



EUROPEAN MEDICINES AGENCY  
SCIENCE MEDICINES HEALTH

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Data Analytics and Methods

## Functionalities in support of the medical literature monitoring service

User manual: EudraVigilance ICSR Downloads and tracking spreadsheets

\* **Note:** Rev 7 contains the following:

- Document substantially rewritten to remove references to the (pre-22/11/2017) ICSR export manager;
- Inclusion of references to MEDLINE search;
- Inclusion of references to and explanations of the MLM RIS format;
- Update of links and references;
- Removal of references to the ICH E2B(R2) message format.

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## Overview

Article 27 of Regulation (EC) No 726/2004 sets out the provisions for the monitoring of medical literature and the entry of relevant information into the EudraVigilance (EV) database by the European Medicines Agency. The [Detailed guide regarding the monitoring of medical literature and the entry of relevant information into the EudraVigilance database by the European Medicines Agency](#) (doc. ref. EMA/161530/2014) further defines the scope of the activities and the applicable business processes.

The medical literature monitoring (MLM) service covers a range of active substances including herbal active substances as well as designated medical literature based on the use of literature reference databases. All of this information is published on [Medical literature monitoring](#) page of the EMA's website.

The outcome of the screening results is published on a daily basis as both "MLM RIS" and "MLM Search Results" at a dedicated area of the [EudraVigilance restricted area](#) – Medical Literature Monitoring (MLM) box.

A list of ICSRs entered in EudraVigilance is published daily as "MLM ICSRs" at the dedicated section of the [EudraVigilance restricted area](#) – Medical Literature Monitoring (MLM) box.

MAHs can access and download the ICSRs from EudraVigilance, via the ICSR Download section, in line with the applicable formats and standards as outlined in Article 25 and 26 of the Commission Implementing Regulation (EC) No 520/2010.

The EudraVigilance "ICSR Download" section allows for filtering based on the following parameters: substance groups, individual substance or substance combinations, dates of transmission of the ICSRs to EudraVigilance, Primary source country, Worldwide Case ID, Seriousness, Report type, Current report only (Yes/No).

# 1. Pre-requisites

## **1.1. Eudravigilance Registration**

To use both EudraVigilance (EV) and the tracking spreadsheets requires registration with EV. If you are not registered with EV, contact your organisation's person responsible for Eudravigilance. This is usually the QPPV or head of pharmacovigilance department. Further information on registering for EudraVigilance is available on the [EudraVigilance: how to register](#) webpage.

## **1.2. Software**

The tracking spreadsheets are published as Microsoft Excel 2007+ format spreadsheets. To access the cases, users will require Google Chrome, Mozilla Firefox or Microsoft Edge. The RIS format files are intended for use in library management software, but can be viewed using Notepad or any equivalent software.

## 2. Accessing the MLM functionalities

All functionalities are accessible from the restricted area of the Eudravigilance website:

<https://eudravigilance.ema.europa.eu/human/restricted/PublicView/list2.asp>.

**EudraVigilance** Home Restricted  
Human Restricted Home Public  
Restricted Area

**Logged In**

Welcome to the restricted area of the Eudravigilance website

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

For the UK, as from 1.1.2021, EU Law applies only to the territory of Northern Ireland (NI) to the extent foreseen in the Protocol on Ireland/NI

**EV Services**

- ▶ EVWEB - ICSR
- ▶ EVWEB - Art 57 / XEVMPD
- ▶ xEVMPD Export
- ▶ xEVMPD Bulk update
- ▶ EV Data Warehouse
- ▶ EV Post - Art 57 / XEVMPD

**CTIS links**

- ▶ Sponsor workspace
- ▶ Authority workspace

**EV Registered Partners**

- ▶ Manage your contact details
- ▶ QPPV List
- ▶ Organisations List

**Medical Literature Monitoring**

- ▶ MLM RIS
- ▶ MLM Search result
- ▶ MLM ICSRs
- ▶ Archive
- ▶ ICSR Export
- ▶ Substances
- ▶ Further MLM info

**User Support**

You will see various menus on the left of the screen. The yellow-ringed link takes you to EVWEB (which is also available directly from <https://eudravigilance-human.ema.europa.eu/#/>) and the red-ringed menu contains the MLM-specific links.

### 3. Tracking tools

Every business day the MLM Service will publish and update the following links:

- **MLM RIS**, which contains the results of the searches and screening of scientific and medical literature that the Agency is monitoring in RIS format<sup>1</sup>.
- **MLM Search Results**, which contains the results of the searches and screening of scientific and medical literature that the Agency is monitoring in Excel format;
- **MLM ICSRs**, which contains the results of the review and assessment of the returned articles and information on the management of the ICSRs created in Excel format.

All links will be updated daily at 9AM & an article and any related cases will remain in the relevant spreadsheet until the day after it has been completed.

An article is considered completed, and is removed from the sum\_screen spreadsheet the following day, once it has been assessed for inclusion/exclusion criteria.

A case is considered completed, and is removed from the sum\_ICSR spreadsheet the following day, either:

- once it has been confirmed that there is no case; or
- once the case has been transmitted to EV and it is assessed that no follow-up is required; or
- that follow-up was received and a follow-up version received; or
- that no follow-up was received by the requested date of reply.

Once an article and/or the cases are completed, they will no longer appear in the daily tracking sheets, and their tracking records will only be the archive, which will be permanently available. However, the cases created and transmitted to EV will be permanently available via **EVWEB** (see 4. ).

All dates in the spreadsheets are in the format DD/MM/YYYY. Dates and times are in the format DD/MM/YYYY hh:mm.

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<sup>1</sup> RIS is a standardized tag format designed to allow the exchange of citation data between programs.

### 3.1. MLM RIS

#### 3.1.1. Accessing the MLM RIS data

To access the MLM Search results in RIS format, click on the "MLM RIS" link:



The following message is displayed:



Click "Open" to open the file, or "Save" to save the file locally.

#### 3.1.2. Data in the MLM RIS file

The RIS file contains the following data fields, which match\* the fields in the MLM Search result spreadsheet:

Field code	Meaning	Data/Format
TY	Type of publication	Free text: usually "JOUR" for 'Journal'
SG	Substance Group	Text: substance group name from the list of Active Substance Groups (see 4.4. )
DB	Reference Database	Text: "AMED", "EMBASE", "IPA" or "MEDLINE"
DA	Date and Time of Search	CCYY/MM/DD/HH:MM
AU	Author [repeatable field]	Free text
PY	Year	YYYY
VL	Volume	Number
IS	Issue/supplement	Number
SP	Pages	Number-number
T2	Journal	Free text
TI	Title	Free text
CY	Primary Source Country	ISO 3166-1 alpha-2 code
LA	Lead Author	Free text
DO	Document Object Identifier	Free text

Field code	Meaning	Data/Format
IE	Inclusion/Exclusion Criteria	Free text - see the bullet "Inclusion/ exclusion criteria" in 3.2.2.
CP	Confirmed/Potential ICSRs	Text: Null/C/P
S	Serious	Text: Null/N/Y
FD	Full Text Request Date	CCYY/MM/DD/
TD	Translation Request Date	CCYY/MM/DD/
ER	End Record	Text: "ER"

\*the following fields of the RIS format do not exactly match the MLM Search result spreadsheet: literature reference, which is broken into separate fields, and the date fields, which are in the format CCYY/MM/DD in RIS and DD/MM/CCYY in the spreadsheet.

The following text provides an example of a search result in the RIS format (converted to text)

```

TY - JOUR
SG - ACARBOSE
DB - EMBASE
DA - 2022/04/26/10:00
AU - Brodosi L
AU - Marchignoli F
AU - Marchesini G
AU - Petroni ML
PY - 2022
VL - 23
IS - 2
SP - 149-53
T2 - Expert Opinion on Pharmacotherapy
TI - Considerations when prescribing pharmacotherapy for metabolic associated fatty
liver disease
CY - IT
LA - Marchesini G
DO - 10.1080/14656566.2021.1980538
ER -

```

### 3.1.3. Flow of data into and out of the MLM RIS file

The same principles apply to the RIS file as the Search result spreadsheet – see 3.2.4.



### 3.2. MLM Search Results

#### 3.2.1. Accessing the MLM Search results spreadsheet

To access the MLM Search results click on the "MLM Search Results" link to view results in an Excel spreadsheet.



The following message is displayed:



Click "Open" to open the file, or "Save" to save the file locally.

