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EudraVigilance User Manual

Marketing Authorisation Holders - EudraVigilance access via the
EudraVigilance Data Analysis System

electronic Reaction Monitoring Reports, Line Listings and Active Substance
Grouping reports

Version 2.1

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Version

Date	Version number	Summary of changes
07 Nov 2017	1.0	Original version
22 Jan 2018	1.1	<p>Warning regarding reports from studies deleted from the overview section.</p> <p>Section 4.2.1.1. data reliability warning message deleted from section 4.2.1.1 and 5.1.1.</p> <p>Sections 9.5 and 9.9 updated to clarify how the 'new columns' of the ad hoc eRMR are populated.</p> <p>Annex II. Description of the eRMR columns updated.</p>
14 May 2018	1.2	<p>Section 2. updated to further clarify general access.</p> <p>Sections 4.2, 4.3 and 5.2 updated to reflect the data lock point for the cases included in the eRMRs and line listing.</p> <p>Section 6 updated to reflect the marketing authorisation status within the active substance grouping reports outputs.</p> <p>Section 8.3.3 updated to clarify the 'hide columns' functionality.</p> <p>Section 9.1 updated to clarify the use of the eRMR in relation to the frequency of monitoring.</p> <p>Section 9.3.1 created to describe the considerations following the updates of the MedDRA versions.</p> <p>Sections 9.5, 9.9 and Annex I updated to reflect how the number of new cases in the ad-hoc eRMR are populated and the corresponding hyperlinks to the line listing.</p> <p>Annex III. Troubleshooting created.</p>
20 April 2020	2	<p>Section 1.1.5. Introduction to EVDAS Terminology – figures updated to reflect the new EVDAS dashboard.</p> <p>Section 3.1 Accessing EVDAS via the EudraVigilance webpage – figures updated to reflect the current webpage.</p> <p>Section 3.3 MAH's Pharmacovigilance Queries dashboard.</p> <p>Section updated to reflect the changes incorporated in the dashboard.</p> <p>Section 4. The electronic Reaction Monitoring Report (eRMR) – Section updated to reflect the new access to fixed reference period eRMRs. The references to the ad-hoc eRMR have been eliminated.</p> <p>Section 5.5 – The line listing output in the EVDAS interface – The cut off dates and cases included in the line listings retrieved via the eRMRs hyperlinks have been further</p>

Date	Version number	Summary of changes
		<p>described.</p> <p>Section 8.3.3 Hide columns – The section has been deleted.</p> <p>Section 9 User manual of the eRMR for MAHs. The references to the ad-hoc eRMR have been deleted. The SDR criteria implemented in EV has been further emphasised.</p>
17 Feb 2021	2.1	<p>New section (9.10.) added to reflect the changes in the EVDAS outputs triggered by the Brexit implementation in EudraVigilance.</p>

Overview

This manual provides guidance for Marketing Authorisation Holders (MAHs) on the use of the EudraVigilance Data Analysis System (EVDAS) to retrieve information for level 1 access as established in the EMA policy on access to EudraVigilance data for medicinal products for human use (Referred in this manual as 'the EudraVigilance access policy') for stakeholder Group III¹. These EVDAS reports permit MAHs to perform signal management activities and therefore comply with the pharmacovigilance obligations established in the Commission Implementing Regulation (EU) No 520/2012 and GVP Module IX on signal management.

The data and information provided at substance level is in the form of an electronic Reaction Monitoring Report (eRMR) containing aggregated data and a line listing with details of the individual cases. Users are also able to retrieve Individual Case Safety Report (ICSRs) forms accessible through the line listing. The ICSR form provides different levels of access driven by the products ownership of the MAHs querying the database.

As the data is provided at the highest level of the active substance in the hierarchy of the *extended EudraVigilance Medicinal Product Dictionary* (xEVMPD), the user will be able learn the substances grouped to a specific scientific composition by using the active substance grouping report in the dashboard.

This manual provides instructions on how to retrieve the data from EVDAS; Moreover, **Section 9** provides guidance on the use of the eRMR for signal detection. Training materials and relevant documents on signal detection and management should also be consulted.

¹European Medicines Agency policy on access to EudraVigilance data for medicinal products for human use
http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000674.jsp

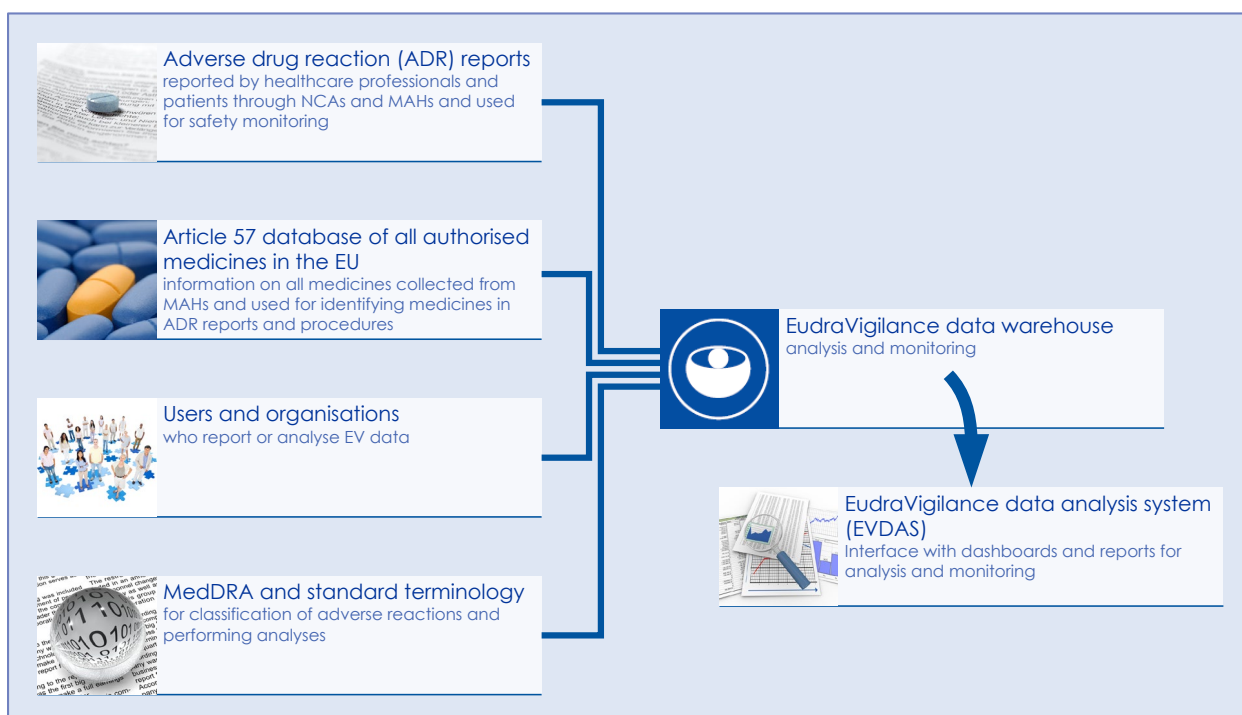
1. Introduction to the EudraVigilance Data Analysis System

This section provides a general introduction about how the *EudraVigilance Data Analysis System* (EVDAS) works, defining at a high level the system architecture. It will also define some of the terms used to describe the system components.

1.1. EudraVigilance Data Analysis System

EVDAS enables users to analyse safety data collected in EudraVigilance so that better-informed decisions can be made about the safety profile of medicinal products.

Figure 1. Components of EVDAS



This architecture consists of the following components:

- Source systems;
- ETL process;
- EudraVigilance data warehouse;
- EVDAS interface.

1.1.1. Source systems

Source systems capture and store the data that are reported to or used by EudraVigilance. These systems include the *EudraVigilance Database Management System (EVDBMS)*, the *extended EudraVigilance Medicinal Product Dictionary (xEVMPD)*, the *EudraVigilance registration database*, the *Medical Dictionary for Regulatory Activities (MedDRA)* and other internationally agreed standard terminologies used within EudraVigilance (e.g. European Pharmacopoeia Dosage Forms).

The EVDBMS contains the following information on suspected adverse drug reactions, which is used to populate the data warehouse:

- *EVPM ICSRs*: Individual Case Safety Reports (ICSRs) transmitted to the EudraVigilance Post-Authorisation Module (EVPM);
- *EVCT ICSRs* (SUSARs): ICSRs transmitted to the EudraVigilance Clinical Trial Module (EVCTM);

The xEVMPD contains information on:

- Authorised Medicinal Products;
- Investigational Medicinal Products that are or have been studied in clinical trials within the European Economic Area (EEA).

Medicinal product and active substance terms reported in cases are recoded against the xEVMPD, and subsequently grouped into 'scientific compositions' for pharmacovigilance activities.

The EudraVigilance registration database contains information about National Competent Authorities (NCAs), MAHs, and sponsors of clinical trials in the EEA that have electronic reporting obligations and are registered with the EudraVigilance system. This information is used to configure data access rights and privileges in the EVDAS.

1.1.2. ETL process

The *extraction, transfer, and loading (ETL)* process is the means by which data are transferred from source systems and loaded into the EudraVigilance Data Warehouse. Specifically, the ETL process does the following:

- Stores information about the structure and contents of source systems and the Data Warehouse;
- Correlates the source systems structure and contents to the structure and contents of the Data Warehouse;
- Provides information to the data extraction tools that physically execute the transfer of data from source systems to the Data Warehouse.

The ETL process is performed nightly so that every day the EudraVigilance Data Warehouse is populated with data updated to the day before.

1.1.3. EudraVigilance Data Warehouse

The *EudraVigilance Data warehouse* is the repository for storing all of the information for analysis from the source systems. Just as the source systems are designed to process capturing and storing data, a data warehouse is optimized for enabling users to report on and manipulate data. Manipulation of data includes transformation of variables, filtering and tabulation.

1.1.4. EVDAS interface

The *EVDAS interface* provides predefined formats for report presentation. Users have functions available for the manipulation of report results. This user manual explains how to use the EVDAS interface to view and manipulate data.

Users interact with the EVDAS interface via a common web browser. The interface layout can change, depending on your internet browser (e.g. if you are using Internet Explorer, Chrome or Firefox). The screenshots in this training manual are taken using Chrome.

Some of the screenshots have been cropped, re-sized or otherwise manipulated to highlight certain features and to enhance legibility. Therefore, the images in the document may not correspond exactly to that which you see on the screen. Although the positioning or size of some elements may be different, the screenshots will be representative of the information the users will encounter in the system.

1.1.5. Introduction to EVDAS Terminology

1.1.5.1. Filters

Filters define the conditions that data must meet to be included in the report result set. A single filter can contain any number of conditions. Only data that meets all of the filter conditions appears in the final result set of a report. The following illustration shows an example of a report filters

Figure 2. Report filters

electronic Reaction Monitoring Report - 1 month
Time run: 30/03/2020 09:30:06

The selected reference period for defining "new" cases is 01/02/2020 to 29/02/2020

Active Substance (High Level) VW is equal to **GEMCITABINE**

and

- none** [View](#)
- or reaction HLGT** [View](#)
- or reaction HLT** [View](#)
- or reaction PT** [View](#)
- or reaction SMQ Level 1 Broad** [View](#)
- or reaction SMQ Level 1 Narrow** [View](#)
- or** '@stdmandatoryfilter10 All' is equal to / is in **MedDRA reaction SOC**
and Reaction SOC is equal to **Cardiac disorders, Gastrointestinal disorders**

and Fixed Period Id is equal to / is in **2**

In this example, the filters have three conditions. The database will return an eRMR with 1 month reference period, for the active substance 'gemcitabine' coded as suspect/interacting; and the reported reaction is a Preferred Term (PT) linked to the System Organ Class (SOC) 'cardiac disorders' or 'gastrointestinal disorders'.

When running the reports in EVDAS, the filters will always appear in the outcome. When exporting data (see [Section 8.1.1.](#)), the filters will be included in the export.

1.1.5.2. Prompts

Prompts are objects that enable users to select the conditions to be included in a report at run time. The following figure shows the prompts available in a report:

Figure 3. A report and its prompts

Report Description

This report provides an electronic Reaction Monitoring Report (eRMR) for one or more active substances and a reference period. The data can be further filtered by MedDRA terms.

Active Substance

* Active Substance (High Level)

Reference Period

Select from the list below the time interval for populating the columns with "new" cases.

All reference periods are refreshed every 3rd of the month with data up to the last day of the previous month. Additionally, the 15 days reference period is also refreshed on 18th of the month with data up to 15th.

* 15 days
 1 month
 3 months
 6 months
 12 months

Reactions from the MedDRA hierarchy to filter the report results

MedDRA Reaction Terms for the Active Substance

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

* The prompt is mandatory

2. EVDAS access to MAHs – General principles

Authorised personnel in the MAHs will be granted access to EVDAS at headquarters level. The Qualified Person responsible for Pharmacovigilance (QPPV)/Deputy QPPV should nominate the authorised personnel with access to EVDAS in line with the EudraVigilance registration process. The QPPV/Deputy QPPV are responsible for updating the user registration for their organisation accordingly.

There are two EVDAS profiles:

- EVDAS '*scientific role*' provides access to the EVDAS reports (eRMRs, active substance groupings and line listings) and ICSRs forms;
- EVDAS '*administrative profile*' provides access to EVDAS reports (eRMRs, active substance groupings and line listings).

It is important to understand that although access to the ICSR form is through the hyperlink provided in the EVDAS line listing, the ICSR form is populated in the EudraVigilance Web application (EVWEB) and therefore to access the ICSR form, the user will be asked to enter the credentials for EVWEB. Users with EVDAS '*scientific role*' are provided with credentials for both EVWEB and EVDAS at the time of the registration. On the contrary, users with EVDAS '*administrative profile*' are provided with EVDAS credentials at the time of the registration.

The EVWEB credentials provided for EVDAS 'scientific role' do not grant automatically level 2B access in EVWEB. Level 2B access is granted by the QPPV within the secure area of EudraVigilance.

Guidance on the registration process and EVWEB training can be found in the EudraVigilance page at the EMA website²

Users working with eRMRs exported (e.g. Excel) should be aware that to access line listings from the hyperlinks (see [Section 9.9](#)) they should have EVDAS credentials. To access ICSR forms from the exported line listings, users should enter the EVWEB credentials.

EVDAS access for MAHs is implemented according to level 1 access for Stakeholders Group III as established in the EudraVigilance access policy. Level 1 access to MAHs is implemented as follows:

- Access is provided to all MAHs with a medicinal product authorised in the EEA.
- Access is provided at substance level using the highest level of the active substance in the hierarchy of the xEVMPD.
- Access is provided for all the substances contained in products authorised in the EEA that have been coded as suspect/interacting in at least one post-marketing ICSR. Access is provided regardless of if the substance is the active substance, an excipient or an adjuvant. MAHs can select any active substance (and not only substances for which they have a product authorised), to retrieve eRMRs and line listings from EVDAS. These outputs are based on level 1 access and the results will be the same regardless of the MAH querying the database. The ICSR form provides different levels of access (level 1, 2a and 3) depending on the products owned by the MAH querying the database.
- Access is provided for all the cases submitted to the EVPM. The report type of the cases are 'spontaneous', 'reports from studies' (including 'individual patient use and other studies'), 'other' and 'not available to sender'.
- Access is provided for all individual cases (regardless of the sender) where the specific substance is coded as suspect or interacting.

3. Accessing EVDAS

MAHs' users registered in EVDAS will be able to access the system through the following ways:

- Via the EudraVigilance page on the EMA corporate website.
- Via EVDAS welcome page.

3.1. Accessing EVDAS via the EudraVigilance webpage

To access EVDAS via the EudraVigilance webpage, go to

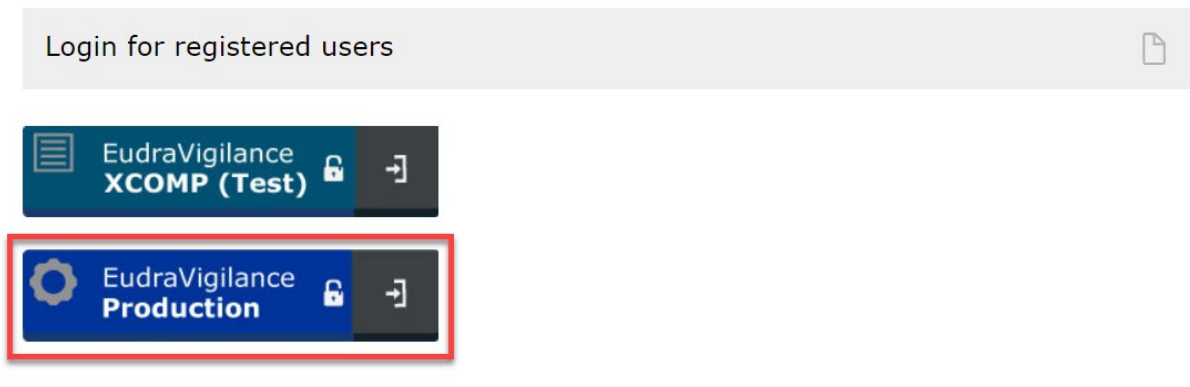
http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000679.jsp&mid=WC0b01ac05800250b5 and then click the **Production** text link (see the image below)

²http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000687.jsp&mid=WC0b01ac0580a69262

Figure 4. The EudraVigilance webpage



Figure 5. EudraVigilance Production



On doing so, you will be prompted to enter your EudraVigilance User Name & Password

Figure 6. EudraVigilance webpage user name & password prompt

Enter your EudraVigilance **User Name** & **Password** and click **Sign In**.

Note: at this prompt, you should enter your EudraVigilance User Name & Password, NOT your EVDAS User Name & Password. Users with an EVDAS 'administrative profile' cannot log in to EVDAS via the EudraVigilance webpage as they are not provided with EudraVigilance credentials.

Select EVHUMANWT (AFF) – EudraVigilance Web trader and click **Select**


Figure 7. Select organisation

Once you have logged-in to the restricted area, click the **EudraVigilance Data Warehouse** text link (see Figure 8 below).

Figure 8. The EudraVigilance webpage restricted area

Figure 10. MAH Pharmacovigilance Queries

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

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MAHs' Pharmacovigilance Queries

The EudraVigilance Data Warehouse is the central repository of ICSR and medicinal product data from where these reports are being generated.
v01.00.00 [EVDAS release notes](#) | [EVDAS user manual](#) | [ICSR form manual](#) | [eRMR calendar](#)

Current MedDRA version is 23.0

For any technical support, please contact [EMA EVDAS support](#).
As of 1.2.2020, the UK is no longer an EU Member State. However, EU law still applies to the UK during the transition period.

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From the welcome page it is possible to access 3 different reports:

- electronic Reaction Monitoring Report (eRMR)
- Line listing
- Active substance grouping

These 3 reports are fully described in the next sections of this Module.

3.4. System idle log-out

Once you are logged-in, you will remain logged-in until

- You close all web browser windows, or
- The system has been inactive for 210 minutes, whereupon you will be automatically logged-out.

Once you have been automatically logged-out, the internet browser will still show the page(s) that you had open. If you then try and perform an action, you will have to re-enter your username and password.

4. The electronic Reaction Monitoring Report (eRMR)

4.1. Introduction

This section describes the EVDAS report to retrieve eRMRs and the report functionalities. Details of the fields provided in the eRMR output are described in [Annex II](#). Moreover, [Section 9](#) of this manual provides with practicalities when using the eRMR for signal detection.

