.



### 5.1.5. EMA change management planning

The following EMA actions have been grouped by area and whether they are obligatory or recommended actions.

People	Information
<p><b>Must Do</b></p> <ul style="list-style-type: none"> <li>• There will be an increase in DCM resource requirement for the quality assurance testing of the data submission in the new format (R3)</li> <li>• There will be a resource requirement for the development of the training material, as well as time required to deliver the training to internal users of the new system</li> <li>• There will be a resource requirement for the development of the training material which is to be rolled out to the external users on the submission of data. (The training will be provided by contractors and is to be rolled out to ~11,000 users)</li> <li>• With the implementation of the EV Access Policy, the larger amount of the requests on access to documents (access to documents, access to information) is anticipated therefore Agency will need to have a plan in place to deal with the queries (mainly SMA, with DCM support)</li> <li>• It is likely that there will be a significant increase in registration requests during the six month period before the system goes live (potentially 25,000 users to be registered in EV and EVDAS). The effect of this additional work on EMA resources will need to be planned for.</li> </ul>	<p><b>Must do</b></p> <ul style="list-style-type: none"> <li>• An increase in helpdesk queries is very likely leading up to the new system implementation and for a period of several months after implementation functionalities to user and organisation management.</li> <li>• The EudraVigilance website contains a wealth of information regarding recent news, information days, helpdesk information, training information and EudraVigilance System information. This website will need to be maintained on a regular basis to ensure that the content is relevant and up-to-date.</li> </ul>
Technology	Process
<p><b>Must Do</b></p> <ul style="list-style-type: none"> <li>• The data structure in SAS will change therefore the Agency's SAS users will need to learn and understand the new data model</li> <li>• Before the go live, the data from the current system will all be migrated to the new E2B(R3) compliant database.</li> </ul> <p><b>Should do</b></p> <ul style="list-style-type: none"> <li>• No new technology is being introduced to the EV system (for data analysis tools), but additional functionalities are implemented and internal training on the new functionalities may be needed</li> <li>• The configuration of rerouting rules is likely to be maintained by the NCAs directly in the system through an interface. If the interface is not accessible to the NCAs at the time when the new system is put in place the EMA will need to maintain these rules on behalf the NCAs.</li> </ul>	<p><b>Must Do</b></p> <ul style="list-style-type: none"> <li>• A new process for MAHs registration with the EVDAS system needs to be established (for companies to be able to fulfil their Pharmacovigilance obligations)</li> <li>• A new internal process for the production and publication of electronic reaction monitoring reports (eRMR) for MAHs is to be established</li> <li>• The Agency will need to develop a new process to meet the requirement of the EU ADR provision to WHO UMC (to forward data to WHO UMC in line with EU data protection legislation)</li> </ul>

### 5.2. NCA change management planning

This section of the change management plan focuses on the IT and business process changes that should be considered by NCAs in the period of time leading up to and after implementation of the new EudraVigilance system.

#### 5.2.1. NCA IT changes

The implementation of the new EudraVigilance system will require the adaptation of existing national IT systems in order to support the new ISO ICSR standard and to the changes in processing the data. The sections below cover specific IT system components that should be considered at a national level.

##### 5.2.1.1. Implementing ISO ICSR (E2B(R3)) support in National pharmacovigilance systems

Once the new EudraVigilance system is implemented all stakeholders will be able to start using the ISO ICSR (E2B(R3)) format for the submission of ICSRs. However, organisation will still be able to use E2B(R2) for the submission of ICSR after the new EudraVigilance system is implemented. Those organisations not implementing fully compliant ISO ICSR systems will need to support the receipt and processing of the new format. The reason for this is that when cases are forwarded by the EudraVigilance system to the NCA that requests them, the format of the message received will not be

changed. In addition, data processed and entered into EudraVigilance by the EMA (such as Master cases for duplicates, cases identified in the Medical Literature and in the future ICSR recoded against the ISO IDMP terminologies) will be made available to NCAs in the ISO ICSR (E2B(R3)) format only.

NCAs therefore will need to either implement support for ISO ICSR (E2B(R3)) in their systems or implement the backwards/forwards conversion tool in order to be able to process ICSR messages in the ISO ICSR (E2B(R3)) format.

#### **5.2.1.2. EV gateway**

NCAs using a local installation of the gateway software provided by the EMA will not need to replace this software. However, configuration changes may be required in order to support the processing of E2B(R3) messages. Guidance and support for making configuration changes will be provided by EMA gateway support ahead of the implementation of the new system.

When centralised reporting comes into effect, the transmission of ICSRs between MAHs and National Competent Authorities will no longer be supported by the EMA. However, the gateway will not prevent organisations exchanging ICSRs, e.g. between NCAs and their regional pharmacovigilance centres.

At the time of implementation organisations should be aware that only submissions of ICSRs to the EudraVigilance system will be considered as fulfilling the legal obligations of the sender. Therefore NCAs should ensure that the transition to centralised reporting is communicated with MAHs within their territory.

#### **5.2.1.3. EVWEB**

NCAs using EVWEB will need to prepare for the implementation of the new version of the application. The application will be changed to only support E2B(R3) ICSR data entry. E2B(R3) will introduce additional fields and different ways of structuring the data, therefore the user interface will be changed to reflect this and will have a different appearance.

These changes will require the users within the NCA to undertake some training in order to become familiar with the new system. Training materials and online training will be made available in advance of the new system being implemented; please see section 4.5. for details.

It is recommended that NCAs plan to start training their staff six months in advance of the new system being implemented followed by regular refresher training at least three months and followed by two weeks before the new EudraVigilance system is implemented.

