



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

New EudraVigilance functionalities and the 2010 pharmacovigilance legislation – preparing for change

Training Module PhV-M1

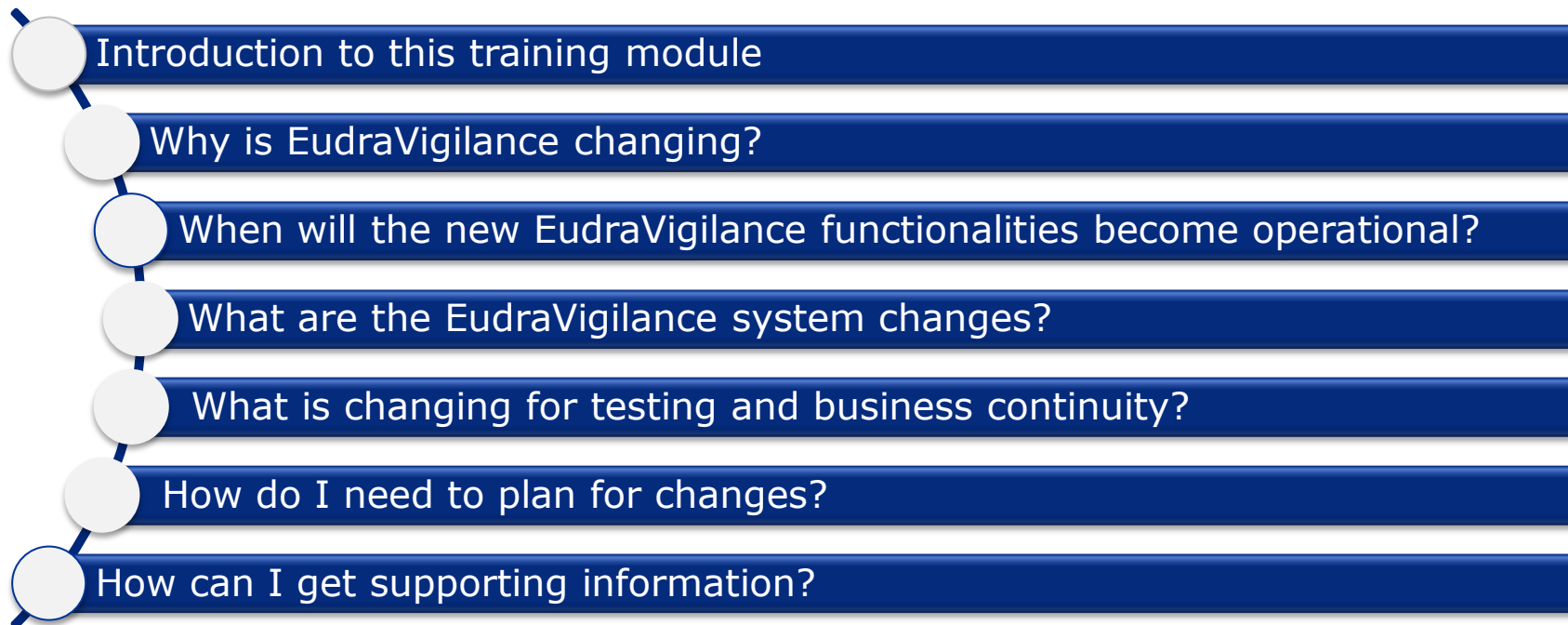
Overview of legal provisions that form the basis for the new EudraVigilance functionalities and steps to be taken to prepare for business change

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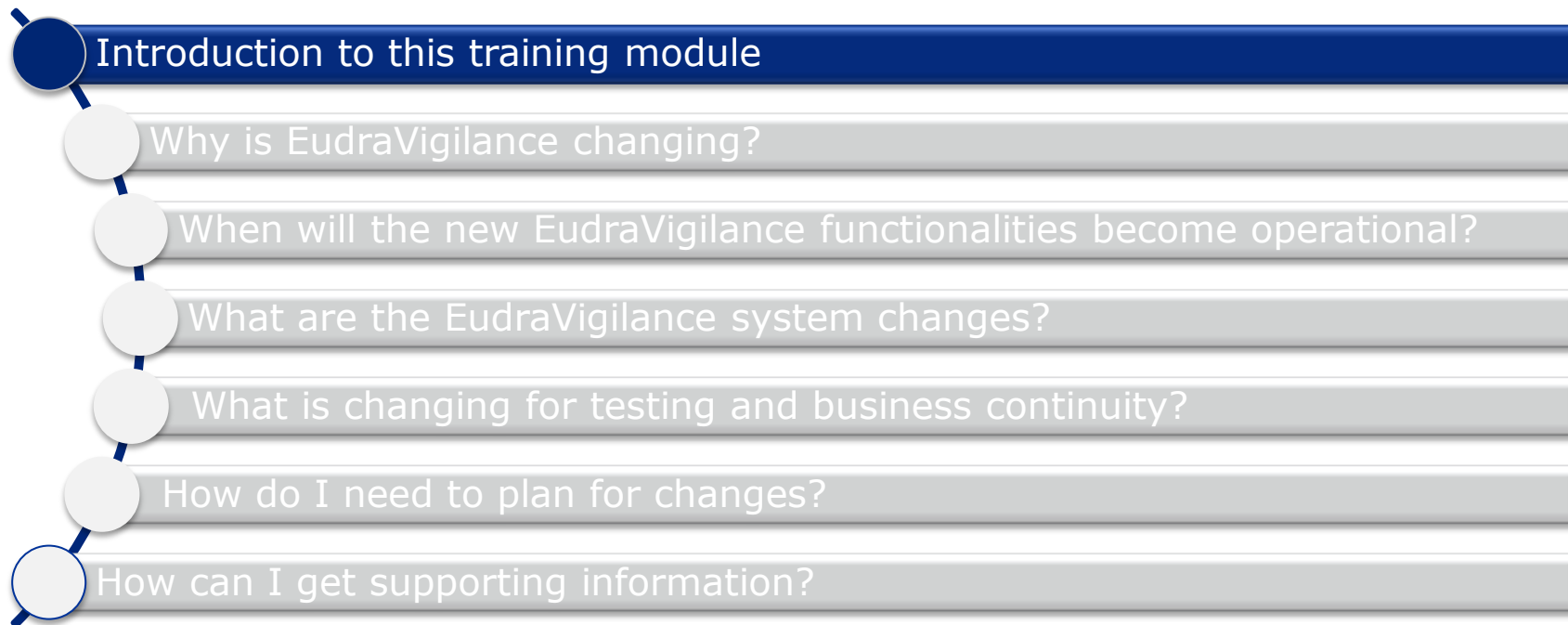
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Overview Module PhV-M1

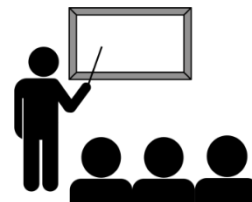


Overview Module PhV-M1



Introduction: Context PhV-M1

- Target audience for this training module:
 - National Competent Authorities (NCAs) in the European Economic Area (EEA)
 - Marketing authorisation holders (MAHs)
 - Commercial and non-commercial sponsors of clinical trials (Sponsors)



Introduction: Context PhV-M1

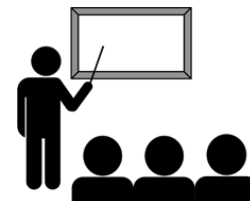


NOTE

–Whilst not impacted by the 2010 pharmacovigilance legislation, Sponsors will be indirectly impacted by the new EudraVigilance functionalities i.e. users of EVWEB

–The impact of the 2014 Clinical Trial Regulation on Sponsors and potential changes to reporting of suspected unexpected serious adverse reactions (SUSARs) will be addressed in a dedicated training module at a later time

–SUSAR reporting requirements for clinical trials authorised under Directive 2001/20/EC currently remain unchanged

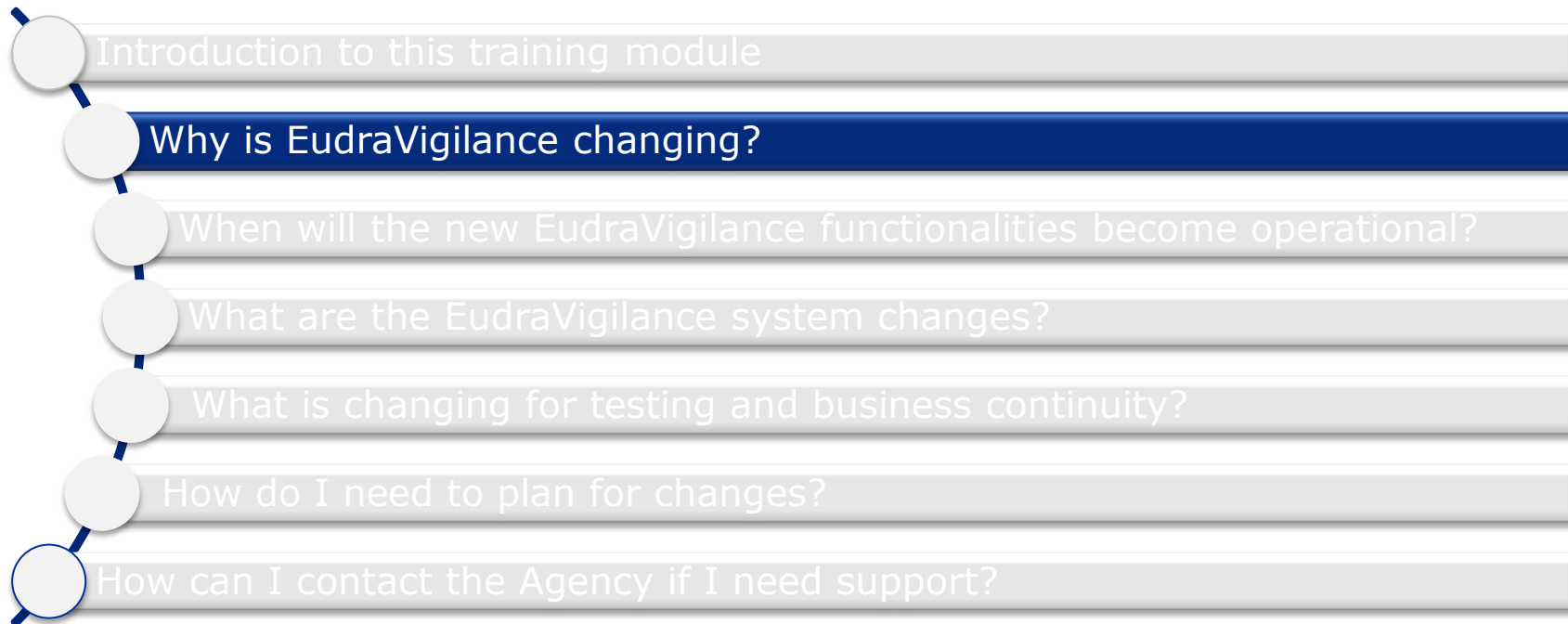


Introduction: Learning Objectives

- At the end of module PhV-M1 you should be able to:
 - Understand the legal requirements for changes of EudraVigilance
 - Describe the EudraVigilance System Implementation Plan
 - Apprehend the EudraVigilance System Changes
 - Prepare for Change Management Planning
 - from the perspective of a NCA, a MAH, a Sponsor of clinical trials
 - Understand where to obtain supporting information



Overview Module PhV-M1





Session overview: Why is EudraVigilance changing?

In this session you will obtain an understanding of:

- The requirements set out in the 2010 pharmacovigilance legislation that form the basis of changes to EudraVigilance

Pharmacovigilance legislation (1)

The legal provisions that form the basis for the enhancements of EudraVigilance are set out in Regulation (EC) 726/2004 and Directive 2001/83/EC, which were amended in 2010

- *Regulation (EC) No 726/2004* of the European Parliament and of the Council of 31 March 2004 laying down Community procedures for the authorisation and supervision of medicinal products for human and veterinary use and establishing a European Medicines Agency (Consolidated version: 05/06/2013)
- *Directive 2001/83/EC* of the European Parliament and of the Council of 6 November 2001 on the Community code relating to medicinal products for human use (Consolidated version: 16/11/2012)

Reference: EudraLex Volume 1 - Pharmaceutical Legislation Medicinal Products for Human Use

Pharmacovigilance legislation(2)

Additionally, in 2012 the Commission adopted the:

- *Commission Implementing Regulation (EU) No 520/2012* of 19 June 2012 on the performance of pharmacovigilance activities provided for in Regulation (EC) No 726/2004 of the European Parliament and of the Council and Directive 2001/83/EC of the European Parliament and of the Council

Reference: EudraLex Volume 1 - Pharmaceutical Legislation Medicinal Products for Human Use

Pharmacovigilance legislation (3)

Summary of legal provisions forming the basis for updates to EudraVigilance:

- *Simplified adverse reaction reporting* in the EU (DIR 2001/83/EC Art 107/107a)
(see training module PhV-M3 and PhV-G2)
- *Reporting to WHO UMC* of suspected adverse reactions occurring in the EU by the Agency (REG (EC) 726/2004, Art 28c)
(see training module PhV-M3 and PhV-G2)
- *Monitoring of selected literature* for a selected number of substances by EMA and the entering of reports of suspected adverse reactions in EudraVigilance (REG (EC) 726/2004, Art 27)
(see training module PhV-M6 and PhV-G2)

Pharmacovigilance legislation (4)

Summary of legal provisions forming the basis for updates to EudraVigilance (continued):

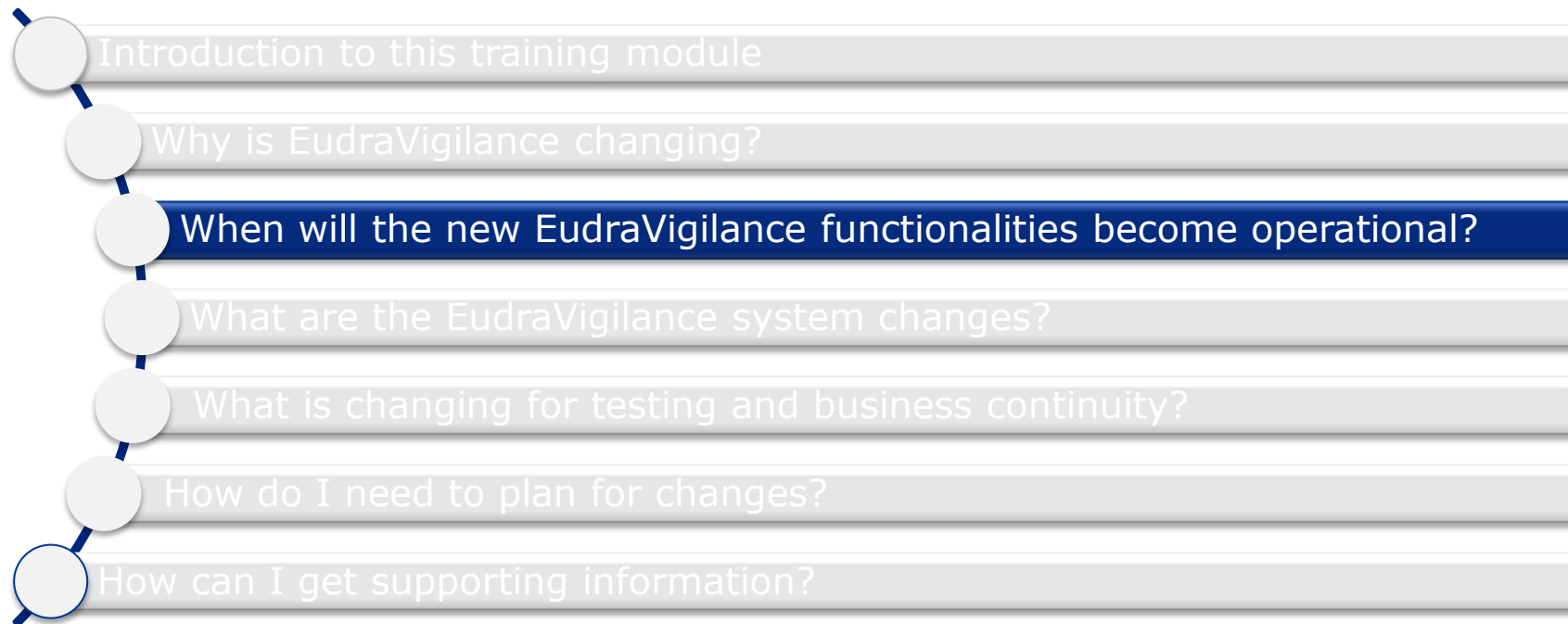
- *Use of internationally agreed formats, standards and terminology*
(IR (EU) 520/2012, chapter IV)
(see training modules PhV-M2a and PhV-G2)
- *Provision of access to EudraVigilance* – EEA medicines regulatory authorities, the Commission, EMA, healthcare professionals, public, research institutions and marketing authorisation holders (REG (EC) 727/2004, Art 24)
(see training module PhV-M4)
- *Signal detection and validation* based on EudraVigilance data
(IR (EU) 520/2012, chapter III)
(see training modules PhV-G1, PhV-M5a-d)

Session summary: Why is EudraVigilance changing?

