23 February 2026
EMA/501718/2018
Data Analytics and Methods

EudraVigilance - EVWEB User Manual

Version 1.11

Note: Revision 1.11 contains the following:

Section(s) added	1.5.2. Unavailability of the EVWEB application/What to do in case of system failure 1.8. Masking of personal data in ICSRs/SUSARs submitted to EudraVigilance 2.6.1.4.1. Searching for units in Immediate Query Fields 3.2.1. Tests and Procedures 3.5.2.3. Viewing the EMA's official receipt date (gateway date) in EVWEB 3.5.2.3.1. Reporting compliance calculation
Section(s) updated	1.4.4.1.8. ICSR Download Screen 1.5.1. Availability of the EVWEB application 1.7. Classification of product information and Level 2A/B access 2.6.1.4. Immediate Query Field 3.2. Creating Safety Messages & ICSRs 3.2.2. Attachments *[and also renumbered from 3.2.1 to 3.2.2]* 3.2.2.1. Literature article 3.2.2.2. Additional (non-literature) document(s) held by sender 3.3. Sending a Safety Message 3.5. ICSRs Screen Functions 3.5.2. Searching ICSRs & Safety Messages in the ICSRs Screen 3.8.1. Case Follow-Up 3.8.2. Case Amendment 3.8.3. Case Nullification 3.9.3. ICSR Download 3.9.3.3.1. "Reports" Criteria *[and also renumbered from 3.9.3.1 to 3.9.3.3.1]* 5.1. Rerouting Rules (NCA Users)
Section(s) removed	N/A
Other change(s)	Additional sub-sections were created in section *3.9.3. ICSR Download*: • 3.9.3.1. User access • 3.9.3.2. Product classification and access to Level 2A/B ICSRs • 3.9.3.3. Downloading of ICSRs • 3.9.3.3.2. Considerations on the "Active Substance Group" and "Active Substance Combination" filters Some editorial changes were made to align the format with other EMA documents

Official address Domenico Scarlattilaan 6 ● 1083 HS Amsterdam ● The Netherlands
Address for visits and deliveries Refer to www.ema.europa.eu/how-to-find-us
Send us a question Go to www.ema.europa.eu/contact **Telephone** +31 (0)88 781 6000
An agency of the European Union

Table of Contents

1. Introduction

1.1. About this User Manual

This user manual is part of the official documentation prepared by the European Medicines Agency (EMA) to support the use of the EudraVigilance Web reporting tool (EVWEB).

The user manual consists of 5 chapters.

Chapter 1 presents a comprehensive overview of the EVWEB application and should be read before the other chapters. It contains basic information regarding the structure, functions and use of EVWEB, which applies to all other sections and needs to be understood before moving on to the more advanced aspects of the system.

Chapter 2 describes the creation and transmission of Safety and Acknowledgement messages (ACKs), as well as the functions available in the **WEB Trader**, **ICSRs**, **Post** and **Workspace** screens.

Chapter 3 explains the integration of MedDRA in EVWEB and how to query the system for specific MedDRA terms.

Chapter 4 provides an insight into the administration tools available in EVWEB.

Chapter 5 lists the abbreviations and acronyms, along with their descriptions, introduced in this user manual.

1.2. Typographical Conventions

The following typographical conventions have been used throughout this user manual:

Table 1 - Typographical Conventions

Format	Description
"Quoted text"	Indicates user interface items such as buttons, text, or icon descriptions.
Bold	Indicates EVWEB screens, for example **Create and send ICSRs, WEB Trader, ICSRs, Post, MedDRA, Workspace etc**. Also denotes external documentation titles referenced in this manual.
Bold italic	Indicates chapter/section titles and figure captions.
CAPS	Indicates keys you should press on your keyboard (i.e. SHIFT, TAB).
`Courier Font`	Indicates back end database items (i.e., schema and table names etc.)

1.3. EudraVigilance (EV)

EudraVigilance (EV) is the European data-processing network and database management system for the exchange, processing and evaluation of Individual Case Safety Reports (ICSRs) related to medicinal products authorised in the European Economic Area (EEA).

EudraVigilance is a key component in supporting the EMA and its committees in the coordination of the supervision, under practical conditions of use, of medicinal products which have been authorised within the European Community. EudraVigilance also provides advice on the measures to ensure the safe and effective use of these products, in particular by evaluating and making available through a pharmacovigilance database information on adverse reactions to the medicinal products in question.

EudraVigilance provides the European Union (EU) with a data-processing network for the rapid transmission of safety information, between the National Competent Authorities (NCAs) in the event of an alert relating to faulty manufacture, serious adverse reactions, and pharmacovigilance data regarding medicinal products marketed in the community.

In addition, EudraVigilance supports the Clinical Trials Directive 2001/20/EC and regulation EU 536/2014, through the EudraVigilance Clinical Trials Module (EVCTM). This module enables Commercial and Non-Commercial Sponsors (NCSs) to report electronically Suspected Unexpected Serious Adverse Reactions (SUSARs) that occur during clinical trials in accordance with the respective community guidance.

Please refer to the release notes for EudraVigilance (available on the EMA's webpage [EudraVigilance training and support]) to get a list of the new functions and amendments to the existing system.

This user manual deals with EudraVigilance version that entered into production on the 22 November 2017.

1.3.1. ICH E2B(R2) & E2B(R3) Standards

1.3.1.1. ICH E2B(R2)

The ICH E2B(R2) standard was introduced in 2001, and its aim was to migrate the industry from the then traditional paper reporting style to a more efficient, electronic submission method. In order for this to be possible, the E2B(R2) standard was designed in such a way as to improve the interoperability between all concerned parties (i.e. regulatory authorities, pharmaceutical companies and healthcare organisations), by standardising the data elements for the transmission of ICSRs.

It should be noted that this standard was fully phased out in favour of the newer and more versatile ICH E2B(R3). Still, the newly re-written EVWEB has retained the ability to import E2B(R2) data. This is **only** possible only through the **Workspace** import function, which allows importing, viewing/editing and sending (see **section 3.7. Workspace Screen Functions**).

1.3.1.2. ICH E2B(R3)

To make the ICH standards and the electronic case reporting more useful and compliant with changing pharmacovigilance practices, a new version referred to as ICH E2B(R3) was finalized in July 2013. ICH agreed to use the International Organization for Standardization (ISO) Individual Case Safety Report (ICSR) standard ISO EN 27953-2:2011 to meet the reporting requirements for E2B(R3).

EVWEB, one of the functional components of EudraVigilance (see **section 1.4.4. EVWEB**), has been re-written to support ICH E2B(R3) messages. Furthermore, additional updates and modifications have been applied to EVWEB and will be described in detail throughout this user manual.

1.4. Main Functional Components of EudraVigilance

1.4.1. EudraVigilance Database Management System (EVDBMS)

The EudraVigilance Database Management System (EVDBMS) is the core component of the European pharmacovigilance database. This web-based information system is designed to handle the safety report information in full compliance with the latest version of the International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use (ICH) specifications, featuring:

- A fully integrated organisation and user management in the EudraVigilance community synchronised with the EudraVigilance Gateway profile management.
- A fully automated safety and message processing mechanism, using XML-based messaging, supporting both asynchronous data interchange and interactive transactions.
- A large reference pharmacovigilance database, which is built by importing and consolidating data from multiple sources, including information on medicinal products and adverse drug reactions.
- An extensive query and tracking/tracing capability, both from a scientific and administrative business perspective.

1.4.2. MedDRA

MedDRA is the Medical Dictionary for Regulatory Activities. It was developed in the frame of the ICH M1 activities as a clinically validated international medical terminology for regulatory authorities, and is maintained by the MedDRA Maintenance and Support Services Organisation (MSSO).

MedDRA is used by regulators and the pharmaceutical industry for data entry, retrieval, evaluation and presentation during all phases of the drug regulatory process (i.e. the pre- and post-authorisation phase). These processes include clinical studies, reports of spontaneous adverse reactions, events, regulatory submissions and regulated product information.

1.4.3. EudraVigilance ESTRI Gateway

The EMA has implemented an electronic regulatory submission environment, the EudraVigilance Gateway, which follows the ICH M2 Gateway Recommendation for the Electronic Standards for the Transmission of Regulatory Information (ESTRI) Gateway.

The purpose of the EudraVigilance Gateway is to operate a single, common, EEA-wide Gateway for receiving regulatory submissions in a fully automated and secure way, including all aspects of privacy, authentication, integrity and non-repudiation of all transactions in pharmacovigilance.

The EudraVigilance Gateway allows the pharmaceutical industry to report to a common reporting point within the EEA, from where the transactions are re-routed to the concerned regulatory authorities. It provides the NCAs with a secure reporting mechanism to the pharmaceutical industry and to the EMA. The pharmaceutical industry, for example Marketing Authorization Holders (MAHs), is responsible for implementing at least one of the supported ESTRI standards in order to ensure electronic communication with any EEA Regulatory Authority.

The EudraVigilance Gateway supports two transmission modes:

- The Gateway transmission mode
- The WEB Trader transmission mode

The Gateway transmission mode refers to an organization that has a pharmacovigilance database that is fully compliant with the applicable exchange standards, which permits the generation and receipt of ICSRs and the electronic transmission of them via a local gateway solution that meets the ICH M2 recommendations and has been successfully tested and connected with the EudraVigilance Gateway.

The WEB Trader transmission mode is an integrated component of the EudraVigilance Gateway designed to support Small and Medium Size Enterprises (SMEs) or Regional Pharmacovigilance Centres (RPCs) to generate, send and receive ICSRs in a secure way, to any registered organisation within the

EudraVigilance community. This transmission mode is achieved through a specially developed internet-based reporting tool called EVWEB.

The WEB Trader transmission mode is not applicable for NCAs that are connected through the EudraVigilance Gateway, but it may be selected as a transmission mode by RPCs, if applicable.

1.4.4. EVWEB

The EVDBMS also provides interactive tools that allow the manual creation of Safety and Acknowledgement messages (ACKs) and their administration by a user via a web interface, called EVWEB.

EVWEB can be used by any MAH or sponsor in the EEA. EVWEB is specifically designed for SMEs, which do not have a fully ICH E2B(R3) compliant pharmacovigilance system and/or ESTRI gateway in place. It provides the necessary tool to allow SMEs secure electronic reporting to the EMA and all NCAs in the EEA.

EVWEB users must register with the EMA (see **section 1.5. Access to EudraVigilance & EVWEB**) of this manual) and also follow EudraVigilance Training courses in order to familiarise themselves with the reporting facilities. Please visit the EudraVigilance training and support webpage of the EMA's website for up-to-date information on training courses.

Access to EVWEB is personal and non-transferable for each user of each organisation. It is achieved through personal login, and password access keys can be obtained following registration with EudraVigilance.

1.4.4.1. EVWEB's Main Functions

1.4.4.1.1. Create & Send Safety Messages

One of the main functions of EVWEB is the ability to create and send ICSRs in relation to both the pre- and post-authorisation phases – WEB Trader users may use EVWEB for this purpose by compiling a new message containing one or more ICSRs using the specific screen of the application.

The tool will automatically display the complete sections of the hierarchical structure of a typical ICSR giving a user the opportunity to insert the information in the various fields as necessary. The application will also take care of displaying mandatory fields and detect basic data entry and consistency mistakes before validating the message and sending it.

Only WEB Trader users are allowed to send Safety messages via EVWEB. Gateway users may use the application, but Safety and Acknowledgement messages can only be sent and received via their local gateway.

Once a Safety message has been created, it can be exported in the XML format (which is the typical format for a Safety message) by clicking on the "Export XML" button (see **Figure 14 - Dynamic buttons set**). However, in order to obtain the case in the RTF format (which is the typical "text" document format), the previously downloaded XML file should be uploaded into the **Workspace** area (see **section 3.7.1. Import Function**) and once that is done, the file can now be exported in the RTF format (see **Figure 114 - Workspace screen: 1 XML file (containing only 1 case) imported**).

Alternatively, if a case was already sent to EV, then it is possible to export both the XML and RTF files by going to the **WEB Trader** "Outbox" section (see **Figure 54 - WEB Trader "Outbox" screen**). In the "Outbox" section of EVWEB, it is possible to obtain the XML and/or RTF file(s) by clicking on "XML" or "RTF".

Note: EVWEB uses the ICH E2B(R3) standard for Safety messages created in its environment, but retains background compatibility for importing ICH E2B(R2) Safety messages as well (see **section 3.7. Workspace Screen Functions**).

1.4.4.1.2. Create & Send Acknowledgement Messages

Acknowledgement messages are used to inform other users that a Safety message has been received and processed. They also announce the outcome of the validation of that Safety message at the receiver's end. EVWEB allows users to create and send Acknowledgement messages for received Safety messages and to read and store the received Acknowledgement messages for the Safety messages they have sent.

Notes:

- Given the phasing out of the old E2B(R2) message format, EVWEB only displays now the applicable ICH E2B(R3) compliant Acknowledgement message form.
- As stated in **section 1.4.4.1.8. ICSR Download Screen**, MAHs should **not** send acknowledgements (ACKs) for any ICSR downloaded from EudraVigilance, including those obtained via the "**ICSR Download**" screen.

1.4.4.1.3. WEB Trader Screen

The **WEB Trader** screen of the application allows WEB Trader users to keep track of sent and received Safety messages, Acknowledgement messages and rejected (invalid) messages.

1.4.4.1.4. ICSRs Screen

The ICSRs screen allows users to view, browse and query ICSRs and Safety messages residing on the EVDBMS. It also provides the "Follow-up" and "Add to follow-ups" options which allow the user to edit or update and resend ICSRs already stored in the EVDBMS. These functions on ICSRs can be performed taking into account the general access rights of the users.

1.4.4.1.5. Post Screen

The **Post** screen provides a quick method to upload and send a Safety message to other compliant organisations (i.e. EVDBMS, MAHs). It accepts only XML files that are compliant with the ICH E2B(R3) standard.

1.4.4.1.6. MedDRA Screen

The user is able to browse and query the complete MedDRA terminology. MedDRA is fully integrated in the EVWEB application.

1.4.4.1.7. Workspace Screen

The Workspace screen is a new addition to EVWEB's supported functions. Its purpose is to act as a temporary, centralised area where multiple EVWEB items (Safety messages, Acknowledgement messages, ICSRs) can be added to for better review and management.

Attention: The **Workspace** screen retains the added EVWEB items only during an active EVWEB session. If a user logs out or terminates the session (i.e. closes the web browser window), the **Workspace** screen will clear all previously added items. The cleared items are not actually deleted since they reside on the remote EVDBMS. Items added to the **Workspace** screen are copies that are loaded from the remote system.

1.4.4.1.8. ICSR Download Screen

The ICSR Download screen allows users to download ICSRs in bulk from the Medical Literature Monitoring (MLM) Service, to fulfil pharmacovigilance obligations (L2A), or to request case narratives in the context of signal management (L2B). Please see **section 3.9.3. ICSR Download** for further details on using this functionality.

1.5. Access to EudraVigilance & EVWEB

Only registered organisations and their registered individual users are granted access to the EVDBMS. When registering with EudraVigilance, all organisations need to specify their transmission mode.

NCAs and RPCs can choose to use the Gateway or the WEB Trader transmission mode.

MAHs need to specify their transmission mode at the level of the Head Quarters and at the level of the affiliates, if the ICSR management is not centralised within a company. Different transmission modes may be used at each level. For MAHs, the chosen transmission mode determines the default access rights to the EVDBMS.

Sponsors of Clinical Trials can register either transmission mode (Gateway or WEB Trader users) and add affiliates/subsidiaries following a Head Quarters registration. As per MAHs, the chosen transmission mode determines the default access rights to the EVDBMS.

Individual users of NCAs have access to all ICSRs (both pre-and post-authorisation) stored in the EVDBMS.

MAHs currently have only restricted access to the EVDBMS. Individual users of a pharmaceutical company can only view the ICSRs that have been submitted by that company to the EudraVigilance post-authorisation module. MAHs may also define specific user rights for their affiliates, and their individual users during the registration process.

MAHs and Sponsors of Clinical Trials do not have access to the pre-marketing reports submitted to the EVCTM.

1.5.1. Availability of the EVWEB application

The EVWEB application will be made available during EMA business hours 08:30 – 18:00 (CET/CEST time)[1], Monday to Friday. The EVWEB will also be made available outside of these hours apart from scheduled maintenance and routine data management tasks.

Note: Please note that generally submissions made via the gateway are not affected by maintenance periods, such submissions will be queued for processing once the overnight process and any maintenance are completed. If the gateway is planned to be specifically unavailable this will be announced in advance.

All service issues/outages are reported on the service desk homepage (see **section 1.6. EVWEB Support** below). Users of EVWEB should check this page first if they encounter issues accessing the service.

[1] EMA Business hours and holidays

The following tasks are performed outside of EMA office hours to support the operation of EudraVigilance:

- classification of ICSRs against the XEVMPD/Art.57 database
- detection and management of duplicate ICSRs
- assignment of the substance-based access (Level 2) for MAHs

These scheduled activities will run every day Monday to Sunday between 23:59 and 04:00 (UK time) in the morning, EVWEB services will resume as soon as these automated tasks have completed. Access to EVWEB will not possible whilst these activities are being performed, and a maintenance page will be displayed.

Please note that if a larger than normal number of ICSRs are received within a day the system may become available again later than 04:00, however in such situations EVWEB should still be accessible from 08:30 (EMA office hours).

Notes:

- Any ICSR download requests launched by MAHs that have not completed before these scheduled activities start will be made available as soon as the EVWEB interface is available gain.
- Submissions made via the EudraVigilance gateway are not affected by these planned activities; however acknowledgements will not be returned until these processes have finished.

1.5.2. Unavailability of the EVWEB application/What to do in case of system failure

In the event of prolonged unavailability of the EudraVigilance web application during EMA's business hours which could affect the sender's ability to meet regulatory reporting timeframes, organisations should follow the guidance of the EMA's webpage EudraVigilance: electronic reporting – section **What to do in case of system failure**.

1.6. EVWEB Support

If you require technical assistance, please contact the EMA service desk by using the following portal: https://support.ema.europa.eu/esc

Please also refer to the EudraVigilance support guide, that provides a detailed overview of different support options available, as well as additional sources of information.

When logging a call please ensure that you provide as much information as possible in order to help with investigating issues or to provide you with the correct support. You should always provide the following information:

- User name
- Organisation ID

For issues related to ICSRs submitted to EudraVigilance please also include:

- Worldwide case ID
- Local report number (EU-EC-nnnnnnnnnn)
- Message number

- Date of submission

For issues related to missing acknowledgements for Gateway submissions please also include:

- XML file name
- Gateway CoreID
- Date and time sent
- Confirmation positive Message Disposition Notification (MDN) was received

For issues and errors seen with the EVWEB application please include:

- The steps taken that lead to the error or issue
- Screenshots of the error/issue seen in the application

The service desk application allows the attachment of files (ZIP, word, excel & image files) and these are useful in providing complete responses in quicker timeframe. However, please note that **files containing sensitive information** (such as **XML files**, **ICSR** or **CIOMS** Forms, **RTF** documents or **print screens**) should **NOT** be added to your Service Desk request - this is also stated in the Data Protection Note in the homepage of ServiceNow and the associated Information Note.

Thus, if your query refers to a case already transmitted to EV, then all that is needed is the full C.1.1 'Sender's (case) safety report unique identifier' or the C.1.8.1 'Worldwide unique case identification number' as EMA can access the cases present in the system.

Alternatively, if your query does not refer to a case already transmitted to EV, and if EMA needs to access sensitive file(s), it/they should, instead, be shared with EMA via Eudralink to an email address that will be provided in the reply to your Service Desk ticket.

1.7. Classification of product information and Level 2A/B access

Access to ICSRs in EudraVigilance is based on linkage between the suspect and interacting drugs within an ICSR and the data held in the XEVMPD for the organisation accessing the system. This is done at the level of the **"scientific product" or "scientific group"** (substance).

Notes:

- MAHs have full access to an ICSR which they have sent regardless of the product/substance information in the ICSR.
- MAH/Sponsor organisations get level 3 access to all MLM ICSRs in accordance with the EMA's EudraVigilance Access Policy.

The first step in performing the linkage for level 2 access is through the Classification of the product/substance information for an ICSR. The diagram shown below **Figure 1** - Classification and linkage of XEVMPD data provides an overview of the process.

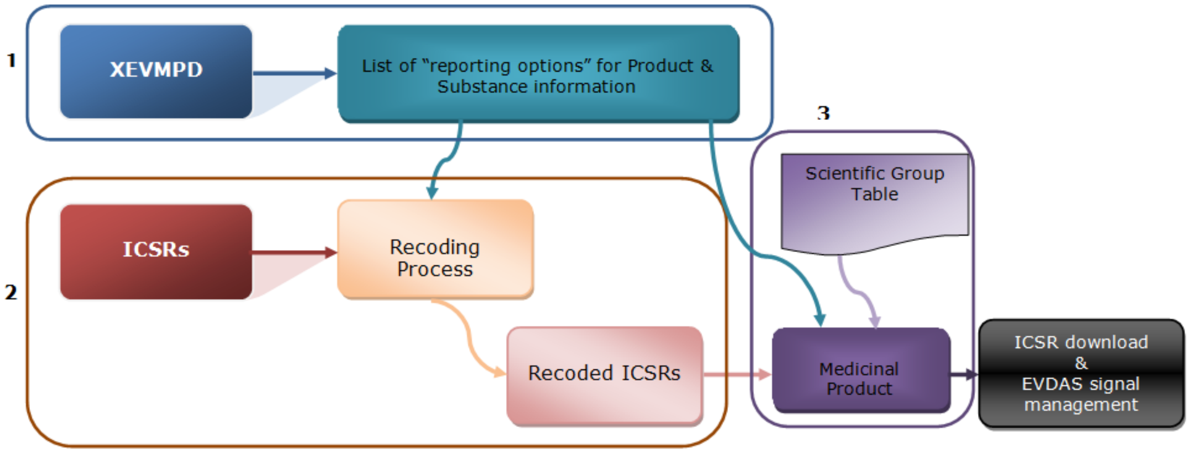


Figure 1 - Classification and linkage of XEVMPD data

The recording process mentioned in the **Figure 1** above identifies the reported text in the ICSR and classifies it against the closest match to XEVMPD data. The matching uses the XEVMPD's "product index", the product index is a list of a possible combinations of the parts of the product name information for authorised medicinal products and also the scientific compositions of those products. **Figure 2** below illustrates how this matching is performed automatically, however some matches require a manual review in order to choose the correct corresponding product index entry.

