



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

# EudraVigilance: Preparing for Change

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EudraVigilance Auditable Requirement project

6<sup>th</sup> Industry Stakeholder Platform Meeting, 18<sup>th</sup> December 2015

Presented by Francois Domergue, Data Standardisation and Analytics, EMA

An agency of the European Union





# Agenda

- Why is EudraVigilance changing?
- How is EudraVigilance changing?
- How to prepare for technical changes?
- How to prepare for business process changes?
- What training will be available?
- What communication will be available?

## Why is EudraVigilance changing? (1/3)

- 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, followed by the addition of Commission Implementing Regulation (EU) No 520/2012 in June 2012.
- The main changes to electronic reporting requirements 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.



## Why is EudraVigilance changing? (2/3)

- Clinical Trials legal requirement changes
  - 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 28th May 2016. According to the Regulation, the Agency shall set up and maintain an electronic database for the reporting of SUSARs and annual safety reports. The database shall be a module of the EudraVigilance database.
- The main planned changes to electronic reporting requirements are:
  - Usage of ISO standards in the reporting of SUSARs, ISO ICSR standard 27953-2:2011
  - 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.

## Why is EudraVigilance changing? (3/3)

- Revision of the EudraVigilance Access Policy
  - Article 24(2) of the Regulation defines the level of EudraVigilance access as follows:
    - EudraVigilance shall be fully accessible to the competent authorities of the Member States and to the Agency and the European Commission.
    - It shall also be accessible to MAHs to the extent necessary for them to comply with their pharmacovigilance obligations.
    - The Agency shall ensure that healthcare professionals and the public have appropriate levels of access to the EudraVigilance database, while guaranteeing personal data protection.
  - Article 28(c) of Regulation (EC) No 726/2004 further states that
    - The Agency shall make available promptly all suspected adverse reaction reports occurring in the Union to the WHO.

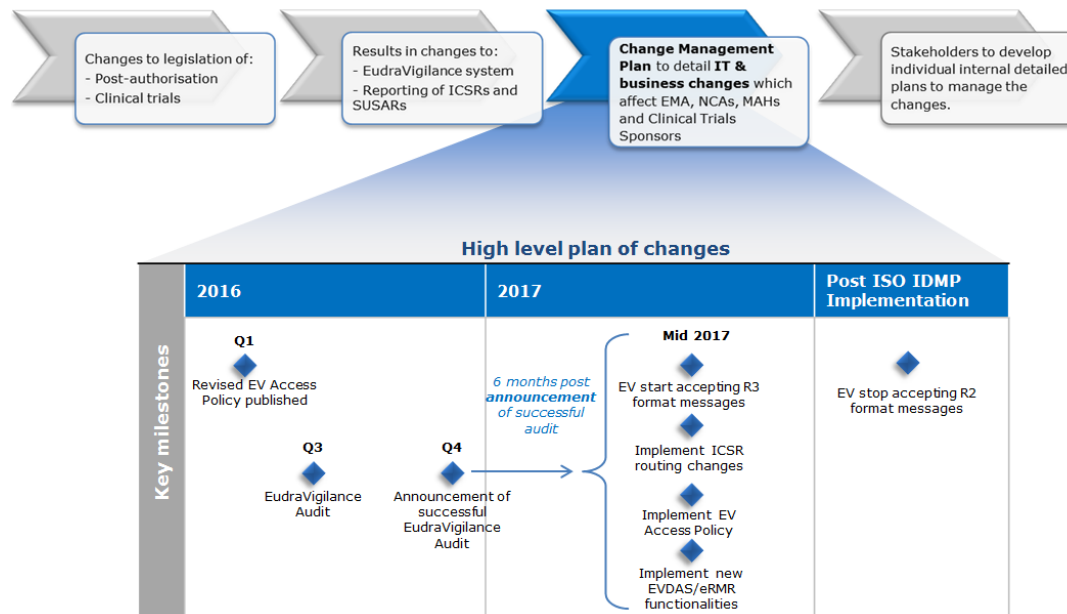
## How is EudraVigilance changing? (1/4)