#### **5.2.1.4. EV Rerouting rules engine**

NCAs will be contacted in advance of the new system being implemented in order to obtain the details of which ICSRs that NCA wishes to be automatically forwarded to them by the system. Details on the options for rerouting are described in the EU ICSR implementation guide.

NCAs will be able to update the rerouting rules at any time; however changes may require a few days to be processed. NCAs are therefore requested to decide in advance which ICSRs they wish to have forwarded. If no response is received, the default setting will be to forward all the cases associated with that NCA's country.

#### **5.2.1.5. EudraVigilance duplicate detection and management system**

Additional message types will be introduced as part of the EU implementation of E2B(R3) in order to support the forwarding of cases created or modified by the EMA e.g. the creation of Master cases for

identified duplicate cases. NCAs should be aware that these new message types do not exist in the current E2B(R2) specifications and the EU backwards-forwards conversion tool will convert the message type for master cases to “masterichicsr” in the field M.1.1 when downgrading an E2B(R3) master case message.

#### **5.2.1.6. NCA Testing**

As NCAs will receive cases rerouted by EudraVigilance, no testing will be required with MAHs or Sponsors of clinical trials that submit cases directly to the new EudraVigilance system. For those NCAs that have eSUSAR reporting forms, testing should be planned to ensure that they are able to send those SUSARs without issues to the new EudraVigilance system.

The testing process with the EudraVigilance system will change in accordance with the details provided in the EU ICSR implementation guide. The EMA will provide a set of sample ICSR files to be uploaded and transmitted to the EudraVigilance external testing system along with a testing script to be followed by the organisation performing the testing.

NCAs should test once they are ready to implement a new system supporting the submission of E2B(R3) ICSRs. Testing of existing E2B(R2) system with the new EudraVigilance system is not required, however it is encouraged to be performed in advance of the new system going live in order to identify any potential issues in the sending or receiving systems. Therefore, NCAs should plan to complete any testing of their existing systems three to six months prior to the new system going live in order to give time for any issues to be addressed. The testing of existing pharmacovigilance systems against the new EudraVigilance test system will not require involvement of the QAT Testing team at the EMA.

### **5.2.2. NCA business process changes**

#### **5.2.2.1. Centralised reporting of ICSRs to EudraVigilance**

The main change to NCA business processes will be that MAHs will no longer provide ICSRs directly to NCAs; these cases will be reported directly to EudraVigilance before being automatically forwarded to the concerned NCA depending on the NCA requirements.

Planning should be put in place at national level in order to inform MAHs about this upcoming change and to ensure that MAHs are able to report directly to EudraVigilance in advance of the move to centralised reporting. Submissions made by MAHs to NCAs after the move to centralised reporting will not be in compliance with the legislation.

In addition to the reporting of serious cases to EudraVigilance system within 15-days, non-serious cases will also need to be submitted by the concerned NCAs within 90-days of receipt.

NCAs using EVWEB will need to plan for an increase in resources for the manual data entry of non-serious cases into EudraVigilance taking into account that the number of non-serious cases received is generally higher than serious cases. However, it should be noted that with the implementation of centralised reporting NCAs will no longer need to re-route data to MAHs. This means for those NCAs without fully automated IT processes this will lead to a reduction of work and can allow a re-allocation of some finances and resources.

#### **5.2.2.2. Reporting of SUSARs to EudraVigilance**

Until the clinical trials regulation is applicable there is no change to the current process for the submission of SUSARs for clinical trials.

Clinical trials approved through the clinical trials Directive 2001/20/EC will continue to have the same SUSAR reporting requirements as specified in the directive for a transition period of three-years after the clinical trials regulation is applicable.

Sponsors that have a clinical trial approved through the clinical trials regulation are normally required to send SUSARs to EudraVigilance only. The EudraVigilance system will then automatically reroute the SUSARs to the concerned NCAs. However, the option remains for small organisations to report SUSARs directly to the NCA that has approved the trial through establishing an agreement between the sponsor and the NCA concerned. The NCA will then forward any SUSARs reported to them under such agreements to the EudraVigilance system.

Planning should also be put in place at national level in order to inform sponsors of these changes and what is required at national level for SUSAR reporting.

#### **5.2.2.3. Nullification requests**

As NCAs have previously forwarded cases originally from MAHs, nullification requests may be received by EudraVigilance from those MAHs directly for cases that are marked in the system as being sent by an NCA. The previous business rules in EudraVigilance would not permit such nullifications to occur and therefore the new EudraVigilance system has amended rules to not reject such submissions.

When an organisation submits a nullification report, the new EudraVigilance will automatically mark an ICSR as nullified if the pre-existing case has been submitted by the same organisation or one of its affiliates.

If a nullification is received for an EEA case where no pre-existing case from the same organisation or one of its affiliates is found in EudraVigilance, then the nullification report will be stored and the nullification retransmitted to the concerned NCA. If an NCA has elected not to receive re-routed cases the EMA will periodically forward the details of nullification requests as a report via e-mail for consideration. The concerned NCA should then review the nullification requests; if a nullification is for a valid reason, the NCA should submit a nullification for the case they have previously submitted to EudraVigilance.

Therefore, NCAs will need to ensure that they establish processes to check if they need to nullify cases they have previously forwarded to EudraVigilance.

#### **5.2.2.4. MAH Signal validation and management process**

As described in section 5.1.2.5. above, MAHs will have a legal obligation to monitor the data available in EudraVigilance and to inform the Agency and NCAs about validated signals.

This will be a new process for NCAs to implement, therefore NCAs should plan for appropriate resources to support this activity. Although it is not currently possible to estimate the amount of validated signals that will be submitted by MAHs, it is anticipated that there will be an increase in the volume of the signals that will have to be tracked, confirmed, prioritised and evaluated.