The eRMR is a tool to perform signal detection in EudraVigilance. This tool provides aggregated data related to the ICSRs submitted to EudraVigilance stratified by different parameters and incorporates the Reporting Odds Ratio (ROR) as a statistical measure.

Users will be able to retrieve different eRMRs depending on the selected reference period. These reports will retrieve valid cases transmitted to the EVPM module only (see Section 9.5. for more details). Identified duplicates will be excluded by default.

To access the EVDAS eRMR report click on the **eRMR** tab in the MAH Pharmacovigilance Queries dashboard.

Figure 11. Access to the eRMR EVDAS report



The EVDAS eRMR report contains the following prompts:

- Active substance high level
- Reference period
- MedDRA level of hierarchy and reaction term to filter the data

Figure 12. EVDAS eRMR report prompts

The image shows a screenshot of the EVDAS eRMR report prompts form. The form has a navigation bar at the top with four tabs: 'Welcome', 'electronic Reaction Monitoring Report - eRMR', 'Line listing', and 'Active substance grouping'. The 'electronic Reaction Monitoring Report - eRMR' tab is selected. Below the navigation bar, there is a text block stating: 'The 1-month, 3-month, 6-month and 12-month eRMRs are available with data up to and including 29/02/2020. The 15-day eRMR is available with data up to and including 15/03/2020'. Below this is a section titled 'Report Description' with the text: 'This report provides an electronic Reaction Monitoring Report (eRMR) for one or more active substances and a reference period. The data can be further filtered by MedDRA terms.' Below the description is a section titled 'Active Substance' with a dropdown menu labeled '* Active Substance (High Level) --Select Value--'. Below this is a section titled 'Reference Period' with the text: 'Select from the list below the time interval for populating the columns with "new" cases. All reference periods are refreshed every 3rd of the month with data up to the last day of the previous month. Additionally, the 15 days reference period is also refreshed on 18th of the month with data up to 15th.' Below this is a list of radio buttons: '* 15 days', '1 month', '3 months', '6 months', and '12 months'. Below the list is a section titled 'Reactions from the MedDRA hierarchy to filter the report results' with a list of radio buttons: 'MedDRA Reaction Terms for the Active Substance', 'none', 'MedDRA reaction PT', 'MedDRA reaction HLT', 'MedDRA reaction HLTG', 'MedDRA reaction SOC', 'MedDRA SMQ Level 1 Broad', and 'MedDRA SMQ Level 1 Narrow'.

4.2. The reference period

The *reference period* in the eRMR defines the start and end of the period for populating the columns labelled as 'New' in the eRMR output. The 'End date' is used for defining the limit for the interval and cumulative data. The dates in the reference period are based on the *EV Message Gateway Date*, which is the precise date and time when a case was transmitted to EudraVigilance.

The concept of 'New' cases in the eRMR is broad and includes not only the cases received for the first time in EudraVigilance, but also follow-ups and 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, this case will appear as new in the eRMR output.

The cases received during the reference period (i.e. new cases, follow-ups and de-duplicated) can be also identified in the eRMR in the column 'Changes' and in the specific columns where the new cases are indicated (e.g. 'New EVPM', 'New Fatal', 'New Paediatric'). See further details in [Annex II](#) and [Section 9](#).

Users can select different reference periods depending on the frequency of monitoring of their substance but cannot modify the dates of the reference period, as these eRMRs are pre-generated by the EMA.

As showed in [Figure 12](#) above, users are able to retrieve the following eRMRs reference periods:

- *15-Day reference period eRMR*
- *1-Month reference period eRMR*
- *3-Month reference period eRMR*
- *6-Month reference period eRMR*
- *12-Month reference period eRMR*

The 15 days reference period eRMRs are available on 03rd and 18th of each month.

- The 15-day eRMR available on 03rd of each month contains a reference period from 16th to the last day of the previous month (30th/31st or 28th/29th in February). The cumulative data is up to and including the last day of the previous month.
- The 15-day eRMR available on 18th of the month contains a reference period from 1st to 15th (both included) of the same month. The cumulative data is up to and including 15th of the same month.

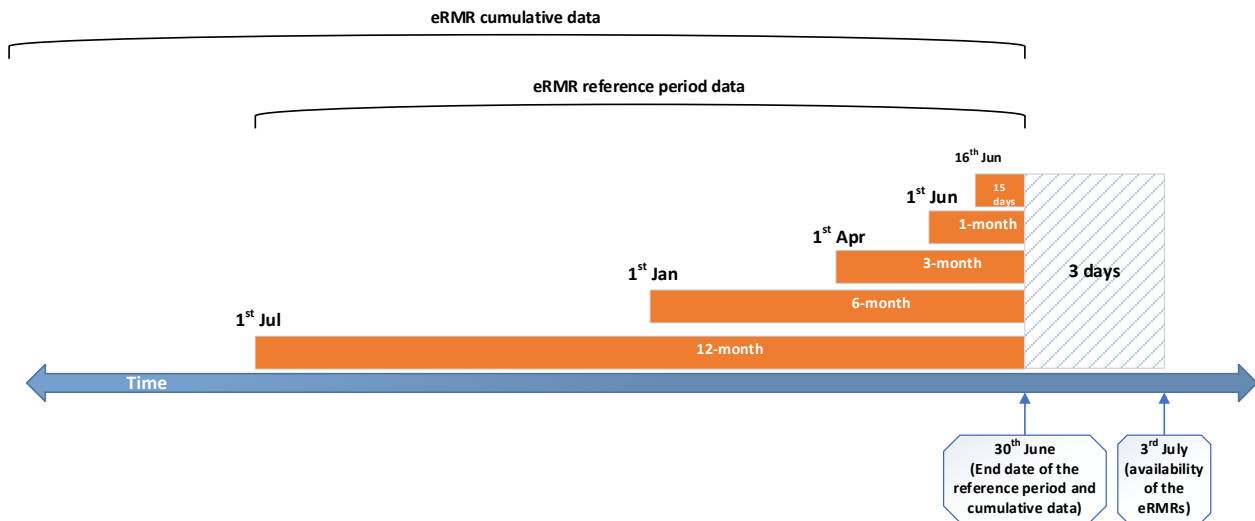
The 3 days delay (03rd and 18th of each month) on the availability of the eRMRs is in order to allow the system to process all the cases received.

The 1-month, 3-month, 6-month and 12-month eRMRs will be available on 3rd of each month and the reference periods will be 1-month, 3-month, 6-month and 12-month in the past being the end date the last day of the previous month (30th/31st or 28th/29th in February). The cumulative data is up to and including the last day of the previous month. For instance, for the 3-month eRMR available on 3rd July 2020, the reference period will be 01st April 2020 to 30th June 2020. The cumulative data is up to and including 30th June.

Exceptionally, in May and November, the eRMRs due on 03rd of the month will be made available some days later in order to accommodate for the 6-monthly MedDRA updates. These eRMRs will therefore be available later than usual but will use the latest MedDRA version. Users will be communicated as

applicable. Figure 13 illustrates the eRMRs fixed reference periods available using the example of 3rd July.

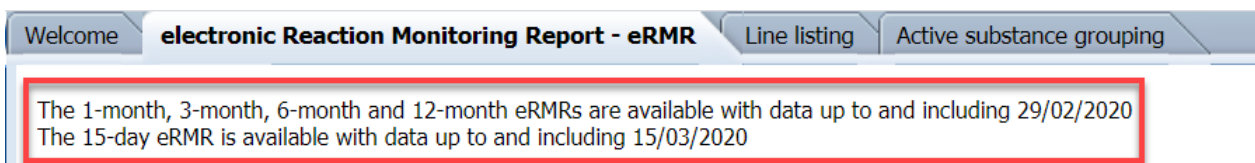
Figure 13. eRMRs reference period - Example 3rd July



The data in the reports will not change until a new report (with a new reference period) is available, therefore running for instance a 1-month eRMR for the same substance on 3rd of the month or the last day of the same month, will provide the same results. It's important to consider this when comparing the number of cases in the eRMR with the number of cases in the line listings, as, unlike the eRMR, the line listing report is updated every day (see [Section 5.5](#)).

Be aware that there is a legend in the eRMR report page that informs the users about the current available reports and the end dates of the available reference periods. This legend is updated when new eRMRs with new reference periods are available. An example of this legend is shown in the following [Figure 14](#). Users are advised to check this legend to ensure that the reports provide the data with the expected cut off dates. The actual reference period will be populated by the system with the results of the report (see [Section 4.6](#))

Figure 14. End dates available



Once a new eRMR is generated by the EMA, the users will not be able to retrieve eRMRs for the previous periods and therefore users are advised to save locally the eRMRs of interest according to the MAHs procedures.

In order to help users to plan the signal detection activities, an eRMR calendar is available in the welcome page of the EVDAS dashboard as shown in [Figure 15](#) below.

Figure 15. eRMR calendar link

MAHs' Pharmacovigilance Queries

The EudraVigilance Data Warehouse is the central repository of ICSR and medicinal product data from where these reports are being generated.
v01.00.00 | [EVDAS release notes](#) | [EVDAS user manual](#) | [ICSR form manual](#) | [eRMR calendar](#)

Current MedDRA version is 23.0

The eRMR calendar provides with the planned eRMR production dates, the eRMR type depending on the reference period and the actual reference period.

Figure 16. eRMR calendar

eRMR production dates and reference periods

Production date	eRMR type	Reference period
03 June 2020	15-day	16 May 2020 – 31 May 2020
03 June 2020	1-month	01 May 2020 – 31 May 2020
03 June 2020	3-month	01 March 2020 – 31 May 2020
03 June 2020	6-month	01 December 2019 – 31 May 2020
03 June 2020	12-month	01 June 2019 – 31 May 2020
18 June 2020	15-day	01 June 2020 – 15 June 2020

The production dates stated in the eRMR calendar are planned production dates. If due to unforeseen technical reasons (e.g. failures in the ETL process), the production date for a specific month has to be postponed, the eRMR type and the reference period will be the same. For instance, if the eRMRs cannot be produced as planned on 3rd June, but are created on 5th June, the reference periods will be up to an including 31st May as per the calendar.

4.3. Active substance

The user should select an active substance using the prompt 'Active substance (high level)'. This is a required prompt and you will not be able to run the report without answering this prompt.

The user will be able to select more than one substance within the same report. The results will provide in one file, independent eRMRs for the different substances organised in alphabetical order.

The data filtered on in this prompt originate from the fields ICH E2B (R3) G.k.2.2 (proprietary medicinal product) and G.k.2.3.r.1 (active substance), which is recoded against the data in the xEVMPD and further grouped into medicinal product/active substance groups ('Active substance high level') for pharmacovigilance activities.

For the users to know which specific substances have been grouped to which 'Active substance high level', please refer to Active substance grouping report in [Section 6](#).

Figure 17. Active substance prompt

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

The 1-month, 3-month, 6-month and 12-month eRMRs are available with data up to and including 29/02/2020
The 15-day eRMR is available with data up to and including 15/03/2020

Report Description

This report provides an electronic Reaction Monitoring Report (eRMR) for one or more active substances and a reference period. The data can be further filtered by MedDRA terms.

Active Substance

* Active Substance (High Level) --Select Value--

Reference Period

Select from the list below the time interval for populating the columns with "new" cases.

All reference periods are refreshed every 3rd of the month with data up to the last day of the previous month. Additionally, the 15 days reference period is also refreshed on 18th of the month with data up to 15th.

* 15 days
 1 month
 3 months
 6 months
 12 months

A substance can be selected by typing the name of the substance in the 'select value' field then clicking with the mouse on the substance name. EVDAS will offer you suggestions for the substance once you have typed the first few letters.

Figure 18. Example of an active substance selection.

Active Substance

* Active Substance (High Level) gemc

Reactions from the MedDRA

MedDRA Reaction Terms for the

the report results

- GEMCITABINE
- GEMCITABINE H
- GEMCITABINE, E
- GEMCITABINE, C
- GEMCITABINE, C
- GEMCITABINE, C
- GEMCITABINE, C

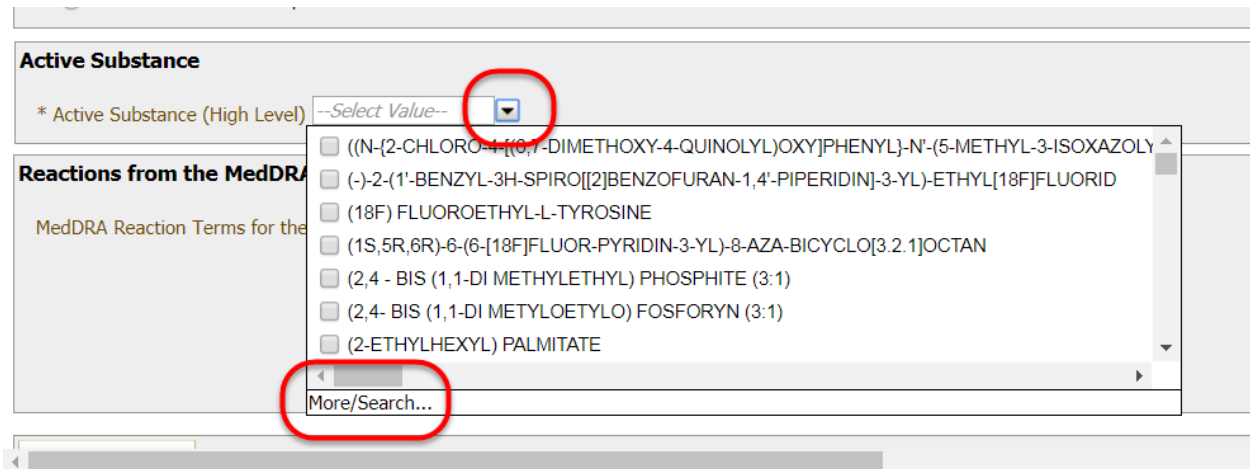
MedDRA reaction PT
MedDRA reaction HLT
MedDRA reaction HLGT
MedDRA reaction SOC
MedDRA SMQ Level 1 Broad
MedDRA SMQ Level 1 Narrow

Search...

If you wish to search for more than one substance, then you can type the substance names, select the substance and separate them by semicolons. Also you can search and select the substances by

opening the 'selection cart' option. This option is by clicking 'More/Search' after opening the drop-down menu in the 'Active Substance' prompt.

Figure 19. Opening the selection cart prompt



Once in the active substance selection cart prompt from the 'available' section, select your operator using the drop down menu in name (orange ring in Figure 20 below); the options are 'Starts', 'Contains', 'Ends' and 'Is like (pattern match)'. Select 'contains' for a broad search.

Once the operator is selected, type or paste your desired term (or part of the term) into the search box (green ring in Figure 20 below).

Select or deselect the 'Match Case' option (red ring in Figure 20 below). Deselect 'Match case' for a broad search and to avoid 'case sensitivity'. As you type, the system will start to offer results. The more you type, the more refined the results are.

Select the desired term and the click the **move arrow** (blue ring in Figure 20 below). The term will be then moved to the 'Selected' list. You can also move the term by double clicking on it.

Figure 20. Example of an active substance selection

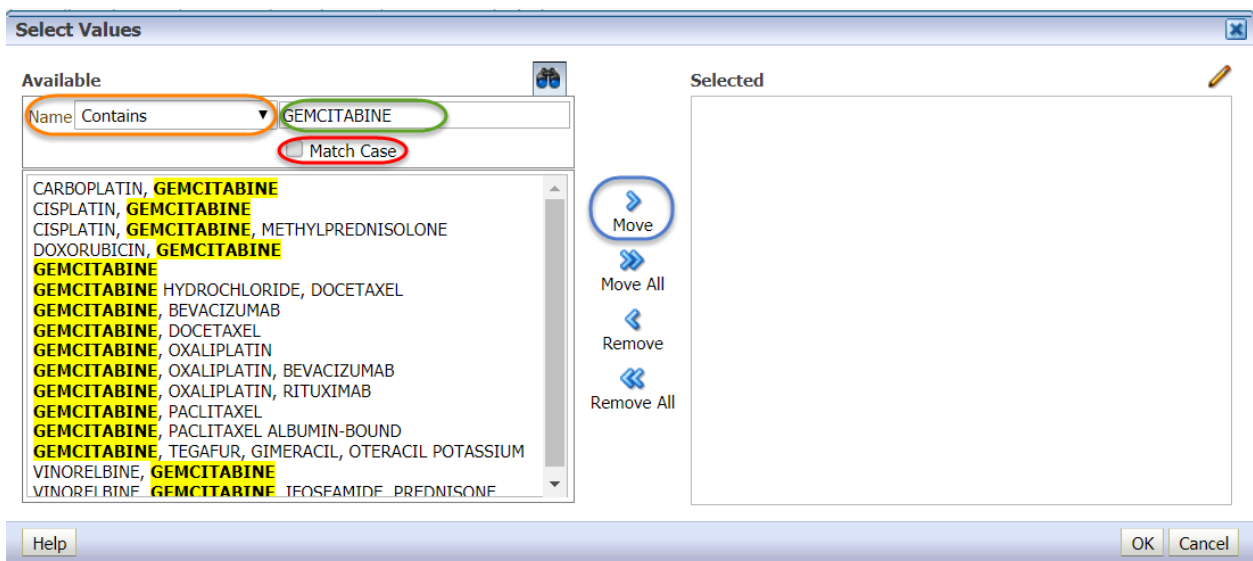
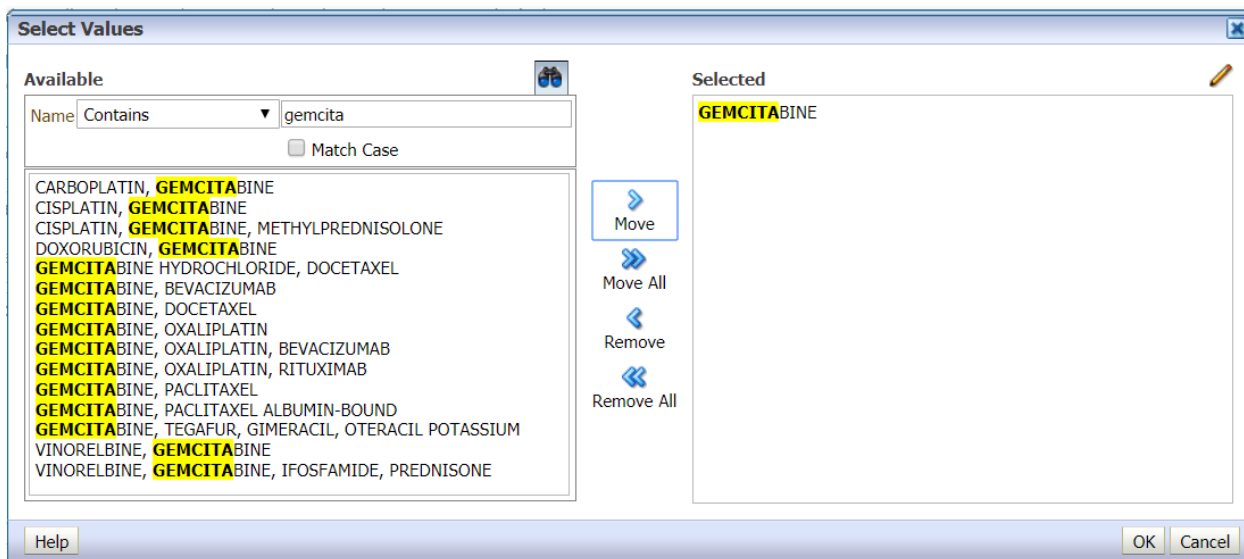
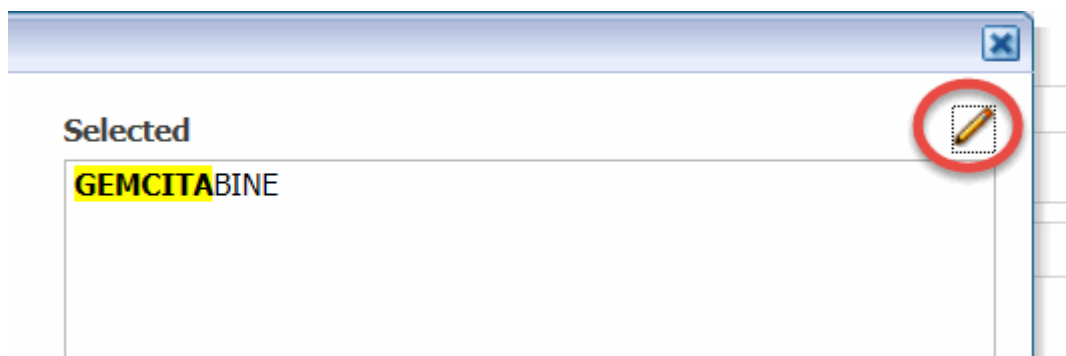


Figure 21. Example of an active substance selection



Search 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.

