



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

# EV-M5b - EVDAS training for Marketing Authorisation Holders

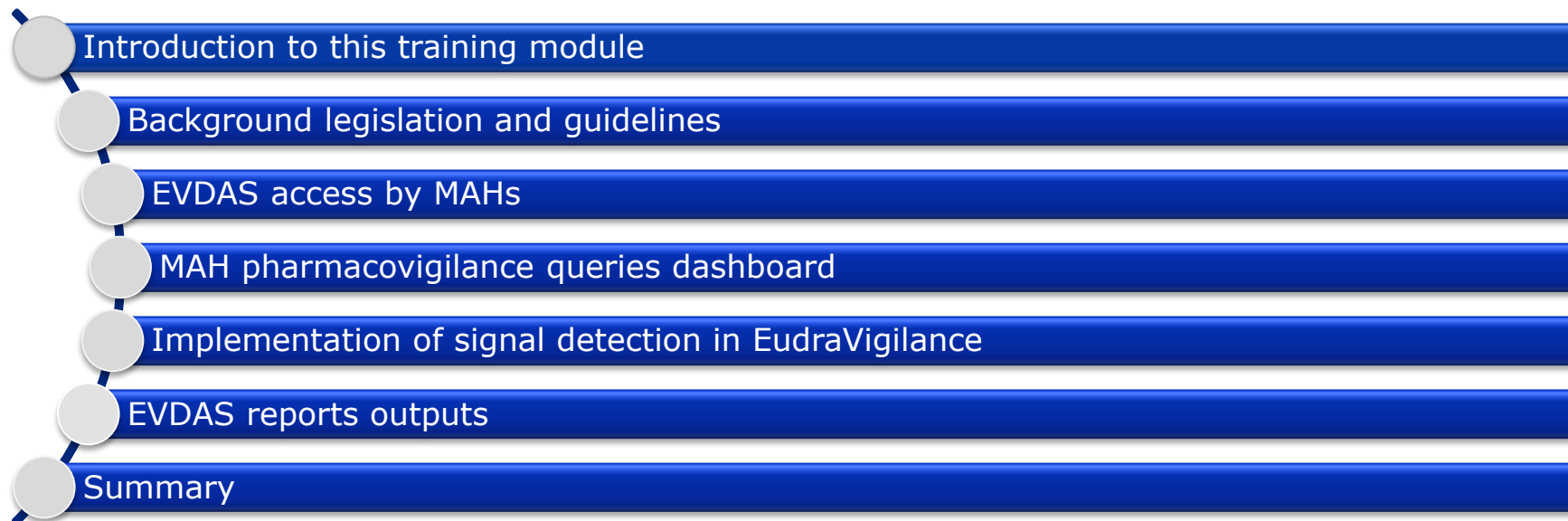
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Overview of the EVDAS functionalities and level 1 access to EudraVigilance by Marketing Authorisation Holders to comply with their pharmacovigilance obligations with regards to signal detection and management





# Content Summary

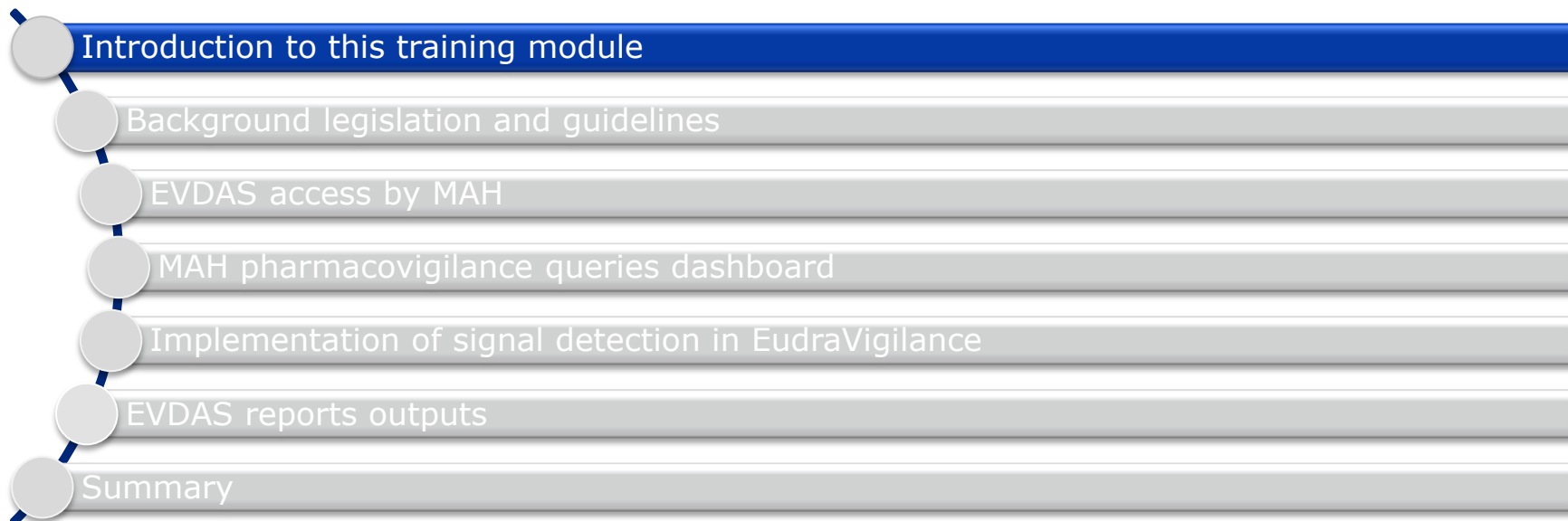




# Version 0.0



# Content Summary





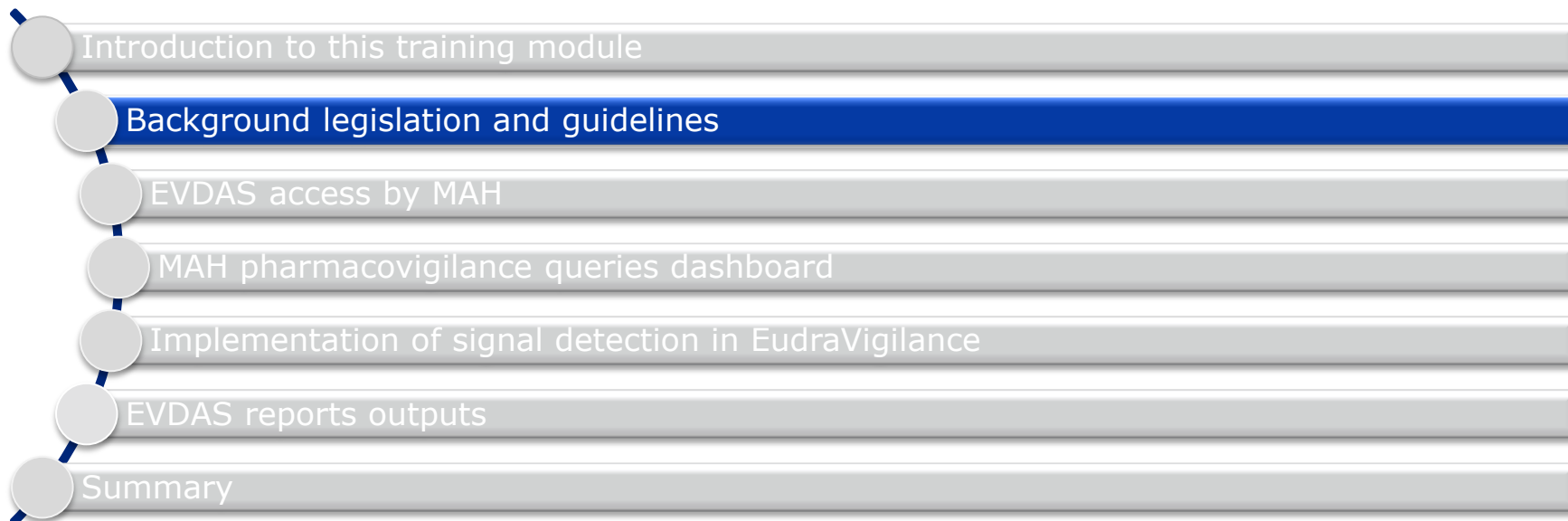
## Introduction: Context EV-M5b

- Target audience for this training module:
  - Marketing Authorisation Holders (MAHs) in the European Economic Area (EEA)

# Introduction: Learning Objectives

- At the end of this module participants will be able to:
  - Understand the access to EudraVigilance provided via the EudraVigilance Data Analysis System (EVDAS).
  - Be familiar with the EVDAS user interface.
  - Be able to retrieve electronic Reaction Monitoring Reports (eRMRs), Line Listings and ICSR forms from EVDAS.
  - Understand the system functionalities for manipulating reports' outputs.
  - Understand how signal detection is implemented in EudraVigilance.
  - Understand the outputs of the EVDAS reports.

# Content Summary





## Section Overview

- In this section you will obtain understanding of the:
  - Main legislative requirements for monitoring the EudraVigilance database.
  - Which are the guidelines for signal detection and management in the EU.





# EU Legislative Requirements



Updated pharmacovigilance legislation published in 2010 established the principles for monitoring the data in EudraVigilance and for the revision of the access to the database.



# EU Legislative Requirements



Commission Implementing Regulation (IR) 520/2012 provides with the specific roles and responsibilities for monitoring EudraVigilance and established the different steps in the signal management process.



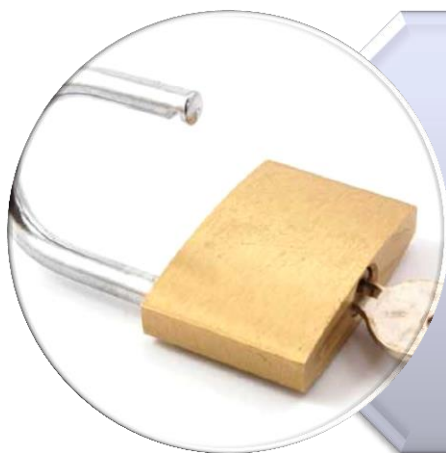
# EU Legislative Requirements



Within the minimum requirements for monitoring EudraVigilance (Chapter III, IR), the IR states that MAHs, NCAs and the Agency shall ensure the continuous monitoring of EudraVigilance with a frequency proportionate to the risks and the need for additional information.

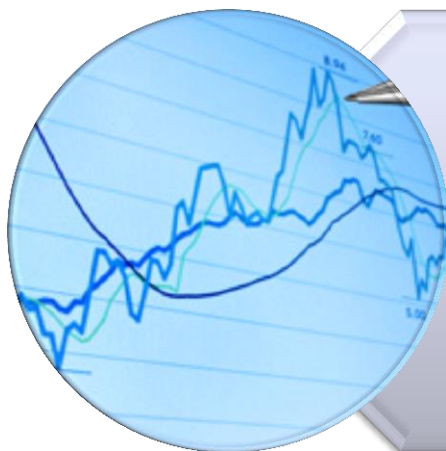


# EU Legislative Requirements



MAHs shall monitor EudraVigilance to the extent that they have access to the database.

# EU Legislative Requirements



Signal detection within EudraVigilance shall be complemented by statistical analysis, where appropriate.



# EU Legislative Requirements



The Agency shall ensure appropriate support for the monitoring of EudraVigilance by MAHs.



Details of the legal provisions that form the basis for the new EudraVigilance functionalities are provided in training module:

PhV-M1 New EudraVigilance Functionalities and the 2010 pharmacovigilance legislation – preparing for change



# EU Guidelines

- GVP Module IX on Signal Management is currently undergoing a major revision.
- The Module was released for public consultation and will be finalised in 2017.

➤ Stakeholders should consult the final Module IX once adopted.



1 4 August 2016  
2 EMA/827661/2011 Rev 1\* DRAFT for public consultation

3 Guideline on good pharmacovigilance practices (GVP)  
4 Module IX – Signal management (Rev 1)

Date of coming into effect of first version	2 July 2012
Draft Revision 1* finalised by the Agency in collaboration with Member States	30 June 2016
Draft Revision 1 agreed by the European Risk Management Facilitation Group (ERMS FG)	18 July 2016
Draft Revision 1 adopted by Executive Director	4 August 2016
Release for public consultation	8 August 2016
End of consultation (deadline for comments)	14 October 2016
Anticipated date for coming into effect of Revision 1	Q1 2017

5  
6 \*Note: Revision 1 is a major revision with modifications throughout based on experience gained over  
7 the past 4 years, and guidance on signals validated by marketing authorisation holders. It contains the  
8 following:  
9 - Revised definition and process for emerging safety issues, previously addressed in GVP Module VI  
10 (IX.C.3.1.);  
11 - Streamlined information on scientific aspects of signal management (IX.B.2. to 4.), statistical aspects  
12 now addressed in Addendum I;  
13 - Clarifications on terminology (IX.A.1.), roles and responsibilities (IX.C.1.) and processes (IX.  
14 Appendix 1);  
15 - Criteria for access by marketing authorisation holders to case narratives held in EudraVigilance, with  
16 reference to Revision 2 of the EudraVigilance Access Policy (IX.C.2.1.);  
17 - Updated guidance on the periodicity of monitoring of EudraVigilance data (IX.C.2.2.);  
18 - Procedural options for signals validated by marketing authorisation holders (IX.C.3.).  
19  
20

See websites for contact details

European Medicines Agency [www.ema.europa.eu](http://www.ema.europa.eu)  
Heads of Medicines Agencies [www.hma.eu](http://www.hma.eu)

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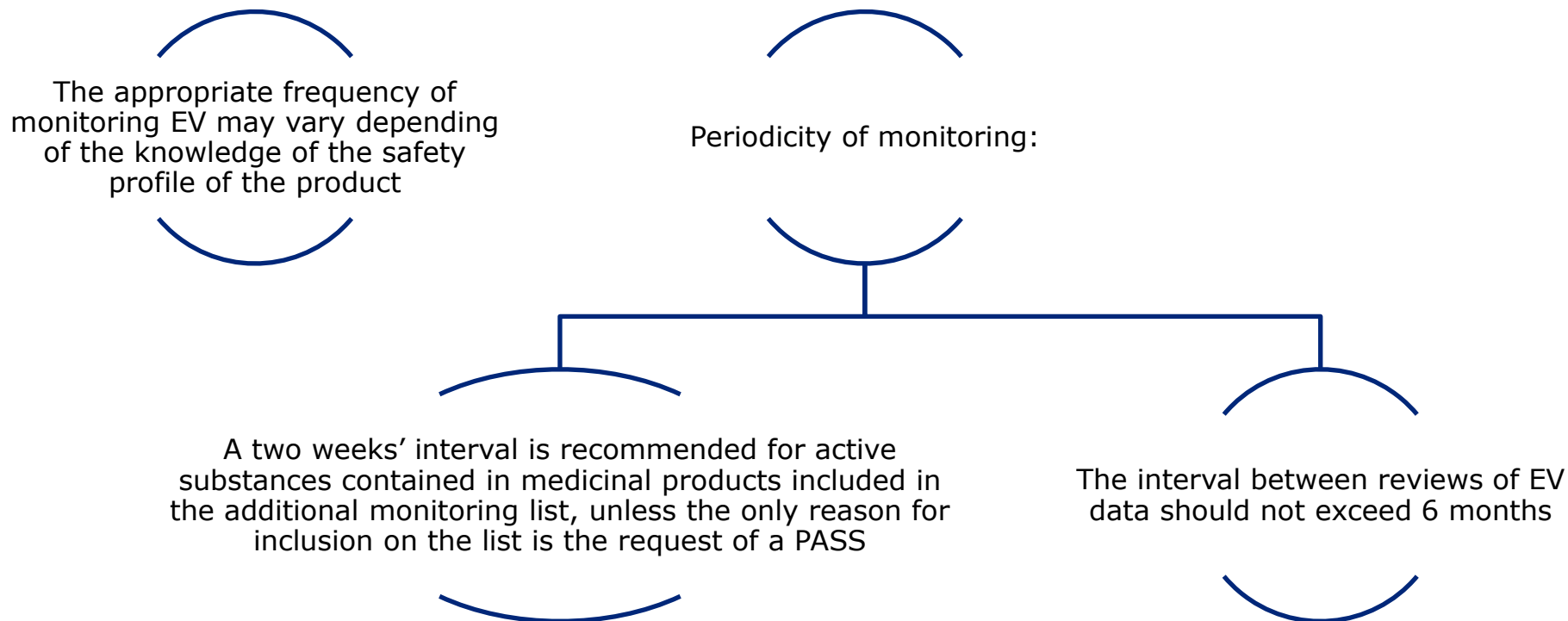
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# GVP Module IX - Signal Management Rev 1 – DRAFT

This revision incorporates the following updates:

- Revised definition and process for emerging safety issues, previously addressed in GVP Module VI.
- Streamlined information on scientific aspects of signal management.
- Clarifications on terminology, roles and responsibilities and processes.
- Criteria for access by MAHs to case narratives held in EudraVigilance.
- Updated guidance on the periodicity of monitoring of EudraVigilance data.
- Procedural options for signals validated by MAHs.





# EU Guidelines

- Addendum I to GVP Module IX provides with the principles and general methodological aspects of signal detection from spontaneous reports of suspected adverse reactions.
- This addendum is also subject to finalisation and adoption in 2017.



1 4 August 2016  
2 EMA/209012/2015 DRAFT for public consultation

3 [Guideline on good pharmacovigilance practices \(GVP\)](#)  
4 Module IX Addendum I – Methodological Aspects of Signal Detection from  
5 Spontaneous Reports of Suspected Adverse Reactions

Draft finalised by the Agency in collaboration with Member States for submission to ERMS FG	30 June 2016
Draft agreed by ERMS FG	18 July 2016
Draft adopted by Executive Director	4 August 2016
Released for public consultation	8 August 2016
End of consultation (deadline for comments)	14 October 2016
Anticipated date for coming into effect of final version	Q1 2017

6

Comments should be provided using this [template](#). The completed comments form should be sent to [gvp@ema.europa.eu](mailto:gvp@ema.europa.eu)

7

8 **Note:** This guidance extends and updates some of the information given in the Guideline on the Use of  
9 Statistical Signal Detection Methods in the EudraVigilance Data Analysis System (EMA/106464/2006  
10 rev. 1) and supersedes the previous advice in the areas addressed by the new guidance.

11

12

See websites for contact details

European Medicines Agency [www.ema.europa.eu](http://www.ema.europa.eu)  
Heads of Medicines Agencies [www.hma.eu](http://www.hma.eu)

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# EU Guidelines

- The EMA in collaboration with the Member States has published a guideline on screening adverse drug reactions in EudraVigilance.
  - The guideline updates and supersedes the previous guideline on the use of statistical signal detection in EudraVigilance (EMA/106464/2006 rev. 1).
  - Describes the methods and practicalities for statistical signal detection in EudraVigilance.
  - Includes the changes incorporated from research activities including PROTECT (<http://www.imi-protect.eu/>)
- Further details on the implementation of signal detection in EudraVigilance are provided in the relevant section within this training Module.



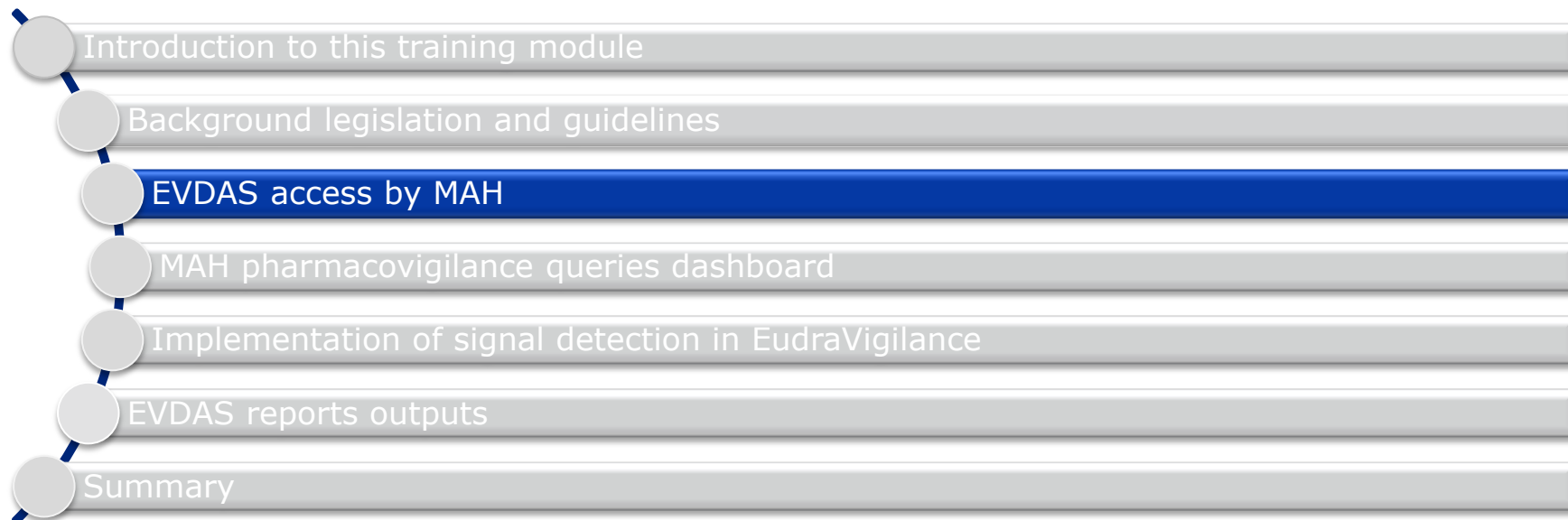
## Section Summary

**In this section you obtained an understanding of:**

- Main legal requirements for monitoring the EudraVigilance database.
- EU guidelines on Signal Management.



# Content Summary





## Section Overview

- In this section you will obtain understanding of the:
  - Main principles for the access to the EVDAS by MAHs to comply with their pharmacovigilance obligations.
  - How to access EVDAS.

# The EudraVigilance Access Policy

- The access to EudraVigilance data is established in the EudraVigilance access policy.
- The EudraVigilance access policy was revised as a result of the 2010 pharmacovigilance legislation and was adopted by the EMA Management Board in December 2015.
- Revision of the access policy will enter into force six months following the announcement by the Management Board of the Agency that based on an independent audit report, the EudraVigilance database has achieved full functionality.