The new process for signals validated by MAHs will be designed, discussed and consulted during the 1st revision of the GVP Module IX on signal management. Other guidance documents including training

materials will be created and provided as relevant. As EPITT is the current system for tracking signals at the EU level, it is expected that this system will be used by NCAs to support this activity.

#### **5.2.2.5. NCAs reporting to WHO-UMC**

The reporting of ICSRs occurring in the EEA to the WHO-UMC will be performed by the EMA instead of directly by the NCAs. These ICSRs will be forwarded automatically using predefined rules that have been agreed with WHO-UMC.

The main change for NCAs will be that they will no longer need to perform this activity. NCAs should plan for the last submission of data to occur around the time of the switch to centralised reporting so that any data for the WHO-UMC covers the period up until the switch to centralised reporting. EudraVigilance will submit data prospectively from the time of the switch.

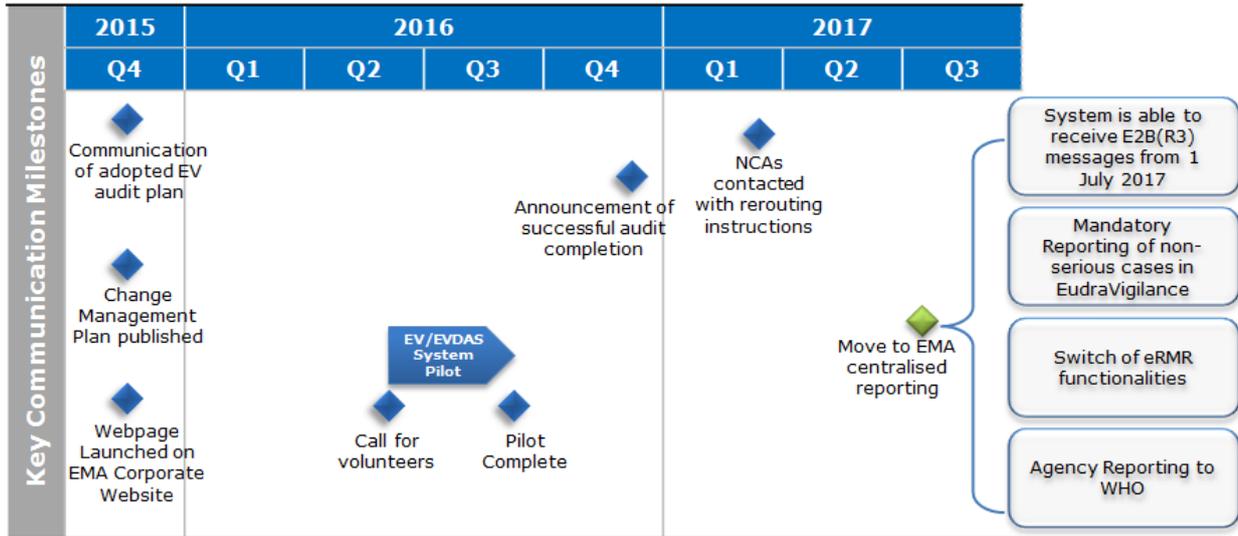
#### **5.2.2.6. EudraVigilance data analysis system**

The main change for NCA will be the implementation of several new functionalities and predefined reports in the EudraVigilance data analysis system to support:

- Pharmacovigilance activities, including the implementation of a new measure of disproportionality (reporting odds ratio), new functionalities for sub-group analyses, new reports and new data elements;
- Data quality monitoring, including reports on organisation reporting to EudraVigilance, safety report monitoring, expedited reporting timelines compliance monitoring, Safety reports data quality;
- Publication of Article 57 data, including reports on authorised medicinal products, legal entity (MAH) and QPPV details, approved substances, pharmacovigilance system master file and listings on authorised medicinal products;
- The electronic reaction monitoring report (eRMR), including the integration with EVDAS, the improvement of data visualization and the clarification on methodology.

### 5.2.3. NCA communications

NCA should consider developing a communications plan in order to ensure that the necessary information is circulated to their relevant stakeholders at the appropriate time so that impacted parties are aware of the changes to the reporting requirements and associated business process. They should also inform their stakeholders of the need to be prepared for the associated IT changes that will be required.



### 5.2.4. NCA training

Training should be planned for NCA staff on the new business process and new IT systems in order to be ready once the new system is implemented. It is advisable to start training around six months in advance of the new system being implemented with refresher training planned at regular intervals in the months leading up to implementation.

If NCAs provide training to its stakeholders, these training courses and training materials should be updated accordingly along with plans for when the new training materials will be implemented.

The EVDAS user manual for pharmacovigilance reports will be updated and new user manuals for Article 57 reports and data quality reports will be created.

eLearning courses will be created for existing NCA users in EVDAS to highlight new functionalities/reports or changes to the existing reports in EVDAS that the NCA users might already be familiar with.

New NCA users will be trained via the standard EVDAS training provided every year to NCAs by the EMA. Training materials will therefore be updated accordingly.

Key Training Milestones	Training type	Training goal	Timeline	
			2016	2017
	<b>User Manual</b> <ul style="list-style-type: none"> <li>Update of existing EV and EVDAS user manuals</li> <li>Creation of new user manuals: ROR reports, Art.57 reports Data quality reports, Duplicate Detection user guide</li> </ul>	Detailed guides to support all EVDAS and EV users	<i>Under Development</i>	Available Online
<b>E-Learning</b> <ul style="list-style-type: none"> <li>New functionalities/ reports in EVDAS (including changes to the existing reports)</li> <li>The move from R2 to R3</li> <li>EudraVigilance R3 Format</li> </ul>	Support existing EVDAS and EV users	<i>Under Development</i>	Available Online	
<b>Face to Face</b> <ul style="list-style-type: none"> <li>Standard EVDAS training by the Signal Management Service</li> <li>Regulatory and procedural aspects</li> <li>EudraVigilance Access Policy</li> <li>Electronic reporting principles based on new ISO ICSR standard</li> </ul>	Support new and existing EVDAS and EV users	Standard EVDAS Training Available on Demand <i>EV Training Under Development</i>	Standard EVDAS Training Available on Demand Available On Demand	

### 5.2.5. NCA change management plan summary

The following NCA actions have been grouped by area and whether they are obligatory or recommended actions.