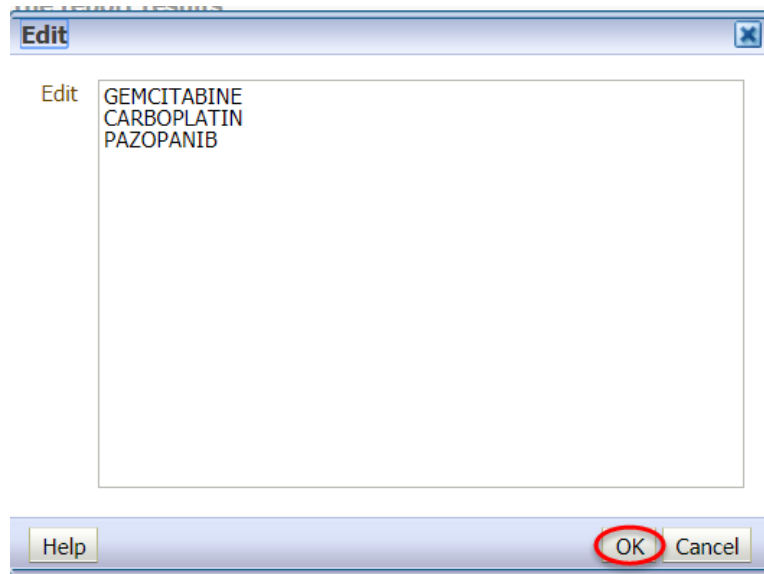
Figure 22. The selection cart prompt edit box



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) that they are spelled completely correctly and (b) that each term is on a separate line and (c) the terms are in capitals. Click **OK** when all the desired terms are included.

Figure 23. The selection cart prompt edit box - Example



To select multiple terms, either repeat the selection process, or use the **Move All** arrow.

To deselect terms repeat the above steps, but clicking on the terms in the selected list and using the **Remove** and **Remove All** arrows or manually deleting them in the edit box.

4.4. MedDRA terms

The user can select MedDRA reaction terms to filter the report. If no terms are to be filtered for, then option '**None**' should be selected (this option is the default option) and the eRMR will contain the data for all the MedDRA PTs reported for that substance.

If the user wants to restrict the data using a MedDRA term, the MedDRA hierarchy level should be selected first. Once this is selected, a new prompt will appear for the user to select the appropriate term.

Figure 24. Example of selection for a MedDRA SOC

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

* Active Substance (High Level) GEMCITABINE

Reactions from the MedDRA hierarchy to filter the report results

MedDRA Reaction Terms for the Active Substance

- 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 Eye disorders

- Blood and lymphatic system disorders
- Cardiac disorders
- Congenital, familial and genetic disorders
- Ear and labyrinth disorders
- Endocrine disorders
- Eye disorders
- Gastrointestinal disorders
- General disorders and administration site conditions

Search...

Clear all prompts

* The prompt is mandatory

Click on link to run report

[electronic Reaction Monitoring Report - 15 days](#)

4.5. Running the report

Once the prompts have been answered, the user will be able to retrieve the eRMR by clicking on the **activated link** at the bottom left of the report.

Figure 25. Running the report

Reactions from the MedDRA hierarchy to filter the report results

MedDRA Reaction Terms for the Active Substance

- 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

* The prompt is mandatory

Click on link to run report

[electronic Reaction Monitoring Report - 15 days](#)

An option to reset all the prompts is also available in the 'Clear All Prompts' button. Users are advised to clear the prompts when running different reports so no previous unwanted filters are included in the new selections.

Figure 26. Clear all prompts option

Reactions from the MedDRA hierarchy to filter the report results

MedDRA Reaction Terms for the Active Substance

- 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

* The prompt is mandatory

4.6. The eRMR output in the EVDAS interface

The returned eRMR will provide you with the type of the report and the criteria you have used to answer the prompts and therefore filter the data (see section on filters 1.1.5).

The output will also state the reference period of the eRMR and the date and time when the report was run. See example below in Figure 27.

Figure 27. eRMR output example

electronic Reaction Monitoring Report - 3 months

Time run: 30/03/2020 16:50:23

The selected reference period for defining "new" cases is 01/12/2019 to 29/02/2020

Active Substance (High Level) VW is equal to **GEMCITABINE**
and Reaction_MedDRA [View](#)
and Fixed Period Id is equal to / is in 3

Active Substance	SOC	HLGT	HLT	SMQ Narrow	PT
GEMCITABINE	Blood and lymphatic system disorders	Anaemias nonhaemolytic and marrow depression	Anaemia deficiencies		Iron deficiency anaemia
GEMCITABINE	Blood and lymphatic system disorders	Anaemias nonhaemolytic and marrow depression	Anaemias NEC	Haematopoietic cytopenias	Anaemia macrocytic

The default eRMR output will be organised following the standard MedDRA hierarchy (SOCs in alphabetical order). A different design can be determined by the user by sorting (ascending or descending in any of the columns) and by moving columns. See [Section 8](#) 'working with returned reports'.

5. The EVDAS line listing report

The EVDAS line listing report provides the user with the listing of individual cases for a specific substance/s and specific MedDRA terms when appropriate. The report also provides the possibility to restrict the data to a specific period.

To access the line listing report, click on the line listing tab in the MAH Pharmacovigilance Queries Dashboard.

Figure 28. Line listing report



The line listing report contains 3 main prompts:

- Search criteria
- Period
- MedDRA terms

Figure 29. EVDAS Line listing report prompts

Report prompts

Search Criteria

* Active Substance (High Level)
 Worldwide Case Number
 EU Local Number

Active Substance

* Active Substance (High Level)

Period

Cases received between 'start date' and 'end date', using the EV Message Gateway Date

Start Date >=
End Date <=

Reactions from the MedDRA hierarchy to filter the report results

MedDRA Reaction Terms for the Active Substance none
 MedDRA reaction PT
 MedDRA reaction HLT
 MedDRA reaction HLGT
 MedDRA reaction SOC
 MedDRA SMQ Level 1 Broad
 MedDRA SMQ Level 1 Narrow

5.1. The line listing search criteria

The 'search criteria' prompt provides the possibility to retrieve a line listing using an 'active substance high level' but also provides the possibility to search for individual cases using the 'Worldwide case identification number' or the 'EU local number'. Once the search criterion is selected, a prompt to select the substance, Worldwide case number or EU local number will be activated. The default setting is search criteria by active substance.

Please note that when the search criteria selected is 'Worldwide case number' or the 'EU local number', the prompts for the period and MedDRA term will not be present as they would not be needed.

Figure 30. Line listing prompts for the search criteria 'Worldwide case number'

Data up to and including 29-09-2017

Report Description
This report generates an individual case line listing for one or more active substances, worldwide case numbers or EU local numbers. The data can also be filtered by MedDRA terms and restricted to a time period.

Report prompts

Search Criteria

* Active Substance (High Level)
 Worldwide Case Number
 EU Local Number

Worldwide Case Number

* Worldwide Case Number

* The prompt is mandatory

Warning
Please complete all mandatory prompts.

The search criteria by 'Worldwide case number' or the 'EU local number' permits the user to retrieve a line listing of individual cases using the identification numbers of the cases.

Once one of these criteria has been selected, the user should introduce the Worldwide case number or the EU local number of the cases of interest in the corresponding prompt. This prompt follows the same logic as the active substance prompt. You can introduce the identification numbers directly in the 'select value' field and wait for the system to find the identification number, and then select the specific number by clicking on in for the prompt to be populated correctly.

Figure 31. Selection of a specific 'Worldwide case number'

The screenshot displays a web form with the following sections:

- Report Description:** This report generates an individual case line listing for one or more cases. The data can also be filtered by MedDRA terms and restricted to a time period.
- Report prompts:** A section for entering search criteria.
- Search Criteria:** Three radio buttons are present: 'Active Substance (High Level)', 'Worldwide Case Number' (which is selected), and 'EU Local Number'.
- Worldwide Case Number:** A text input field contains 'PHHO2016FR018809'. A dropdown menu is open below it, showing a search result 'FR-002147023-PHH' with a blue checkmark icon.
- Clear all prompts:** A button located below the dropdown menu.
- * The prompt is mandatory:** A label next to a search input field containing 'Search...'.
- Click on link to run report:** A blue button with the text 'Line listing'.

Be aware that when you type the system will start offering possibilities, the more you type, the more refined the results will be.

Figure 32. Selection of a specific 'Worldwide case number'

Report Description
This report generates an individual case line listing for one or more
The data can also be filtered by MedDRA terms and restricted to a

Report prompts

Search Criteria

* Active Substance (High Level)
 Worldwide Case Number
 EU Local Number

Worldwide Case Number

* Worldwide Case Number FR-0021470

Clear all prompts

* The prompt is mandatory

Click on link to run report
[Line listing](#)

FR-002147023-A
FR-002147023-A
FR-002147023-C
FR-002147023-C
FR-002147023-C
FR-002147023-C
FR-002147023-C
FR-002147023-C

Search...

To include more than one identification number a 'more/search' option is available to open the selection cart prompt.

Figure 33. Selection cart prompt for the selection of identification numbers

Select Values

Available

Name Starts
Starts
Contains
03- Ends
#201 is Like (pattern match)
#80
#81
\$>-002147023-PHFR2011IE02900
(ID 2011-03657

-01054554290-1999-05-0726
-01054554290-2005-09-0822
-01054554290-2006-06-0994
-01054554290-2006-06-0995
-01054554290-2008SP010934
-01054554290-2009SP017937
-01054554290-2009SP017950
Choices Returned: 1 - 1000 + More...

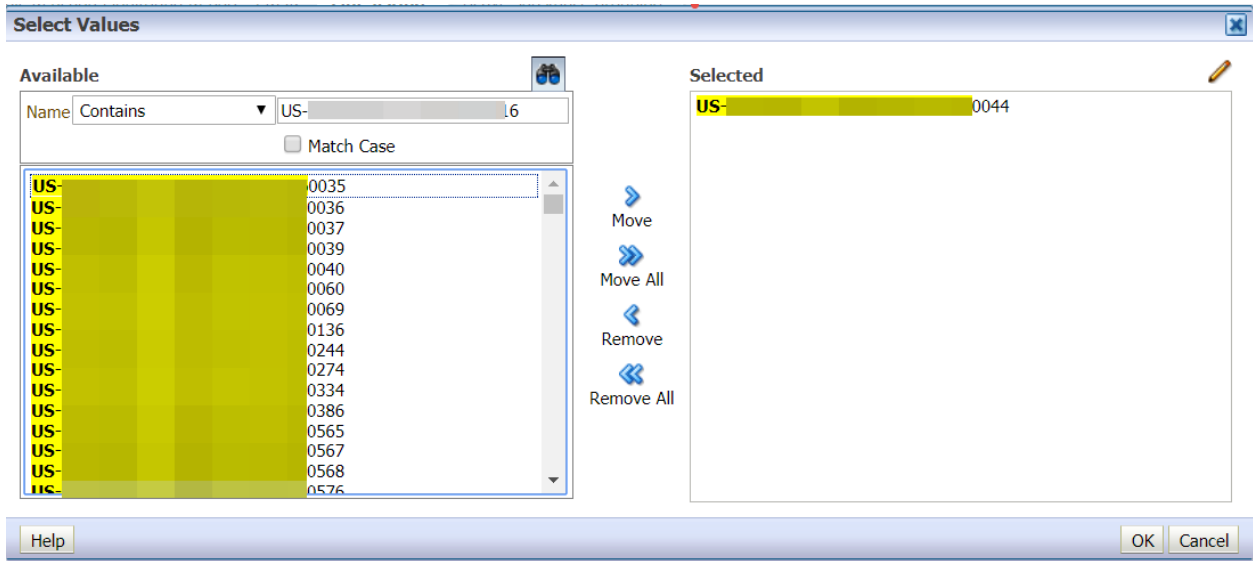
Match Case

Move
Move All
Remove
Remove All

Help OK Cancel

Select the desired operator in the 'name' drop down menu (blue ring in Figure 33 above), the possibilities are 'Starts', 'Contains', 'Ends', and 'is like (pattern match)', select or deselect the 'Match case' option (red ring in Figure 33 above) and type or paste the identification number in the selection field (green ring in Figure 33 above). If you type the identification number in the selection box, the system will start offering results. Select the desired term and the click the **move arrow**. The term will be then moved to the 'Selected' list. You can also move the term by double clicking on it. Please ensure the identification numbers are correct, before making any conclusion.

Figure 34. Selection of a Worldwide case number - Example

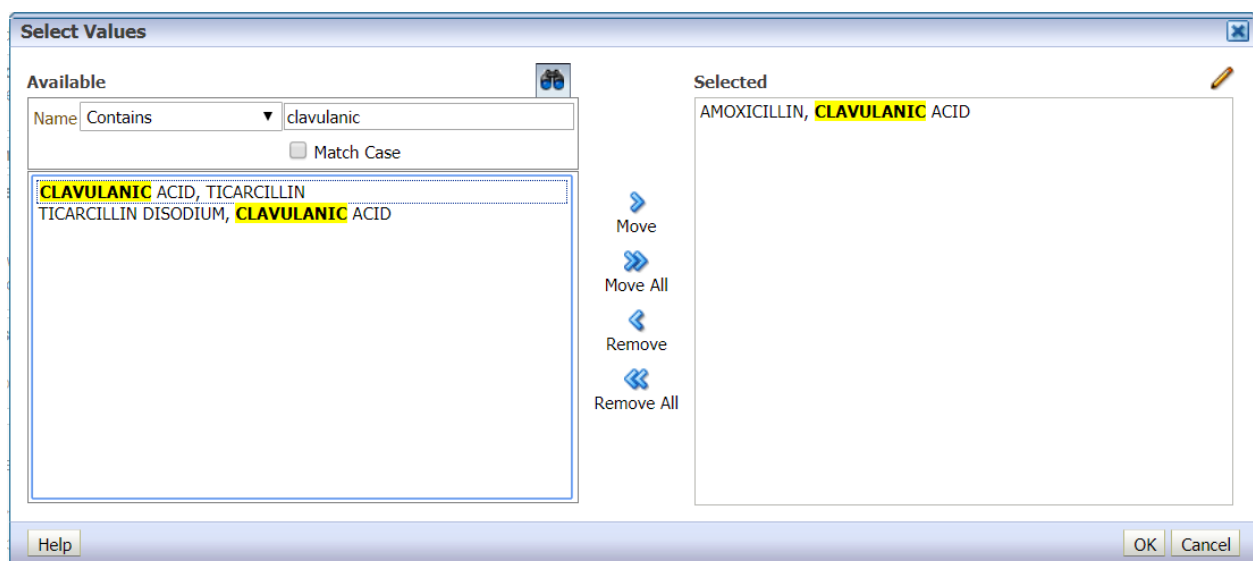


The line listing can also be retrieved using 'active substance high level' as search criteria. Users can select one or more active substances to retrieve the line listing. See [Section 4.3.](#) for the substance's selection.

Please note that if you select more than one 'active substance high level', the system will operate with an 'OR' criteria. The line listing will provide you with all the cases where any of the substances selected is coded as suspect/interacting in the cases. For instance, if you select 'paracetamol' and 'ibuprofen' and the MedDRA PT: 'anaemia', the system will retrieve all the cases of anaemia with suspect/interacting paracetamol plus all the cases of anaemia with suspect/interacting ibuprofen.

When a fixed combination of substances forms a unique 'active substance high level', the system will provide you with the cases where the fixed combination is coded as suspect/interacting. This is different than selecting 2 independent active substances high level.

Figure 35. Selection of a fixed combination of substances



5.2. The line listing period

The line listing EVDAS report offers the possibility to retrieve the cases received in EudraVigilance during a specific period using the 'EV Gateway Receipt Date'. To select a period, the users should enter the 'start date' and 'end date' of the period. There are no restrictions when selecting the period. The dates can be entered directly or can be selected by opening the calendars. The period is not a mandatory prompt and therefore if no period is selected, all the cases that meet the criteria specified in the rest of the prompts will be retrieved, this will provide us with a line listing containing all cases received in EV up until 'yesterday' (today -1) at 18:00 pm. In the line listing report the cut-off date of - 3 days is not applied as in the eRMRs (see [Section 4.2](#)). This is because the intention of the line listing is to provide the most possible updated information on the individual cases as these are normally used to validate signals at a specific time.

By including a period in the line listing users are filtering the cases according to the 'EV Gateway Receipt Date' but the information included in the cases (e.g. MedDRA terms coded) is according to the most updated information (today -1 at 18:00 pm). For instance, if on 15th November 2020 we retrieve a line listing using a period from 1st September 2020 to 30th September 2020, the EVDAS report will retrieve only the cases received during September 2020, but the information included in the cases will be according to the most updated information received in EudraVigilance up to and including 14th November 2020 at 18:00 pm.

Figure 36. Selection of a period within the line listing EVDAS report

The screenshot shows a web interface for selecting a period. At the top, there is a section for 'Active Substance' with a dropdown menu showing 'GEMCITABINE'. Below this is a section for 'Period' which is highlighted with a red rounded rectangle. The text in this section reads: 'Cases received between 'start date' and 'end date', using the EV Message Gateway Date'. Underneath, there are two date input fields: 'Start Date >=' with the value '04/09/2017' and 'End Date <=' with the value '30/09/2017'. A 'Select Date' calendar pop-up is open, showing the month of September 2017. The calendar grid shows days from 28 to 1. The 30th of September is highlighted in blue. At the bottom of the calendar are 'OK' and 'Cancel' buttons.

5.3. The line listing by MedDRA Terms

The line listing report offers the possibility to retrieve the cases using MedDRA terms following the steps specified in [Section 4.4](#). This prompt is not mandatory.

5.4. Running the line listing report

Once all the criteria are selected the user should click on the Line listing activated link to run the report.

Figure 37. Running the EVDAS line listing report

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

Data up to and including 30-09-2017

Report Description
This report generates an individual case line listing for one or more active substances, worldwide case numbers or EU local numbers. The data can also be filtered by MedDRA terms and restricted to a time period.