### 3.2.2. Columns in the MLM Search results spreadsheet

Substance Group	Reference database	Date & Time Of Search	Literature reference (Vancouver Style: Author(s). Title. Journal. Year;Vol:1st page-last page)	Primary Source Country	Lead Author	Document Object Identifier	Inclusion/exclusion criteria	Confirmed/potential ICSRs (C/P)	Serious?	Full text request date	Translation request date
ACETYLSALICYLIC ACID	EMBASE	25/08/2015 09:52	Hatty CR, Banati RB. Protein-ligand and membrane-ligand interactions in pharmacology: The case of the translocator protein (TSPO). Pharmacological Research. 2015;100 : 58-63	AU	Hatty CR	10.1016/j.phrs.2015.07.029	Aggregated data on patients			N/A	
ACETYLSALICYLIC ACID	EMBASE	25/08/2015 09:55	He JQ, Yu XP, Peng C, Li Q, Luo YW, Gao YC et al. Predictive ability of the SYnergy between percutaneous coronary intervention with TAXus and cardiac surgery score II for long-term mortality in patients with three-vessel coronary artery disease undergoing percutaneous coronary intervention treated with second-generation drug-eluting stents. Chinese Medical Journal . 2015;128(16) : 2176-2182	CN	He JQ	10.4103/0366-6999.162510	Aggregated data on patients			N/A	
ACETYLSALICYLIC ACID	EMBASE	26/08/2015 09:36	Goverde P, Taeymans K, Lauwers K, Schroë H, Vermassen F. How to ameliorate the disappointing: 1-year results of bioabsorbable stents in superficial femoral artery lesions (the Belgian Remedy registry). EuroIntervention. 2015; :	BE	Goverde P	<a href="http://www.embase.com/search/results?suction=viewrecord&amp;rid=19&amp;page=1">http://www.embase.com/search/results?suction=viewrecord&amp;rid=19&amp;page=1</a>				N/A	
ACETYLSALICYLIC ACID	EMBASE	26/08/2015 09:36	Kefer J, Tzikas A, Shakir S, Gafoor S, Berti S, Santoro G et al. Left atrial appendage occlusion for stroke prevention in patients with atrial fibrillation and chronic renal failure: A substudy of the multicentre registry with the Amplatzer cardiac plug. EuroIntervention. 2015; :	BE	Kefer J	<a href="http://www.embase.com/search/results?suction=viewrecord&amp;rid=12&amp;page=1">http://www.embase.com/search/results?suction=viewrecord&amp;rid=12&amp;page=1</a>				N/A	
ACETYLSALICYLIC ACID	EMBASE	26/08/2015 09:36	Deharo P, Pankert M, Quilici J, Bonnet JL, Cuisset T. Body mass index has no impact on platelet inhibition induced by ticagrelor after ACS, conversely to prasugrel. EuroIntervention . 2015; :	FR	Deharo P	<a href="http://www.embase.com/search/results?suction=viewrecord&amp;rid=17&amp;page=1">http://www.embase.com/search/results?suction=viewrecord&amp;rid=17&amp;page=1</a>				N/A	
ACETYLSALICYLIC ACID	EMBASE	26/08/2015 09:36	Buzon J, Roignot O, Lemoine S, Perez P, Kimmoun A, Levy B et al. Takotsubo cardiomyopathy triggered by influenza A virus. Internal Medicine. 2015;54(16) : 2017-2019	FR	Buzon J	10.2169/internalmedicine.54.3606				N/A	
ACETYLSALICYLIC ACID	EMBASE	26/08/2015 10:22	Escasany AA, Iavecchia L, Safiya A, Foix DS, Ferrer MB, Gallego MS et al. Perioperative management and outcomes of patients treated with antithrombotics admitted for hip fracture surgery. Basic and Clinical Pharmacology and Toxicology. 2014;115(3) : 17	ES	Escasany AA	10.1111/bcpt.12300				N/A	
ACETYLSALICYLIC ACID	EMBASE	26/08/2015 10:22	Elia C, Graupera I, Barreto R, Solà E, Moreira R, Huelin P et al. Severe acute kidney injury associated with non-steroidal anti-inflammatory drugs in cirrhosis: A case-control study. Journal of Hepatology. 2015;63(3) : 593-600 Article Number 5640	ES	Elia C	10.1016/j.jhep.2015.04.004				N/A	
ACETYLSALICYLIC ACID	EMBASE	26/08/2015 10:22	Schroeter T, Meyer A, Lehmann S, Garbade J, Mohr FW. Complications associated with implantable cardioverter-defibrillator implantation or replacement in patients with left ventricular assist device. Thoracic and Cardiovascular Surgeon. 2015;63(1) :	DE	Schroeter T	10.1055/s-0035-1544276				N/A	
ACETYLSALICYLIC ACID	EMBASE	26/08/2015 10:22	Bolz J, Meves SH, Kara K, Reinacher-Schick A, Gold R, Krogias C. Multiple cerebral infarctions in a young patient with heroin-induced hypereosinophilic syndrome. Journal of the Neurological Sciences. 2015;356(1-2) : 193-195 Article Number 13860	DE	Bolz J	10.1016/j.jns.2015.06.031				N/A	
ACETYLSALICYLIC ACID	EMBASE	26/08/2015 09:36	Niemann B, Sheybani B, Rohrbach S, Grieshaber P, Möller A, Sommerbeck S et al. Dual platelet inhibition before cardiac surgery-perioperative prospective analysis in 499 patients. Thoracic and Cardiovascular Surgeon. 2015;63(1) :	DE	Niemann B	10.1055/s-0035-1544342				N/A	

As you can see from the image on the previous page, the spreadsheet has the following columns:

- Substance group
  - The substance group for which the search was run that returned this article,
  - If an article is returned in more than one search, then it will appear in the spreadsheet once for each substance group, but duplicate cases will NOT be created,
  - Results are sorted by substance group;
- Reference database
  - The database against which the search was run – this will either be AMED, Embase, IPA or MEDLINE,
  - For spreadsheets from the archive this may also be EBSCO
- Date & time of search;
- Literature reference (Vancouver Style: Author(s). Title. Journal. Year;Vol:1st page-last page. DOI)
  - The literature reference is entered in accordance with the Vancouver Style, as described in the following article: International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals. N Engl J Med. 1997; 336:309-15;
- Primary source country
  - This is the country of the lead author &, in accordance with the ICH E2B(R3) guideline, the two-letter country code will form the first two characters of the WW Case Safety ID. For example, an article by an author based in Paris will see this field populated with "FR",
  - In rare circumstances, this country may not correspond to the occurrence country. In such instances, the occurrence country would take precedence for the purposes of reporting;
- Lead author;
- Document Object Identifier
  - This is a unique identifier for the article & will appear in all spreadsheets to allow easy traceability,
  - If there is no DOI available then a URL for the article will be provided and if there is no URL then the internal tracking number used by the MLM Service will be provided,
  - If there are multiple cases from an article, all will have the same Document Object Identifier or URL;
- Inclusion/ exclusion criteria
  - If the cases arising from an article are **included**, then this is populated with "5.2.1 - Valid ADR",
  - If an article is definitively excluded, then it is assigned the first exclusion criterion that it meets, in accordance with those detailed in the [Monitoring of medical literature and the entry of relevant information into the EudraVigilance database by the European Medicines Agency - Inclusion and exclusion criteria for processing of Individual Case Safety Reports](#) and the flowcharts therein,

- If there are potential cases in an article, then all possible exclusion criteria, in accordance with those detailed in the [Monitoring of medical literature and the entry of relevant information into the EudraVigilance database by the European Medicines Agency - Inclusion and exclusion criteria for processing of Individual Case Safety Reports](#), are assigned;
- Confirmed/ potential ICSRs (C/P)
  - If the article contains **confirmed** ICSRs, this is populated with "C",
  - If the article contains **potential** ICSRs, this is populated with "P";
- Serious?
  - If the case is **serious**, this is populated with "Y",
  - If the case is **not serious**, this is populated with "N";
- Full text request date
  - If applicable, this is the date the full-text was requested,
  - The full text will always be requested for a confirmed ICSR;
- Translation request date
  - If applicable, this is the date the translation was requested.

### 3.2.3. Cumulative tabs in the MLM Search results spreadsheet

In addition to the daily updates to the MLM Search Results spreadsheet, the MLM Service also provides cumulative tabs.