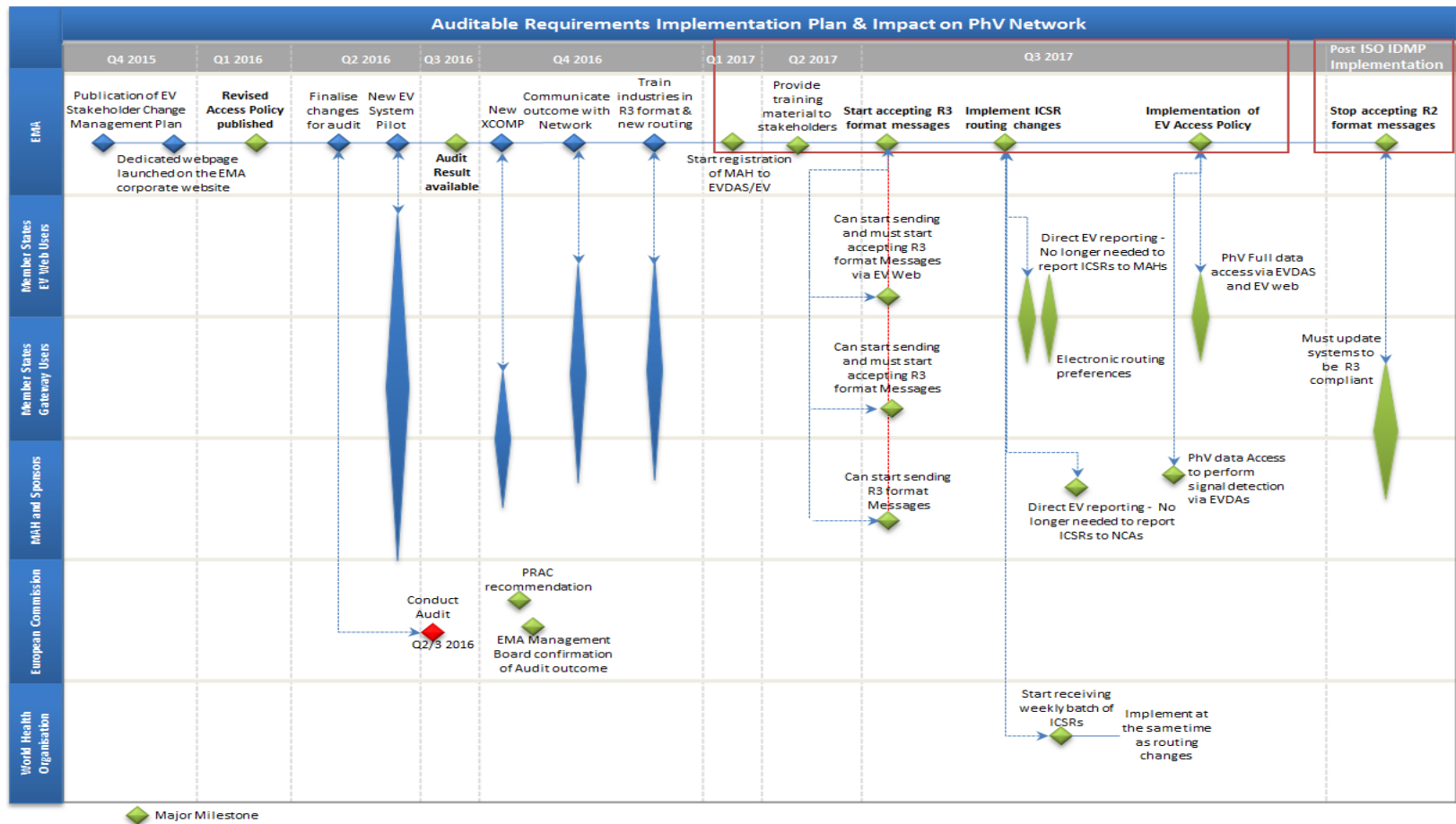
In December 2013, the EMA Management Board endorsed the “**EudraVigilance Auditable requirements**” :

- **Simplified reporting of side effect reports for MAHs with re-routing to NCAs**
- **Provision of reports to WHO** (respecting EU data protection legislation)
- **EV access for MAHs** to conduct product monitoring including signal detection (respecting EU data protection legislation)
- **Publication of data and search availability for healthcare professionals and the public for all medicines** authorised in the EU
- **Compliance with international ICSR standards** (and compatibility with IDMP standards based on Article 57 data) by 1 July 2016 including backwards and forwards conversion tools for E2B(R2)/(R3) messages
- **Conversion of legacy data (> 7 mill. ICSRs currently held in EV)**
- **System performance and scalability** based on increased number of users and volume of data
- **Security** (authentication, authorisation and data transaction to limit the risks of unauthorised access)

# How is EudraVigilance changing? (2/4)

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.