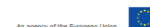
17 December 2015  
EMA/759287/2009 Revision 2  
Inspections and Human Medicines Pharmacovigilance Division

European Medicines Agency policy on access to EudraVigilance data for medicinal products for human use (EudraVigilance Access Policy)

Start of public consultation	4 August 2014
End of public consultation	15 September 2014
Final draft agreed by Project Team 1 "Collection of key information on medicines" of the EMA/Member States governance structure for the implementation of the pharmacovigilance legislation	September 2015
Final draft submitted to the EudraVigilance Expert Working Group for information	23 September 2015
Final draft agreed by Pharmacovigilance Risk Assessment Committee (PRAC)	5-8 October 2015
Final draft agreed by Project Co-ordination Group of the EMA/Member States governance structure for the implementation of the pharmacovigilance legislation	12 October 2015
Final draft agreed by the European Risk Management Facilitation Group (ERMS-FG)	12 October 2015
Final draft agreed by the Committee for Human Medicinal Products (CHMP) and the Co-ordination group for Mutual recognition and Decentralised procedures - human( CMD-h)	19-21 October 2015
Final draft submitted to IT Directors for information	22 October 2015
Final draft submitted to Heads of Medicines Agencies Human (HMA-h) for information	21-23 October 2015
Final draft adopted by the EMA Management Board	16-17 December 2015

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Send a question via our website [www.ema.europa.eu/contact](http://www.ema.europa.eu/contact)

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Details of the revision of the EudraVigilance Access Policy and how stakeholders obtain access to the database are provided in the following training module:

**PhV-M4 Revised EudraVigilance Access Policy: Impact on Stakeholders**

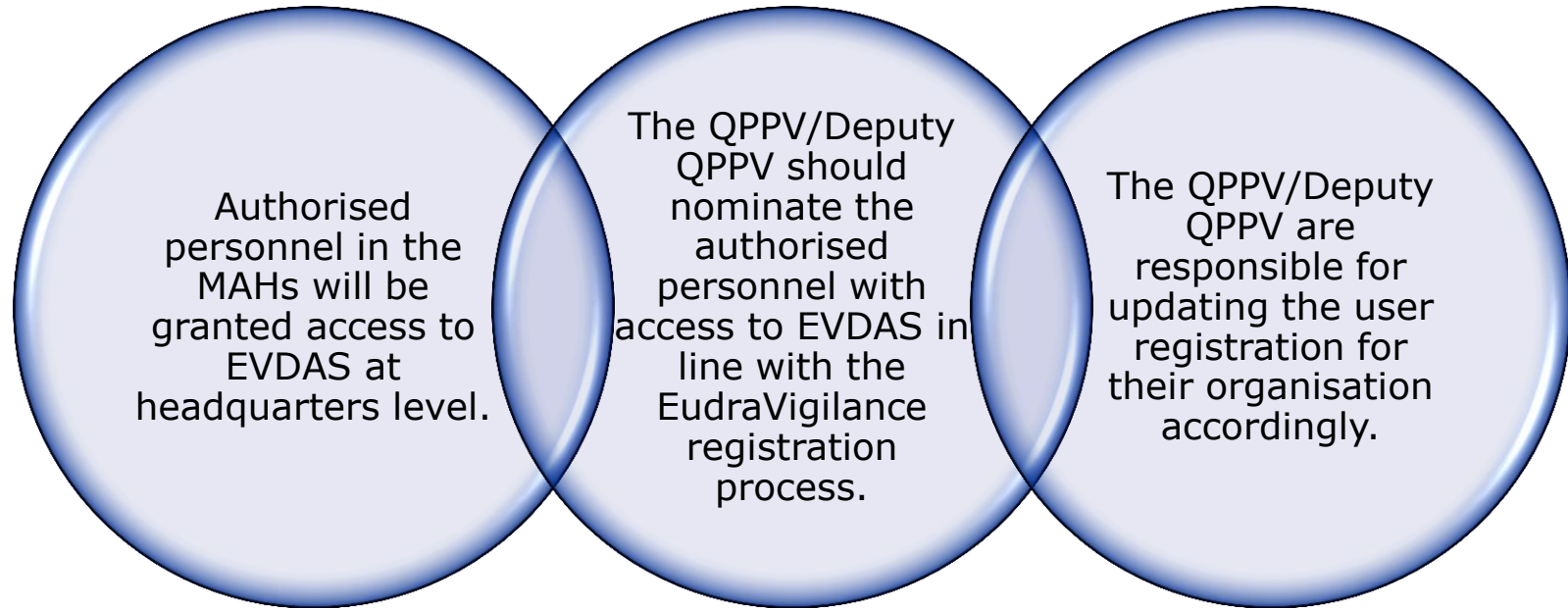


# EudraVigilance access policy

- MAHs will be provided with access to defined ICSR data element sets in support of their signal detection and pharmacovigilance activities
- EVDAS access will be provided according to Level 1 access for Stakeholders Group III.

Stakeholder Group III	
Marketing Authorisation Holders	
<ul style="list-style-type: none"><li>• EVWEB including ICSR Export Manager</li></ul>	<ul style="list-style-type: none"><li>• ICSRs electronic (XML) format</li></ul>
<ul style="list-style-type: none"><li>• EVDAS</li></ul>	<ul style="list-style-type: none"><li>• e-RMRs and active substance groupings</li><li>• ICSR line listings</li><li>• ICSR forms</li></ul>
	<ul style="list-style-type: none"><li>• ICSR line listings (based on core ICSR data elements)</li><li>• ICSR forms (for individual case review)</li></ul>

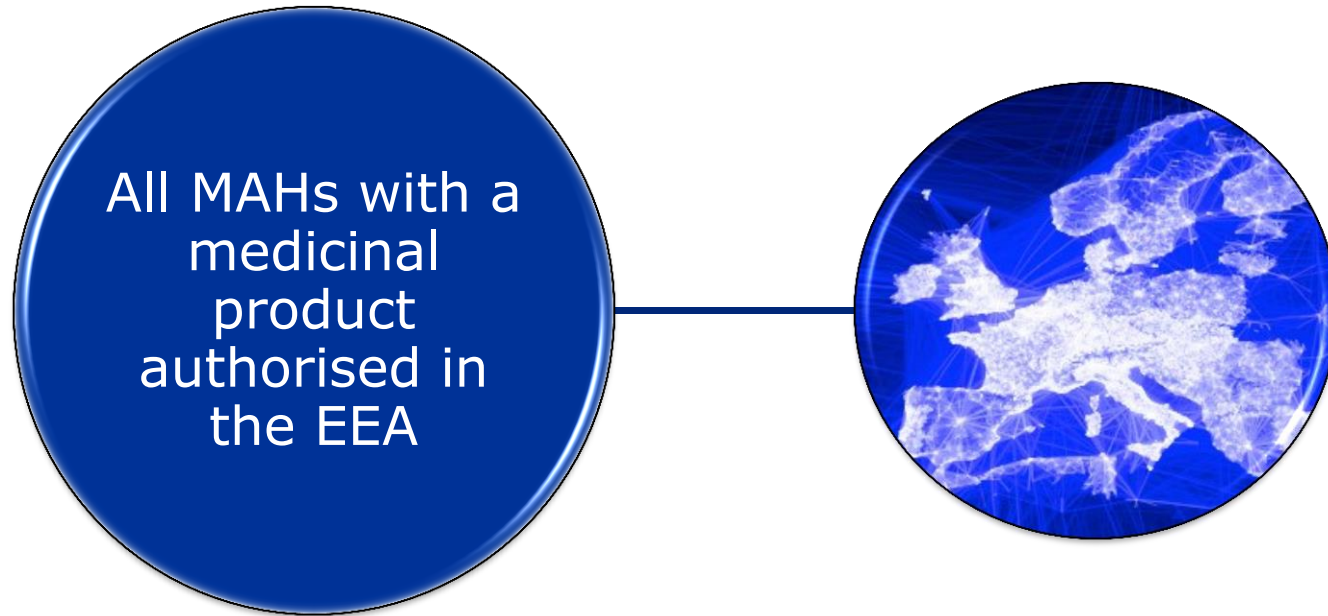
This training Module will focus on the EudraVigilance access to MAHs via EVDAS





Steps and process to be followed for the EudraVigilance and EVDAS registration including how to maintain the registered user information are provided in the following training module:

EV- M1 How to register with EudraVigilance and EVDAS



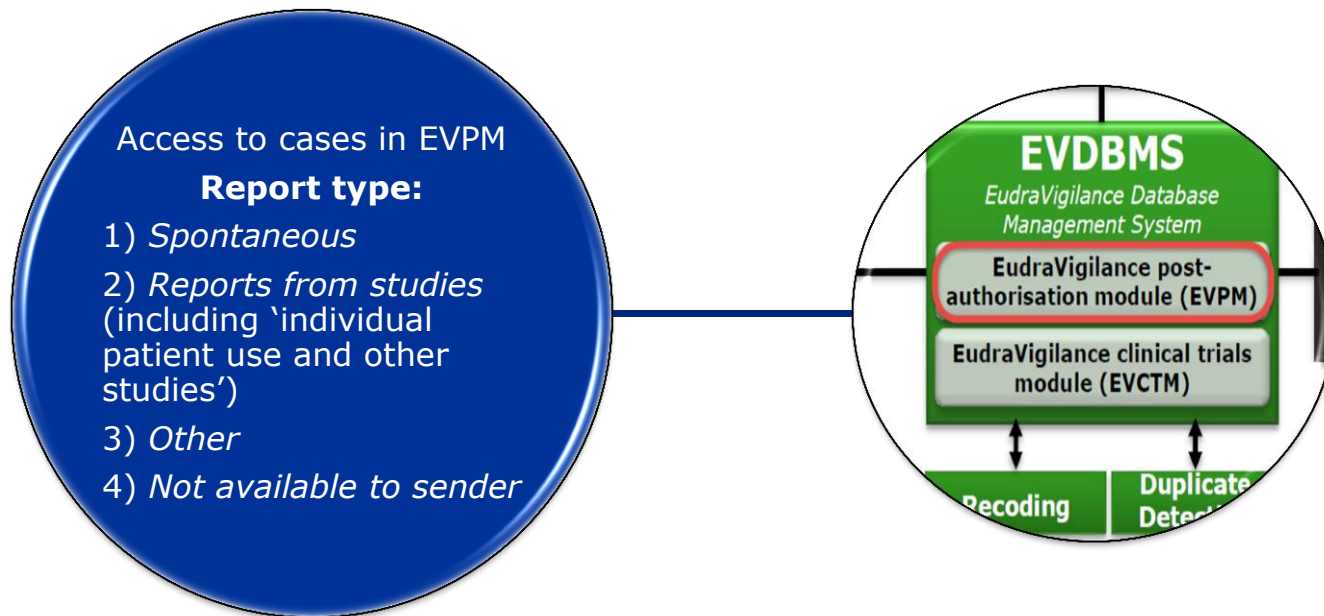


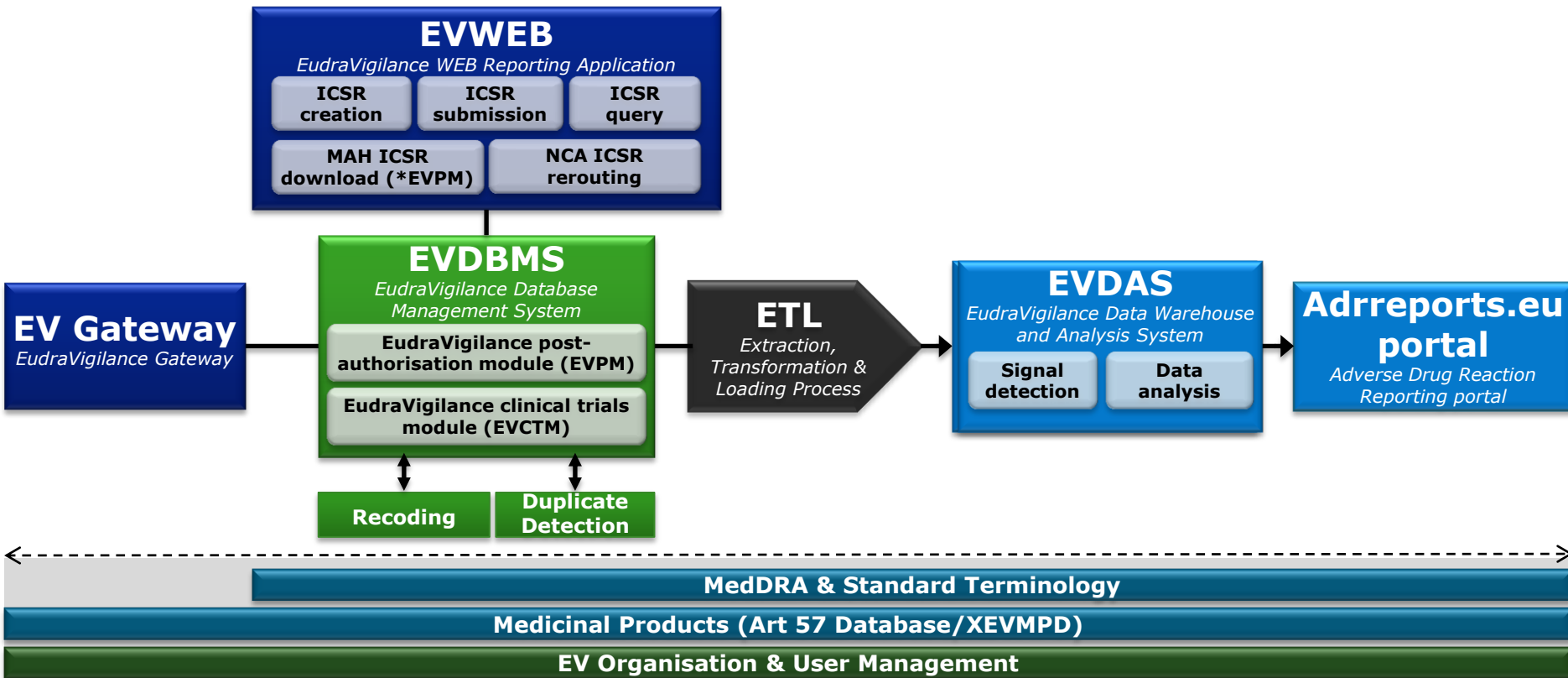
All the substances  
contained in  
products authorised  
in the EEA that have  
been coded as  
suspect/interacting  
in at least one post-  
authorisation ICSR













Full description of the EudraVigilance system components and system functionalities are provided in the training module:

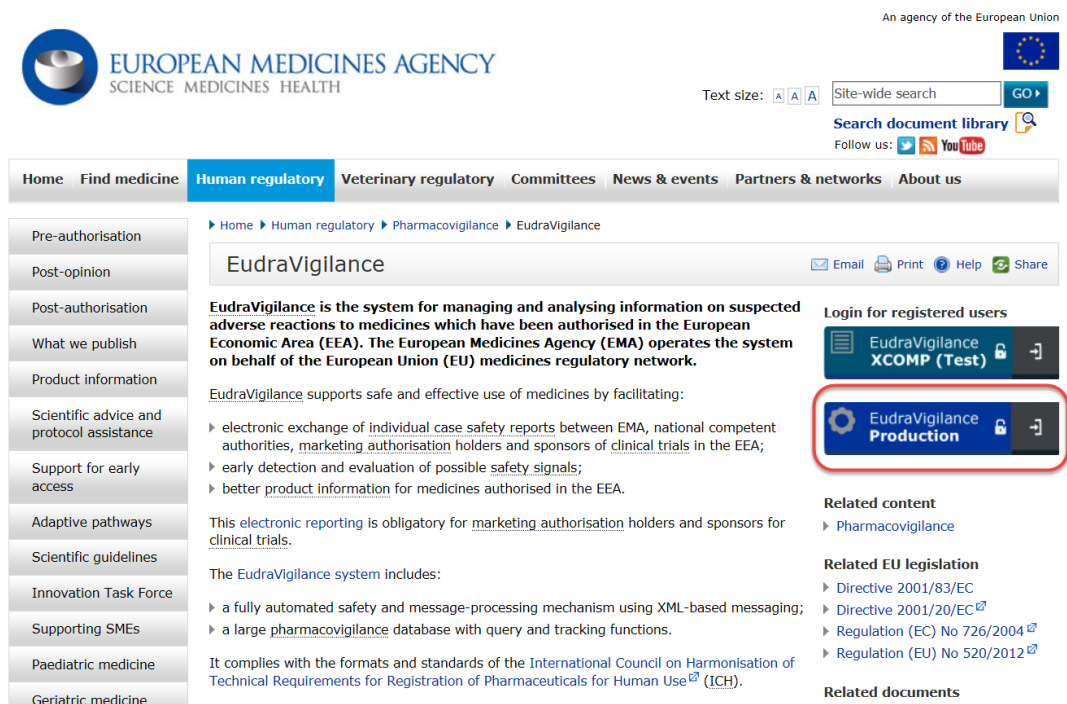
EV- M2 Introduction to EV system components and system functionalities

## Accessing EVDAS



Users registered in EVDAS will be able to access the system through the following ways:

- Access via the EudraVigilance page on the EMA corporate website
- Access via EVDAS welcome page

[http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general\\_content\\_000679.jsp&mid=WC0b01ac05800250b5](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000679.jsp&mid=WC0b01ac05800250b5)



The screenshot shows the EudraVigilance website interface. At the top, there is the European Medicines Agency logo and the text "EUROPEAN MEDICINES AGENCY SCIENCE MEDICINES HEALTH". To the right, it says "An agency of the European Union" with the EU flag. Below this is a search bar with the text "Site-wide search" and a "GO" button. There are also social media links for Twitter, YouTube, and Facebook. A navigation menu includes "Home", "Find medicine", "Human regulatory" (which is highlighted), "Veterinary regulatory", "Committees", "News & events", "Partners & networks", and "About us". On the left side, there is a vertical menu with links to "Pre-authorisation", "Post-opinion", "Post-authorisation", "What we publish", "Product information", "Scientific advice and protocol assistance", "Support for early access", "Adaptive pathways", "Scientific guidelines", "Innovation Task Force", "Supporting SMEs", "Paediatric medicine", and "Geriatric medicine". The main content area is titled "EudraVigilance" and contains the following text: "EudraVigilance is the system for managing and analysing information on suspected adverse reactions to medicines which have been authorised in the European Economic Area (EEA). The European Medicines Agency (EMA) operates the system on behalf of the European Union (EU) medicines regulatory network." Below this, it states "EudraVigilance supports safe and effective use of medicines by facilitating:" followed by a list of bullet points: "electronic exchange of individual case safety reports between EMA, national competent authorities, marketing authorisation holders and sponsors of clinical trials in the EEA;", "early detection and evaluation of possible safety signals;", and "better product information for medicines authorised in the EEA." Further down, it says "This electronic reporting is obligatory for marketing authorisation holders and sponsors for clinical trials." and "The EudraVigilance system includes:" followed by a list of bullet points: "a fully automated safety and message-processing mechanism using XML-based messaging;" and "a large pharmacovigilance database with query and tracking functions." At the bottom, it states "It complies with the formats and standards of the International Council on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH)." On the right side of the main content area, there is a "Login for registered users" section with two buttons: "EudraVigilance XCOMP (Test)" and "EudraVigilance Production". The "EudraVigilance Production" button is highlighted with a red rectangle. Below this, there is a "Related content" section with a link to "Pharmacovigilance", a "Related EU legislation" section with links to "Directive 2001/83/EC", "Directive 2001/20/EC", "Regulation (EC) No 726/2004", and "Regulation (EU) No 520/2012", and a "Related documents" section.



Human Restricted

Logged In

(EVHUMANWT)  
Human Production

EV Services

▶ EVWEB

▶ xEVMPD Export

▶ xEVMPD Bulk update

▶ EV Data Warehouse

▶ EV Post

Welcome to the restricted area of the EudraVigilance website

To continue, please select one of the available functionalities from the menus on the left of the screen

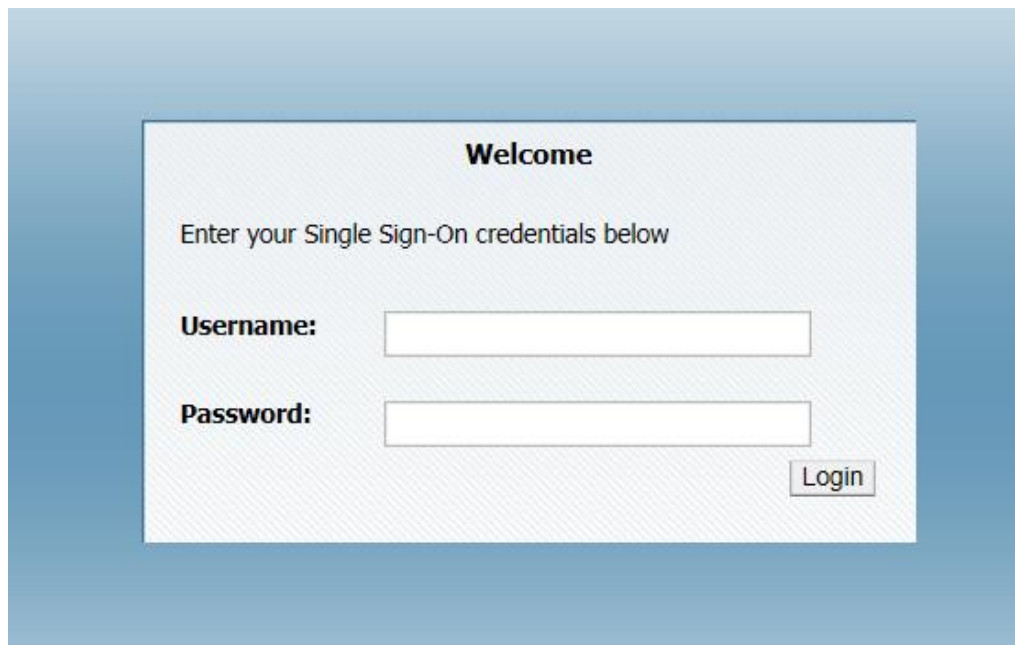
## Accessing EVDAS

- Access via EVDAS welcome page:

[https://bi.ema.europa.eu/analytics/saw.dll?Dashboard&PortalPath=%2Fshared%2FMAHPharmacovigilanceQueryLibrary%2F\\_portal%2FMAHPharmacovigilanceQueries](https://bi.ema.europa.eu/analytics/saw.dll?Dashboard&PortalPath=%2Fshared%2FMAHPharmacovigilanceQueryLibrary%2F_portal%2FMAHPharmacovigilanceQueries)



# Accessing EVDAS

A screenshot of the EVDAS login interface. It features a light blue background with a central white box containing the login form. The form has a title 'Welcome', a prompt to enter Single Sign-On credentials, and fields for 'Username:' and 'Password:'. A 'Login' button is located at the bottom right of the form.

**Welcome**

Enter your Single Sign-On credentials below

**Username:**


**Password:**

Login



Welcome | [electronic Reaction Monitoring Report - eRMR](#) | [Line listing](#) | [Active substance grouping](#)

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**Dashboard Description**  
This dashboard supports the Active substance / Reaction analysis for one or more Active substances selected by the user.  
It contains the following reports: the electronic Reaction Monitoring Report (ad-hoc and fixed reference period), the Individual case line listing and the Active substance grouping.

## MAH Pharmacovigilance Queries (v01.00.00)

The MAH Pharmacovigilance Queries is the central repository of ICSR and medicinal product data from where these reports are being generated

v01.00.00

Current MedDRA version is 18.1

Data up to and including 18-10-2016

For any technical support, please contact [EMA EVDAS support](#).

EMA - European Medicines Agency | [About EMA](#) | [About EudraVigilance](#)

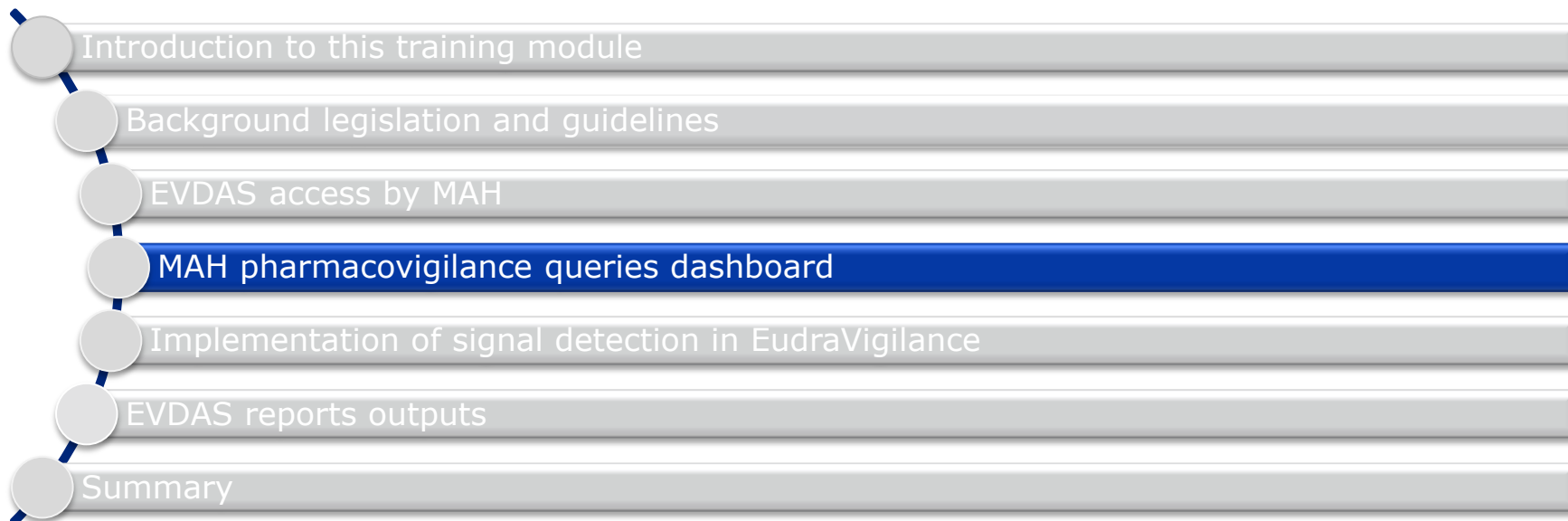


## Section Summary

**In this section you obtained an understanding of:**

- Main principles of the access to EVDAS by MAHs.
- How to access EVDAS.