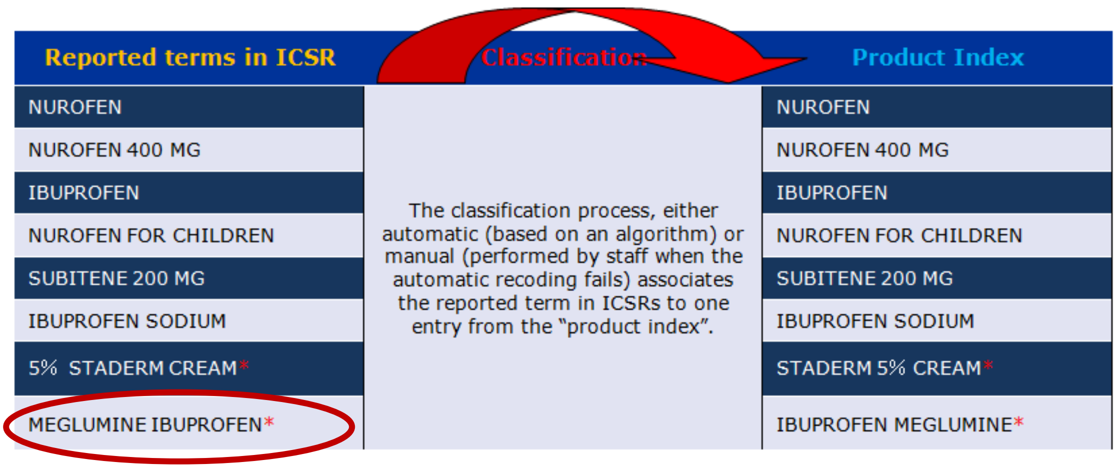


Figure 2 - Classification of reported terms against the XEVMPD product index

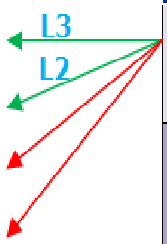
After the product index is assigned to the drug information in the ICSR, the EudraVigilance system is able to link this information to the corresponding Scientific product and the Scientific group. Examples of this linkage are shown in **Figure 3** below.

Product Index	Product Index Group	Scientific Product	Scientific Group
NUROFEN	NUROFEN	IBUPROFEN	IBUPROFEN
NUROFEN 400 MG	NUROFEN	IBUPROFEN	IBUPROFEN
IBUPROFEN	IBUPROFEN	IBUPROFEN	IBUPROFEN
NUROFEN FOR CHILDREN	NUROFEN FOR CHILDREN	IBUPROFEN	IBUPROFEN
SUBITENE 200 MG	SUBITENE	IBUPROFEN SODIUM DIHYDRATE	IBUPROFEN
IBUPROFEN SODIUM	IBUPROFEN	IBUPROFEN SODIUM	IBUPROFEN
STADERM 5% CREAM	STADERM	IBUPROFEN PICONOL	IBUPROFEN
IBUPROFEN MEGLUMINE	IBUPROFEN	IBUPROFEN MEGLUMINE	IBUPROFEN

Figure 3 - Product Index link to Scientific product and scientific group

The final step the system takes is to link the ICSR drug Scientific product or scientific group (depending on search criteria chosen, the default is the scientific group) to the XEVMPD authorised medicinal product scientific product or scientific group. **Figure 4** below shows a search being performed using the Scientific product linkage, the user will retrieve one Level 2A (L2A) ICSR (case 2), access to case 1 will be level 3 and would not be included in a L2A download request. If the query is changed to use the Scientific group (default level) instead cases 3 & 4 will be returned in addition to case 2.

Case	MAH sending the ICSR	Reported terms in ICSR	Scientific Product	Scientific Group
1	MAH A	NUROFEN	IBUPROFEN	IBUPROFEN
2	MAH B	IBUPROFEN	IBUPROFEN	IBUPROFEN
3	MAH C	IBUPROFEN SODIUM	IBUPROFEN SODIUM	IBUPROFEN
4	MAH D	IBUPROFEN MEGLUMINE	IBUPROFEN MEGLUMINE	IBUPROFEN



MAH owning the Medicinal Product	Active Substance of the Medicinal Product
MAH A	IBUPROFEN
MAH B	IBUPROFEN SODIUM

Figure 4 - Example matching of Scientific product information

1.8. Masking of personal data in ICSRs/SUSARs submitted to EudraVigilance

Following the publication of GVP Module VI Addendum II – Masking of Personal Data in Individual Case Safety Reports Submitted to EudraVigilance in July 2025, the Agency implemented the necessary technical changes to update the EudraVigilance (EV) system accordingly.

The XCOMP and Production environments were updated in November 2025 to reflect these changes. As part of this process, changes to the EV parsers were made to:

A) Not extract any data from the Sender fields listed in **Table VI.Add.II.2**, as detailed in Chapter **VI.Add.II.4. ICH-E2B(R3) data elements to be left blank**:

> *In instances where data are submitted to EudraVigilance by a sender for any of these 11 data elements due to failure of compliance with the instructions in this Addendum, the Agency will not make the data available to the EudraVigilance users. Similarly, for legacy data held in EudraVigilance related to these 11 data elements, the Agency will remove the data.*

Case senders remain obligated to comply with the requirements outlined in **VI.Add.II.4. ICH-E2B(R3) data elements to be left blank**, which mandate that the 11 data elements are to be left blank when submitting ICSRs and SUSARs to EudraVigilance. The update to EV parsers, which prevents extraction of data from those fields, does not remove this obligation. This adjustment is a technical safeguard to ensure that any data inadvertently populated by an organisation is not recorded within the EV system.

Note: For organisations operating as EVWEB **WebTraders** (i.e., using the EVWEB tool to submit ICSRs to EV), the data in the E2B section "C.3 Information on sender of case safety report" is automatically populated by the EV system based on the login credentials of the user. This information cannot be altered by the user and will not be processed. Therefore, no additional action is required from you for this specific section when creating or sending a case with the EVWEB tools.

B) Mask the 13 data elements provided in **Table VI.Add.II.1**, as detailed in Chapter **VI.Add.II.3. ICH-E2B(R3) data elements to be masked**:

> *In instances where unmasked data are submitted to EudraVigilance by a sender for any of these 13 data elements due to failure of compliance with the instructions in this Addendum, the Agency will not make the unmasked data available to the EudraVigilance users. Similarly, for legacy data held in EudraVigilance related to these 13 data elements, the Agency will mask the data.*

Organisations must continue to comply with the requirements set out in **VI.Add.II.3. ICH-E2B(R3) data elements to be masked**, which stipulate that the 13 specified data elements must be masked when submitting to EV, provided that that data are available to the sender of the case. Please note that this technical amendment serves as a safeguard to ensure that any data unintentionally left unmasked by an organisation is not captured in an unredacted form within the EV system.

Note: This automated masking is only applied by the system if any of those 13 fields contains a value other than a nullflavor. If a field is blank or already set to a nullflavor, then no changes will be made by the system.

2. EVWEB

The EudraVigilance WEB (EVWEB) application is a web-based tool designed for the transmission of ICSRs to EudraVigilance for pharmacovigilance purposes through the internet. It also allows follow-ups to ICSRs and exchange of Acknowledgement messages. System users also have full access to MedDRA for coding and analytical processing.

EVWEB can be accessed by modern web browsers, the browsers, MS Edge, Firefox & Chrome have been tested and are therefore recommended.

2.1. General Description

EVWEB is available to registered users only. It can be accessed from the following website:

https://eudravigilance.ema.europa.eu/Decommissioned/Decommissioned.html

The transmission of information through this system is secure. Security is achieved in a first instance by a username/password combination to access the reserved area of the website, and in a second instance by the use of a HTTPS (SSL) protocol. Secure Sockets Layer (SSL) provides security by the use of a public key to encrypt data that is then transferred over the SSL connection. In HTTP (SHTTP), SSL creates a secure connection between a client and a server, through which any amount of data can be sent securely. SSL and S-HTTP, therefore, are complementary technologies.

2.1.1. Login

EVWEB is accessible by clicking on the "EVWEB" link in the restricted area of the EudraVigilance webpage or via the EudraVigilance links available on the EudraVigilance pages of the EMA website.

Figure 5 - Accessing EVWEB

By accessing EVWEB via the restricted area, the user will need to select an organization.

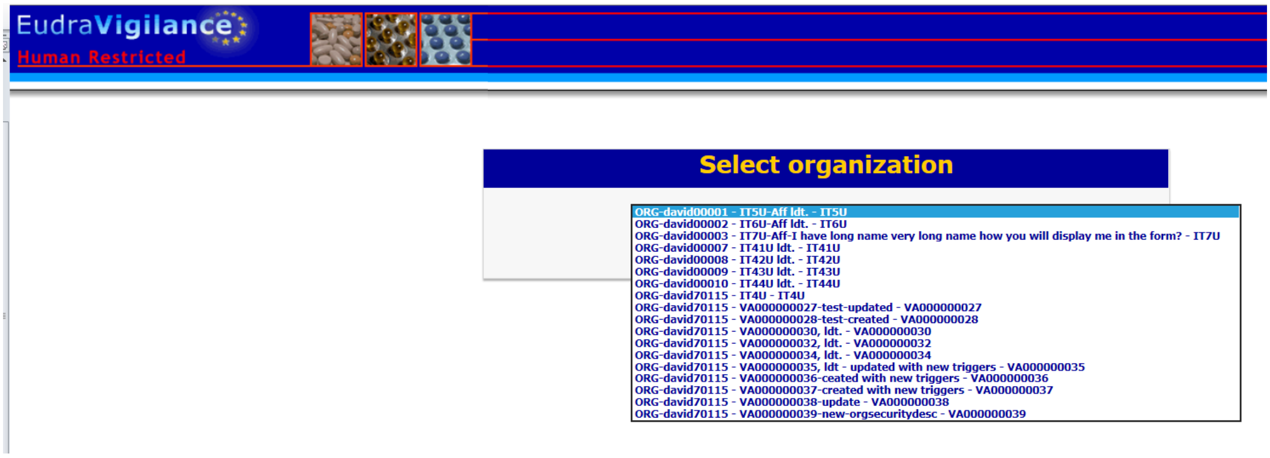


Figure 6 - Selection of organisation

The EVWEB application can also be access directly without going through the secure area of the EudraVigilance website by using the following URLs.

EudraVigilance XCOMP (test): https://eudravigilance-human-xcomp.ema.europa.eu/#/

EudraVigilance production: https://eudravigilance-human.ema.europa.eu/#/

Tip: You can add these URLs as bookmarks to your Internet browser in order to quickly access the application without going through the secure area of the EudraVigilance website.

The application will open in a new web browser window. If the user has not been authenticated already, a login dialog will appear prompting them to login:

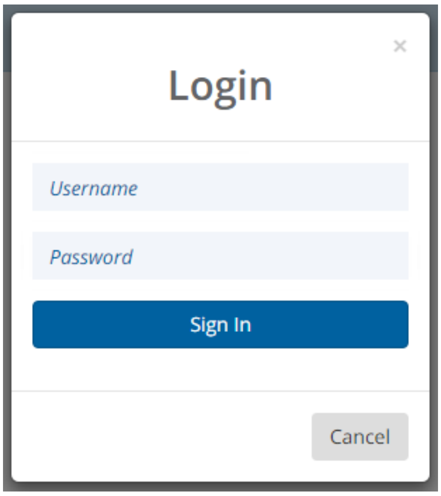


Figure 7 - Login dialog

When logged in, the user will be prompted to select an organisation.

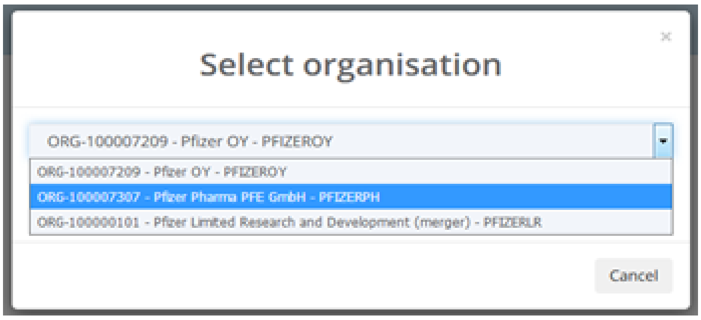


Figure 8 - Organisation selection dialog

2.1.2. User Interface Layout

The main menu is located on the top of that window and below it is the dynamic buttons set **(Please note: the buttons will vary depending on the EVWEB screen you are currently accessing).** Below the main menu and the dynamic buttons set, the screen will usually be divided vertically into two parts: on the left side will be the tree view area and on the right the active area.

The following screenshot, which shows the 'Create and send ICSRs' screen, and accompanying table provide a general outline of the EVWEB interface:

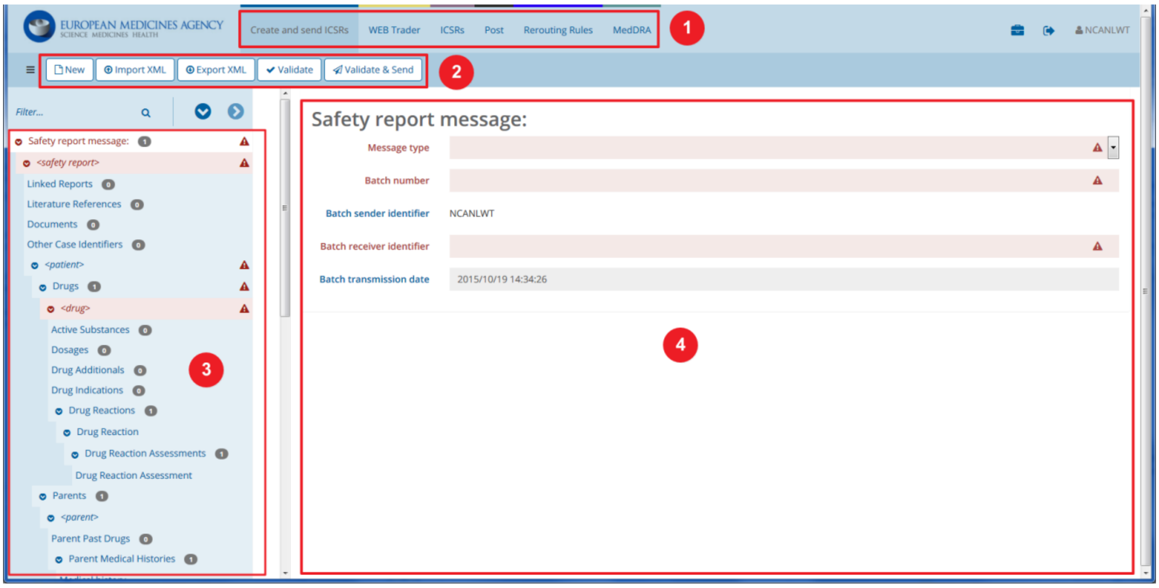


Figure 9 - EVWEB Interface

Table 2 – Description of the Interface Options

Interface Option	Description
(1) Main menu	EVWEB's main menu is always present in every screen of the application. EVWEB is divided into different screens according to the kind of information you are going to operate with (i.e. **Create and send ICSRs**, **WEB Trader**, **ICSRs**, **Post**, **MedDRA**, etc.).

Interface Option	Description
(2) Dynamic buttons set	This area represents the dynamic buttons set. It will vary depending on the EVWEB screen you are accessing.
(3) Tree view area	Displays the hierarchy of the ICSR, Safety or Acknowledgement message sections in a tree view style.
(4) Active area	Displays content of a selected section or search results from a query.

Attention: The case examples used in this user manual to describe the functions of the EVWEB application are fictitious, and are intended for demonstration purposes only.

2.1.3. Session Time Out

The EVWEB tool allows a maximum period of inactivity of 25 minutes before a user is automatically logged out of the system. **Figure 10** below shows the session expiry warning that will come up when the maximum period of inactivity is being reached. In order to prevent the automatic log out, users should click on the "Renew Session" button.

Note: There is **no** "auto-save" functionality in EVWEB. Users are therefore advised to **periodically save their work** by clicking on the "Export XML" button - see **Figure 14 - Dynamic buttons set**. This way, they can resume their work once the previously saved XML file is uploaded into EVWEB, by clicking on the button "Import XML" - see **Figure 14 - Dynamic buttons set**.

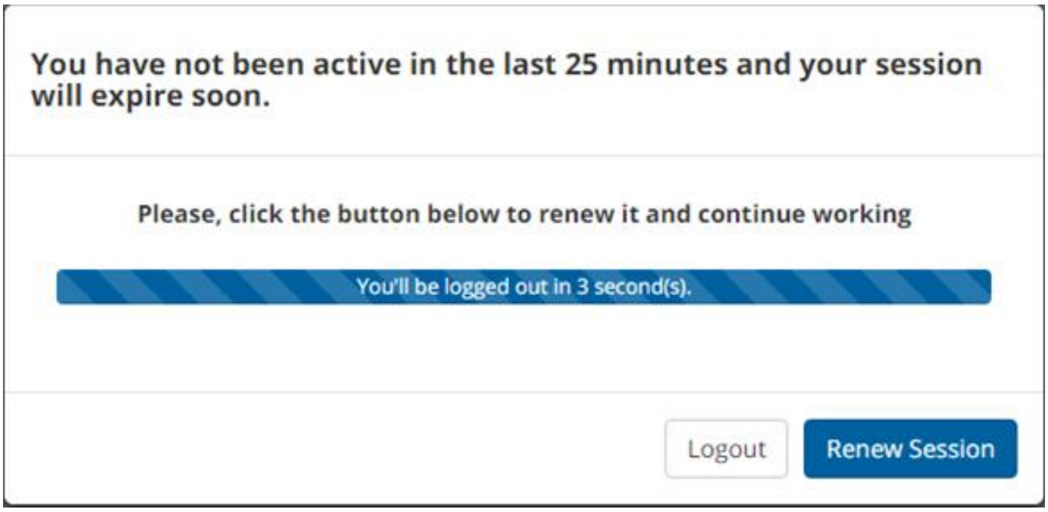


Figure 10 - Session expiry warning

2.2. The Main Menu & Dynamic Buttons Set

2.2.1. 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.

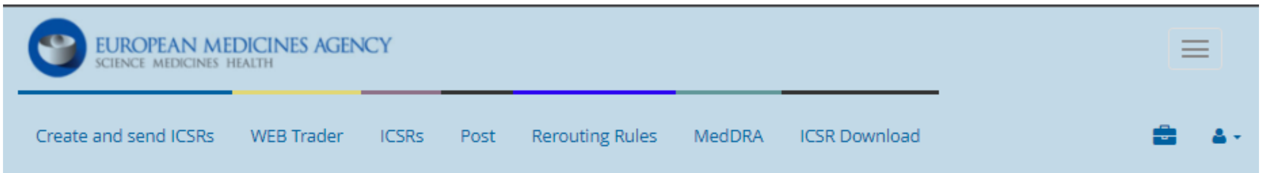
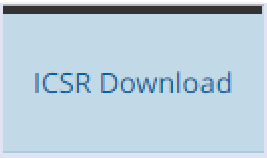
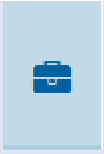


Figure 11 - The main menu

A typical EVWEB main menu consists of the following links:

Table 3 – EVWEB main menu

Menu Option	Description
Create and send ICSRs	Allows user access to the part of the application dedicated to the creation and transmission of ICH E2B(R3) Safety messages (see chapter **3. ICSRs & Messages** of this manual).
WEB Trader	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 (see chapter **3. ICSRs & Messages** of this manual).
ICSRs	Allows you to view, browse and query ICSRs and Safety messages located in the EVDBMS (see chapter **3. ICSRs & Messages** of this manual).
Rerouting Rules	The re-routing rules administration tool is accessible only to NCA user accounts.
Post	Provides a quick method to upload and send ICH E2B(R3) compliant Safety messages to the system.
MedDRA	This area of the application allows you to browse and perform searches at all levels of MedDRA (see chapter **4. MedDRA** of this manual)

	Allows the bulk export of ICSRs and Safety messages based on pre-defined criteria options.
	The Workspace screen 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: .

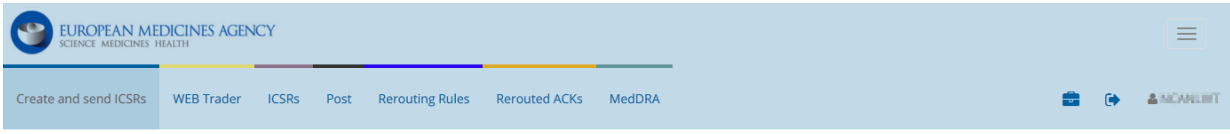


Figure 12 - Main menu: Normal screen/window size

Figure 13 - Main menu: Small screen/window size

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

2.2.2. Dynamic Buttons Set

This set of buttons, located under the main menu and on the left side of your window, displays a variable number of buttons that change according to the screen of the application and the related section selected in the tree view area.

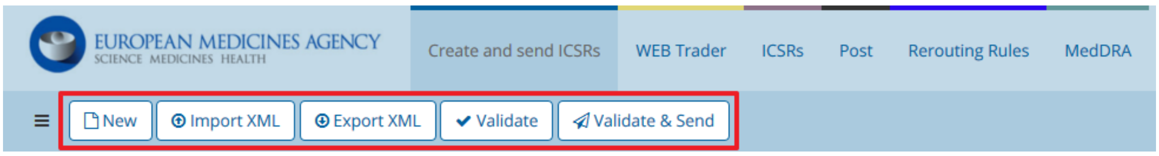


Figure 14 - Dynamic buttons set

These buttons and the different screens and functions of EVWEB will be described in further detail in the following sections of this user manual.

2.3. The Tree View Area

The tree view area is located on the left side of the application, below the main menu and the dynamic buttons set. It shows sections in a tree view style (similar to Windows File Explorer). The mandatory sections, such as Patient or Summary, are pre-selected by the system; others, such as Linked reports or Literature references have to be entered by the user if needed.

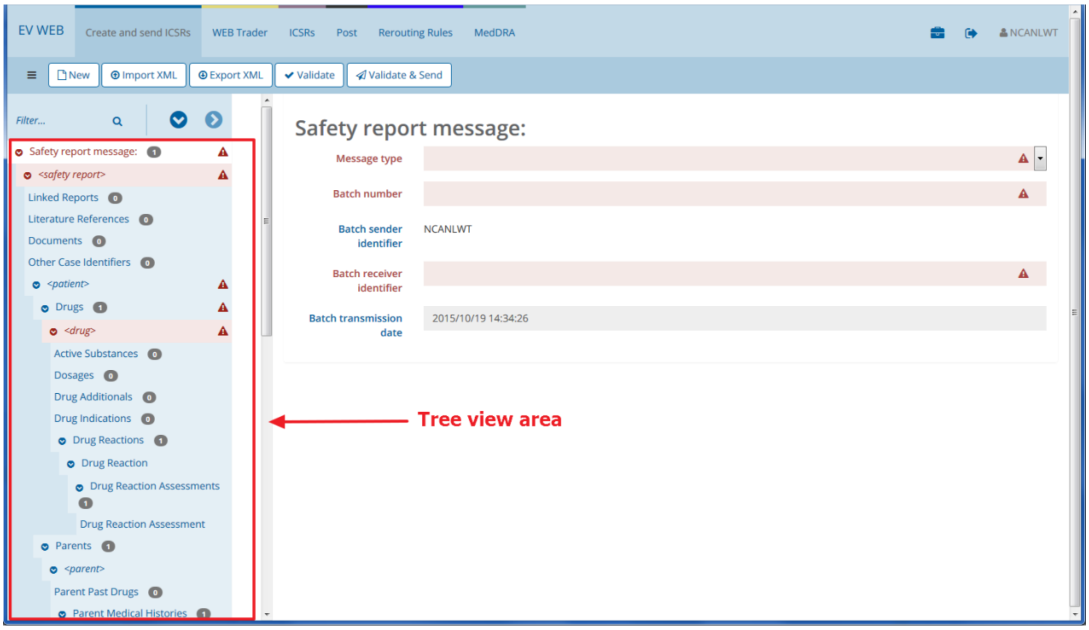


Figure 15 - The tree view area

To select a section (either pre-entered by the system or entered by the user) in the tree view area, the user has to click on the section’s name. If applicable data needs to be entered into a section that is not automatically added when creating a new report, the user needs to manually add the section to the form. To do this the user should place their mouse pointer over the section to be added and then use the Plus symbol that appears, the new section will then be added to the form.