## How is EudraVigilance changing? (3/4)

- Eudravigilance Audit:
  - Functional specifications were prepared by the Agency in collaboration with Member States and the Commission to address required changes
  - Functional specifications were endorsed by EMA Management Board in December 2013 and are subject to an independent audit (“auditable requirements”)
  - EMA Management Board is to announce when Eudravigilance database has achieved full functionality and the system meets the functional specifications based on
    - Independent audit report
    - Recommendation of the Pharmacovigilance Risk Assessment Committee
  - Simplification of adverse reaction reporting will apply six months following the announcement by the Board



## How is EudraVigilance changing? (4/4)

- Key milestones:
  - New EV system stakeholder testing: start End of Q2 2016
    - Scope: to provide opportunity to selected MAHs to test the new functionalities implemented in the EV system.
  - New XCOMP available to stakeholder for testing: Q4 2016
  - Training launch: Q1 2017
  - Go-live: July 2017

## How to prepare for technical changes? (1/3)

- **Implementing ISO ICSR (E2B(R3)) support in MAH's PhV systems:**
  - 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 acknowledgements from EV.
  - Understand and apply new E2B(R3) principles (e.g. seriousness at event level, amendment reports, additional drug role characterisation)
- **Electronic Gateway for ICSR transmission:**
  - current software solution will remain the same, however configuration changes may be needed to support E2B(R3) messages including acknowledgments from EV.
  - As only submissions of ICSRs to the EV will be considered as fulfilling the MAH's legal obligations, MAHs should ensure that modifications to their submission systems are configured and tested well in advance of the planned implementation.

## How to prepare for technical changes? (2/3)

- **MAH Testing:**
  - No more testing with NCAs will be required.
  - MAHs are required to test once they are ready to implement the new system supporting the submission of E2B(R3) ICSRs, using the new simplify testing process with EMA.
  - MAHs should plan to complete any testing of their existing systems 6 to 3 months prior to the new system going live in order to give time for any issues to be addressed
- **EV-WEB:**
  - a new version of this application will be released to support E2B(R3) format ICSRs data entry. MAHs should plan to start training of their staff 6 months in advance of the new system being implemented followed by regular refresher training at least 3 months and 2 weeks before implementation.
- **EV Downloading ICSRs concerning MAH's products:**
  - a download tool will be made available in order for MAH to download ICSRs concerning their products.

## How to prepare for technical changes? (3/3)

- **Synergy between the new EV system and ISO IDMP, xEVMPD/Article 57**
- The future use of the ISO IDMP standard in the context of the new ICH E2B(R3) format is further elaborated in the EU Individual Case Safety Report (ICSR) Implementation Guide (EMA/51938/2013 )
- Art.57/xEVMPD database, which contains core data elements from the ISO IDMP standard, serves as the dictionary for medicinal product information until the ISO IDMP standards implementation
- For the ISO IDMP standards and terminologies, an incremental introduction is planned over time taking into account the migration of the existing xEVMPD/Article 57 content as the starting point
- Please refer to dedicated webpage “Implementation of the ISO IDMP standards” on the EMA website for ongoing activities and next steps  
([http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general\\_content\\_000645.jsp&mid=WC0b01ac058078fbe2](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000645.jsp&mid=WC0b01ac058078fbe2))

## How to prepare for Business process changes? (1/3)

- **Centralised reporting of ICSRs to EudraVigilance:**

- MAH will need to ensure that all reportable ICSRs are submitted to EudraVigilance only, including EEA non-serious within 90 days.
- Planning should be put in place to ensure MAHs are ready to report directly to EudraVigilance prior to move to centralised reporting .
- MAHs using EV-WEB 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.

## How to prepare for Business process changes? (2/3)

- **MAH Signal validation and management process:**

- MAHs will have the legal obligation to monitor data available in EV and to inform the Agency and NCAs about any validated signals they identify.
- 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 (Public consultation planned for 2<sup>nd</sup> quarter of 2016). Other guidance documents, including training materials, will be created and provided as relevant. MAHs should put in place training for their staff concerning this new process.
- MAHs will be granted access to the EudraVigilance Data Analysis system in order to comply with their pharmacovigilance obligations and use the signal detection and analytical reporting functions (e.g. electronic reaction monitoring report and ICSR line listings). MAHs should put in place training for their staff concerning this new tool and register their staff to have access to it.