Report prompts

Search Criteria

* Active Substance (High Level)
 Worldwide Case Number
 EU Local Number

Active Substance

* Active Substance (High Level) GEMCITABINE

Period
Cases received between 'start date' and 'end date', using the EV Message Gateway Date

Start Date >= 04/09/2017
End Date <= 30/09/2017

Reactions from the MedDRA hierarchy to filter the report results

MedDRA Reaction Terms for the Active Substance 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 Anaemia

Clear all prompts
* The prompt is mandatory

click on link to run report
[Line listing](#)

5.5. The line listing output in the EVDAS interface

The output of the line listing will provide you with the filters selected in the prompts followed by the line listing of individual cases. The filters in the line listing report shows some technical information not relevant for the users (e.g. current case – SR is equal to/ in in 1).

When a period has been selected to retrieve the line listing, the end date for the period could be different than today - 1

Figure 38. Line listing output in the EVDAS interface

Line listing Report
 Data up to and including 02-10-2017
 Time run: 03/10/2017 09:42:05

Current Case - SR is equal to / is in 1
 and Current Case - DR is equal to / is in 1
 and EV Document Type is equal to **EVPM ICSR(s), EVPM BACKLOG ICSR(s), EVPM MASTER ICSR(s), PSUR ICSR(s), PSUR MASTER ICSR(s)**
 and Cluster Role ID is equal to / is in 1
 and Characterisation is equal to **Interacting, Suspect**
 and Active Substance (High Level) is equal to **PAZOPANIB**
 and

and	none	View
or	reaction SOC	View
or	reaction HLG	View
or	reaction HLT	View
or	"@{stdmandatoryfilter10}{All}" is equal to / is in MedDRA reaction PT	
and	Reaction PT is equal to Polycythaemia	
or	reaction SMQ Level 1 Broad	View
or	reaction SMQ Level 1 Narrow	View

and "Line Listing Objects"."EV Message Gateway Date" BETWEEN date '1990-01-01' AND date '2050-12-31'

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)
EU-EC-12117562	FR-002147023-PH02016FR018809	04/05/2017	Spontaneous	Healthcare professional (Other health professional, Physician)	EEA	Not available	18-64 Years	Not Specified

In this section we have described how to retrieve a line listing using the EVDAS line listing report in the MAH Pharmacovigilance Queries dashboard. A line listing can also be retrieved via the hyperlinks in the eRMR columns 'new EVPM' and 'total EVPM'.

Figure 39. Line listing hyperlinks in the eRMR output

Active Substance	SOC	HLGT	HLT	SMQ Narrow	PT	IME/DME	New EVPM	New EVPM	Tot EVPM	Tot EVPM	New EEA	Tot EEA	M
GEMCITABINE	Gastrointestinal disorders	Abdominal hernias and other abdominal wall conditions	Abdominal hernias NEC		Abdominal hernia		2 New EVPM	2 Total EVPM			0	0	
GEMCITABINE	Gastrointestinal disorders	Abdominal hernias and other abdominal wall conditions	Abdominal hernias NEC		Abdominal strangulated hernia	IME	0 New EVPM	1 Total EVPM			0	0	

As the cut-off date of the eRMRs is fixed, cannot be modified by the users and is only updated once the new eRMRs are available, it is important to understand the differences with the cut-off dates of the Line Listings that are retrieved via the hyperlinks in the eRMR.

The 'new EVPM' link will retrieve a line listing containing the cases received in EV during the eRMR reference period, nevertheless follow-up reports, nullifications and deduplications received from the end date of the reference period until today -1 at 18:00 pm will be taken into consideration. This could be the reason why the number of 'New EVPM' cases in the eRMR differs from the number of cases retrieved in the line listing.

The 'total EVPM' link will follow the same rationale as the Line Listing EVDAS report and will retrieve the cases considering the most updated information (today -1 at 18:00 pm).

While it is acknowledged that some users would prefer to see exactly the same number of cases in the eRMR and the line listing, as the line listings are normally used for signal validation and assessment, it would make sense to make scientific decisions based on the most updated information in the database and that is the reason why the line listing retrieved via the 'total EVMP' link provides data up to today - 1 at 18:00 pm.

The line listing output also contains a link to access the ICSR form. For more information on the ICSR form, please consult the ICSR form training manual: [EudraVigilance User Manual - Individual Case Safety Report form](#)

Figure 40. Link to the ICSR Form

PT (Duration – 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])	ICSR Form
Duration (n/a - Fatal - Death, Other Medically Important Condition),	[redacted] for unknown indication - Not applicable - [n/a - n/a - Unknown]],	Not reported	ICSR
Test abnormal (n/a - Fatal - Death, Other Medically Important Condition),	[redacted] for unknown indication - Not applicable - [n/a - n/a - Transdermal]],		
n/a - Fatal - Results in Medically Important	[redacted] for unknown indication - Not applicable - [n/a - 800mg		

Details of the fields provided in the line listing are described in [Annex I](#) of this manual.

6. The EVDAS active substance grouping report

The 'Active substance grouping' EVDAS report provides the user with an overview of the active substances and medicinal products in the xEVMPD that are grouped under a specific 'Active Substance high Level'. The report provides also the possibility to visualise the corresponding MAHs and serves MAHs in the identification of active substances of medicinal products for which they hold a marketing authorisation in the EEA.

The grouping of active substances is a manual activity performed by the EMA. The active substances are grouped in 'active substance high level' terms for the purpose of pharmacovigilance activities (e.g. signal detection). These terms are used to retrieve eRMRs and line listings in the EVDAS MAH Pharmacovigilance Queries dashboard.

The values referenced in the output come from the latest validated version of the products. Only products with a valid authorisation status appear in the grouping.

As changes can occur at any time within the grouping of the active substances and the composition of the products, the active substance grouping report should be used before retrieving data from EVDAS to ensure that any potential changes in the substance grouping, product composition and ownership are being taken into consideration and therefore the correct active substance high level is selected.

To access this report, click on the **active substance grouping** tab in the MAH Pharmacovigilance Queries dashboard.

Figure 41. EVDAS Active substance grouping report



The active substance grouping report contains one main prompt:

- Search criteria.

Figure 42. Active substance grouping report prompt

The image displays a 'Report prompts' section. It has a title 'Report prompts' and a sub-section 'Search Criteria'. Under 'Search Criteria', there are four radio button options: 'Active Substance (High Level)' (which is selected), 'Active Substance', 'Medicinal Product', and 'Marketing Authorisation Holder'. Below these options is a dropdown menu with the text '* Active Substance (High Level) --Select Value--'. A 'Clear all prompts' button is located below the dropdown. A note states '* The prompt is mandatory'. At the bottom, there is an orange warning box with the text 'Warning Please complete all mandatory prompts.'

Users have the possibility to select one of the following search criteria:

- Active substance high Level
- Active substance
- Medicinal product [short name]
- MAH name [at headquarter (HQ) level].

The selection of the specific terms in this prompt follows the same rationale as the selection of active substances for the other reports in the MAH Pharmacovigilance Queries dashboard.

Once the prompt has been completed users should run the report by clicking in the hyperlink 'active substance grouping'

Figure 43. Running the active substance grouping report

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

Data up to and including 30-09-2017

Report Description
This report shows the active substances and medicinal products that are grouped under an Active Substance (High Holders).

Report prompts

Search Criteria

- * Active Substance (High Level)
- Active Substance
- Medicinal Product
- Marketing Authorisation Holder

* Active Substance

* The prompt is mandatory

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

6.1. 'Active substance high level' criterion

If the database is queried by 'Active Substance high Level', the output will display all the 'active substances' that are grouped to the specific 'active substance high level'. More than one term can be selected.

Figure 44. Example selection by 'Active substance high level' terms using the selection cart

Select Values

Available

Name: Contains | amlopidin

Match Case

- AMLODIPINE BESILATE, CANDESARTAN CILEXETIL
- AMLODIPINE BESILATE, PERINDOPRIL ARGININE, ATORVASTAT
- AMLODIPINE BESILATE, PERINDOPRIL TOSILATE
- AMLODIPINE, ACETYLSALICYLIC ACID
- AMLODIPINE, ALISKIREN
- AMLODIPINE, ATORVASTATIN
- AMLODIPINE, BENAZEPRIL
- AMLODIPINE, BISOPROLOL
- AMLODIPINE, CANDESARTAN CILEXETIL
- AMLODIPINE, ENALAPRIL
- AMLODIPINE, HYDROCHLOROTHIAZIDE, ALISKIREN
- AMLODIPINE, IRBESARTAN
- AMLODIPINE, LISINAPRIL
- AMLODIPINE, OLMESARTAN
- AMLODIPINE, PERINDOPRIL

Selected

- LITHIUM
- AMLODIPINE

Figure 45. Example outcome for active substance grouping report selecting 'lithium' and 'amlodipine'

Active Substance (High Level)	Active Substance
AMLODIPINE	AMLODIPINE
	AMLODIPINE BESILATE
	AMLODIPINE MALEATE
	AMLODIPINE MESILATE
	AMLODIPINE MESILATE MONOHYDRATE
LITHIUM	LITHIUM
	LITHIUM ACETATE
	LITHIUM CARBONATE
	LITHIUM CHLORIDE
	LITHIUM CITRATE
	LITHIUM GLUCONATE
	LITHIUM SULFATE

This example is used to illustrate that when the user selects 'lithium' in the 'Active substance high level' prompt, they will see all the lithium salts that are grouped within that high level. This means that all the cases in which one of the grouped lithium salts was reported are grouped and appear in the eRMR and line listing of the 'lithium' active substance high level.

6.2. 'Active Substance' criterion

If the database is queried by 'active substance', the output will contain the name of the 'active substance high level' that should be used to retrieve data from EVDAS for the specific 'active substance'. More than one term can be selected.

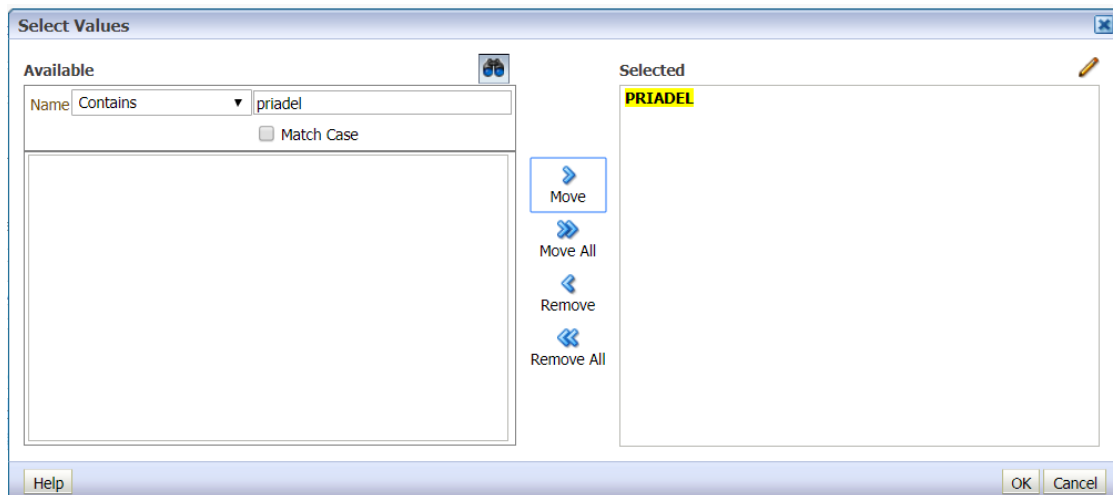
Figure 46. Example output for active substance grouping report selecting 'lithium acetate' and 'amlodipine maleate' as active substances.

Active Substance (High Level)	Active Substance
AMLODIPINE	AMLODIPINE MALEATE
LITHIUM	LITHIUM ACETATE

6.3. 'Medicinal product' short name criterion

Users can also retrieve the data querying by using the 'Medicinal product short name'

Figure 47. Example of selection by medicinal product



If the dataset is queried for a Medicinal Product name, the output of the report will contain the 'active substance high level', the 'active substance', the 'medicinal product' and the 'MAH' terms.

Figure 48. Example of active substance grouping output when Medicinal product name is selected

Active substance grouping
 Data up to and including 02-10-2017
 Time run: 03/10/2017 10:47:15

Active Substance (High Level)	Active Substance	Medicinal Product	Marketing Authorisation Holder
LITHIUM	LITHIUM CARBONATE	PRIADEL	
	LITHIUM CITRATE	PRIADEL	

6.4. Marketing Authorisation Holder search criteria

The MAH prompt and field in the output contain the values of the product owner HQ in order to comply with the implementation of the EudraVigilance access policy, as the ownership of products at HQ level will define the level of access to ICSR information the MAH will have for a specific substance.

If the dataset is queried for a MAH name, then the output of the report will contain the 'active substance high level', the 'active substance', the 'medicinal product' and the 'MAHs' terms, as in **Figure 48**.

If a product has been transferred to another MAH, the product will no longer appear in the output of the report for the MAH that no longer holds the marketing authorisation.

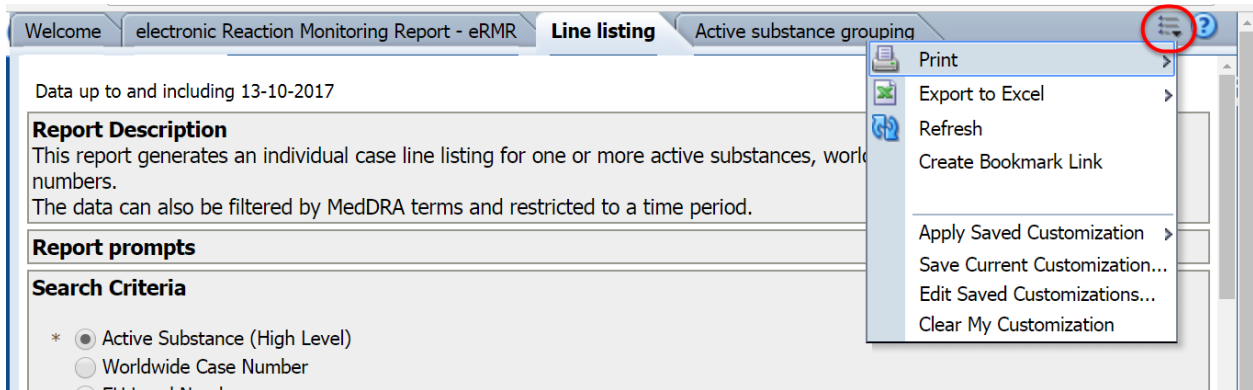
The output of the report will not include the products with a 'Not valid' marketing authorisation status.

7. Prompts page options

When you are on the prompts page, as well as answering the prompts and running the reports, there are a variety of options to customise your selections.

To access the prompt page options menu, click the **page options** button in the top right-hand corner of the prompts page.

Figure 49. Position of the page options button



The following options are available:

1. Create Bookmark Link.
2. Apply Saved Customization.
3. Save Current Customization.
4. Edit Saved Customization.
5. Clear My Customization.

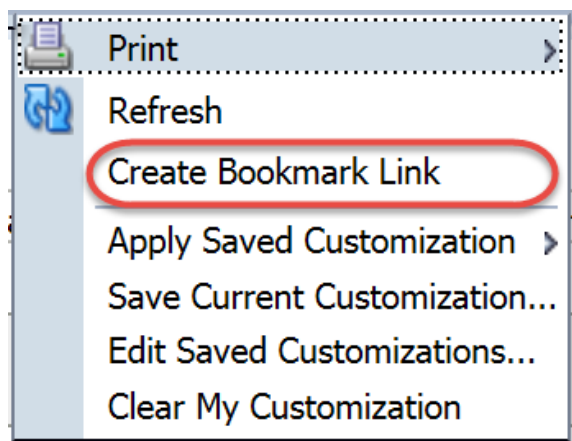
Be aware that the Print and Refresh options are not active.

7.1. Create a Bookmark link

By selecting this option, you will be able to create a dedicated URL suitable for saving or sharing the prompt page. It is shown in the browser's address bar.

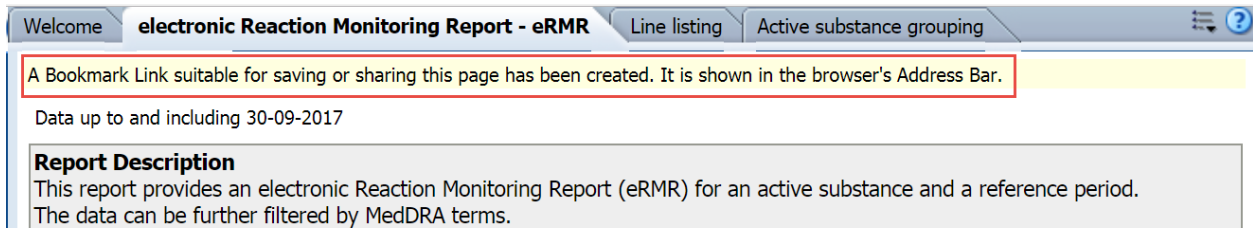
Once you have entered your prompt selections, click on '**Create Bookmark link**' in the prompt page options.

Figure 50. Create a Bookmark link option



A message will appear in the prompt page stating that a bookmark link is available in the browser address bar.

Figure 51. Bookmark link available

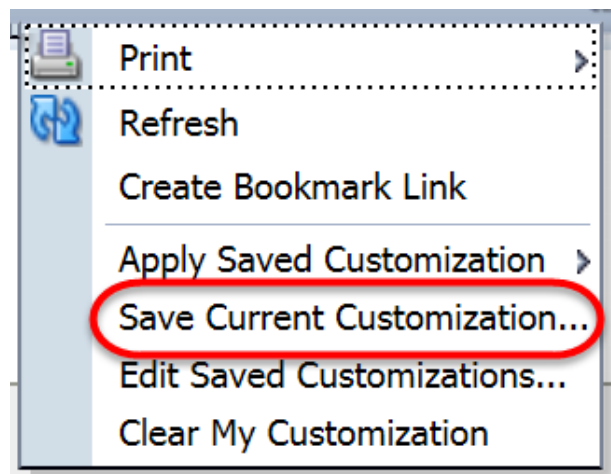


7.2. Save Current Customization

Once you have completed the prompts in a report, you can choose to save these selections for future reports, either as a default for this report or as a specific customisation via the '**Save current customization**' functionality. To save your prompt answers, before you run the report, you should apply '**save current customisation**' in the page prompt options (see Figure 52).

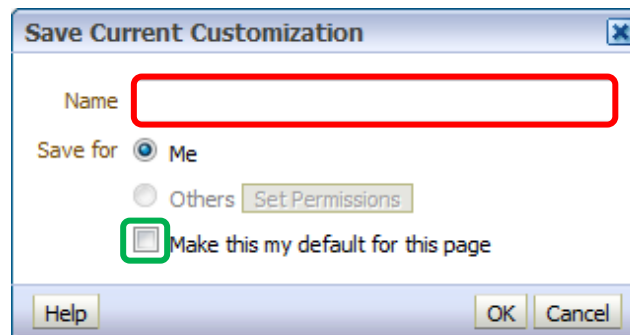
If you forgot to save your prompt answers before running the report, you can always return to the prompts page from the returned results via the 'Return link' in the standard report options (see Section 8.1 for using 'Return') and then open the prompt page options menu.

Figure 52. Save Current Customisation option



Once you click on '**Save Current Customization**', a dialogue box will appear.

Figure 53. The 'Save Current Customization' menu



You will need to enter a descriptive name for your customisation in the '**Name**' box. The name should be one which enables you to recall which customisation you require at a later day. Click '**OK**' once the name is entered.