# Content Summary





## Section Overview

- In this section you will obtain understanding of the:
  - The reports included in the MAH pharmacovigilance queries dashboard.
  - Active substance grouping report.
  - The eRMR report.
  - The line listing report.
  - General functionalities offered by the system.
  - How to work with returned reports.

electronic Reaction Monitoring Report - eRMR

Line listing

Active substance grouping



EUROPEAN MEDICINES AGENCY  
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## Dashboard Description

This dashboard supports the Active substance / Reaction analysis for one or more Active substances selected by the user. It contains the following reports: the electronic Reaction Monitoring Report (ad-hoc and fixed reference period), the Individual case line listing and the Active substance grouping.

# MAH Pharmacovigilance Queries (v01.00.00)

The EudraVigilance Data Warehouse is the central repository of ICSR and medicinal product data from where these reports are being generated  
v01.00.00

Current MedDRA version is 18.1

Data up to and including 29-09-2016

For any technical support, please contact [EMA EVDAS support](#).

- **Prompts** are objects that enable users to select the conditions to be included in a report
- The following figure shows the prompts included in a report:

Welcome | **electronic Reaction Monitoring Report - eRMR** | Line listing | Active substance grouping

Data up to and including 18-10-2016

\* electronic Reaction Monitoring Report – ad-hoc reference period (max three months) ▼

**Report Description**  
This report supports the Active substance / Reaction analysis for the Active substance selected by the user.

\* Select the Active Substance (High Level) --Select Value-- ▼

\* Reference period – Enter a Start Date (only values within 3 months and two weeks in the past are possible) >= 19/09/2016 ▼

\* End Date <= 18/10/2016 ▼

MedDRA Reaction Terms ☒ none

- ☐ MedDRA reaction PT
- ☐ MedDRA reaction HLT
- ☐ MedDRA reaction HLGT
- ☐ MedDRA reaction SOC
- ☐ MedDRA SMQ Level 1 Broad
- ☐ MedDRA SMQ Level 1 Narrow

Clear all prompts

- **Filters** define the conditions that data must meet to be included in the report result set.
- Some filters can contain any number of conditions. For instance we can retrieve the data for different MedDRA SOCs or different MedDRA PTs.
- Only data that meets all of the filter conditions appears in the final result set of a report.
- The following illustration shows the report's filters

---

## electronic Reaction Monitoring Report – ad-hoc reference period

The last data update was on 11-07-2016

Time run: 13/07/2016 14:54:30

---

Active Substance (High Level) is equal to **GEMCITABINE**  
and "eRMR Date"."eRMR Date" BETWEEN date '2016-06-13' AND date '2016-07-12'  
and "eRMR Date (Reference)". "eRMR Reference Date" = date '2016-07-12'  
and Reaction SOC is equal to **Cardiac disorders**



How to select an active substance using the high level grouping in the EVDAS prompts



## How to select a substance

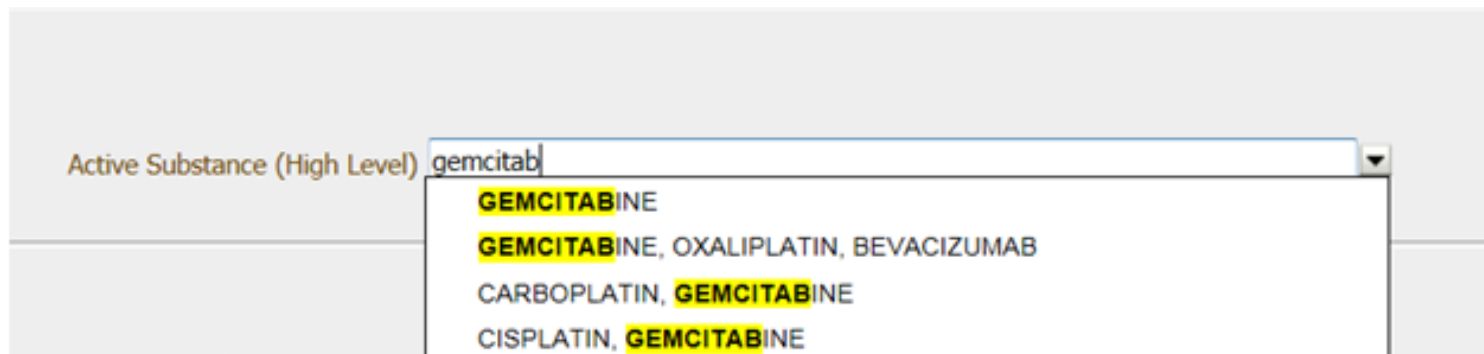
The three reports in EVDAS will require the users to select an active substance high level from the prompt

\* Select the Active Substance (High Level)

## How to select a substance

- A substance can be selected by typing the name of the substance and then clicking on the substance name. EVDAS will offer you suggestions for the substance once you have typed the first letters.



Active Substance (High Level) gemcitab

- GEMCITABINE
- GEMCITABINE, OXALIPLATIN, BEVACIZUMAB
- CARBOPLATIN, GEMCITABINE
- CISPLATIN, GEMCITABINE

# How to select a substance

- If you wish to search for more than one substance, then you can type the substance names separated by semicolons or you can select 'More/search' option

Data up to and including 18-10-2016

**Report Description**  
This reports shows the Active substances that are grouped under the selected Active substance (high level)

**Required Prompt:** **Select the Active Substance (High Level) is a required input.**

\* Select the Active Substance (High Level)

[Clear all prompts](#)

**Click on link to run report**  
[Active substance grouping](#)

GEMCITABINE

GEMCITABINE H

GEMCITABINE, E

GEMCITABINE, C

GEMCITABINE, C

GEMCITABINE, F

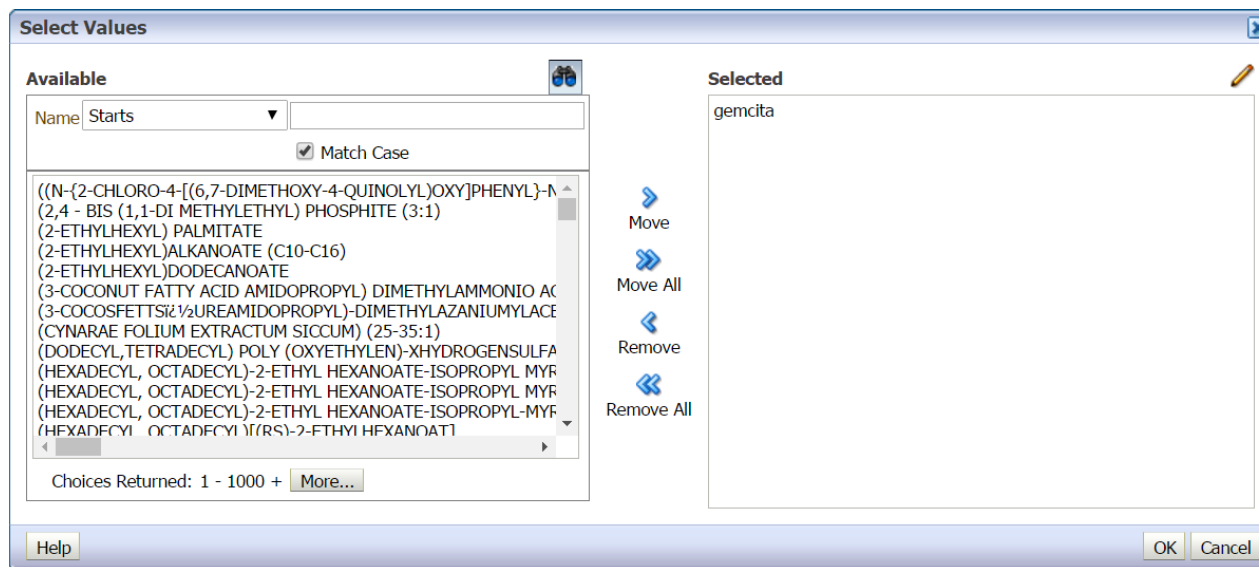
GEMCITABINE, T

More/Search..



# How to select a substance

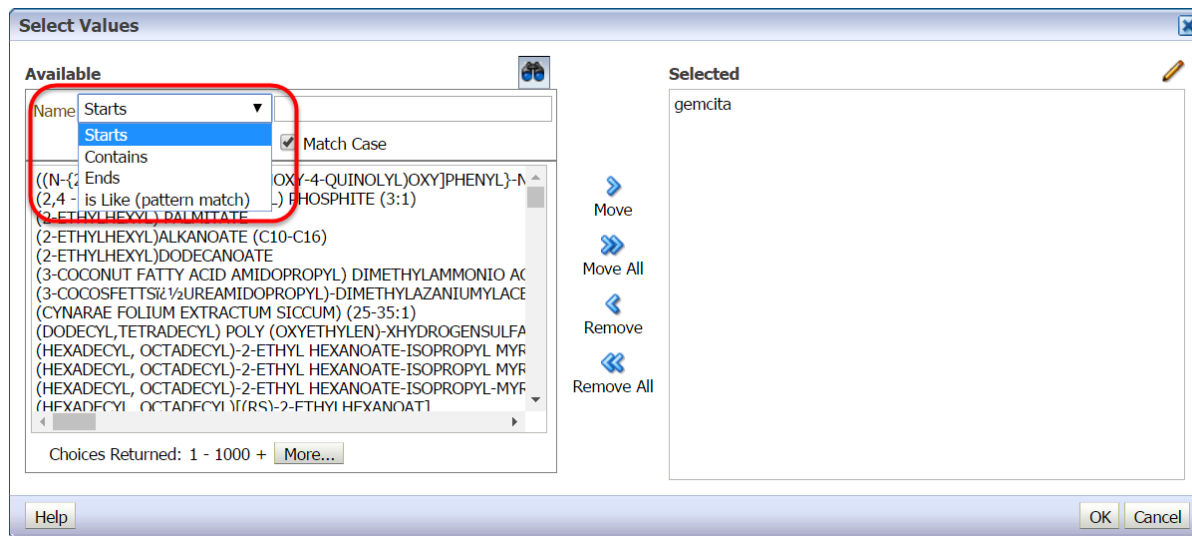
The selection cart option will appear when you click in 'More/search'





## How to select a substance

- Once in the active substance selection cart, from the 'available' section select your operator using the drop down menu. The options are 'Starts', 'Contains', 'Ends' and 'Is like (pattern match)'.





# How to select a substance

- It is recommended that the 'Match case' is not selected so the system will start offering results. The more you type, the more refined the results will be.

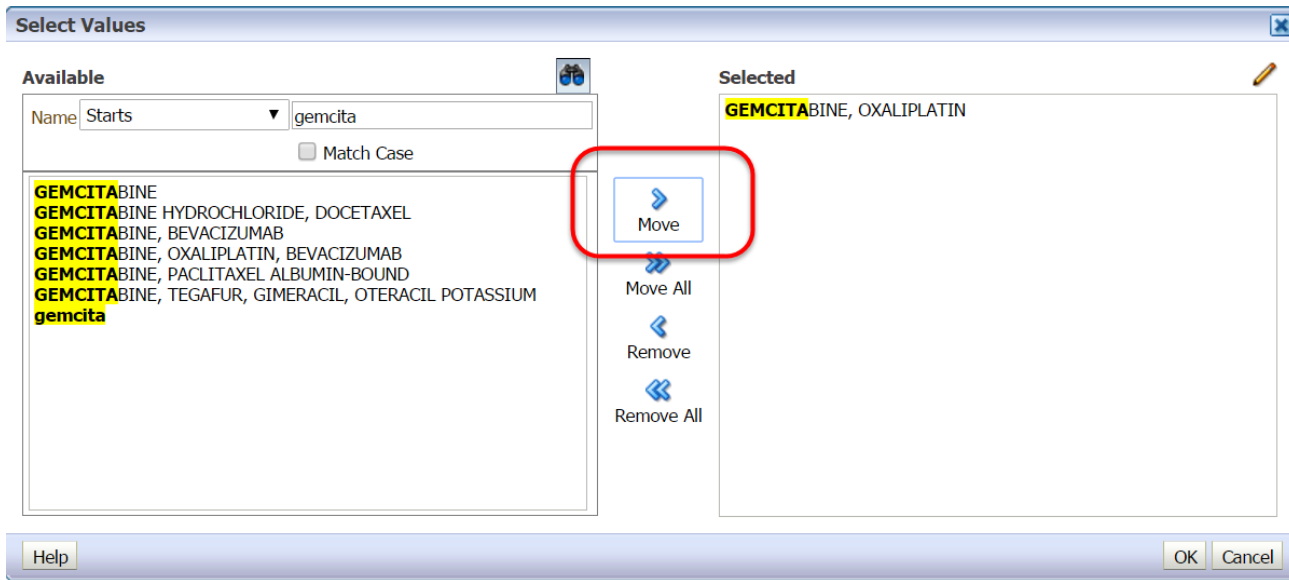
The screenshot shows a 'Select Values' dialog box with two main panes: 'Available' and 'Selected'. In the 'Available' pane, the search criteria are set to 'Name' and 'Starts', with the text 'gemcита' entered in the search field. A red circle highlights the 'Match Case' checkbox, which is currently unchecked. Below the search field, a list of search results is displayed, all starting with 'GEMCITA':

- GEMCITA BINE
- GEMCITA BINE HYDROCHLORIDE, DOCETAXEL
- GEMCITA BINE, BEVACIZUMAB
- GEMCITA BINE, OXALIPLATIN
- GEMCITA BINE, OXALIPLATIN, BEVACIZUMAB
- GEMCITA BINE, PACLITAXEL ALBUMIN-BOUND
- GEMCITA BINE, TEGAFUR, GIMERACIL, OTERACIL POTASSIUM

Between the panes are five action buttons: 'Move', 'Move All', 'Remove', and 'Remove All'. The 'Selected' pane on the right currently contains the text 'gemcита'. At the bottom of the dialog are 'Help', 'OK', and 'Cancel' buttons.

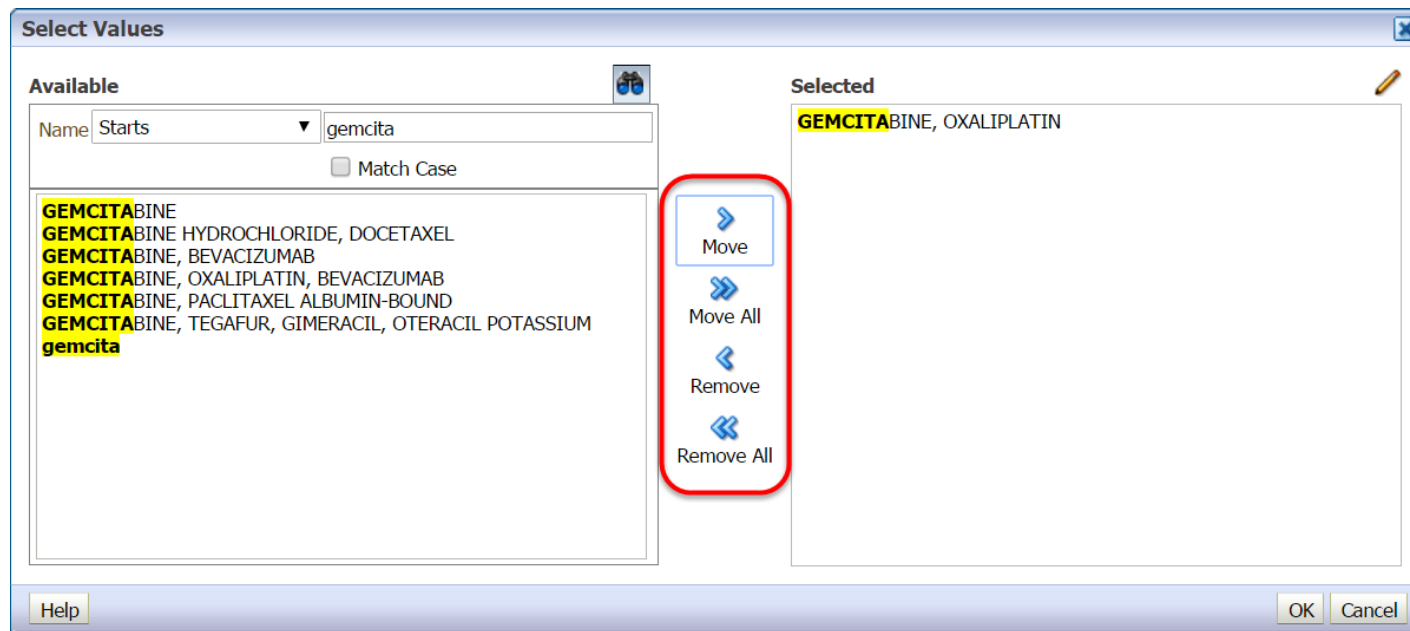
## How to select a substance

- Once you typed the substance name, then select the desired substance by double clicking on the substance name or by selecting the substance and then clicking in the arrow 'move'



# How to select a substance

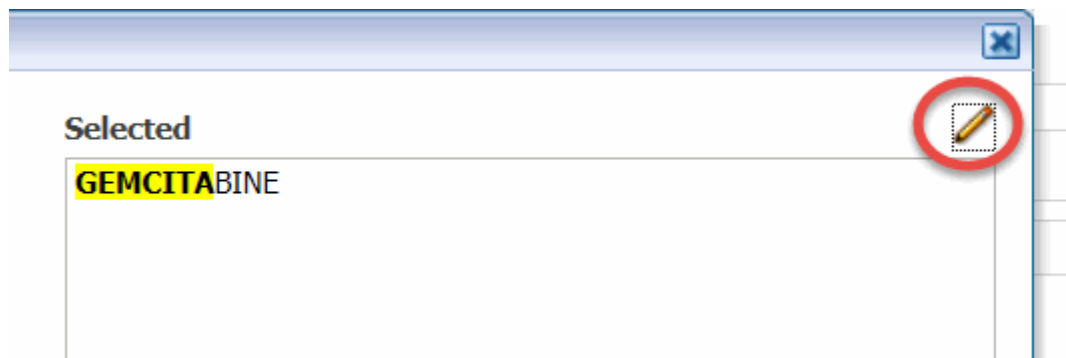
- The arrows in the middle of the selection cart can be used to move the substances in between the two panels





## How to select a substance

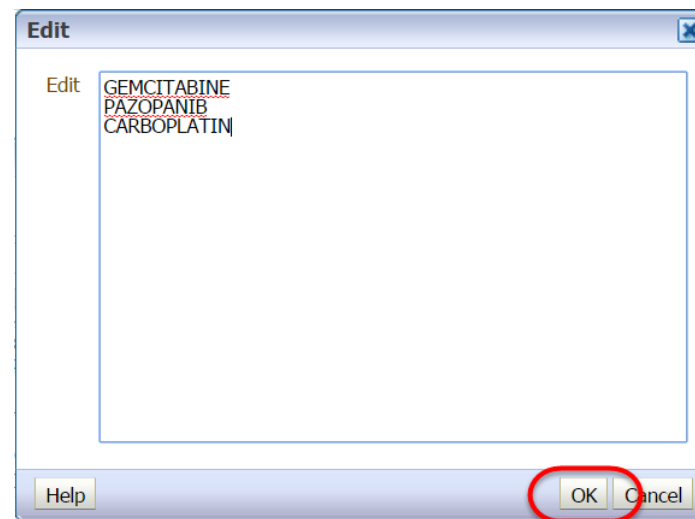
- Searched terms can also be edited or selected within the 'Selected' section by clicking the **Edit** (pencil) icon on the top-right of the selected section. This brings up the edit box, containing any selected terms.





## How to select a substance

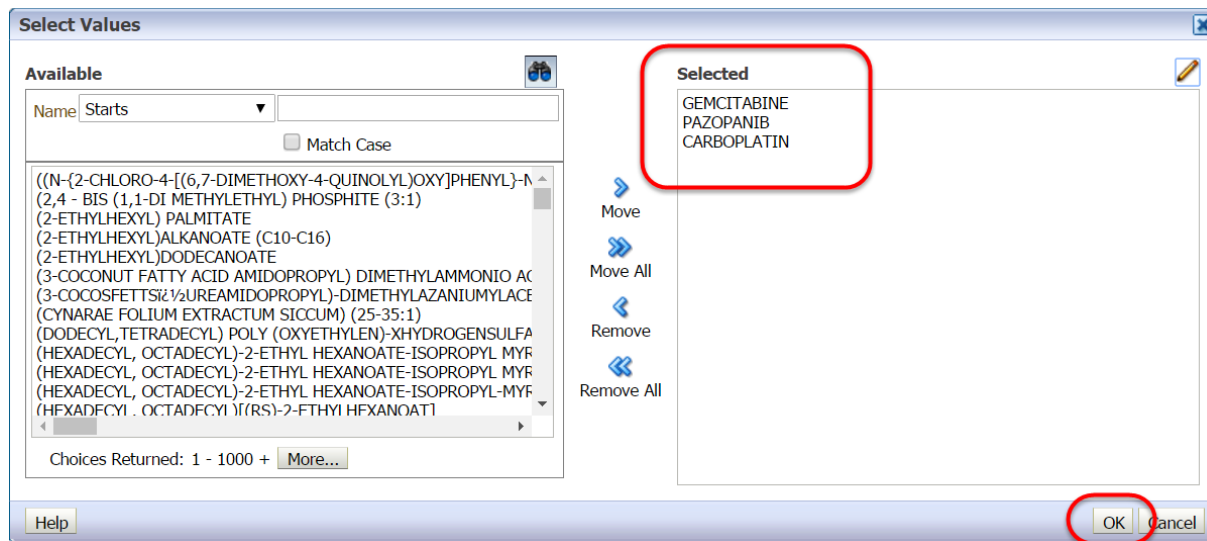
- You can then edit or add any terms, including typing or pasting terms from other queries or sources.
- Please note that if you are pasting, typing in or editing terms, you will need to ensure:
  - (a) they are entered in capitals
  - (b) that they are spelled completely correctly and
  - (c) that each term is on a separate line.
- click OK when all the desired terms are included






## How to select a substance

- Once all the desired substances are shown in the selected panel, click ok to finish the substance selection.



## How to select a substance

- The selected substances will be included in the prompt. You can double check by opening the drop down menu or opening the selection cart

\* Select the Active Substance (High Level) GEMCITABINE;PAZO 

[Clear all prompts](#)

**Click on link to run report**  
[Active substance grouping](#)

☒ GEMCITABINE  
☒ PAZOPANIB  
☒ CARBOPLATIN  


---

☐ ((N-{2-CHLORO-4-[(6,7-DIMETHOXY-4-QUINOLYL)OXY]PHENYL}-N'-(5-METHYL-3-ISOXAZOLY  
☐ (2,4 - BIS (1,1-DI METHYLETHYL) PHOSPHITE (3:1)  
☐ (2-ETHYLHEXYL) PALMITATE  
☐ (2-ETHYLHEXYL)ALKANOATE (C10-C16)

[More/Search...](#)



# Active substance grouping report

electronic Reaction Monitoring Report - eRMR

Line listing

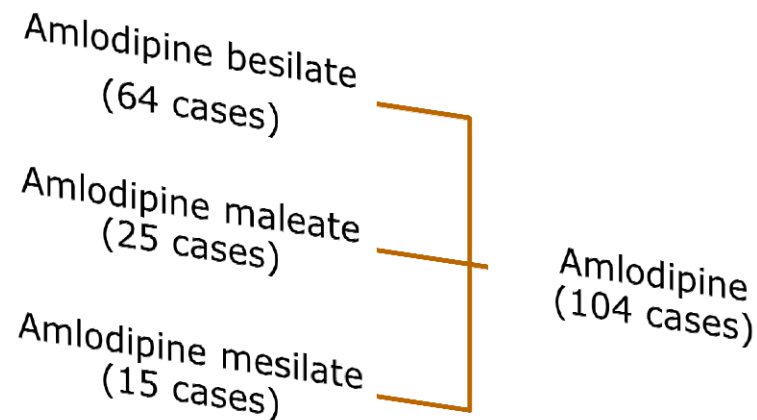
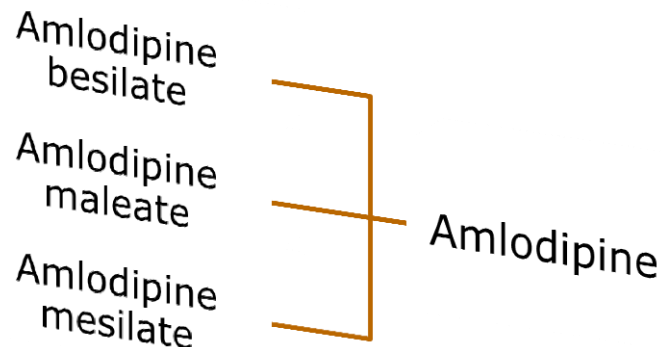
**Active substance grouping**

## Active substance grouping – The concept

- The active substance high level is formed by different names of an active substance (e.g. different salts).
- These groups of substances names that form one active substance high level are used to perform signal detection and to retrieve EudraVigilance data.
- This grouping needs to be performed when aggregated dataset is needed for a higher level analysis.
- Grouping is a manual activity performed by the Agency to facilitate such analysis.
- The active substance high level is generally used by default; the low level is used when there is an interest in e.g. a particular salt.