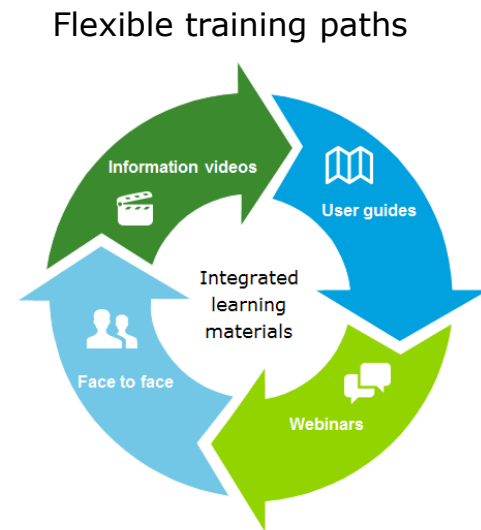


## How to prepare for Business process changes? (3/3)

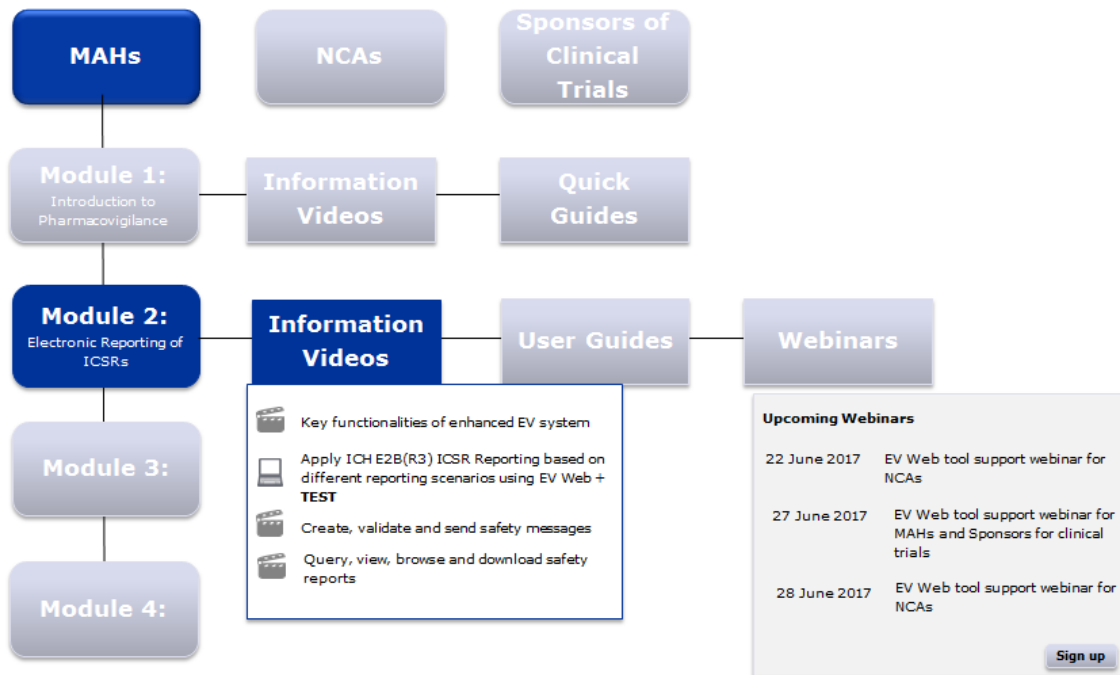
- ***Reporting of SUSARs to EudraVigilance:***
  - Until the Clinical Trials regulation is applicable, there is no change to the current process for the submission of SUSARs for clinical trials approved through the Clinical Trials directive 2001/20/EC.
  - Clinical Trials approved through the Clinical 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.
  - Note: Option will remain 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 these SUSARs to EV.

## What training will be available? (1/2)

- Training should be planned for MAH staff on the new business process and new IT systems at least 6 months prior to implementation in order to be ready once the new EudraVigilance system is implemented.
- Module based online training approach for all users accessible through the EMA website
- The online learning comprises the use of:
  - Information videos,
  - Contextual help in EV Web
  - User Manuals,
  - Demo videos,
  - Competency assessments.
- Limited face to face trainings based on a train the trainer approach might be offered.



# What training will be available? (2/2)





# MAH Learning Path (under finalisation)



E-learning

- Introduction to training offering by the EMA
- New EV functionalities and 2010 pharmacovigilance legislation
- Implementing ISO ICSR/ICH E2B R3
- How to prepare for simplified adverse reaction reporting in the EU
- Revised EV Access policy – how does it impact on MAHs and NCAs
- Revised GVP guidelines – updates and impact
- Medical Literature Monitoring by EMA – what’s new

Guidance

- Revised Signal Detection Guideline
- Revised GVP Module VI
- Revised GVP Module IX

Webinars

Pharmacovigilance Operations Support webinar

## New EudraVigilance Functionalities

- How to register with EudraVigilance and EVDAS
- Introduction to EV system components and system functionalities
- Overview of reporting process for EV users
- EudraVigilance export manager and ICSR download
- EVDAS training for MAHs
- Medical Literature Monitoring service

- MAH’s level 1 access via EVDAS
- EVDAS Report Manual
- Webport user guide for ADR website