#### Monthly cumulative tabs

- The full results of the previous month's screening & reviewing on the first working day of each month,
  - Tab name format: MMM YYYY (e.g. Mar 2017);
- The aforementioned monthly tab, filtered to display only special circumstances with no adverse reaction – the exclusion criteria numbered 5.3.2, 5.3.3, 5.3.4, 5.4.2, 5.5.2, 5.6.3 & 5.8.2 in the [Monitoring of medical literature and the entry of relevant information into the EudraVigilance database by the European Medicines Agency - Inclusion and exclusion criteria for processing of Individual Case Safety Reports](#) (doc. ref. EMA/119265/2015) – on the first working day of each month,
  - Tab name format: MMM YYYY special situation (e.g. Mar 2017 special situation).

#### Daily cumulative tabs

- Running in-month cumulative screening and reviewing results on every other working day of the month,
  - Tab name format: "MMM YYYY to date" (e.g. Feb 2017 to date);
- The aforementioned in-month cumulative tab, filtered to display only special circumstances with no adverse reaction – the exclusion criteria numbered 5.3.2, 5.3.3, 5.3.4, 5.4.2, 5.5.2, 5.6.3 & 5.8.2 in the [Monitoring of medical literature and the entry of relevant information into the EudraVigilance database by the European Medicines Agency - Inclusion and exclusion criteria for processing of](#)

[Individual Case Safety Reports](#) (doc. ref. EMA/119265/2015) – on every other working day of the month,

- Tab name format: "MMM YYYY special sit to date" (e.g. Feb 2017 special sit to date).

### 3.2.4. Flow of data into and out of the MLM Search results spreadsheet

Each day the MLM team will run the search criteria in AMED, Embase, IPA and MEDLINE against each substance group. The results of the searches will be entered into the Agency's tracking tool.

If a substance returns no articles, this will be recorded as "NO RESULTS RECEIVED".

If an article concerns more than one substance being monitored by the MLM service, then it will be retrieved & recorded for each substance group.

Once the articles are entered into the tracking tool, they will be screened & reviewed to see if they meet the inclusion/exclusion criteria & whether they contain any confirmed or potential ICSRs. The screening & reviewing will take place either the same day as the searching or on the next working day.

At the end of each day, the MLM Service exports the data entered into the tracking tool that day as an Excel spreadsheet & uploads it to the EMA's system, where it is virus-checked and, at 9AM the following morning, it is made available for download.

The retrieved articles will be presented in the tracking sheet and will remain there until the screening & reviewing is complete. For example, an article was retrieved on 25 August 2015. Later that day the data was extracted & uploaded. The sum\_screen spreadsheet with this article was available for download from 9AM on the 26<sup>th</sup>. Also, on the 26<sup>th</sup>, the article was reviewed & determined not to contain any valid ICSRs. Later that day the data was extracted & uploaded. The sum\_screen spreadsheet with this article was available for download from 9AM on the 27<sup>th</sup>. In the sum\_screen spreadsheet available for download the following day did not contain that article.

## 3.3. MLM ICSRs

### 3.3.1. Accessing the MLM ICSRs spreadsheet

To access the MLM ICSRs spreadsheet, click on the "MLM ICSRs" link to view results in an Excel spreadsheet.



The following message is displayed:



Click "Open" to open the file, or "Save" to save the file locally.

### 3.3.2. Columns in the MLM ICSRs spreadsheet

Substance Group	Reference database	Date & Time Of Search	Literature reference (Vancouver Style: Author(s). Title. Journal. Year;Vol:1st page-last page)	Primary Source Country	Lead Author	Document Object Identifier	Inclusion/ exclusion criteria	Confirmed/ potential ICSRs (C/P) Serious?	Full text request date	Full text receive date	Translation request date	Translation receive date	Suspect or interacting products/ substances (semicolon delimited)	Initial/FU/ Amendment	WWID (A.1.10.2)	Version	Receive date	Latest receipt date (Day Zero)
ACETYLSALICYLIC ACID	EMBASE	26/09/2017 09:30	Gallo M, Mineur L, Emptas H, Costes V, Ramos J. Hepatic myelolipoma: A rare entity, case report and review of the literature. <i>Annales de Pathologie</i> . 2017; :	FR	Gallo M	10.1016/j.aa	Article in P P											
ACETYLSALICYLIC ACID	EMBASE	11/03/2016 09:02	Li YF, Gao WQ, Li YX, Feng QZ, Zhu P. Management of acute perioperative myocardial infarction: A case report of concomitant acute myocardial infarction and tumor bleeding in the transverse colon. <i>Clinical Interventions in Aging</i> . 2016;11 : 159-166	CN	Li YF	10.2147/Ci	5.2.1 - Vali C	Y	14/03/2016	14/03/2016							11/03/2016	
ACETYLSALICYLIC ACID	EMBASE	04/04/2016 11:42	Calvo Campoverde K, Giner-Muñoz MT, Martínez Valdez L, Rojas Votquez M, Lozano Blasco J, Machinena A et al. Hypersensitivity reactions to non-steroidal anti-inflammatory drugs and tolerance to alternative drugs	ES	Calvo Campoverde	10.1016/j.aa	5.2.1 - Vali C	Y	06/04/2016	07/04/2016							07/04/2016	
ACETYLSALICYLIC ACID	EMBASE	20/05/2016 11:50	Yu WS, Jung HS, Lee JG, Kim DJ, Chung KY, Lee CY. Safety of thoracoscopic surgery for lung cancer without interruption of anti-platelet agents. <i>Journal of Thoracic Disease</i> . 2016;7(11) : 2024-2032	KR	Yu WS	http://www	5.2.1 - Vali C	N	24/05/2016	24/05/2016							20/05/2016	
ACETYLSALICYLIC ACID	EMBASE	13/01/2017 11:00	Ankay Yilbas A, Kanburoglu C, Uzumcuoglu F, Cifci C, Saralp OO, Karagoz H, et al. [Progressive hematoma in anterior neck after endovascular treatment of middle cerebral artery aneurysm]. <i>Rev Bras Anesthesiol</i> . 2016; :	TR	Ankay Yilbas A	DOI: 10.101	Article in P P											
ACETYLSALICYLIC ACID	EMBASE	29/05/2017 09:40	Roganovic B, Obradovic S, Micic A, Petrovic S. Hereditary hemorrhagic telangiectasia associated with inherited thrombophilia. <i>Vojnosanitetski Pregled</i> . 2017;74(5) : 489-493	RS	Roganovic B	10.2298/V	5.2.1 - Vali C	Y	30/05/2017	30/05/2017							29/05/2017	
ACETYLSALICYLIC ACID	EMBASE	06/06/2017 09:40	Kahyaoglu M, Gecmen C, Guner A, Celik M, Izgi IA. A rare complication: Diffuse alveolar haemorrhage following acute coronary syndrome. <i>Kardiologia Polska</i> . 2017;75(5) : 507	TR	Kahyaoglu M	10.5603/KP	5.2.1 - Vali C	Y	07/06/2017	07/06/2017			Acetylsalicylic acid; Ticagrelor	FU	TR-MLMSERVICE-20170607-0757395-1	1	06/06/2017	27/09/2017
ACETYLSALICYLIC ACID	EMBASE	04/08/2017 09:30	Zhou LQ, Chen SM, Zhang YZ, He LY, Gao W. Two case of preoperative bridging therapy for patients undergoing non-cardiac surgery after coronary stent implantation. <i>Journal of Geriatric Cardiology</i> . 2017;14(7) : 488-490	CN	Zhou LQ	10.11909/j	5.2.1 - Vali C	Y	07/08/2017	07/08/2017							04/08/2017	
ACETYLSALICYLIC ACID	EMBASE	01/09/2017 09:30	Kawamura R, Mizuma A, Kouchi M, Nagata E, Takahashi W, Takizawa S. A Recurrent Case of Ischemic Stroke Caused by Vasospasm due to Giant Cell Arteritis. <i>Journal of Stroke and Cerebrovascular Diseases</i> . 2017; :	JP	Kawamura R	10.1016/j.js	Article in P P											
ACETYLSALICYLIC ACID	EMBASE	08/09/2017 09:30	Sugino K, Nakamura Y, Sekiya M, Kobayashi H, Shibuya K, Homma S. Fatal diffuse alveolar haemorrhage mimicking acute exacerbation in idiopathic pulmonary fibrosis treated with nintedanib. <i>Respirology Case Reports</i> . 2017;5(6) : Article Number e00258	JP	Sugino K	10.1002/rcr	5.2.1 - Vali C	Y	11/09/2017	11/09/2017			Acetylsalicylic acid; Nintedanib		JP-MLMSERVICE-20170911-0884321-1		08/09/2017	
ACETYLSALICYLIC ACID	EMBASE	14/09/2017 09:30	Hassan OA, Moey MY, Papegeorgiou CN. From anemia to polycythemia in 4 weeks. <i>Clinical Case Reports</i> . 2017;5(9) : 1526-1530	NL	Hassan OA	10.1002/ccr	Follow-Up P		15/09/2017	15/09/2017								
ACETYLSALICYLIC ACID	EMBASE	15/09/2017 09:30	Rubin RN. Medication management after an 88-year-old man's gastrointestinal bleed. <i>Consultant</i> . 2017;57(9) : 543-544	US	Rubin RN	https://ww	5.2.1 - Vali C	Y	18/09/2017	18/09/2017							15/09/2017	
ACETYLSALICYLIC ACID	EMBASE	15/09/2017 09:30	Johal K, Welch K, Peters A. Immunoglobulin G4 sinusitis in association with aspirin-exacerbated respiratory disease. <i>American Journal of Rhinology and Allergy</i> . 2017;31(5) : 302-304	US	Johal K	10.2500/ajr	5.2.1 - Vali C	Y	18/09/2017	18/09/2017			Acetylsalicylic acid		US-MLMSERVICE-20170918-0893758-1		15/09/2017	
ACETYLSALICYLIC ACID	EMBASE	21/09/2017 10:00	Akca F, Verberkmoes NJ, Verstraeten SE, van Laar CV, van Putte BP, van Straten AHM. Is there an alternative treatment for patients intolerant to antiplatelet therapy if percutaneous left atrial appendage closure is considered?. <i>Netherlands Heart Journal</i> . 2017;25(9) : 510-515	NL	Akca F	10.1007/s1	5.2.1 - Vali C	Y	22/09/2017	22/09/2017					NL-MLMSERVICE-20170922-0899696-1		21/09/2017	
ACETYLSALICYLIC ACID	EMBASE	27/09/2017 10:00	Enjor Martín R, Gutiérrez-Madrid E, Martín-Sánchez FJ, Cuervo Pinto R. Iatrogenic rhabdomyolysis in a patient with ischemic heart disease. <i>Medicina Clinica</i> . 2016;146(10) : e57-e58	ES	Enjor Martín R	10.1016/j.m	Translatio P		29/09/2017	29/09/2017	29/09/2017							
ACETYLSALICYLIC ACID	EMBASE	28/09/2017 09:30	Koksal V, Yavasi O. Controversies in the differential diagnosis of Brown-Sequard syndrome due to cervical spinal disease from stroke: A case series. <i>Turkish Journal of Emergency Medicine</i> . 2017;17(3) : 115-120	TR	Koksal V	10.1016/j.tj	5.2.1 - Vali P	Y	29/09/2017	29/09/2017							28/09/2017	
ACETYLSALICYLIC ACID	EMBASE	02/10/2017 09:30	Stierlin FB, Cook S, Stadelmann M. Incomplete stent apposition resolves one year after implantation. <i>Kardiologiske Mediziner</i> . 2017;20(9) : 216-218	CH	Stierlin FB	10.4414/cvr	Follow-Up P											
ACETYLSALICYLIC ACID	EMBASE	03/10/2017 09:30	Quah C, Bayley E, Bhamber N, Howard P. Fatal pulmonary embolism following elective total knee replacement using aspirin in multi-modal prophylaxis — A 12 year study. <i>Knee</i> . 2017;24(5) : 1187-1190	GB	Quah C	10.1016/j.k	Full text re P		04/10/2017									