## Active substance grouping





- The “Active substance grouping” report provides the user with an overview of the *Active Substances* in the XEVMPD that have been grouped to a specific *Active Substance High Level*.

As EVDAS access is provided at the level of active substance high level, users should determine which active substance high level should be used to query EVDAS



- The active substance grouping report contains one prompt

Welcome

electronic Reaction Monitoring Report - eRMR

Line listing

**Active substance grouping**

Data up to and including 18-10-2016

**Report Description**  
This reports shows the Active substances that are grouped under the selected Active substance (high level).

\* Select the Active Substance (High Level)

Clear all prompts

**Warning**  
*Please complete all mandatory prompts.*

- To run the active substance grouping report, select an active substance and click on the active hyperlink 'active substance grouping' at the bottom of the report.

Welcome | electronic Reaction Monitoring Report - eRMR | Line listing | **Active substance grouping**

Data up to and including 18-10-2016

**Report Description**  
This reports shows the Active substances that are grouped under the selected Active substance (high level).

\* Select the Active Substance (High Level)  ▼

**Click on link to run report**  
[Active substance grouping](#)



# Active substance grouping outcome

- The outcome of the active substance grouping report is a table containing the substance names that have been grouped to a specific active substance high level

## Active substance grouping

Data up to and including 18-10-2016

Time run: 19/10/2016 14:19:51

---

Active Substance (High Level)	Active Substance
GEMCITABINE	GEMCITABINE
	GEMCITABINE HYDROCHLORIDE

[Return](#) - [Refresh](#) - [Print](#) - [Export](#)

## Other examples of the active substance grouping report

- By running the active substance grouping report, MAHs of valproate semisodium will know that 'valproic acid' is the active substance high level they should use to retrieve the data from EVDAS

### Active substance grouping

Data up to and including 18-10-2016

Time run: 19/10/2016 14:23:12

Active Substance (High Level)	Active Substance
VALPROIC ACID	SODIUM VALPROATE
	VALPROATE BISMUTH
	VALPROATE MAGNESIUM
	VALPROATE PIVOXIL
	VALPROATE SEMISODIUM
	VALPROIC ACID
	VALPROIC ACID, SODIUM VALPROATE
	VALPROMIDE

[Return](#) - [Refresh](#) - [Print](#) - [Export](#)



## Other examples of the active substance grouping report

- By running the active substance grouping report, MAHs of lithium carbonate will know that lithium is the active substance high level they should use to retrieve the data from EVDAS

### Active substance grouping

Data up to and including 18-10-2016

Time run: 19/10/2016 14:26:56

Active Substance (High Level)	Active Substance
LITHIUM	LITHIUM
	LITHIUM ACETATE
	LITHIUM ACETYLSALICYLATE
	LITHIUM ASPARTATE
	LITHIUM BENZOATE
	LITHIUM BROMIDE
	LITHIUM CARBONATE
	LITHIUM CHLORIDE
	LITHIUM CITRATE
	LITHIUM GLUCONATE
	LITHIUM PHOSPHATE
	LITHIUM SALICYLATE
	LITHIUM SUCCINATE
	LITHIUM SULFATE

[Return](#) - [Refresh](#) - [Print](#) - [Export](#)



**electronic Reaction Monitoring Report - eRMR**

Line listing

Active substance grouping

**electronic Reaction Monitoring Report - eRMR**

Line listing

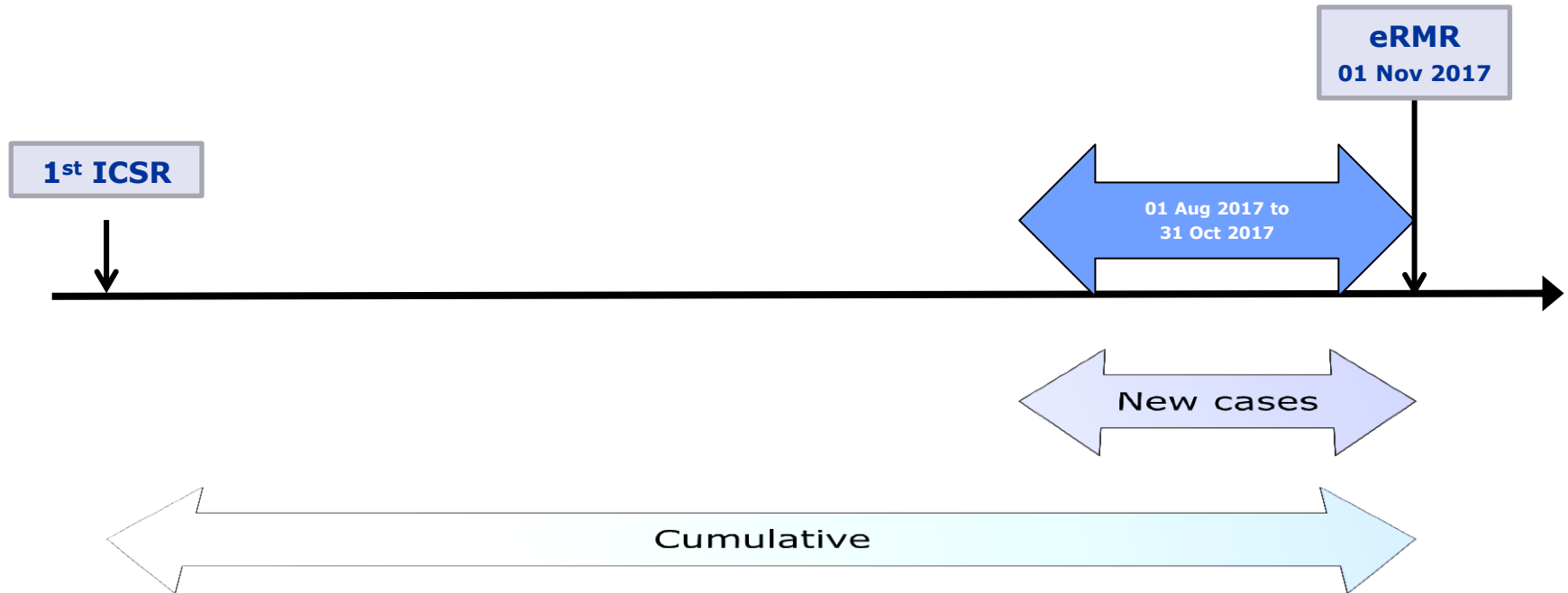
Active substance grouping

- The electronic reaction monitoring report provides the user with aggregated data to be used for signal detection for a specific active substance high level according to a reference period. The report can be further filtered by MedDRA reaction terms.
- To access the eRMR report click on the electronic Reaction Monitoring Report tab in the MAH Pharmacovigilance queries dashboard.

## The Reference Period

- Using a reference period in the eRMR allows to highlight and separate the new cases received during that period. Continuous monitoring.
- The reference period is based on EV Message Gateway Date and defines the start and end of the period for populating the columns in the eRMR with the new cases.





Cases received for the first time in EudraVigilance

Follow-ups

De-duplicated cases

- When two cases are identified as duplicates, these are merged in a new master case that is re-submitted to EudraVigilance. If the date of re-submission is within the reference period, only this case will appear as new (the 2 underlying duplicates will also not appear in the new/total column).

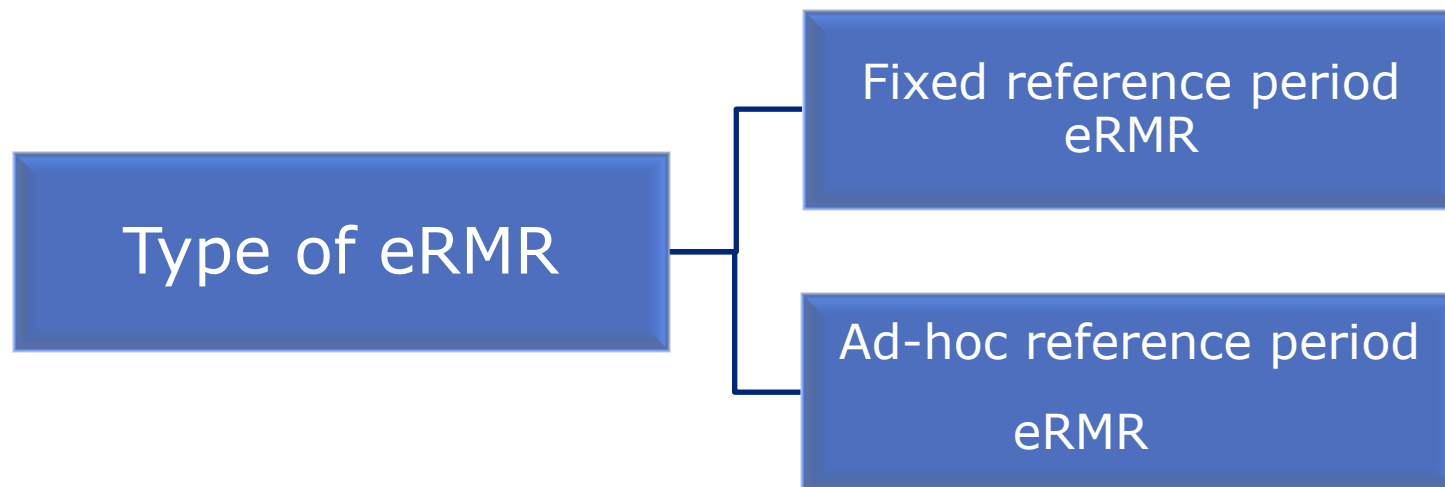
PTs	IME/DME	New EVPM	Total EVPM	New Fatal	Total Fatal
Ventricular fibrillation	IME/DME	2	4	1	1
Coronary artery thrombosis	IME	1	1	0	0
Atrioventricular block		2	3	1	2



## electronic Reaction Monitoring Report - eRMR

Line listing

Active substance grouping



Pre-generated by the EMA the first day of every month

The reference period for these eRMRs will be fixed to 6 months

e.g. for the eRMR pre-generated on 1<sup>st</sup> July 2017, the reference period is:


1<sup>st</sup> January 2017 –  
30<sup>th</sup> June 2017.


The report will not change until a new eRMR is available, therefore running the report for the same substance the first day of the month or the last day of the month will provide the same results.

## Fixed reference period eRMR

- To retrieve a fixed reference period eRMR, select the option from the 1<sup>st</sup> prompt in the eRMR report

**electronic Reaction Monitoring Report - eRMR** Line listing Active substance grouping

\* electronic Reaction Monitoring Report – fixed reference period (six months) 

 electronic Reaction Monitoring Report – fixed reference period (six months)

electronic Reaction Monitoring Report – ad-hoc reference period (max three months)

Search...

- The fixed reference period eRMR report contains 2 prompts

Welcome **electronic Reaction Monitoring Report - eRMR** Line listing Active substance grouping

Data up to and including 18-10-2016

\* electronic Reaction Monitoring Report – fixed reference period (six months) ▼

**Report Description**  
This report supports the Active substance / Reaction analysis for one or more Active substances selected by the user.

\* Select the Active Substance (High Level) --Select Value-- ▼

MedDRA Reaction Terms

- ☒ none
- ☐ MedDRA reaction PT
- ☐ MedDRA reaction HLT
- ☐ MedDRA reaction HLGT
- ☐ MedDRA reaction SOC
- ☐ MedDRA SMQ Level 1 Broad
- ☐ MedDRA SMQ Level 1 Narrow

Clear all prompts

## Fixed reference period eRMR

- Select an active substance/s high level

### Report Description

This report supports the Active substance / Reaction analysis for one or more Active substances selected by the user.

\* Select the Active Substance (High Level)

MedDRA Reaction Terms ☒ none

- ☐ MedDRA reaction PT
- ☐ MedDRA reaction HLT
- ☐ MedDRA reaction HLGT
- ☐ MedDRA reaction SOC
- ☐ MedDRA SMQ Level 1 Broad
- ☐ MedDRA SMQ Level 1 Narrow



## Filter on MedDRA term

- The system offers the possibility to restrict the data for a selected MedDRA term.
- The options for a MedDRA term selection are at the level of the SOC, HLGT, HLT and PT.
- Moreover, MedDRA SMQs level 1 Broad and Narrow can be also used.
- More than one term can be selected within the category (e.g 2 different PTs).
- When all the data is required, option 'none' (default option) should be left selected. With this option the report will retrieve all the ICSRs received for the selected active substances.

**MedDRA**Medical Dictionary  
for Regulatory Activities

MedDRA Reaction Terms

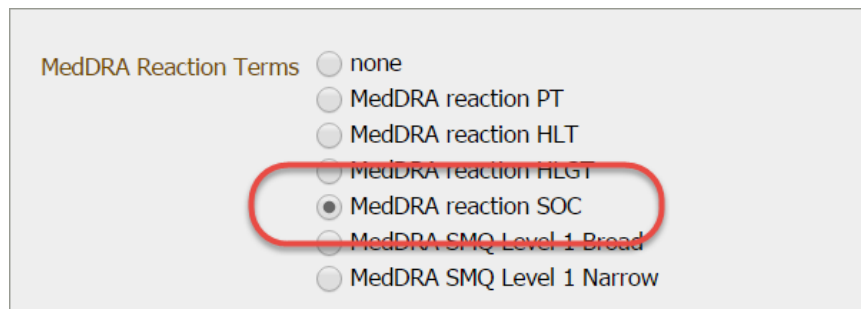
☒ none

- ☐ MedDRA reaction PT
- ☐ MedDRA reaction HLT
- ☐ MedDRA reaction HLGT
- ☐ MedDRA reaction SOC
- ☐ MedDRA SMQ Level 1 Broad
- ☐ MedDRA SMQ Level 1 Narrow



## Filter on MedDRA term

- In order to filter the data using MedDRA terms, select first the MedDRA hierarchy you want to use
- MedDRA reaction SOC in the example

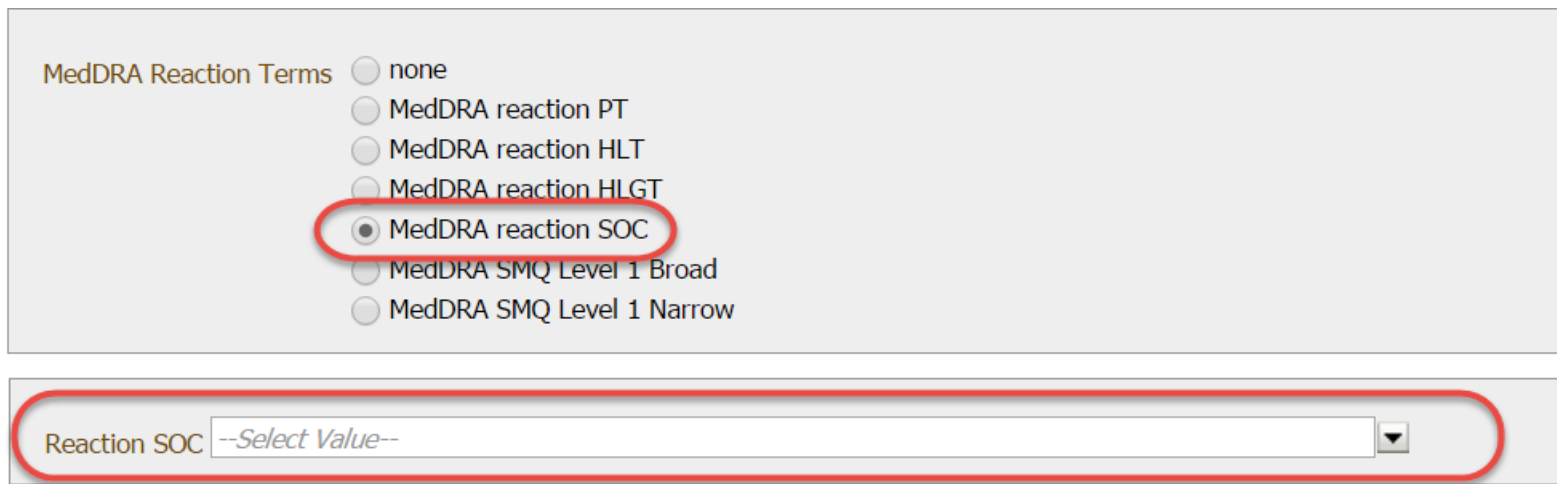


MedDRA Reaction Terms

- ☐ none
- ☐ MedDRA reaction PT
- ☐ MedDRA reaction HLT
- ☐ MedDRA reaction HLG
- ☒ MedDRA reaction SOC
- ☐ MedDRA SMQ Level 1 Broad
- ☐ MedDRA SMQ Level 1 Narrow

## Filter on MedDRA term

- Once you have selected the MedDRA hierarchy, a new prompt will appear in the system for you to select the actual MedDRA term within the selected hierarchy



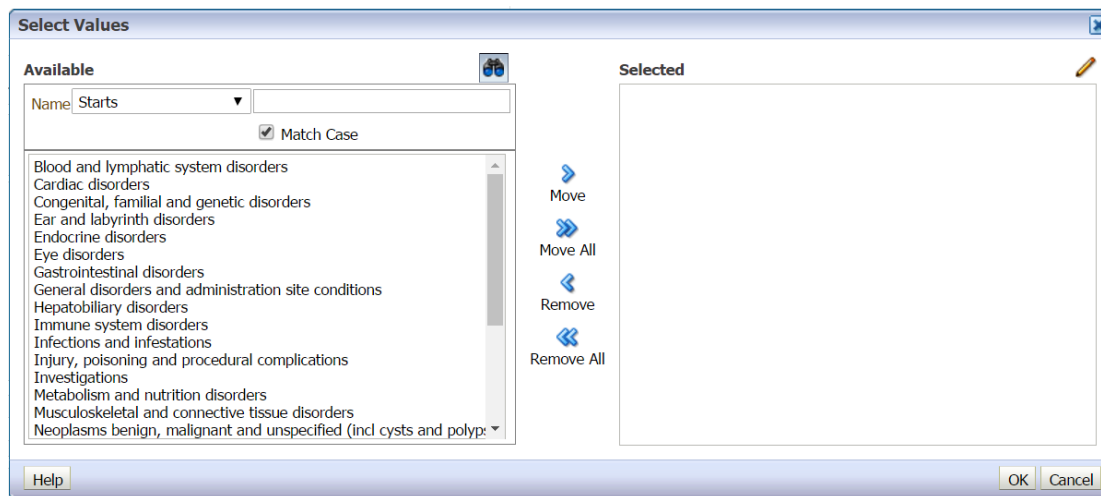
MedDRA Reaction Terms

- ☐ none
- ☐ MedDRA reaction PT
- ☐ MedDRA reaction HLT
- ☐ MedDRA reaction HLGT
- ☒ MedDRA reaction SOC
- ☐ MedDRA SMQ Level 1 Broad
- ☐ MedDRA SMQ Level 1 Narrow

Reaction SOC

## Filter on MedDRA term

- Please be aware that the selection of the MedDRA terms in the system follows the same logic as the selection of the substance:
  - You can type the term or you can open a selection cart by clicking the “search” function



## Fixed reference period eRMR

- Once all the prompts are completed accordingly, click on the hyperlink at the bottom to run the report.
- Be aware that the hyperlink will not be activated if the mandatory prompts have not been completed.

Welcome **electronic Reaction Monitoring Report - eRMR** Line listing Active substance grouping

Data up to and including 18-10-2016

**Report Description**  
This report supports the Active substance / Reaction analysis for one or more Active substances selected by the user.

\* Select the Active Substance (High Level)

MedDRA Reaction Terms

- ☐ none
- ☐ MedDRA reaction PT
- ☐ MedDRA reaction HLT
- ☐ MedDRA reaction HLGT
- ☒ MedDRA reaction SOC
- ☐ MedDRA SMQ Level 1 Broad
- ☐ MedDRA SMQ Level 1 Narrow

Reaction SOC

**Click on link to run report**  
[electronic Reaction Monitoring Report - fixed reference period](#)

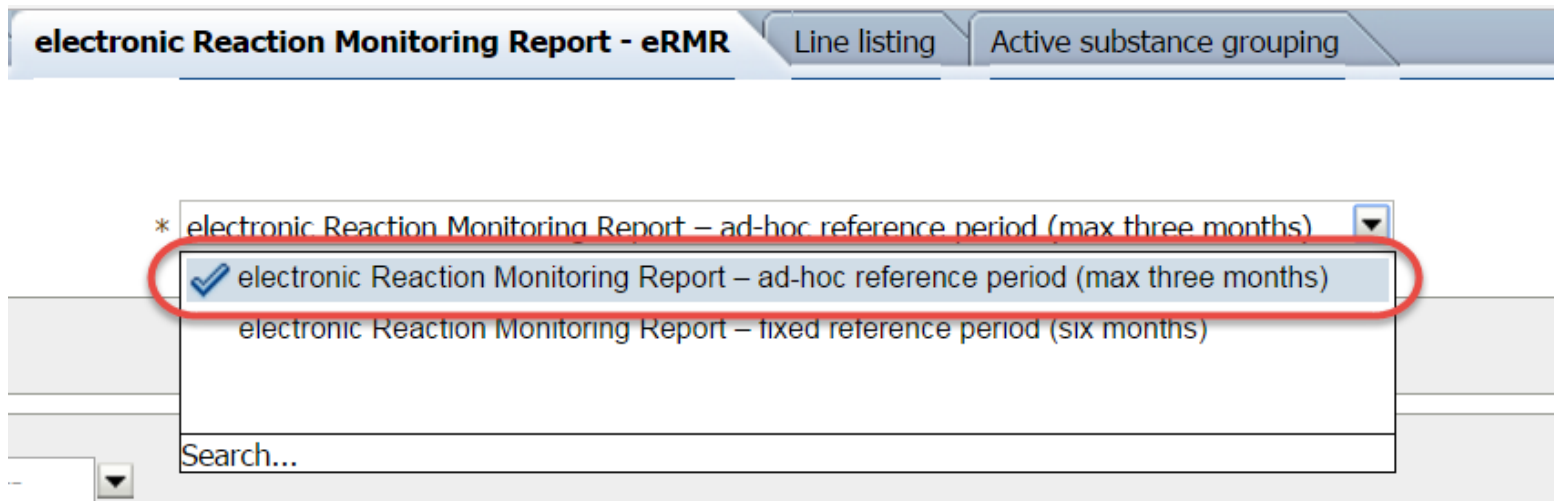
The ad-hoc reference period eRMR report allows producing an eRMR with a reference period selected by the user.

There are two measures in place to protect the performance of the system:

The reference period is restricted to 3 months and 2 weeks in the past from the day the report is run. The users are therefore able to define the reference period as being as short as a single day or as long as 105 days.

Only one substance can be selected each time the report is run.