EV/EVDAS Functionalities webinar

## New EudraVigilance Functionalities - IT

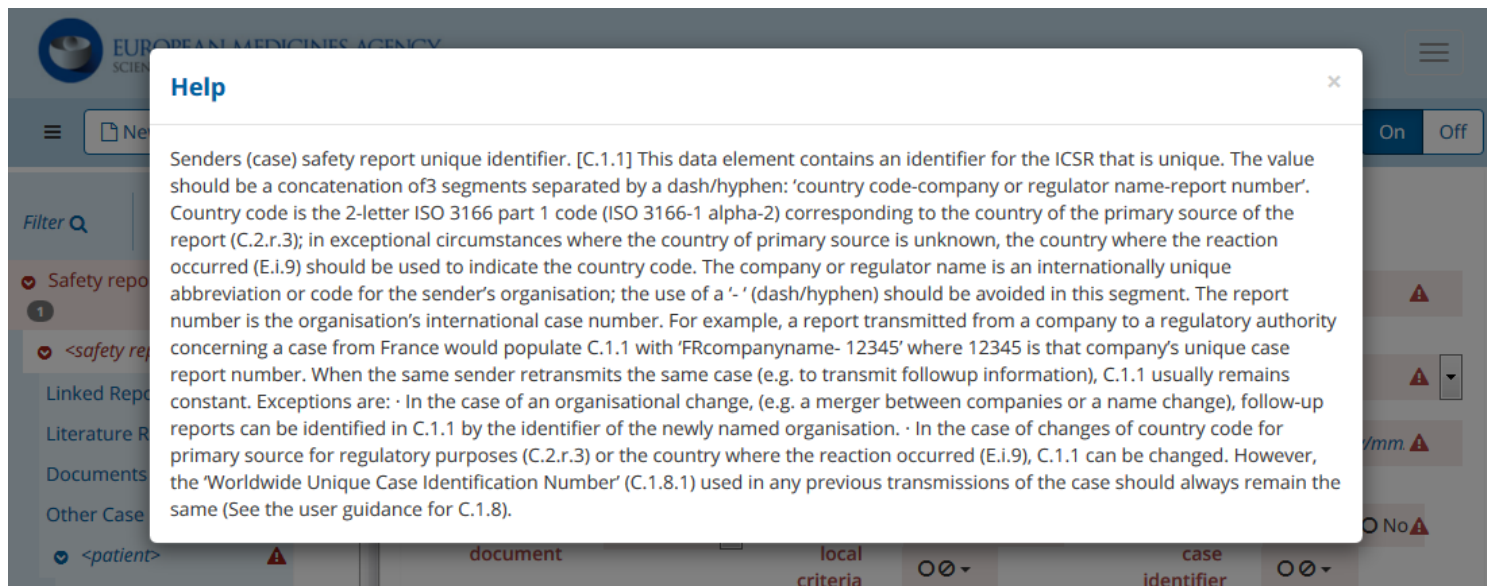
- ISO ICSR standard implementation for IT system developers
- Gateway adaptations for ISO ICSR/ACK message exchange with Eudravigilance
- Instructions on how to test ICSR submissions to EV



# Built-in help in EV web (1/2)

The screenshot displays the European Medicines Agency (EMA) EV web interface. At the top left is the EMA logo and the text 'EUROPEAN MEDICINES AGENCY SCIENCE MEDICINES HEALTH'. A navigation bar contains buttons for 'New', 'Import XML', 'Export XML', 'Validate', and 'Validate & Send'. On the right of this bar is a 'Show Help' toggle set to 'On'. Below the navigation bar, a search filter is visible. A central tooltip provides help for the 'Safety report identifier' field, stating: 'Senders (case) safety report unique identifier. [C.1.1] This data element contains an identifier for the ICSR that is unique. The value should be a concatenation of 3 segments separated by a dash/hyphen: 'country code-company or regulator name-report number'....more'. The main form area shows a 'Safety report identifier' field with a red warning triangle, a 'Creation date' field with the value '2015/12/15 15:22:32', and a 'Report type' field with a red warning triangle and a dropdown arrow. On the left side, there are sections for 'Safety report message:' with a count of 1 and a warning triangle, and 'Linked Reports' with a count of 0.