In this session we discussed:

- The legal requirements set out in the 2010 pharmacovigilance legislation related to EudraVigilance: to meet these requirements, EudraVigilance functionalities need to be adapted or enhanced acknowledging that many legal requirements have already been addressed and the applicable business processes put in operation

Overview Module PhV-M1





Session overview: When will the new EudraVigilance functionalities become operational?

In this session you will learn to describe:

- The EudraVigilance Implementation Plan including the milestones and the timelines when EudraVigilance with its new functionalities will become operational

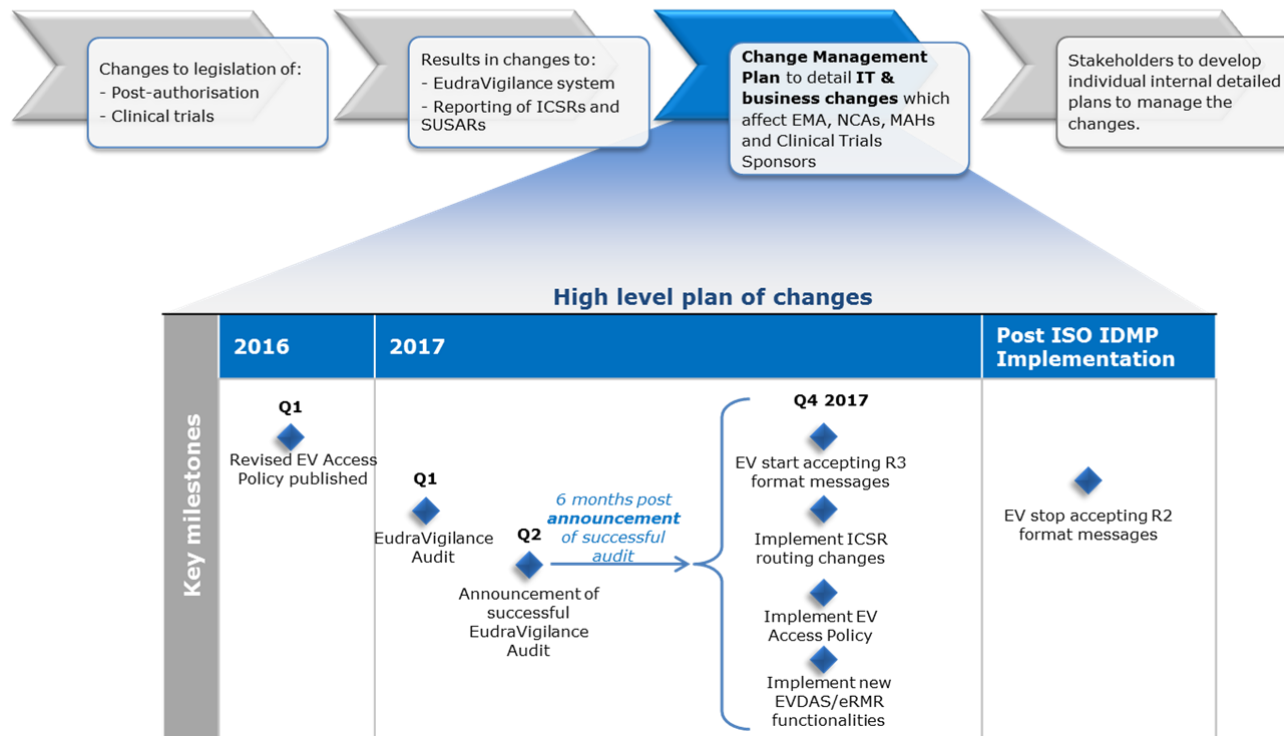
EudraVigilance Implementation Planning (1)

- **New and enhanced EudraVigilance functionalities** were agreed by PRAC and endorsed by the EMA Management Board in December 2013
- The '**EudraVigilance Auditable Requirements Project**' has been set-up to complete the implementation of the new Pharmacovigilance legislation, to **deliver the new EV system** and **prepare EV for its audit**.
- Revision 2 of the EudraVigilance Access Policy was adopted by the EMA Management Board in December 2015
- **Stakeholder testing** with a selected number of participants of the EV-EWG (MAHs) and PMG1 (NCAs) is **scheduled for Q4 2016**
- The EV functionalities are subject to an **independent audit**, which is scheduled for Q1 2017

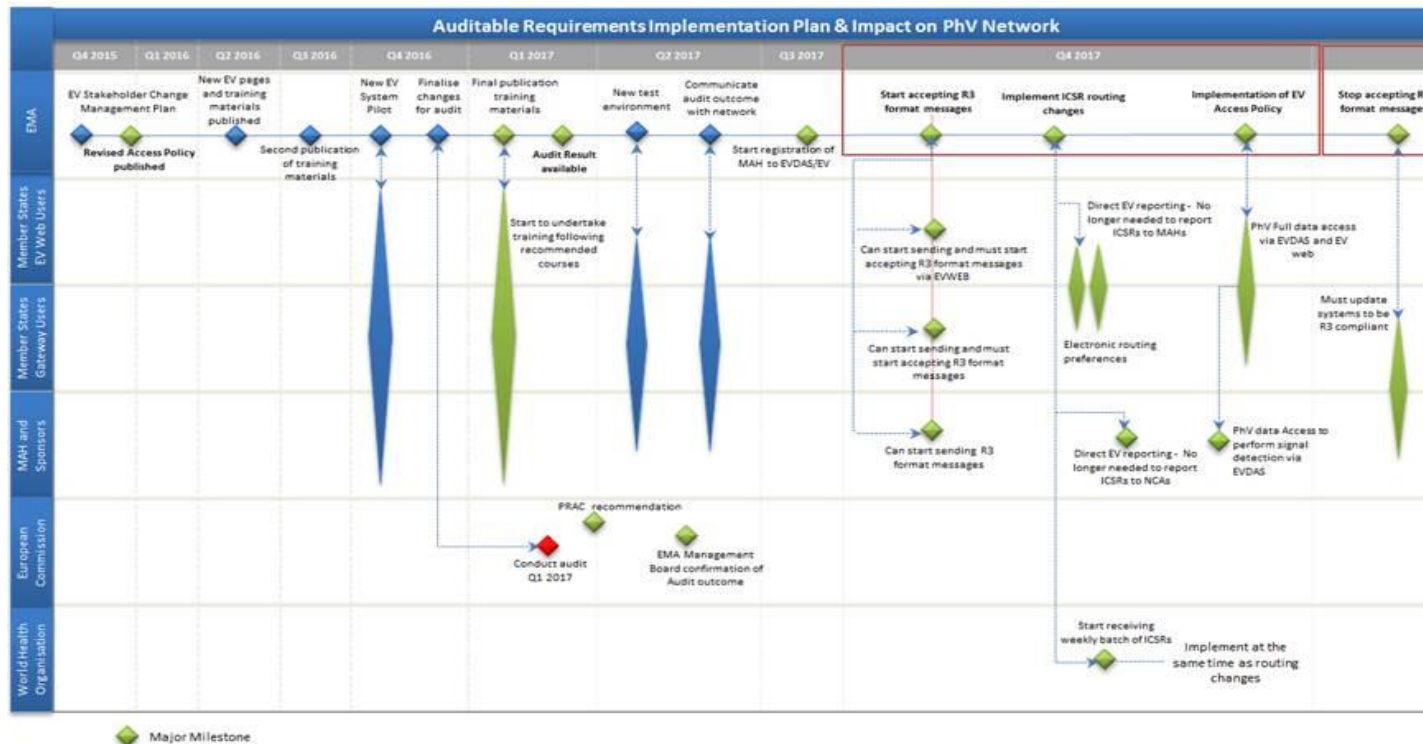
EudraVigilance Implementation Planning (2)

- The **audit report along with a PRAC recommendation** will be presented to the EMA Management Board, which will announce if the EV functionalities have been implemented; this is scheduled for **Q2 2017**
- Six months following the announcement by the Board, the move to the simplified reporting and the release of the new EudraVigilance functionalities will take effect; **this is expected to be Q4 2017**

EudraVigilance System Implementation Planning (3)



EudraVigilance System Implementation Planning (4)

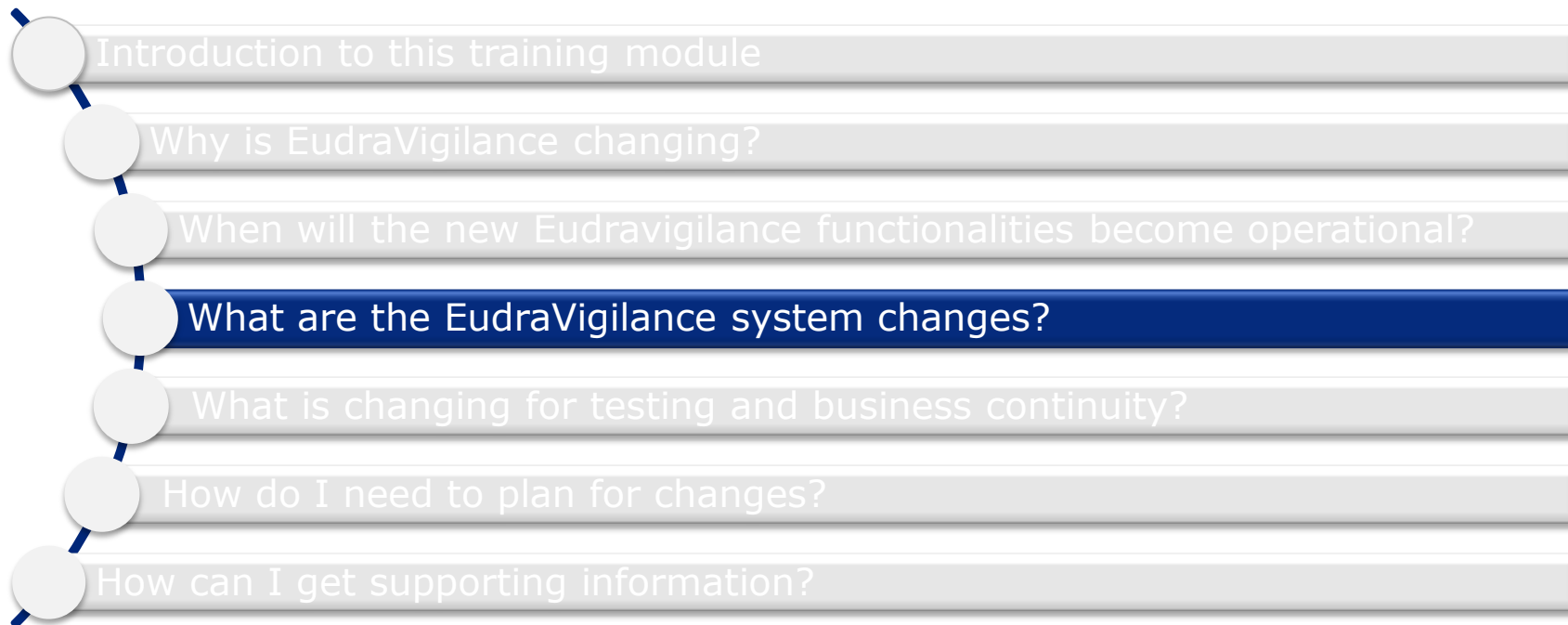


Session summary: When will the new EudraVigilance functionalities become operational?

In this session we discussed:

- The milestones and the timelines by when the new EudraVigilance functionalities will go live taking into account that this will trigger the start of the simplified reporting to EudraVigilance (please see training module PhV-M3): this should allow you to prepare for the change management planning within your own organisation

Overview Module PhV-M1

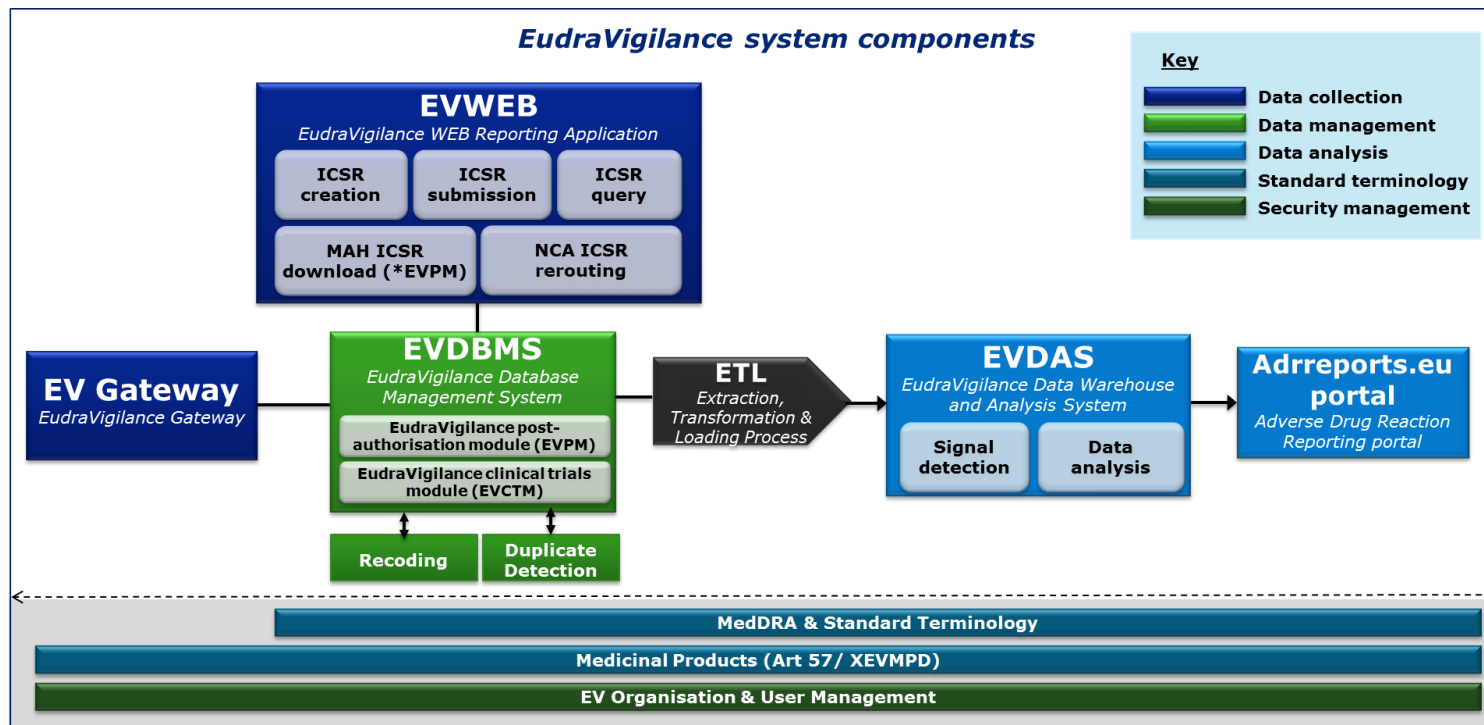


Session overview: What are the EudraVigilance system changes?