**Note:** This image has been cropped to improve legibility. Not all columns are shown.



As you can see from the image on the previous page, the spreadsheet contains more information than the "MLM Search Results" spreadsheet. It contains the following columns (new columns from October 2017 are described in red text):

- Substance group
  - The substance group for which the search was run that returned this article,
  - If an article is returned in more than one search, then it will appear in the spreadsheet once for each substance group, but duplicate cases will NOT be created;
- Reference database
  - The database against which the search was run,  
This will be either AMED, Embase, IPA or Medline  
For searches tracked in the archive, this may also be EBSCO;
- Date & time of search;
- Literature reference (Vancouver Style: Author(s). Title. Journal. Year;Vol:1st page-last page),
  - The literature reference is entered in accordance with the Vancouver Style, as described in the following article: International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals. N Engl J Med. 1997; 336:309-15,
  - If an article has more than one confirmed or potential case, then the article will appear once for each case, as in the rows highlighted in yellow in the image on the previous page;
- Primary source country
  - This is the country of the lead author & the two-letter country code will form the first two characters of the WW Case Safety ID,
  - In rare circumstances, this country may not correspond to the occurrence country. In such instances, the occurrence country would take precedence for the purposes of reporting;
- Lead author;
- Document Object Identifier
  - This is a unique identifier for the article & will appear in all spreadsheets to allow easy traceability,
  - If there is no DOI available, then a URL for the article will be provided and if there is no URL then the internal tracking number used by the MLM Service will be provided,
  - If there are multiple cases from an article, all will have the same Document Object Identifier or URL;
- Inclusion/ exclusion criteria
  - If the cases arising from an article are **included**, then this is populated with " 5.2.1 - Valid ADR",
  - If an article is definitively excluded, then the first exclusion criterion that it meets, in accordance with those detailed in the [Monitoring of medical literature and the entry of relevant information into the EudraVigilance database by the European Medicines Agency - Inclusion](#)

[and exclusion criteria for processing of Individual Case Safety Reports](#) and the flowcharts therein, is assigned,

- If there are potential cases in an article, then all possible exclusion criteria, in accordance with those detailed in the [Monitoring of medical literature and the entry of relevant information into the EudraVigilance database by the European Medicines Agency - Inclusion and exclusion criteria for processing of Individual Case Safety Reports](#), are assigned;
- Confirmed/ potential ICSRs (C/P)
  - If the article contains **confirmed** ICSRs, this is populated with "C",
  - If the article contains **potential** ICSRs, this is populated with "P";
- Serious?
  - If the case is **serious**, this is populated with "Y",
  - If the case is **not serious**, this is populated with "N";
- Full text request date
  - If applicable, this is the date the full-text was requested,
  - The full text will always be requested for a confirmed ICSR;
- Full text receive date
  - If applicable, this is the date the full-text was received;
- Translation request date
  - If applicable, this is the date the translation was requested;
- Translation receive date
  - If applicable, this is the date the translation was received;
- Suspect or interacting products/substances (semicolon delimited)
  - This contains the precise names of all substances or combinations of substances are considered suspect or interacting in each case,
  - This may include substances which are not monitored by the MLM Service as long as at least one of the substances,
  - Each different substance or substance combination will be separated by a semicolon,
  - Each substance combination will have a + between the substances,
  - Therefore a case containing both ibuprofen & a combination product containing codeine & paracetamol would see the field populated thus: Ibuprofen; Paracetamol+Codeine;
- Initial/FU/Amendment
  - If this is the **first** version of a case, this is populated with "Initial"
  - If this is a **follow-up** version of the case **based on new information**, this is populated with "FU",
  - If this is a **follow-up** version of a case **correcting an error** from the previous version, with **no new information received**, this is populated with "Amendment",
  - If the follow-up is a nullification of the case, then this column will be left blank and the nullification column will be populated instead;



- WWID (C.1.8.1)
  - The worldwide unique case safety identifier of the case;
- Version
  - If this is the **first** version of a case, this is populated with "0",
  - If this is the first follow-up version of a case, this is populated with "1",
  - If this is the second follow-up version of a case, this is populated with "2",
  - This pattern continues for all subsequent versions;
- Receive date
  - The day that the minimum criteria for a confirmed case were first received by the MLM Service. If there is a definite case from the initial search, then day zero will be the same as the search date, if not then it will be later,
  - This corresponds to E2B(R3) field C.1.4;
- Latest receipt date (Day zero)
  - The date of receipt of most recent information,
  - This corresponds to E2B(R3) field C.1.5;
- Transmission date (EV)
  - Date the case was first transmitted to Eudravigilance;
- Transmission date (NCA)
  - Date the case was first transmitted to an NCA (as applicable),
  - This column will be removed from December 2017 as all cases will be transmitted only to EV;
- FU to be initiated? (Y/N)
  - If the case **does** require follow-up (FU), this is populated with "Y",
  - If the case **does not** require follow-up, this is populated with "N";
- Date FU initiated
  - If applicable, this is the date the follow-up was requested;
- Date reply requested by
  - This is the date by which a reply was requested from the author;
- Reply received? (Y/N)
  - If applicable, if a reply **was** received, this is populated with "Y",
  - If applicable, if a reply **was not** received by the date a reply was requested by, this is populated with "N";
- Date FU received
  - If applicable, this is the date the follow-up was received;
- Duplicate? (Y/N)

- If this case has been confirmed as a duplicate of another case or cases, then this will be populated with "Y"; otherwise it will be blank;
- Master WWID; Other case numbers
  - If this case has been merged under a master, then the worldwide case safety ID of the master and/or of all confirmed duplicates will be entered here, separated by a semicolon; otherwise it will be blank;
- Nullified?
  - If this case has been nullified, then this will be populated with "Y", otherwise it will be blank;
- Nullification date
  - If the case has been nullified, the date the nullification ICSR was submitted to EudraVigilance will be populated.