You will notice that most section names are followed by a numbered grey circle icon (i.e.). These icons indicate how many additional sub-sections are available under the main section. If the number in the grey circle is greater than zero, then the section name will be in bold.

When the icon appears on the left of a tree view section, this indicates it contains a sub-section that can be expanded by clicking on the icon.

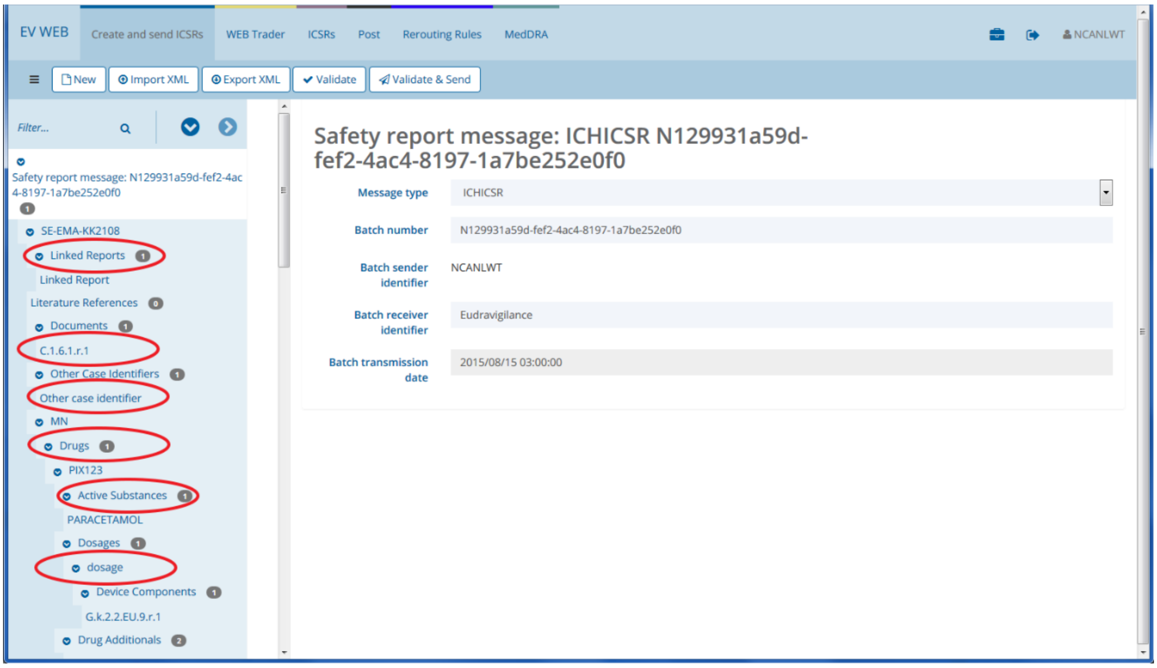


Figure 16 - Tree view area with sub-sections

Tip: You can expand or collapse at once all tree view sections by clicking on the corresponding icons ( ) located at the top of the tree view area.

After a tree view section is expanded, the icon changes into . To collapse the section again, click on the icon.

The tree view can grow, expand and become extensive while using the application. The active section of the tree view area is always marked on a white background.

Note: Located within the tree view area and at the top, is a simple query type field containing the text "Filter…" in it (Filter...).You can use this query field to search for any matching section/sub-section in the current tree view area.

When the expanded tree grows beyond the size of the tree view area, scroll bars will appear on the side, to allow you to move up and down and reach any part of the tree.

2.4. The Active Area

The active area displays the content of the currently selected section in the tree view area.

The active area is located below the main menu and the dynamic buttons set. If a tree view area is present, the active area appears on the right side of the application.

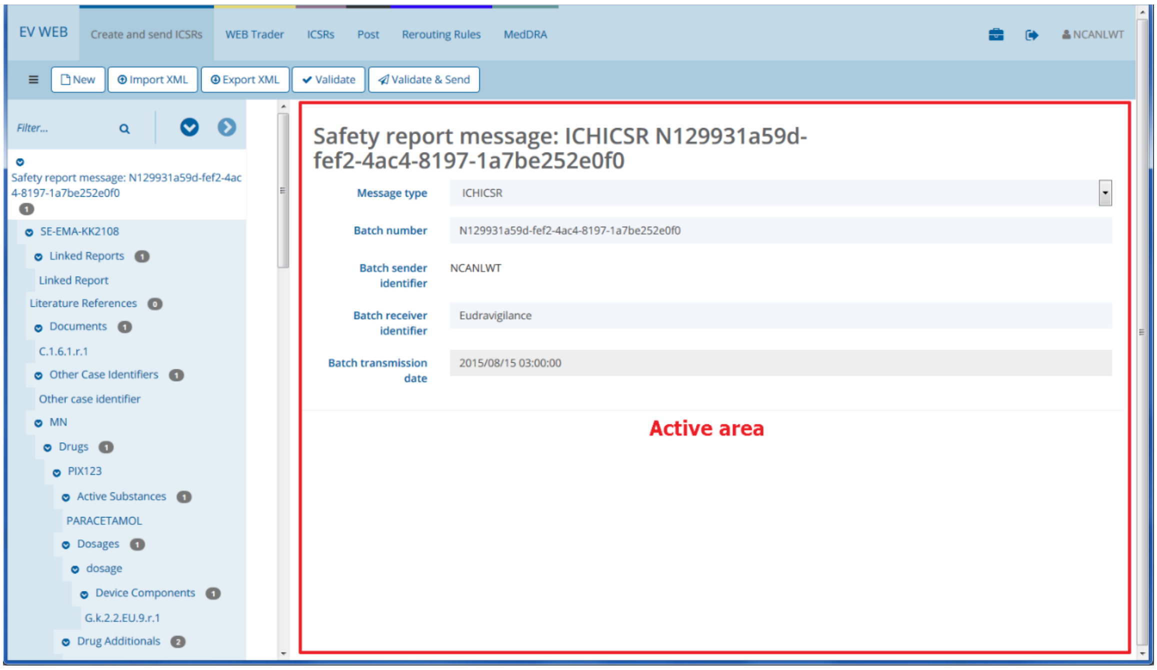


Figure 17 - Active area

The main difference between the tree view area and the active area is that the active area is interactive and displays information that can be edited and modified by the user (see **section 2.6. Data Entry** of this manual).

The active area displays information in 2 different ways:

- Section view: Used for displaying information and/or data entering. A typical example of a section view is the editing of a new Safety message.

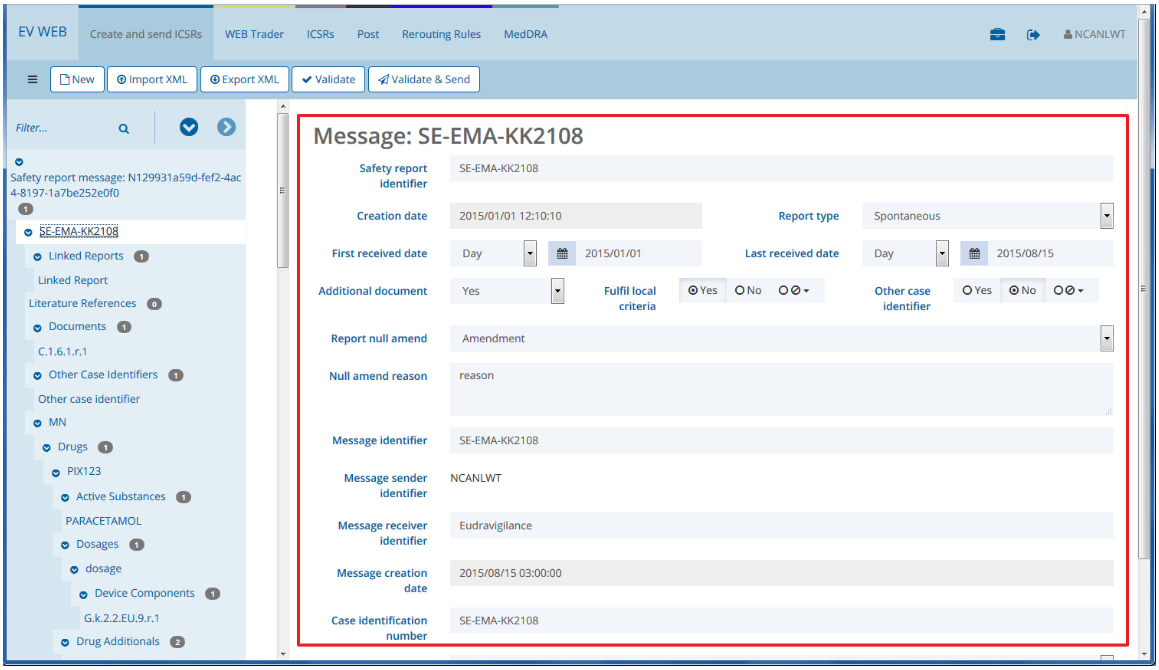


Figure 18 - Active area section view

- List view: Used for displaying items that can be selected. A typical example of a list view is the result of a query.

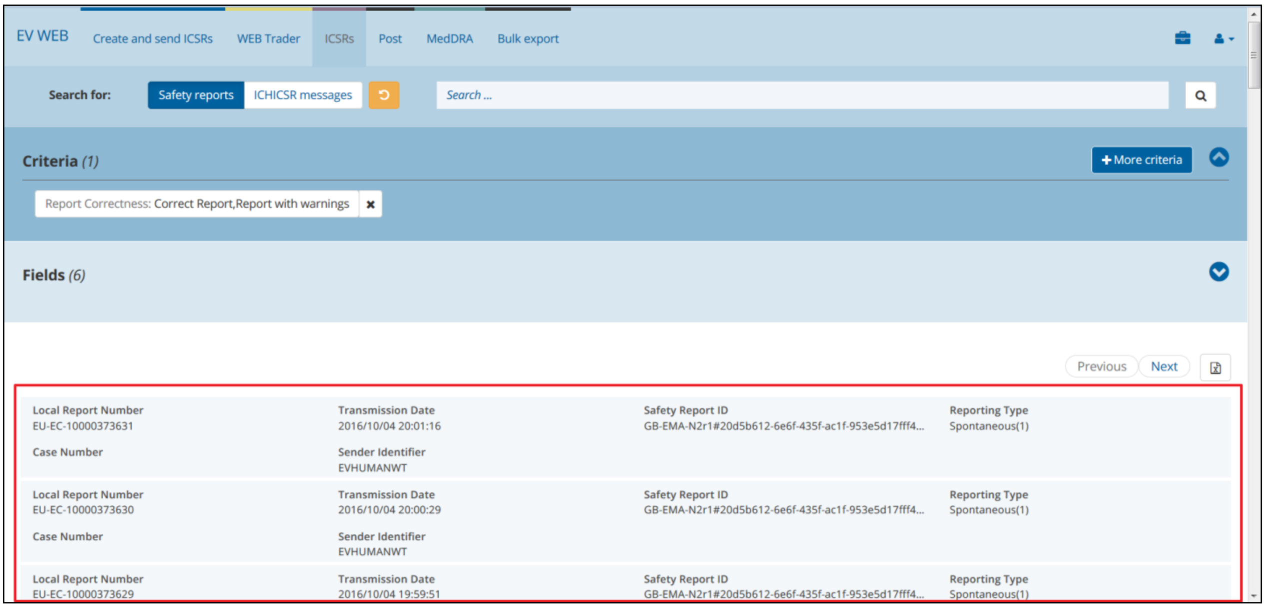


Figure 19 - Active area list view

The main body of the active area may display editable or non-editable information. Sometimes it shows information to the user, other times it requests information or an action from the user.

2.5. Interaction Between the Tree View & Active Area

The tree view area enables you to browse sections by selecting them, and by expanding or collapsing them into sub-sections. Functionally, the tree view area can be considered a navigation system. The active area displays the content of the selected section in the tree view area and allows the user to view, input, modify and nullify information.

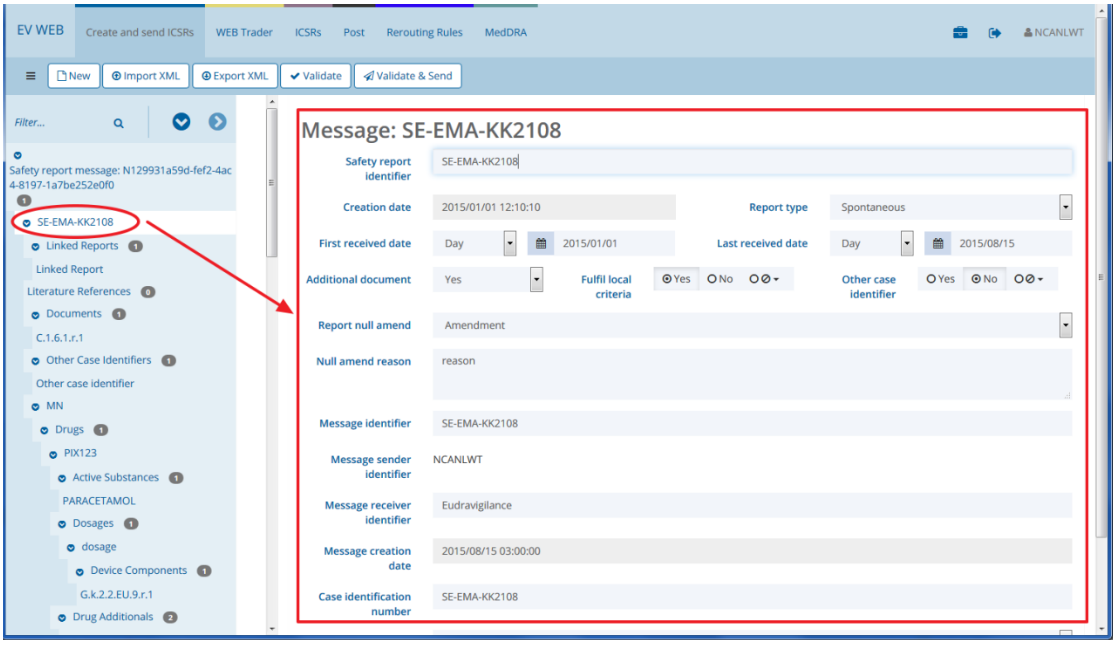


Figure 20 - Tree view & active area interaction

The information displayed in the active area can be presented in two different formats: section view and list view (see **section 2.4. The Active Area** of this manual). To display the details of any of your sections you have to click once on the section's name in the tree view area.

2.6. Data Entry

This part deals with all specific actions that you can perform to insert data in the EVWEB application.

2.6.1. Input Field Types

EVWEB has basically five different types of fields for the user to input information into the system. These are:

1. Text fields
2. Date fields
3. Drop-down list fields
4. Immediate query fields
5. Checkbox/radio button fields
6. Null Flavour flags

These are explained in detail below. You do not necessarily need to know what type of field you are dealing with when you are entering information. The system will guide you through the necessary steps for each type of field.

During the input phase the application performs a real-time validation of the inserted data. Fields that contain erroneous or incomplete information have their title/description and field box highlighted in red. The relative error message is displayed when you hover the mouse pointer over the icon which appears on the far right of the invalid field. In addition to that, the section that contains errors is also displayed in red both in the tree view area and the active area.

2.6.1.1. Text Field

This is the most common type of field that you will find in EVWEB. Text fields require information that is entered using the keyboard.

To enter information in a text field, you first need to select it by clicking in its text box.

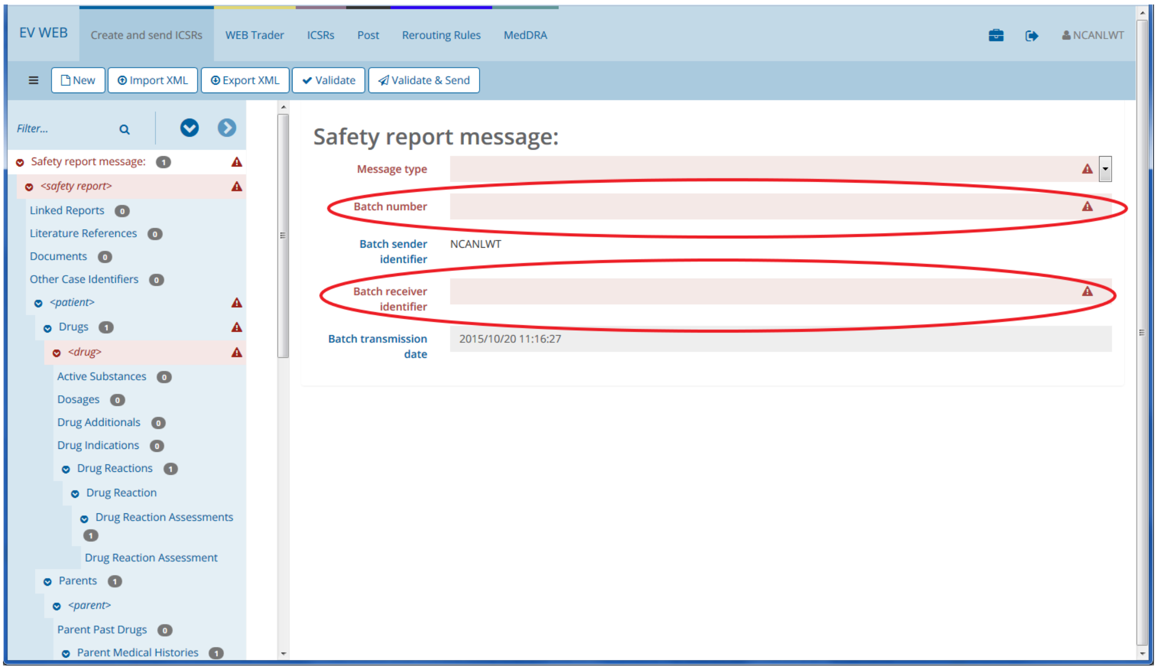


Figure 21 - Text fields

Once you enter the required data, you can click anywhere outside of the text field to finish the input process for that field. You also have the ability to copy and paste information from/to text fields.

Tip: To quickly move to the next field, you can press the TAB key on your keyboard. This will activate the next field for you. Similarly, you can press SHIFT+TAB to activate the previous field.

A special type of text field is the resizable text field. This kind of field allows you to insert a long description that contains more than one line of text. EVWEB has specific fields designated as resizable text fields, thus not all text fields are resizable.

A resizable text field is distinguished by its larger text box and the dotted triangle located at the bottom right corner of the box. To resize the text box, click and hold the left mouse button on the dotted triangle and move your mouse downwards, as much as needed, to properly display your input.

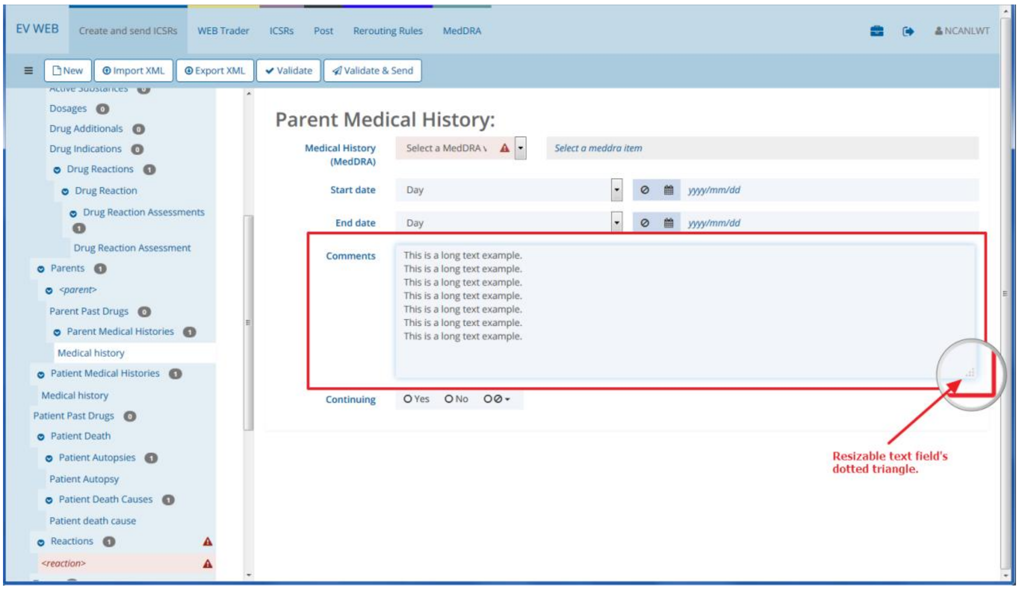


Figure 22 - Resizable text field

This type of field is used in EVWEB to enter date information using either a graphical interface that resembles a calendar, or by typing it in the available date field text box.