In this session you will learn to apprehend:

- The main components of the EudraVigilance Systems
- The new and enhanced functionalities of the EudraVigilance system
- Which areas remain unchanged
- The impact of the changes to EudraVigilance on the way you create and send Individual Case Safety Reports (ICSRs) and the way you perform signal detection and validate signals

EudraVigilance System Description (1)



EudraVigilance System Description (2)

EudraVigilance is comprised of the following system components:

- **EudraVigilance Gateway** in support of the secure electronic transmission of safety and acknowledgment (ACK) messages
- **EudraVigilance WEB application (EVWEB)**, which is the interface to the EDBMS allowing to create, send and view ICSRs, safety and ACK messages and to perform queries
- **EudraVigilance Database Management System (EDBMS)** in support of the processing and administration of safety and ACK messages and ICSRs; this includes the EudraVigilance Post-authorisation module (EVPM) and the EudraVigilance clinical trial module (EVCTM)

EudraVigilance System Description (3)

EudraVigilance system components continued:

- The **EudraVigilance Database Management System (EDBMS)** includes:
 - *EudraVigilance Post-Authorisation Module (EVPM)* dedicated to the collection of ICSRs related to all medicinal products authorised in the EEA in line with Regulation (EC) No 726/2004 and Directive 2001/83/EC. The following ICSR types are collected in EVPM: "Spontaneous Report", "Report from Study" with study type "Individual patient use" and "Other studies", "Other" and "Not available to sender (unknown)"
 - *EudraVigilance Clinical Trial Module (EVCTM)* dedicated to the collection of ICSRs of Suspected Unexpected Serious Adverse Reactions (SUSARs) in accordance with Directive 2001/20/EC and Regulation (EU) No 536/2014. The following ICSR types are collected in EVCTM: "Report from Study" with study type "Clinical Trials"

EudraVigilance System Description (4)

The following EV functionalities are available:

- **ICSR creation, submission and query** – allowing to create ADR reports, electronically submit them and perform queries on reports
- **Rerouting Functionality** allowing to send ICSRs reported to EV by MAHs to NCAs of Member States where the reaction occurred
- **ICSR Download Functionality** allowing MAHs to access ICSRs that were reported by NCAs of Member States to EudraVigilance; this applies to active substances of medicinal products, for which they hold marketing authorisations in the EEA
- **Duplicate Detection and Management Functionality** allowing EMA to detect and manage duplicates in EudraVigilance
- **Medicinal Product Recoding Functionality** in support of the coding of medicinal product information in ICSRs against the XEVMPD (Article 57 product submissions)

EudraVigilance System Description (5)

EudraVigilance system components continued:

- [EudraVigilance Data Analysis System \(EVDAS\)](#) dedicated to support the EU pharmacovigilance safety monitoring activities with the main focus on signal detection and evaluation of ICSRs
- [Adrreports.eu portal](#), a publicly accessible portal that allows to search and view EudraVigilance data on suspected adverse reactions for authorised medicinal products in the EEA and that provides general information to aid the understanding of the reports

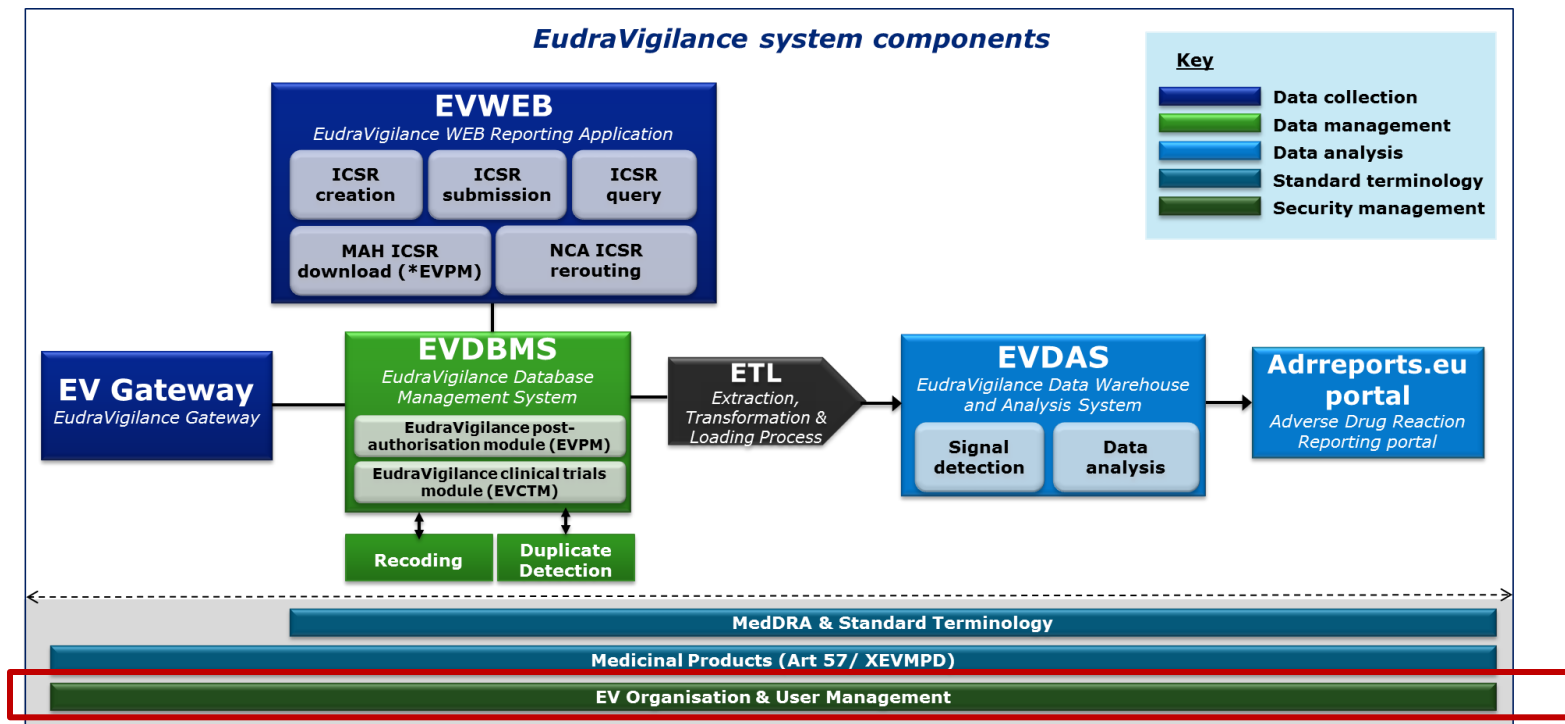
EudraVigilance System – Reference sources and services (1)

- Organisation and User management
- The **Medical Dictionary for Regulatory Activities (MedDRA)** as developed by the International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) (multidisciplinary topic M1) is used for the coding of medical information
- The **eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD)**, is used as a reference source for the coding of substances and medicinal products reported in ICSRs based on the information provided by MAHs in line with Article 57(2), second subparagraph of Regulation (EC) Regulation (EC) No 726/2004

EudraVigilance System – Reference sources and services (2)

- The lists of Standard Terms published by the European Pharmacopoeia Commission are applied for the coding of pharmaceutical forms of medicines and routes of administrations
- The Medical Literature Monitoring service, performed by EMA to monitor selected medical literature to identify suspected adverse reactions with medicines authorised in the European Union, and to entering the relevant information into the EudraVigilance database
- European Pharmacovigilance Issues Tracking Tool (EPITT), which is not a specific part of the EudraVigilance system, however it provides the functionalities for medicines regulatory authorities in the EEA and EMA to track signals at EU level

EudraVigilance System Changes



EV Organisation and User Management (1)

- EudraVigilance and the electronic transmission of ICSRs requires organisations and users to be registered
- This is to
 - Ensure that adequate privacy and security measures are in place
 - Warrant that principles of data integrity, accountability and availability are adhered to
 - Provide access to EudraVigilance to authorised users in line with the EudraVigilance Access Policy

EV Organisation and User Management (2)

- The registration process will not change
- Registrations for existing organisations and users will remain unchanged for accessing EVWEB and the secure area of EudraVigilance
- Existing registered users will be migrated to the new EudraVigilance system with the same configuration settings
- All registered users at the time of the go live will be automatically granted access to the new EV system functionalities and therefore there will be no action required by existing users
- New organisations or users will need to follow the existing registration process

EV Organisation and User Management (3)



NOTE 1: Check if you require additional registrations for the new XCOMP test system (EVTEST) so your users can access the new test system when it goes live after completion of the audit



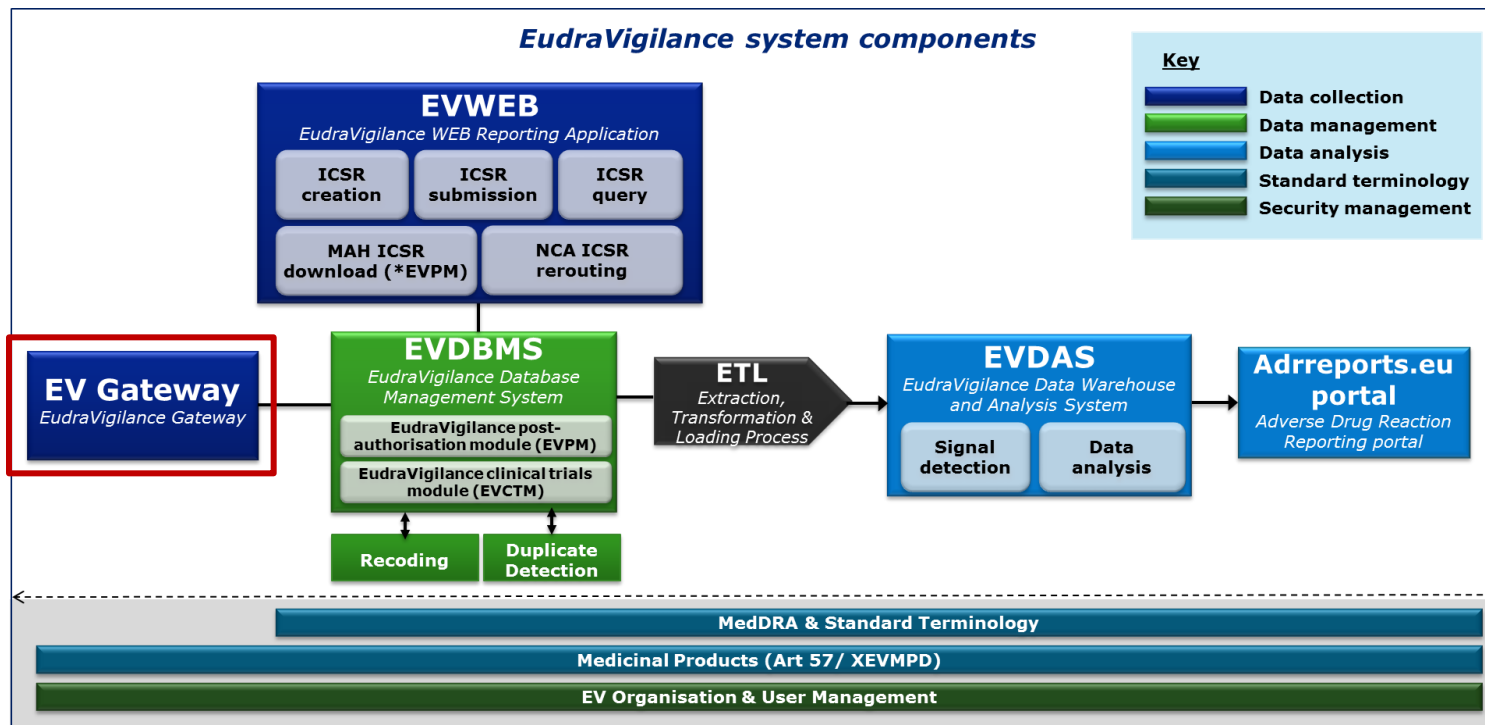
NOTE 2: For XEVMPD (Art57) the registration process will remain as is for new users responsible for the submission of medicinal product information in accordance with Article 57(2) of REG (EC) 726/2004

EV Organisation and User Management (4)

Specific to MAHs

- MAHs will be granted with access to EVDAS in accordance with the EudraVigilance Access Policy
- The EU QPPV or the appointed Deputy will need to designate authorised users who will obtain permission to access EVDAS
- The Agency will contact the EU QPPV/Appointed Deputy for all registered MAHs in Q2 2017 to inform when the registration of their authorised EVDAS users can be initiated

EudraVigilance System Changes



EV Gateway (1)

- There are no changes expected for the data-processing network and the secure electronic exchange of safety and ACK messages
- The Gateway configuration will be able to accept ICH E2B(R3) files
- When the simplified reporting becomes effective, the transmission of ICSRs by MAHs to NCAs will no longer be supported



NOTE 1: Gateway users will not be prevented from sending ICSRs to other registered organisations but there will be no technical support from the Agency for these types of transactions



NOTE 2: The EVPOST function, which allowed organisations without a local gateway solution to send safety and ACK messages in a secure manner, will become an integral part of EVWEB

EV Gateway (2)

- At the time of implementation, organisations should be aware that only submissions of ICSRs to EudraVigilance will be considered as fulfilling the legal electronic reporting obligations (see training module PhV-M3)
- Organisations need to ensure that the transition to simplified reporting is adequately coordinated with all stakeholders they usually interact with; this includes the configuration of their pharmacovigilance systems and local gateway solutions, if necessary

EV Gateway (3)

NCAs

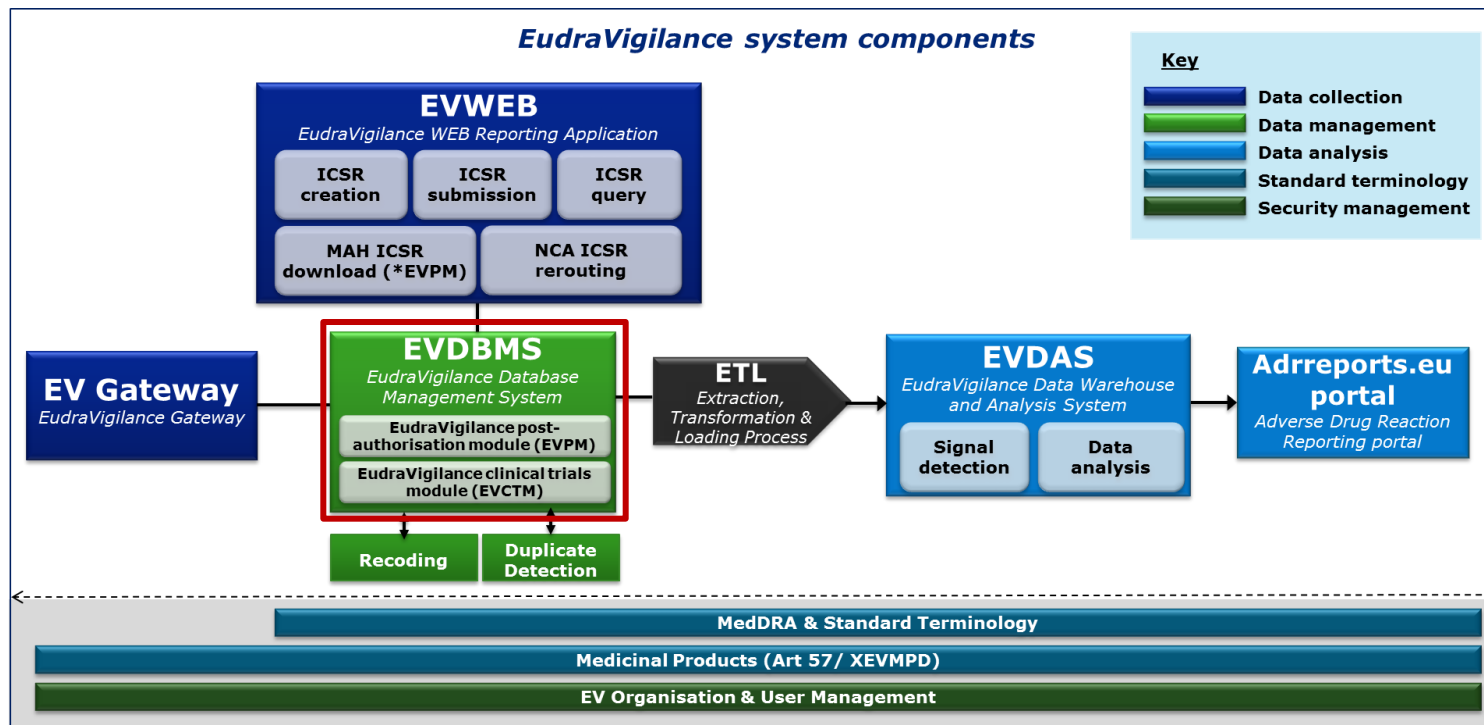
- NCAs using a local gateway connector provided by the Agency will not need to replace this software
- No configuration changes are needed and existing communities maintained
- Safety messages will be larger (e.g. due to the attachments) and a review of the space required in their installations may be necessary

MAHs

- MAHs using a gateway solution will not need to replace this software
- The need for configuration changes should be assessed to support processing of E2B(R3) safety & ACK messages incl. the review of space requirements (larger safety messages) depending on the Gateway solution used
- Guidance and support will be provided by the Agency, if required