### **3.3.3. Flow of data into and out of the MLM ICSRs spreadsheet**

Once an article has been reviewed and been determined to contain one or more confirmed or potential cases, then the article will appear in the MLM ICSRs spreadsheet with one row for each case (confirmed or potential). Each case will have one row for each suspect or interacting substance the subject of monitoring by the MLM Service.

For example, if an article contains 2 cases, the first of which has a suspect drug of paracetamol and the second of which has both paracetamol & ibuprofen as suspect, then there will be one row for the first case & 2 rows for the second case, making a total of 3 rows for the article.

Once assessed as confirmed (C) or potential (P) a case will stay in the MLM ICSRs spreadsheet until the day after it has been completed. A case is considered completed in the following situations:

- Potential cases will always have follow-up sought (including requesting the full-text article if it has not yet been received). Once received, this date will be added to the spreadsheet and the potential case will be reassessed and the status amended to either confirmed or non-valid:
  - For a once-potential case that is now confirmed, the date of receipt of the FU which permitted confirmation is day zero for reporting timelines,
  - A confirmed case stays in the spreadsheet until completed (see below),
  - Once a case is changed to non-valid, the final exclusion criterion must be entered in the tracking tool,
  - The rejected (non-valid) case will appear in the spreadsheet extracted that day with the exclusion criterion,
  - It will no longer be available in the sum\_ICSR spreadsheet for the following days, but the previous days' sheets in the archive will retain the record of the case & the decisions taken;
- The day a confirmed cases is transmitted to EV (and the relevant NCA, if applicable), the following columns are populated for the case:
  - Suspect or interacting products/substances (semicolon delimited),
  - WWID (C.1.8.1),
  - Day zero,

- Transmission date (EV),
- Transmission date (NCA),
- FU to be initiated? (Y/N),
- Date FU initiated,
- Date reply requested by;
- This data will be extracted into that day's spreadsheet, which will be available from 9AM the following day
  - That day's spreadsheet will be available permanently in the archive;
- If no follow-up was required, then the transmitted case will be considered closed and will not appear in subsequent spreadsheets unless follow-up or duplicates are received or a correction made
  - If a correction was made, then there should be a footnote added to the bottom of the spreadsheet explaining why the case has returned & was corrected;
- A confirmed case transmitted to EV which requires follow-up will stay in the spreadsheet until either:
  - FU has been received, processed & a follow-up version transmitted to EV,
  - FU has been received, but contained no new information,
  - The date by which a reply was requested has passed;
- The day that follow-up is received, the field "Reply received? (Y/N)" will be populated with Y & the field "Date FU received" is populated with that date
  - The tracking sheet for that day will contain this information & it will remain in the tracking sheet with the case for as long as the case remains there;
- If the follow-up contains no new information (an unlikely, but not impossible, scenario), then no follow-up version will be created and the following day the case will disappear from the tracking sheet;
- If the follow-up does contain new information, then a follow-up version will be created & on the day that the follow-up is transmitted the fields "FU creation date", "FU transmission date (EV)" and, if applicable, "FU transmission date (NCA)" will be populated
  - This information will appear in that day's MLM ICSRs spreadsheet, which will be available the following day from 9AM,
  - Once the follow-up has been sent, the case will not appear in subsequent days' tracking sheets, but the previous sheets will remain in the archive as a record of what happened;
- If no follow-up is received by the date that FU was requested, then on the following day the field "Reply received? (Y/N)" will be populated with N, thus closing the case. This will appear in that day's MLM ICSRs spreadsheet, which will be available the following day from 9AM
  - This case will not appear on subsequent days' spreadsheets, but the record of what happened will remain in the previous days' spreadsheets in the archive.

### 3.3.4. Cell highlighting function

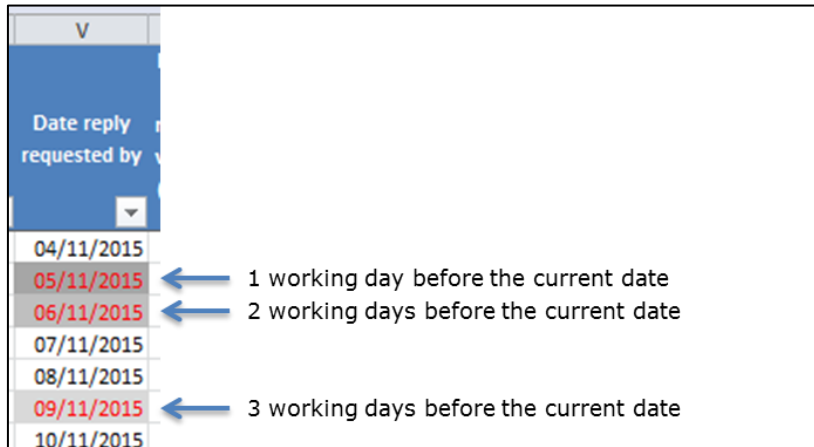
In order to improve usability and easily track how long a case is to remain in the ICSRs spreadsheet, the following cell highlighting rules apply:

**1. For new data in sum\_ICSR:**

- a. When the initial (or any FU version) of a case is transmitted to EV the previous day, the entire row is highlighted in yellow.

**2. For cases that are due to leave the ICSRs spreadsheet:**

- a. When column V "date reply requested by" is 3 working days before the current date, the cell is highlighted in light grey and the text is red.
- b. When column V "date reply requested by" is 2 working days before the current date, the cell is highlighted in dark grey and the text is red.
- c. When column V "date reply requested by" is 1 working day before the current date, the cell is highlighted in a darker grey and the text is red.



The above screenshot displays the different shades of grey that are used in column V at each stage before a case is removed from the ICSRs spreadsheet.

### 3.4. Archive

The archive is a record of each day's tracking sheets, both MLM Search results & MLM ICSRs. The spreadsheets, once archived, are not updated & form a permanent record of the information available to MAHs on each day.

To access the archives of daily sheets, click on the "Archive" link to view results in an Excel spreadsheet. (ringed in red in the image below)



The following screen will appear.

**EudraVigilance**  
Human Restricted

Home Restricted  
Home Public

Restricted Area

**Logged In**  
evhumanwtu03  
(ORG-100006777 -  
1-Y KMRSRVUWLV,  
SSW - 3VBIO)  
Human Internal Test

**EV Services**

- ▶ EVWEB - ICSR
- ▶ EVWEB - Art 57 / XEVMPD
- ▶ xEVMPD Export
- ▶ xEVMPD Bulk update
- ▶ EV Data Warehouse
- ▶ EV Post - Art 57 / XEVMPD

**Archive**

Archive\  
2013  
2014  
2015  
2016  
2018  
2022  
2024

Select the required year...

**Archive**

Archive\2015

June  
July  
August

Select a month to access that month's archive of daily tracking sheets.

**Archive**

Archive\2015\August

sum\_ICSR\_2015\_08\_03.xlsx  
sum\_ICSR\_2015\_08\_04.xlsx  
sum\_ICSR\_2015\_08\_05.xlsx  
sum\_ICSR\_2015\_08\_06.xlsx  
sum\_ICSR\_2015\_08\_07.xlsx  
sum\_ICSR\_2015\_08\_10.xlsx  
sum\_ICSR\_2015\_08\_11.xlsx  
sum\_ICSR\_2015\_08\_12.xlsx  
sum\_screen\_2015\_08\_03.xlsx  
sum\_screen\_2015\_08\_04.xlsx  
sum\_screen\_2015\_08\_05.xlsx  
sum\_screen\_2015\_08\_06.xlsx  
sum\_screen\_2015\_08\_07.xlsx  
sum\_screen\_2015\_08\_10.xlsx  
sum\_screen\_2015\_08\_11.xlsx  
sum\_screen\_2015\_08\_12.xlsx

Note:

- Archived MLM Search Results spreadsheets will have file names beginning "sum\_screen";
- Archived MLM Search results in RIS format will have file names beginning "sum\_screen\_RIS";
- Archived MLM ICSRs spreadsheets will have file names beginning "sum\_icsr".