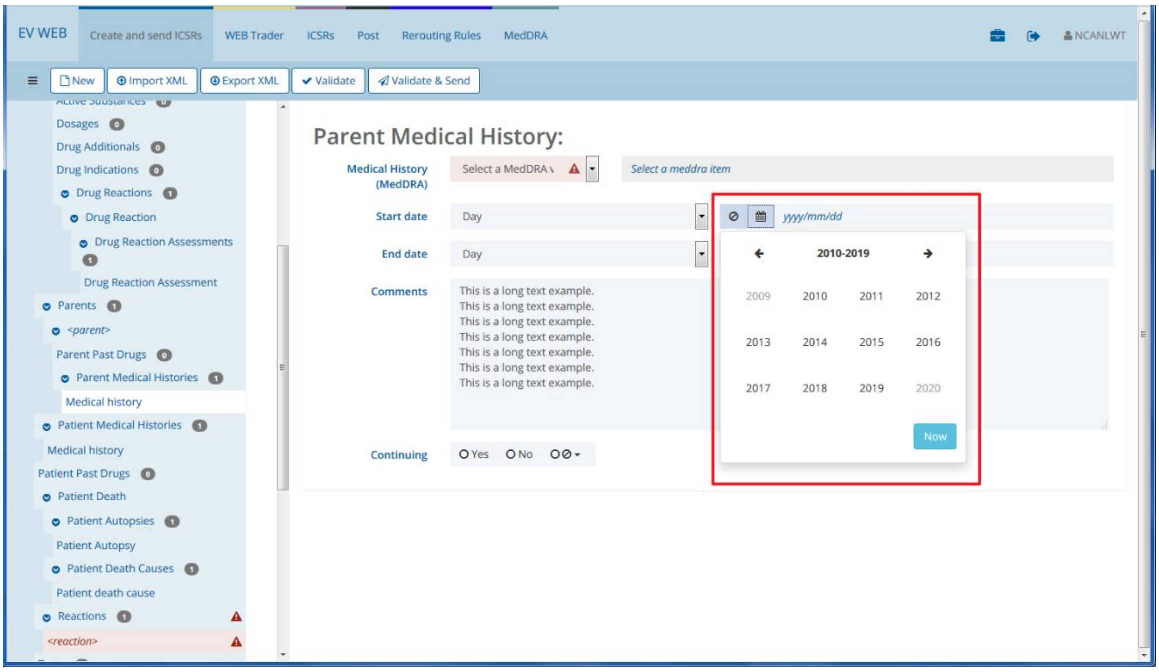


Figure 23 - Date field

Using the graphical interface: Clicking on the  icon displays the calendar. The calendar provides a grid layout for the successive selection of year, month and day.

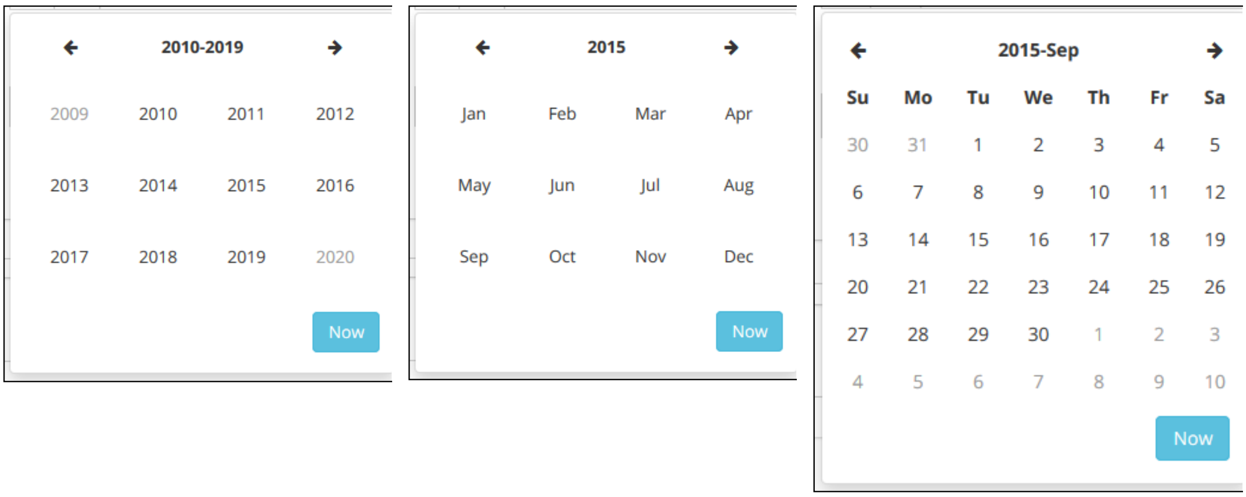


Figure 24 - Date field: Selection by year, month and day

If the date you wish to enter is the current one then you can simply click on the "Now" button on the bottom right of the calendar. This will automatically set the date field to the current date.

While in the calendar, you can retrace your selection(s) by clicking on the calendar's title (bolded text between arrows). This will move you a step backwards, allowing you to correct/change your previous selection.

2.6.1.2. Adding Precision

In some cases, your date input requirements could necessitate additional accuracy such as defining exact hours, minutes and/or seconds. EVWEB facilitates this need by providing the "precision" drop-down list field that precedes the date field. Here, you can set the precision of the date value and extend its accuracy to the required level.

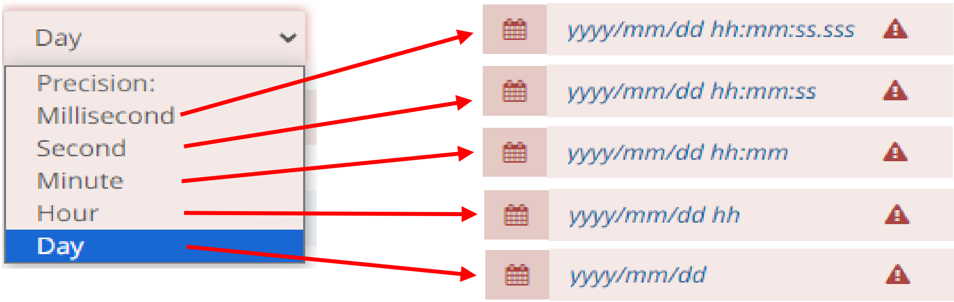


Figure 25 - Precision field options (left) in correlation with the date field (right)

For example:

- Using the date field text box

  Click within the date field text box to activate it. Then insert a date in the format yyyy/mm/dd, where yyyy is the year (i.e. 2017), mm the month (i.e. 06) and dd the day (i.e. 22). If you have enabled the precision option (from the preceding drop-down list field) then you should also insert the hours, minutes and/or seconds in the format hh:mm (i.e. 12:15), or hh:mm:ss (i.e. 12:15:30) if you have enabled a precision that includes seconds.

  Thus, we have:

  Without precision

  2017/06/22 translates into **22 June 2017**

  With precision (including seconds)

  2017/06/22 12:15:30 translates into **22 June 2017 12h 15m 30s**

Please pay special attention to the date format of the date field box, and always make sure it follows the instructed format yyyy/mm/dd (or yyyy/mm/dd hh:mm:ss if you require additional accuracy). Failing to do so will introduce a validation error.

2.6.1.3. Drop-Down List Field

In this type of field you are presented with a drop-down list from which you can select the required information.

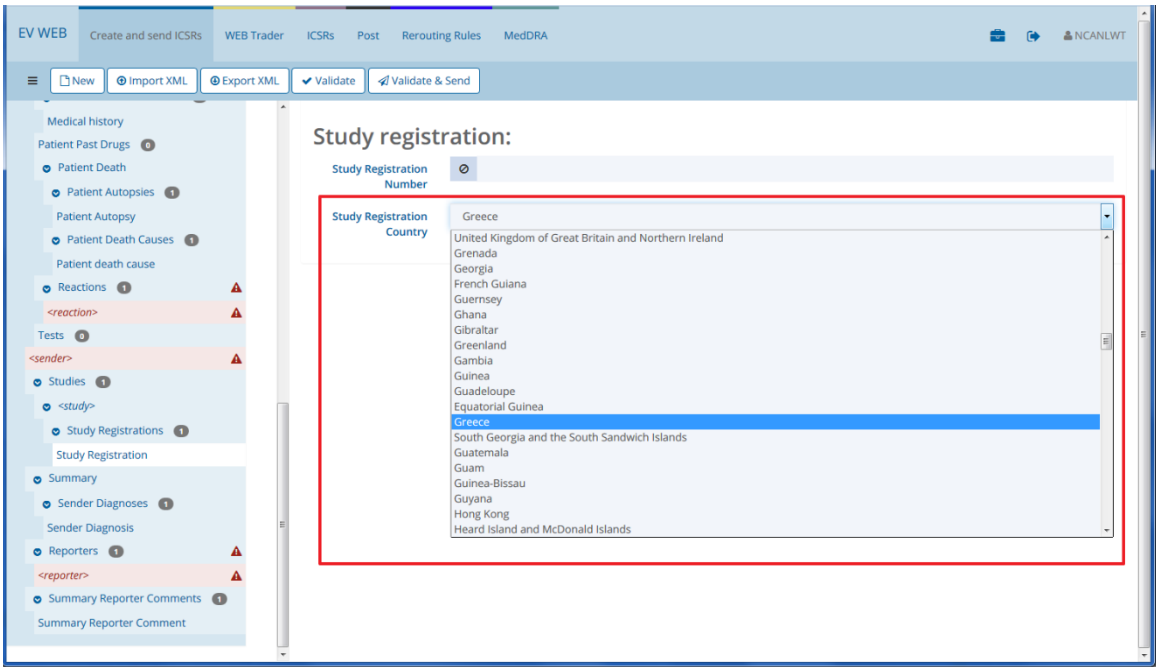


Figure 26 - Drop down list field

Select the field by clicking in it, in the same way you do to complete a text field. A drop-down list will be displayed. Choose the required information from the list by clicking on any element using your mouse pointer.

2.6.1.4. Immediate Query Field

This type of field, which is also known as a look-up field, automatically shows data from the EVDBMS as a result from the query performed in it.

Proceed as you do with a text field, by clicking in the field's box to activate it. Now start typing a few characters or words that are part of the entry you would like to insert in this field. For example, you can type "**parace**" in the field G.k.2.2 'Medicinal product name as reported by the primary source' when searching for a product name – see figure below. Soon, a drop-down list will appear with all entries that match the characters/words you have typed in. Then, you click on the suitable entry and it will be inserted into the immediate query field.

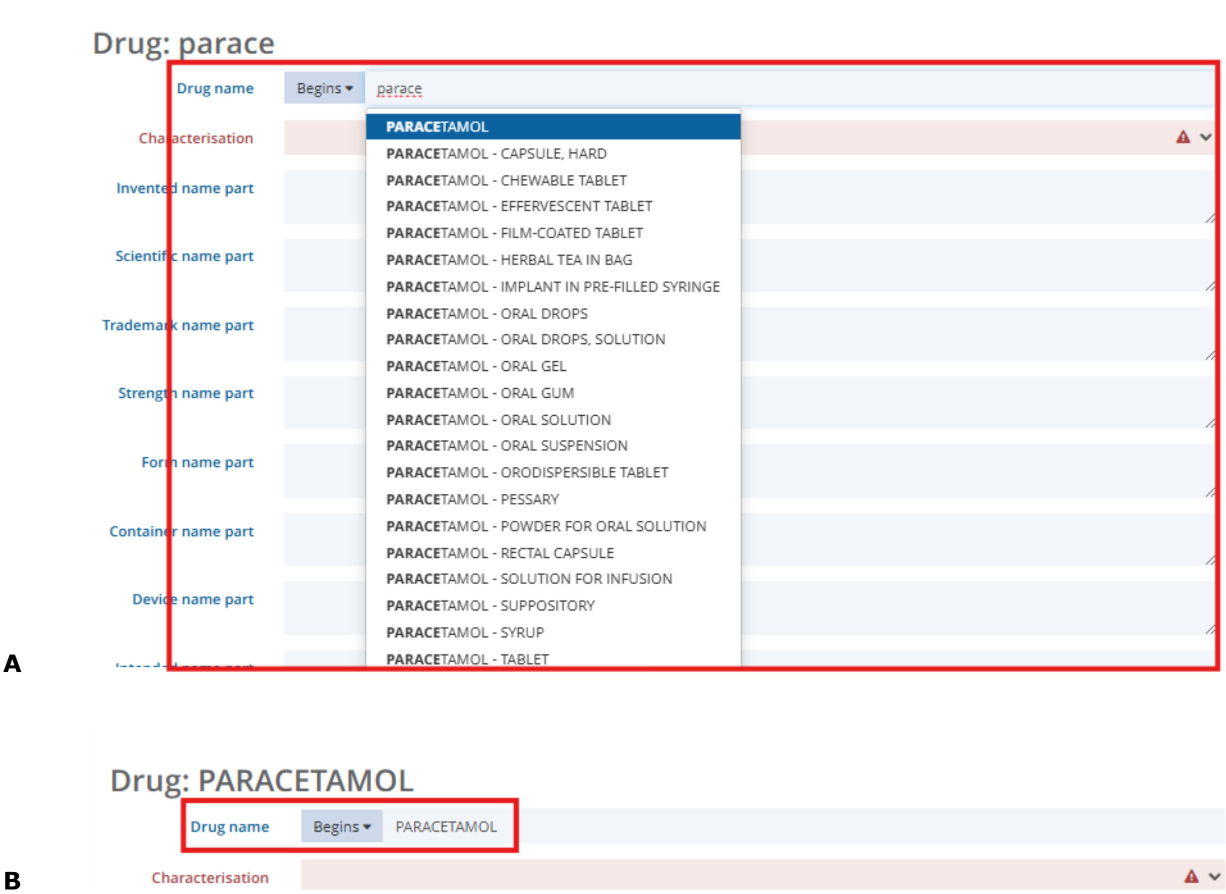


Figure 27 - Immediate query field: (A) searching for a product name and (B) name added to the field

Tip: The characters or words you type into an immediate query field are also called keywords. A keyword is text that indicates to the information retrieval systems (or search engines) what to look for and, thus, allow for the best possible match upon retrieval of that information.

Your keyword(s) can be any part of an EVDBMS entry. For example, if you type "**ulm**" as a keyword the immediate query field will include the following EVDBMS entries for you to select from:

P**ulm**atrix Inc

P**ulm**agen Therapeutics LLP

Universitaetsklinikum **Ulm**

V**ULM** SK s.r.o.

Also evident in the above immediate query field results example is that the search is not case sensitive. This means that you can query the following keywords Eudra, eudra, eUdra, and still obtain the same search results.

There are many fields in which this kind of query is used in EVWEB. Some examples are:" "Message receiver identifier" and "Drug name" (see figure below).

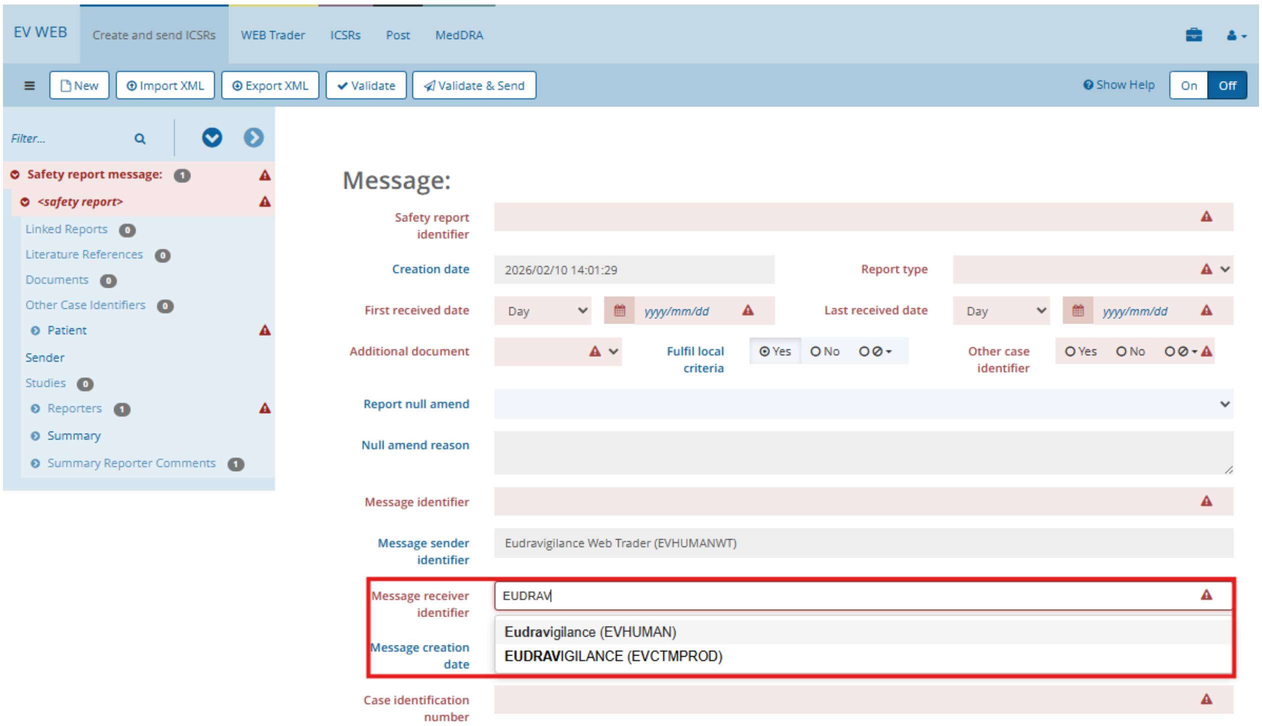


Figure 28 - Immediate query field: Message receiver identifier

2.6.1.4.1. Searching for units in Immediate Query Fields

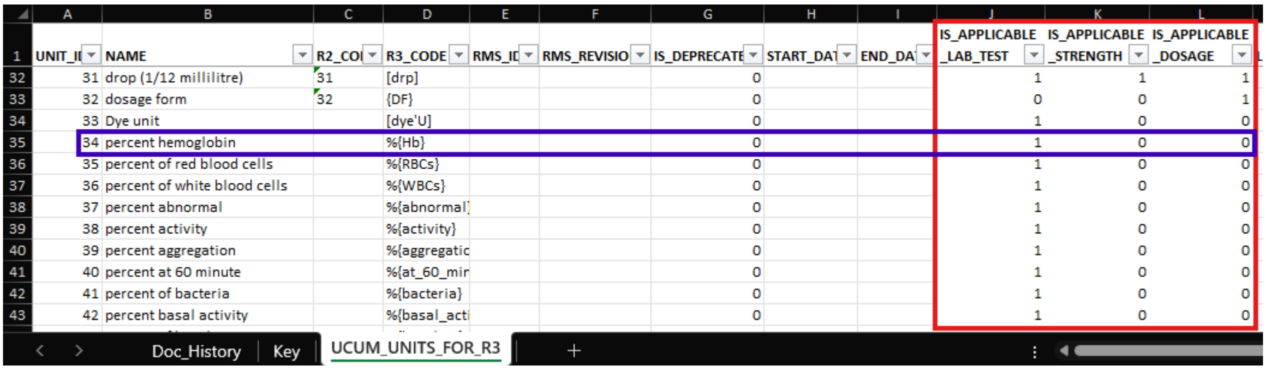
As explained above, many fields in EVWEB are Immediate Query Fields, meaning that as you type, a drop-down list of matching results will appear. Because the list of results depends entirely on the keywords you enter, accurate and relevant keywords will yield the best matches.

For some E2B fields, such as the F.r.3.3 'Test result (unit)', G.k.2.3.r.3b 'Strength (unit)' and G.k.4.r.1b 'Dose (unit)', it may not always be easy to retrieve a given unit or to ascertain whether a certain unit is a valid for that field. Therefore, in those situations it is advisable to check the Unified Code for Units of Measure (UCUM) list published by EMA.[2]

This excel file lists, on the third spreadsheet (see figure below), the different R3 units and indicates whether they are currently listed either as a **Test unit** ('IS_APPLICABLE_LAB_TEST'), as a **Strength unit** ('IS_APPLICABLE_STRENGTH') and/or as a **Dosage unit** ('IS_APPLICABLE_DOSAGE').

Note: The value '1' indicates that that unit is accepted for that field whereas the value '0' means that the unit is not accepted. In the figure below, the unit "**percent hemoglobin**" is accepted as a test unit ('IS_APPLICABLE_LAB_TEST'=1) but not as a strength unit ('IS_APPLICABLE_STRENGTH'=0) nor as a dosage unit ('IS_APPLICABLE_DOSAGE'=0).

[2] This list is currently published as an Excel file in the '**Guidance**' section of the EMA webpage Change management for the EudraVigilance system, under the '**Guidance on the enhanced EudraVigilance system**' topic (sub-topic: '**EU implementation guidance**').



1	UNIT_I	NAME	R2_COI	R3_CODE	RMS_ID	RMS_REVISIO	IS_DEPRECATE	START_DAT	END_DA	IS_APPLICABLE _LAB_TEST	IS_APPLICABLE _STRENGTH	IS_APPLICABLE _DOSAGE
32	31	drop (1/12 millilitre)	31	[drp]			0			1	1	1
33	32	dosage form	32	{DF}			0			0	0	1
34	33	Dye unit		[dye'U]			0			1	0	0
35	34	percent hemoglobin		%{Hb}			0			1	0	0
36	35	percent of red blood cells		%{RBCs}			0			1	0	0
37	36	percent of white blood cells		%{WBCs}			0			1	0	0
38	37	percent abnormal		%{abnormal}			0			1	0	0
39	38	percent activity		%{activity}			0			1	0	0
40	39	percent aggregation		%{aggregatic			0			1	0	0
41	40	percent at 60 minute		%{at_60_mir			0			1	0	0
42	41	percent of bacteria		%{bacteria}			0			1	0	0
43	42	percent basal activity		%{basal_acti			0			1	0	0

Figure 29 – UCUM Excel file snippet

2.6.1.5. Checkbox/Radio Button Fields

The checkbox/radio button fields allow the selection of a true or false state (checkbox field) or the selection of a mutually exclusive state (radio button field). Consequently, the checkbox field usually contains a single item for you to state as true (ticked box) or false (unticked box), whereas the radio button field always contains two or more items of which only one can be selected.

Figure 30 - Checkbox/radio button fields

2.6.1.6. Nullflavour flags

The ICH E2B(R3) ICSR standard requires that mandatory data fields must always be completed in an ICSR and should not be empty.

In some situations, though, mandatory data fields might be required to appear empty for specific reasons and still have the ICSR considered valid. The issue of such required empty fields is handled through the use of "Null Flavour" flags. These flags allow a mandatory field to appear valid and provide the receiver of the ICSR with a reason for the lack of data for that field. Therefore, valid ICSRs can be created containing mandatory fields without actually including real values in them.

The reason for a blank field is referred to as the “flavour” of the null value. Currently, EVWEB provides the following Null Flavour flags:

Table 4 – Nullflavor flags

Nullflavour flag	Description
Masked (MSK)	There is information on this item available, but it has not been provided by the sender due to security, privacy or other reasons.
Unknown (UNK)	A proper value is applicable but not known.
Asked but unknown (ASKU)	Information was requested but not received (i.e. patient was asked but didn't know what to reply).
Not asked (NASK)	Information was not requested.

When an EVWEB field supports a Null Flavour flag, the icon will appear next to it. If you click on the icon, you will be presented with the applicable values for the specific field.

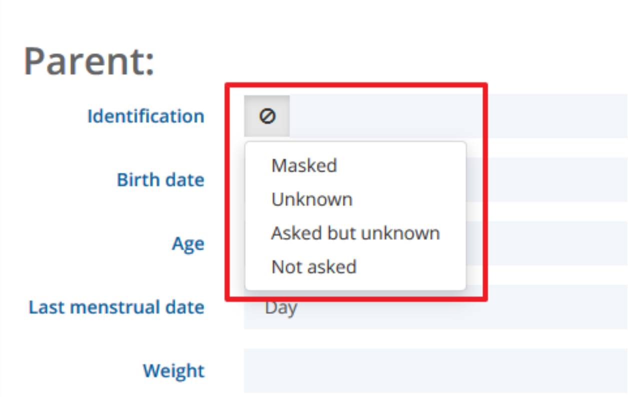


Figure 31 - Null Flavour flags

2.6.2. Adding & Removing/Deleting Tree View Area Sections/Sub-sections

During the data entry process you may be required to add a new sub-section to the tree view area. This can be done by clicking on the icon that appears once you hover the mouse pointer over a tree view section that allows such an action. An example of this process can be found in the **Create and send ICSRs** screen of the EVWEB application.