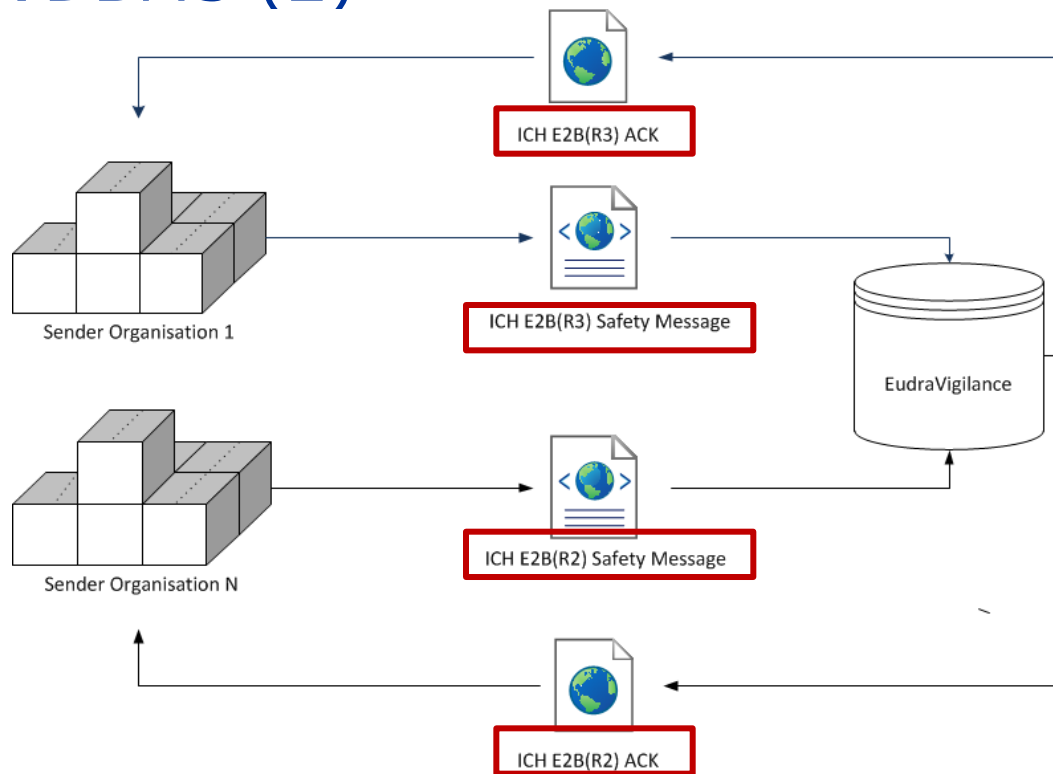
EudraVigilance System Changes



EVDBMS (1)

- EVDBMS will undergo the most significant changes
- EVDBMS will be updated to support the ICH E2B(R3) format and new data elements
- All existing ICSRs in ICH E2B(R2) format will be migrated
- The XML parser will be updated to be able to:
 - Process ICH E2B(R2) safety and ACK messages
 - Process ICH E2B(R3) safety and ACK messages in line with the ISO ICSR standard
 - Support the business rules as outlined in the EU ICSR Implementation Guide based on the ISO/ICH E2B(R3) standard

EVDBMS (2)



- If an ICH E2B(R3) message is sent to EV, an E2B(R3) ACK will be returned to the sender
- If an ICH E2B(R2) message is sent to EV, an E2B(R2) ACK will be returned to the sender

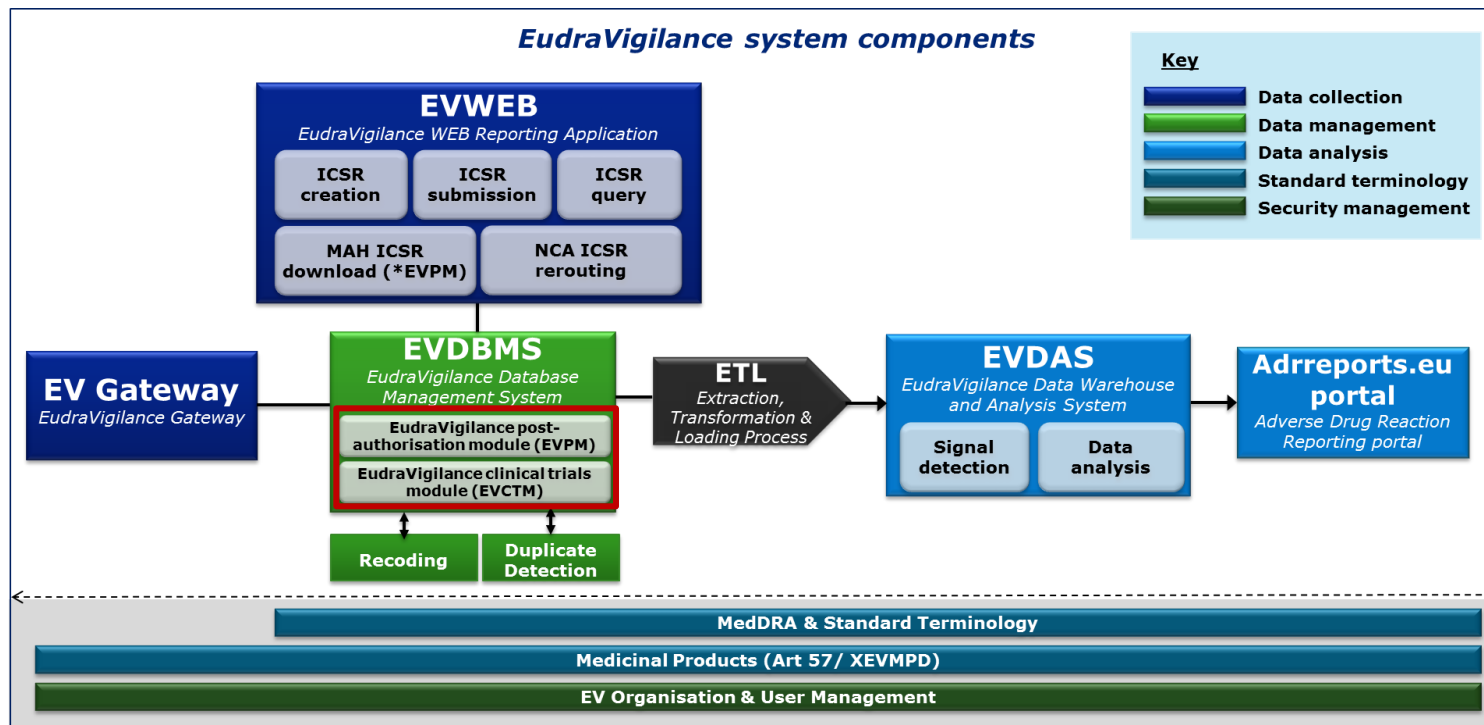


EVDBMS (3)



NOTE: If an initial ICSR was submitted in ICH E2B(R3) format it is not possible for the same sender to submit a follow-up ICSR in ICH E2B(R2) format

EudraVigilance System Changes



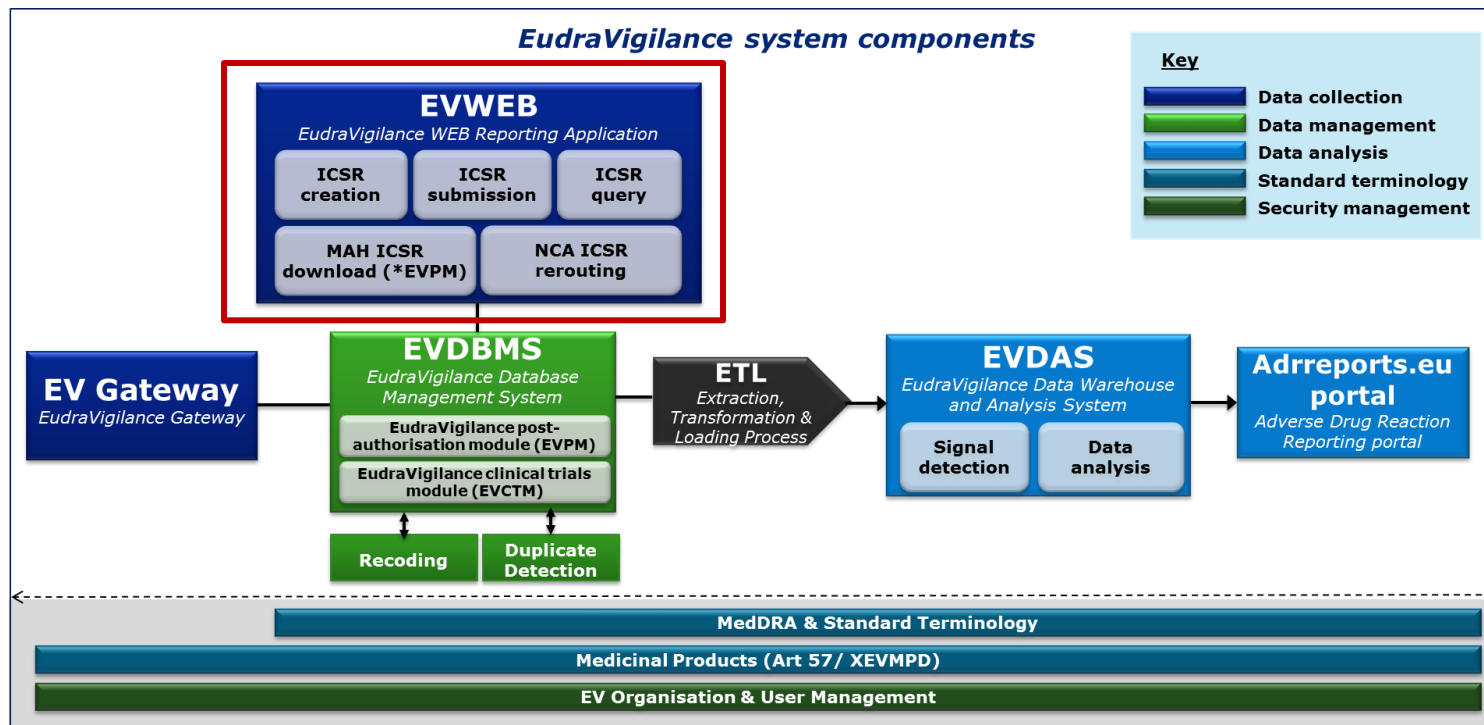
EVPM and EVCTM

- EVPM and EVCTM will accept ICSRs in ICH E2B(R2) or ICH E2B(R3) format
 - For ICSRs submitted in ICH E2B(R2) format to EudraVigilance, the business rules are applied as set out in the Note for guidance – EudraVigilance Human – Processing of safety messages and individual case safety reports (ICSRs) (EMA/H/20665/04/Final Rev. 2)
 - For ICSRs submitted in ICH E2B(R3) format to EudraVigilance, the business rules are applied as set out in the EU Individual Case Safety Report (ICSR) Implementation Guide (EMA/51938/2013)



Make sure that your pharmacovigilance system complies with the applicable business rules

EudraVigilance System Changes



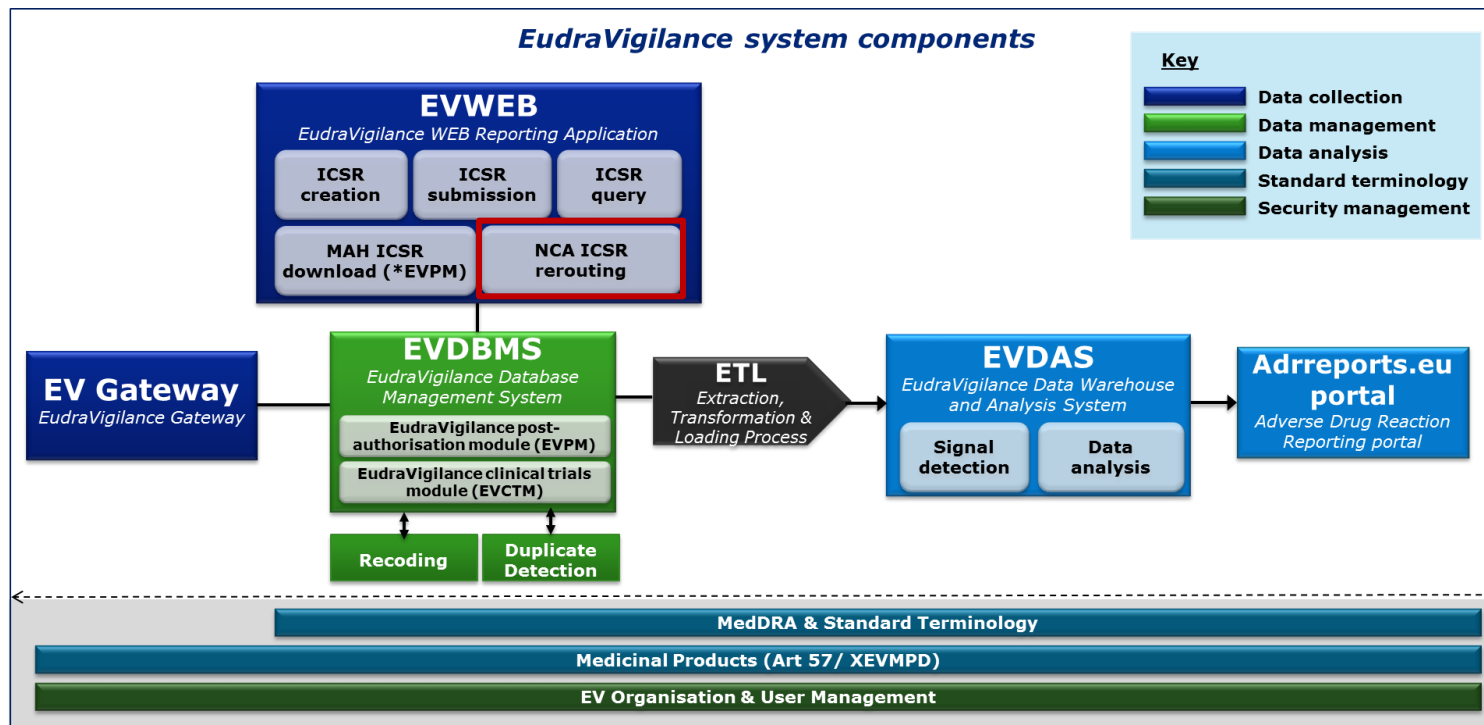
EVWEB

- The EVWEB application will be rewritten in a different technology, which will support additional browsers (Firefox, Chrome, Internet Explorer version 10 or above)
- EVWEB will support the sending of ICSRs in ICH E2B(R3) format only
(EVWEB will allow E2B(R2) files to be loaded/reviewed in the application and these can be converted into E2B(R3) files if needed)
- The EVWEB user interface will change
- EVWEB will incorporate the former EVPOST function



Existing EVWEB users should follow the applicable training modules to get familiar with the new functions and the new ICH E2B(R3) format

EudraVigilance System Changes



Rerouting for NCAs (1)



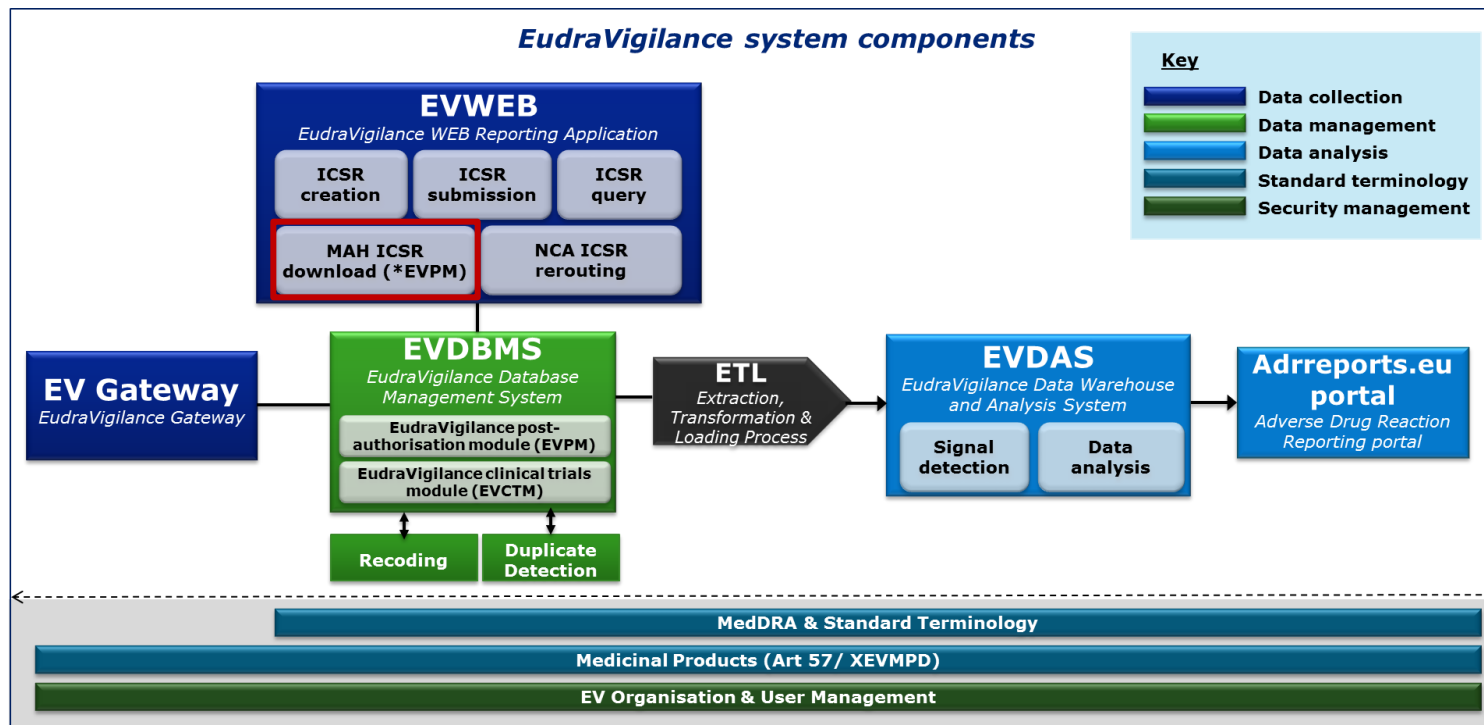
- This new component will allow for automatic forwarding of ICSRs to the applicable NCA in a Member State
- The EV rerouting functionality is only applicable to NCAs in EEA Member States
- ICSRs will be rerouted in the format received i.e. no conversions between ICH E2B(R2) and ICH E2B(R3) will be applied
- The rerouting of ICSRs with recoded medicinal product information will be put in place following implementation of the ISO IDMP terminologies
- The Agency will liaise with each NCA to set up the first configuration of the rerouting rules in line with the EU ICSR Implementation Guide