## 4. Accessing MLM ICSRs

Since 22 November 2017, all MLM ICSRs have been accessed via the new EVWEB, both for single-case downloads and bulk downloading.

The [EVWEB User Manual](#) explains all the functions for downloading cases, whether as single cases, as a listing in an Excel spreadsheet or as bulk downloading, including the following features:

- the functions of the ICSR single case download screen,
  - performing simple queries,
  - performing advanced queries,
  - the Excel list export;
- how to load data into EV for further processing or exporting if desired;
- the single item export (exporting cases as XML files or as human-readable ICSR forms, RTFs or HTML documents);
- the ICSR download functionality. This is also covered in 4.3. of this manual
  - Tips on creating filters and amending existing filters are covered in 4.5. of this user manual.

### 4.1. Log in

There are two methods to access the ICSR Export Manager: Either you can click on the EVWEB link in the restricted area, as described in 2. or you can go directly to EVWEB via the following URL:

<https://eudravigilance-human.ema.europa.eu/#/>.

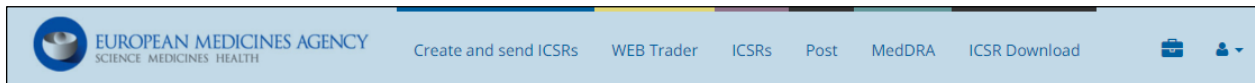
This will take you to the entry page of EVWEB.



Click the “Login” button and a login dialogue will appear.

### 4.2. Main Menu

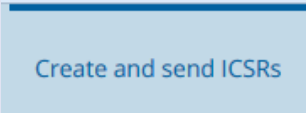
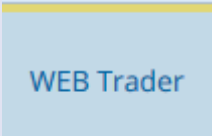

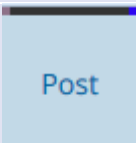

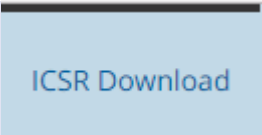

Once you have logged-in, you will be presented with the main menu.




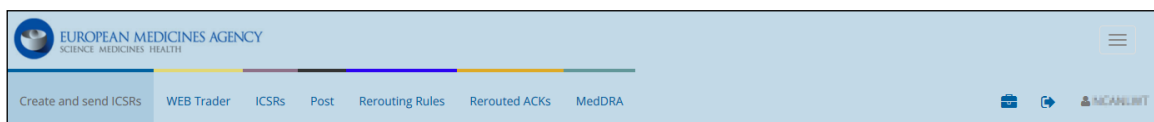
EVWEB’s main menu will vary in available options, depending on the user’s account access rights. In this user manual we will describe the menu entries and system functionality available to regular MAH users (i.e. non-administrators) of the interface. Depending on your account’s rights, you may see all of these options or a limited set of them.

**Note:** Additional locked features are available, such as tools for administrators of the EVWEB system, but these will only be available to user accounts that have the necessary permissions.

A typical EVWEB main menu consists of the following links:

Menu Option	Description
	Allows access to the part of the application dedicated to the creation and sending of ICH E2B(R3) Safety messages.
	Allows access to review your own messages, both sent and received. You will be able to see messages sent to you and by you, in the "Inbox" and "Outbox" views. The "Inbox" and "Outbox" view options will only be available to WEB Trader users. Users sending information via their locally established Gateway will not see these view options.
	Allows you to view, browse and query ICSRs and Safety messages located in the EVDBMS.
	Provides a quick method to upload and send either ICH E2B(R3) compliant Safety messages to the system.
	This area of the application allows you to browse and perform searches at all levels of MedDRA.
	Allows the bulk export of ICSRs and Safety messages based on pre-defined criteria options.
	The <b>Workspace screen</b> is a new addition to EVWEB's supported functions. It acts as a temporary, centralised area where multiple EVWEB items (Safety and Acknowledgement messages, ICSRs) can be added to for better review and management.

**Note:** The EVWEB interface has been designed to utilise the latest WEB user interface (UI) approach called responsive UI. This approach automatically adjusts the EVWEB interface to the best possible viewing layout based on the size of your screen or web browser window. For example, if the screen or window is too small, the main menu may be hidden within the following menu icon: .



Main menu: Normal screen/window size



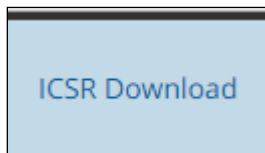
Main menu: Small screen/window size

The link corresponding to the currently active screen of EVWEB will have a darker background.

This user manual will describe the functions of the "ICSRs" link and the "ICSR Download" link. For all other functions, please see the [EudraVigilance - EVWEB user manual](#).

### 4.3. ICSR Download

EVWEB offers a dedicated screen that allows the bulk export of ICSRs and Safety messages. To access this screen, click on the **ICSR Download** link in the main menu.



You will be presented with the **ICSR Download** interface as shown in the following screenshot.

The screenshot shows the ICSR Download interface. It features a top ribbon with a 'Criteria (3)' section (callout 1) containing filters for Reports, Start Date (2016/09/18), and End Date (2016/10/03). Below the ribbon is a toolbar with 'Count', 'Reset', and 'Count: 74027' (callout 2), and a search bar for 'Request name...' (callout 3). The main area is titled 'History (4)' and shows a table of pending requests (5) with columns for Requested on, Completion status, Request name, File size (MB), and Status. Below the table is a 'Resolved (38)' section.

To perform a bulk export procedure, you first define a set of criteria which will return a set of matches; then you export all of them as a single compressed (.zip) file.

**Note:** The exported items contained in the single compressed file are in ICH E2B(R3) XML format.

To proceed with the bulk export process, you need to follow the steps outlined in the below table (the numbers reference the screenshot above):





ICSR Download Screen Option	Description
(1) Criteria	<p>Define the criteria that will narrow down the items you wish to bulk export.</p> <p>The default, pre-selected criteria available in the ribbon are:</p> <ul style="list-style-type: none"> <li><b>Reports:</b> Select "MLM reports". See 4.3.1. for more information;</li> </ul>




- **Start Date:** Select the start date of a date range on which messages containing ICSRs are received;
- **End Date:** Select the end date of date range on which messages containing ICSRs are received,
  - Start and end-dates are mandatory and cannot be more than 15 days apart;

To further fine-tune the results, the user can select a series of criteria options available from the "More criteria" button:

- **Active Substance:** Insert one or more active substances that should be present in the matching items;
- **Reporter Country:** Select the country of the primary source for regulatory reporting purposes,
  - Only one country can be selected;
- **World Wide Case ID:** Insert the worldwide unique case ID number,
  - Multiple WWIDs can be entered;
- **Active Substance Group:** Select the active substance group;
  - EMA does **NOT** recommend using this criterion for MLM Downloads. See 4.4.1.
- **Active Substance Combination:** Select the active substance combination;
  - EMA does **NOT** recommend using this criterion for MLM Downloads. See 4.4.1.
- **Active Substance MLM Group:** Select the active substance MLM group,
  - You should use the Active Substance MLM Group or combination when searching for MLM reports;
- **Active Substance MLM Combination:** Select the active substance MLM combination,
  - **NOTE: These filters are combined with an AND.** If you select both 'Active Substance MLM Group' **AND** 'Active substance MLM Combination', then only ICSRs which have suspect drugs meeting both criteria will be returned. See 4.4. "Active substances being monitored" for more information;
- **Serious:** Select whether you want only serious or non-serious cases.