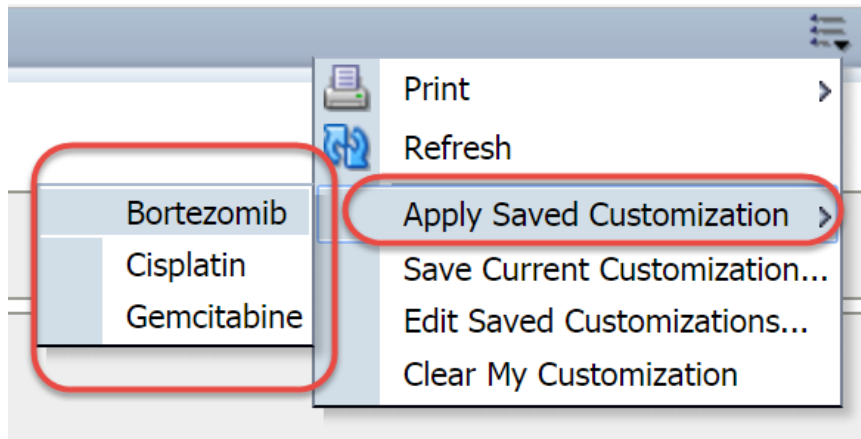
You can make these your default answers for this report by ticking the **'Make this my default for this page'** box, see [Figure 53](#), above.

Please note that 'saving for others' is not possible.

7.3. Apply Saved Customization

To apply a saved set of prompt answers to a report, click **'Apply Saved Customization'**. The system will show the list of customisations you have previously saved.

Figure 54. The 'Apply Save Current Customization' menu – Example



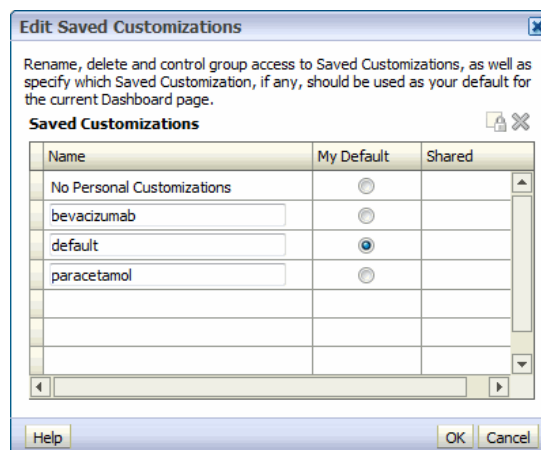
You can then run the report which will contain the search criteria according to the prompts.

Previously saved customisation can only be applied within the same report. For instance, you cannot run a line listing with a customisation saved for the eRMR report.

7.4. Edit Saved Customizations

To edit your saved customizations for a report you are currently in, click the **'Edit Saved Customizations'** link. The system will provide you with a list of your saved customisations see example in [Figure 55](#).

Figure 55. Result of clicking 'Edit Saved Customizations' – Example



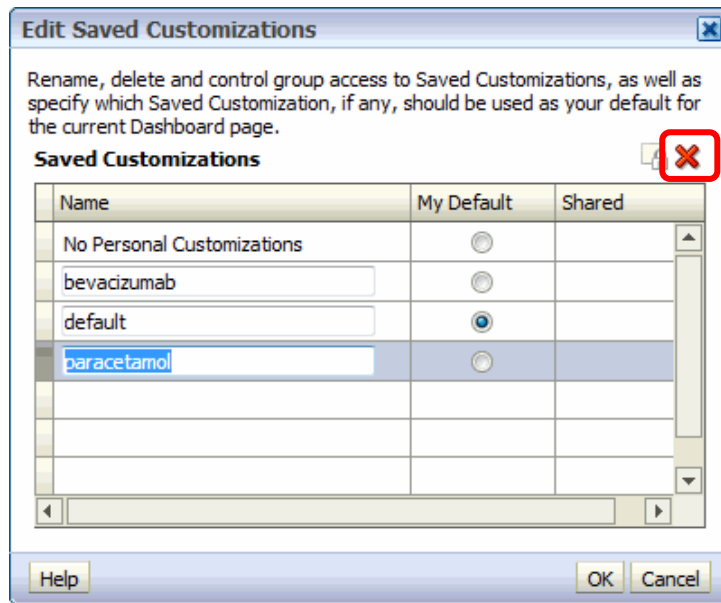
Note: The column 'Shared' is not presently usable.

You can switch the default option, including restoring the default to the system defaults ('No Personal Customizations'), by clicking the relevant radio button in the 'My Default' column.

To edit the name of a customization, click on the customisation name and type or paste your desired alternative.

Once a saved customisation has been selected a delete button will be enabled for you to delete the customisation if required.

Figure 56. A selected customization and delete button - Example

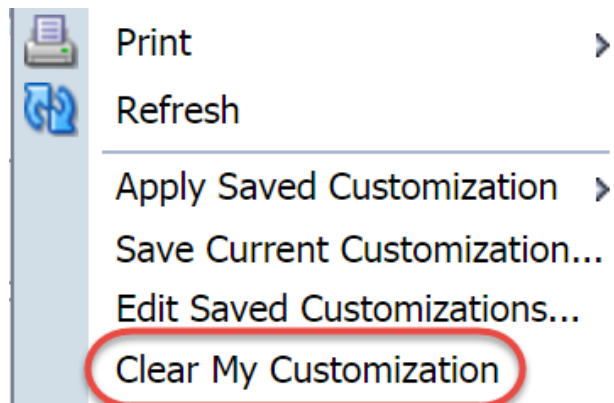


7.5. Clear My Customization

By selecting 'clear my customisation' the system removes all the answers you have entered in the prompts and restores the prompt page to the default answers. Please be aware that this function will not delete your saved customisations.

It is advised to clear your customisations when new reports are run so you do not carry over by mistake previous prompt selections.

Figure 57. Clear my customisation option



8. Working with returned reports

This section explains the format of returned reports and how to perform manipulations to the outputs in the EVDAS interface. This section describes how to change the display level, standard report options, drilling-down and other data and appearance manipulations. In EVDAS, reports always run at the default display level, which you can amend after the results have returned.

There is a limit of 100,000 rows that the EVDAS reports (eRMR and line listing) can generate. If the user selects substances that would generate an output larger than 100,000 rows, no results will be given, and an error message will be displayed. In these cases, users should look for alternative ways to retrieve the data, for instances dividing the data in two different reports.


8.1. Standard report options

All reports have the following four options at the foot of the page (Figure 58):

1. 'Return': This option takes you back to the prompt page with the options you selected for that report.
2. 'Refresh': This option re-runs the report with the options previously selected.
3. 'Print': This option exports the returned results in a printable format. You have two options for exporting, PDF or HTML. Both options will open in a new internet browser window.
4. 'Export': This option permits the user to export the data in different formats. (see Section 8.1.1)

Figure 58. Standard report options

	system disorders	thrombocytopenic)			
GEMCITABINE	Blood and lymphatic system disorders	Coagulopathies and bleeding diatheses (excl thrombocytopenic)	Coagulation factor deficiencies	Hepatic Disorders	Hyp
GEMCITABINE	Blood and lymphatic system disorders	Coagulopathies and bleeding diatheses (excl thrombocytopenic)	Coagulopathies		Acti resi:

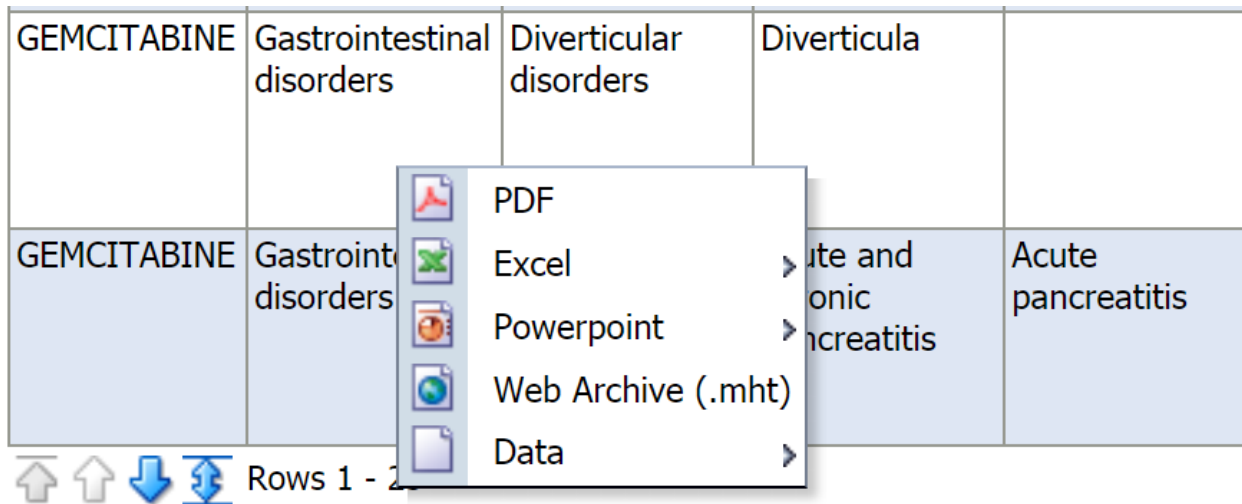
 Rows 1 - 25

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

8.1.1. Export

The 'Export' option provides the possibility to export the 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:

Figure 59. The Export menu



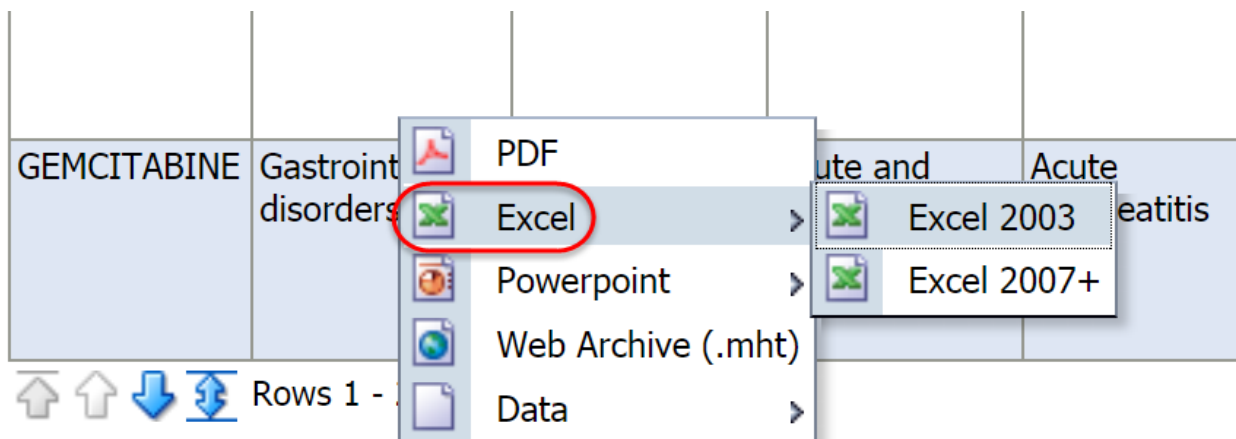
[Return](#) - [Refresh](#) - [Print](#) - [Export](#)

There are five options for exporting: PDF, Excel, PowerPoint, Web Archive (.mht) and Data. Users can select the desired option to export the results.

If you select 'Excel', you are then presented with a dialogue box offering you the option to export as Excel 2003 or Excel 2007+. If you have Excel 2007, or above, then this is the recommended option.

Please be aware that Excel has the limitation of 200,000 cells for exporting the data. CSV format is advisable in these situations.

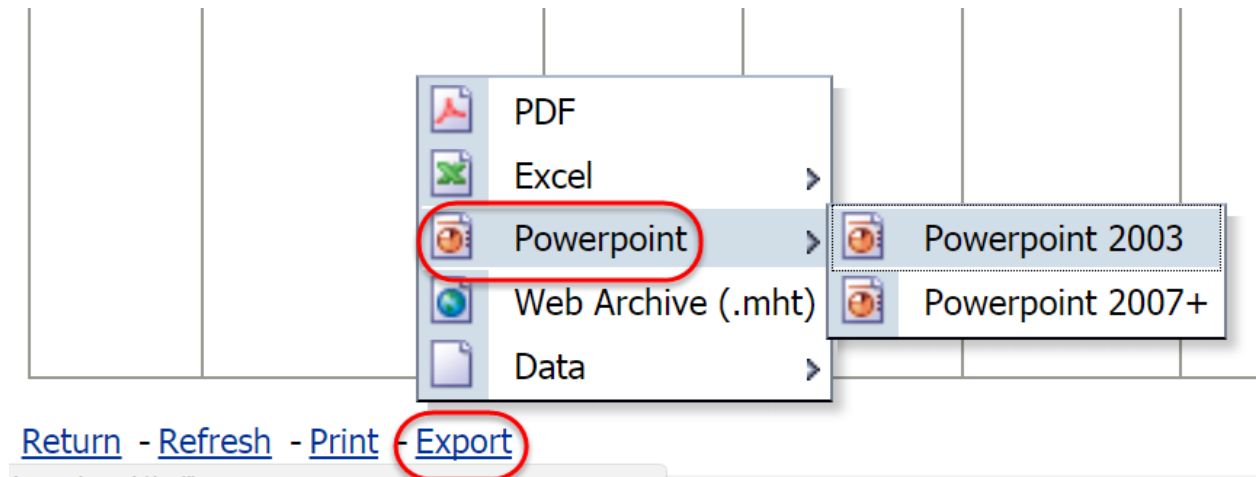
Figure 60. The Excel version dialogue box



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

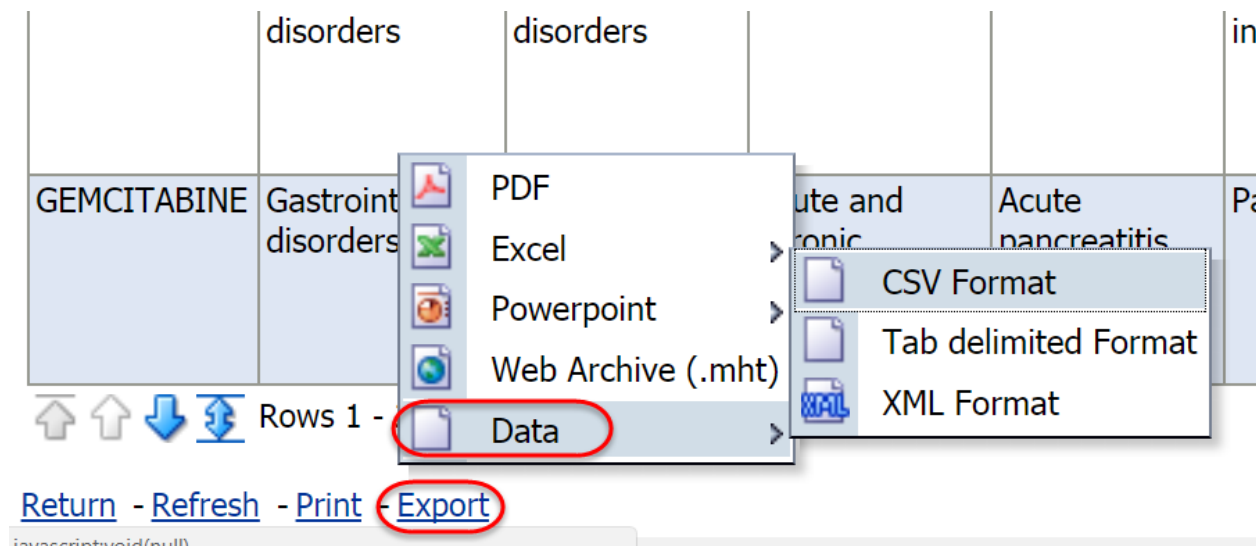
If you select PowerPoint, you are then presented with a dialogue box offering you the option to export as PowerPoint 2003 or PowerPoint 2007+. If you have PowerPoint 2007, or above, then this is the recommended option.

Figure 61. The PowerPoint version dialogue box



If you select 'Data', you are then presented with a dialogue box offering you the option to export as CSV Format, Tab delimited Format and XML Format:

Figure 62. Data export options



If you select 'CSV Format' or 'Tab delimited Format', these formats will open in your default programme for these formats. In the example below, the default programme for CSV and Tab delimited formats is Excel

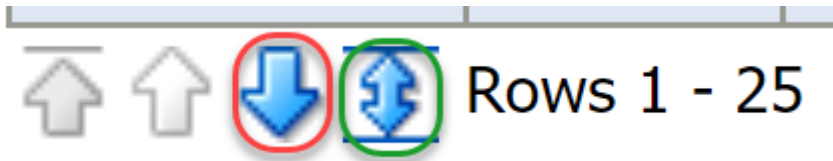
Figure 63. Data exported as CSV or Tab delimited format and opened in Excel 2007

	A	B	C	D	E	F	G	H	I	J	K	L	M
1	Active Sub	PTs	HLTs	HLGTs	SOCs	SMQ Narr	SMQ Broa	IME/DME	New EVPN	Total EVPN	New Fatal	Total Fatal	New Medi
2	GEMCITAE Abdominal	Gastrointe	Gastrointe	Gastrointe	Gastrointestinal disorders				<a target=	<a target=	0	0	0
3	GEMCITAE Abdominal	Gastrointe	Gastrointe	Gastrointe	Gastrointestinal disorders				<a target=	<a target=	2	45	0
4	GEMCITAE Abdominal	Gastrointe	Gastrointe	Gastrointe	Gastrointestinal disorders				<a target=	<a target=	1	4	0
5	GEMCITAE Anal fissur	Anal and r	Anal and r	Gastrointe	Gastrointestinal disorders				<a target=	<a target=	0	2	0
6	GEMCITAE Anal fistul	Gastrointe	Gastrointe	Gastrointe	Gastrointestinal disorders				<a target=	<a target=	0	0	0
7	GEMCITAE Ascites	Peritoneal	Peritoneal	Gastrointe	Gastrointestinal disorders		IME		<a target=	<a target=	2	40	0
8	GEMCITAE Colitis	Colitis (exc	Gastrointe	Gastrointe	Gastrointestinal disorders				<a target=	<a target=	3	13	0
9	GEMCITAE Colitis isch	Colitis (exc	Gastrointe	Gastrointe	Gastrointestinal disorders		IME		<a target=	<a target=	0	2	0
10	GEMCITAE Constipati	Gastrointe	Gastrointe	Gastrointe	Gastrointestinal disorders				<a target=	<a target=	0	21	0
11	GEMCITAE Diarrhoea	Diarrhoea	Gastrointe	Gastrointe	Gastrointestinal disorders				<a target=	<a target=	9	84	0
12	GEMCITAE Diverticula	Gastrointe	Gastrointe	Gastrointe	Gastrointestinal disorders		IME		<a target=	<a target=	1	3	0
13	GEMCITAE Duodenal	Duodenal	Gastrointe	Gastrointe	Gastrointestinal disorders		IME		<a target=	<a target=	0	0	0
14	GEMCITAE Duodenal	Duodenal	Gastrointe	Gastrointe	Gastrointestinal disorders				<a target=	<a target=	0	3	0

8.2. Expanding table views

Tables with the results in the EVDAS interface are limited to 25 rows when they first return, however these can be increased by clicking the arrows which appear below any table that has >25 rows:

Figure 64. Expand table arrows



Note: the two left-most arrows are not available for selection when you are on the first page of results

The single arrow (ringed in red) takes you to next 25 rows, the double arrow (ringed in green) expands page size to 500 rows. The two arrows to the left of the ringed arrows contract the table and take you to the previous page respectively.