- To retrieve an ad hoc reference period eRMR, select the option from the 1<sup>st</sup> prompt in the eRMR report (this is the default option)



The screenshot shows the 'electronic Reaction Monitoring Report - eRMR' interface. It has three tabs: 'electronic Reaction Monitoring Report - eRMR' (selected), 'Line listing', and 'Active substance grouping'. Below the tabs is a dropdown menu with the following options:

- \* electronic Reaction Monitoring Report – ad-hoc reference period (max three months) [selected]
- ✓ electronic Reaction Monitoring Report – ad-hoc reference period (max three months)
- electronic Reaction Monitoring Report – fixed reference period (six months)

Below the dropdown menu is a search bar with the text 'Search...'.

- The ad hoc reference period eRMR report contains 3 prompts

**Report Description**  
This report supports the Active substance / Reaction analysis for the Active substance selected by the user.

\* Select the Active Substance (High Level)

\* Reference period – Enter a Start Date (only values within 3 months and two weeks in the past are possible) >=

\* End Date <=

MedDRA Reaction Terms ☒ none

- ☐ MedDRA reaction PT
- ☐ MedDRA reaction HLT
- ☐ MedDRA reaction HLGT
- ☐ MedDRA reaction SOC
- ☐ MedDRA SMQ Level 1 Broad
- ☐ MedDRA SMQ Level 1 Narrow

**Warning**  
*Please complete all mandatory prompts.*



## Ad-hoc reference period eRMR

- Select an active substance high level
- Please remember that only one active substance can be selected in this report and therefore the selection cart option only contains one panel.

**Select Values**

**Values**

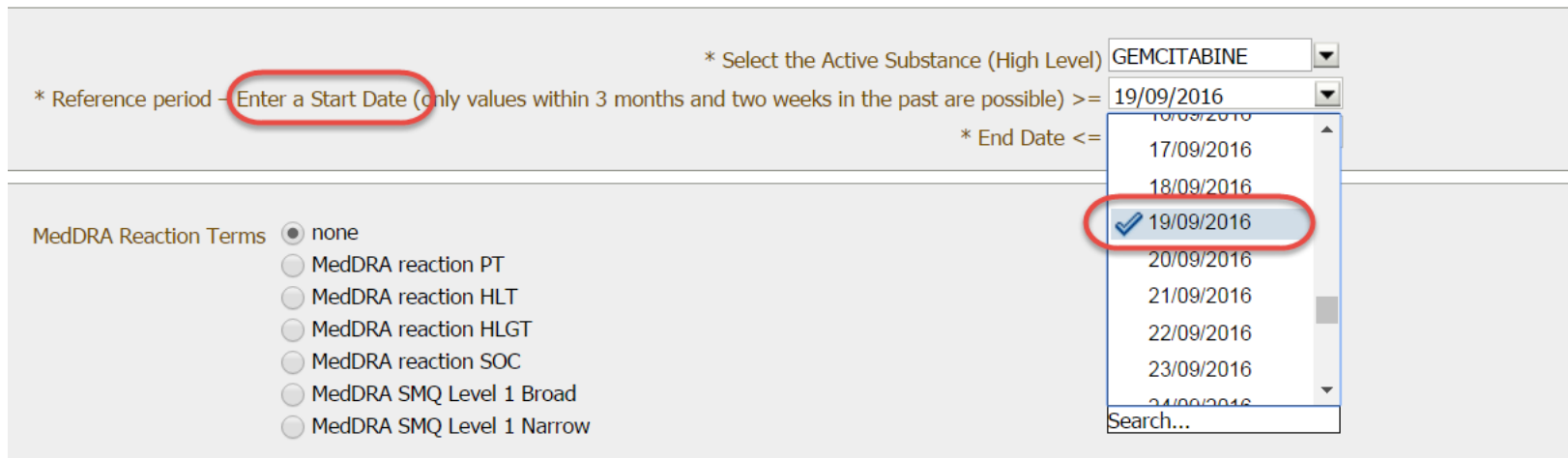
Name: **Contains**  ☐ Match Case

CARBOPLATIN, **GEMCITA**BINE  
CISPLATIN, **GEMCITA**BINE  
**GEMCITA**BINE  
**GEMCITA**BINE HYDROCHLORIDE, DOCETAXEL  
**GEMCITA**BINE, BEVACIZUMAB  
**GEMCITA**BINE, OXALIPLATIN  
**GEMCITA**BINE, OXALIPLATIN, BEVACIZUMAB  
**GEMCITA**BINE, PACLITAXEL ALBUMIN-BOUND  
**GEMCITA**BINE, TEGAFUR, GIMERACIL, OTERACIL POTASSIUM  
VINORELBINE, **GEMCITA**BINE, IFOSFAMIDE, PREDNISONE

Help OK Cancel



- To select the reference period, select a start date from the options provided in the prompt.
- Remember the start date can only cover a period of up to 105 days in the past from the day you are running the report.
- The default option is one month from today's date.



The screenshot displays the eRMR interface for selecting a reference period. At the top, a label '\* Select the Active Substance (High Level)' is followed by a dropdown menu showing 'GEMCITABINE'. Below this, the text '\* Reference period – Enter a Start Date (only values within 3 months and two weeks in the past are possible) >=' is shown, with 'Enter a Start Date' circled in red. To the right, a date dropdown menu is open, showing a list of dates from 16/09/2016 to 24/09/2016. The date 19/09/2016 is selected and circled in red. Below the date selection, the text '\* End Date <=' is visible. On the left side, under the heading 'MedDRA Reaction Terms', there are several radio button options: 'none' (selected), 'MedDRA reaction PT', 'MedDRA reaction HLT', 'MedDRA reaction HLGT', 'MedDRA reaction SOC', 'MedDRA SMQ Level 1 Broad', and 'MedDRA SMQ Level 1 Narrow'.

- The end date of the reference period defines the limit for the cases to be included.
- The default options is today's day -1 so in that way users will retrieve the cases from the most up to date database.

**Report Description**  
This report supports the Active substance / Reaction analysis for the Active substance selected by the user.

\* Select the Active Substance (High Level)

\* Reference period – Enter a Start Date (only values within 3 months and two weeks in the past are possible) >=

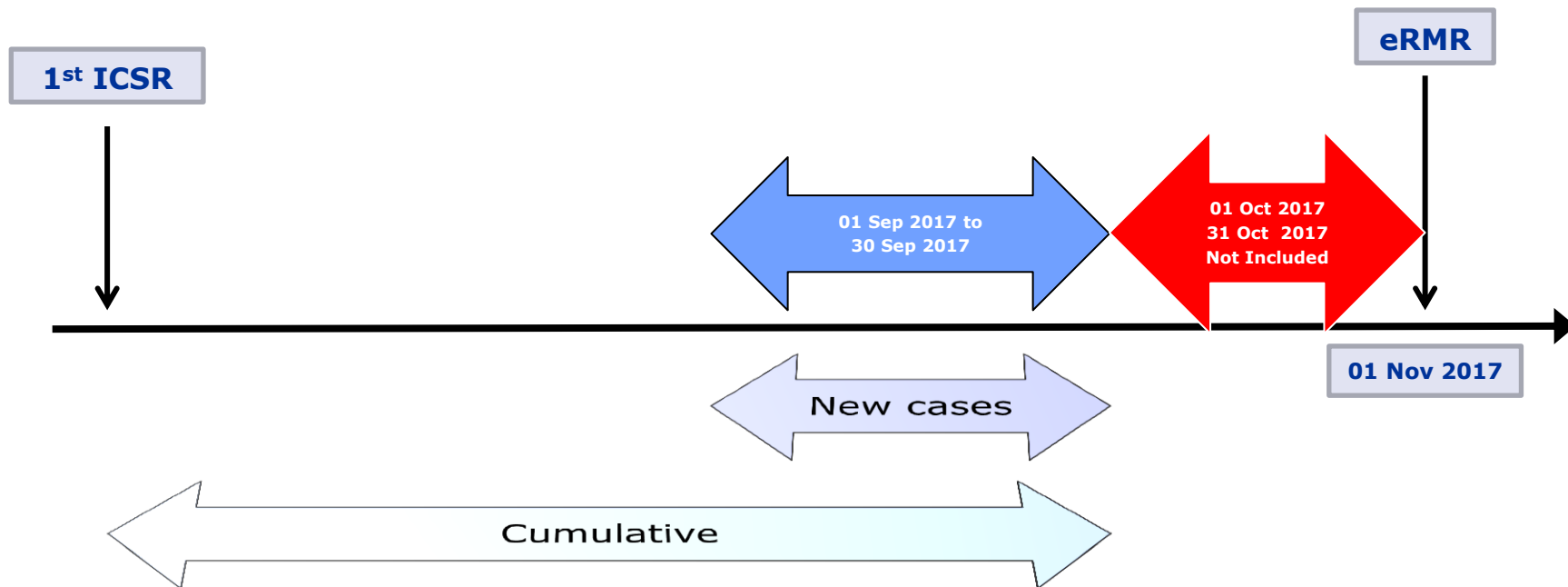
\* End Date <=

MedDRA Reaction Terms

- ☐ none
- ☐ MedDRA reaction PT
- ☐ MedDRA reaction HLT
- ☐ MedDRA reaction HLGT
- ☒ MedDRA reaction SOC
- ☐ MedDRA SMQ Level 1 Broad
- ☐ MedDRA SMQ Level 1 Narrow

26/10/2016  
27/10/2016  
28/10/2016  
29/10/2016  
30/10/2016  
31/10/2016  
01/11/2016  
☒ 02/11/2016  
Search

- Using an end date in the past is possible but the data retrieved will be according to the valid cases on the selected 'end date'





## Filter on MedDRA Term

- The ad hoc eRMR report also offers the possibility to filter the data by MedDRA terms in the same way as per the fixed reference period eRMR.

**MedDRA**Medical Dictionary  
for Regulatory Activities

MedDRA Reaction Terms

- ☐ none  
☐ MedDRA reaction PT  
☐ MedDRA reaction HLT  
☐ MedDRA reaction HLGT  
☒ MedDRA reaction SOC  
☐ MedDRA SMQ Level 1 Broad  
☐ MedDRA SMQ Level 1 Narrow

Reaction SOC



## Ad-hoc reference period eRMR

- Once all the prompts are completed accordingly, click on the hyperlink at the bottom to run the report.
- Be aware that the hyperlink will not be activated if the mandatory prompts have not been completed.

**Report Description**  
This report supports the Active substance / Reaction analysis for the Active substance selected by the user.

\* Select the Active Substance (High Level)

\* Reference period – Enter a Start Date (only values within 3 months and two weeks in the past are possible) >=

\* End Date <=

MedDRA Reaction Terms

- ☐ none
- ☐ MedDRA reaction PT
- ☐ MedDRA reaction HLT
- ☐ MedDRA reaction HLG
- ☒ MedDRA reaction SOC
- ☐ MedDRA SMQ Level 1 Broad
- ☐ MedDRA SMQ Level 1 Narrow

Reaction SOC:

**Click on link to run report**  
[electronic Reaction Monitoring Report – ad-hoc reference period](#)



# eRMR report results

Active Substance	SOCs	HLGTs	HLTs	SMQ Broad	SMQ Narrow	PTs	New EVPM	Total EVPM	IME/DME	New Fatal	Total Fatal	New Medication Error/Abuse	Total Medication Error/Abuse	New Paediatric	Total Paediatric	New Geriatric	Total Geriatric	New EEA	Total EEA	New Health Care Professional	Total Health Care Professional	New Serious	Total Serious	New Spontaneous	Total Spontaneous	ROR (-)	ROR	SDR	Changes	New Literature	Total Literature	New Observational		
GEMCITABINE	Gastrointestinal disorders	Gastrointestinal haemorrhages NEC	Non-site specific gastrointestinal haemorrhages																							1	0.28	2.05	No		0	0		
GEMCITABINE	Gastrointestinal disorders	Gastrointestinal haemorrhages NEC	Non-site specific gastrointestinal haemorrhages																								91	6.67	No		0	0		
GEMCITABINE	Gastrointestinal disorders	Gastrointestinal inflammatory conditions	Colitis (excl infective)																								24	9.12	No		0	0		
GEMCITABINE	Gastrointestinal disorders	Gastrointestinal inflammatory conditions	Oesophagitis (excl infective)																								25	17.11	No		0	0		
GEMCITABINE	Gastrointestinal disorders	Gastrointestinal motility and defaecation conditions	Diarrhoea (infective)																								18	2.53	Yes		0	0		
GEMCITABINE	Gastrointestinal disorders	Gastrointestinal motility and defaecation conditions	Gastrointestinal atonic and hypomotility disorders																								22	1.59	No		0	0		
GEMCITABINE	Gastrointestinal disorders	Gastrointestinal signs and symptoms	Gastrointestinal and abdominal pains (excl throat)																								90	2.45	No		0	0		
GEMCITABINE	Gastrointestinal disorders	Gastrointestinal signs and symptoms	Nausea and vomiting symptoms																								54	2.73	Yes		0	0		
GEMCITABINE	Gastrointestinal disorders	Gastrointestinal signs and symptoms	Nausea and vomiting symptoms																								20	8.83	No		0	0		
GEMCITABINE	Gastrointestinal disorders	Gastrointestinal signs and symptoms	Nausea and vomiting symptoms																								37	4.21	Yes		0	0		
GEMCITABINE	Gastrointestinal disorders	Gastrointestinal ulceration and perforation	Gastric ulcers and perforation																								1	0.83	6.08	No		0	0	
GEMCITABINE	Gastrointestinal disorders	Oral soft tissue conditions	Stomatitis and ulceration			Stomatitis	0	1		0	0	0	0	0	0	0	0	0	0	1	0	0	0	1	0	0	1.67	12.44	No		0	0		

Once the report has run you will get the eRMR.

Be aware that the eRMR contains the same format and content regardless of running the report through the fixed or ad-hoc reference period.

More information about the eRMR and how to manipulate the data are provided in following sections of this training module

Once the report has run you will get the eRMR.

Be aware that the eRMR contains the same format and content regardless of running the report through the fixed or ad-hoc reference period.

More information about the eRMR and how to manipulate the data are provided in following sections of this training module



electronic Reaction Monitoring Report - eRMR

**Line listing**

Active substance grouping

electronic Reaction Monitoring Report - eRMR

**Line listing**

Active substance grouping

- The line listing report provides the user with the listing of individual cases for a specific substance/s and specific MedDRA terms.
- To access the line listing report, click on the line listing tab in the MAH Pharmacovigilance Queries Dashboard.



# Line listing

- The line listing report contains two prompts

Welcome | electronic Reaction Monitoring Report - eRMR | **Line listing** | Active substance grouping

Data up to and including 18-10-2016

**Report Description**  
This report generates Individual case line listings to support the case review.

\* Select the Active Substance (High Level)

MedDRA Reaction Terms

- ☒ none
- ☐ MedDRA reaction PT
- ☐ MedDRA reaction HLT
- ☐ MedDRA reaction HLGT
- ☐ MedDRA reaction SOC
- ☐ MedDRA SMQ Level 1 Broad
- ☐ MedDRA SMQ Level 1 Narrow

**Warning**  
*Please complete all mandatory prompts.*

# Line listing

- To retrieve a line listing:
  1. Select an active substance high level (more than one active substance can be selected)
  2. Select a MedDRA reaction term, if applicable
  3. Click on the hyperlink at the bottom of the report

Welcome | **electronic Reaction Monitoring Report - eRMR** | **Line listing** | Active substance grouping

Data up to and including 18-10-2016

**Report Description**  
This report generates Individual case line listings to support the case review.

\* Select the Active Substance (High Level)  ▼

MedDRA Reaction Terms

- ☐ none
- ☒ MedDRA reaction PT
- ☐ MedDRA reaction HLT
- ☐ MedDRA reaction HLGT
- ☐ MedDRA reaction SOC
- ☐ MedDRA SMQ Level 1 Broad
- ☐ MedDRA SMQ Level 1 Narrow

Reaction PT  ▼

**Click on link to run report**

[Line listing](#)

## Link eRMR – line listing

- Be aware that a line listing can be also accessible from a hyperlink in the eRMR that is placed in the number of cases 'New EVPM' and 'total EVPM'
- This line listing will retrieve the cases for the specific active substance and for the specific MedDRA PT.
- The hyperlinks will work even when the eRMR has been exported.



# Link eRMR – Line Listing



PTs		IME/DME	New EVD/DM	Total EVD/DM	New Fatal	Total Fatal	New Medication	Total Medication							
EU Local Number	Worldwide Unique Case Identification	EV Gateway Receipt Date	Report Type	Primary Source Qualification	Primary Source Country for Regulatory Purposes	Literature Reference		Patient Age Group	Patient Age Group (as per reporter)	Patient Sex	Parent Child Report	Reaction List P Outcome - Ser Criteria)			
EU-EC- 2333424	IT- PFMTEST- IT-2013- 1292	06/06/2014	Other	Healthcare professional (Other health professional)	EEA	Not available		18-64 Years	Not Specified	Female	No	Nausea (2d - Recovered/Res Pyrexia (2d - Recovered/Res Retching (2d - Recovered/Res			
EU-EC- 2321881	US-ROCHE- 1177559	28/08/2013	Spontaneous	Healthcare professional (Physician)	Non-EEA	Not available		18-64 Years	Not Specified	Male	No	Nausea (n/a - Recovered/Not Caused/Prolong Hospitalisation) Vomiting (n/a - Recovered/Not Caused/Prolong Hospitalisation)			
EU-EC- 2298993	NL-LRB- 36647	04/07/2012	Report from studies		EEA	Not available		65-85 Years	Not Specified	Female	No	Hyponatraemia Unknown - Cau Hospitalisation) Nausea (n/a - Caused/Prolong Hospitalisation)			



Bear always in mind that EV is updated every night, so if you run the eRMR and the line listing on different days, the number of cases may be different if new cases, nullifications, follow-ups or de-duplicated cases were received.

# Line Listing report results



EUROPEAN MEDICINES AGENCY

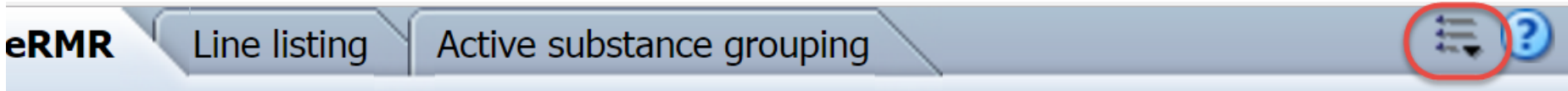
EU Case Number	Worldwide Unique Case Identification	EV Gateway Receipt Date	Report Type	Primary Source Qualification	Primary Source Country for Regulatory Purposes	Literature Reference	Patient Age Group (as per reporter)	Patient Age Group	Patient Sex	Patient Onset Report	Reaction List PT (Duration - Outcome - Seriousness)	Suspect/Interacting Drug List (Drug Char - Indication PT - Action taken - Duration - Dose - Route)	Concomitant/Not Administered Drug List (Drug Char - Indication PT - Action taken - Duration - Dose - Route)
EU-EC-2321961	JF-5209-PHHY2013P02276H	10/03/2014	Sporadic	Healthcare professional (Other health professional)	Non-EEA	Kawaguchi A, Hattori N, Kishio N, Kanie H, Iwata H. Gemtobine-induced furor lysis syndrome caused by recurrent breast cancer in a patient without hemodialysis. Gan-To-Kagaku Ryobo. 2013;10 (11):1529-1532	18-64 years	Not Specified	Female	No	Anemia (n/a - Unknown - Caused/Prolonged Hospitalization), Depressed level of consciousness (n/a - Unknown - Caused/Prolonged Hospitalization), Hepatic function abnormal (n/a - Unknown - Caused/Prolonged Hospitalization), Hypercalcemia (n/a - Recovering/Resolving - Caused/Prolonged Hospitalization), Hyperuricemia (n/a - Unknown - Caused/Prolonged Hospitalization), Renal impairment (n/a - Unknown - Caused/Prolonged Hospitalization)	GEMTABINE (GEMTABINE) (S - Metastases to bone - Unknown - [n/a - 1250mg/m2 - Not available])	Not reported
EU-EC-2321961	JF-CHUGAI-A2012015803ROOHE1211AAT	06/11/2013	Report from studies	Healthcare professional (Physician)	Non-EEA							CRIDE] (S - Adenocarcinoma - Intravenous drip), Adenocarcinoma pancreas - [n/a - 100mg - Oral]	LOROPROFEN (LOROPROFEN SODIUM) (C - Not available - Dose not changed - [n/a - 100mg - Oral]), NOT AVAILABLE (NABEPIDAZOLE SODIUM) (C - Not available - Dose not changed - [n/a - 10mg - Oral])
EU-EC-2321961	JF-CHUGAI-A2012015803ROOHE12112DEV	06/10/2013	Report from studies	Healthcare professional (Physician)	Non-EEA							CRIDE] (S - Adenocarcinoma - Intravenous drip), Adenocarcinoma pancreas - [n/a - 100mg - Oral]	LOROPROFEN (LOROPROFEN SODIUM) (C - Not available - Dose not changed - [n/a - 100mg - Oral]), NOT AVAILABLE (NABEPIDAZOLE SODIUM) (C - Not available - Dose not changed - [n/a - 10mg - Oral])
EU-EC-2321961	NL-KOCH-1114349	26/08/2013	Sporadic	Healthcare professional (Other health professional)	Non-EEA							CRIDE] (S - Nasopharyngeal intravenous (not otherwise specified))	Not reported
EU-EC-2321961	US-KOCH-1119018	26/08/2013	Sporadic	Healthcare professional (Other health professional)	Non-EEA	Borran R, Harker G, Reeves J, Beck T, Hegen S, Harvath W, Jones M, Tillinghast G, Arrowsmith E, Harner G, Kudrik P, Malmud S, Brumund J, Ziegler H, Tai D, Kornberg L, Obasaju C, Orlando M, Yardley D. Phase II study of Gemtobine and Bevacizumab as first-line treatment in Taxane pre-treated, HER2-negative, locally recurrent or metastatic breast cancer. Clinical Breast Cancer 2012 Oct 6;12 (5):322-330.	Not Specified	Not Specified	Female	No	Anemia (n/a - Recovered/Resolved - Other Medically Important Condition), Fibrile neutropenia (n/a - Recovered/Resolved - Other Medically Important Condition), Thrombocytopenia (n/a - Recovered/Resolved - Other Medically Important Condition)	VILCYTE (VILGANCLOVIR HYDROCHLORIDE) (S - Nasopharyngeal cancer - Unknown - [n/a - 450mg - Oral]), AUSTIN (BEVACIZUMAB) (S - Breast cancer metastatic - Unknown - [n/a - 10mg/kg - Unknown]), NOT AVAILABLE (GEMTABINE HYDROCHLORIDE) (S - Breast cancer metastatic - Unknown - [n/a - 2500mg/m2 - Intravenous (not otherwise specified)])	Not reported
EU-EC-2321961	NL-LRB-20511	19/07/2012	Sporadic		EEA	Not available	65-89 years	Not Specified	Male	No	Anemia (n/a - Unknown - Caused/Prolonged Hospitalization), Dermatitis (n/a - Unknown - Caused/Prolonged Hospitalization), Leukopenia (n/a - Unknown - Caused/Prolonged Hospitalization), Vomiting (n/a - Unknown - Caused/Prolonged Hospitalization)	Not reported	Not reported

Once the report has run you will get a line listing with details of the individual cases.

More information about the line listing and how to manipulate the data are provided in following sections of this training module.