People	Information
<p><b>Must Do</b></p> <ul style="list-style-type: none"> <li>Undergo training for data submission in the new format (R3) and for the implementation of the new data analysis tools (EVDAS)</li> </ul> <p><b>Should Do</b></p> <ul style="list-style-type: none"> <li>Undertake training on EVWEB to become familiar with application changes</li> <li>Plan to complete any testing of their existing systems six to three months prior to the new system going live</li> <li>Consider resource implications and budget to implement the new standard and support the receipt of R3 messages (IT system developers)</li> </ul>	<p><b>Should Do</b></p> <ul style="list-style-type: none"> <li>EEA non-serious cases should also be reported to EudraVigilance within 90 days of receipt in order to meet reporting obligations.</li> <li>Should report seriousness at an event level rather than case level</li> <li>If a nullification is retransmitted, the concerned NCA should review the nullification and if it is for a valid reason the NCA should submit a nullification for the case they have previously submitted to EudraVigilance.</li> <li>Ensure that transition to centralised reporting is communicated with MAHs within their territory</li> </ul>
Technology	Process
<p><b>Must Do</b></p> <ul style="list-style-type: none"> <li>Upgrade and move to R3 compliant systems (no deadline yet established)</li> <li>Gateway Users: Software does not need to be replaced but configuration changes will be necessary to support E2B(R3)</li> <li>EVWEB Users: Will need to implement the new version of the application. The application will be updated to only support E2B(R3)</li> </ul> <p><b>Should Do</b></p> <ul style="list-style-type: none"> <li>NCA's should prepare internal plans concerning the implementation of the new EudraVigilance system and the resulting changes that will occur to reporting, downloading and analysis of data</li> </ul>	<p><b>Must Do</b></p> <ul style="list-style-type: none"> <li>Update existing processes for rerouting information to MAHs and WHOs</li> <li>Adapt own business processes to screen the new aggregated data (PhV Data, Art57 data) which will be made available by the EMA</li> <li>Update existing processes for Data analysis within the NCAs</li> <li>Implement a new process to support the submission of signals by MAHs</li> <li>Change the standards and the process according to E2B R3 and PhV legislation.</li> </ul> <p><b>Should Do</b></p> <ul style="list-style-type: none"> <li>ICSR submissions in the EEA should only be made to the EudraVigilance in order to meet reporting compliance</li> <li>ICSR submissions for cases occurring in the EEA should only be made by the EudraVigilance system to WHO-UMC.</li> <li>Ensure that transition to centralised reporting is coordinated with the new systems implementation</li> </ul>

### **5.3. MAH Change management planning**

This section of the change management plan focuses on the IT and business process changes that should be considered by MAHs in the period of time leading up to and after the implementation of the new EudraVigilance system.

#### **5.3.1. MAH IT changes**

The implementation of the new EudraVigilance system will require the adaption of existing IT systems at the level of MAHs in order to support the new ISO ICSR standard and to the changes to the processing of the data. The sections below cover specific IT system components that should be considered by MAHs.

##### **5.3.1.1. Implementing ISO ICSR (E2B(R3)) support in MAH's PhV systems**

Once the new EudraVigilance system is implemented, MAHs will have the choice to start using the ISO ICSR (E2B(R3)) format for the submission of ICSRs, assuming that all testing has been completed beforehand. It should be noted that MAHs can continue to use E2B(R2) for the submission of ICSR after the new system is implemented. However, MAHs that choose not to implement a fully compliant ISO ICSR system will still need to support the ability to process the new format. The reason for this is that when ICSRs are made available for MAHs to download from the EudraVigilance system in accordance with the EudraVigilance access policy, these will be in the E2B(R3) format only.

MAHs need to consider implementing a fully ISO ICSR compliant system or to use a backwards/forwards conversion tool in order to support the processing of the E2B(R3) format ICSRs and the ICSR acknowledgements.

##### **5.3.1.2. Electronic gateway**

MAHs using an electronic gateway solution will not need to replace their current software solution. However, configuration changes may be required in order to support the processing of E2B(R3) messages including the acknowledgments returned (EudraVigilance will only return E2B(R3) acknowledgments). Guidance and support for making these configuration changes will be provided by EMA gateway support.

When centralised reporting becomes effective the transmission of ICSRs between MAHs and National Competent Authorities will no longer be supported by the EMA. However, the gateway will not prevent MAHs exchanging ICSRs with other MAHs or sponsors of clinical trials. It should be noted that, organisations performing such transmissions will not be able to contact the gateway helpdesk for support if issues occur with these transmissions.

At the time of implementation MAHs should be aware that only submissions of ICSRs to the EudraVigilance system will be considered as fulfilling the MAH's legal obligations. Therefore, MAHs should ensure that modifications to their submission systems are configured and tested well in advance of the planned implementation.

##### **5.3.1.3. EVWEB**

MAHs using EVWEB will need to prepare for the implementation of the new version of the application. The application will be changed to only support E2B(R3) ICSR data entry. The E2B(R3) standard will introduce additional fields and different ways of structuring the data; therefore the user interface will be changed and have a different appearance.