Rerouting for NCAs (2)



- NCAs will be able to update the rerouting parameters at any time in line with the EU ICSR Implementation Guide through EVWEB
 - Changes to rerouting rules may take a few days to be processed
 - NCAs need to decide in advance, which ICSRs are to be automatically rerouted to their national pharmacovigilance system
 - The default setting will be to forward all the ICSRs associated with that NCA's country (ICH E2B(R3) data element C.2.r.5 "Primary Source for Regulatory Purposes")

EudraVigilance System Changes



ICSR Download for MAHs (1)

MAHs

- After the switch to simplified reporting, MAHs will no longer receive ICSRs directly from NCAs (see training module PhV-M3)
- A download function will be made available to MAHs to obtain access to these ICSRs
- MAHs will be able to download ICSRs for active substances of medicinal products, for which the MAHs hold a marketing authorisation in the EEA (see PhV-M4 training module)
- *ICSRs will be made available in ICH E2B(R3) format only*

ICSR Download for MAHs (2)

MAHs

- The ICSR download functionality will be accessible to registered users by means EVWEB
- Access to ICSRs will be determined based on the medicinal product information submitted by MAHs to the XEVMPD (Article 57 product submissions) (Access Level 2A of the revised EudraVigilance Access Policy)




MAHs must ensure that the XEVMPD is updated as regards the medicinal products for which the MAHs hold a marketing authorisation in the EEA

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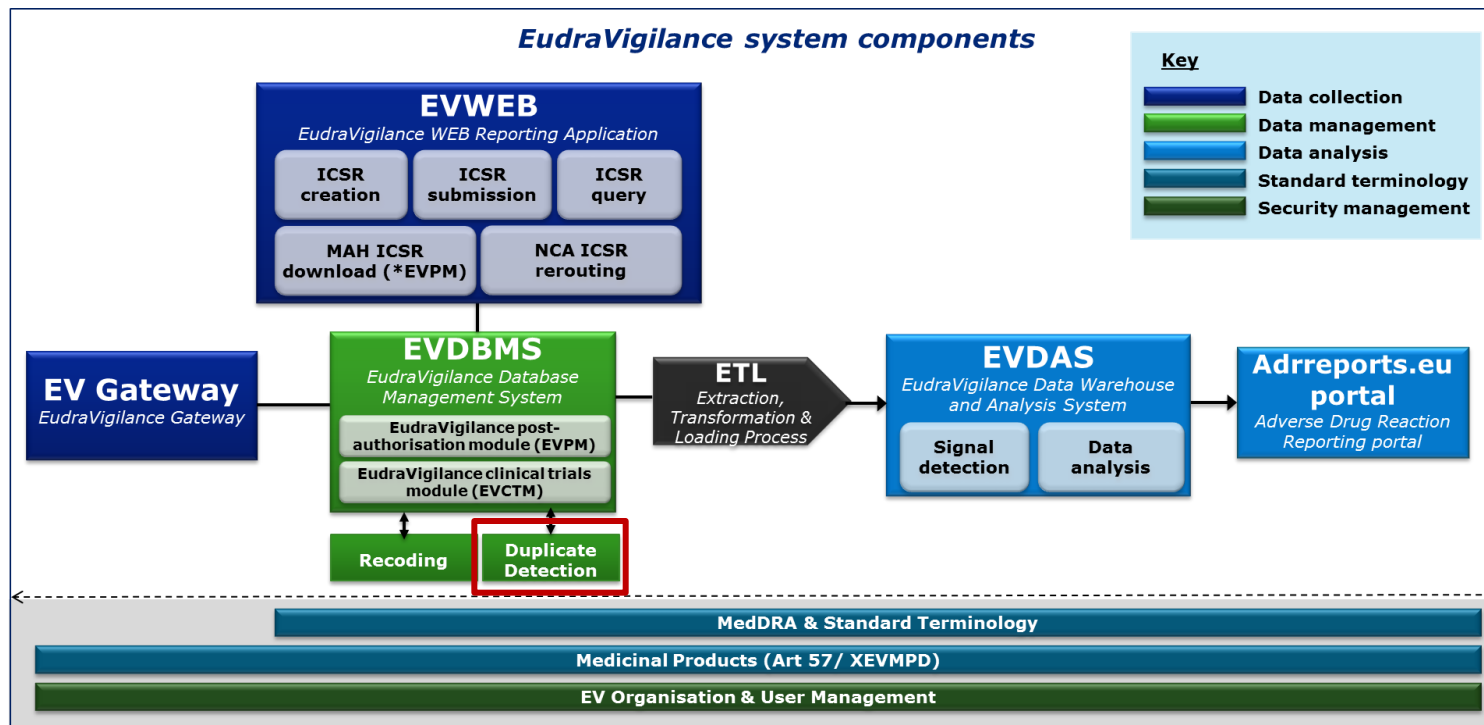
ICSR Download Function for MAHs (3)

MAHs

-  **NOTE 2:** MAHs should make sure that their pharmacovigilance systems can process the ICH E2B(R3) ICSRs downloaded from EudraVigilance. This can be achieved by implementing:
- Native ICH E2B(R3) or
 - Backwards/Forwards conversion (BFC) using a BFC tool to convert E2B(R3) files into E2B(R2) files

An extended E2B(R3) BFC tool is made available in the EU, which includes the additional EU specific data fields

EudraVigilance System Changes



Duplicate Detection and Management (1)

- The duplicate detection algorithm does not change
- The duplicate detection client is for use by EMA only and will be amended to handle duplicates in ICH E2B(R2) and ICH E2B(R3) format and to create E2B(R3) Master cases including cluster information (linking all associated duplicate ICSRs as initially received from senders)
- An additional message type will be implemented to be able to process Master Cases (“masterichicsr”); a master case is created in EudraVigilance when duplicates are merged and associated with a master
 - This message type currently does not exist as part of the ICH E2B(R2) specifications; the EU backwards-forwards conversion tool will reflect the “masterichicsr” in the data element M1.1 when converting an E2B(R3) master case message

Duplicate Detection and Management (2)

MAHs

- Will be able to download “master cases” from EudraVigilance in line with the revised EudraVigilance Access Policy
- The message type (equivalent to E2B(R2) - M.1.1) will have the code “master” to distinguish it from all other ICSR messages, which will have the message type “ichicsr” (see EU ICSR Implementation Guide, chapter I.C.3.1.1)
- Will also be able to download from EudraVigilance the original ICSRs that have been merged under the “master case” and also any nullification to these ICSRs, where applicable (see EU ICSR Implementation Guide, chapter I.C.6.1.2)

Duplicate Detection and Management (3)

MAHs

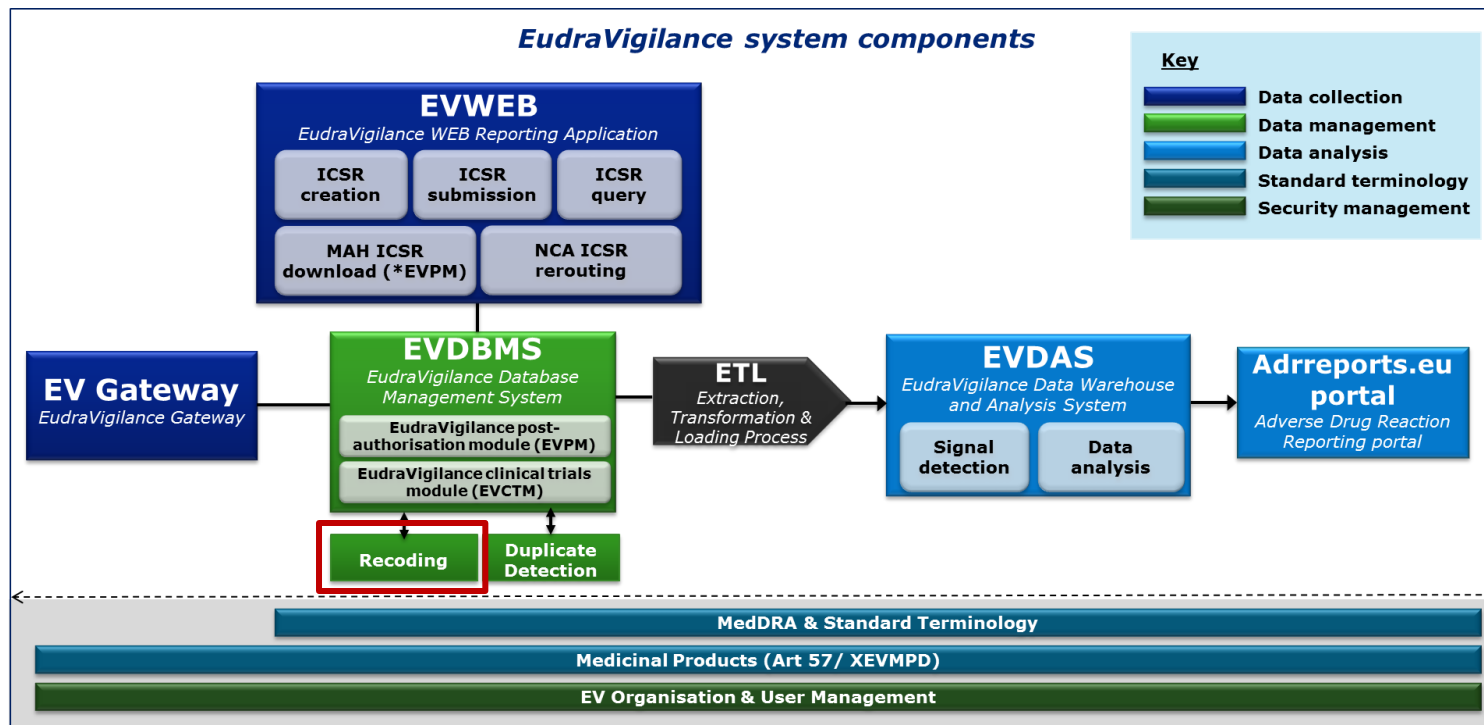
- Can decide if they wish to process “master cases” or not
- If an MAH does process the “master case” and it involves updating one of their own individual cases with information from the EudraVigilance master case, the MAH **MUST NOT** resubmit an updated version of this individual case to EudraVigilance
- A table of master cases and associated duplicates will be made available to aid duplicate management by Sender organisations

Duplicate Detection and Management (4)

NCAs

- Can use the EudraVigilance Rerouting functionality to update the rerouting rules to determine if they wish to receive EudraVigilance “master cases” or not (see also further guidance as outlined in EU ICSR Implementation Guide, chapter I.C.2.3 and I.C.6.1.2)
- The “master cases” must not be retransmitted by the NCA to EudraVigilance if there is no receipt of new information that warrants a follow-up report
- A table of master cases and associated duplicates will be made available to aid duplicate management by Sender organisations

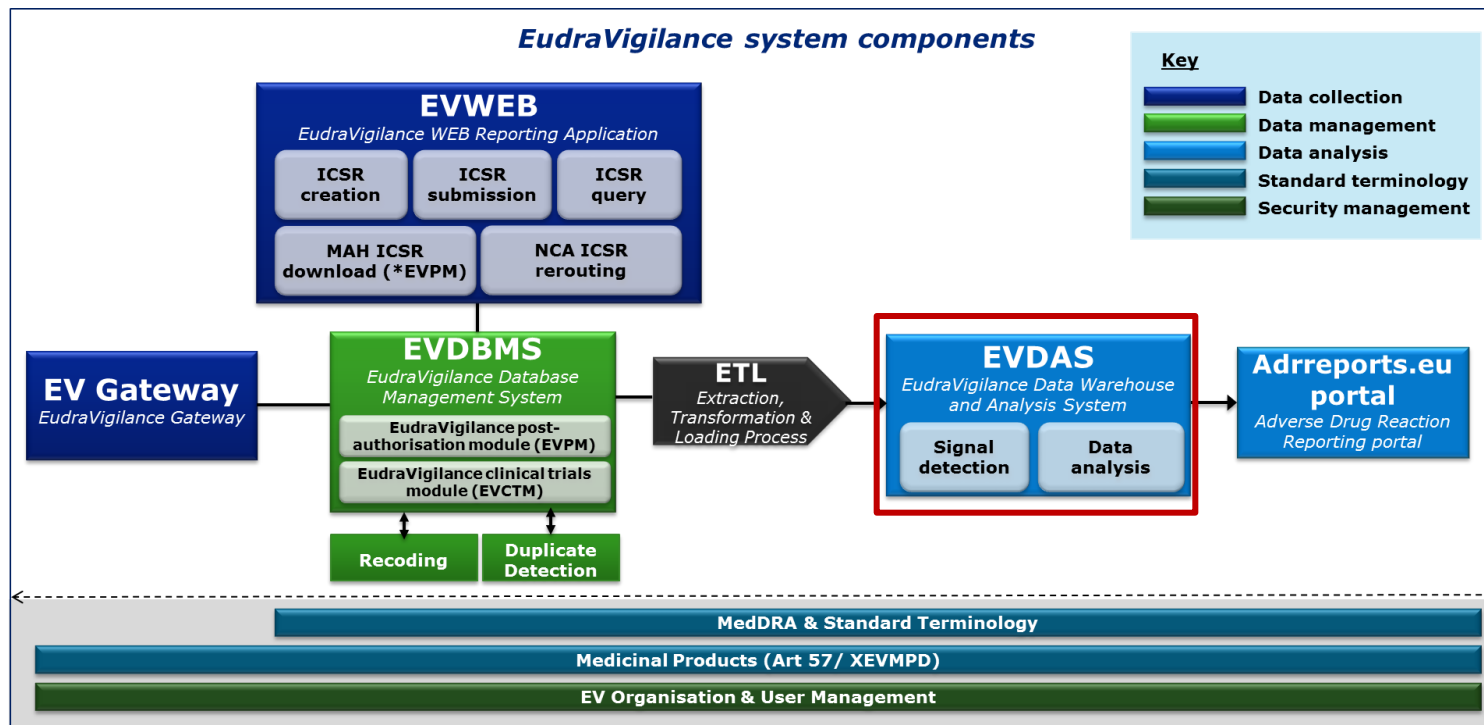
EudraVigilance System Changes



Medicinal Product Recoding

- The recoding process remains unchanged and is only for use by EMA
- XEVMPD will be used to support recoding of medicinal product information in ICSRs until ISO IDMP terminologies are available and implemented
- The recoding application and the recoding interface will be updated using new software technology
- NCAs and MAHs will not be affected by these changes

EudraVigilance System Changes





EVDAS (1)

EVDAS will be updated to:

- Be compliant with the new ICH E2B(R3) data structure and data elements
- Include a new measure of disproportionality (reporting odds ratio (ROR) is replacing the currently used proportional reporting ratio (PRR))
- Generate eRMRs, line listings, individual case report forms
 - The CIOMS I individual case report form will be replaced with a new case report form that is compliant with the ICH E2B(R3) format

EVDAS (2)