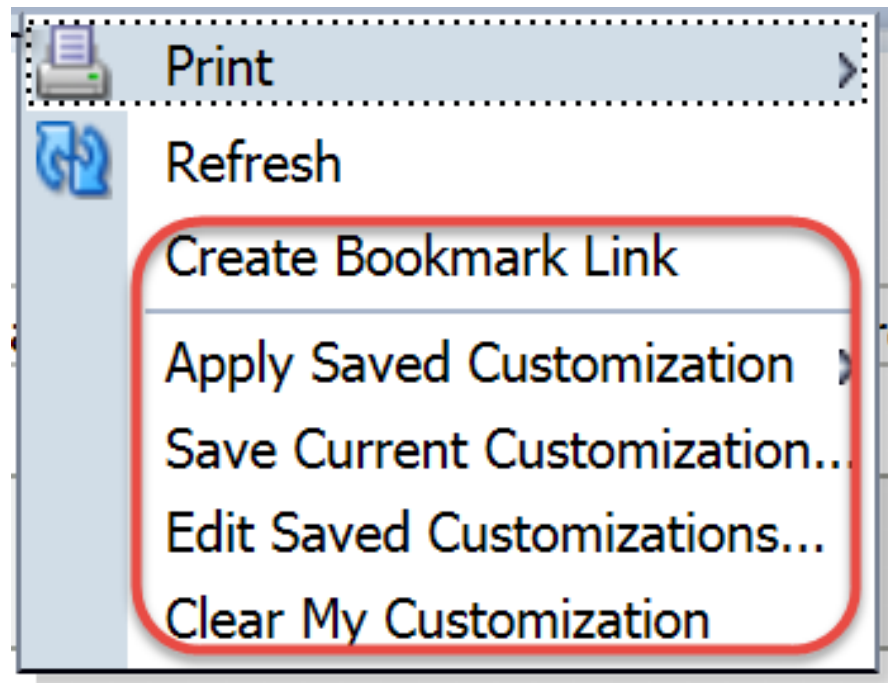
## EVDAS - General functionalities – Prompt Page options

- When you are on the prompts page, as well as answering the prompts and running the report, the system offers options to customise your selections.
- To access these, click the **page options button** in the top right-hand corner of the prompts page.



## General functionalities – Prompt Page options

- Be aware that the Print and Refresh options are not active.

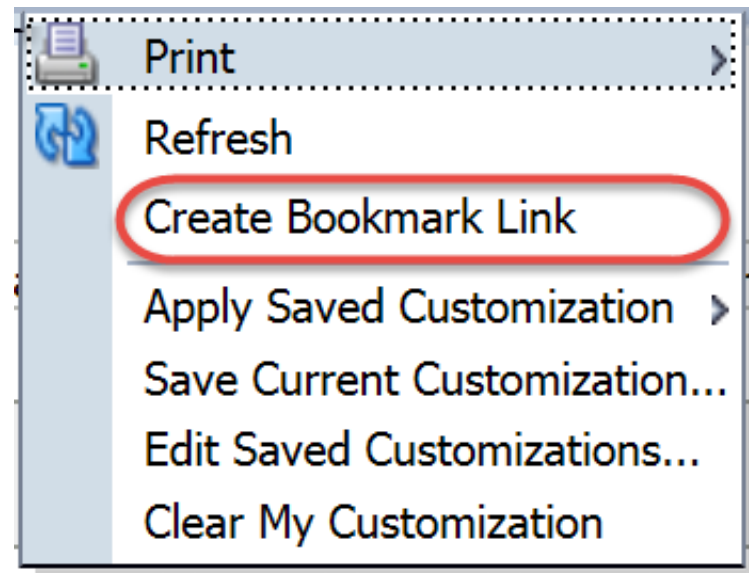




## General functionalities – Prompt Page options

### Bookmark link

- This option creates a dedicated URL suitable for saving or sharing the prompt page. It is shown in the browser's Address Bar



Welcome **electronic Reaction Monitoring Report - eRMR** Line listing Active substance grouping

A Bookmark Link suitable for saving or sharing this page has been created. It is shown in the browser's Address Bar.

Data up to and including 28-11-2016

\* electronic Reaction Monitoring Report – ad-hoc reference period

**Report Description**  
This report supports the Active substance / Reaction analysis for the Active substance selected by the user.

\* Select the Active Substance (High Level)

\* Reference period – Enter a Start Date (only values within 3 months and two weeks in the past are possible) >=

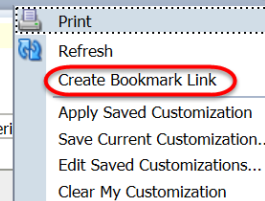
\* End Date <=

MedDRA Reaction Terms ☐ none

- ☐ MedDRA reaction PT
- ☐ MedDRA reaction HLT
- ☐ MedDRA reaction HLG
- ☒ MedDRA reaction SOC
- ☐ MedDRA SMQ Level 1 Broad
- ☐ MedDRA SMQ Level 1 Narrow

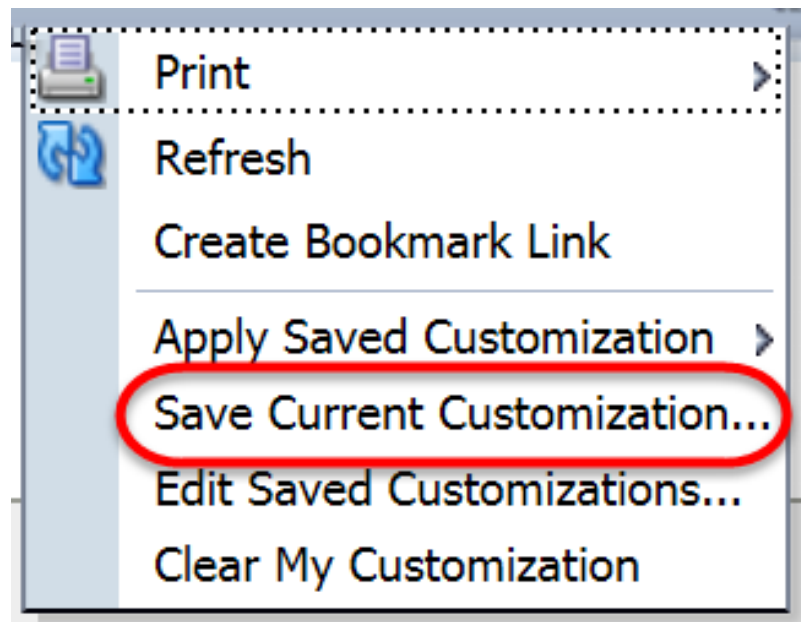
Reaction SOC

**Click on link to run report**  
[electronic Reaction Monitoring Report – ad-hoc reference period](#)



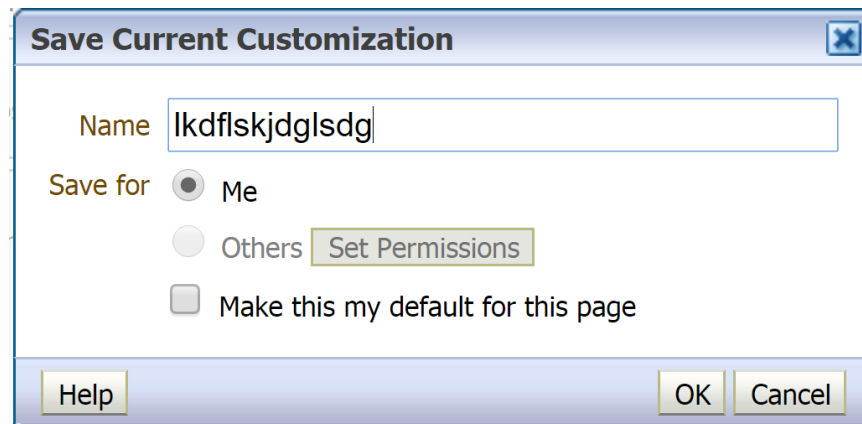
## Prompt customisations – Save current customisation

- Once you have entered your prompt selections, you can choose to save these for future searches.
- To do so, once all the prompts are completed, click on 'Save Current Customization' in the prompt page options.



## Prompt customisations - Save current customisation

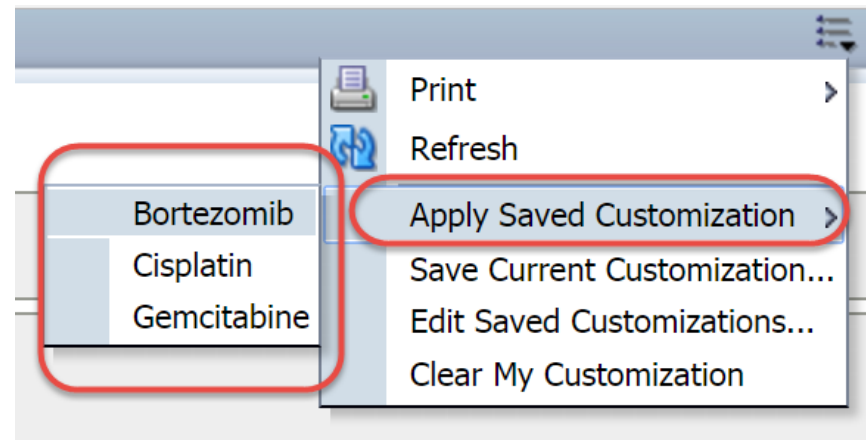
- The system will offer you the possibility to name that customisation and to make this customisation the default option, so next time you open this report, the prompts will be populated with this default customisation.
- Be aware that saving customisations for other users is not an active option.



The screenshot shows a dialog box titled "Save Current Customization" with a close button in the top right corner. Inside the dialog, there is a text input field labeled "Name" containing the text "lkdfjskjdglsdg". Below this, under the "Save for" section, there are three options: "Me" (selected with a radio button), "Others" (with an unselected radio button and a "Set Permissions" button next to it), and "Make this my default for this page" (with an unselected checkbox). At the bottom of the dialog, there are three buttons: "Help", "OK", and "Cancel".

## Prompt customisations – Apply saved customisation

- To apply a saved customisation to the report, click on 'Apply Saved Customisations' and the system will show the list of customisations you have previously saved.
- To apply one of the saved customisations simply click on the desired option.
- Please be aware that customisations can only be applied within the same report. You cannot run an eRMR report with a customisation saved for the line listing report.



## Prompt customisations – Edit saved customisations

- The option edit customisations gives you the possibility to modify your list of saved customisations.
- From here you can delete, rename or change the default option.
- If no default options is desired, then no personal customisations should be selected.

Edit Saved Customizations

Rename, delete and control group access to Saved Customizations, as well as specify which Saved Customization, if any, should be used as your default for the current Dashboard page.

**Saved Customizations**

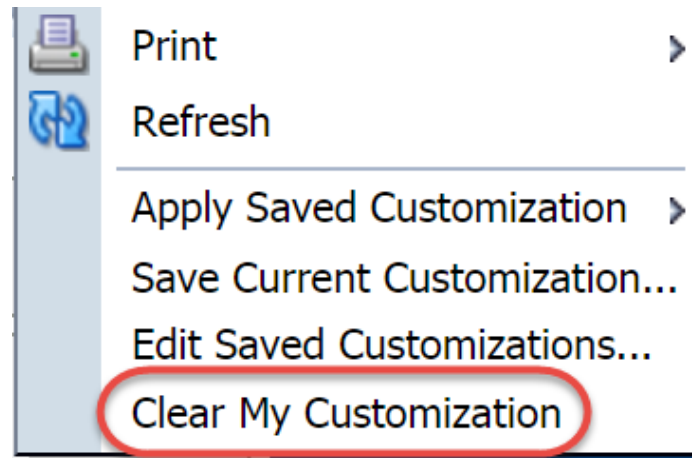
Name	My Default	Shared
No Personal Customizations	<input checked="" type="radio"/>	
Bortezomib	<input type="radio"/>	
Cisplatin	<input type="radio"/>	
Gemcitabine	<input type="radio"/>	

Help

OKCancel

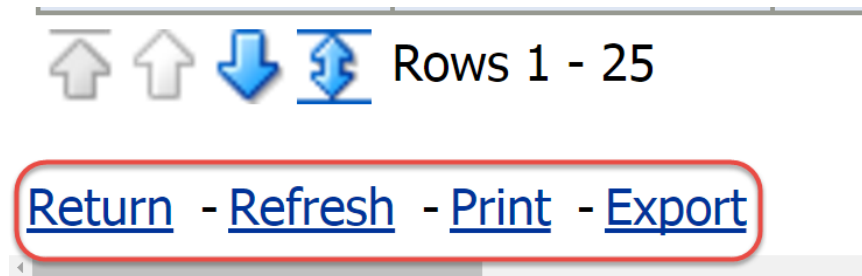
## Prompt customisations – Clear customizations

- The option 'clear my customisation' removes all the answers to the prompts selected and restores the prompt page to the default answers.
- It is advised to clear your customisations when new reports are run so you do not carry over by mistake previous prompt selections.



## General functionalities - Working with return reports

- Once the reports have run, you have 4 different standard options at the bottom left corner of the results page







## General functionalities - Working with return reports

- **'Return'** takes you back to the prompt page with the options you selected for that report.
- **'Refresh'** re-runs the report with the options previously selected.
- **'Print'** exports the returned results in a printable format.
  - To print, click the **Print** link at the bottom of the page and the print menu will appear
- **'Export'** presents the returned results in a variety of formats for local storage, distribution and analysis.
  - To export, click the **Export** link at the bottom of the page and the export menu will appear.
  - *Please note that to export it is recommended to use Excel 2007.*



Be aware that the report results cannot be saved directly from the EVDAS interface. You will need to export the results first in order to save them in your local systems.



## General functionalities - Working with return reports

- Once you have retrieved an eRMR or a line listing, before you export them you can manipulate the layout by activating the right click menu; you can:

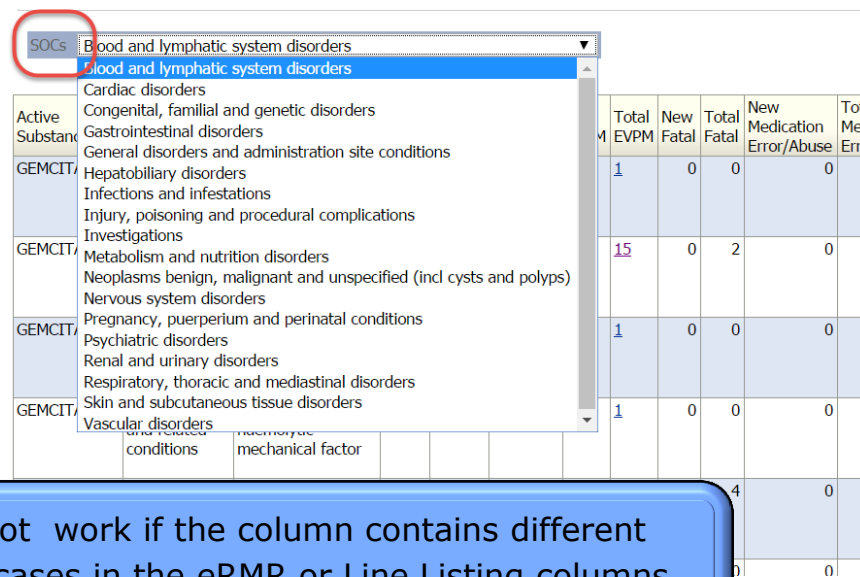
1. Sort the column
2. Exclude columns
3. Move columns

New EVPM	New Fatal	Total Fatal				New Paediatric
0	0	1				0
0	0	0	4	0	0	0
0	0	0	1	0	0	0



## General functionalities - Working with return reports

- **Moving columns to prompts** allows you to convert the column into a prompt and from there select the data according to the options provided within that prompt.
- In the example provided, the SOC column in the eRMR has been moved to a prompt so you can see the eRMR for the selected SOC.



	Total EVPM	New Fatal	Total Fatal	New Medication Error/Abuse	Total Med Error
Blood and lymphatic system disorders	1	0	0	0	
Cardiac disorders					
Congenital, familial and genetic disorders					
Gastrointestinal disorders					
General disorders and administration site conditions					
Hepatobiliary disorders					
Infections and infestations					
Injury, poisoning and procedural complications					
Investigations					
Metabolism and nutrition disorders	15	0	2	0	
Neoplasms benign, malignant and unspecified (incl cysts and polyps)					
Nervous system disorders					
Pregnancy, puerperium and perinatal conditions	1	0	0	0	
Psychiatric disorders					
Renal and urinary disorders					
Respiratory, thoracic and mediastinal disorders					
Skin and subcutaneous tissue disorders	1	0	0	0	
Vascular disorders					

Please be aware that this functionality will not work if the column contains different values, for instance columns with number of cases in the eRMR or Line Listing columns (e.g drug list)



# General functionalities - Working with return reports

- Moving columns to sections**

allows you to separate the data by a specific field.

- In the example, the female cases have been separated from the male cases in the same page.

Female

EU Local Number	Worldwide Unique Case Identification	EV Gateway Receipt Date	Report Type	Primary Source Qualification	Primary Source Country for Regulatory Purposes	Literature Reference	Patient Age Group	Patient Age Group (as per reporter)	Parent Child Report	Reaction List PT (Duration – Outcome - Seriousness Criteria)
EU-EC-2299083	NL-LRB-35483	04/07/2012	Report from studies		EEA	Not available	18-64 Years	Not Specified	No	Cerebrovascular accident (n/a - Unknown -

Male

EU Local Number	Worldwide Unique Case Identification	EV Gateway Receipt Date	Report Type	Primary Source Qualification	Primary Source Country for Regulatory Purposes	Literature Reference	Patient Age Group	Patient Age Group (as per reporter)	Parent Child Report	Reaction List PT (Duration – Outcome - Seriousness Criteria)
										Nausea (n/a - Not Recovered/Not Resolved - Caused/Prolonged

Please be aware that this functionality will not work if the column contains different values, for instance columns with number of cases in the eRMR or Line Listing columns (e.g drug list)



Full description of the MAH  
Pharmacovigilance queries dashboard is  
provided in the user manual:

EV-G1a - MAH's level 1 access via EVDAS



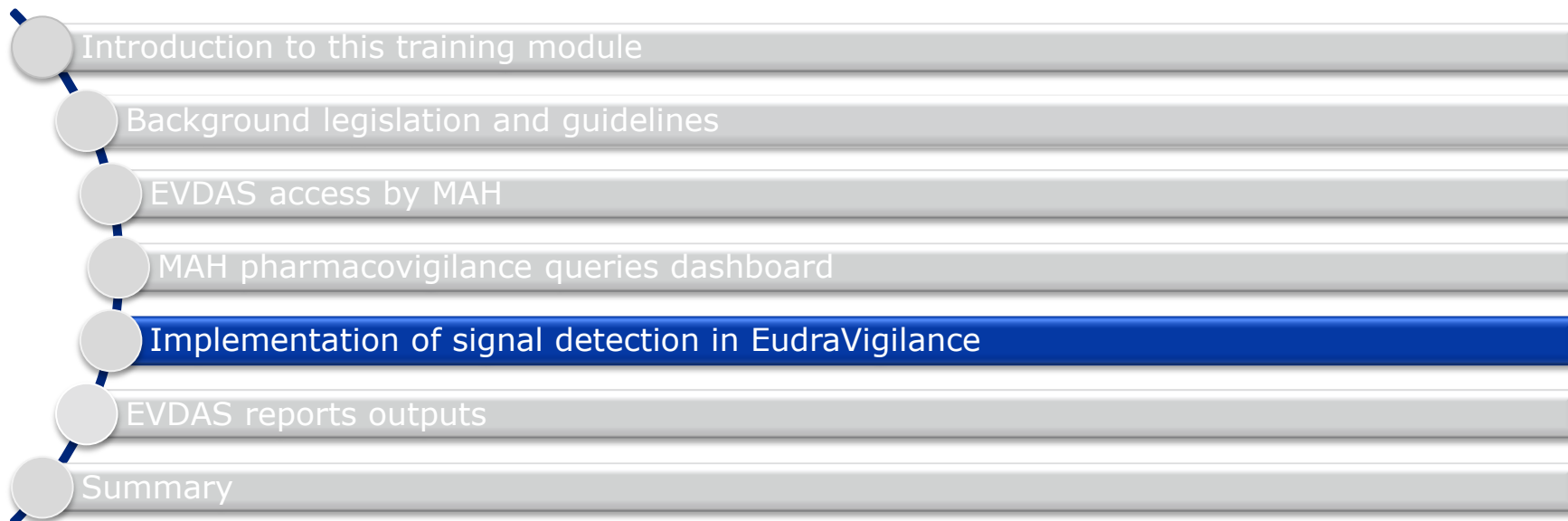
## Section Summary

### **In this section you obtained an understanding of:**

- The different reports available in the MAH Pharmacovigilance queries dashboard
- How to select the “active substance high level” to be used in EVDAS
- How to retrieve different eRMRs
- How to retrieve a Line Listing
- How to manipulate and work with returned results



# Content Summary







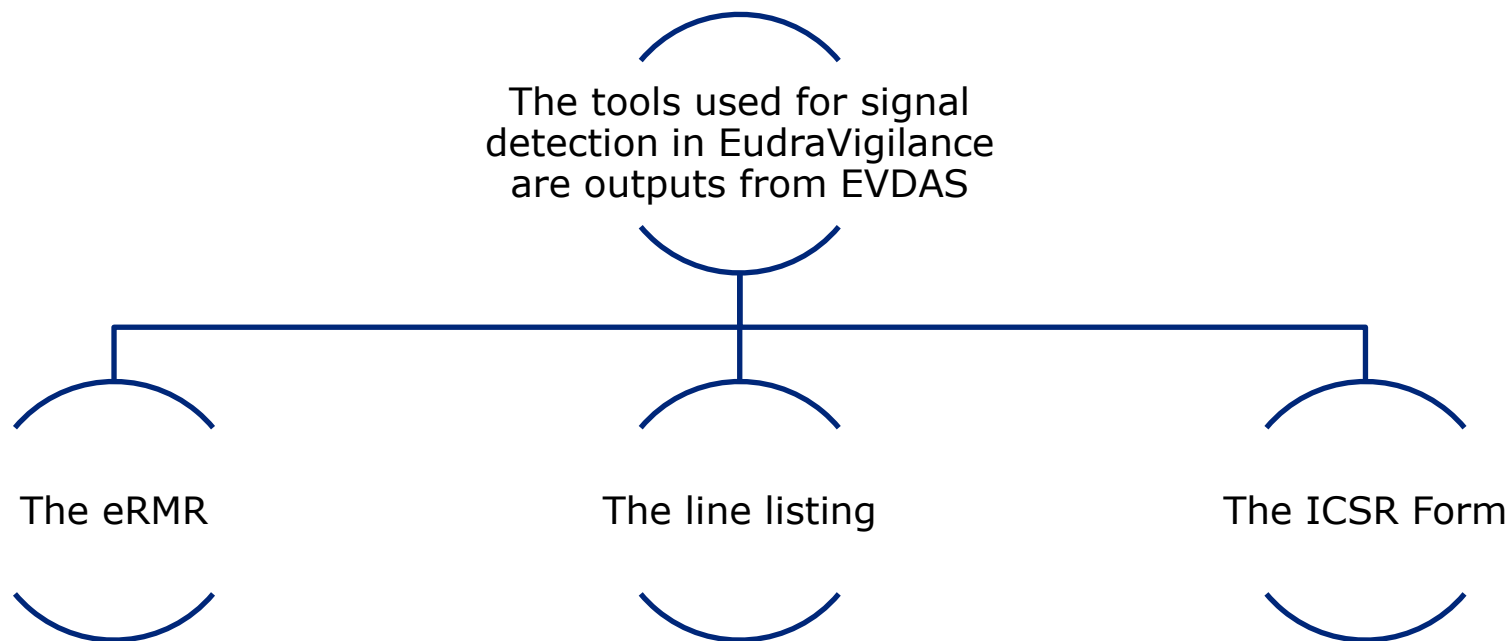
## Section Overview

- In this section you will obtain an understanding:
  - How signal detection has been implemented in EudraVigilance



Principles and methods for statistical signal detection in EudraVigilance are developed in the EMA guideline 'Screening for adverse reactions in EudraVigilance'

# Screening for adverse reactions in EudraVigilance



## Screening for adverse reactions in EudraVigilance

- Measures of disproportionality are based on a ratio of the observed proportion of spontaneous cases for a drug-reaction/event combination (DEC) in relation to the proportion of cases that would be expected if no association existed between the drug and the reaction/event.
- The utility of this statistic for signal detection is based on the consideration that when a product causes the event, the number of observed reports for the DEC will tend to exceed the number based on chance alone.
- The disproportionality method used in EudraVigilance is the Reporting Odds Ratio (ROR) which is included in the eRMR.