Tree view area sections also allow the creation of multiple sub-sections within them. In order to do this you should click on the icon more than once, depending on the number of sub-sections required.

Another useful option when dealing with sub-sections is the ability to create a copy of them within the same section. This is very handy when data is quite similar (or identical) between multiple sub-sections. To create a copy of a sub-section, hover the mouse pointer over it and click on the icon that appears on the right side of the sub-section.

The sub-sections you add can, of course, be removed/deleted. To do this, you have to hover the mouse pointer over the sub-section you need to remove in the tree view area and click on the icon that becomes available in these situations.

Note: Please note that there is no "undo" function in EVWEB, so it is **not** possible to recover a deleted item/sub-section.

2.7. Search Methods

2.7.1. Simple Query

When applicable, the simple query field is located below the main menu as shown in the screenshot below. Here you can enter keywords and initiate the search by clicking on the magnifying glass icon ( ).

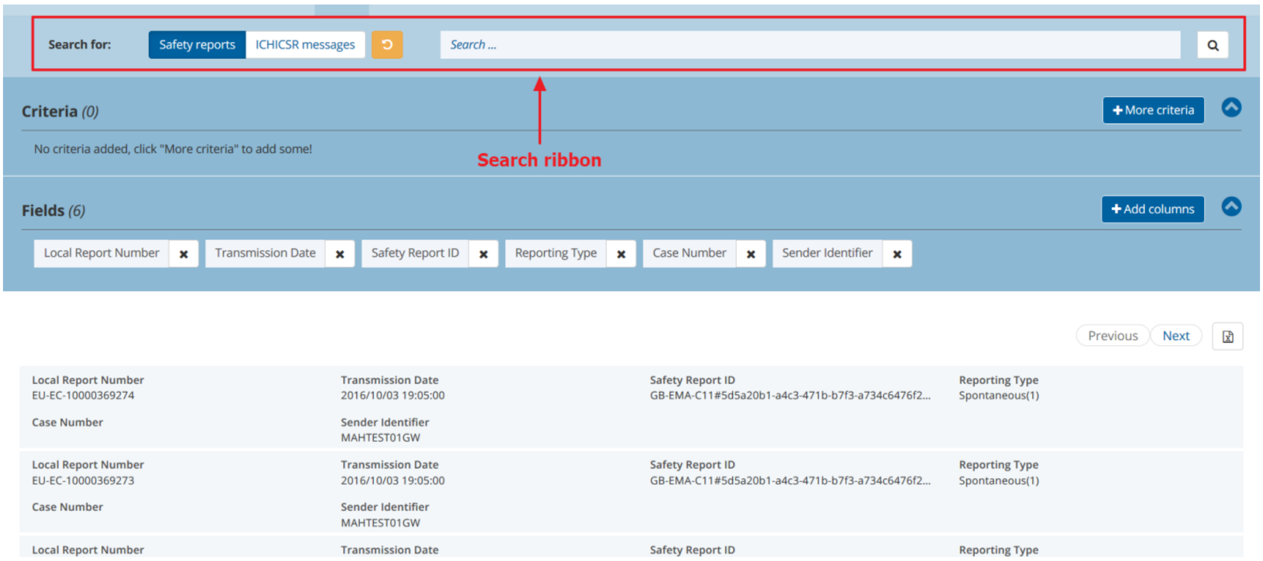


Figure 32 - Simple query in the ICSRs screen

You can perform a simple query on ICSRs or Safety messages in the **ICSRs** screen of the EVWEB application. You can choose the type of simple query by clicking on one of the buttons (Safety reports / ICHICSR messages) that reside in the Search ribbon.

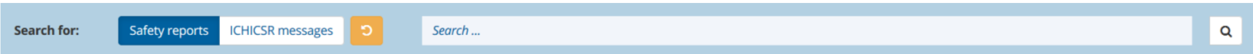


Figure 33 - The search ribbon in the ICSRs screen

Note: In contrast to the previous version of EVWEB, in which the query functions supported the use of wildcards such as "*" and "?", the newly re-written EVWEB supports only queries carried out with the "contains" clause (wildcards are not supported). This means that your keyword(s) can be any part of an EVDBMS entry (i.e. characters from the beginning, middle or end of an EVDBMS entry). Furthermore, this type of query is not case sensitive, allowing for the use of capital or small characters, or even a combination of them.

The following example shows how to perform a simple query on ICSRs. Click on the **ICSRs** screen in the main menu to enter it.

Figure 34 - ICSRs screen link

Type an ICSR worldwide case ID, Safety report identifier or local message number in the simple query field and click on the magnifying glass icon (). The active area will display your results in a list view layout.

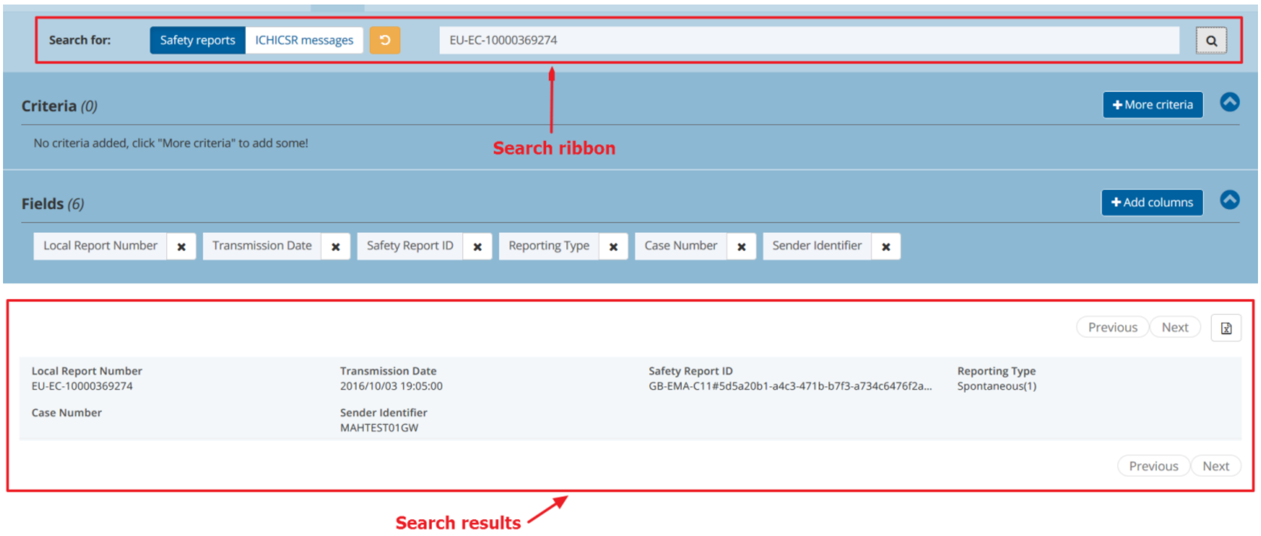
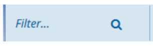


Figure 35 - Simple query on Safety reports (ICSRs)

Note: An additional simple query feature is available in the Create and send ICSRs screen. Located within the tree view area and at the top, is a simple query type field containing the text "Filter…" in it (

). You can use this query field to search for any matching section/sub-section in the current tree view area.

2.7.2. Advanced Query

EVWEB allows you to perform elaborate queries in the EVDBMS (i.e. MedDRA terms, ICSRs, Safety messages).

The advanced query parameters that describe and define such a query are available as separate ribbons under the Search ribbon. As an example, the advanced query parameters available for ICSRs in the **ICSRs** screen are displayed.

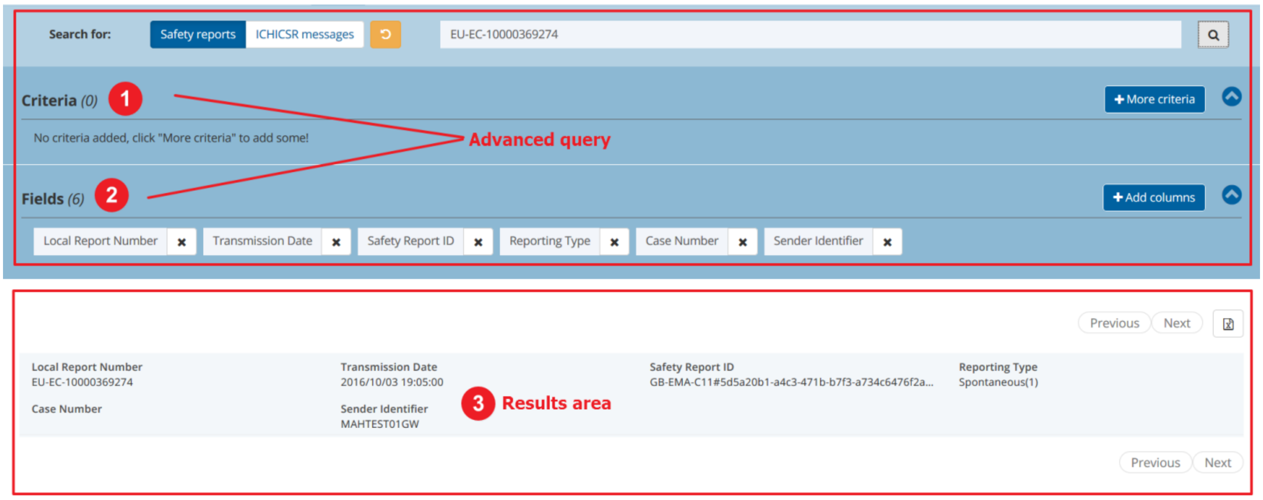


Figure 36 - Advanced query fields

Every advanced query is divided in 3 different areas (see above screenshot for reference):

1. Criteria ribbon
2. Fields ribbon

3. Results area

Criteria and fields are used in combination, to better target the scope of the query. The results area in this query case is actually the active area of the **ICSRs** screen.

Note: In contrast to the previous version of EVWEB, in which the query functions supported the use of wildcards such as "*" and "?", the newly re-written EVWEB supports only queries carried out with the "contains" clause (wildcards are not supported). This means that your keyword(s) can be any part of an EVDBMS entry (i.e. characters from the beginning, middle or end of an EVDBMS entry). Furthermore, this type of query is not case sensitive, allowing for the use of capital or small characters, or even a combination of them.

2.7.2.1. Criteria Ribbon

The criteria ribbon is used to define the conditions of an advanced query. This area allows you to select one or more items and define their value. These items are then used as criteria to filter the results of the advanced query.

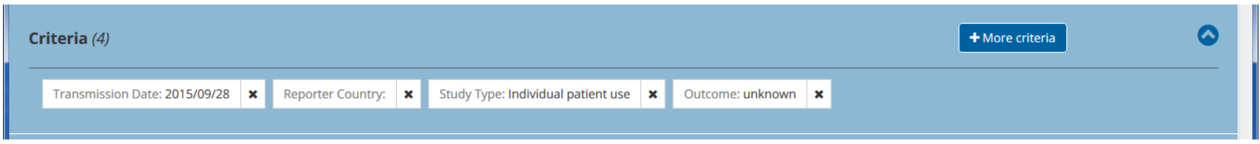


Figure 37 - Criteria ribbon

To add a criteria item you need to click on the "+More criteria" button that is located in the criteria ribbon. This will produce a drop-down list from which you can select the desired criteria item. You can repeat this process as many times as necessary to obtain all criteria items required for your advanced query.

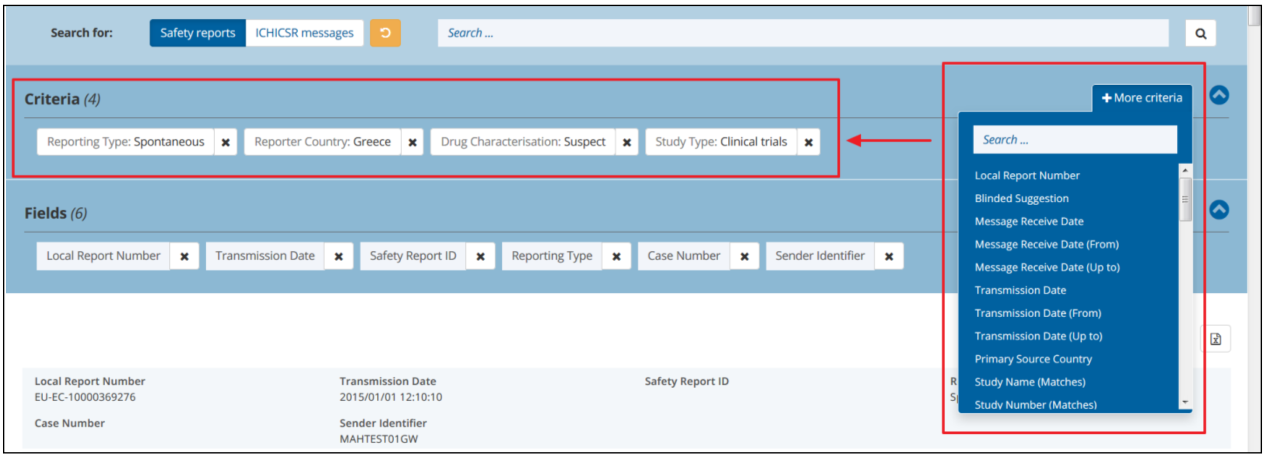


Figure 38 - Adding a criteria item

Tip: If the "+More criteria" button is not visible in the criteria ribbon then this means that the ribbon is in collapsed mode. You should click on the icon which will expand the ribbon, allowing access to the "+More criteria**"** button.

Once you have selected your criteria items, and before you perform the query, you should define their values. This is accomplished by clicking on each criteria item that you have inserted in the criteria ribbon, and defining their value using the available options presented.

Depending on criteria type, when you click on an inserted criteria item you will be presented with a drop-down list (or a calendar in the case of date criteria items) from which you can choose the required option.

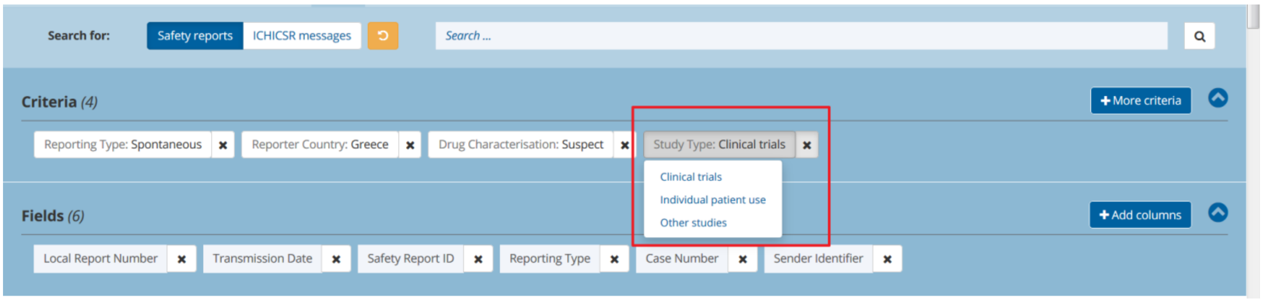


Figure 39 - Defining criteria item values

To remove a criteria item you simply need to click on the ✖ icon located on the right-hand side of the item.

Alternatively, and if you need to remove all inserted criteria items at once, you can click on the "Reset and start over" button ( ) which is located in the Search ribbon. <u>Note, though, that this action will reset all options and values on the current page</u>.

2.7.2.2. Fields Ribbon

The fields ribbon is used to define the output of an advanced query. This means that the items displayed in the results area will contain only the fields previously inserted in this ribbon.

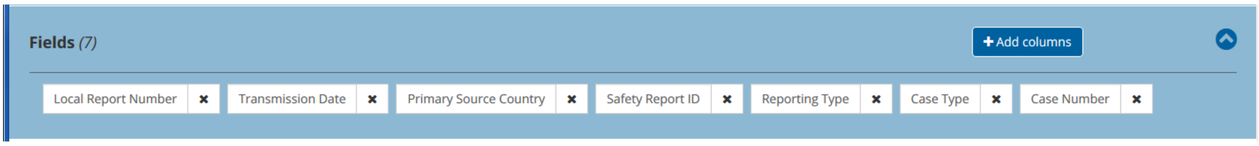


Figure 40 - Fields ribbon

Usually, some of the items displayed in the fields ribbon are the default ones. This means that if you run the query without inserting any new items in the fields ribbon, the default ones will be considered as active.

To add a field item you need to click on the "+Add columns" button that is in the fields ribbon. This will produce a drop-down list from which you can select the desired field item. You can repeat this process as many times as necessary to obtain all field items required for your advanced query.

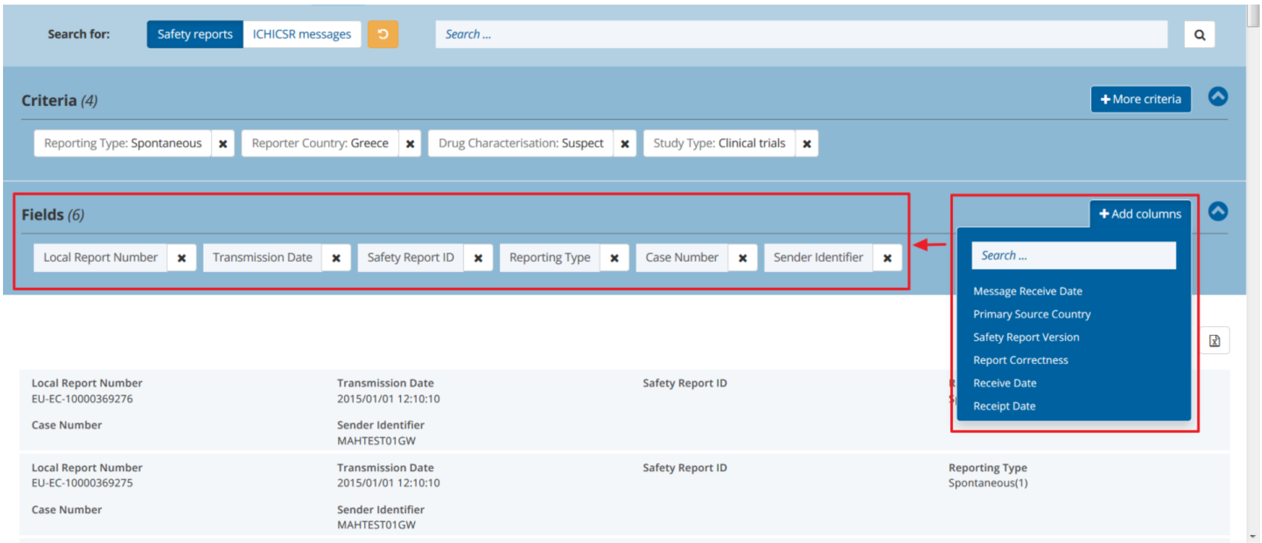


Figure 41 - Adding a field item

Tip: If the "+Add columns" button is not visible in the fields ribbon then this means that the ribbon is in collapsed mode. You should click on the icon which will expand the ribbon, allowing access to the "+Add columns" button.

If you insert your own field items, and after having run the query at least once, you will notice that these inserted items remain active in the fields ribbon throughout the current EVWEB session.

To remove a field item you simply need to click on the ✖ icon located on the right-hand side of the item.

Note: The default fields ribbon items can be restored either by clicking on the "Reset and start over" button ( ) which is located in the Search ribbon, or by initiating a new EVWEB session. Keep in mind, though, that these actions will reset all options and values on either the current page (when clicking on the "Reset and start over" button), or in the entire EVWEB session (when initiating a new EVWEB session).

2.7.2.3. Results Area

To initiate a query, after having specified the criteria and fields, you need to click on the magnifying glass icon ( ) in the Search ribbon. The results of the query will be displayed in the active area of the current EVWEB screen in a list view layout.

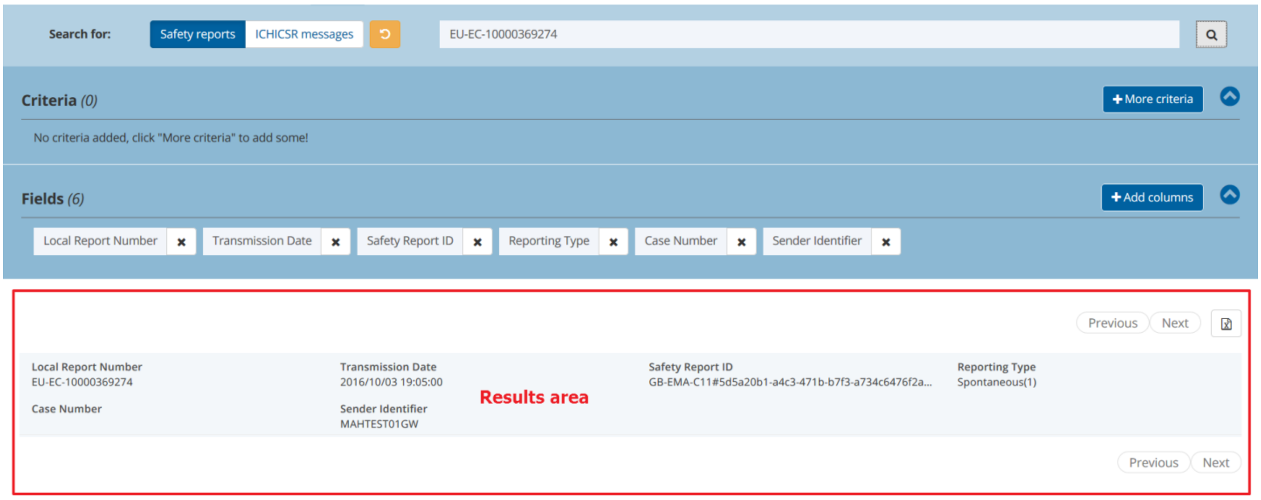


Figure 42 - Results area

When running a query, the system will always return, as the result, a maximum of 50 search items. When the number of items exceeds that limit then one of the following options becomes available to the user, depending on the active EVWEB screen:

- For the screens **ICSRs**, **ICSR Recode** and **Terms** (Recoding/Management/Activity Log/System Log/Interpretation), the following navigation buttons will appear at the top and bottom right of the active area:

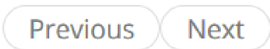


Figure 43 - Previous/Next page navigation buttons

These navigation buttons allow you to move forward or backward on the results currently displayed on your screen.

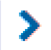
- For the screens **WEB Trader**, **Rerouted ACKs** and **MedDRA**, a set of numbered page navigation buttons will appear at the top and bottom right of the active area:

Figure 44 - Numbered page navigation buttons

These numbered page navigation buttons allow you to move forward or backward on the results currently displayed on your screen. The table below provides further information on each button type included in the set.