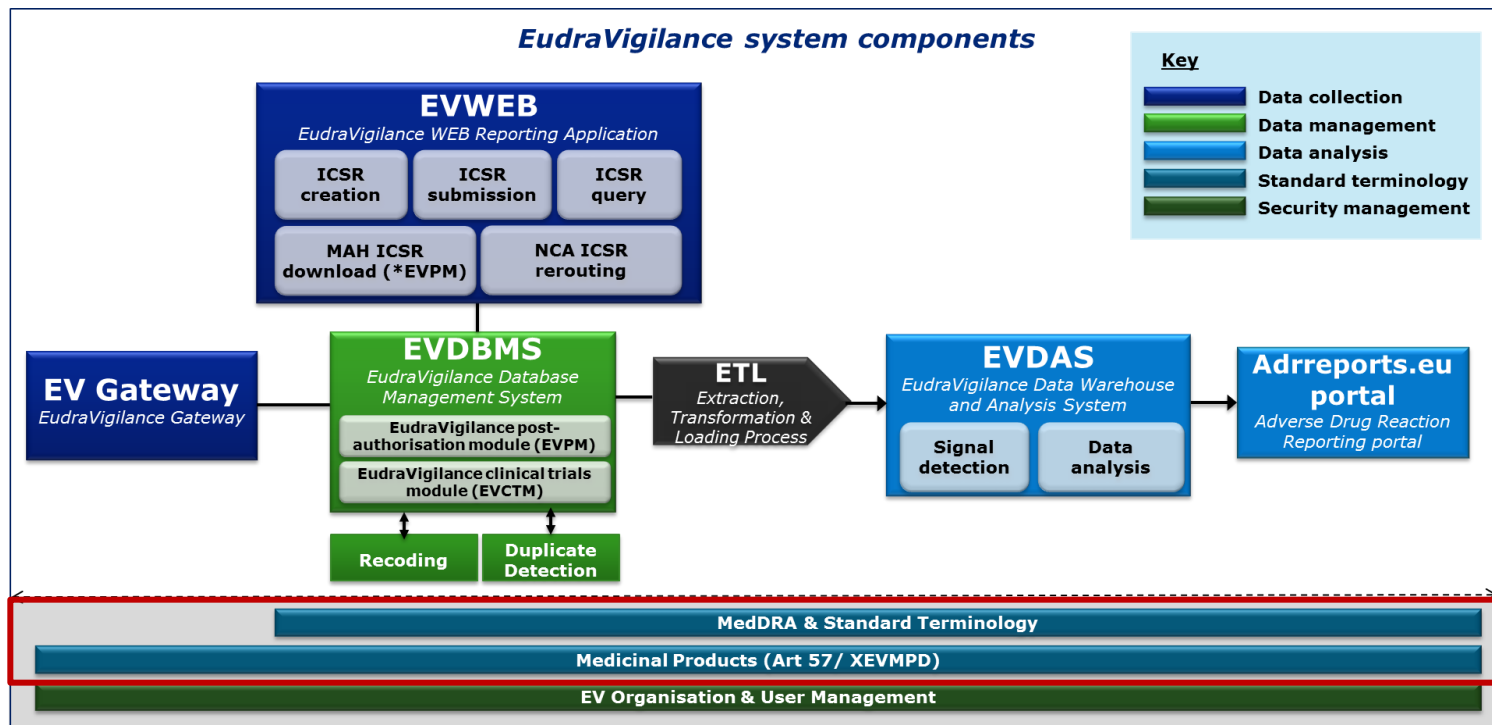


- New functionalities and predefined reports will be available to support
 - New measure of disproportionality (reporting odds ratio), new sub-group analyses
 - eRMR integration, improved data visualisation
 - Data quality monitoring and reporting compliance reports
 - Reporting on Article 57 data (EU QPPV, PSMF, MAH legal entity, product listings)



- Access to signal detection and analytical/reporting functions to the extent necessary to comply with their pharmacovigilance obligations, incl.
 - eRMRs as used by the EU regulatory network for signal detection/validation
 - Individual case line listing (Level 1 of revised EudraVigilance Access Policy)
 - ICSR forms
- See also training module PhV-M4

EudraVigilance System Changes



References

- The use of the MedDRA terminology for ICSR reporting will remain unchanged
- The use of XEVMPD data for the recoding of medicinal product information reported in ICSRs will remain unchanged
- The XEVMPD data will be used to determine the level of access to be granted to MAHs to EudraVigilance data in line with revision 2 of the EudraVigilance Access Policy adopted in December 2015
- The European Pharmacopoeia standard terms may be used for the description of the pharmaceutical dose form in E2B(R3) in free text (G.k.4.r.9.1) until the applicable ISO IDMP standard terms are available
- The existing code list attached in Appendix I of the ICH ICSR IG is used for routes of administration (G.k.4.r.10.2b, G.k.4.r.11.2b) until the applicable ISO IDMP standard terms are available

References



NOTE:

The EudraVigilance list of EDQM dosage forms can be found here:

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

- This list is not required but organisations can continue to use it for ICSR submissions in ICH E2B(R2) format and for ICSR submissions in ICH E2B(R3) format in free text (G.k.4.r.9.1)

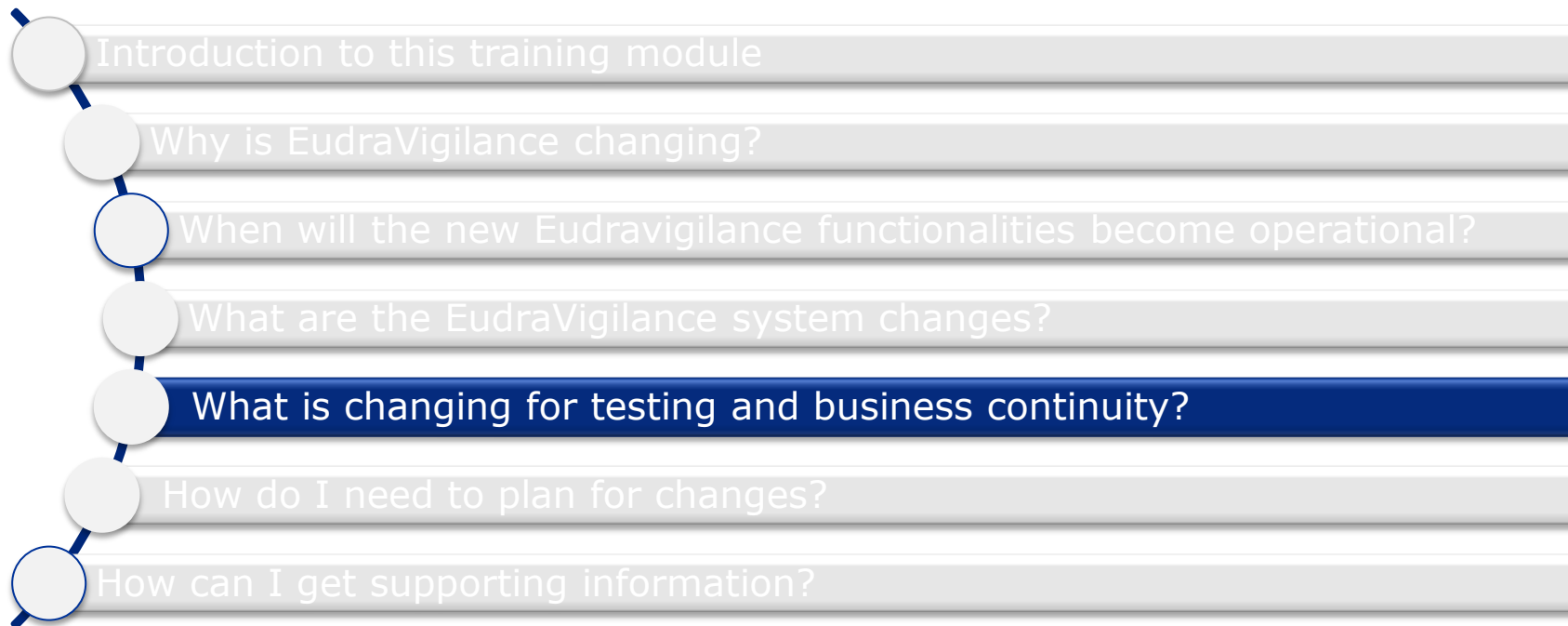
Session summary: What are the EudraVigilance system changes?

In this session you have learned to apprehend:

- The main components of the EudraVigilance Systems
- Which functionalities of the EudraVigilance system will change and which components remain unchanged
- The impact of the changes to EudraVigilance on the way you create and report Individual Case Safety Reports and the way you perform signal detection and validate signals

This should allow you to prepare for the change management planning within your own organisation, which will be further addressed in the next session

Overview Module PhV-M1





Session overview: What is changing for testing and business continuity?

In this session you will learn to describe:

- How to perform System Testing
- Changes to the currently established testing process
- How to plan for business continuity in case of system failure

Testing Process (1)

- Details on System Testing Requirements are provided in the EU ICSR Implementation Guide, chapter I.C.2.1.5; this includes communication, development, validation and XML testing
- Once the audit is completed, all organisations can start testing: **XCOMP is planned to be made available in Q2 2017** (see also the EV Communication Plan published by the Agency and await further announcements)
- For testing purposes, all organisations need to have a valid Test EudraVigilance (XCOMP) account (*see EV organisation and user Management*)
- Using XCOMP, organisations can test the EVWEB functionalities

Testing Process (2)

- A set of E2B(R3) sample XML ISO ICSR files will be made available by the Agency covering a range of different reporting scenarios in line with the ISO ICSR 27953-2:2011/ICH E2B(R3) standard and EU specific requirements
- Testers are expected to upload these sample files into their phv system and follow the test script to produce additional test files
- Once uploaded these test files should be transmitted to XCOMP for review by the EMA, who will provide feedback on any potential issues
- The sample test files will be also made available to EVWEB users
- *See also training module IT-M3*

Testing Process (3)

NCAs

- No testing with MAHs is required
- The re-routing process should be tested
- Where the local phv system is not yet ICH E2B(R3) compliant, a local conversion tool should be tested
- Testing should be initiated once the NCA's local phv system is ICH E2B(R3) compliant
- Testing will follow the steps as outlined in the EU ICSR Implementation Guide

MAHs

- MAHs will need to test with EMA only
- Gateway adaptations should be tested to support processing of E2B(R3) messages & ACKs
- Where the local phv system is not yet ICH E2B(R3) compliant, a local conversion tool should be tested
- Testing should be initiated once the MAH's local phv system is ICH E2B(R3) compliant
- Testing will follow the steps as outlined in the EU ICSR Implementation Guide

What to do in case of system failure (1)

- The process to follow in case of a failure of submission of ICSRs will change; details are provided in the EU ICSR Implementation Guide, chapter I.C.2.1.6
- *Failure occurring at the sender's side*
 - The process of submission of CIOMS forms via fax or other methods (CD) is no longer permitted
 - An organisation must submit ICSRs electronically to EudraVigilance as soon as their system is available again

What to do in case of system failure (2)

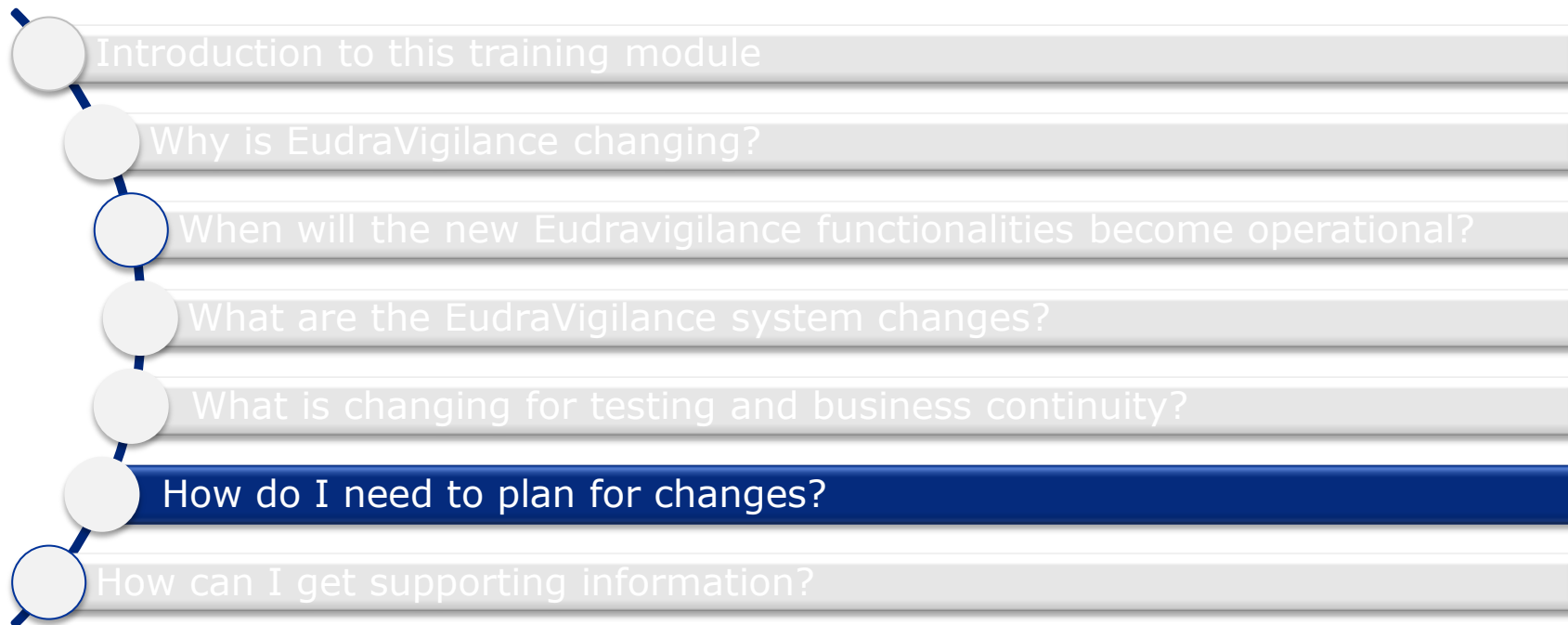
- *Failure occurring at the level of EudraVigilance*
 - Organisations will need to submit cases within **two calendar days after the system failure has been resolved**
 - Cases received late due to the system failure at the level of the EudraVigilance system will be excluded from reporting compliance 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)/C.1.5 E2B(R3)), whichever is greater

Session summary: What is changing for testing and business continuity?

In this session you have learned to describe:

- Where you can find detailed information in the EU ICSR Implementation Guide as regards the conduct of system testing and
- The planning for business continuity in case of system failure

Overview Module PhV-M1



Session overview: How do I need to plan for changes?

In this session you will learn:

- What to take into account when preparing a Change Management Plan for your organisation focusing on People, Technology, Process and Information
- We will highlight points you “must do” and “should do” to be prepared

We have structured this session on the type of organisation you belong to:

- National Competent Authority
- Marketing Authorisation Holder
- Sponsor of Clinical Trials

NCA Change Management Planning



Summary of changes for which NCAs need to plan and prepare for

PEOPLE - NCA Change Management Planning Summary

Must Do

- Staff to undergo training on:
 - Use of the new ICH E2B(R3) format
 - EVDAS
 - GVP Modules VI (revision 2)
 - GVP Modules IX (revision 1)
 - EudraVigilance Access Policy
- Refer to detailed training catalogue for all training modules

Should Do

- Undertake training on the use of EVWEB to familiarise with the new functionalities and changes
- Plan to complete any testing of local phv systems 6 to 3 months prior to the enhanced EV functionalities going live
- Consider resource implications for local phv system adaptations to become ICH E2B(R3) compliant



TECHNOLOGY - NCA Change Management Planning

IT	Change summary
Use of ISO/ICH E2B(R3) standard	<ul style="list-style-type: none">• ICSRs from EV will be rerouted to NCAs in the format they were received i.e. E2B(R2)/(R3) format• ICSRs resulting from the Agency's MLM service will be rerouted in E2B(R3) format• ICSR "Master Cases" from EV will be rerouted in E2B(R3) format• NCAs may still report ICSRs in ICH E2B(R2) format• NCAs will need to update their local phv system to be compliant with the new E2B(R3) format and standard• Until the E2B(R3) format is implemented, NCAs may use a backwards/forwards conversion tool

TECHNOLOGY - NCA Change Management Planning

IT	Change summary
EV Rerouting Function	<ul style="list-style-type: none">• NCAs to confirm to EMA the initial rerouting settings in accordance with the EU ICSR Implementation Guide• NCAs may update rerouting rules any time
EudraVigilance Duplicate Detection	<ul style="list-style-type: none">• NCAs need to accommodate for the new message type "masterichicsr"• As part of the EU backwards/forwards conversion tool provided by the EMA, "masterichicsr" will be reflected in M1.1 when converted from E2B(R3) to E2B(R2)



TECHNOLOGY - NCA Change Management Planning

IT

Change summary

Testing

- NCAs should follow the testing process in line with the EU ICSR Implementation Guide
- Testing is encouraged before moving to simplified reporting as regards gateway adaptations, rerouting and backwards/forwards conversion where applicable
- Testing of changes of the local phv system in compliance with the ICH E2B(R3) format should be performed 6 months prior to go live date with the EMA