## Built-in help in EV web (2/2)

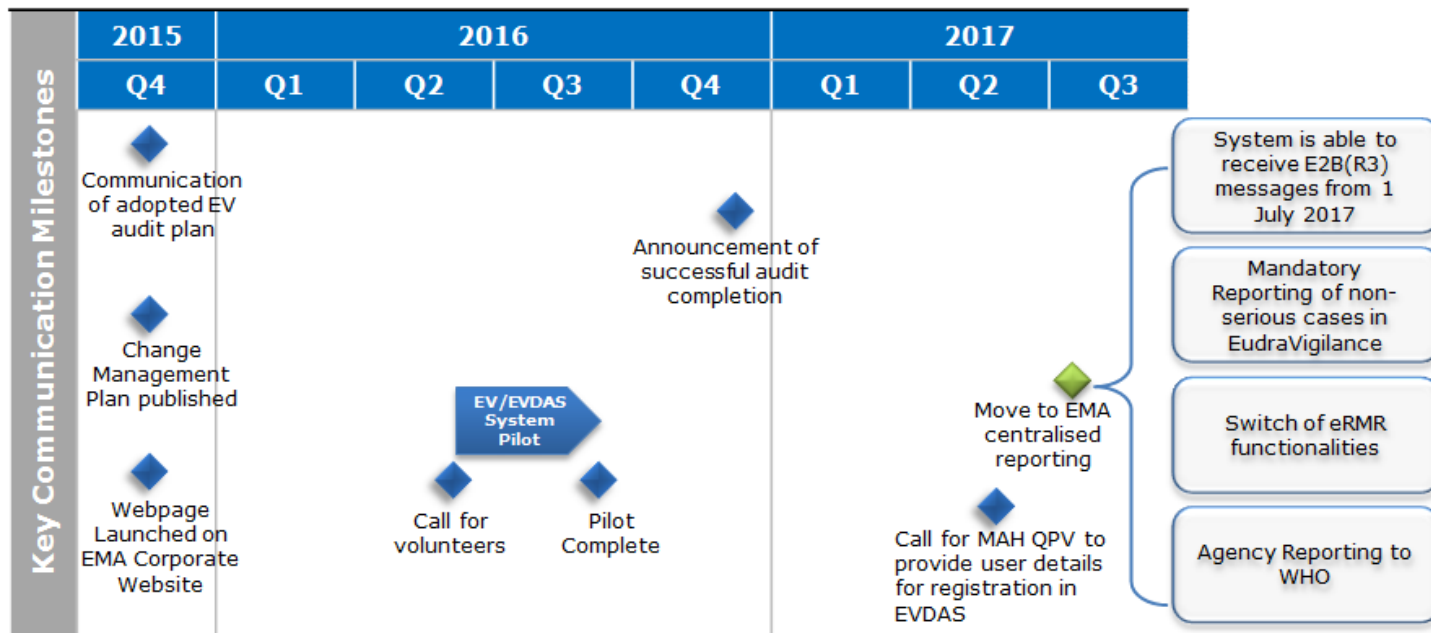


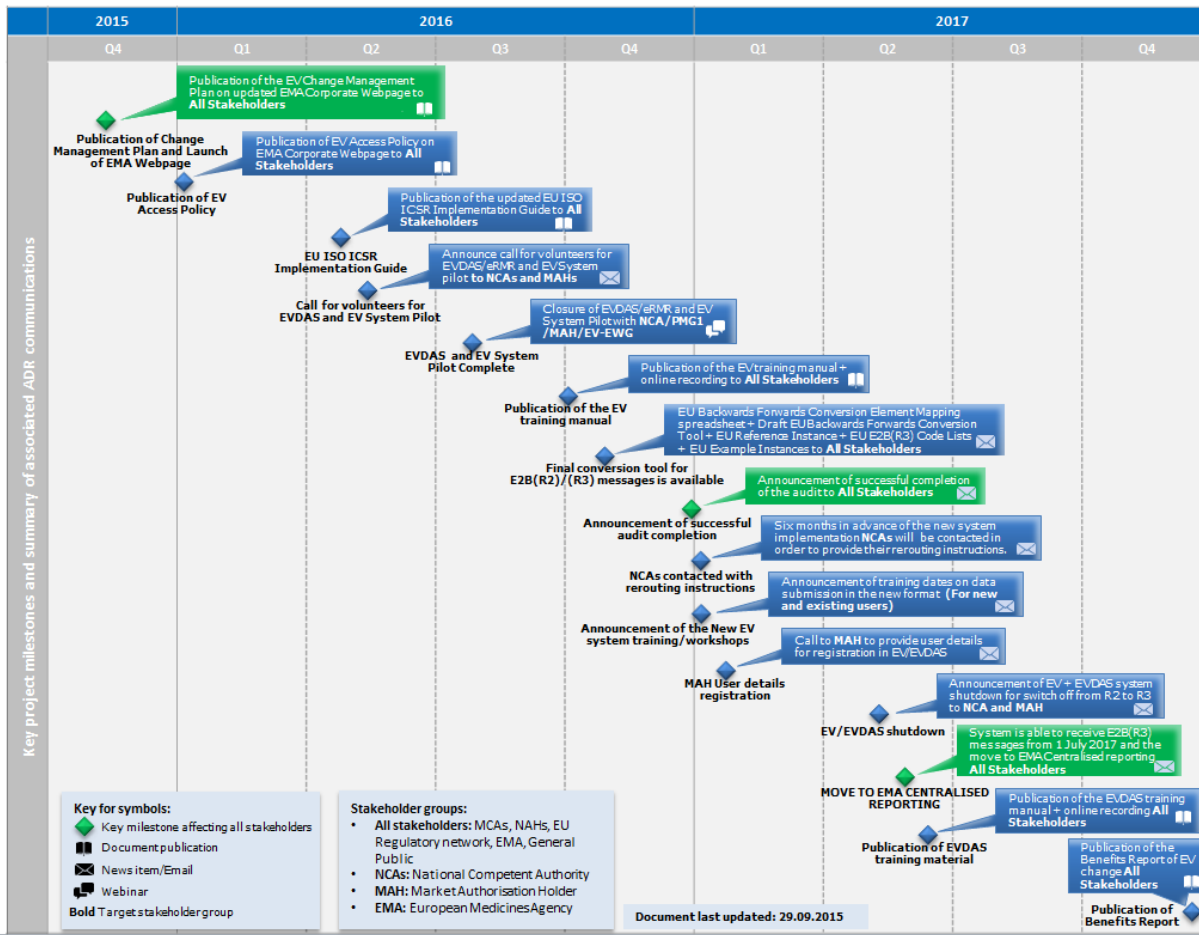
**Help**

Senders (case) safety report unique identifier. [C.1.1] This data element contains an identifier for the ICSR that is unique. The value should be a concatenation of 3 segments separated by a dash/hyphen: 'country code-company or regulator name-report number'. Country code is the 2-letter ISO 3166 part 1 code (ISO 3166-1 alpha-2) corresponding to the country of the primary source of the report (C.2.r.3); in exceptional circumstances where the country of primary source is unknown, the country where the reaction occurred (E.i.9) should be used to indicate the country code. The company or regulator name is an internationally unique abbreviation or code for the sender's organisation; the use of a '-' (dash/hyphen) should be avoided in this segment. The report number is the organisation's international case number. For example, a report transmitted from a company to a regulatory authority concerning a case from France