8.3. Right click menu.

Once you have retrieved the data, you can manipulate the layout in the EVDAS interface by activating the right click menu, you can:

1. Sort the columns
2. Exclude/include columns
3. Move columns

Figure 65. Right click menu

EV Gateway Receipt Date	Report Type	Primary Source Qualification	Primary Source Country for Regulatory Purposes	Patient Age Group	Patient Age Group	Patient Sex	Parent Child	Reaction List PT (Duration – Outcome – Seriousness Criteria)
04/12/2019	Report from studies	Healthcare professional (Physician)	Non-EEA	65-85 Years				Anaemia (134d - Recovered/Resolved - Caused/Prolonged Hospitalisation), Haemorrhage subcutaneous (50d - Recovered/Resolved

- Sort Column >
- Exclude column
- Include column >
- Move Column >

8.3.1. Sort the column


Tables can be sorted by any of the columns. To sort by a column, hover the mouse over the column header the sort buttons  will appear. Click the downwards-pointing arrow (the arrow on the right) to sort descending (highest to lowest/Z to A) or the upwards-pointing arrow (the arrow on the left) to sort ascending (lowest to highest/A to Z).

Figure 66. An eRMR showing the sort buttons

Active Substance	SOC	HLGT	HLT	SMQ Narrow	PT	IME/DME	New EVPM	New EVPM	Tot EVPM	Tot EVPM	New EEA	Tot EEA	New HCP	Tot HCP	New Serious	Tot Serious	New Obs	Tot Obs	New Fata
GEMCITABINE	Gastrointestinal disorders	Gastrointestinal signs and symptoms	Nausea and vomiting symptoms	Gastro_nonspec_inflam & dysf_cond	Nausea		30	New EVPM	1015	Total EVPM	15	309	28	939	0	0	8	0	

8.3.2. Exclude/include column

You can exclude a column by selecting 'exclude column'. Once a column has been removed the right click menu will offer you the possibility to include the column again using the 'Include column' option.

Figure 67. Include column option

SOC	HLGT	HLT	PT	IME/DME	New EVPM	New EVPM	Tot EVPM	Tot EVPM	New EEA	Tot EEA
Gastrointestinal disorders	Gastrointestinal signs and symptoms	Gastrointestinal and abdominal pains (exc and throat)			1	New EVPM	357	Total EVPM	0	107
Gastrointestinal disorders	Peritoneal and retroperitoneal conditions	Peritoneal retroperitoneal disorders			1	New EVPM	258	Total EVPM	0	56
Renal and urinary disorders	Urinary tract signs and symptoms	Bladder and urethral symptoms	Urinary retention	IME	1	New EVPM	37	Total EVPM	0	8

8.3.3. Moving columns

You can manipulate reports by moving columns left or right, moving columns to 'prompts' and moving columns to 'sections'.

8.3.3.1. Moving columns to Prompts

This functionality allows you to convert the column into a 'prompt' and from there; you select the data according to the option provided within that prompt. In the following example, we are going to move the column 'MedDRA SOC' to a prompt section. Please be aware that this option will not work when the selected column contains numbers or multiple values.

Figure 68. SOC column converted into a prompt.

Active Substance	SOC	HLGT	HLT	SMQ Narrow	PT	IME/DME	New EVPM
BEVACIZUMAB	Blood and lymphatic system disorders				Iron deficiency anaemia		
BEVACIZUMAB	Blood and lymphatic system disorders	Anaemias nonhaemolytic and marrow depression	Anaemia		Anaemia macrocytic		
BEVACTIZUMAB	Blood	Anaemias	Anaemias	Haematopoietic	Microcytic		

Once the column has moved to a prompt, the prompt will display a drop down menu with the different options that column had, in the example the drop down menu offers the different MedDRA SOC. Users can select one MedDRA SOC and the system will display the data for the specific SOC.

Figure 69. SOC column converted into a prompt.

Active Substar	IME/DME	New EVPM	New EVPM	Tot EVPM	Tot EVPM	New EEA	Tot EEA
BEVACI		0	New EVPM	1	Total EVPM	0	0
BEVACI		0	New EVPM	527	Total EVPM	0	214
BEVACI		0	New EVPM	2	Total EVPM	0	0

Moving columns to prompts would be especially useful when retrieving eRMRs for more than one substance. In the following example an eRMR have been created for gemcitabine and cisplatin. The report brings the 2 eRMR together in alphabetic order by the substances (1st cisplatin and 2nd gemcitabine). By moving the column active substance to a prompt, you will be able to separate both eRMRs by selecting the substances from the new created prompt. Be aware that the column active substance will disappear from the eRMR outputs.

Figure 70. Moving columns to a prompt - Example.

electronic Reaction Monitoring Report – six months reference period
 Time run: 04/03/2016 14:16:07

Active Substance (High Level) is equal to **GEMCITABINE, CISPLATIN**
 and Reaction SOC is equal to **Gastrointestinal disorders**

Active Substar	Sort Column	HLTs	SMQ Broad	SMQ Narrow	PTs
CISPLA	Move Column				Gingival pain
CISPLATIN	Gastrointestinal disorders	Exocrine pancreas conditions			Pancreatitis
CISPLATIN	Gastrointestinal disorders	Exocrine pancreas conditions	Acute and chronic pancreatitis		Pancreatitis acute
CISPLATIN	Gastrointestinal disorders	Gastrointestinal conditions NEC	Gastrointestinal disorders NEC		Gastrointestinal disorder

Figure 71. Moving columns to prompts example

electronic Reaction Monitoring Report – six months reference peri
 Time run: 04/03/2016 14:16:07

Active Substance (High Level) is equal to **GEMCITABINE, CISPLATIN**
 and Reaction SOC is equal to **Gastrointestinal disorders**

SOCs	HLGTs	HLTs	SMQ Broad	SMQ Narrow	PTs
Gastrointestinal disorders	Dental and gingival conditions	Gingival pains			Gingival pain
Gastrointestinal disorders	Exocrine pancreas conditions	Acute and chronic pancreatitis			Pancreatitis
Gastrointestinal disorders	Exocrine pancreas conditions	Acute and chronic pancreatitis			Pancreatitis acute
Gastrointestinal disorders	Gastrointestinal conditions NEC	Gastrointestinal disorders NEC			Gastrointestinal disorder
Gastrointestinal disorders	Gastrointestinal conditions NEC	Gastrointestinal fistulae			Colonic fistula

You can put the prompt back to the table by selecting the prompt and dragging and dropping the prompt back to the table.

8.3.3.2. Moving columns to Sections

This functionality allows you to separate the data by a specific field. As an example, in the [Figure 72](#) below, the column gender has been moved to sections, in that way the female cases have been separated from the male cases. Please be aware that this option will not work when the selected column contains numbers or multiple values.

Figure 72. Moving the column header to Sections – Example

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 (Duration – Outcome – Seriousness Criteria)
EU-EC-12117562		04/05/2017	Spontaneous	Healthcare professional	EEA	Not available	18-64 Years	Not Specified	No	Polycythaemia -

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 (Duration – Outcome – Seriousness Criteria)
EU-EC-11084914		01/09/2016	Spontaneous	Healthcare professional (Consumer or other Non-Health	Non-EEA	Not available	65-85 Years	Not Specified	No	Intestinal per (n/a - Fatal - In Death, Ot Medically Im Condition).

9. User manual of the eRMR for MAHs

9.1. Introduction

The aim of this section is to provide the reader with an understanding of how to use the eRMR for signal detection including useful tips for prioritisation, yet not to describe the methodological aspects of signal detection which are discussed in Addendum I to Module IX of Guideline on Good Pharmacovigilance Practices (GVP)³ and in the Guideline for Screening for Adverse Reactions in EudraVigilance⁴.

The eRMR is a tool that allows the monitoring of the safety of drug use by facilitating the surveillance, detection, and documentation of suspected ADRs reported in EudraVigilance. The eRMR is designed to support signal detection activities, yet it is not a tool for signal validation or evaluation, for which more extensive data review and analysis are required.

The eRMR displays summary statistics on both the new cases (received within the period of interest) and all cases submitted cumulatively. Thus, it draws particular attention to new information available into the context of the total number of cases submitted to the EVPM. For the best use of the eRMR, the frequency of monitoring of the substance should be in line with the eRMR reference period. For instance to monitor substances every 15 days, the 15-day reference period eRMR report should be used.

Each reference period for the new updated eRMR will start at the time that the previous period finished, in that way, the eRMR allows for the continuous monitoring of the database.

3 http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/document_listing/document_listing_000345.jsp&mid=WC0b01ac058058f32c

4 http://www.ema.europa.eu/docs/en_GB/document_library/Other/2016/12/WC500218606.pdf

The eRMR provides the number of cases, disproportionality analysis, seriousness, patient outcomes (e.g. fatal, rechallenge) and details for different subgroups of interest, to assist with the prioritisation of reviews but the eRMR does not state which Drug Event Combination (DEC) should be further analysed. MAHs should exercise scientific rationale when deciding which DECs from the eRMR deserve further analysis; this should be based on the knowledge of the safety profile of the product, exposure, patient population, previous assessments etc.

During the selection of the DECs for further analysis, users should take into consideration what is known about the products, the products information, risk minimisation already in place, the identified risks, the potential risks and the missing information. In the same way, it should be considered signals that were already assessed by the MAHs and the PRAC in the context of the EU signal assessment procedure or other pharmacovigilance procedures such as PSURs or safety referrals. In some circumstances it may be useful to consult information on the class and product information for other products containing the same substance (e.g. generic products vs innovators).

Statistical signal detection has to be always complemented with clinical and scientific assessment and judgement. A signal of disproportionate reporting (SDR) is not the same as a validated signal and on the other hand there could be real safety signals that do not show as SDRs at a certain point in time.

EVDAS access for MAHs provides us the possibility to retrieve eRMRs for any substance regardless of the MAHs and that allows for comparison and statistical analysis within products in the same pharmacological class if relevant.

The screenshots included in this section are based on an eRMR exported in Excel and formatted for presentation purposes.

The eRMR is structured at DEC level, which means that each line of the eRMR contains the name of one drug (at active substance high level) and the name of one event at MedDRA PT level.

The figures displayed in the columns of the eRMR are computed from the EVPM.

Data in EVPM include reports classified as EVPM ICSRs⁵, EVPM backlog ICSRs⁶, EVPM Master ICSRs⁷, PSUR ICSRs⁸, Master PMPSUR⁹.

The eRMR contains hyperlinks whereby the user can directly access the line listing of cases for the DEC of choice.

Annex II describes the columns included in the eRMR output.

9.2. How to select the Reaction Monitor Report

Regardless of the reference period selected, the eRMR contains the cumulative summary table of suspected ADRs for the concerned active substance (or combination of active substances) since the first report was received in EV. To display only the DECs received during the reference period, in the column 'Changes' filter out the 'Blanks' option:

5 ICSRs transmitted to the EudraVigilance Post-Authorisation Module (EVPM)

6 ICSRs transmitted retrospectively to EVPM

7 Master ICSRs created after duplicate detection, transmitted to EVPM

8 ICSRs from Periodic Safety Update Reports transmitted to the EVPM

9 Master ICSRs from PSURs created after duplicate detection, transmitted to EVPM

Figure 73. Selection of the ADRs received for the specific reference period

B	C	G	AU	AU	AV	AW
Active Substances	SOCs	PTs	Tot Spontaneous	ROR (-) All	SDR	Changes
Active substance	Blood	Anaemia				
Active substance	Blood	Coagulopathy				
Active substance	Blood	Leukocytosis				
Active substance	Blood	Neutropenia				
Active substance	Blood	Thrombocytopenia				
Active substance	Card	Cardiovascular Insufficiency				
Active substance	Card	Cardiac Failure				
Active substance	Card	Acute Myocardial Infarction				
Active substance	Card	Myocardial Infarction				
Active substance	Card	Cardiac Tamponade				

The eRMR will display all reports received during the reference period for the three categories: 'new', 'increased fatal' and 'increased'.

- *New* = Filter on 'New' in the column 'Changes' to display only the DECAs that appear for the first time for the concerned active substance.
- *Increased fatal* = Filter on 'Increased fatal' in the column 'Changes' to select the DECAs with an increased number of fatal cases in the column 'Tot EVPM' or for which a follow-up of a fatal report has been received or a master fatal case (following de-duplication) has been created for the concerned active substance during the reference period covered by the eRMR.
- *Increased* = Filter on 'Increased' in the column 'Changes' to select the DECAs 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 for the concerned active substance during the reference period covered by the eRMR.

Remember that the concept of 'new cases' during the reference period in the eRMR is broad and include the following:

- Initial cases received in the EVPM during the reference period;
- Follow-up cases received in the EVPM during the reference period;
- 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, this case will be considered as 'new' for the population of the columns in the eRMR.

Using the column 'Changes' in the eRMR users can switch the eRMR view to check the totality of the DECAs that have been submitted cumulatively. During the screening of the eRMR and to decide the DECAs that should be further analysed, users may find useful to have an overview of the whole safety

profile of the substance and to consider other MedDRA PTs that can be related to the DEC of interest but for which no new cases have been received during the reporting period.

In the following example in **Figure 74** we can observe that a new case of 'pancreatitis acute' has been received during the reference period, but when we switch the view to observe all the cumulative data, we find that there are cases for 'pancreatitis', 'amylase increased' and 'lipase increased' that we should also consider during the analysis of the issue.

Figure 74. Example of ADRs related considering the cumulative data

Active Substances	SOCs	PTs	IME / DME	New EVPM	Total EVPM
Active substance	Gastr	Pancreatitis	Ime / Dme	0	8
Active substance	Gastr	Pancreatitis Acute	Ime / Dme	1	4
Active substance	Inv	Amylase Increased		0	5
Active substance	Inv	Lipase Increased		0	9

9.3. Use of MedDRA in the eRMR

As already explained, the eRMR is built using the MedDRA hierarchy and the number of cases is provided for the MedDRA PT. Having the MedDRA hierarchy in the eRMR allow us to visualise the System Organ Class (SOC), High Level Group Term (HLGT), High Level Term (HLT), Standardised MedDRA Queries (SMQ) narrow the MedDRA PT belongs to.

In line with the explanations provided in **Section 9.2**, during the screening of the eRMR it may be useful to extend the search at the level of the SOC/HLGT/HLT/SMQ in order to have an overview of other PTs that could be related to the event of interest.

For example, to visualise the data at the SOC level, the following steps can be followed:

- a) Identify the MedDRA PT of interest:

Figure 75. Example of a PT of interest

Active Substances	SOCs	HLGTs	HLTs	SMQ Narrow	PTs
Active substance	Renal	Renal Disorders (Excl Nephropathies)	Renal Disorders Nec		Renal Disorder
Active substance	Renal	Renal Disorders (Excl Nephropathies)	Renal Failure And Impairment	Acute Renal Failure	Acute Kidney Injury
Active substance	Renal	Renal Disorders (Excl Nephropathies)	Renal Failure And Impairment	Acute Renal Failure	Anuria
Active substance	Renal	Renal Disorders (Excl Nephropathies)	Renal Failure And Impairment	Chronic Kidney Disease	Chronic Kidney Disease

- b) Filter by the correspondent SOC by selecting or typing in the field the SOC's name:

Figure 76. SOC selection

Active Substances	SOCs	HLGTs	HLTs	SMQ Narrow	PTs
		Renal Disorders (Excl Nephropathies)	Renal Disorders Nec		Renal Disorder
		Renal Disorders (Excl Nephropathies)	Renal Failure And Impairment	Acute Renal Failure	Acute Kidney Injury
		Renal Disorders (Excl Nephropathies)	Renal Failure And Impairment	Acute Renal Failure	Anuria
		Renal Disorders (Excl Nephropathies)	Renal Failure And Impairment	Chronic Kidney Disease	Chronic Kidney Disease
		Renal Disorders (Excl Nephropathies)	Renal Failure And Impairment	Acute Renal Failure	Oliguria
		Renal Disorders (Excl Nephropathies)	Renal Failure And Impairment	Acute Renal Failure -- Chronic Kidney Disease	Renal Failure
		Renal Disorders (Excl Nephropathies)	Renal Failure And Impairment	Acute Renal Failure	Renal Impairment

The same steps can be followed to filter at the level of the HLGT and HLT in the related columns.

Please be aware of other filters you may have applied. If you want to see cumulatively all the DECs submitted to the EVMP for an specific SOC (regardless of the reporting period), you will need to ensure that there are no filter applied to the column 'changes' in order to include all the DECs submitted cumulatively.

As a general rule, the combination of filters in the eRMR can help users during the screening and prioritisation of DEC analysis (e.g. fatal cases or cases with positive rechallenge). While the focus should be for the new information received during the reference period, the holistic overview of the safety profile of the product should be always considered, especially during signal validation and assessment.

The eRMR provides the possibility to filter using narrow MedDRA SMQs. To filter for a specific SMQ the process would similar to the example for the SOC filter provided in this section. There will be scenarios where a single MedDRA PT belongs to different SMQs and users may consider filtering for different SMQs.

To filter by the SMQ of interest, the text filtering function 'Contains' can be used:

Figure 77. Selection of text filter within the 'SMQ column' - Example

B	C	D	E	F	G
Active Substances	SOCs	HLGTs	HLTs	SMQ Narrow	PTs
Active substance	Renal	Renal Disorders (Excl Nephropathies)	Renal Obstructive Disorders	Sort A to Z	Renal Disorder
Active substance	Renal	Renal Disorders (Excl Nephropathies)	Renal Obstructive Disorders	Sort Z to A	Acute Kidney Injury
Active substance	Renal	Renal Disorders (Excl Nephropathies)	Renal Obstructive Disorders	Sort by Color	Anuria
Active substance	Renal	Renal Disorders (Excl Nephropathies)	Renal Obstructive Disorders	Clear Filter From "SMQ Narrow"	Equals...
Active substance	Renal	Renal Disorders (Excl Nephropathies)	Renal Obstructive Disorders	Filter by Color	Does Not Equal...
Active substance	Renal	Renal Disorders (Excl Nephropathies)	Renal Obstructive Disorders	Text Filters	Begins With...
Active substance	Renal	Renal Disorders (Excl Nephropathies)	Renal Obstructive Disorders	Search	Ends With...
Active substance	Renal	Renal Disorders (Excl Nephropathies)	Renal Obstructive Disorders	<input checked="" type="checkbox"/> (Select All)	Contains...
Active substance	Renal	Renal Disorders (Excl Nephropathies)	Renal Obstructive Disorders	<input checked="" type="checkbox"/> Acute Renal Failure	Does Not Contain...
Active substance	Renal	Renal Disorders (Excl Nephropathies)	Renal Obstructive Disorders	<input checked="" type="checkbox"/> Acute Renal Failure -- Chronic Kidney Disease	Custom Filter...
Active substance	Renal	Renal Disorders (Excl Nephropathies)	Renal Obstructive Disorders	<input checked="" type="checkbox"/> Chronic Kidney Disease	Azotaemia
Active substance	Renal	Renal Disorders (Excl Nephropathies)	Renal Obstructive Disorders	<input checked="" type="checkbox"/> Retroperitoneal Fibrosis	Nephrolithiasis
Active substance	Renal	Urolithiasis	Renal Obstructive Disorders	(Blanks)	Hydronephrosis
Active substance	Renal	Renal Disorders (Excl Nephropathies)	Renal Obstructive Disorders	OK	
Active substance	Renal	Renal Disorders (Excl Nephropathies)	Renal Obstructive Disorders	Cancel	

Figure 78. Filtering on two SMQs - Example

B	C	D	E	F	G	H	I	J	K
Active Substances	SOCs	HLGTs	HLTs	SMQ Narrow	PTs				
Active substance	Renal	Renal Disorders (Excl Nephropathies)	Renal Failure And Impairment	Acute Renal Failure	Oliguria	0	y And	0	2
Active substance	Renal	Renal Disorders (Excl Nephropathies)	Renal Failure And Impairment	Acute Renal Failure	Oliguria	0	y And	0	2
Active substance	Renal	Renal Disorders (Excl Nephropathies)	Renal Failure And Impairment	Acute Renal Failure	Oliguria	0	y And	0	2
Active substance	Renal	Renal Disorders (Excl Nephropathies)	Renal Failure And Impairment	Acute Renal Failure	Oliguria	0	y And	0	2
Active substance	Renal	Renal Disorders (Excl Nephropathies)	Renal Failure And Impairment	Acute Renal Failure	Oliguria	0	y And	0	2

Please be aware that in the example above (Figure 78) if you filter for 'Acute Renal Failure ---Chronic Kidney Disease', you will retrieve only the DEC's that belong to both SMQs.