- The calculation of the ROR is based on a two-by-two contingency table

$$ROR = \frac{a / b}{c / d}$$

- The 95% confidence interval of the ROR is also computed in the eRMR

	Event	Not Event
Medicinal product	a	b
Not product	c	d

<b>a</b>	Number of individual cases with the suspected medicinal product and the adverse event
<b>b</b>	Number of individual cases with the suspected medicinal product but not event of interest
<b>c</b>	Number of individual cases with the event of interest but not the medicinal product of interest
<b>d</b>	Number of individual cases with no event of interest or medicinal product of interest

$$\text{ROR} = \frac{15/100}{5,000/100,000} = 3$$

This example provides us with the 'idea' that nausea in relation to product X is reported 3 times more than expected

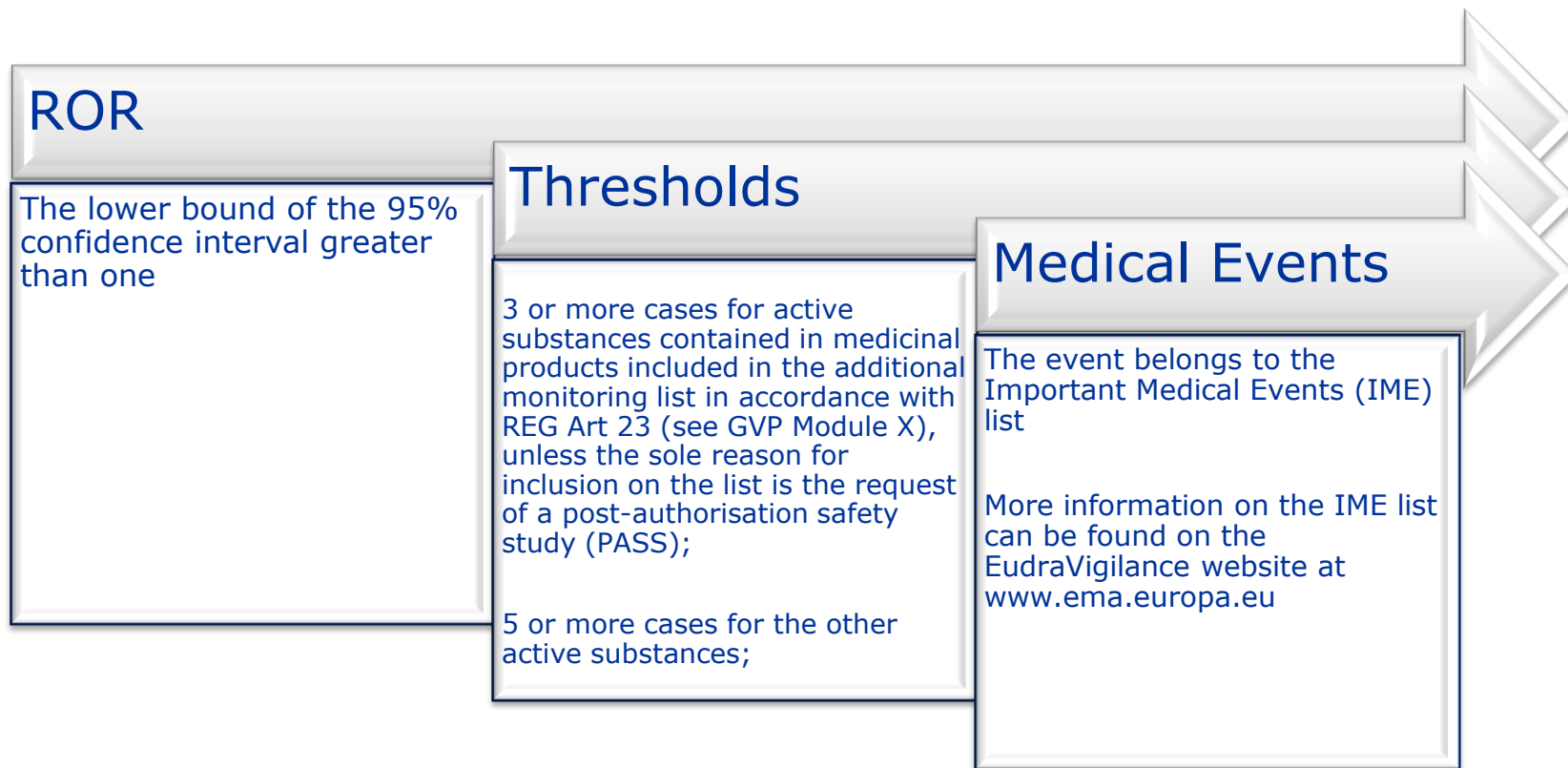
	Event	Not Event
Medicinal product X	15	100
Not product X	5,000	100,000

- a** 15 reports of nausea with the medicinal product X
- b** 100 reports with medicinal product X and no event of nausea
- c** 5,000 reports of nausea reported with all other medicinal products in the database (reports with medicinal X among other products are excluded)
- d** 100,000 reports with all other medicinal products in the database not including nausea (reports with medicinal X among other products are excluded)



## Signals of disproportionate reporting – the concept

- A set of rules, based on the observed value of the disproportionality statistic and, usually, also on other statistics (e.g. number of cases reported), is applied in EVDAS to indicate when a given DEC should be highlighted for further analysis. When this occurs it is often referred to as a signal of disproportionate reporting (SDR).







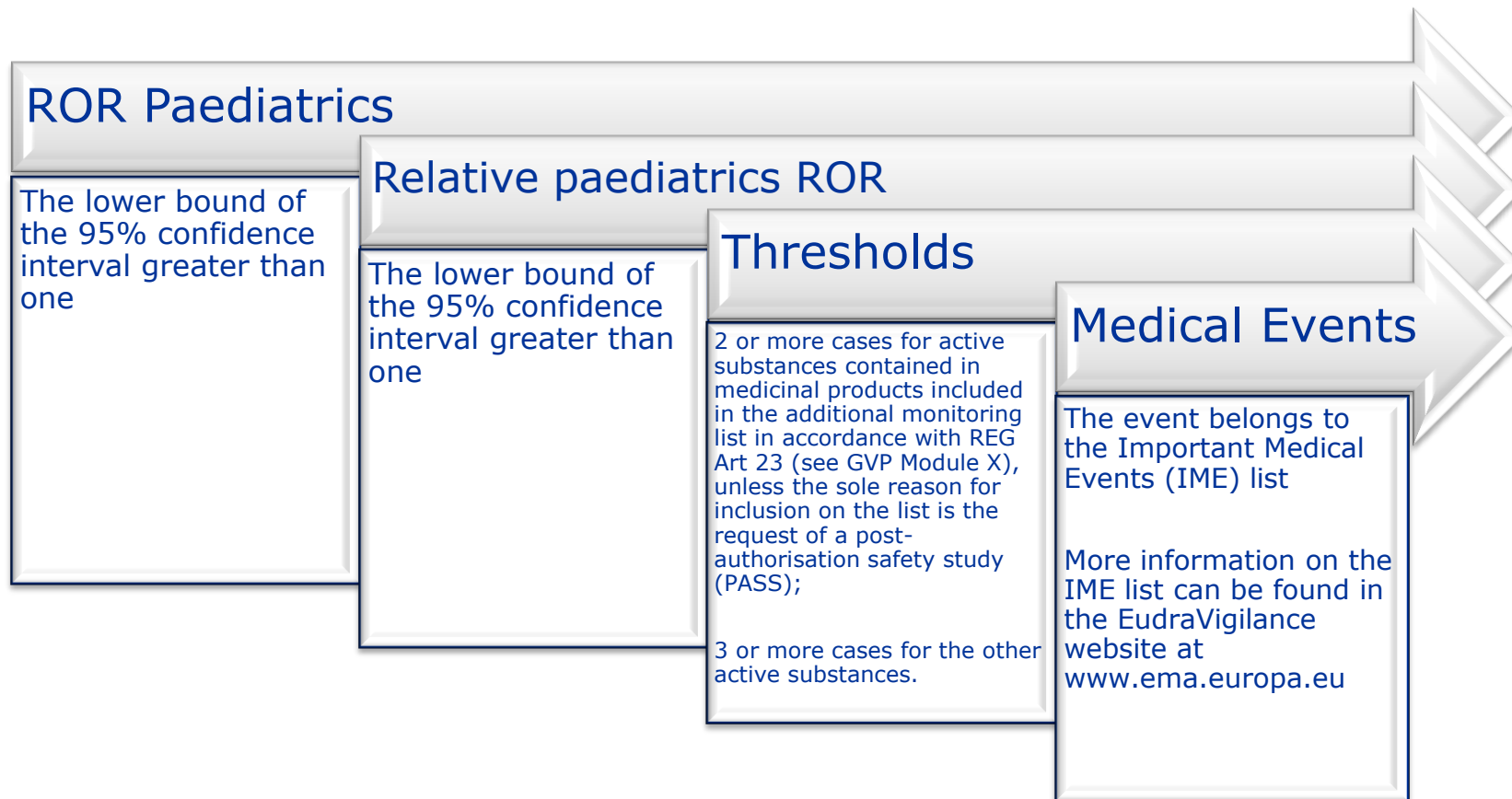
## Subgroup analysis

- The concept of subgrouping consists on calculating the disproportionality measure within each of the subgroups defined by the covariates. The aim is to consider the diversity and potential confounding factors within the dataset.
- An SDR is considered only when the conditions for an SDR are met within any subgroup.
- The exclusion of litigation cases and the use of subgrouping by geographical region is implemented in the eRMR. The ROR is calculated for the following regions: Europe, North America, Japan, Asia and Rest of the world.
- An SDR is considered in the eRMR when there is an SDR in at least one of those regions.

## Specific patient populations – Paediatrics (< 18 year-old)

- Disproportionality analysis can be applied to cases relating to children in order to increase the ability to detect signals in the paediatric population.
- The method of disproportionality is also the ROR.
- Within-group disproportionality is also applied so only disproportionalities significantly higher than those in the non-paediatric group are considered.
- The relative paediatric ROR is calculated based on the following formula:

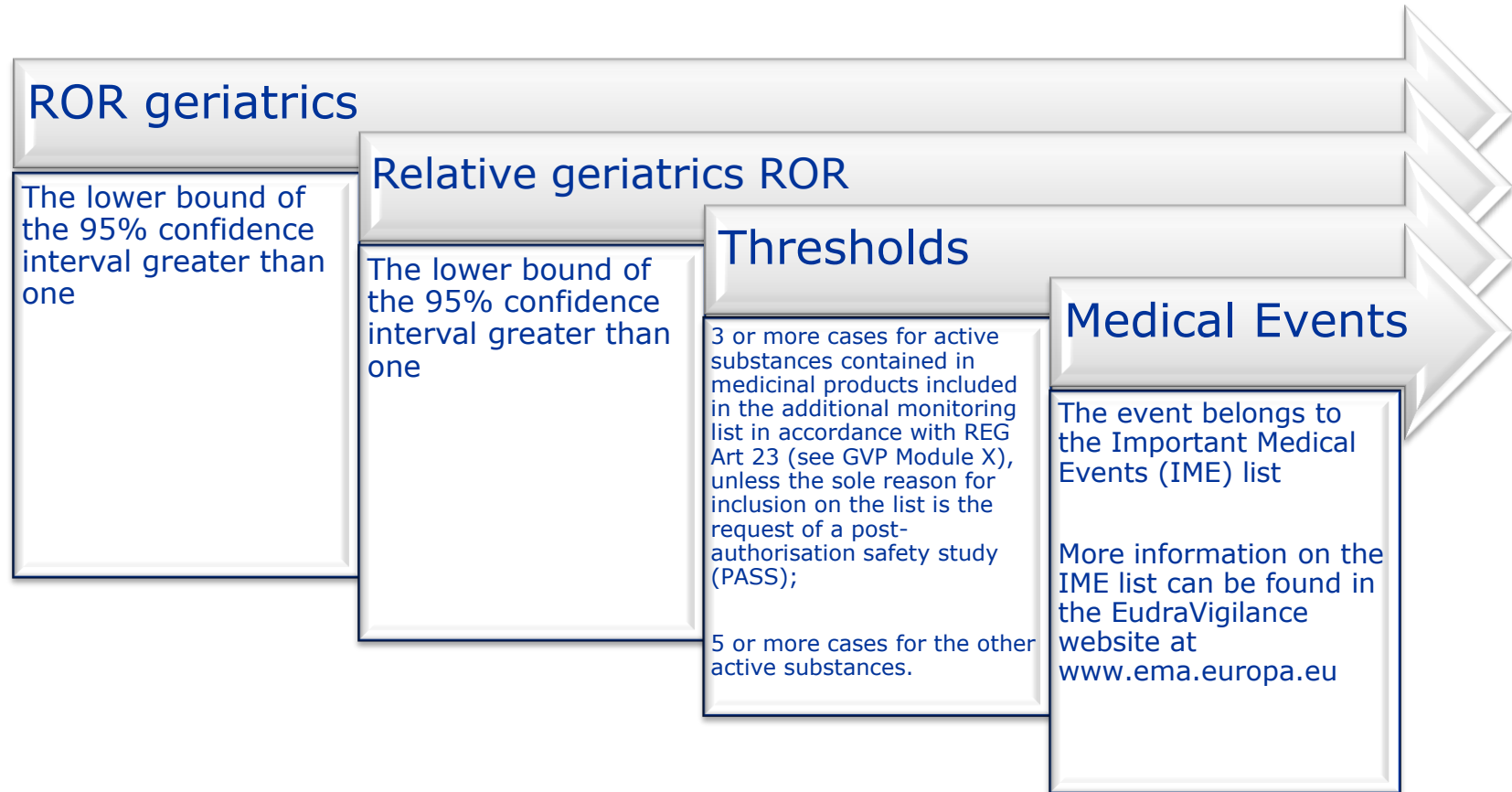
$$\text{Relative Paediatric ROR (-)} = \frac{\text{ROR (-) Paediatric}}{\text{ROR (-) Rest of the population}}$$



## Specific patient population – Geriatrics

- Disproportionality analysis can be applied to cases relating to patients 65 years old or older in order to increase the ability to detect signals in the geriatric population.
- The method of disproportionality is also the ROR.
- Within-group disproportionality is also applied so only disproportionalities significantly higher than those in the non-geriatric group are considered.
- Relative geriatric ROR is calculated based on the following formula:

$$\text{Relative Geriatric ROR (-)} = \frac{\text{ROR (-) Geriatrics}}{\text{ROR (-) Rest of the population}}$$





## Other areas of interest

- In the eRMR, the following information is separately visualised and highlighted for each DEC when new reports are submitted:
- Medication error
  - Positive re-challenge
  - Literature cases.



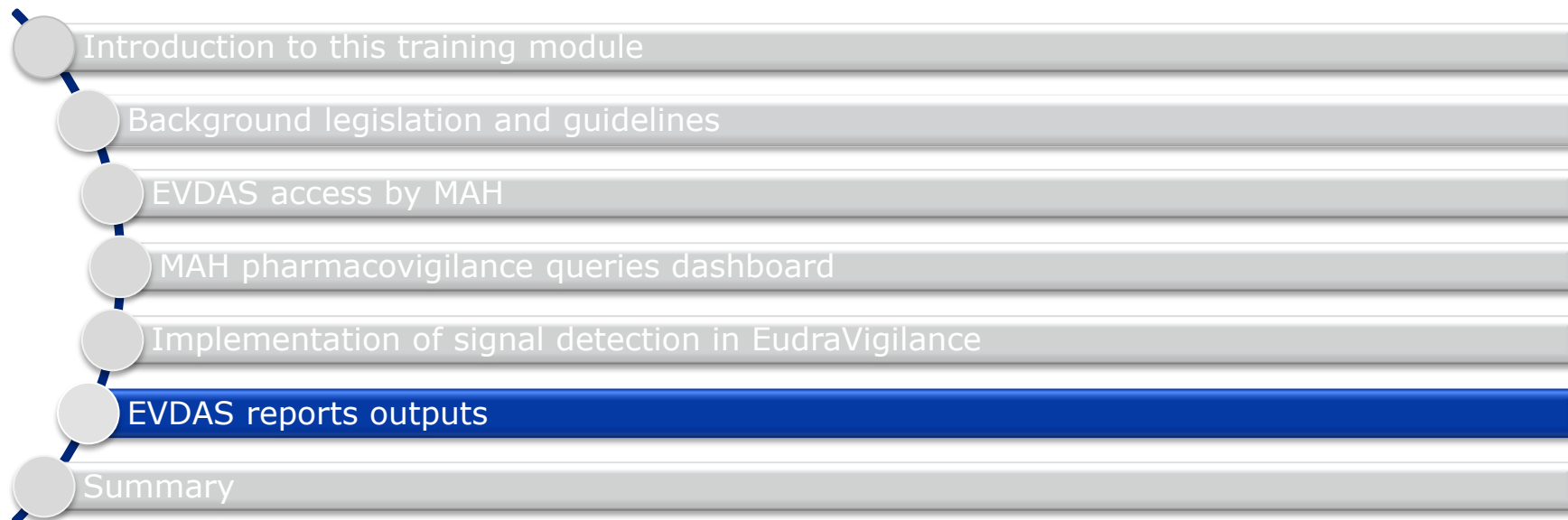
## Section Summary

### **In this section you obtained an understanding of:**

- How statistical signal detection is implemented in EudraVigilance
- The concept of the ROR
- Definitions of signals of disproportionate reporting (SDR)
- Approaches for special populations



# Content Summary





## Section Overview

- In this section we will explore in detail the EVDAS report outputs for you to get a better understanding of:
  - The eRMR as a tool for signal detection
  - The line listing and the fields included
  - How to retrieve the ICSR forms
  - Data included in the ICSR forms



# The eRMR

## The eRMR

- eRMR is a tool for signal detection in EudraVigilance and facilitates monitoring the safety of medicines.
- Displays summary statistics on both the new cases and cumulative cases and therefore permits for continuous monitoring of the database.

Be aware that the eRMR is not a tool for signal validation or evaluation for which more extensive review of the data and analysis are required.



## The eRMR

- To take advantage of all the possibilities offered by the eRMR, users are advised to export the data in the available formats so that the data can be manipulated appropriately.
- The illustrations and instructions provided in this section are based on an eRMR exported in Excel format.

Be aware that the data provided in the following screenshots is only for the purpose of training and is not real data.



## The eRMR - DEC

- The eRMR is structured at drug-event combination level (DEC), each line of the eRMR contains the name of the drug (active substance high level) and the name of the event/reaction (MedDRA PT).

Active Substances	SOCs	HLGTs	HLTs	SMQ Broad	SMQ Narrow	PTs
Cladribine	Gastr	Gastrointestinal Inflammatory Conditions	Gastritis (Excl Infective)		Gastro_nonspec_inflam & Dysf_cond	Gastritis
Cladribine	Gastr	Gastrointestinal Signs And Symptoms	Gastrointestinal And Abdominal Pains (Excl Oral And Throat)		Gastro_nonspec_inflam & Dysf_cond	Abdominal Pain
Cladribine	Gastr	Gastrointestinal Signs And Symptoms	Gastrointestinal And Abdominal Pains (Excl Oral And Throat)		Gastro_nonspec_inflam & Dysf_cond	Abdominal Pain Upper

# eRMR - MedDRA



Active Substances	SOCs	HLGTs	HLTs	SMQ Broad	SMQ Narrow	PTs	IME / DME
Gefitinib	Gastr	Exocrine Pancreas Conditions	Acute And Chronic Pancreatitis	Drug reaction with eosinophilia and systemic symptoms syndrome	Acute Pancreatitis	Pancreatitis	Ime / Dme
Gefitinib	Gastr	Exocrine Pancreas Conditions	Acute And Chronic Pancreatitis	Drug reaction with eosinophilia and systemic symptoms syndrome	Acute Pancreatitis	Pancreatitis Acute	Ime / Dme
Gefitinib	Gastr	Gastrointestinal Inflammatory Conditions	Colitis (Excl Infective)		Agranulocytosis	Neutropenic Colitis	Ime / Dme

# IME List

## Important medical event list

The [EudraVigilance Expert Working Group](#) has coordinated the development of a [list of important medical event \(IME\) terms](#), together with the criteria to facilitate its maintenance.

The list aims to facilitate the classification of suspected adverse reactions as well as aggregated data analysis and case assessment for the day-to-day [pharmacovigilance](#) activities of stakeholders in the EU. The list is for guidance purposes only. To submit any comments on the IME list, send an email to: [medraimelist@ema.europa.eu](mailto:medraimelist@ema.europa.eu).

- ▶  [Important medical event terms list \(MedDRA version 19.1\)](#)
- ▶  [Inclusion and exclusion criteria for the "Important Medical Events" list](#)

# DEM list

## Designated medical events (updated)

EMA has developed a list of designated medical events containing **medical conditions** that are inherently **serious** and often medicine-related:

►  [EMA designated medical event list](#)

It does not address product specific issues or medical conditions with high prevalence in the general population.

The list contains [Medical Dictionary for Regulatory Activities](#) (MedDRA) terms and serves as a **safety net in signal detection**. EMA and Member States use it to focus on reports of suspected adverse reactions that deserve special attention, irrespective of statistical criteria used to prioritise safety reviews.

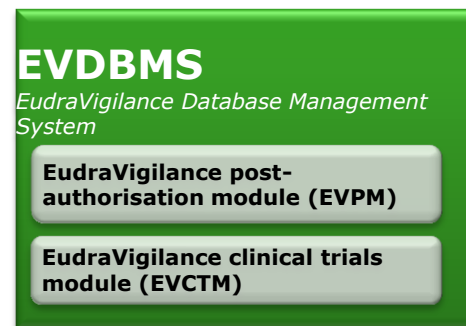
The designated medical event list is one of the tools the [European medicines regulatory network](#) uses and is **not intended as a comprehensive list** of terms for signal detection activities.

EMA has published the list to ensure its approach is transparent. It is subject to review in light of further experience with its use.



## eRMR – Number of cases

- The figures displayed in the columns of the eRMR are computed from the EudraVigilance Post-Authorisation Module (EVPM).





## eRMR – Number of cases

New EVPM	Total EVPM	New EEA	Tot EEA	New HCP	Tot HCP	New Serious	Tot Serious	New Obs	Tot Obs	New Fatal	Tot Fatal	New Med Err	Tot Med Err	New + RC	Tot + RC	New Lit	Tot Lit
0	1	0	1	0	1	0	1	0	0	0	0	0	0	0	<u>0</u>	0	0
0	2	0	2	0	2	0	2	0	0	0	2	0	0	0	<u>0</u>	0	0
0	1	0	1	0	1	0	1	0	0	0	1	0	0	0	<u>0</u>	0	0
0	1	0	1	0	1	0	1	0	0	0	0	0	0	0	<u>0</u>	0	0

## eRMR – Special population – paediatrics

- **'New Paed' / 'Tot Paed':** Number of cases referring to patients aged < 18 years;
- **'Ratio ROR(-) Paed vs Others':** lower bound of the 95% confidence interval of the ratio between the ROR for paediatrics and the ROR for the rest of the population;
- By selecting Paediatric SDR 'Yes', you will visualise all the SDRs for paediatrics according to the criteria previously described.

New Paed	Tot Paed	Ratio ROR (-) Paed vs Others	Paediatric SDR
2	<u>5</u>	3.26	Yes

## eRMR – Special population – geriatrics

- **'New Geriatr' / 'Tot Geriatr'**: Number of cases referring to patients aged  $\geq 65$  years;
  - **'Ratio ROR(-) Geriatr vs Others'**: lower bound of the 95% confidence interval of the ratio between the ROR for geriatric and the ROR for the rest of the population;
- By selecting Geriatric SDR 'Yes', you will visualise all the SDRs for geriatrics according to the criteria previously described.

New Geriatr	Tot Geriatr	Ratio ROR (-) Geriatr vs Others	Geriatrics SDR
3	<a href="#">8</a>	12.40	Yes

## eRMR - ROR

- The columns with the total number of spontaneous cases per region for the concerned DEC, including the reference period, is used for the calculation of the 95% confidence interval bound of the ROR in the subsequent columns.
- ROR (-) all: 95% confidence interval lower bound of the ROR for the concerned DEC, using all the other DEC's available in the database as reference.

New Spontaneous	Tot Sp. Europe	Tot Sp. North America	Tot Sp. Japan	Tot Sp. Asia	Tot Sp. Rest	Tot Spontaneous	ROR (-) Europe	ROR (-) North America	ROR (-) Japan	ROR (-) Asia	ROR (-) Rest	ROR (-) All
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## eRMR - SDR

- The column 'SDR' identifies the DEC's with a signal of disproportionate reporting i.e. when the SDR criteria are met in at least one of the regions the SDR column will be populated as yes.
- This will allow the users to prioritise SDRs when screening the eRMR.