Table 5 – Page navigation buttons

Page Navigation Button	Description
	Moves you to the first page of the results.
	Moves you one page backward.

Page Navigation Button	Description
	Moves you one page forward.
	Moves you to the last page of the results.

Tip: For a more fine-tuned navigation on the query results, you can click on the individual page numbers that appear in the page navigation buttons.

Numeric indicators of the displayed search items' range, along with the total number of items resulting from the query, appear at the top and bottom left of the active area.

1-50 of 863

Figure 45 - Numeric indicator of query results

Note: To clear the results area and initiate a new simple or advanced query click on the "Reset and start over" button () which is located in the Search ribbon.

2.7.3. Advanced List Criteria Query

This special search method deserves its own paragraph, despite belonging to the criteria ribbon functionality. The advanced list criteria query method provides a more refined way of looking up EV data within a criteria item, leading in turn to a quicker and easier set up of a simple or advance query.

Furthermore, this search method offers extra query modes and, thus, is not restricted to EVWEB's regular "contains" clause which is used in simple and advanced queries. These modes are as follows:

Table 6 – Description of the Query Modes

Query Mode	Description
Begins	Finds only matches which start with the search term.
Matches	Finds only matches which are identical with the search term.
Contains	Finds the search term anywhere in the name – beginning, middle, or end.
Sounds Like	Searches for a similar combination of consonants in the search term. This query ignores vowels and is useful where spelling is uncertain. **Note:** This query mode appears in select criteria items.

The abovementioned query modes can be defined and utilised within a selected criteria item that supports this functionality. Such criteria items can be located in the **ICSRs** screen and, as of this writing, are the following:

- Case Number
- Safety Report ID
- Medicinal product
- Local Report Number

- Message Number
- Sender identifier (Matches)
- Drug indication (code)
- Reaction Low Level Term (code)
- Reaction Preferred Term (code)
- Reaction System Organ Class (code)
- Active substance
- Active Substance Group
- Active Substance Combination
- Active Substance MLM Group
- Active Substance MLM Combination

Once you add such an item in the criteria ribbon and click on it, you'll be presented with options to select the query mode and enter your search term. In the following screenshot the user has selected the "Begins" query mode and has inserted the search term "NCA":

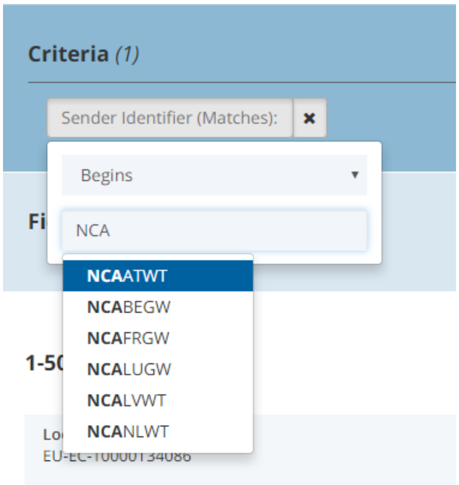


Figure 46 - Advanced List Criteria Query

As is evident in the screenshot, the search term field behaves as an immediate query field type (aka look-up field), assisting the user in finding the proper term and selecting it for the main **ICSRs** screen query.

2.8. Loading Data

Loading data is the action of transferring information from different sources into EVWEB.

There are 3 different loading processes available:

1. Load from the EVDBMS (ICSRs and WEB Trader screens)
2. Load from a local file (Import XML function)
3. Load from within EVWEB (Follow-up function)

Notes:

- When utilising the last two abovementioned loading processes (Import XML and/or Follow-up functions), the MedDRA version of the loaded data will be automatically updated to the latest MedDRA version. This may lead to some terms being invalidated (due to terms following older MedDRA version naming schemes); in such cases, the user must correct them accordingly to be able to proceed with the intended process.
- The above loading processes are also available from the **Workspace** screen ( ) once you have added the data (i.e. ICSR, Safety and Acknowledgements messages) to it. The **Workspace** screen allows for better data review and management when dealing with multiple items. You can find more information regarding the **Workspace** screen and its functions in section **3.7. Workspace Screen Functions** of this manual.

2.8.1. Load from the EVDBMS

2.8.1.1. ICSRs Screen

One way to load from the EVDBMS is to initiate a simple or advance query in the **ICSRs** screen of EVWEB. Once the search results area has been populated with ICSRs or Safety messages, you can click on a search result item to display the contextual actions menu (see **section 2.9. Contextual Actions Menu** for more information regarding this feature). This menu will appear above the selected search result item.

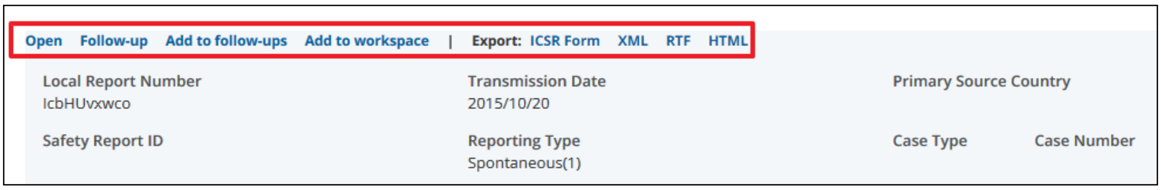


Figure 47 - Contextual actions menu

To load the selected item into your EVWEB session, you need to click on the “Open” option in the contextual actions menu. This will retrieve and display the item in a typical, read-only, tree view and active area layout.

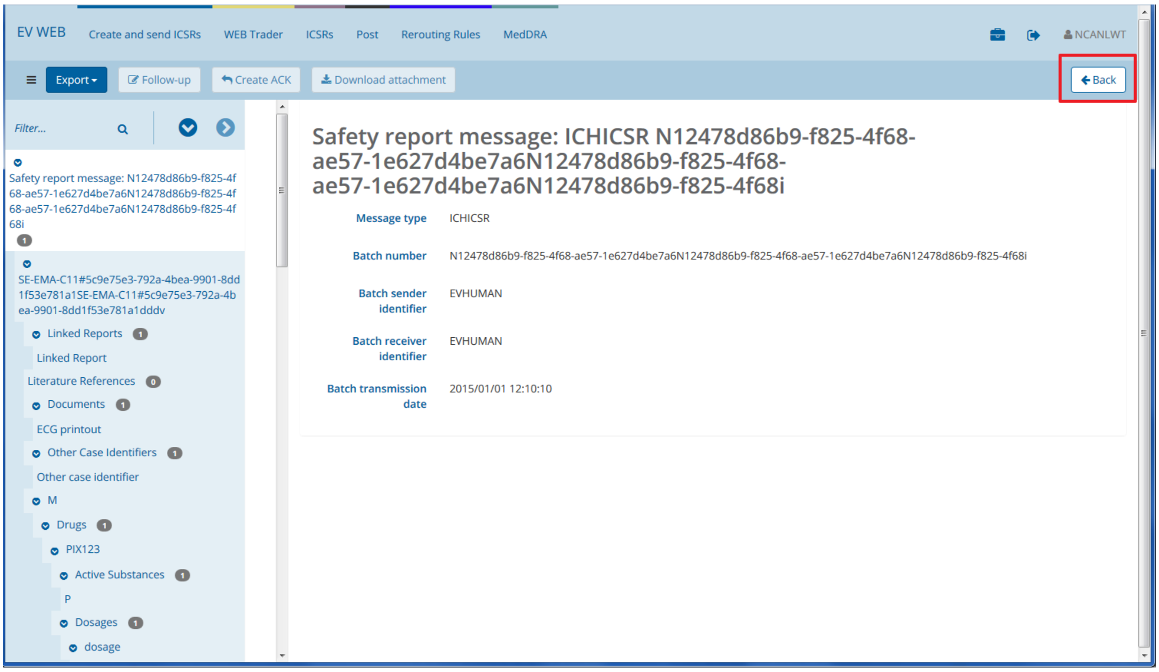


Figure 48 - Loading of an ICSR from the ICSRs screen

Note: If the loaded ICSR or Safety message has been received and processed by the receiving party, then basic information of its Acknowledgement message will be displayed in the tree view layout of the opened ICSR or Safety message.

To close the loaded search result item and return to the previous screen, click on the "Back" button which is located on the far right of the dynamic buttons set (see above screenshot for reference).

Note: It is also possible to load a search result item in the **Workspace** screen of EVWEB. This allows for better review and management since you can add multiple items to the **Workspace** screen and concentrate specifically on those items. To do this, you need to click on the option "Add to workspace" in the contextual actions menu which appears above the selected search result item. You can find more information about the **Workspace** screen and its functions in section **3.7. Workspace Screen Functions** of this manual.

2.8.1.2. Download Attachments

After opening an ICSR for viewing it is possible to view associated attachments, <u>if allowed by the level of access the user has to that ICSR</u>. The EudraVigilance system associates all attachments submitted for different versions of the same ICSR (linked by the worldwide case ID) regardless of the organisation that sent the ICSR. Master ICSR cases will also link to the associated documents in the underlying identified duplicate cases.

Figure 49 below shows the buttons that are available when viewing an ICSR, these buttons will retrieve a list of all associated document attachments or literature attachments.

Figure 49 - Download attachments

Figure 50 and **Figure 51** below show the list of available documents that can be downloaded for the different versions of the same ICSR, the list includes the safety report ID and the date the safety report that included the attachment(s) was received.

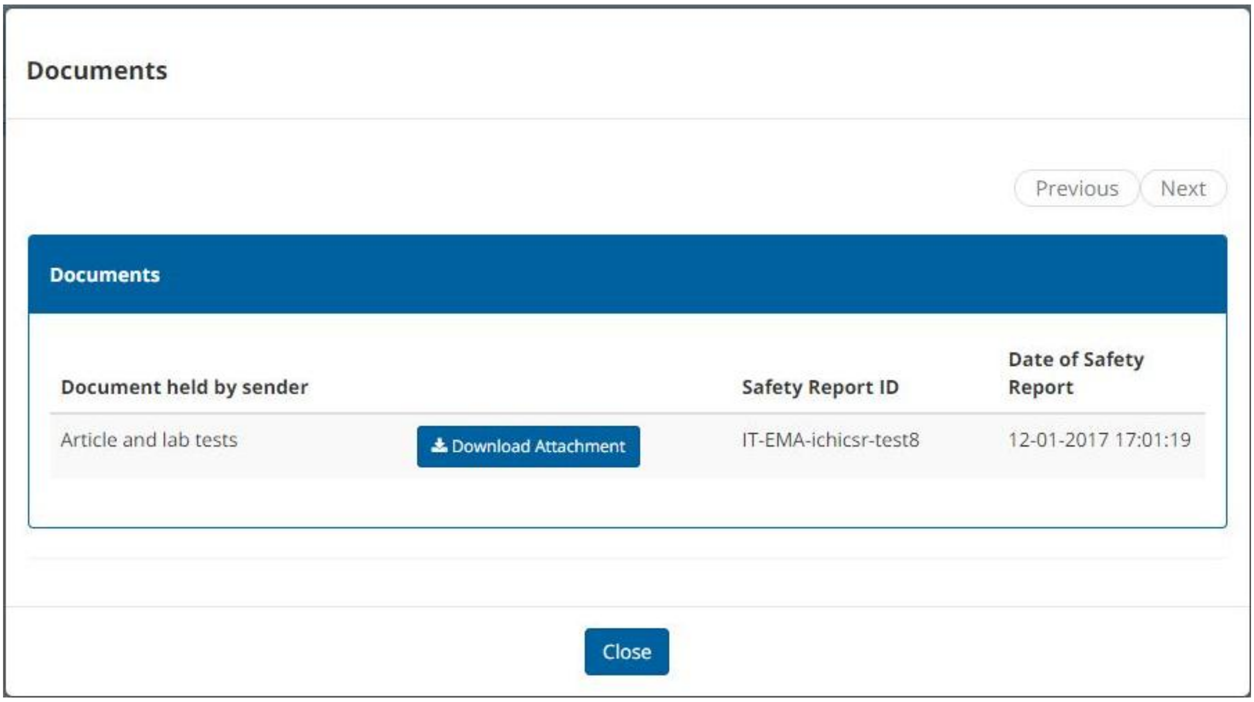


Figure 50 - Download associated documents

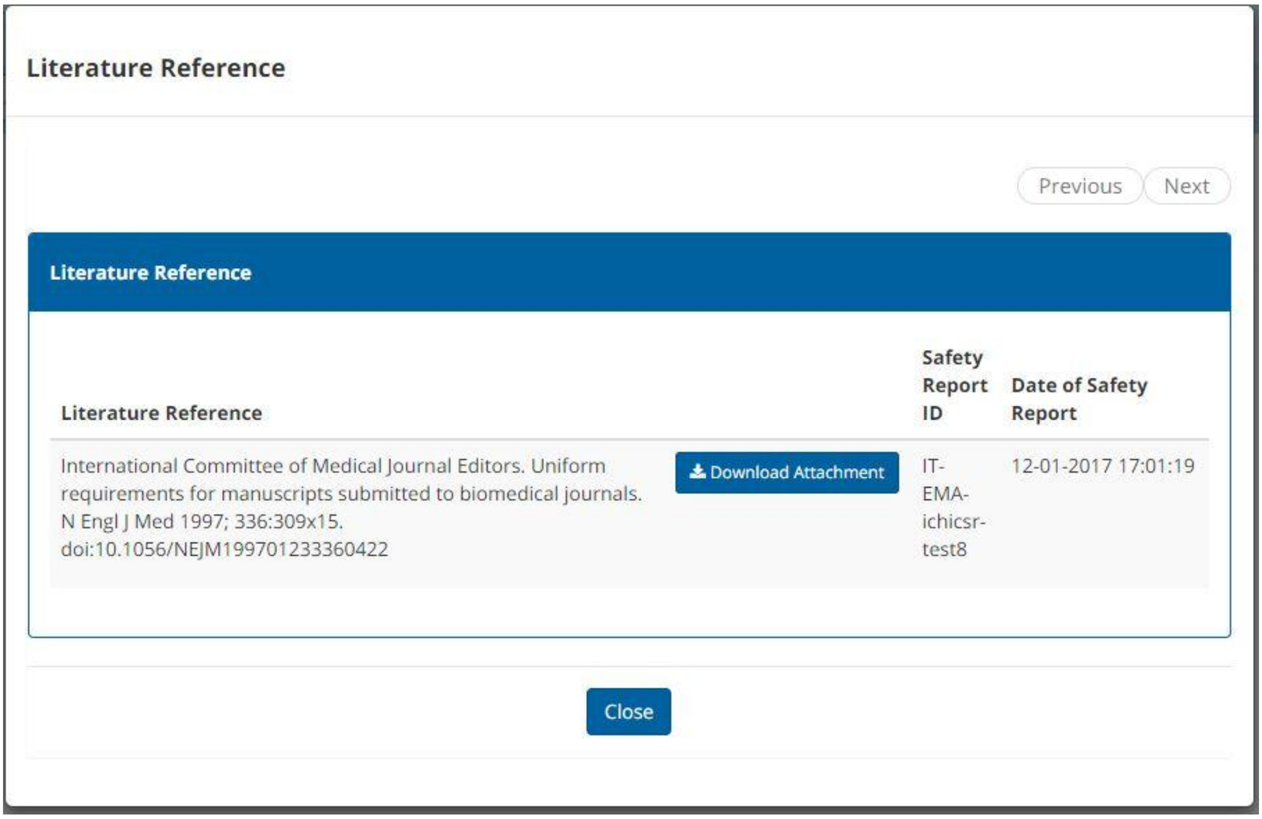


Figure 51 - Download associated literature articles

In addition to accessing all associated attachments for different versions of an ICSR, it is also possible to download the attachment in the ICSR being viewed. In order to do this, select the literature reference or document of interest from the tree view and then press the **download attachment** as shown in **Figure 52** below.

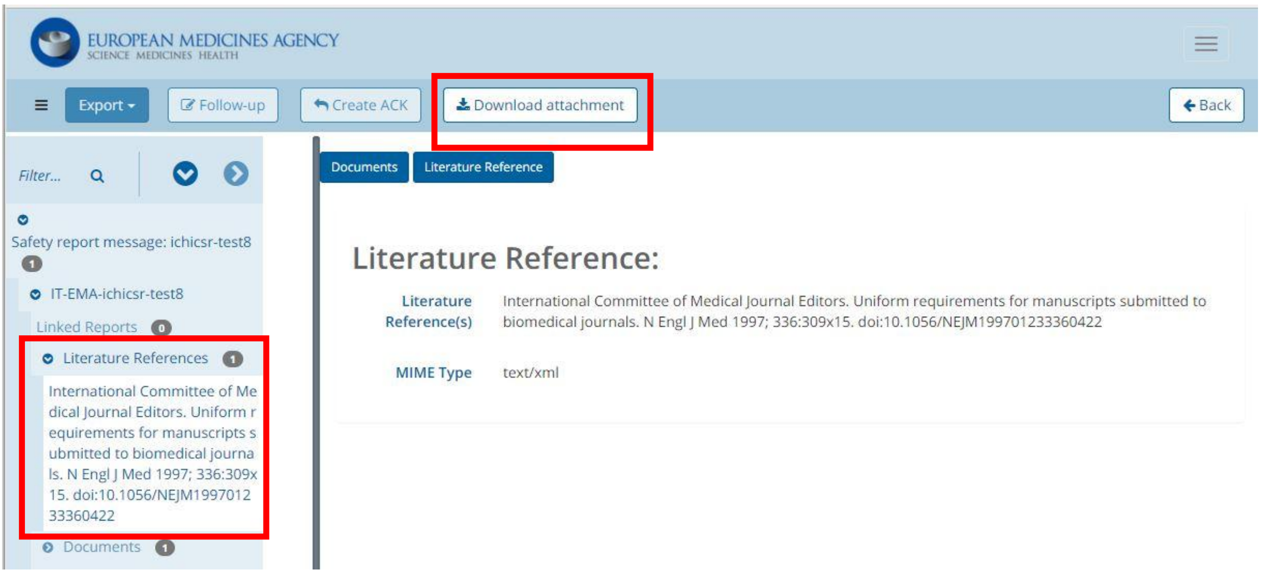


Figure 52 - Download a document from the currently viewed ICSR

2.8.1.3. WEB Trader Screen

Another way to load data from the EVDBMS is from the **WEB Trader** screen in EVWEB. WEB Trader keeps track of sent and received Safety and Acknowledgement messages. To load one of these messages you need to click on it in the active area and select the "Open" option from the contextual actions menu that appears above the selected WEB Trader message.

Note: To toggle between the received ("Inbox" view) and sent ("Outbox" view) messages you should click on the icon that appears next to the "Search" button.

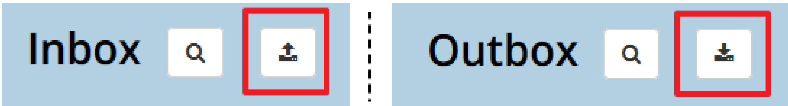


Figure 53 - WEB Trader Inbox & Outbox views

Figure 54 - WEB Trader "Outbox" screen

This will retrieve and display the item in a typical, read-only, tree view and active area layout.

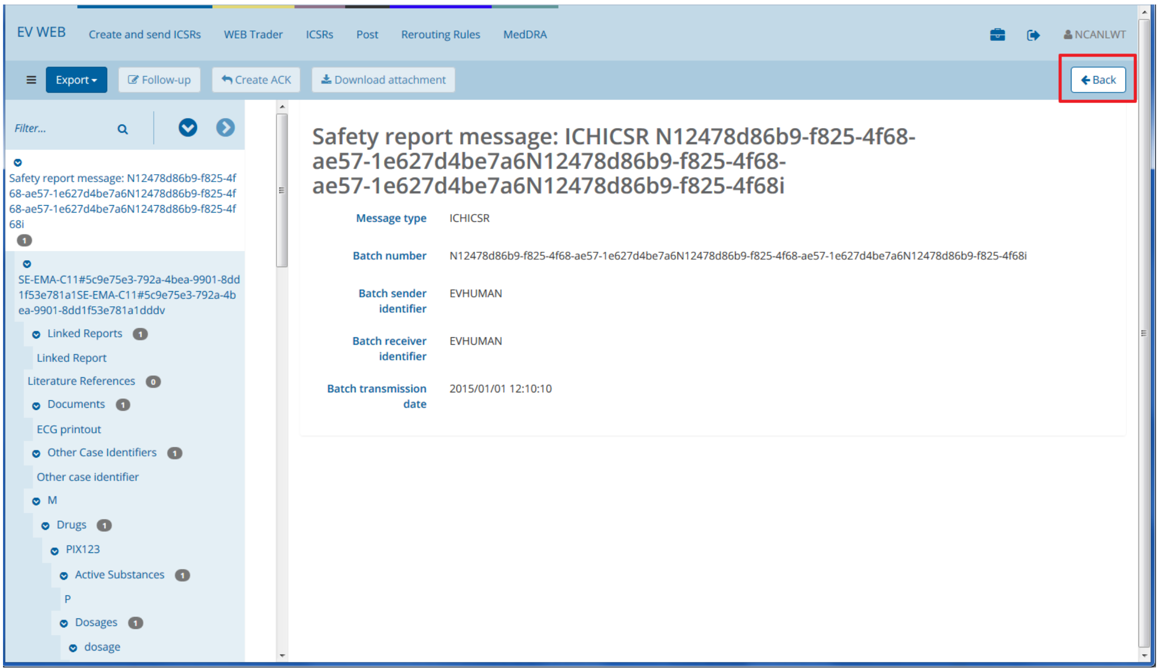


Figure 55 - Displaying retrieved data from the WEB Trader screen

To close the loaded message and return to the previous screen, click on the “Back” button which is located on the far right of the dynamic buttons set (see above screenshot for reference).

Note: It is also possible to load a WEB Trader message in the **Workspace** screen of EVWEB. This allows for better review and management since you can add multiple messages to the **Workspace** screen and concentrate specifically on those items. To do this, you need to click on the option “Add to workspace” in the contextual actions menu which appears above the selected WEB Trader message. You can find more information about the **Workspace** screen and its functions in section **3.7. Workspace Screen Functions** of this manual.

2.8.2. Load from a Local File

This kind of loading process is used to import data from an XML file available locally (on your computer or your local network) into the EVWEB application. It is possible to load from a local file any kind of message handled by EVWEB, such as Safety and Acknowledgement messages.

Load from a local ICH E2B(R3) file is available from different EVWEB screens such as:

1. **Create and send ICSRs**
2. **WEB Trader** (when creating an Acknowledgement message)
3. **Post**
4. **Workspace** (“Messages” tab only)

The following example loads a local file in EVWEB from the **Workspace** screen.

While in the “Messages” tab, click on the single XML file import button (), which is located in the top left side of the **Workspace** screen area.