9.3.1. MedDRA version updates

Following the release by the MedDRA MSSO, EudraVigilance is updated with the new MedDRA version in May and November every year and the new MedDRA version is applied retrospectively to the terminology for all historic data.

There could be differences within the new version for the categorisation of specific terms [e.g. a MedDRA PT can be demoted to a MedDRA Lowest Level Term (LLT)] that can affect the number of cases per MedDRA PT in the eRMR and therefore the interpretation of the data. Figure 79 reflects an example of a MedDRA PT ('local swelling') that has been demoted to a MedDRA LLT. The MedDRA PT corresponding to the MedDRA LLT 'Local swelling' is the MedDRA PT 'Swelling' and therefore in the EVDAS outputs the cases reflected coded with local swelling before the MedDRA update are included under the MedDRA PT 'Swelling' after the MedDRA update.


Figure 79. MedDRA update example

Before MedDRA update		After MedDRA update	
PT1	Swelling	PT1	Swelling
PT2	Local Swelling		

Users should be conscious about the MedDRA updates when data is retrieved previous to the MedDRA update but it is used for analysis after the MedDRA update. In an eRMR retrieved and exported previous to the MedDRA update, the hyperlinks from the terms that have changed between MedDRA versions will not retrieve any results from MedDRA PTs that have been downgraded. Taking the [Figure 79](#) example, clicking on the hyperlinks for 'local swelling' will not retrieve any results after the MedDRA update ([Figure 80](#))

Figure 80. MedDRA update example

PT	New EVPM	New EVPM	Tot EVPM	Tot EVPM
Local swelling	1	New EVPM	2	Total EVPM



No Results
The specified criteria didn't result in any data.

9.4. Important Medical Events (IME) and Designated Medical Events (DME)

The column 'IME/DME' states whether the MedDRA PT is part of the IME and DME lists. Filters can be used to visualise only the 'IME/DME' or the terms not considered 'IME/DME'.

The development of the IME list and the criteria to facilitate its maintenance has been coordinated by the EudraVigilance Expert Working Group. Further information on the IME list can be found in the EudraVigilance website:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/q_and_a/q_and_a_detail_000166.jsp&mid=WC0b01ac0580a68f78

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.

Figure 81. Filter on 'IME/DEM' column

Active Substances	SOCs	HLGTS	HLTs	SMQ Narrow	PTs	IME / DME
Active substance	Renal	Renal Disorders (Excl Nephropathies)	Renal Disorders Nec			
Active substance	Renal	Renal Disorders (Excl Nephropathies)	Renal Failure And Impairment	Acute Renal Fail		
Active substance	Renal	Renal Disorders (Excl Nephropathies)	Renal Failure And Impairment	Acute Renal Fail		
Active substance	Renal	Renal Disorders (Excl Nephropathies)	Renal Failure And Impairment	Chronic Kidney Di		
Active substance	Renal	Renal Disorders (Excl Nephropathies)	Renal Failure And Impairment	Acute Renal Fail		
Active substance	Renal	Renal Disorders (Excl Nephropathies)	Renal Failure And Impairment	Acute Renal Failu	Chronic Kidney Di	
Active substance	Renal	Renal Disorders (Excl Nephropathies)	Renal Failure And Impairment	Acute Renal Fail		
Active substance	Renal	Urolithiasis	Renal Lithiasis			
Active substance	Renal	Renal Disorders (Excl Nephropathies)	Renal Obstructive Disorders	Retroperitoneal Fil		

Remember, for a DEC to be considered an SDR in EudraVigilance, the MedDRA PT should be included in the IME list.

The DME list has been developed by the EMA and contains MedDRA PTs related to medical conditions that are inherently serious and often medicine-related. The list does not address product specific issues or medical conditions with high prevalence in the general population.

The EMA and Member States use the DME list to focus on reports of suspected adverse reactions that deserve special attention, irrespective of statistical criteria used to prioritise safety reviews.

The DME list can be found in the Signal Management website at the EMA corporate website:

http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000587.js&mid=WC0b01ac0580727d1b

9.5. Number of cases in the eRMR

The sections in the eRMR related to the number of cases provide with the number of 'new' cases received during the reference period and the 'total' number of cases in the EVPM. Remember the columns with new cases will also include follow-ups and de-duplications as described in Section 9.2.

Figure 82. Number of cases in the eRMR – Example

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	0	0	1	0	1	0	0	0	1	0	0	0	0	0	0
0	11	0	3	0	11	0	11	0	1	0	5	0	1	0	0	0	0
0	2	0	2	0	2	0	2	0	0	0	0	0	0	0	0	0	0
0	3	0	0	0	3	0	3	0	0	0	0	0	0	0	0	0	0
0	1	0	0	0	1	0	1	0	0	0	1	0	0	0	0	0	1

The DEC is considered serious in the eRMR when they are included in a serious case. The criteria for a case to be considered serious, are described in Annex II.

In the same way, DEC is considered fatal when they are included in a 'fatal case' according to the criteria specified in Annex II.

The eRMR enables the retrieval of the cases in which a positive re-challenge was described in the case report. A positive rechallenge refers to an adverse reaction reoccurring after restarting the suspect or

interacting drug. Positive rechallenge for the DEC in the eRMR is considered when the drug is reported with positive rechallenge for any of the reactions included in the case.

Users should also be aware of the different approach to report seriousness criteria and positive rechallenge between ICH-E2B (R2) and ICH-E2B (R3) and how legacy cases submitted under ICH-E2B (R2) have been migrated to ICH-E2B (R3) data structure in EVDAS outputs.

Further training on the implementation of ICH-E2B (R3) in EudraVigilance can be found in the following eLearning Modules in the EudraVigilance training website:

- [Implementing ISO ICSR/ICH E2B\(R3\): Impact on adverse reaction reporting \(PhV-M2a\)](#)
- [EVDAS training for Marketing Authorisation Holders \(EV-M5b\)](#)

9.6. Screening ADRs in the General Population

According to the 'Guideline for Screening for Adverse Reactions in EV', three are the criteria to consider a DEC to be an SDR in EudraVigilance for the general population. These criteria are also outlined in [Annex II](#).

By selecting in the 'SDR All' column 'Yes', the eRMR groups all DEC that met the criteria of an SDR.

Figure 83. Filter selection in the 'SDR All' column

Active Substance	SOC	PT	IME/DME	SDR All	Changes
Substance1	Gastr	Abdominal Discomfort			Increased
Substance1	Gastr	Abdominal Mass			
Substance1	Infec	Abdominal Sepsis			
Substance1	Gastr	Abdominal Tenderness			
Substance1	Gastr	Abdominal Wall Haematoma			
Substance1	Psych	Abnormal Behaviour			Increased
Substance1	Psych	Abnormal Dreams			
Substance1	Metab	Abnormal Loss Of Weight			
Substance1	Surr	Abortion Induced			No

Additional data can be revealed by looking at the 'Total EVPM' 'Total Spon' and the 'ROR (-) All' and the ROR (-) by geographical regions. Assessing the disproportionality by geographical regions may help to consider the occurrence of a given ADR based on any geographical clusters, indication for use, different route of administration authorised etc.

Figure 84. Number of cases and RORs by geographical region and totals – Example

Tot Spont Europe	Tot Spont N America	Tot Spont Japan	Tot Spont Asia	Tot Spont Rest	Tot Spont	ROR (-) Europe	ROR (-) N America	ROR (-) Japan	ROR (-) Asia	ROR (-) Rest	ROR (-) All
15	19	4	2	3	44	1.2476	1.641375	0.5342	0.62163	0.69038	1.47041
0	1	0	0	0	1		0.729339				0.21484
1	0	0	0	0	1	1.5412					0.76376
0	3	0	1	0	5		1.6717		0.53986		0.98992

The ROR values are calculated only using spontaneous reports (ICSRs with report type 'other' and 'not available to sender' are considered spontaneous for the purpose of the ROR calculation) and litigation cases are excluded. The ROR values 'ROR (-) All' are calculated using the total cumulative number of spontaneous reports.

If the ROR is not available for any of the DEC's despite the fact that there are cases in the 'total EVPM', this is because the cases showed in the total EVPM would be reports from studies or litigation cases.

To consider the threshold on the ROR lower bound of the 95% confidence interval greater than one, subgrouping by the geographical regions is applied and that means that the ROR should be greater than one in at least one of the regions. The column in the eRMR 'ROR (-) ALL' provides information on the ROR using all the spontaneous cases in the database regardless of the country, but the definition of SDR in EudraVigilance does not take into consideration the 'ROR (-) ALL' values.

The ROR threshold per region should be combined with the number of spontaneous reports in the same region so in conclusion, an SDR is considered in the eRMR when the thresholds on the number of cases in one specific region and the lower bound of the 95% confidence interval of the ROR are met in the same specific region and the DEC is included in the IME list. For instance, if an IME term has ROR(-) > 1 in the EEA, we will need at least 3/5 spontaneous reports (excluding litigation cases) in the EEA for that DEC to be an SDR. The SDR criteria could be met in different regions at the same time. The total number of spontaneous reports for a DEC regardless of the region is not a parameter used to determine SDRs.

Figure 85 provides us with examples of DEC's that did not meet the criteria for SDRs in the general population at a certain point in time despite being IMEs, having a total of spontaneous reports above 3/5 and having 'ROR (-) All' above one.

Figure 85. Examples of DEC's that did not meet the criteria for SDRs

PT	IME/D ME	New EVPM	Tot EVPM	New Spont	Tot Spont Europe	Tot Spont N America	Tot Spont Japan	Tot Spont Asia	Tot Spont Rest	Tot Spont	ROR (-) Europe	ROR (-) N America	ROR (-) Japan	ROR (-) Asia	ROR (-) Rest	ROR (-) All
Epilepsy	Ime	2	11	0	3	2	3	0	0	8	0.42	4.00	0.71			1.18
Toxic Epidermal Necrolysis	ImeDme	1	6	0	2	0	4	0	0	6	0.42		0.90			1.09
Pneumonia	Ime	1	28	0	0	4	4	1	0	9		0.72	0.79	0.74		1.32
Sepsis	Ime	2	24	1	3	2	0	0	2	7	0.54	0.78			4.14	1.03
Retinal Detachment	Ime	0	13	0	2	1	1	0	2	6	1.38	0.22	3.03		3.99	2.30

9.7. Screening ADRs in the paediatric population

To enhance the focus of the screening on the paediatric population, the eRMR contains a separate presentation of paediatric suspected ADRs including a column with SDR dedicated to paediatrics only.

Figure 86. Paediatric SDR examples

Active Substance	SOC	PT	IME/DME	New Paed	Tot Paed	Relative ROR (-) Paed vs Others	SDR Paed
Substance1	Infec	Bacterial Sepsis	Ime	1	3	2.92	Yes
Substance1	Genrl	Death	Ime	1	4	1.05	Yes
Substance1	Hepat	Hepatitis Acute	Ime	2	3	1.90	Yes

The criteria for paediatric SDRs are developed in the 'Guideline for Screening for Adverse Reactions in EV' and outlined in [Annex II](#).

9.8. Screening ADRs in the Geriatric population

To enhance the focus of the screening on the geriatric population, the eRMR contains a separate presentation of suspected ADRs in geriatrics, including a column with SDR dedicated to geriatrics only.

Figure 87. Geriatric SDR examples

Active Substance	SOC	PT	IME/DME	New Geriatr	Tot Geriatr	Relative ROR (-) Geriatr vs Others	SDR Geriatr
Substance1	Nerv	Altered State Of Consciousness	Ime	0	16	1.04	Yes
Substance1	Genrl	Death	Ime	0	29	1.03	Yes
Substance1	Psych	Drug Use Disorder	Ime	2	5	1.02	Yes

The criteria for geriatrics SDRs are developed in the 'Guideline for Screening for Adverse Reactions in EV' and outlined in [Annex II](#).

9.9. Hyperlinks to the line listing

The eRMR provides hyperlinks that take you directly to the line listing in EVDAS for the DEC selected. By clicking on the hyperlink placed on the 'new EVPM link' and 'Tot EVPM link' you can retrieve the case line listing of interest from EVDAS.

These hyperlinks work directly from the EVDAS interface and also after the eRMR has been exported (e.g. excel, PDF) but please remember that to access the line listing in EVDAS, users should have credentials to use EVDAS.

The cases included in the line listings retrieved from the eRMR hyperlinks are driven by the cut off dates. This is fully described in [Section 5.5](#) of this manual.

The hyperlinks are placed in the columns 'New EVPM link' and 'Tot EVPM link';

Figure 88. Hyperlinks to the line listing

Active Substance	SOC	PT	IME/DME	New EVPM	New EVPM link	Tot EVPM	Tot EVPM link	New EEA	Tot EEA	New HCP
Substance1	Gastr	Abdominal Discomfort		1	1	48	48	0	15	1
Substance1	Psych	Abnormal Behaviour		2	2	12	12	0	1	2
Substance1	Musc	Arthropathy		1	1	8	8	0	1	0

Details of the line listing can be found in the [Annex I](#).

Although there is a duplicate detection algorithm implemented in the EudraVigilance system, it is possible that MAHs may find duplicates when analysing the data that have not been detected by the system. As outlined in GVP Module VI. Add I Chapter VI Add I.3.1., users are encouraged to send those cases to the EMA by email for deduplication to the following email address:

duplicates@ema.europa.eu

To report suspected duplicates, the EMA encourages that the sender sends each suspected cluster of duplicates as a single row in a table similar to Table VI. Add I.2. in GVP Module VI. Add I.

9.10. Changes in the EVDAS outputs triggered by the Brexit implementation in EudraVigilance.

From 01 January 2021, due to the implementation of the Brexit and the Northern Ireland protocol¹⁰ in EudraVigilance, the following changes should be taken into consideration in the eRMR and line listing EVDAS outputs.

- A New ISO 3166-1 alpha-2 Country Code 'XI' is implemented in EudraVigilance in order to identify the cases from Northern Ireland (UK) from the rest of the UK. The 'XI' country code should be used in the field 'Primary source country for regulatory purposes' (C.2.r.3.).
- Cases received from 01 January 2021 with 'GB' as primary source country for regulatory purposes, are considered and counted as 'Non-EEA' cases.
- Cases received before 01 January 2021 with 'GB' as primary source country for regulatory purposes, remain and are counted as 'EEA cases' in the column 'Total EEA cases' of the eRMR.
- An initial case with 'GB' as primary source country for regulatory purposes received before 01 January 2021, with a follow up after 01 January 2021 will remain and will be counted as 'EEA case' in the columns 'Total and new EEA cases' of the eRMR.
- Cases received with 'XI' as primary source country for regulatory purposes will be considered and counted as 'EEA' cases in the columns 'Total and new EEA cases' of the eRMR.

¹⁰ Commission Notice – Application of the Union's pharmaceutical acquis in markets historically dependent on medicines supply from or through Great Britain after the end of the transition period

[https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52021XC0125\(01\)&from=EN](https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:52021XC0125(01)&from=EN)

The Brexit related changes do not affect the ROR calculations by region (i.e. 'ROR (-) Europe', ROR (-) Rest of the World) or the number of total spontaneous cases by region (i.e. 'Total Spontaneous Europe', 'Total Spontaneous Rest of the World') as these figures reflect a geographical distribution of the cases (e.g. Europe) rather than a distribution based on the countries that belong to the EEA.

10. List of acronyms used in the document

Acronym	Meaning
ADR	Adverse Drug Reaction
DEC	Drug Event Combination
DEM	Designated Medical Event
EEA	European Economic Area
EMA	European Medicines Agency
eRMR	Electronic Reaction Monitoring Report
ETL	Extraction, Transfer, and Loading
EU	European Union
EV	EudraVigilance
EVCTM	EudraVigilance Clinical Trial Module
EVDAS	EudraVigilance Data Analysis System
EVDBMS	EudraVigilance Database Management system
EVPM	EudraVigilance Post-Authorisation Module
EVWEB	EudraVigilance Web application
GVP	Good Pharmacovigilance Practice
HQ	Headquarter
HLGT	High Level Group Term
HLT	High Level Term
ICH	International Conference on Harmonisation
ICSR	Individual Case Safety Report
IME	Important Medical Event
MAH	Marketing Authorisation Holder
MedDRA	Medical Dictionary for Regulatory Activities
MLM	Medical Literature Monitoring
NCA	National Competent Authority of an EEA Member State
PRAC	Pharmacovigilance Risk Assessment Committee
PSUR	Periodic Safety Update Report
PT	Preferred Term
QPPV	Qualified Person responsible for Pharmacovigilance

Acronym	Meaning
ROR	Reporting Odds Ratio
SDR	Signal of Disproportionate Reporting
SOC	System Organ Class
SMQ	Standardised MedDRA Query
SUSAR	Suspected Unexpected Serious Adverse Reaction
xEVMPD	Extended EudraVigilance Medicinal Product Dictionary

11. Supporting documents

- European Medicines Agency policy on access to EudraVigilance data for medicinal products for human use (EMA/759287/2009 Revision 4)
http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000674.jsp
- Screening for adverse reactions in EudraVigilance (EMA/849944/2016)
http://www.ema.europa.eu/docs/en_GB/document_library/Other/2016/12/WC500218606.pdf
- EudraVigilance User Manual - Individual Case Safety Report form (EMA/249220/2016)
http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2017/06/WC500229803.pdf
- Guideline on good pharmacovigilance practices (GVP) - Module IX – Signal management (Rev 1)
http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2017/10/WC500236408.pdf
- Guideline on good pharmacovigilance practices (GVP) - Module IX Addendum I – Methodological aspects of signal detection from spontaneous reports of suspected adverse reactions
http://www.ema.europa.eu/docs/en_GB/document_library/Scientific_guideline/2017/10/WC500236405.pdf
- Guideline on good pharmacovigilance practices (GVP) - Module VI Addendum I – Duplicate management of suspected adverse reaction reports
http://www.ema.europa.eu/docs/en_GB/document_library/Regulatory_and_procedural_guideline/2017/08/WC500232765.pdf
- eLearning: Implementing ISO ICSR/ICH E2B(R3): Impact on adverse reaction reporting (PhV-M2a):
[Implementing ISO ICSR/ICH E2B\(R3\): Impact on adverse reaction reporting \(PhV-M2a\)](#)
- eLearning: EVDAS training for Marketing Authorisation Holders (EV-M5)
[EVDAS training for Marketing Authorisation Holders \(EV-M5b\)](#)