TECHNOLOGY - NCA Change Management Planning Summary

Must Do

- Install EU backwards/forwards conversion tool (where applicable)
- Configure local pharmacovigilance system in line with ICH E2B(R3) format

Should Do

- Prepare internal testing plans for your pharmacovigilance system in relation to the changes that will occur to the reporting, receiving and analysis of data

PROCESS - NCA Change Management Planning

Process	Change summary
Simplified Reporting	<ul style="list-style-type: none">• NCAs should inform MAHs at national level in a timely manner about the changes in reporting to EudraVigilance• NCAs will need to start reporting non-serious adverse reactions occurring in their territory within 90days of receipt
Reporting of SUSARs	<ul style="list-style-type: none">• SUSAR reporting will remain unchanged until the implementation of the Clinical Trials Regulation – further information will be provided by EMA• NCAs should inform commercial and non-commercial sponsors at national level in a timely manner when process changes will be required

PROCESS - NCA Change Management Planning

Process	Change summary
ICSR Nullification Requests	<ul style="list-style-type: none">• During the transition phase, MAHs may submit nullification requests for ICSRs previously reported by NCAs to EV• NCAs will need to ensure to establish processes to check if they need to nullify cases they have previously reported to EV<ul style="list-style-type: none">– If a nullification report for an EEA case is received in EV where no pre-existing case from the sender organisation is found, the nullification report is submitted to the concerned NCA– If a NCA does not wish to receive rerouted ICSRs from EV, the EMA will periodically inform the NCA about these reports so they can validate the nullification

PROCESS - NCA Change Management Planning

Process	Change summary
Signal management process and EVDAS	<ul style="list-style-type: none"> • NCAs will need to update their business processes in line with revision 1 of GVP Module IX • NCAs will need to plan for the notification of validated signals by MAHs in line with revision 1 of GVP Module IX • NCAs will need to continue to use EPITT for tracking signals at EU level • NCAs will need to familiarise with several new EVDAS functionalities and predefined reports
Reporting to WHO-UMC	<ul style="list-style-type: none"> • NCAs no longer need to submit ICSRs for suspected adverse reactions that occurred on their territory to WHO-UMC; these reports will be made available by the EMA to WHO

PROCESS - NCA Change Management Planning Summary

Must Do

- Update existing processes to:
 - Receive rerouted ICSRs from EV
 - Stop sending ICSRs from patients and healthcare professionals to MAHs
 - Stop sending local ICSRs to WHO-UMC
 - Align ADR reporting in line with GVP Module VI (revision 2)
 - Align signal detection/validation with GVP Module IX (revision 1) and new EVDAS reports/data outputs
 - Support submission of validated signals by MAHs

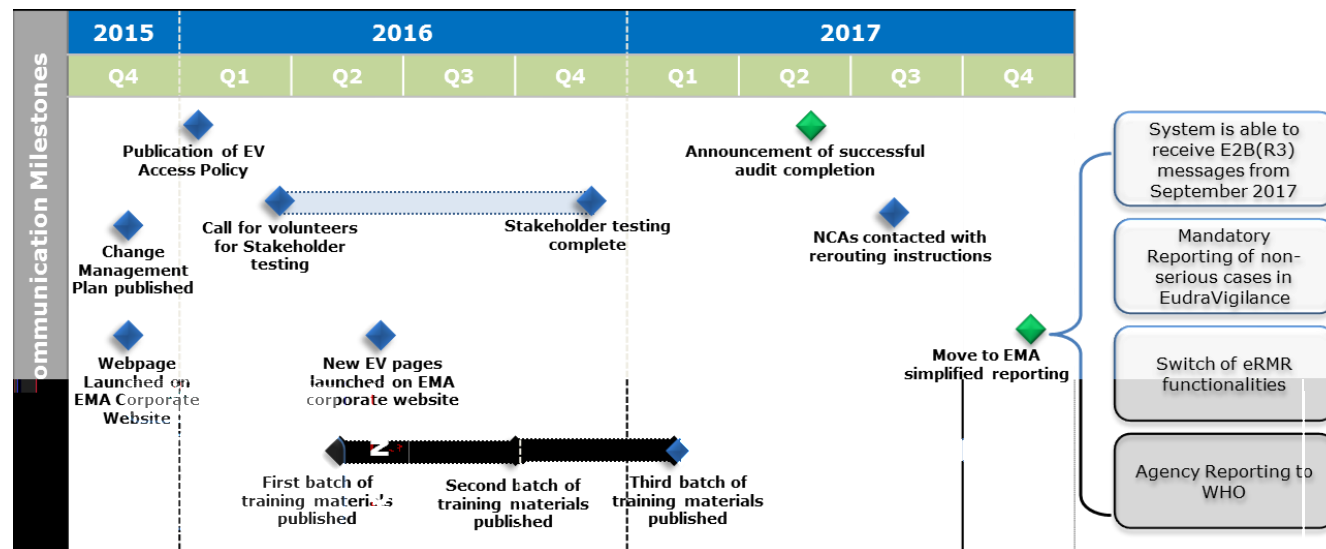
Should Do

- Ensure that the transition to simplified reporting to EV is coordinated with all stakeholders
- Follow the specific nullification process during the transition phase as outlined in the EU ICSR Implementation guide

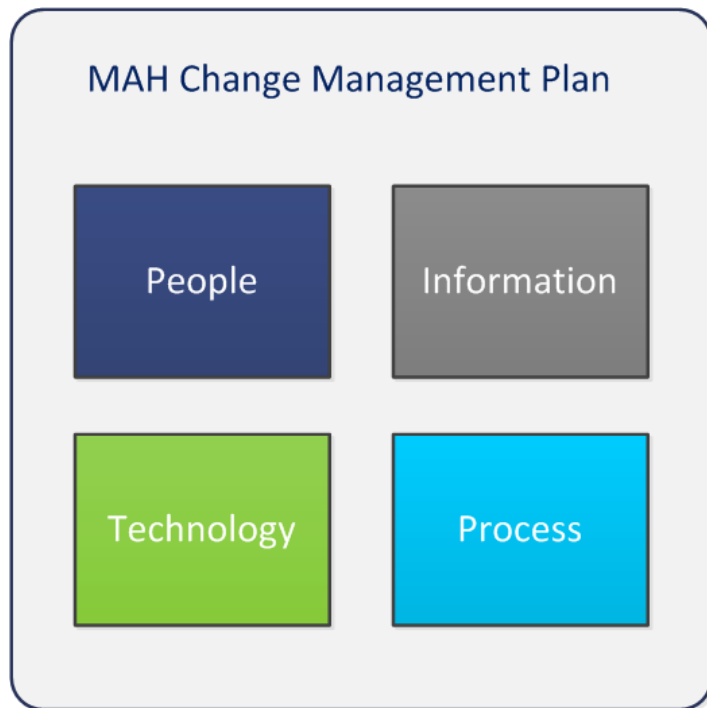
INFORMATION - NCA Change Management Planning

Should Do

- Prepare a communication plan to keep local stakeholders informed about the switch to the simplified reporting and the process changes related to signal management



MAH Change Management Planning



Summary of changes for which MAHs need to plan and prepare for

PEOPLE - MAH Change Management Planning Summary

Must Do

- EU QPPV or Deputy to identify and register users who will be authorised to access EVDAS
- Staff to undergo training on:
 - Use of the new ICH E2B(R3) format
 - EVDAS
 - GVP Modules VI (revision 2)
 - GVP Modules IX (revision 1)
 - EudraVigilance Access Policy
 - For details refer to detailed training catalogue

Should Do

- Undertake training on the use of EVWEB/EVDAS to familiarise with new functionalities and changes
- Plan to complete any testing of local phv system 6 to 3 months prior to the enhanced EV going live in Q3 of 2017
- Consider resource implications for:
 - Local phv system adaptations to be ICH E2B(R3) compliant/BFC during transition phase
 - Operating the new signal management process
 - Accessing and processing ICSRs and other data outputs from EV
 - Training of staff

TECHNOLOGY - MAH Change Management Planning

IT	Change summary
Use of ISO/ICH E2B(R3) standard	<ul style="list-style-type: none">• MAHs may use the E2B(R3) format for reporting of ICSRs to EV or continue to report based on the E2B(R2) format (no deadline is yet established for discontinuation of R2)• ICSRs from NCAs in the EEA will need to be downloaded from EV in E2B(R3) format –the EU backwards/forwards conversion tool may be used to facilitate conversion where necessary• Local phv system should be upgraded to be compliant with the ICH E2B(R3) format

TECHNOLOGY - MAH Change Management Planning

IT	Change summary
MAH Gateway solutions	<ul style="list-style-type: none">• There may be a need to undertake configuration changes to be able to process ICH E2B(R3) Safety and ACK messages
EVWEB	<ul style="list-style-type: none">• MAHs using EVWEB will need to be familiar in working with the new ICH E2B(R3) data structure and additional data elements; there will be also a new interface and improved functionalities• EVPOST function users will need to familiarise with new EVWEB where this function will become an integral part



TECHNOLOGY - MAH Change Management Planning

IT	Change summary
Testing	<ul style="list-style-type: none">• MAHs are only required to test with EudraVigilance, no testing with NCAs will be necessary• MAHs should follow the testing process in line with the EU ICSR Implementation Guide• Testing is encouraged before moving to simplified reporting as regards potential gateway adaptations and backwards/forwards conversion where applicable• Testing of changes of the local phv system in compliance with the ICH E2B(R3) format should be performed 6 months prior to go live date with the EMA

TECHNOLOGY - MAH Change Management Planning

IT	Change summary
EudraVigilance Download function	<ul style="list-style-type: none">• After the switch to simplified reporting, MAHs will no longer receive ICSRs directly from NCAs• MAHs will have access to the download functionality of EVWEB, which requires users to be registered• The download functionality will allow staff of the company to search, request and download ICSRs for active substances of medicinal products, for which the MAH holds a marketing authorisation in the EEA• The download functionality will also allow to download ICSRs from the literature resulting from the Agency's MLM service

TECHNOLOGY - MAH Change Management Planning Summary

Must Do

- Configure local Gateway to support ICH E2B(R3) messages (where applicable)
- Install backwards/forwards conversion tool (where applicable) – E2B(R3) format will need to be accepted as of Q3 2017
- Configure local phv system in line with ICH E2B(R3) format

Should Do

- Familiarise with HL7 messaging format for the electronic transmission of ICSRs in E2B(R3) format
- Plan testing of local phv system

PROCESS - MAH Change Management Planning Summary

Must Do

- Update existing processes to:
 - Retrieve ICSRs from EEA NCAs using EV
 - Comply with simplified reporting to EV
 - ICSR reporting in line with GVP Module VI (revision 2)
 - Signal detection and validation based on GVP Module IX (revision 1) and new EVDAS reports and data outputs
 - Support submission of validated signals to NCAs and the Agency
 - Ensure that Article 57 product submissions are kept up to date

Should Do

- Reporting of ICSRs (for medicinal products authorised in the EEA) occurring within or outside the EEA should only take place to EV in compliance with phv legislation
- Ensure that the transition to simplified reporting is coordinated in line with the guidance and communication provided by EMA and NCAs in EEA Member States

PROCESS - MAH Change Management Planning

Process	Change summary
Signal detection and management	<ul style="list-style-type: none">• MAHs will need to monitor the data available in EV and to inform the Agency and NCAs about any validated signals they identify• The requirements as outlined in GVP Module IX (revision 1) will need to be applied• Access will be granted to EVDAS and the signal detection/analytical and reporting functions – MAHs will need to familiarise in working with eRMRs, line listings, ICSR forms• A Confidentiality undertaking must be signed by the EU QPPV and authorised personnel to obtain access to case narratives as part of the signal validation process

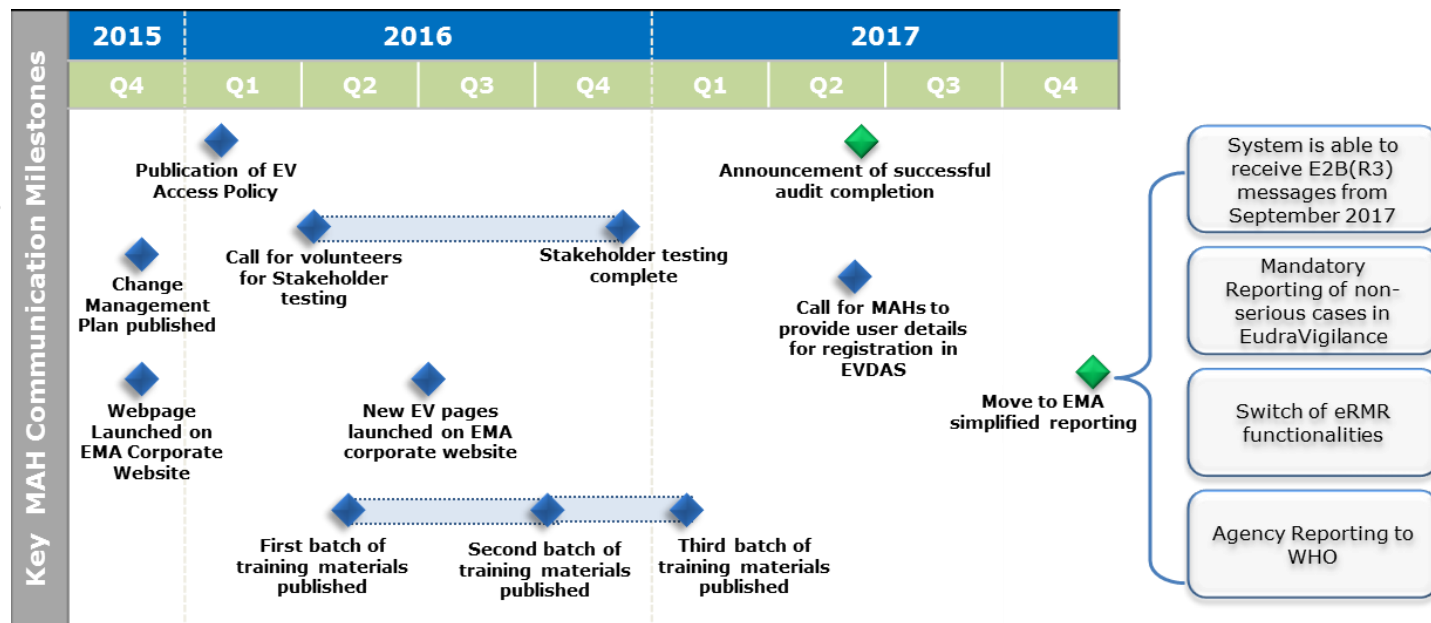
PROCESS - MAH Change Management Planning

Process	Change summary
Simplified Reporting	<ul style="list-style-type: none">• MAHs need to ensure that all reportable ICSRs are transmitted to EV only in line with GVP Module VI, revision 2• Besides serious adverse reactions reportable within 15-days, MAHs will need to start reporting non-serious adverse reactions with occurrence in the EEA within 90 days of receipt
XEVMPD/Article 57 submissions	<ul style="list-style-type: none">• No changes will be made to the existing XEVMPD tool and therefore the functionalities and interface will remain the same• Article 57 product submissions remain unchanged, the data must be kept up to date to ensure appropriate access to EV

INFORMATION - MAH Change Management Planning

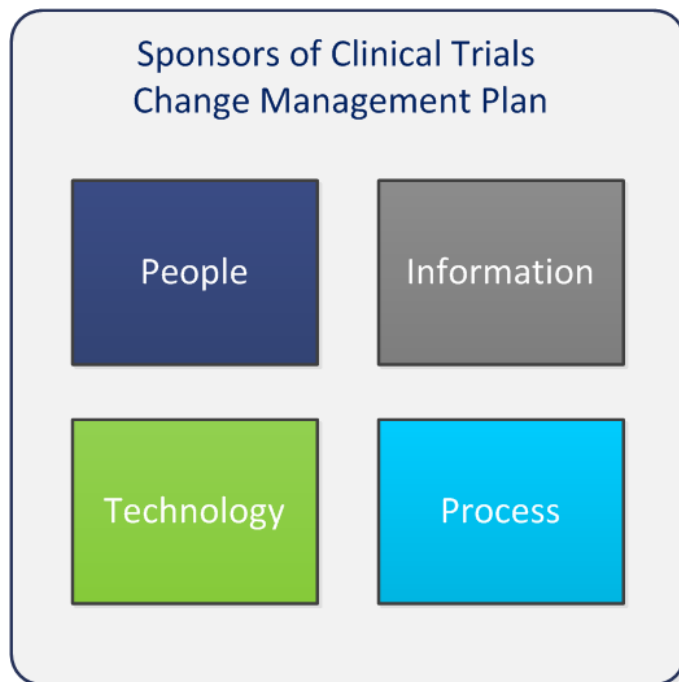
Should Do

- Prepare a communication plan to inform affiliates, contractual partners and other stakeholders about the changes to take place with the launch of the enhancements of EudraVigilance and related process changes