ICSR Download Screen Option	Description
(2) "Count", "Reset", "Save Criteria" (  ) & "Load Criteria" (  ) Buttons	<p>The buttons available in this area provide additional actions that help the user with the overall bulk export process.</p> <ul style="list-style-type: none"> <li>• <b>Count:</b> Click on this button to see the number of items that match the defined criteria.</li> <li>• <b>Reset:</b> Clears all changes (including criteria options) and initiates a new count process.</li> <li>• <b>Save Criteria</b> (  ): Saves the applied criteria options to a file, allowing you to perform a future bulk export process using the same criteria settings.</li> <li>• <b>Load Criteria</b> (  ): Loads criteria options that were saved using the "Save Criteria" button.</li> </ul>
(3) "Request" Field & Button	<p>Enter a 'request name' to distinguish the bulk export process that will initiate when clicking on the "Request" button. It also provides the filename to the compressed file that becomes available for download.</p>

ICSR Download Screen Option	Description
(4) ICSR Download Status	<p>This area offers information regarding running ("Pending") and completed ("Resolved") bulk export processes.</p> <p>The common feedback fields are:</p> <ul style="list-style-type: none"> <li>• <b>Requested on:</b> Indicates the date on which the bulk export process was requested.</li> <li>• <b>Completion status:</b> Provides metrics on the succeeded (S) and total (T) number of matches processed for bulk exporting (S/T).</li> <li>• <b>Request name:</b> The name of the process and resulting compressed file. Originates from the "Request" field.</li> <li>• <b>File size:</b> The size of the resulting compressed file.</li> <li>• <b>Status:</b> Indicates the status of the bulk export process. The available conditions are: <ul style="list-style-type: none"> <li>– <b>STARTED:</b> A bulk export request has just been initiated and is in progress.</li> <li>– <b>COMPLETED:</b> A bulk export request has been successfully processed and resolved.</li> <li>– <b>COMPLETED_WITH_ERROR:</b> A bulk export request has been resolved but one or more reports failed to be exported.</li> <li>– <b>ARCHIVED:</b> A resolved bulk export request that has passed the 5<sup>th</sup> day from its creation date.</li> </ul> </li> <li>• <b>Exported Reports:</b> The number of exported reports originating from the resolved bulk export request.</li> </ul> <p><b>Note:</b> The rounded arrows icon () next to "History", when clicked, refreshes the status area and displays the latest information updates.</p>

After initiating a bulk export process the user waits for it to complete which, in turn, will force it to move from the "Pending" group section to that of the "Resolved" group section. Once in the "Resolved" section, the user can proceed to export the compressed file by selecting the bulk export process row, and then clicking on the "Download" option that appears at the top left.

Download	Requested on	Request name	File size (MB)	Status	Exported Reports
	2016/09/29 12:13	11	0.01	ARCHIVED	2

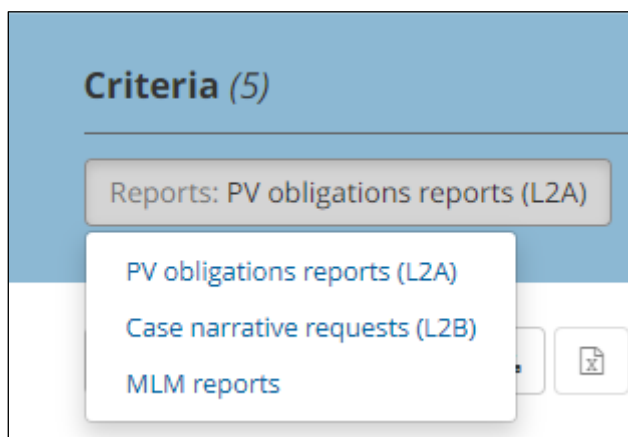
**Note:** All completed bulk export processes remain in the "Resolved" group section, and do not get deleted. However, after 5 days from the date of their creation they acquire the status of "ARCHIVED" and cannot be downloaded again.

### 4.3.1. "Reports" Criteria

The "Reports" criteria item is used to filter-down the results of a bulk export request, based on the type (i.e. EMA/NCA, MAH etc.) and assigned access rights of the logged-in user. For MAH users, this criterion is mandatory.

As you can see from the screenshot below, there are 3 options:

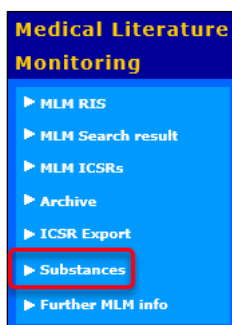
- PV obligations reports (L2A);
- Case narrative requests (L2B);
- MLM reports;



To download MLM cases, you should select "MLM reports".

### 4.4. Active substances being monitored

The Active Substance Groups, as described in Chapter 1 of the detailed guide on literature monitoring, are available from the EMA's [Medical literature monitoring](#) webpage and from the Medical Literature Monitoring menu on the Eudravigilance website.



Each Substance Group includes all substances including various salts, and substance combinations under the group. The Substance Groups are ranked by the greatest number of MAHs that hold MAs for a product containing this substance.

For example, the Paracetamol substance group contains paracetamol on its own, and paracetamol in combination with everything that it is in combination with in the xEVMPD; however, if a substance is included as part of a combination with another monitored substance, then the specific combination will be found under the earliest combination group. Therefore, the combination of paracetamol & codeine is under the Paracetamol substance group, and not the Codeine group, because the Paracetamol Substance Group is ranked before the Codeine Substance Group. Therefore, if you are searching using

the Substance Groups and you want a case with codeine as a suspect or interacting drug, whether alone or in combination, you will need to select the Codeine substance group &, in a separate query, all substance combinations containing codeine from higher-ranked groups. You should do this as two separate filters, since selecting the CODEINE active substance group & the PARACETAMOL, CODEINE active substance combination in the same query will return only cases where both a substance under the codeine group **AND** the combination product were considered suspect or interacting.

Conversely, when selecting **only** multiple active substance groups **or only** multiple active substance combinations, an "OR" operator is applied. Therefore, if you select active substance group PARACETAMOL and then active substance group CODEINE, the search will return all cases containing **either** paracetamol **or** codeine.

If selecting only combinations, you will need to carefully select from the list of substances before entering your filtering criteria, taking into account how information is likely to be reported in articles. You should generally ensure that you include a substance or substance combination which matches the substance group since salts or specific grade are unlikely to be reported in an article. For example, the Paracetamol active substance group includes the following substances:

- PARACETAMOL;
- PARACETAMOL COMPAP PVP 3;
- PARACETAMOL DC;
- PARACETAMOL PH. EUR.

If you are an MAH for a product containing "Paracetamol DC" as the active substance, your filter should include both "Paracetamol DC" and "Paracetamol", since you cannot reasonably exclude the possibility that the cases reported as having "Paracetamol" as the active substance refer to your product; but you would not need to include "Paracetamol compap PVP 3" or "Paracetamol Ph. Eur", since if those were reported then they would clearly not be your product.

You will not need to select substances every time, since, as described in 4.5. , above, you can save & load filters.

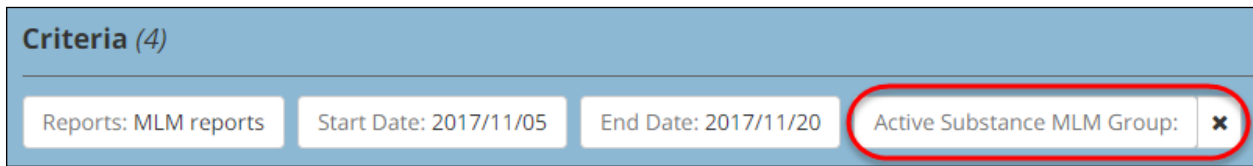
#### 4.4.1. Active Substance MLM Group

Searching on Active Substance MLM Groups is optional. If you wish to retrieve cases concerning all substances, do not filter of this criterion.

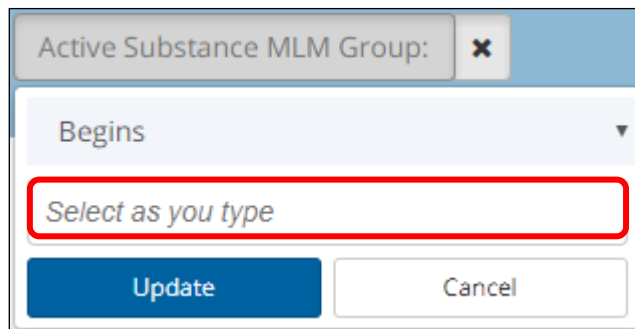
To search on an Active Substance MLM Group, select the criterion from the "More criteria" menu.