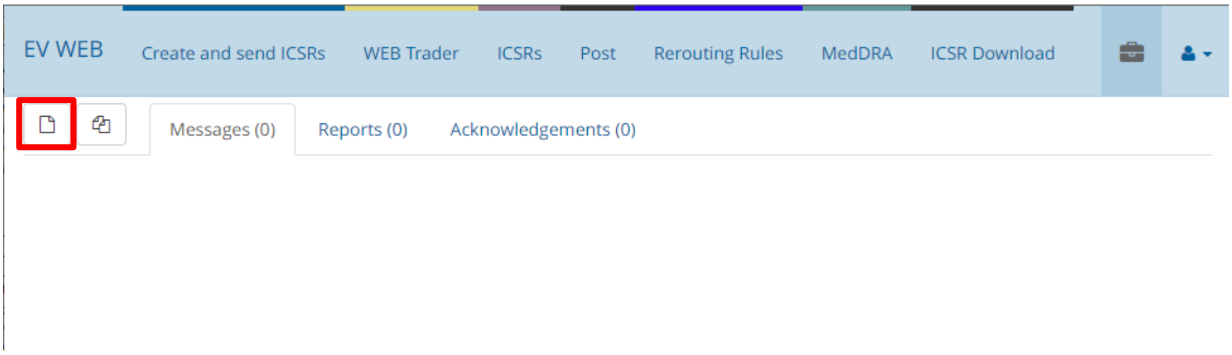


Figure 56 - Loading a local file from Workspace

A file selection window will appear in which you can locate and select your local XML file.

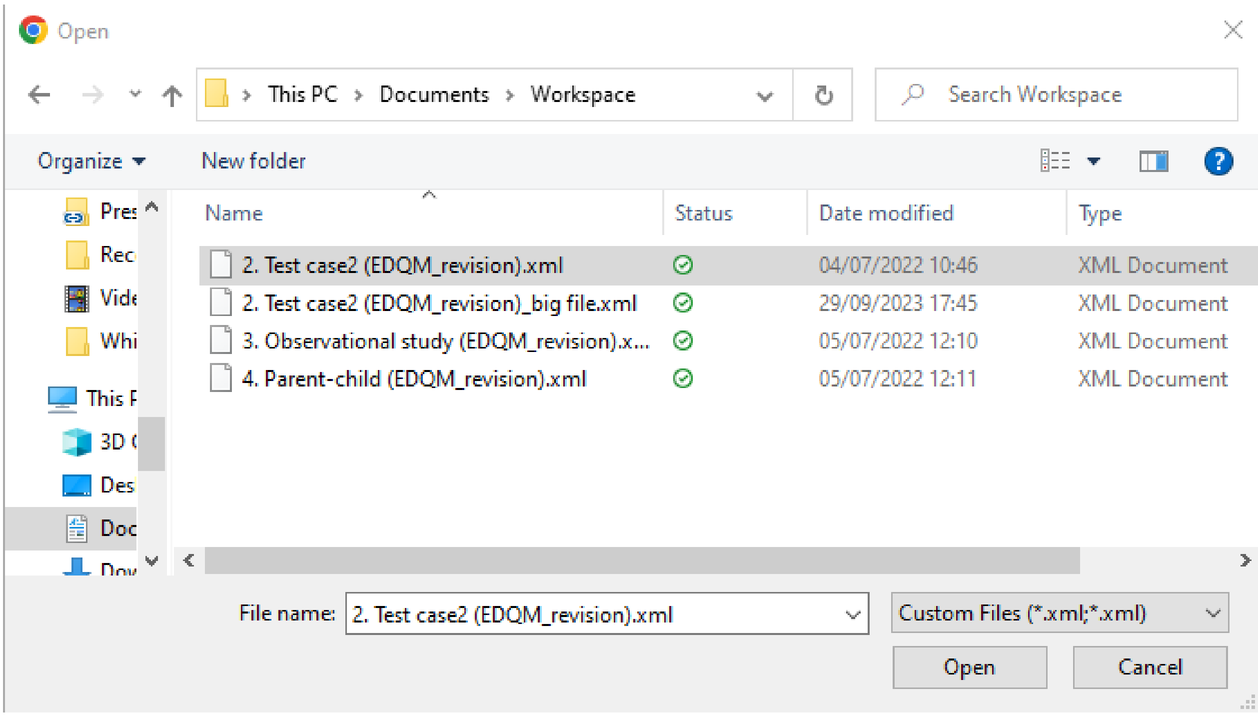


Figure 57 - File selection window

Once the process is completed, the imported XML file appears in the "Messages" tab of the **Workspace** screen.

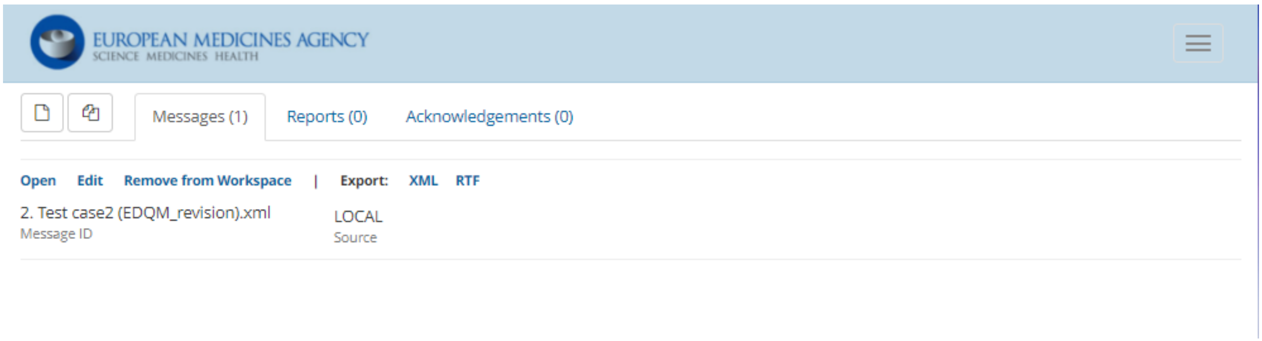


Figure 58 - Imported XML file in "Messages" tab of Workspace screen

You now have the ability to review and manage the imported message. Click on it to display the contextual actions menu which will show the acceptable functions applicable to this message.

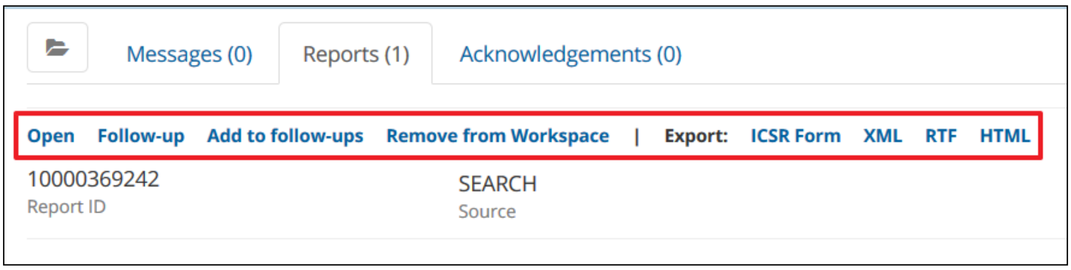


Figure 59 - Contextual actions menu in the Workspace screen

2.8.3. Load from Within EVWEB

This operation does not actually load any external data. Instead, it creates new items in a data entry screen (i.e. **Create and send ICSRs**) and eventually fills in some of the newly created sections with data taken from other screens (i.e. "Follow-up" option in the **ICSRs** screen).

As an example of this loading process, we will look at the creation of a new ICSR in the **Create and send ICSRs** screen.

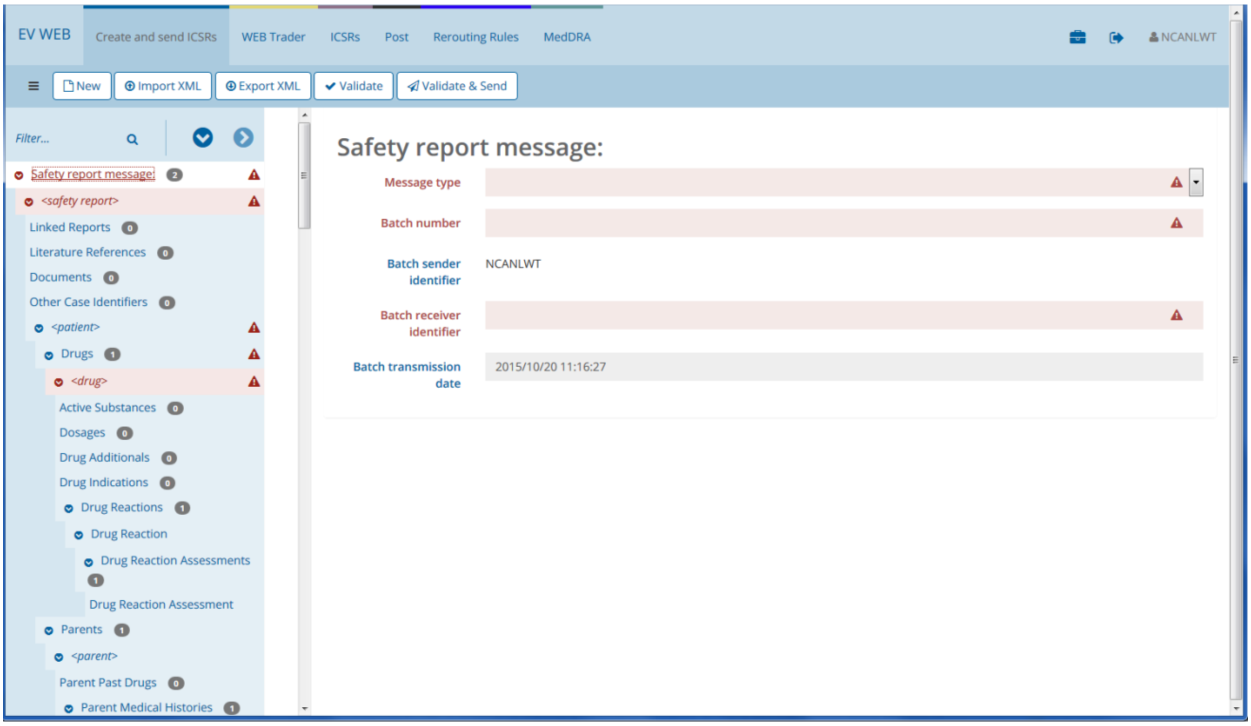


Figure 60 - Load from within EVWEB – Create and send ICSRs screen

As you can see, all the fields are empty because in this case we have created a new ICSR and it is supposed to be completed by the user. In other situations (like the "Follow-up" option), you will find some fields already completed.

2.9. Contextual Actions Menu

In certain screens of the EVWEB application (**WEB Trader**, **ICSRs**, **Workspace**) you will be presented with a contextual actions menu when selecting items in the active area (or in the search results area after performing a query). This applies only to list view layouts of the active area.

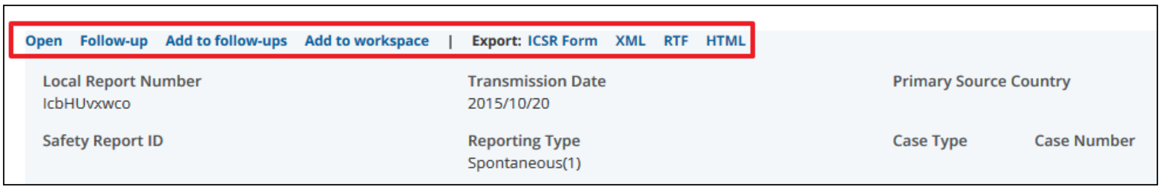


Figure 61 - Contextual actions menu

Contextual action menus provide specific operations that can be applied to a selected item. Based on the selected item type (i.e. ICSR, Safety or Acknowledgement message), the available options in a contextual actions menu will vary, displaying only the applicable actions for the specific item type.

For a detailed description of contextual actions menu options per EVWEB application screen, see the relevant parts of the following sections:

- **3.4.1. Handling Messages in WEB Trader**
- **3.5.1. Handling ICSRs & Safety Messages in the ICSRs Screen**
- **3.7. Workspace Screen Functions**

3. ICSRs & Messages

A Safety message is like an envelope, which may contain one or more ICSRs. Every message contains required information about the sender, receiver, the date, and a unique identification number among other things.

An Acknowledgement message is a particular type of message, which contains the acknowledgement of a received Safety message and the acknowledgements of each ICSR contained within it.

An Acknowledgement message is sent by the receiver of a Safety message, to inform the sender about the receipt of the Safety message and the outcome of the validation of that message.

This chapter deals with the creation, sending, receipt, validation, acknowledgement and follow-up of ICSRs using EVWEB.

3.1. Contextual Help

EVWEB offers a useful feature called contextual help. This interactive assistance aids the user whilst creating/editing ICSRs, Safety or Acknowledgement messages, as well as Follow-Ups.

While in EVWEB, you can check whether the current screen you are in supports contextual help by looking at the far right of the dynamic buttons set toolbar. If you see the text "Show Help" followed by "On" and "Off" buttons, then the screen supports this feature.

Figure 62- Contextual help buttons

With the contextual help feature enabled (the button "On" is active), you can take advantage of this user assistance feature by placing the mouse pointer over a field label. If available help exists for the field, the mouse pointer will change to , and a tooltip will appear above the field label containing a descriptive message with further context regarding the specific field.

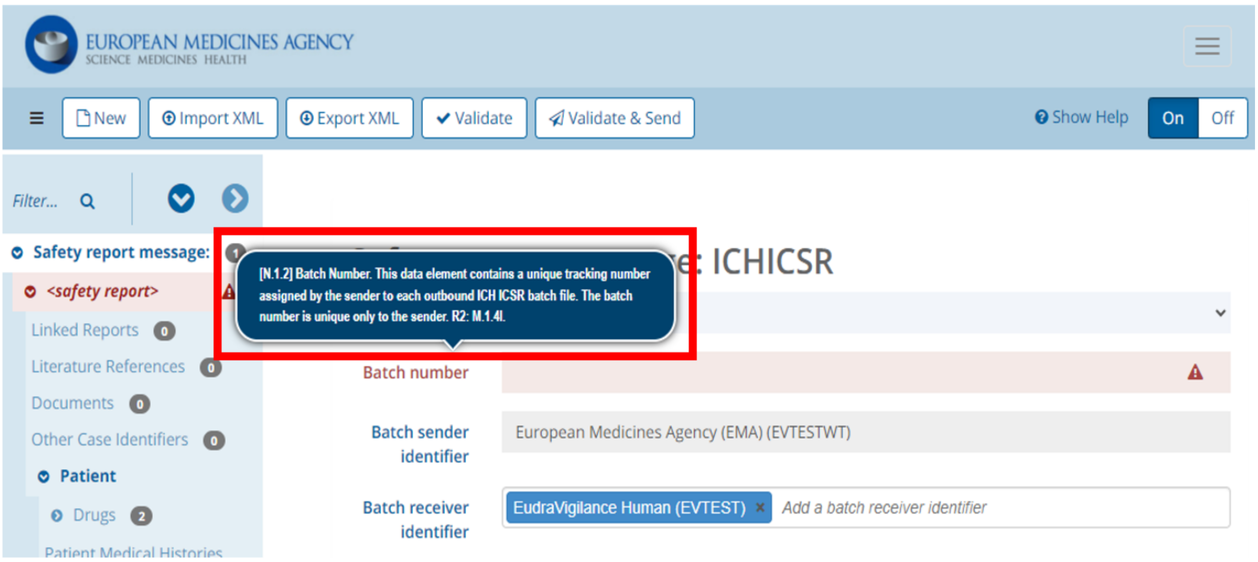


Figure 63 - Contextual help tooltip

3.2. Creating Safety Messages & ICSRs

EVWEB allows WEB Trader EVWEB users to create Safety messages and ICSRs. If you are a WEB Trader Post function user, you may also use EVWEB to send the Safety messages generated by your own safety database.

You can create one or more ICSRs using EVWEB. The system automatically creates a message whenever you decide to send or export any created ICSRs.

We will now go through the process of creating one or more ICSRs.

Click on the **Create and send ICSRs** link in the main menu.

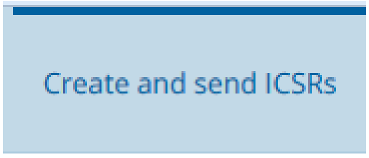


Figure 64 - Create and send ICSRs screen link

In the dynamic buttons set click on "New". The tree view area will display the structure of a new Safety message.

Since this process involves data entry, please refer to Chapter 1 for a detailed description on how to manage the different types of fields when creating an ICSR.

Clicking on any section in the tree view area will display the corresponding fields available for data entry in the active area.

For a detailed guide of all the fields and sections of an ICSR see the Field Definitions document.

A separate, step-by-step instruction set on how to create an ICSR is also available as part of the EVWEB training course materials.

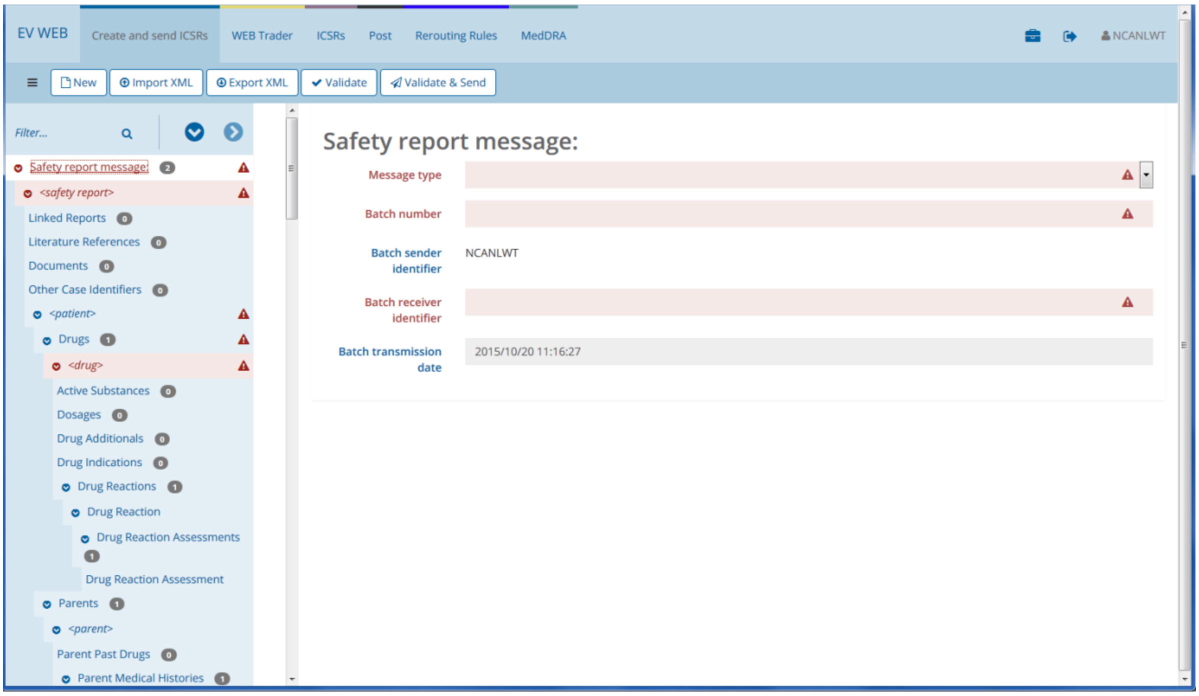


Figure 65 - Creating an ICSR

By default, any mandatory fields in the active area will be highlighted in red denoting that they are invalid or incomplete. This is also the case for sections in the tree view area, which will appear in red text and background (this indicates that these invalid tree view sections contain invalid active area fields).

Note: EVWEB uses an internal auto-validation process that determines whether a field contains the correct input or not. This process is also responsible for providing a descriptive error message when hovering your mouse pointer over the icon that appears on the right edge of the field.

Thus, at this stage, you should correctly complete all invalid/incomplete fields, and fill in any other necessary fields, before proceeding with the ICSR creation process. When successfully done, all sections in the tree view and active area should appear in blue text, indicating that no errors are present in the Safety message.

All populated sections should appear in bold text, indicating clearly which sections you have entered data in.

Note: When creating a Safety message, its MedDRA version will default to the latest MedDRA version available by the system. This value is not editable by the user.

The next step involves validating the entire Safety message which, in turn, will validate all included ICSRs. EVWEB provides two methods for this function:

- Validate
- Validate & Send

These two methods appear in the dynamic buttons set of the **Create and send ICSRs** screen.

While the "Validate" button might seem redundant, since it is already part of the "Validate & Send" method, it has been included for specific validation scenarios. One such scenario is the importing of a local XML file which only needs to be validated and not sent to any receiver. For all other regular Safety message creation cases, you can choose "Validate & Send".

If there are errors when running the validation process on the created Safety message, you will be presented with a validation result window in which all invalid fields will be listed, along with a description of their errors.

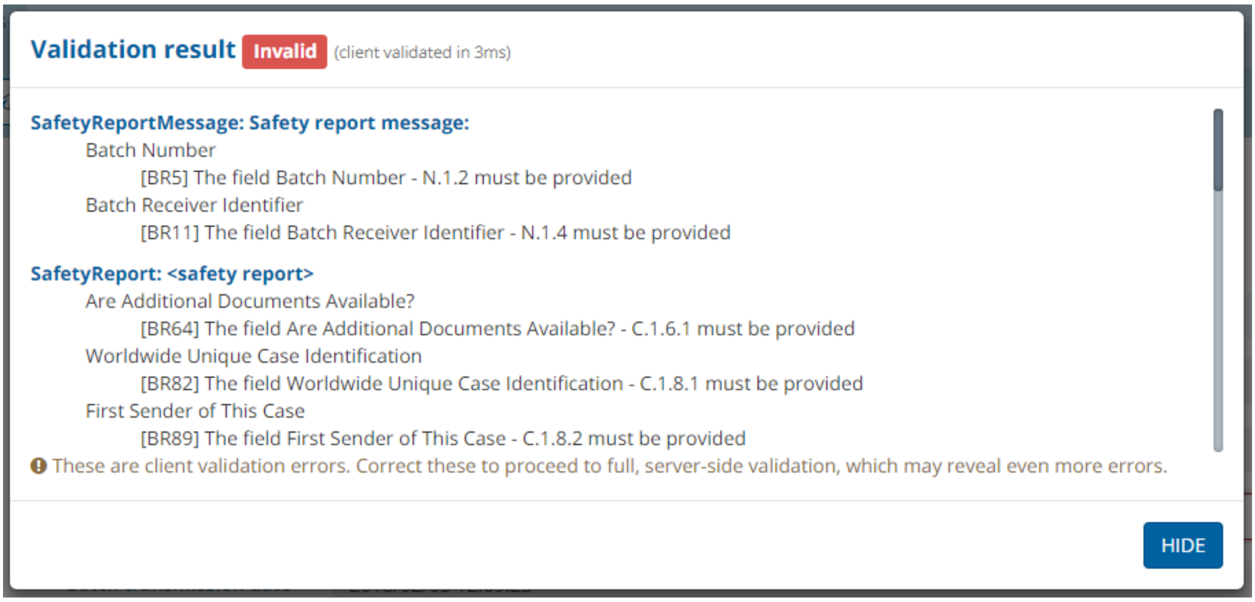


Figure 66 - Validation result window with errors (Safety Message)

The errors displayed in the validation result window are grouped per tree view section of the validated Safety message. To correct a reported validation error you can either close the validation result window (by clicking on the "HIDE" button) and fix the issue in the **Create and send ICSRs** screen, or click on a tree view section error from within the validation result window (the bold blue text); this will take you directly to the invalid fields of that tree view section. If there are no errors, the "HIDE" button will be replaced by an "OK" button.