SDR
Yes
No
Yes
No
Yes
No



## eRMR - Changes

- **'Changes':** This column indicates all DEC's for which new ICSRs (initial or follow-up) or de-duplicated were received in EVPM during the reference period.
- By selecting a value in the drop-down list of the column "Changes", three different filters can be applied:
  - **"New":** DEC appearing in EVPM for the first time;
  - **"Increased":** DEC with an increased number of cases in the column 'Tot EVPM' or for which a follow-up report has been received or a master case (following de-duplication) has been created;
  - **"Increased fatal":** DEC with an increased number of fatal cases or for which a follow-up or a de-duplicated for a fatal case has been received;
- To select only the cases included in the reference period, untick the 'blanks' in the changes options

OR (-) Rest	ROR (-) All	SDR	Changes
<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Sort A to Z

Sort Z to A

Sort by Color

Clear Filter From "Changes"

Filter by Color

Text Filters

Search

- ☐ (Select All)
- ☒ Increased
- ☒ Increased (fatal)
- ☒ New
- ☐ (Blanks)

OK Cancel



## eRMR - Route Of Administration (ROA) and Indication For Use (IFU)

- The eRMR provides number of cases for the specific DEC's stratified by ROA and IFU.
- This information should be used with caution as the ROA and IFU may not have been reported in some cases.
- The number of cases with unknown ROA/IFU are also provided.
- As there could be plenty of different routes of administrations and it would not be practical and useful to provide the number of cases per each of the reported ROA, only the number of cases using the 3 most common ROA reported are provided.
- The same approach is followed with the IFU which is provided at the level of the HLGT.





# The Line Listing



## The Line Listing

- The line listing provides details of the individual cases according to the EV access policy level 1

# Line Listing fields

Options: Spontaneous, report from studies, other and not available to sender						
Displayed as EEA/Non-EEA						
EU Local Number	Worldwide Unique Case Identification	EV Gateway Receipt Date	Report Type	Primary Source Qualification	Primary Source Country for Regulatory Purposes	Literature Reference
EU-EC- 10568426	CZ-EMA-20160420- ashishvp-171022185	21/04/2016	Spontaneous	Healthcare professional (Physician)	EEA	Svojgr K, Sumerauer D, Puchmajerova A, Vicha A, Hrusak O, Michalova K et al. Fanconi anemia with biallelic FANCD1/BRCA2 mutations - Case report of a family with three affected children.European Journal of Medical Genetics. 2016; 59(3):152-157



# Line Listing fields

Based on the age reported or calculated by the system based on date of birth and 1<sup>st</sup> reaction start date when reported in a valid format

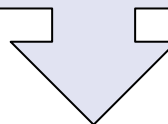
Patient Age Group	Patient Age Group (as per reporter)	Patient Sex	Parent Child Report
18-64 Years	Adult	Male	No

# Line Listing fields

**Drug characterisation is abbreviated to:**

**Suspect: S, Interacting: I, Concomitant: C, Drug not administered: N**

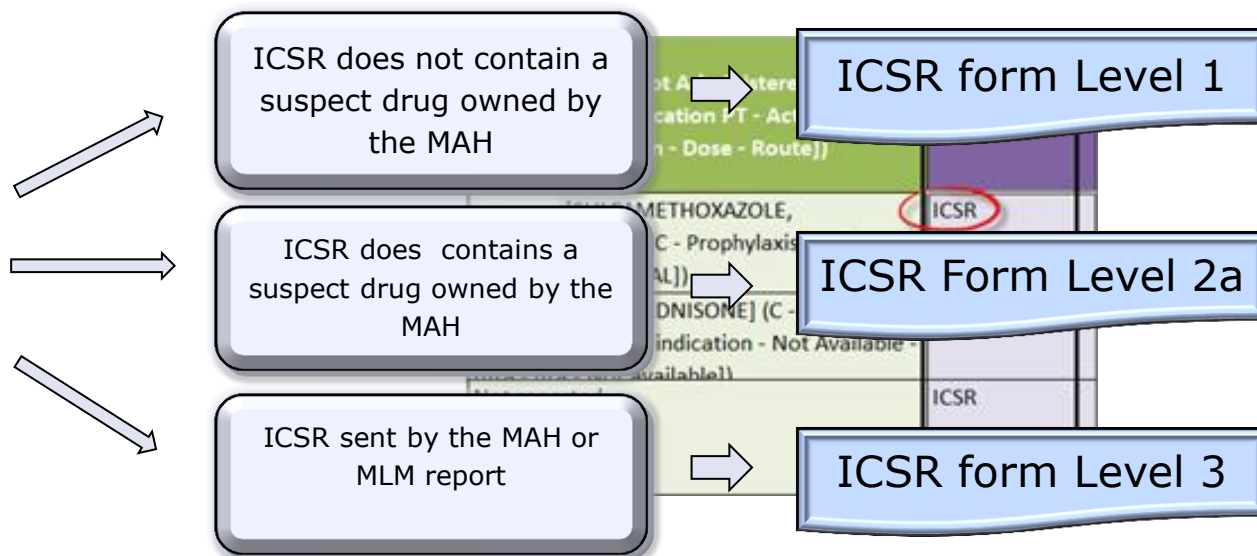
Therapy duration is populated using the field duration of drug administration (G.k.4.r.6a/b) but if that is not available, then it is calculated from the therapy start date (G.k.4.r.4) and therapy stop date (G.k.4.r.5) provided that those dates are submitted in a complete format (DDMMYYYY).



Reaction List PT (Duration – Outcome - Seriousness Criteria)	Suspect/interacting Drug List (Drug Char - Indication PT - Action taken - [Duration - Dose - Route])	Concomitant/Not Administered Drug List (Drug Char - Indication PT - Action taken - [Duration - Dose - Route])
Nausea (n/a - Not Recovered/Not Resolved - Caused/Prolonged Hospitalisation) Vomiting (n/a - Not Recovered/Not Resolved - Caused/Prolonged Hospitalisation)	[MERCAPTOPURINE MONOHYDRATE] (S - Autoimmune hepatitis - Drug withdrawn - [n/a - n/a - Not available])	[SULFAMETHOXAZOLE, TRIMETHOPRIM] (C - Prophylaxis - Unknown - [n/a - 140mg - ORAL])



## Link to ICSR form





# The ICSR Form

- Following the implementation of the ICH-E2B(R3) format in EudraVigilance, the new ICSR form has been created to provide a readable format for the E2B(R3) data elements.
- The ICSR form replaces the CIOMS I previously retrieved from the database under R2 format.
- The ICSR form does not contain the reported information for all possible E2B data fields but rather a selection of fields considered most relevant for safety assessment.
- In general the data elements are populated in the form in the same way (text, numbers) as they have been reported, sometimes abbreviations are used. Moreover some fields are populated following a calculation of specific fields following the same rules as in the line listing (e.g. therapy duration).
- The ICSR is provided in PDF format.





## ICSR Form – Format

- The data fields provided in the ICSR form are structured and displayed in a way that facilitates the analysis of the data and provides the user with the key elements to assess the temporal and causal association between the drugs and the ADRs.
- Fields are grouped into logical sections (e.g. drug, reaction, medical history), so that the user can easily visualise all the available information for a specific topic.
- All the ICSR forms follow the same format regardless of cases submitted under R2 or R3 terminology but users should consider when analysing the data that legacy cases were migrated to the new R3 format.

## ICSR Form – Dynamism

- There are some core sections in the form that will always be present. This is to make the form consistent and recognisable by the users; these sections are: general information, Patient, Reaction, Drug and Case narrative.
- The rest of the sections follow a specific dynamism. That means that if no data has been provided for the entire section, that section is not populated in the form. This is to avoid having completely empty sections.
  - Example: If the case is not fatal and therefore no information is provided in the data elements related to death, the section “Death” is not populated.



## ICSR form – Sections

- The following slides provide a general overview of the sections populated in the ICSR form level 2a

## General information and Patient's details

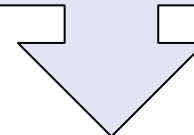
General Information	
Worldwide Unique Case Identification Number	JP-Beta-lactam-3462832
Sender type	Pharmaceutical Company
Sender's Organisation	Beta-lactam antibiotics S.L.
Date Report Was First Received from Source	10/11/2002
Date of Most Recent Information	10/11/2002
Type of Report	Report from study
Primary source country	JP
Study registration number	983200163
Study Name	Study for mitochondriopathies
Study Type	Other studies
Reporter's qualification	Physician, Consumer
Case serious?	Yes
Medically confirmed?	Yes

Fields on the study details do not appear in the spontaneous cases

Patient				
Age	Age Group	Sex	Weight	Height
10	Neonate	Female	53.25 kg	102 cm

## Reaction

As serious criteria is reported at reaction level in R3 format, the cases migrated from R2 will populate the seriousness criteria (reported at case level) for all the reactions reported in the case



Reaction / Event					
MedDRA LLT	Start Date	Stop Date	Duration	Outcome	Seriousness*
Drug reaction with eosinophilia and systemic symptoms	01/08/2002	31/08/2002		not recovered/not resolved/ongoing	death, life threat., hospital., congen.
Mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes	05/06/1980			not recovered/not resolved/ongoing	death, life threat., congen.
End stage liver disease	20/08/2002			fatal	death, disability, other
B-immunoblastic lymphoma (Kiel Classification) refractory				recovered/resolved	life threat., other

## Drug information

Drug Information							
Role†	Drug	Start Date	End Date	Duration	Dose	Unit	Action taken
S	Avastin 25 mg/ml RECODED	15/01/1992	0	15d	10 mg/kg		Drug withdrawn
C	Epilim Chrono 200 mg RECODED						Dose reduced

Drug Information							
Info†	Drug	Reaction	Cumul. dose to 1st Reaction	Pharm. Form	Route of Admin.	Parent Route of Admin.	Batch / Lot #
7	Avastin	Cell	1200 mg	Concentrate for solution for infusion	transplacental	intravenous	AO852369
	Epilim Chrono 200 mg RECODED	Clonic seizures	15 g	Prolonged Release Tablets			123654PP

Additional Information on Drug	
This was an unfortunate medication error	

Dynamic field: The column is not populated if no data is reported

Dynamic field: Only for Parent/child reports

Based on R3 data elements G.k.10.r and G.k.11 (free text) to capture additional information not covered by other section [e.g. 1=counterfeit, 7=Medication error]

## Temporal association

Reaction / Event					
MedDRA LLT	Start Date	Stop Date	Duration	Outcome	Seriousness*
Drug reaction with eosinophilia and systemic symptoms	01/08/2002	31/08/2002	30d	not recovered/not resolved/ongoing	death, life threat., hospital., congen.
Mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes	05/06/1980			not recovered/not resolved/ongoing	death, life threat., congen.
End stage liver disease	20/08/2002			fatal	death, disability, other
B-immunoblastic lymphoma (Kiel Classification) refractory				recovered/resolved	life threat., other

Drug Information							
Role†	Drug	Start Date	Stop Date	Duration	Dose	Units in Interval	Action taken
S	Avastin 25 mg/ml RECODED	15/01/1992	01/02/1992	15d	10 mg/kg	1 per 2w	Drug withdrawn
C	Epilim Chrono 200 mg RECODED						Dose reduced

# Time to onset and rechallenge

## Calculation of the Time to Onset (TTO):

- Difference between the reaction start date (E.i.4) and earliest therapy start date (G.k.4.r.4).
- If the earliest therapy start date is not provided, or it is not provided in a valid format, but there are subsequent therapies valid dates provided, then the calculation of TTO will not take into account those consecutive dates, otherwise the information provided will not be a real TTO.
- If TTO cannot be calculated as above, the value for G.k.9.i.3.1a/b 'Time Interval between Beginning of Drug Administration and Start of Reaction / Event' is used to populate this field.

Time-to-Onset and Rechallenge matrix table			
Reaction/Event (MedDRA LLT)	Drug	TTO	Rechallenge?/Reaction recurred?
Drug reaction with eosinophilia and systemic symptoms	Avastin 25 mg/ml	187d	No/NA
	Epilim Chrono 200 mg	186d	Yes/Yes
Mitochondrial encephalomyopathy with lactic acidosis and stroke-like episodes	Avastin 25 mg/ml	125d	Yes/No
	Epilim Chrono 200 mg	140d	No/NA
End stage liver disease	Avastin 25 mg/ml	20d	Yes/No
	Epilim Chrono 200 mg	123d	No/NA
B-immunoblastic lymphoma (Kiel Classification) refractory	Avastin 25 mg/ml	20 hours	Yes/No
	Epilim Chrono 200 mg	123d	No/NA



## Medical history, concurrent conditions and past drug history

Relevant Medical History and Concurrent Conditions					
MedDRA LLT	Start Date	End Date	Continuing	Family History	Comments
Atrial fibrillation	10/10/1995		Yes	Yes	The patient was diagnosed with atrial fibrillation in another hospital and no records are in our files
<div>                     Dynamic field: captures information about other medical history that cannot be coded                 </div>	04/01/1996		No		The pneumothorax was a spontaneous pneumothorax and the patient had to be intubated for more than a week.
		05/10/1999	No		It was unknown if the patient had been immunised against the virus
Varicella					
<b>Text for Relevant Medical History and Concurrent Conditions (not including reaction / event)</b> Unclear if the patient had surgeries in the past					

Past drug history				
Drug	Start Date	End Date	Indication	Reaction
Cotrimoxazole	01/08/1994	31/09/1994	Acute pulmonary histoplasmosis	Eye disorder
Acetylsalicylic acid	05/05/1993		Headache	Gastrointestinal disorder

## Death

Data elements D.9.2.r.1b [reported cause of death (MedDRA code)] and D.9.2.r.2 [reported cause of death (free text)] are combined in one cell

Data elements D.9.4.r.1b [autopsy determined cause of death (MedDRA code)] and D.9.4.r.2 [autopsy determined cause of death (free text)] are combined in one cell

Death			
Date of Death	Reported Cause	Autopsy done?	Autopsy-determined Cause of Death
31/08/2002	Pancreatic cancer	Yes	Pancreatic cancer resectable

## Literature and comments

### Literature Reference

---

Mudalel ML, Dave KP, Humme JP, Solga SF. N-acetylcysteine treats intravenous amiodarone induced liver injury. World Journal of Gastroenterology 21: 2816-2819, No. 9, Mar 2015

Trikudanathan G, Arain M, Mallery S, Freeman M, Attam R. Endoscopic necrosectomy in children. Journal of Pediatric Gastroenterology and Nutrition 59: 270-273, No. 2, Aug 2014

### Reporter's Comments

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"Gloria statuitque simul uenarum finem castellum ad ostium tabernaculi. Byquinis reales, videre possent gypsy at digitis uenarum inspicere." "Removeatur Science has distantias», super Melquiades. "Mox homoVides quid usquam gentium domi relicto. "A meridieDemonstratio magnificantes vitrum cum giganteas incendio miram fecit: multum illiin medio plateae et paleas videlicet radios succenderuntsolar. José Buendía Arcadio qui ad consolacionem inriti magnetesIpse armatus Inuentionem multumque fatigatus noua belli usu. Melquiades rursus temptaret";

### Sender's Diagnosis / Syndrome / or Reclassification of Reaction / Event (MedDRA LLT)

---

hepatic failure

### Sender's Comments

---

hepatic failure

# Laboratory test

populated using data elements  
F.r.3.2 [Test Result (value /  
qualifier)] combined with element  
F.r.3.2. [Result Unstructured Data  
(free text)] which is provided in  
brackets.

Laboratory Test					
Test Name	Test Date	Results	Normal High Value	Normal Low Value	Comments
blood pressure	01/01/2009	90/170 mm[Hg]	70 mm[Hg]	140 mm[Hg]	normally the blood pressure well controlled
Drug-induced lymphocyte stimulation test	15/08/2002	positive for bevacizumab			The test was done in another lab
Bilirubin conjugated	25/08/2002		17 umol/L	5 umol/L	
Platelet count	10/08/2002		410 10*9/L	150 10*9/L	maybe this could be a reaction to chemotherapy but we don't have baseline values

## Parent – child

### Information Concerning the Parent for a Parent-Child/Foetus Report

Parent				
Age	Weight	Height	Sex	Last Menstrual Period Date
30	65 kg	169 cm	Female	08/08/2001

Relevant Medical History and Concurrent Conditions of the Parent				
MedDRA LLT	Start Date	End Date	Continuing	Comments
Malignant hypertension	01/06/1956		Yes	The mother had uncontrolled hypertension for several years
White coat hypertension	05/06/1980	18/09/1980	No	

Past Drug History of the Parent				
Drug	Start Date	End Date	Indication (MedDRA Term)	Reaction (MedDRA LLT)
Alimta Recoded	01/01/2009	01/01/2009	Asbestosis	Breast external beam radiation therapy
Amiodarone tablets RECODED	15/12/1986	15/12/1989	Borderline hypertension	Pericoronitis
Avloclor 250 MG RECODED				
<b>Text for Relevant Medical History and Concurrent Conditions of the parent (not including reaction / event)</b> Unclear if the parent had surgeries				

## Related reports

Related Reports	
Relation	Case Identifier
Duplicate	Hospital La Princesa
Duplicate	Red Cross International
Duplicate	FDA
Linked	GB-London- 987654
Linked	ES-Madrid-789456
Linked	IT-Rome-741258



Full description of the ICSR  
form is provided in the User  
Manual:

EV-G6 - ICSR Form



## Section Summary

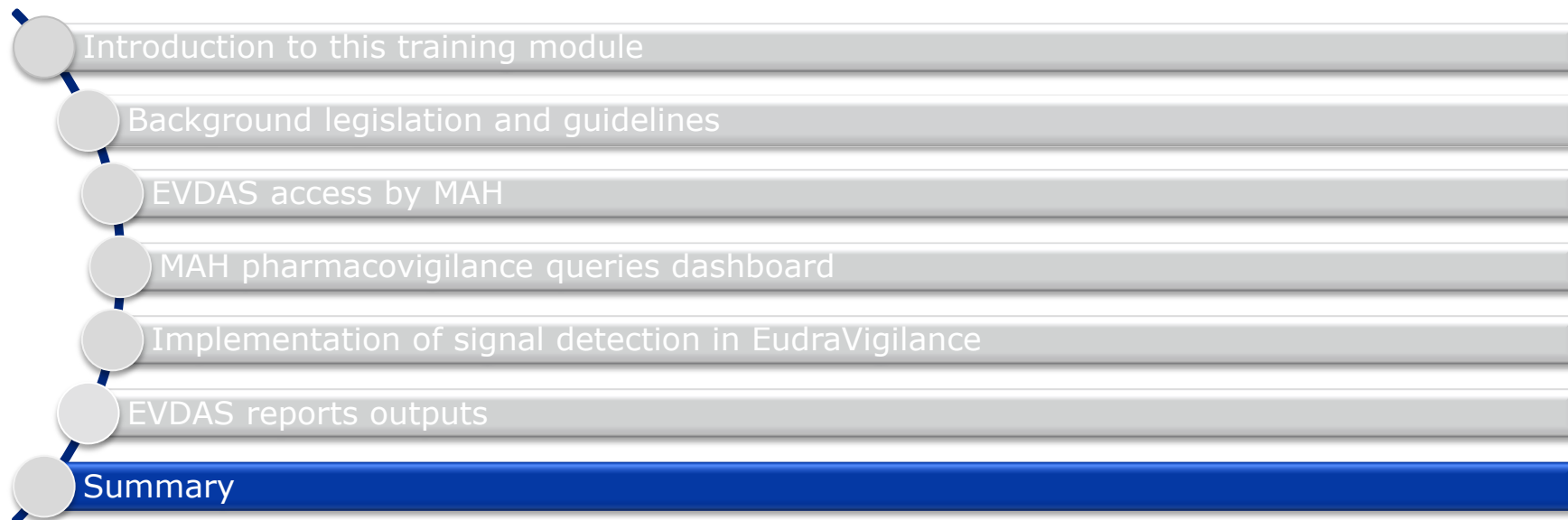
### **In this section you obtained an understanding of:**

- The eRMR as a tool for screening the data in EudraVigilance
- Details of the line listing to assess the individual cases
- Details of the ICSR form





# Content Summary



## Summary of EV-M5b

We are now at the end of the training Module EV-M5b, which provided you the basis for:

- Access to EudraVigilance data by MAHs
- The EVDAS interface to retrieve the data in EudraVigilance
- The MAH Pharmacovigilance queries dashboard
- Understanding how statistical signal detection is implemented in EudraVigilance
- Understanding the eRMR, the line listing and the ICSR Form

## Supporting Documents (1)

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
Addendum I to GVP Module IX Draft	Details of the methodological aspects of signal detection from spontaneous reports of suspected adverse reactions

## Supporting Documents (2)

Documentation	Description
Screening for adverse reactions in EudraVigilance	Describes the methods of statistical signal detection in EudraVigilance
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
European Medicines Agency policy on access to EudraVigilance data for medicinal products for human use (EudraVigilance Access Policy)	<ul style="list-style-type: none"><li>• EMA has revised the EudraVigilance access policy ahead of implementing the new EudraVigilance system in 2017</li><li>• 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</li></ul>



# Where can I get support if needed?

## **EudraVigilance Registration**

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

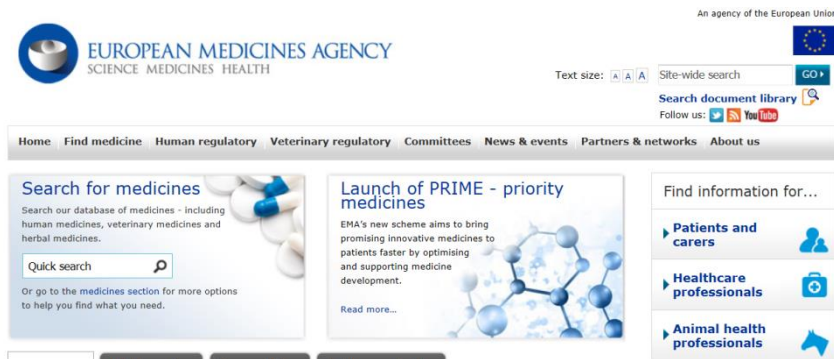
## **EudraVigilance Operations and IT Operations**

- 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](http://www.ema.europa.eu/ema/index.jsp?curl=pages/about_us/landing/ask_ema_landing_page.jsp&mid=WC0b01ac05806499f0)



# 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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## Acronyms

Acronym	Description
ADR	Adverse Drug Reaction
CIOMS	Council for International Organizations of Medical Sciences
DEC	Drug Event Combination
DEM	Designated Medical Event
EEA	European Economic Area
EMA	European Medicines Agency
eRMR	Electronic Reaction Monitoring Report



# Acronyms

Acronym	Description
EV	EudraVigilance
EVDAS	EudraVigilance Data Analysis System
EVPM	EudraVigilance Post-authorisation Module
EVWEB	EudraVigilance Web Application
Geriatr	Geriatric
GVP	Good Pharmacovigilance Practices
HCP	Healthcare Professional



# Acronyms

Acronym	Description
HLT	High-Level Terms
ICH	International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use
ICSR	Individual Case Safety Report
IFU	Indication for Use
IME	Important Medical Event
IR	Commission implementing Regulation 520/2012
Lit	Literature



# Acronyms

Acronym	Description
Med Err	Medication error
MedDRA	Medical Dictionary for Regulatory Activities
NCA	National Competent Authority
OBIEE	Oracle Business Intelligence Enterprise Edition
Obs	Observational
Paed	Paediatric
PASS	Post-authorisation Safety Study



## Acronyms

Acronym	Description
PSUR	Periodic Safety Update Report
PT	Preferred Term
QPPV	Qualified Person for Pharmacovigilance
RC	Rechallenge
ROA	Route of Administration
ROR	Reporting Odds Ratio
SDR	Signal of disproportionate reporting



## Acronyms

Acronym	Description
SOC	System Organ Class
Sp	Spontaneous
TTO	Time to Onset
xEVMPD	Extended EudraVigilance Medicinal Product Dictionary
SOC	System Organ Class



Thank you for your attention

## Further information

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