These changes will require the users within the MAH organisation to undertake training in order to become familiar with the new system. Training materials and online training will be made available in advance of the new system being implemented, please see section 4.5. for details.

It is recommended that MAHs plan to start training their staff six months in advance of the new system being implemented followed by regular refresher training at least three months and two weeks before implementation.

#### **5.3.1.4. EV downloading ICSRs concerning MAH's products**

After the switch to centralised reporting, MAHs will no longer receive ICSRs directly from NCAs. In order for MAHs to receive ICSRs concerning their products, a download function will be made available. Access to the download tool will be through the secure area of the EudraVigilance website and will therefore require a user to be registered. The download tool will allow individuals within an MAH organisation to search, request and download ICSRs.

MAHs will be able to request ICSRs for any substance and product that has been indicated as a suspect or interacting drug. However, the data fields that will be provided for the ICSR will be restricted to the fields defined in the EV access policy. The higher levels of access will be determined based on the Article 57 substance and product information submitted to the xEVMPD and in the future system that will replace it.

#### **5.3.1.5. MAH Testing**

As MAHs will only send cases to EudraVigilance, no testing will be required with NCAs.

The testing process with the EudraVigilance system has changed in accordance with the details provided in the EU ICSR implementation guide. The EMA will now provide a set of sample ICSR files to be uploaded and transmitted to the EudraVigilance external testing system along with a testing script to be followed by the organisation testing.

MAHs are required to test once they are ready to implement the new system supporting the submission of E2B(R3) ICSRs. Testing of existing E2B(R2) system with the new EudraVigilance system is not required, however it is encouraged in advance of the new system going live in order to identify any potential issues in advance. Therefore, MAHs should plan to complete any testing of their existing systems six to three months prior to the new system going live in order to give time for any issues to be addressed. The testing of existing pharmacovigilance systems against the new EudraVigilance test system will not require the involvement of the QAT Testing team at the EMA.

### **5.3.2. MAH business process changes**

#### **5.3.2.1. Centralised reporting of ICSRs to EudraVigilance**

The main change to MAH business processes will be that MAHs will no longer provide ICSRs directly to NCAs. MAH will need to ensure that all reportable ICSRs are submitted to EudraVigilance only. In addition to the reporting of serious cases to EudraVigilance system within 15-days, non-serious cases will also need to be submitted within 90-days of receipt.

Planning should be put in place by each MAH to ensure that they are able to report directly to EudraVigilance in advance of the move to centralised reporting. Any submissions made by MAHs to NCAs after the move to centralised reporting will result in the MAH not being compliant with their legal obligations.

MAHs using EVWEB will need to plan for an increase in resources for the manual data entry of non-serious EEA cases into EudraVigilance, taking into account that the number of non-serious cases received is generally higher than serious cases.

#### **5.3.2.2. MAH signal validation and management process**

As described in section 4.1.3.5. above, MAHs will have a legal obligation to monitor the data available in EudraVigilance and to inform the Agency and NCAs about any validated signals they identify. This will be a new process for MAHs to implement; therefore MAHs should plan for appropriate resources to support this activity.

The new process for signals validated by MAHs will be designed, discussed and consulted during the 1st revision of the GVP Module IX on signal management. Other guidance documents, including training materials, will be created and provided as relevant. MAHs should therefore put in place training for their staff concerning this new activity.

#### **5.3.2.3. EudraVigilance data analysis system**

Access will be granted to the EudraVigilance data analysis System to Marketing Authorisation Holders to use signal detection and analytical/reporting functions to the extent necessary to comply with their pharmacovigilance obligations. Such functions include:

- The electronic Reaction Monitoring Report (eRMR), based on the eRMR used within the EU network and the EMA for signal detection activities:
- The individual case line listing and ICSR form.

### **5.3.3. MAH training**

Training should be planned for MAH staff on the new business process and new IT systems in order to be ready once the new EudraVigilance system is implemented. It is advisable to start training around six months in advance of the new system being implemented with refresher training planned at regular intervals in the months leading up to implementation.

An EVDAS user manual for the electronic Reaction Monitoring Reports (eRMR) (including individual case line listing and ICSR form) will be created.

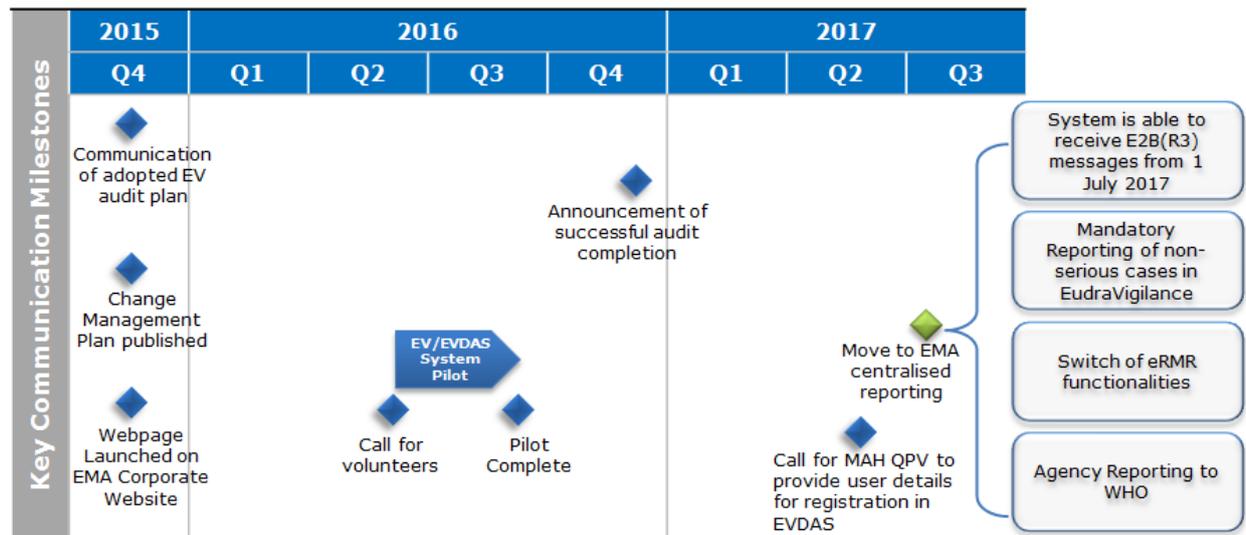
Signal detection guidance for MAH on how to use the eRMR in the context of signal detection/validation will also be created by the EMA Signal Management service.