12. Annex I. Details of the line listing

ICH/EU	ICSR ICH E2B(R3) Element Reference	DATA ELEMENT NAME	EVDAS name	Example	Comment
EU	N/A	EU local number	EU local number	EU-EC-12345	
ICH	C.1.8.1	Worldwide Unique Case Identification	Worldwide Unique Case Identification	GB-EMA-12345	
EV	N/A	EV Gateway Date	EV Gateway Receipt Date	01/01/2014	
ICH	C.1.3	Type of Report	Report type	Spontaneous	
ICH	C.2.r.4	Qualification	Primary source qualification	Healthcare Professional	
ICH	C.2.r.5	Primary Source for Regulatory Purposes	Primary source country for regulatory purposes	EEA	The country is displayed as a classification EEA/non EEA. For legacy data, country classification will use the following country algorithm: - use 'occurrence country', - if missing use 'primary source country', - if missing, use country code for 'worldwide case unique identifier'.
ICH	C.4.r.1	Literature Reference(s)	Literature Reference(s)		
ICH	D.2.2a	Age at Time of Onset of Reaction / Event (number)	Patient age group	18-64 Years	The Patient age is populated using an age group used in EVDAS. The age is calculated as follows: - use reported patient age, - if missing, use age calculated based on difference between date of birth and first reaction start date (if available in a valid date format dd/mm/yyyy).
ICH	D.2.2b	Age at Time of Onset of Reaction / Event (unit)			

ICH/EU	ICSR ICH E2B(R3) Element Reference	DATA ELEMENT NAME	EVDAS name	Example	Comment	
					Note: in case of multiple reactions which occurred beyond a 12 months onset period, age should not be calculated.	
ICH	D.2.3	Patient Age Group (as per reporter)	Patient Age Group (as per reporter)	Adult		
ICH	D.5	Sex	Patient sex	Female		
EU	EU	N/A	Parent/Child report	Yes	If any data has been populated in section D.10	
ICH	E.i.2.1b	Reaction / Event (MedDRA code) ¹¹	Reaction List PT (Duration – Outcome - seriousness criteria)	Rash (3d – Resolved - Life Threatening, Caused / Prolonged Hospitalisation) Nausea (1d - Resolved) Headache (3d – Not resolved)	Will be displayed only if marked as yes	
ICH	E.i.3.2a	Results in Death				Will be displayed only if marked as yes
ICH	E.i.3.2b	Life Threatening				Will be displayed only if marked as yes
ICH	E.i.3.2c	Caused / Prolonged Hospitalisation				Will be displayed only if marked as yes
ICH	E.i.3.2d	Disabling / Incapacitating				Will be displayed only if marked as yes
ICH	E.i.3.2e	Congenital Anomaly / Birth Defect				Will be displayed only if marked as yes
ICH	E.i.3.2f	Other Medically Important Condition				Will be displayed only if marked as yes
ICH	E.i.7	Outcome of Reaction / Event at the Time of Last Observation				
ICH	E.i.6a/b	Duration of Reaction / Event				Displayed in days
ICH	G.k.1	Characterisation				Suspect/interacting

¹¹ Displayed as MedDRA Term

ICH/EU	ICSR ICH E2B(R3) Element Reference	DATA ELEMENT NAME	EVDAS name	Example	Comment
		of Drug Role	Drug List (Drug Char - Indication PT - Action taken - [Duration - Dose - Route])	withdrawn - [1d - 25mg - oral])	columns: 'Suspect/interacting Drug list' and 'Concomitant/Not Administered Drug list'
ICH	G.k.2.3.r.1	Substance / Specified Substance Name	AND	If there are multiple indications, the drug list will be: Lyrica [Pregabalin] (S - Epilepsy, anxiety - Drug withdrawn - [1d - 25mg - oral])	Only if not recorded
EU	N/A (EMA element)	Substance / Specified Substance Name	Concomitant/Not Administered Drug List (Drug Char - Indication PT - Action taken - [Duration - Dose - Route])	If there is multiple information reported for any of the fields 'drug start date, duration, dose, route, the drug list will be: Lyrica [Pregabalin] (S - Epilepsy - Drug withdrawn - [1d - 0.5mg - oral - More in ICSR])	This corresponds to the Scientific composition in EVDAS.
ICH	G.k.2.2	Reported Medicinal product		If there are multiple indications and multiple information reported for any of the fields 'drug start date, duration, dose, route', the drug list will be: Lyrica [Pregabalin] (S - Epilepsy, anxiety - Drug withdrawn - [1d - 0.5mg - oral - More in ICSR])	This will be displayed as the recorded medicinal product in EVDAS for Centrally authorised products. For Non-Centrally authorised products: The substance as recorded, retrieved from the recorded medicinal product, will be displayed. If no recorded information, blank value will be displayed.
ICH	G.k.7.r.2b	Indication (MedDRA code)			if there are multiple indications reported, these will be concatenated in the field.
ICH	G.k.4.r.6a	Duration of Drug Administration			each time one of these data elements is repeated, the string 'More in ICSR' will be inserted as follows:
ICH	G.k.4.r.1a/b	Dose			Drug List (Drug Char - Indication PT - Action taken - [Duration - Dose - Route - More in ICSR])
ICH	G.k.4.r.10.2	Route of Administration			The 'duration - dose - route' will contain the data of the 1st occurrence of the repeated block (based on earliest Drug start date). If no repeated value is reported, the string 'More in ICSR' will not be

ICH/EU	ICSR ICH E2B(R3) Element Reference	DATA ELEMENT NAME	EVDAS name	Example	Comment
ICH	G.k.8	Action(s) Taken with Drug			inserted.
EU	N/A (EMA element)	Hyperlink to the ICSR form	ICSR form		The ICSR form level is implemented according to the EV access policy.

13. Annex II. Description of the eRMR columns

eRMR Column name	Description
Active substance	Name of the monitored active substance (or combination of active substances) using the active substance high level
SOCs	MedDRA System Organ Class classification
HLGTs	MedDRA High Group Level Term classification
HLTs	MedDRA High Level Term classification
SMQ Narrow	Standardised MedDRA Query (Narrow) classification. This column contains: <ul style="list-style-type: none"> • Empty cells when the MedDRA PT is not associated with any SMQ; • One single SMQ per cell when the MedDRA PT is associated with one unique SMQ; • Different SMQs in one single cell when the MedDRA PT belongs to more than one SMQ according to the multi-axiality of MedDRA. The different SMQs are separated by `---`.
PTs	MedDRA Preferred Term classification
IME / DME	This column indicates whether the MedDRA PT corresponds to an 'Important Medical Event' or 'Designated Medical Event' <input type="checkbox"/>
New EVPM	Number of cases for the concerned DEC received in the EVPM during the reference period
Total EVPM	Total number of cases for the concerned DEC received in the EVPM, including the reference period
New EEA	Number of cases for the concerned DEC originating from the European Economic Area (EEA) ¹² and received in the EVPM during the reference period
Total EEA	Total number of cases for the concerned DEC originating from the EEA ¹² and received in the EVPM, including the reference period

¹² A case is considered originated from the European Economic Area if the E2B field C.2.r.3 (Reporter's Country Code) that has been chosen as the E2B field C.2.r.5 (Primary Source for Regulatory Purposes) has a country belonging to the European Economic Area (EEA)

eRMR Column name	Description
New Health Care Professional	Number of cases for the concerned DEC originating from a Health Care Professional (HCP) ¹³ and received in the EVPM during the reference period
Total Health Care Professional	Total number of cases for the concerned DEC originating from a HCP ¹³ and received in the EVPM, including the reference period
New Serious	Number of cases for the concerned DEC reported as 'Serious' ¹⁴ and received in the EVPM during the reference period
Total Serious	Total number of cases for the concerned DEC reported as 'Serious' ¹⁴ and received in the EVPM, including the reference period
New Observational	Number of cases for the concerned DEC originating from solicited reports received in EVPM during the reference period. These cases are not included in the 'New Spontaneous' cases
Total Observational	Total number of cases for the concerned DEC from solicited reports received in EVPM, including the reference period. These cases are not included in the 'Total Spontaneous' cases nor in the calculation of the ROR
New Fatal	Number of fatal ¹⁵ cases for the concerned DEC received in the EVPM during the reference period
Total Fatal	Total number of fatal ¹⁵ cases for the concerned DEC received in the EVPM, including the reference period
New Medication Error	Number of cases for the concerned DEC received in the EVPM during the reference period and reported with at least one reaction contained in the SMQ 'Medication Error'
Total Medication Error	Total number of cases for the concerned DEC received in the EVPM, including the reference period and reported with at least one reaction contained in the SMQ 'Medication Error'
New + Rechallenge	Number of cases for the concerned DEC reported with positive rechallenge ¹⁶ , received in the EVPM during the reference period

¹³ A case is considered originated from a Health Care Professional if the E2B field C.2.r.4 (Qualification) has at least one of the following values: 'Physician', 'Pharmacist' or 'Other health professional'

¹⁴ A case is considered serious if any of the following E2B E.i.3.2 fields has the value 'Yes': Results in Death, Life Threatening, Caused / Prolonged Hospitalisation, Disabling / Incapacitating, Congenital Anomaly / Birth Defect, Other Medically Important Condition.

¹⁵ A case is considered fatal if either the E2B field E.i.3.2a (Results in Death) has the value 'Yes' or the E2B field E.i.7 (Outcome of Reaction) has the value 'Fatal'

eRMR Column name	Description
Total + rechallenge	Total number of cases for the concerned DEC reported with positive rechallenge ¹⁶ received in the EVPM, including the reference period
New Literature	Number of cases for the concerned DEC originating from literature ¹⁷ reports received in the EVPM during the reference period
Total Literature	Total number of cases for the concerned DEC originating from literature ¹⁷ reports received in the EVPM, including the reference period
New Paediatric	Number of cases for the concerned DEC referring to patients aged < 18 years and received in the EVPM during the reference period
Total Paediatric	Total number of cases for the concerned DEC referring to patients aged < 18 years and received in the EVPM, including the reference period
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
Paediatric SDR	<p>It indicates the DEC's when the following criteria are applied:</p> <ul style="list-style-type: none"> • Classified as IME • The lower bound of the 95% confidence interval of the ROR for the paediatric population is greater than one • The lower bound of the 95% confidence interval of the Relative ROR Paed vs Others is greater than one • The number of spontaneous¹⁸ (excluding litigation) cases in the paediatric population is greater than or equal to 2 for products under the additional monitoring and 3 for the other products

¹⁶ In the cases reported under ICH-E2B(R2) , positive re-challenge is recorded at the level of the drug and this information is kept in the eRMR. Therefore, if one drug (suspect or interacting) in a case was reported with positive re-challenge, all reactions belonging to the same case will be highlighted as such for the given drug. For the cases reported under ICH-E2B(R3) positive rechallenge in the eRMR is populated only for the reactions that recurred following the rechallenge of the drug

¹⁷ A case is considered from literature if the E2B field C.4.r.1 (Literature reference) has the value 'Yes'

¹⁸ In the eRMR the number of spontaneous cases includes the cases with report type 'spontaneous' 'other' and 'not available to sender (unknown)'

eRMR Column name	Description
New Geriatric	Number of cases for the concerned DEC referring to patients aged ≥ 65 years and received in the EVPM during the reference period
Total Geriatric	Total number of cases for the concerned DEC referring to patients aged ≥ 65 years and received in the EVPM, including the reference period
Ratio ROR (-) geriatric 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
Geriatrics SDR	<p>It indicates DEC's when the following criteria are applied:</p> <ul style="list-style-type: none"> Classified as IME The lower bound of the 95% confidence interval of the ROR for the geriatric population is greater than one The lower bound of the 95% confidence interval of the Relative ROR Geriatr vs Others is greater than one The number of spontaneous¹⁸ (excluding litigation) cases in the geriatric population greater than or equal to 3 for products under the additional monitoring and 5 for the other products
New Spontaneous	Number of spontaneous ¹⁸ cases for the concerned DEC received in the EVPM during the reference period; this number does not include the new reports from observational studies (see column 'New Observational')
Total Spontaneous by Geographical Regions	The columns 'Total spontaneous Europe, North America, Japan, Asia (excluding Japan), Rest of the World contain the total number of spontaneous ¹⁸ cases for the concerned DEC, including the reference period with Primary Source Country respectively in Europe, North America, Japan, Asia (excluding Japan) and the Rest of the World.
Total Spontaneous	Total number of spontaneous ¹⁸ cases for the concerned DEC, received in EVPM, including the reference period; this number does not include reports from observational studies (see column 'Tot Observational').
ROR (-) by geographical regions	The columns named 'ROR(-) Europe, North America, Japan, Asia, Rest of the World contain the 95% confidence interval lower bound of the ROR for the spontaneous ¹⁸ (excluding litigation) cases related to the concerned DEC originated respectively in those regions using all other DEC's originated in those regions as background distribution
ROR (-)	Lower bound of the 95% confidence interval of the ROR for the concerned DEC, using all other DEC's available in the database as

eRMR Column name	Description
	reference
SDR	<p>This column identifies the DEC's with an SDR. The following SDR criteria are met in at least one of the regions:</p> <ul style="list-style-type: none"> • Classified as IME • ROR (-) > 1 • Total number of spontaneous (excluding litigation) cases: <ul style="list-style-type: none"> – greater than or equal to 3 for substances under Additional Monitoring (unless the sole reason for inclusion on the list is the request of a post-authorisation safety study). – greater than or equal to 5 for all other substances
Changes	<p>Indicates all DEC's for which new cases were received in EVPM during the reference period. There are 3 different values:</p> <ul style="list-style-type: none"> • 'New': DEC's appearing in EVPM for the first time • 'Increased': DEC with an increased number of cases in the column 'Tot EVPM' • 'Increased fatal': DEC's with an increased number of fatal cases

14. Annex III. Troubleshooting

14.1. Browser compatibility

EVDAS uses OBIEE 11.1.1.7.140715. This version officially supports the following browser versions:

Firefox	Google Chrome	Internet Explorer	Safari
3.5+	19+	7.x	4.x
6+		8.x	5.x
13+		9.x	
		10.x	
		11.x	

14.2. Login or display issues

If you experience login or display issues, there are some basic steps you can check before contacting IT Service Desk:

- Clear your browser cache, history and saved passwords. Close and reopen the browser to try again.
- Check login details and remember the distinction between EVDAS and EVWEB login details (also used to connect to EVDAS from EudraVigilance page and to open ICSR forms)

14.3. Errors when exporting data

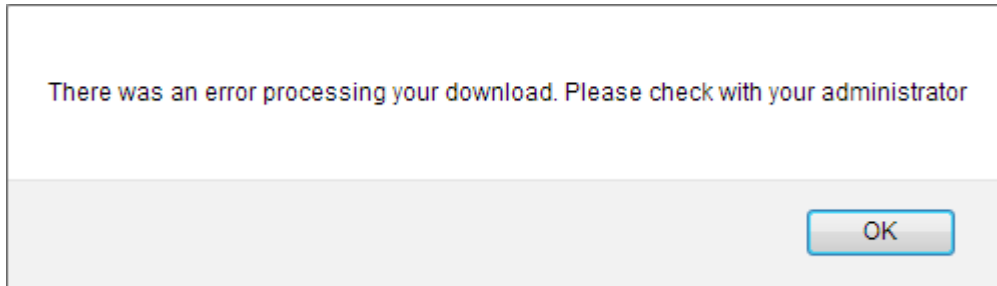
In EVDAS there are several options to export data. There are limitations however to the amount of data you can export. Please realise that even one row in the eRMR or line listing already contains a vast amount of data, thus a line listing with thousands or records is a strain on the system. To avoid errors when exporting, please follow these points:

- If you need to export data, narrow your query down as much as possible before exporting. If it leads to errors in the download, consider a different file format or splitting the query in two or more batches.
- Consider which format you want the data in: .xlsx is the Excel 2007 format suitable for most exports. The .xls format is the more conservative Excel 2003 format and is generally safer if you experience problems with layout or graphical artefacts. The Excel option always exports the data as presented on-screen.
- For large amounts of data .CSV is suitable. Opening a CSV file in Excel will show the data in a plain tabular format.
- If you ran a report and export the results, always scroll down to the bottom of the file to check if all records have been exported. Errors may not always be obvious and only show after the file truncates.

Specific examples of errors are:

- Export to Excel 2007 doesn't work.

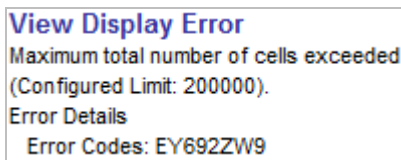
Reason: processing the export in Excel 2007 format violates a 65 MB limit, leading to the following error:



Workaround:

- Export to Excel 2003;
 - Export to CSV;
 - Repeat the query splitting it into batches (e.g. split by MedDRA reaction SOC: the file to export will be smaller).
- Export to Excel (2003 or 2007) is successful but the output is cut off

Reason: the limit of exportable cells (200,000 cells) was reached, leading to an error at the bottom of the file (error might not be directly visible in file):



Workaround:

- Export to CSV;
- Repeat the query splitting it into batches (e.g. split by MedDRA reaction SOC: the file to export will be smaller).

14.4. Opening hyperlinks (ICSR/E2B forms) from eRMR and line listings

Information for users

An error can occur when you try to open a hyperlink for the line listings, ICSR, or E2B forms in a downloaded Excel file. The error will read "System error. Please re-try your action. If you continue to get this error, please contact the Administrator":



This is a known issue in Microsoft Office. As temporary workaround you can copy and paste the hyperlink yourself in the browser. For a permanent solution contact the IT department in your organisation with the below information, as they need to apply a registry fix.

Information for the IT department

If you click on a hyperlink inside Word/Excel/PowerPoint then by default Office itself is handling link activation. As Office however cannot provide full browser capabilities comparable to e.g. IE there are scenarios where we are unable to access the referenced resource.

In most cases reason are special authentication schemes being used (e.g. when accessing a file on a web server it replies with a 401 page and some java code that is supposed to get a security token for the user. As we are not executing such java scripts authentication would fail and Office would not be able to verify the linked resource. So, if you click on a link in such an environment hyperlinks could not be opened from inside an Office document. If you however copy/paste the link URL into a browser then we are typically able to open the link.

With ForceShellExecute registry key enabled Office will not try anymore to open the hyperlink itself.

It will simply pass it over to the shell in order to get it handled there. So, with this registry key we basically do the same as when pasting an URL into the browser.

In the last call we created a DWORD registry key with the name "ForceShellExecute" and value "1", to this location

HKEY_LOCAL_MACHINE\SOFTWARE\Wow6432Node\Microsoft\Office\9.0\Common\Internet\

This path is valid only if you have a 32 bit version of Office.

If you install the 64 bit version then you need to add the key to this path: HKEY_LOCAL_MACHINE \Software\Microsoft\Office\9.0\Common\Internet (<https://support.microsoft.com/en-us/kb/2596545>)

Making this modification, Office will not handle anymore the link activation and problems can appear.

In the below article you can find the problems that can appear but also a solution for the issues:

<https://blogs.technet.microsoft.com/emeaoffice/2013/06/13/impact-of-using-forceshellexecute1-in-office-2007-2010-and-2013/>

In order to add the register key to all the users you can create the domain policy

([https://technet.microsoft.com/en-us/library/cc753835\(v=ws.11\).aspx](https://technet.microsoft.com/en-us/library/cc753835(v=ws.11).aspx)) that can apply this modification.

(courtesy of Microsoft)