would populate C.1.1 with 'FRcompanyname- 12345' where 12345 is that company's unique case report number. When the same sender retransmits the same case (e.g. to transmit followup information), C.1.1 usually remains constant. Exceptions are: · In the case of an organisational change, (e.g. a merger between companies or a name change), follow-up reports can be identified in C.1.1 by the identifier of the newly named organisation. · In the case of changes of country code for primary source for regulatory purposes (C.2.r.3) or the country where the reaction occurred (E.i.9), C.1.1 can be changed. However, the 'Worldwide Unique Case Identification Number' (C.1.8.1) used in any previous transmissions of the case should always remain the same (See the user guidance for C.1.8).

## What communication will be available?

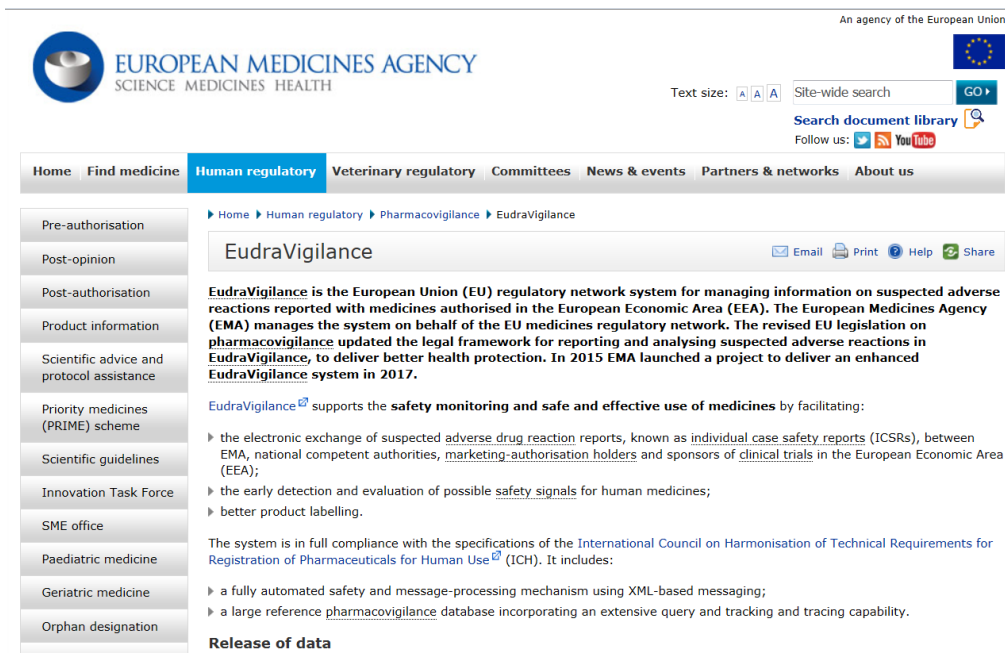
MAHs should consider developing a communication plan to ensure that the necessary information is circulated within their own organisation and with other organisations that they work with.