eLearning courses will also be created for MAH users to train themselves on how to use the eRMR reports.

Key Training Milestones	Training type	Training goal	Timeline	
			2016	2017
	<b>User Manual</b> <ul style="list-style-type: none"> <li>Update of existing EV and EVDAS user manuals</li> <li>Creation of new user manuals: ROR reports, Art.57 reports, Data quality reports, Duplicate Detection user guide</li> </ul>	Detailed guides to support all EVDAS and EV users	<i>Under Development</i>	Available Online
<b>E-Learning</b> <ul style="list-style-type: none"> <li>New functionalities/ reports in EVDAS (including changes to the existing reports)</li> <li>The move from R2 to R3</li> <li>EudraVigilance R3 Format</li> </ul>	Support existing EVDAS and EV users	<i>Under Development</i>	Available Online	
<b>Face to Face</b> <ul style="list-style-type: none"> <li>Standard EVDAS training by the Signal Management Service</li> <li>Regulatory and procedural aspects</li> <li>EudraVigilance Access Policy</li> <li>Electronic reporting principles based on new ISO ICSR standard</li> </ul>	Support new and existing EVDAS and EV users	Standard EVDAS Training Available on Demand <i>EV Training Under Development</i>	Standard EVDAS Training Available on Demand Available On Demand	

### 5.3.4. MAH communications

MAHs should consider developing a communication plan to ensure that the necessary information is circulated within their own organisation and with other organisations that they work with. These communications should be made at appropriate times to ensure that impacted parties are aware of the changes to the reporting requirements and associated business process. They should also inform their IT departments of the need to be prepared for the associated IT changes that will be required to be made.



### 5.3.5. MAH change management summary

The following MAH actions have been grouped by area and whether they are obligatory or recommended actions.

People	Information
<p><b>Must Do</b></p> <ul style="list-style-type: none"> <li>•Assign specific users the permission to access the EVDAS system in addition to EVWEB and the secure area of EudraVigilance</li> <li>•Staff will need to undergo the training for the data submission in the new format (R3). Gateway users to review Agency guidance on new configuration. EVWEB users to undergo training on new application.</li> </ul> <p><b>Should Do</b></p> <ul style="list-style-type: none"> <li>•Undertake training on EVWEB to become familiar with application changes</li> <li>•Consider resource implications and budget to implement the new standard and support the receipt of R3 messages (IT system developers)</li> <li>•The increase in resources may be needed to meet the new signal detection requirement, using the EV data and eRMR</li> <li>•An increase in resources is anticipated to meet the legal requirement to report non-serious cases in EudraVigilance</li> <li>•May require interim increases in staffing requirements to undertake logging, searching and downloading activities. The mechanism for companies to access ADR cases in EudraVigilance is to be manual.</li> </ul>	<p><b>Must do</b></p> <ul style="list-style-type: none"> <li>•Legally obliged to monitor the data available in the system and to inform the Agency and NCAs about validated signals</li> </ul> <p><b>Should Do</b></p> <ul style="list-style-type: none"> <li>•EEA non-serious cases should also be reported to EudraVigilance within 90 days of receipt in order to meet reporting obligations.</li> <li>•Report seriousness at an event level rather than case level, therefore if any event is considered serious, then the whole case should be considered serious.</li> </ul>
Technology	Process
<p><b>Must Do</b></p> <ul style="list-style-type: none"> <li>• Upgrade and move to R3 compliant systems (no deadline yet established)</li> <li>• Gateway Users: Software does not need to be replaced but configuration changes will be necessary to support E2B(R3)</li> <li>• EVWEB Users: Will need to implement the new version of the application. The application will be updated to only support E2B(R3)</li> <li>• The new E2B R3 format messages will need to be accepted as of Q2 2017</li> </ul>	<p><b>Must Do</b></p> <ul style="list-style-type: none"> <li>•The centralised reporting will no longer require NCAs and EMA to reroute the information, therefore the companies will retrieve data from EV directly.</li> <li>•A new process is to be established to retrieve data from EV</li> <li>•A new process for signals validated by MAHs will need to be designed, discussed and consulted during the 1st revision of the GVP Module IX on signal management.</li> <li>•The new functionalities in EVDAS will require changes to the current processes for performance of data analysis activities within the MAHs</li> <li>•Change business processes for a single data submission in EudraVigilance</li> </ul> <p><b>Should Do</b></p> <ul style="list-style-type: none"> <li>•ICSR submissions in the EEA should only be made to the EudraVigilance in order to meet reporting compliance</li> <li>•Ensure that transition to centralised reporting is coordinated with the new systems implementation</li> </ul>

## **5.4. Sponsors of clinical trials change management planning**

This section of the change management plan focuses on the IT and business process changes that should be considered by sponsors of clinical trials in the period of time leading up to and after implementation of the new EudraVigilance system.