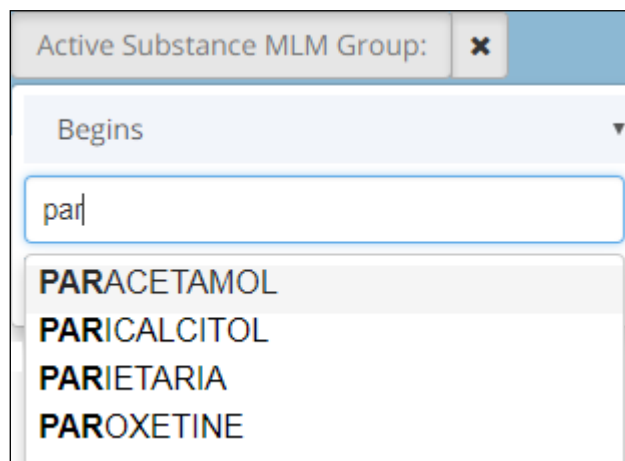
Then click the button that appears on the ribbon.



A text box will appear. Enter the name, or part of the name, of the desired substance group into the search box (ringed in red in the image below).

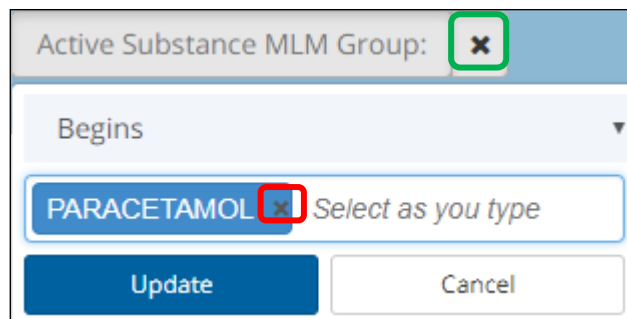


As you type the system will offer you options, as in the image below.



Once your desired substance group is presented, click on it and it will be added to the filter.

Even if only one active substance group is returned, you still need to click it to select it.



To remove a substance group, click on the x, ringed in red in the image above. To add more substance groups, click on the typing area and begin to type the name as before.

Click "Update" to save the filtering criterion.

To amend a saved filtering criterion, click on the saved criterion, to remove it click on the X to the right of the criterion, ringed in green in the image above.

**IMPORTANT NOTE:** EMA strongly recommends that, if you wish to filter the MLM ICSRs for specific substances or substance groups, you should use the options "Active substance **MLM** Group" or "Active Substance **MLM** Combination"



Users are advised NOT to filter using the options "Active Substance Group" or "Active Substance Combination".

#### 4.4.2. Active Substance MLM Combination

Searching on active substance combinations is performed in the same manner as for active substance groups; however there are many more combinations than groups and so you may need to use more iterations of the field to be able to select all of your substance combinations.

While it is technically possible to combine searches for groups and combinations at the same time, it is very strongly recommended **NOT** to do so. If you search for both a substance group & a substance combination, then only ICSRs containing both will be returned.

To return ICSRs containing either a substance group (or groups) or a specific substance combination (or combinations), you would need to make two or more different queries.

#### 4.4.3. Interaction between "Active Substance MLM Group", "Active Substance MLM Combination" and the "Medical literature monitoring: substance and herbal substance groups" spreadsheet

All the substance groups and combinations covered by the MLM Service are listed in the document "[Medical literature monitoring: substance groups 1-309 and herbal substance groups 1-100 valid from 1 June 2020](#)" published on the [MLM webpage](#) under the section "Substances and medical literature covered by EMA's service".

Medical literature monitoring: substance and herbal substance groups spreadsheet.

A	B	C
ID	Substance Group	Substances
1	PARACETAMOL	ACETYLCYSTEINE, PARACETAMOL
1	PARACETAMOL	ACETYLSALICYLIC ACID, ANHYDROUS CAFFEINE, PARACETAMOL DC
1	PARACETAMOL	ASCORBIC ACID, CHLORPHENAMINE, PARACETAMOL
1	PARACETAMOL	ASCORBIC ACID, PARACETAMOL
1	PARACETAMOL	ASCORBIC ACID, PARACETAMOL, ACETYLSALICYLIC ACID
1	PARACETAMOL	ASCORBIC ACID, PARACETAMOL, ANHYDROUS CAFFEINE
1	PARACETAMOL	ASCORBIC ACID, PARACETAMOL, CAFFEINE
1	PARACETAMOL	ASCORBIC ACID, PARACETAMOL, CODEINE PHOSPHATE HEMIHYDRATE
1	PARACETAMOL	ASCORBIC ACID, PARACETAMOL, PHENYLEPHRINE

Note how even though only the Substance Group Paracetamol is displayed, column C, "Substances", contains combinations of paracetamol with other substances monitored by the MLM Service, e.g. ascorbic acid. These combinations are only displayed under the paracetamol group because all fixed drug combinations are displayed under the first substance group in which they appear.


The column "Substance Group" corresponds to the EVWEB ICSR Download filtering criterion "Active Substance MLM Group". As mentioned in 4.4. , combination products containing multiple substances monitored by the MLM Service are grouped under the earliest substance group and not necessarily under the substance you expect.

The column "Substances" corresponds to the EVWEB ICSR Download filtering criterion "Active Substance MLM Combination" and only exact matches of these combinations will be indexed (although the order the substances are entered in the active substance field (ICH E2B(R3) G.k.2.3.r.1) is irrelevant because they are entered as separate substances & the EudraVigilance indexing tool combines them to match the list).

The substance combinations and groups are created based on the data entered in the xEVMPD (also known as the Article 57 database); but in the literature substances might be described only by the active moiety and not include the salt form, so when you are creating filters to search for reportable cases you should include the forms both with and without the salts.

#### **4.5. Saving, amending, validating & loading filters**

##### **4.5.1. Saving filters**

Once you have created your filter, you can save it for re-use at a later date. To do this, click the "Save criteria" button (  ) and follow your browser's normal process for downloading and saving files.

##### **4.5.2. Amending filters**

If you have a pre-existing filter, or have a list of the active MLM substance combinations that you need to search for, then you can add the substances into the filter offline by editing a saved file using a programme such as Notepad++ or similar. If you are doing this, you will need to pay particular attention to the syntax used.

Within an individual filtering criterion, any selections you make will expand your search (an "OR" operator is applied), so if you select both 'Paracetamol' & 'Codeine' as the Active Substance MLM Groups, then cases containing either Paracetamol or Codeine will be returned.

Among different filtering criteria, any selections you make will contract your search (an "AND" operator is applied), so if you select the country of occurrence as 'Spain' and the active substance group as 'Paracetamol', then only ICSRs occurring in Spain where paracetamol was the suspect or interacting drug will be returned.


**Note:** There is a filter limit of approximately 1000 selections in total for any given search. If you require more than 1000 selections you will need to create another query.

##### **4.5.3. Validating filters**

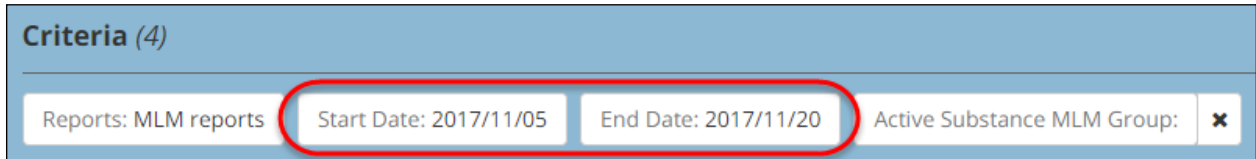
Once you have built and saved a filter, you may need to validate it to ensure that it returns the same data as you would have received previously. You can use the data that you previously downloaded & compare the same date range.



#### 4.5.4. Loading filters

To load a saved filter, click the "Load criteria" button (  ) and select the filter to upload following your browser's normal process for uploading files.

You will need to amend the start and end dates, ringed in red in the image below, to fit the time period that you need to search for, since they will be the dates you had entered the last time you saved your filters.



The image shows a user interface for filter criteria. At the top, it says "Criteria (4)". Below this, there are four input fields: "Reports: MLM reports", "Start Date: 2017/11/05", "End Date: 2017/11/20", and "Active Substance MLM Group: x". A red circle highlights the "Start Date" and "End Date" fields.

## 5. List of acronyms used in the document

Acronym	Meaning
EV	Eudravigilance
EVWEB	Eudravigilance Web application
FU	Follow-up
HTML	Hypertext Markup Language
ICH	International Conference on Harmonisation
ICSR	Individual case Safety Report
JSON	JavaScript Object Notation
MLM	Medical Literature Monitoring
NCA	National Competent Authority of an EEA Member State
RIS	RIS is a standardized tag format designed to allow the exchange of citation data between programs
RTF	Rich Text Format
XCOMP	The EudraVigilance External Compliance environment, used for QA testing
XML	Extensible Markup Language