Sponsors of Clinical Trials Change Management Planning



Summary of changes for which Sponsors of clinical trials need to plan and prepare for



PEOPLE - Sponsors of Clinical Trials

Change Management Planning - Summary

Should Do

- Sponsors, which are using EVWEB should undergo training on EVWEB and the new ICH E2B(R3) format to familiarise with new functionalities and changes (for all training offerings, refer to detailed training catalogue)

TECHNOLOGY - Sponsors of Clinical Trials Change Management Planning - Summary

Should Do (if not a EVWEB user)

- Can continue to use E2B(R2) for SUSAR submissions (no deadline is yet established for discontinuation of R2)
- In case of upgrades of the local SUSAR submission system/clinical trial database to become compliant with the ISO ICSR standard/ICH E2B(R3) format, ensure that testing is performed well in advance with the Agency



TECHNOLOGY - Sponsors of Clinical Trials

Change Management Planning

IT

Change summary

Use of
ISO/ICH E2B(R3)
standard

- Sponsors of clinical trials may continue to use the E2B(R2) format for reporting of ICSRs to EV (no deadline is currently set)
- Sponsors of clinical trials may also use the E2B(R3) format for reporting of ICSRs to EV once all required testing has been completed successfully beforehand
- Sponsors should plan to develop their systems to become compliant with the E2B(R3) format

TECHNOLOGY - Sponsors of Clinical Trials

Change Management Planning

IT

Change summary

Sponsor Gateway solutions

- There may be a need to undertake configuration changes to be able to process ICH E2B(R3) Safety and ACK messages

EVWEB

- Sponsors using EVWEB will need to be familiar in working with the new ICH E2B(R3) data structure and additional data elements; there will be also a new interface and improved functionalities
- EVPOST function will become an integral part of EVWEB

PROCESS - Sponsors of Clinical Trials

Change Management Planning

Should Do

- Sponsors using EVWEB for data entry may continue their process to report SUSARs directly to the NCA that authorised the clinical trial
- Sponsors who use EVWEB for SUSAR reporting should adapt their processes of reporting in line with the new ICH E2B(R3) format, data elements and business rules
- Sponsors should adapt their business processes in line with the communication and instructions provided on the dedicated [Clinical trials in human medicines](#) webpage of the Agency
- No changes will be made to the existing XEVMPD tool and therefore the functionalities and interface will remain the same

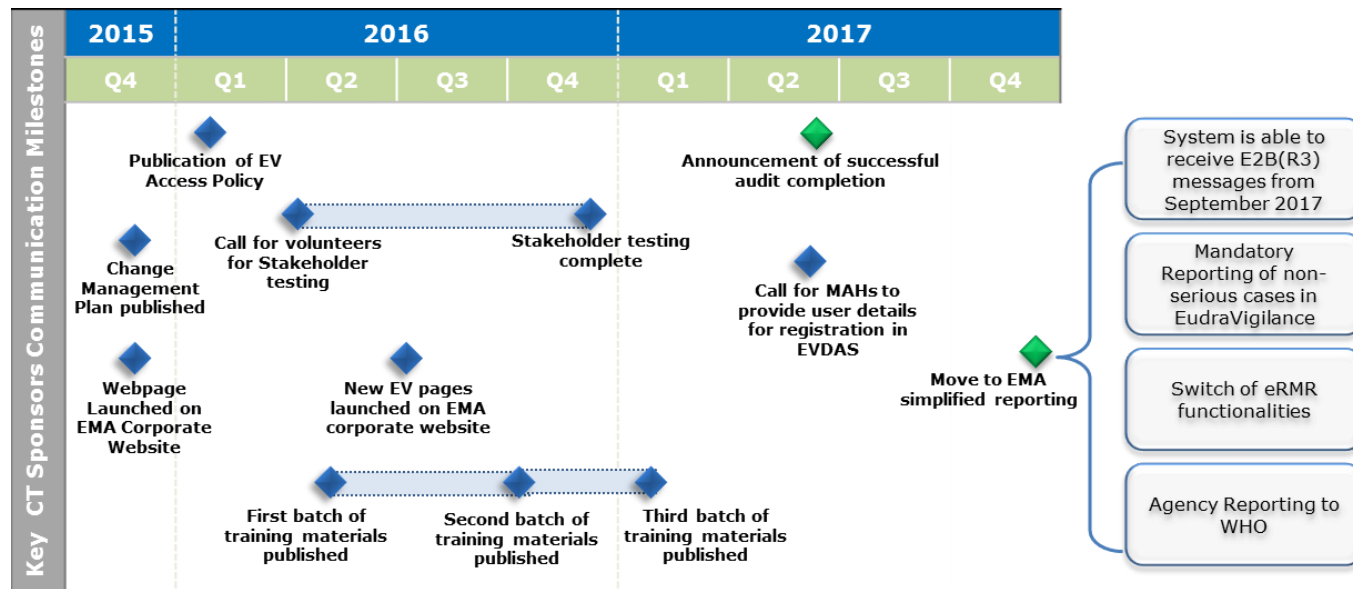


INFORMATION - Sponsors of Clinical Trials

Change Management Planning - Summary

Should Do

- Prepare communication to inform their partners about the changes to take place with the launch of the enhancements of EudraVigilance

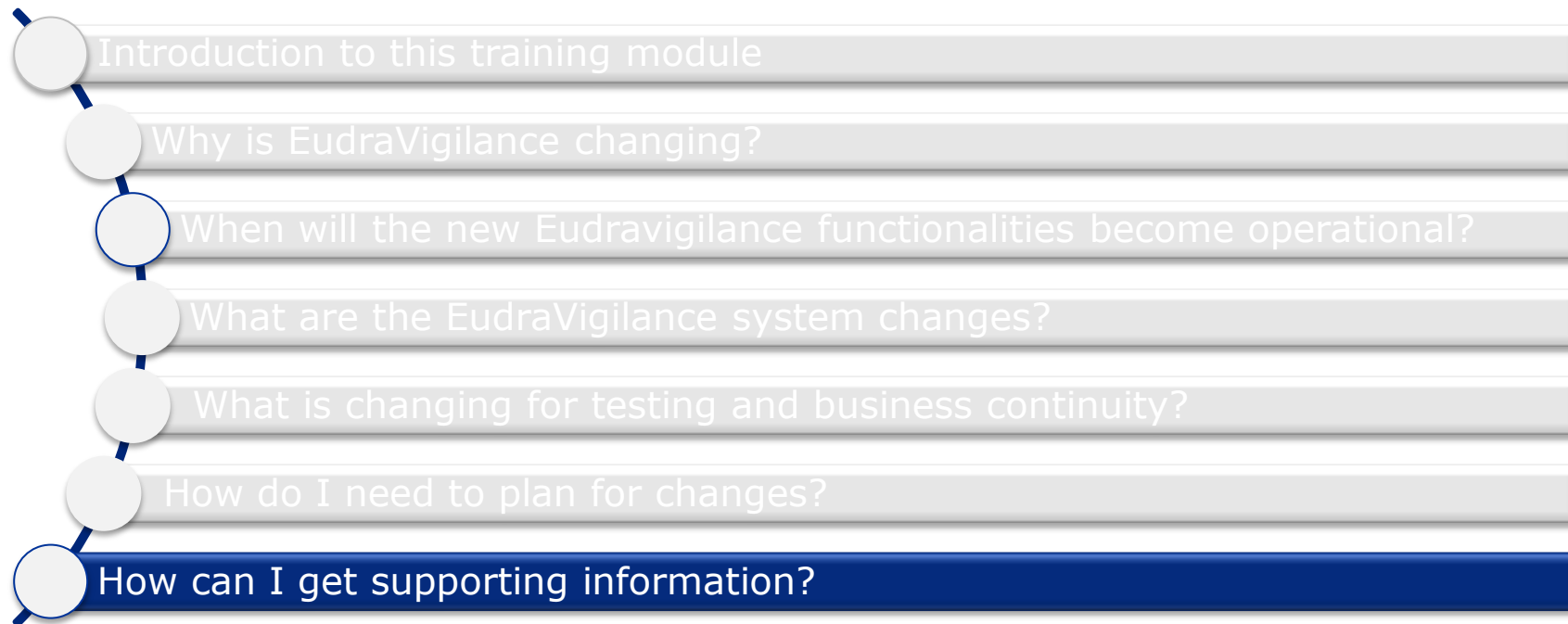


Session summary: How do I need to plan for changes?

In this session you have learned:

- What to take into account when preparing a Change Management Plan focusing on four areas: People, Technology, Process and Information
- To describe the changes specific to your organisation being either a NCA, MAH or a Sponsor of a clinical trial

Overview Module PhV-M1





Session overview: How I can I get supporting information?

In this session you will learn:

- What documents are essential for you to prepare for the launch of the new EudraVigilance System functionalities and to assess the impact on your organisation
- How to contact the Service Desk in case you require support or further information

Supporting Documents (1)

Documentation	Description
Guideline on good pharmacovigilance practices (GVP) Module VI – Management and reporting of adverse reactions to medicinal products (Rev 1) <i>Revision 2 in draft</i>	<ul style="list-style-type: none">Addresses the legal requirements detailed in Title IX of Directive 2001/83/EC and chapter 3 of Regulation (EC) No 726/2004 as regards the collection, data management and reporting of suspected adverse reactions (serious and non-serious) associated with medicinal products for human use authorised in the European Union (EU).

Supporting Documents (2)

Documentation	Description
Guideline on good pharmacovigilance practices: Module IX – Signal management <i>Revision 1 in draft</i>	Describes the signal management process in the EU
EudraVigilance stakeholder change management plan	Details the changes taking place in the EudraVigilance system and to the process of reporting Individual Case Safety Reports (ICSRs)

Supporting Documents (3)

Documentation	Description
Delivery time frame for the EU portal and EU database	<ul style="list-style-type: none">The purpose of the document is to describe the planned time frame for the implementation of the EU portal and EU database
Clinical trials in human medicines webpage of the Agency	

Supporting Documents (4)

Documentation	Description
European Union individual case safety report (ICSR) implementation guide	<ul style="list-style-type: none">• This guidance describes the EU-specific requirements to generate a valid ICSR safety and acknowledgment messages in the international format EN ISO ICSR 27953-2:2011 in accordance with ICH E2B(R3) guidance.• This guidance should be read in conjunction with the ICH E2B(R3) implementation guide and related materials published on the ICH website.

[Implementation of the ISO IDMP standards](#) webpage of the Agency

[EudraVigilance](#) webpage of the Agency

Supporting Documents (5)

Documentation	Description
EU ICSR implementation guide business rules spreadsheet	<ul style="list-style-type: none">This spreadsheet includes all the ICH E2B(R3) and EU specific business rules in a format to help system developers.
EU backwards forwards conversion element mapping spreadsheet	<ul style="list-style-type: none">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-forwards conversion rules. It covers additional EU-specific rules for the conversion back and forth between E2B(R2) and E2B(R3).

Supporting Documents (3)

Documentation	Description
Draft EU BFC conversion	<ul style="list-style-type: none">The ICH backwards-forwards conversion tool updated to include additional EU-specific data fields.
EU E2B(R3) code lists	<ul style="list-style-type: none">The list of codes for EU-specific data fields.
EU reference instances	<ul style="list-style-type: none">ICH reference instances amended to include EU-specific data fields.

Reference: EudraVigilance webpage

Supporting Documents (4)

Documentation	Description
EU example instances	Additional example instances to be used for testing E2B(R3) transmissions to the EudraVigilance. A European database of suspected adverse reactions to medicines that are authorised or being studied in clinical trials in the European Economic Area (EEA).

Supporting Documents (5)

Documentation	Description
ICH Implementation guide package	<ul style="list-style-type: none">• A set of documents including the ICH ICSR implementation guide, backwards and forwards compatibility recommendations and element mapping
ICH E2B(R3) Questions and answers	<ul style="list-style-type: none">• A question-and-answer document relevant for technical E2B questions

Supporting Documents (6)

Documentation	Description
European Medicines Agency policy on access to EudraVigilance data for medicinal products for human use (EudraVigilance Access Policy)	<ul style="list-style-type: none">• EMA has revised the EudraVigilance access policy ahead of implementing the new EudraVigilance system in 2017• This revised access policy was adopted by the EMA Management Board in December 2015 and will enter into force six months after the Management Board announces that the EudraVigilance database has achieved full functionality, based on an independent audit report in 2017



Where can I get support if needed?

EudraVigilance Registration

- Email - eudravigilanceregistration@ema.europa.eu
- Tel - 44 (0) 20 3660 7523

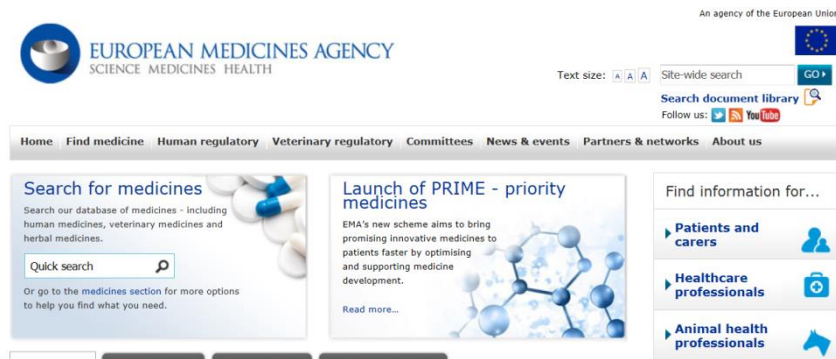
EudraVigilance Operations and IT Operations

- Visit the EMA Service Desk portal: <https://servicedesk.ema.europa.eu>
- Urgent helpline for technical enquiries: +44 (0)20 3660 8520

Where can I get support if needed?

Pharmacovigilance operations

- Send a question to EMA (accessible from the EMA homepage)




Web address:
http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/landing/ask_ema_landing_page.jsp&mid=WC0b01ac05806499f0

Session summary: How can I get supporting information?

In this session we have learned:

- What documents to consult to prepare for the launch of the new EudraVigilance System functionalities and to assess the impact on your organisation
- How to contact the Service Desk in case you require support

Overview Module PhV-M1

- 
- Introduction to this training module
 - Why is EudraVigilance changing?
 - When will the new Eudravigilance functionalities become operational?
 - What are the EudraVigilance system changes?
 - What is changing for testing and business continuity?
 - How do I need to plan for changes?
 - How can I get supporting information?

Summary of PhV-M1

We are now at the end of the training module PhV-M1, which provided you to basis for:

- Understanding the legal requirements for changes of EudraVigilance
- Describing the EudraVigilance System Implementation Plan
- Apprehending the EudraVigilance System changes
- Preparing for Change Management Planning
from a perspective of a NCA, a MAH, a Sponsor of clinical trials
- Understanding where to obtain supporting information





Feedback

- Please provide us with feedback on this E-learning module and any attendant guidance documents you have viewed by taking the EMA training survey.
- The survey is accessible via [this link](#).

☒ Save a backup on your local computer (disable if you are using a public/shared computer)

EudraVigilance training feedback survey

Fields marked with * are mandatory.

Disclaimer
The European Commission is not responsible for the content of questionnaires created using the EUSurvey service - it remains the sole responsibility of the form creator and manager. The use of EUSurvey service does not imply a recommendation or endorsement, by the European Commission, of the views expressed within them.

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Useful links
[EudraVigilance training page](#)

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[European Medicines Agency service desk](#)
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Acronyms (1)

Acronym	Description
ACK	Acknowledgement
BFC	Backwards and Forwards Conversion
EEA	European Economic Area
EDQM	European Directorate for the Quality of Medicines & Healthcare
eRMRs	Electronic Reaction Monitoring Reports
EU	European Union
EV	EudraVigilance
EVCTM	EudraVigilance Clinical Trials Module

Acronyms (2)

Acronym	Description
EVDAS	EudraVigilance Data Analysis System
EVPOST	EudraVigilance Post function (WEB-TRADER)
EVPM	EudraVigilance Post-Authorisation Module
EVWEB	EudraVigilance Web Application
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
ICSR	Individual Case Safety Reports
IG	Implementation Guide
ISO	International Organization for Standardization

Acronyms (3)

Acronym	Description
MAH	Marketing authorisation holder
MedDRA	Medical Dictionary for Regulatory Activities
NCA	National competent authority
OID	Object Identifier
PhV	Pharmacovigilance
PRR	Proportional Reporting Ratio
ROR	Reporting Odds Ratio



Acronyms (4)

Acronym	Description
SUSAR	Suspected Unexpected Serious Adverse Reaction
XEVMPD	Extended EudraVigilance Medicinal Product Dictionary



Thank you for your attention

Further information

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