### **5.4.1. Sponsor of clinical trials IT changes**

#### **5.4.1.1. Implementing ISO ICSR (E2B(R3)) support in clinical trial systems**

Once the new EudraVigilance system is implemented, sponsors of clinical trials will have the choice to start using the ISO ICSR (E2B(R3)) format for the submission of ICSRs, assuming that all testing has been completed beforehand.

It should be noted that sponsors can continue to use E2B(R2) for the submission of SUSARs after the new EudraVigilance system is implemented. However, sponsors of clinical trials should plan to develop their systems in order to support the new format.

#### **5.4.1.2. Electronic gateway**

Sponsors of clinical trials using an electronic gateway solution will not need to replace their current software solution. However, configuration changes may be required in order to support the processing of E2B(R3) messages including the acknowledgments returned (EudraVigilance will only return E2B(R3) acknowledgments). Guidance and support for making these configuration changes will be provided by EMA gateway support.

When centralised reporting becomes effective, the gateway will not prevent sponsors of clinical trials exchanging SUSARs with MAHs or other sponsors of clinical trials; however, this type of exchange will not be supported by the EMA. It should be noted that organisations performing such transmissions will not be able to contact the gateway helpdesk for support if issues occur with these transmissions.

At the time of implementation sponsors of clinical trials should be aware that for trials approved through the clinical trials regulation, only electronic submissions of SUSARs to the EudraVigilance system will be considered as fulfilling their legal obligations, unless the sponsor has a prior agreement with the concerned NCAs to submit those SUSARs through national systems. Sponsors should ensure that modifications to their submission systems are configured and tested well in advance of the planned implementation.

#### **5.4.1.3. EVWEB**

Sponsors of clinical trials using EVWEB will need to prepare for the implementation of the new version of the application. The application will be changed to only support E2B(R3) ICSR data entry. The E2B(R3) standard will introduce additional fields and different ways of structuring the data; therefore the user interface will be changed and have a different appearance.

These changes will require the users within the sponsor's organisation to undertake training in order to become familiar with the new system. Training materials and online training will be made available in advance of the new system being implemented; please see section 3.6. for details.

It is recommended that sponsors plan to start training their staff six months in advance of the new system being implemented, followed by regular refresher training at least three months and two weeks before implementation.

## **5.4.2. Sponsor of clinical trials business process changes**

### **5.4.2.1. Reporting of SUSARs to EudraVigilance**

Until the clinical trials regulation is applicable there is no change to the current process for the submission of SUSARs for clinical trials approved through the clinical trials directive 2001/20/EC.

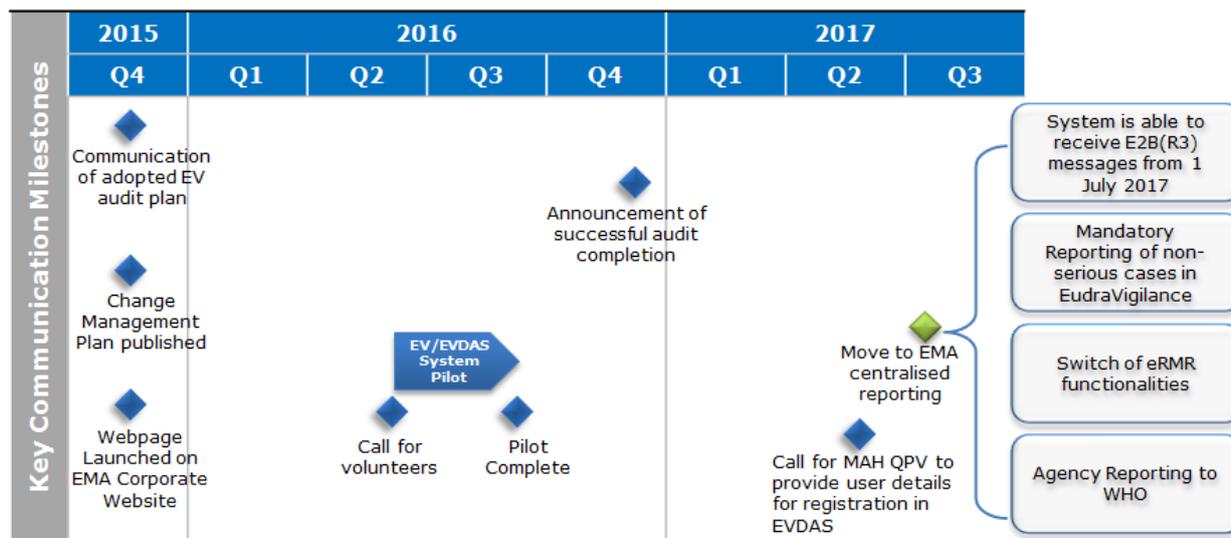
Clinical trials approved through the clinical trials directive 2001/20/EC will continue to have the same SUSAR reporting requirements as specified in the directive for a transition period of 3 years after the clinical trials regulation is applicable.

Sponsors that have a clinical trial approved through the clinical trials regulation are normally required to send SUSARs to EudraVigilance only. The EudraVigilance system will then automatically reroute the SUSARs to the concerned NCAs. However, the option remains for small organisations to report SUSARs directly to the NCA that has approved the trial through establishing an agreement between the sponsor and the NCA concerned. The NCA will then forward any SUSARs reported to them under such agreements to the EudraVigilance system. It is expected that this will be for the submission of SUSARs by small organisations that are not able to create electronic submissions and do not have the resources to use EVWEB. The majority of SUSAR submissions are expected to occur through the centralised reporting to EudraVigilance and a set of business rules will be put in place for the automated forwarding of these SUSARs to the NCA requesting them.