# Where to find further guidance and detailed information? (1/3)

- Dedicated EudraVigilance webpage at the Agency's corporate website



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## EudraVigilance

Email Print Help Share

**EudraVigilance is the European Union (EU) regulatory network system for managing information on suspected adverse reactions reported with medicines authorised in the European Economic Area (EEA). The European Medicines Agency (EMA) manages the system on behalf of the EU medicines regulatory network. The revised EU legislation on pharmacovigilance updated the legal framework for reporting and analysing suspected adverse reactions in EudraVigilance, to deliver better health protection. In 2015 EMA launched a project to deliver an enhanced EudraVigilance system in 2017.**

EudraVigilance supports the **safety monitoring and safe and effective use of medicines** by facilitating:

- ▶ the electronic exchange of suspected adverse drug reaction reports, known as individual case safety reports (ICSRs), between EMA, national competent authorities, marketing-authorisation holders and sponsors of clinical trials in the European Economic Area (EEA);
- ▶ the early detection and evaluation of possible safety signals for human medicines;
- ▶ better product labelling.

The system is in full compliance with the specifications of the International Council on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use<sup>®</sup> (ICH). It includes:

- ▶ a fully automated safety and message-processing mechanism using XML-based messaging;
- ▶ a large reference pharmacovigilance database incorporating an extensive query and tracking and tracing capability.

**Release of data**

<http://www.ema.europa.eu>










# Where to find further guidance and detailed information? (2/3)

## ICH implementation guidance

Documentation	Description
<a href="#">ICH Implementation guide package</a>	A set of documents including the ICH ICSR implementation guide, backwards and forwards compatibility recommendations and element mapping.
<a href="#">ICH E2B(R3) Questions and answers</a>	A question-and-answer document relevant for technical E2B questions.

## EU implementation guidance

Documentation	Description
 <a href="#">EU ICSR Implementation Guide</a>	A guide describing the additional EU-specific requirements to generate a valid ICSR and message acknowledgment to implement EN ISO ICSR in accordance with ICH E2B(R3).
 <a href="#">EU ICSR implementation guide business rules spreadsheet</a>	This spreadsheet includes all the ICH E2B(R3) and EU specific business rules in a format to help system developers.
 <a href="#">EU backwards forwards conversion element mapping spreadsheet</a>	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).
 <a href="#">Draft EU BFC conversion</a>	The ICH backwards-forwards conversion tool updated to include additional EU-specific data fields.
 <a href="#">EU E2B(R3) code lists</a>	The list of codes for EU-specific data fields.
 <a href="#">EU reference instances</a>	ICH reference instances amended to include EU-specific data fields.
 <a href="#">EU example instances</a>	Additional example instances to be used for testing E2B(R3) transmissions to the <a href="#">EudraVigilance</a> system.

<http://www.ema.europa.eu>



# Where to find further guidance and detailed information? (3/3)

  
**EUROPEAN MEDICINES AGENCY**  
SCIENCE MEDICINES HEALTH

26 October 2015  
EMA/797114/2014  
Information Management Division

## EudraVigilance stakeholder change management plan

Consultation of Project Maintenance Group 1	15 July 2015
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
Consultation of the Pharmacovigilance Risk Assessment Committee (PRAC)	7-10 September 2015
Implementation Group (IG) for information	14 September 2015
IT Directors for information	22 October 2015
EU Telematic Management Board (EUTMB) for information	15 September 2015
Endorsement by European Risk Management Facilitation Group (ERMS-FG)	12 October 2015
Heads of Medicines Agencies (HMA) for information	22 October 2015

<http://www.ema.europa.eu>



## Discussion

Few questions to start the discussion:

- Is the proposed training strategy supported by the Industry?
- Is the EMA communication strategy supported by the Industry?
- Any other suggestions to better prepare industry to changes?



# Thank you for your attention

## Further information

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