In accordance with the requirement of Article 40(2) of the new clinical trials regulation (Regulation (EU) No 536/2014) the Agency, in collaboration with the Member States, will develop a standard web-based structured form for the reporting of SUSARs to EudraVigilance by sponsors. This new form will aim to help primarily non-commercial sponsors and small organisations involved in the conduct of clinical trials, which do not have the resources to report SUSARs through EVWeb. The form will be based on the E2B(R3) fields, but will be designed in a user friendly way, which would not require extensive face to face training in order to be used.

## **5.4.3. Sponsor of clinical trials communications**

Sponsors should consider developing a communication plan to ensure that the necessary information is circulated within their own organisation and with other organisations that they work with. These communications should be made at appropriate times to ensure that impacted parties are aware of the changes to the reporting requirements and associated business process. They should also inform their IT departments of the need to be prepared for the associated IT changes that will be required to be made.



#### 5.4.4. Sponsor of clinical trials training

Training should be planned for the staff of sponsors in order to explain the new business process and changes to IT systems in order to be ready once the new EudraVigilance system is implemented. It is advisable to start training around 6-months in advance of the new EudraVigilance system being implemented along with refresher training planned at regular interval in the months leading up to implementation.

Key Training Milestones	Training type	Training goal	Timeline	
			2016	2017
	<b>User Manual</b> <ul style="list-style-type: none"> <li>Update of existing EV and EVDAS user manuals</li> <li>Creation of new user manuals: ROR reports, Art.57 reports, Data quality reports, Duplicate Detection user guide</li> </ul>	Detailed guides to support all EVDAS and EV users	Under Development	Available Online
	<b>E-Learning</b> <ul style="list-style-type: none"> <li>New functionalities/ reports in EVDAS (including changes to the existing reports)</li> <li>The move from R2 to R3</li> <li>EudraVigilance R3 Format</li> </ul>	Support existing EVDAS and EV users	Under Development	Available Online
	<b>Face to Face</b> <ul style="list-style-type: none"> <li>Standard EVDAS training by the Signal Management Service</li> <li>Regulatory and procedural aspects</li> <li>EudraVigilance Access Policy</li> <li>Electronic reporting principles based on new ISO ICSR standard</li> </ul>	Support new and existing EVDAS and EV users	<ul style="list-style-type: none"> <li>Standard EVDAS Training Available on Demand</li> <li>EV Training Under Development</li> </ul>	<ul style="list-style-type: none"> <li>Standard EVDAS Training Available on Demand</li> <li>Available On Demand</li> </ul>

#### 5.4.5. Sponsor of clinical trials change management summary

The following Sponsor actions have been grouped by area and whether they are obligatory or recommended actions.

<p style="text-align: center;"><b>People</b></p> <p><b>Should Do</b></p> <ul style="list-style-type: none"> <li>• Users of EVWEB within the sponsor's organisation should undertake training in order to become familiar with the new system</li> <li>• Sponsors should plan to start training their staff six months in advance of the new system being implemented, followed by regular refresher training at least three months and two weeks before implementation.</li> </ul>	<p style="text-align: center;"><b>Information</b></p> <p><b>Should Do</b></p> <ul style="list-style-type: none"> <li>• Should be aware that only electronic submissions of SUSAR to the EudraVigilance system will be considered as fulfilling their legal obligations</li> <li>• Sponsors should consider developing a communication plan to ensure that the necessary information is circulated and inform their IT departments of the need to be prepared for the associated IT changes</li> </ul>
<p style="text-align: center;"><b>Technology</b></p> <p><b>Should Do</b></p> <ul style="list-style-type: none"> <li>• Can continue to use E2B(R2) for the submission of SUSARs after the new EudraVigilance system is implemented. However, Sponsors of Clinical Trials should plan to develop their systems in order to support the new format.</li> <li>• If using an electronic gateway solution configuration changes may be required in order to support the processing of E2B(R3) messages</li> <li>• Should ensure that modifications to their submission systems are configured and tested well in advance of the planned implementation.</li> </ul>	<p style="text-align: center;"><b>Process</b></p> <p><b>Should Do</b></p> <ul style="list-style-type: none"> <li>• The majority of SUSAR submissions should occur through the centralised reporting to EudraVigilance and a set of business rules will be put in place for the automated forwarding of these SUSARs to the NCA requesting them.</li> <li>• Small organisations that are not able to create electronic submissions and do not have the resources to use EVWEB can still report SUSARs directly to NCAs. A new standard web-based structured form will be developed by the Agency to help non-commercial sponsors and small organisations to support SUSARs.</li> </ul>

## 5.5. WHO-UMC change management planning

This section of the change management plan focuses on the IT and business process changes that should be considered by the WHO-UMC in the period of time leading up to and after implementation of the new EudraVigilance system.

### 5.5.1. Implementing ISO ICSR (E2B(R3))

Once the new EudraVigilance system is implemented, the WHO will start to receive ISO ICSR E2B(R3)) format messages from the EMA for ICSRs originating in the EEA. Therefore, the WHO-UMC will need to ensure that support for the new format is implemented and that testing is conducted before hand.

### 5.5.2. Business process change

The reporting of ICSRs occurring in the EEA to the WHO-UMC will be performed by the EMA instead of directly by NCAs. These ICSRs will be forwarded automatically using predefined rules.

The main change for WHO-UMC will be that they will no longer need to receive ICSRs from EEA NCAs. The NCAs will provide a last submission of data around the time of the switch to centralised reporting. The WHO-UMC will receive EEA data for the period up until the switch to centralised reporting from EEA NCAs and then EudraVigilance will submit EEA data to the WHO-UMC prospectively from the time of the switch.