The validation process applied by "Validate" or "Validate & Send" occurs locally (client-side validation) without the involvement of the remote EVDBMS. Only when a Safety message validates without errors will it be submitted for final validation to the EVDBMS (server-side validation).

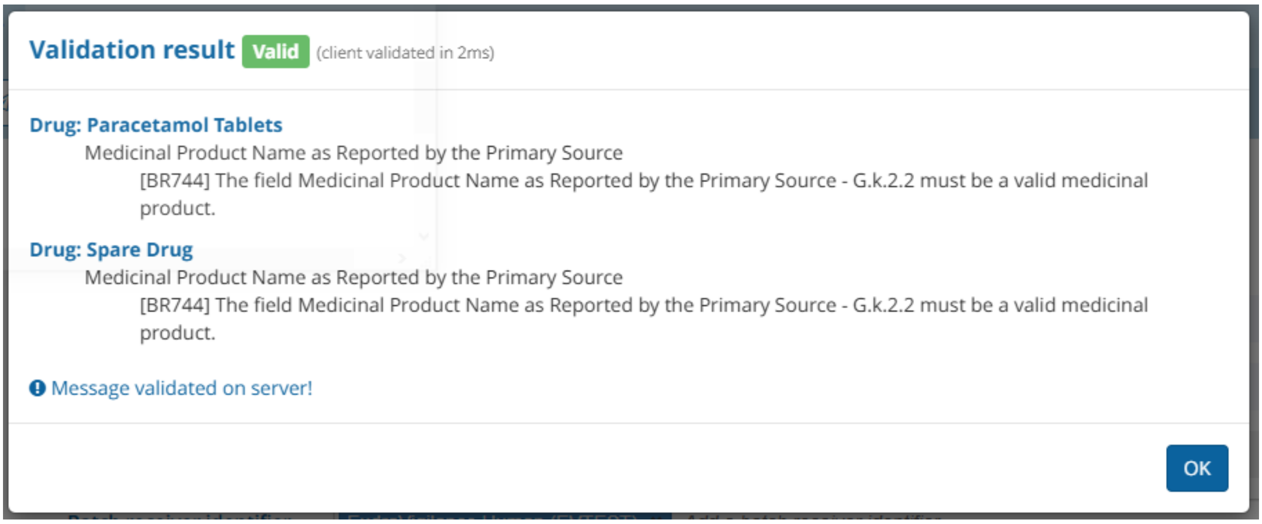


Figure 67 - Validation result window with no errors (Safety Message)

Once you have validated a report, if it contains errors then the dynamic buttons set will have a new button added to it: "Errors". You can use this button to remind yourself of which errors were reported on validation and go directly to them.

Figure 68 - Dynamic buttons showing "Errors" button

Note: If the receiver is not an EMA organisation (i.e. EVHUMAN, EVTEST, EVCTMPROD or EVCTMTEST), EVWEB will require from the user to select the validation target type before allowing him/her to proceed with the server-side validation process. In this case, the user should choose between "PM" (Post-authorisation Module; default for submissions to EVHUMAN or EVTEST), and "CT" (Clinical Trial Module; default for submissions to EVCTMPROD or EVCTMTEST), then click on the "Proceed to server side validation" button, as shown in the dialog box below:

Figure 69 - Validation target selection for non-EMA receivers

Please also note that the server-side validation may reveal additional errors, even if the client-side validation was error-free.

For a more detailed description of the validation process and other related information, you can refer to the EU Individual Case Safety Report (ICSR) Implementation Guide (EMA/51938/2013) for E2B(R3) messages.

3.2.1. Tests and Procedures

Investigational data (i.e., information derived from tests and procedures) that is relevant to the assessment of the patient's medical condition and adverse drug reaction(s) can be provided in the ICSR. This encompasses tests and procedures performed to either diagnose/confirm the reaction/event and those tests done to investigate (exclude) a non-drug cause, (e.g. serologic tests for infectious hepatitis in suspected drug-induced hepatitis). Both positive and negative results should be included in the report. Naturally, all other tests performed to the patient that are **not** relevant for the diagnosis of the ADR or for the exclusion of a non-drug cause, should **not** be included in the case.

The coding of investigations should be performed in line with the latest version of the MedDRA® Term Selection: Points to Consider.

As far as investigational data is concerned, it can be expressed in one of the three ways:

- As a coded result: e.g. "Positive (+ve)".
- As a physical quantity: e.g. "30 mg/ml".
- As text: e.g. "shadowing of right lung".

Still, and similarly to other sections of the ICSR, the investigational data should be provided in a structured manner as much as possible – i.e., via the E2B(R3) field 'F.r.3.1 Test result (code)' or in the fields 'F.r.3.2 Test result (value / qualifier)' and 'F.r.3.3 Test result (unit)' (see Figures below).

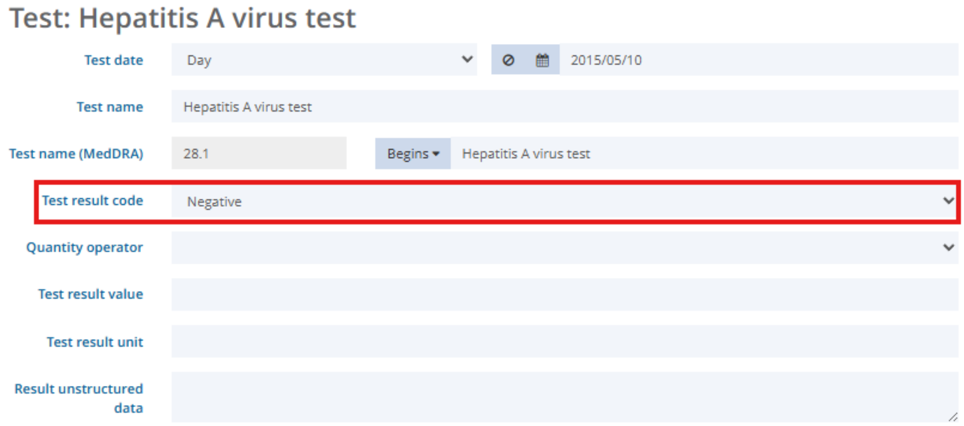


Figure 70 – Result of a test coded in the E2B(R3) field 'F.r.3.1 Test result (code)'

Note: The "Test result code" field has 4 options listed ('Positive', 'Negative', 'Borderline' or 'Inconclusive'), of which one may be selected by the user:

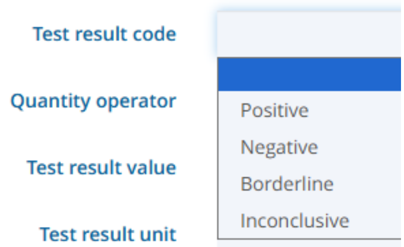


Figure 71 – Options of the "Test result code" field

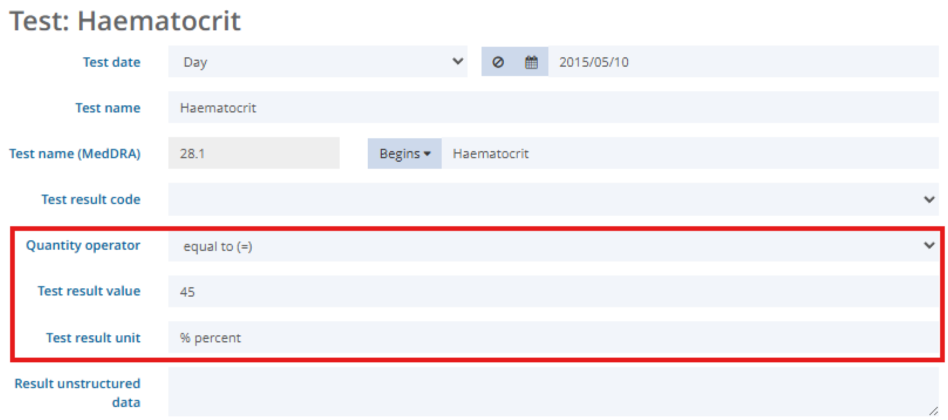


Figure 72 – Result of a test coded in the E2B(R3) fields 'F.r.3.2 Test result (value / qualifier)' and 'F.r.3.3 Test result (unit)'

Notes:

- In EVWEB, the E3B(R3) field **F.r.3.2 Test result (value / qualifier)** is split into 2 fields: "**Quantity operator**" and "**Test result value**".

- The "Quantity operator" field has 5 options listed ['Equal to (=)', 'Less than (<)', 'Less than or equal to (<=)', 'Greater than (>)', 'Greater than or equal to (>=)'], of which one may be selected by the user.

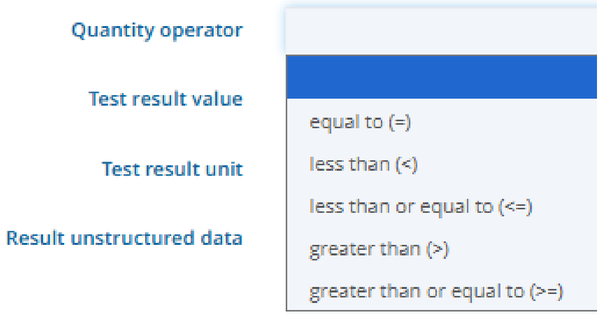


Figure 73 – Options of the "Quantity operator" field

- The field "Test result unit" is an 'Immediate query field' meaning that you have to start typing to activate this field (please refer to **section 2.6.1.4. Immediate Query Field** for more information on these look-up fields). For example, by typing "mm" or "heart", the system will present you with a list of available options – see the figure below.

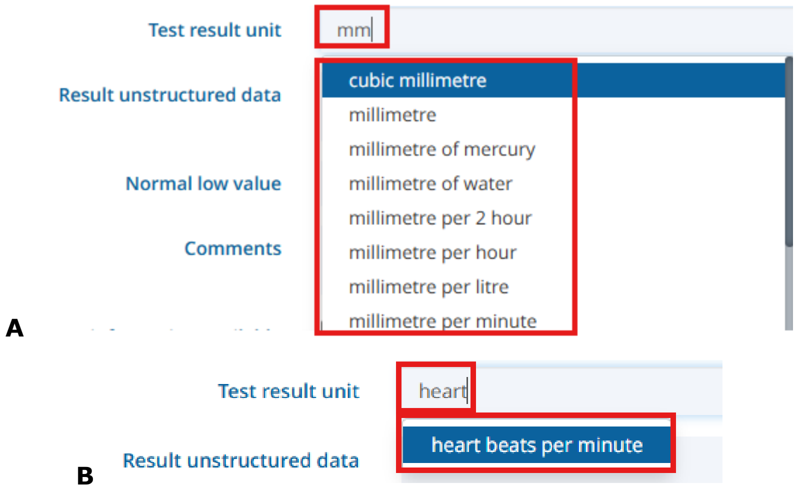


Figure 74 – Searching for test units by typing (A) "mm" or (B) "heart"

Tip: If, some reason, a specific unit cannot be retrieved within a given field, then you should follow the guidance of **section 2.6.1.4.1. Searching for units in Immediate Query Fields.**

If it is not possible to provide information on tests and test results in a structured manner, then provisions have been made to allow for the presentation of the information in free text. In this situation, the data should be entered in field **F.r.3.4 Result unstructured data (free text)**.

Tip: For the blood pressure test and considering that, normally, the systolic and diastolic blood pressures are measured and reported together, the combined result can be provided in the E2B field 'F.r.3.4 Result unstructured data (free text)' (if they were to be coded individually, then the case receiver might perceive them as having not been measured/obtained simultaneously, at the same time).

Figure 75 – Result of a blood pressure test coded in the E2B(R3) field 'F.r.3.4 Result unstructured data (free text)'

In line with ICH-E2B, the following applies:

Table 7 - ICH E2B(R3) requirements

Reference	E2B(R3) requirements
ICH-E2B(R3)	• Section F.r 'Results of tests and procedures relevant to the investigation of the patient' should be used to structure the information on the date the test was performed (data element F.r.1 'Test date'), the test (section F.r.2 'Test name'), the outcome (section F.r.3 'Test result') and the normal low (data element F.r.4 'Normal low value') and normal high (data element F.r.5 'Normal high value'). • Data element F.r.2.1 'Test Name (free text)' should be used for the description of a test when an appropriate MedDRA code is unavailable for use in data element F.r.2.2b 'Test Name (MedDRA code)'. • Data element F.r.3.4 'Result Unstructured Data (free text)' should be used when the data elements F.r.3.1 'Test results (code)', F.r.3.2 'Test results (value / qualifier) and F.r.3.3 'Test result (unit)' cannot be used (often because a Unified Code for Units of Measure (UCUM) code is not available for the test unit). • Data elements F.r.4 'Normal low value' and F.r.5 'Normal high value' should be used to capture the lowest and highest values in the normal range for the test. The same units as used in F.r.3.3 are implied. • Data element F.r.6 'Comments (free text)' should be used to capture any relevant comments made by the reporter about the test result. • Data element F.r.7 'More information available' should be used to indicate that more information is held by the sender about the test and test result. For example, 'true' means that more documentation is available upon request e.g. ECG strips, chest X-ray. 'False' means that no more documentation is

available from the sender. If this data element is set to 'true', then C.1.6.1 should be set to 'true'.

- A separate block (r) should be used for each test/procedure.

3.2.2. Attachments

In order to provide supplemental information, the sender of an ICSR might need to attach documents to the ICSR message itself. The ICH E2B(R3) message format therefore allows for the inclusion of such files – either literature articles (see **section 3.2.2.1. Literature articles**) and/or additional document(s) held by the Sender (see **section 3.2.2.2. Additional (non-literature) document(s) held by sender**). The attachments can be presented in-line within the ICSR message itself using the encapsulated data type; however, a reference to a document URL is not permitted. By attaching those documents to the ICSR message itself, the sender of an ISO ICSR can provide supplemental information that could not be provided other way.

The main usage of these elements will thus be the provision of literature articles and any associated translation of the literature article into English. Other documents made available by a primary source (e.g. autopsy reports, ECG strips, chest X-ray, or photographs, etc.) can also be provided as attachments. However, **additional documents should not be routinely attached to ICSRs**. The main reasons for attaching these additional documents should either be at the request of the receiver on a case-by-case basis or where the correct medical interpretation of the ICSR cannot be made without access to the attachment(s).

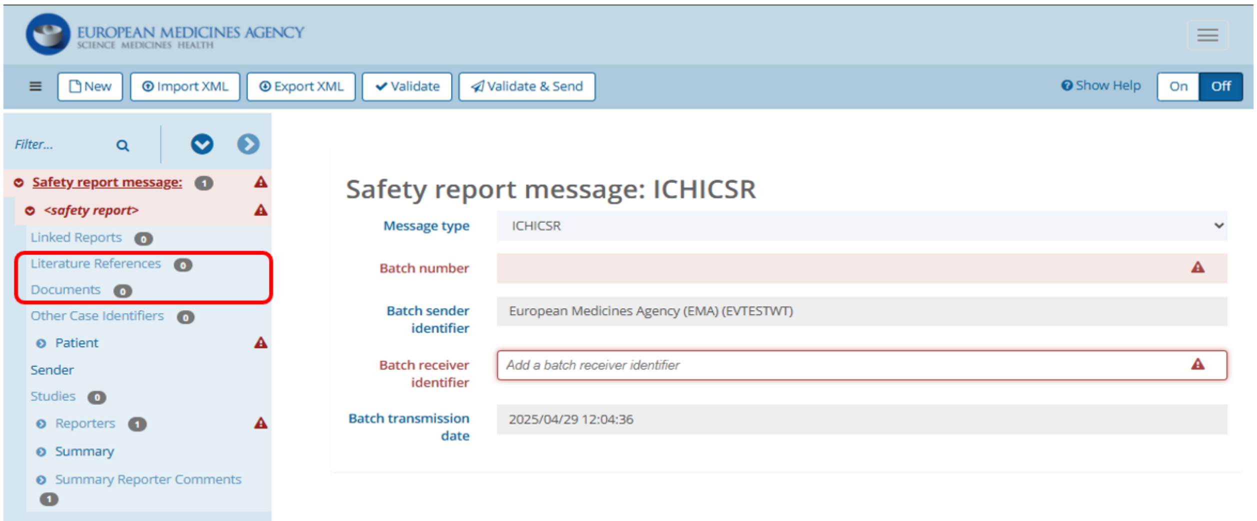


Figure 76 - EVWEB snippet showing the literature and additional documents sections

Note: Case narratives should **not** be provided as file attachments. The data element H.1 'Case Narrative Including Clinical Course, Therapeutic Measures, Outcome and Additional Relevant Information' allows for 100,000 characters (this is enough for around 25 pages of average A4 text). If it is not possible to capture a focused, factual and clear description of the case in 100,000 characters the repeatable data element H.5.r.1a 'Case summary and reporter's comments text' can also be used. Therefore, the case narrative has no actual limit. However, it should be noted that in accordance with ICH E2D (replaced by the E2D(R1) once implemented) and GVP Module VI, organisations creating ICSRs should aim to provide concise narratives containing all known relevant clinical information that supports or refutes the reported suspected adverse reactions. The case narratives should avoid repetitions or listing information included in structured data elements and which is of limited relevance for the reported suspected adverse reaction (e.g. listing all lab test results).

The table below lists the file formats that are supported in the EU along with the Media type that should be provided in the relevant ICSR data element.

Table 8 - Supported file types in the EU

File type extension	File type	Media Type (values)
PDF	Portable Document Format	application/pdf
JPEG/JPG	Joint Photographic Experts Group	image/jpeg
TXT	Text file	text/plain
RTF	Rich text file	text/rtf
TIFF/TIF	Tagged Image File Format	image/tiff
HTML	HyperText Markup Language	text/html
Doc	Word document	application/msword
Docx	Office Open XML (ISO/IEC 29500) wordprocessing	application/vnd.openxmlformats-officedocument.wordprocessingml.document
XLS	Excel document	application/vnd.ms-excel
XLSX	Office Open XML (ISO/IEC 29500) spreadsheet	application/vnd.openxmlformats-officedocument.spreadsheetml.sheet
DICOM	Digital Imaging and Communications in Medicine	application/dicom

3.2.2.1. Literature articles

The E2B section C.4.r.1 'Literature reference(s)' should be used for literature article(s) that describe individual case(s), but not for articles used for data analysis.

The literature citations should be provided in data element C.4.r.1 'Literature reference(s)' in the style specified by the Vancouver Convention, known as 'Vancouver style', which has been developed by the International Committee of Medical Journal Editors. The conventional styles, including styles for special situations, can be found in the following reference: *International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals. N Engl J Med 1997; 336:309-15.*

If available, the Digital Object Identifier (DOI) for the article should also be included as shown in the image below. E.g.:

International Committee of Medical Journal Editors. Uniform requirements for manuscripts submitted to biomedical journals. N Engl J Med 1997; 336:309-15. ***doi:10.1056/NEJM199701233360422****.*

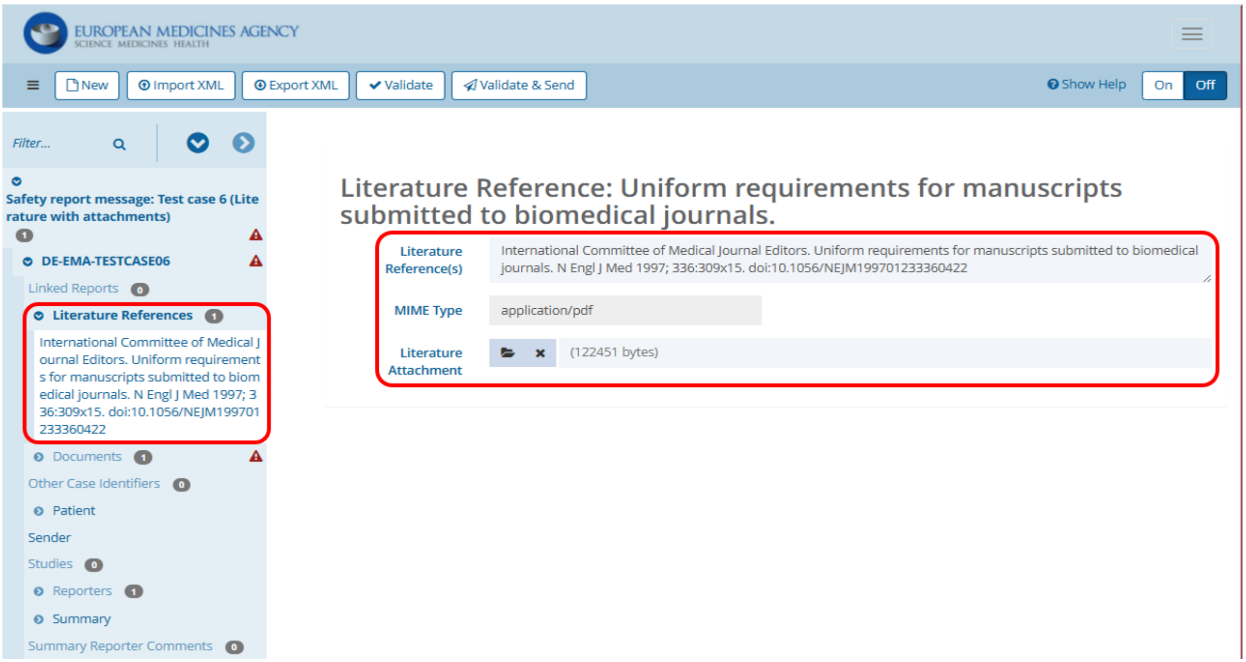


Figure 77 - EVWEB snippet showing the literature-related fields populated

As mentioned in GVP Module VI, Chapter **VI.C.6.2.3.2. Suspected adverse reaction reports published in the medical literature**, upon request of the Agency, for a specific safety review, a full translation in English and a copy of the relevant literature article shall be provided by the marketing authorisation holder that transmitted the initial report, taking into account copyright restrictions.

Therefore, whenever the receiver of the case requests the literature article, it should be sent as an attachment within the ICSR/XML message. The electronic version of the document should be attached to the ICSR in the data element C.4.r.2 'Included documents' (and thus **not** in C.1.6.1.r.2 'Included documents'). If an article has been previously submitted with an ICSR, **the same article document should not be resubmitted for any subsequent follow-up reports**.

Within one ICSR, multiple document descriptions (C.1.6.1.r 'Are additional documents available?') and literature references (C.4.r.1 'Literature reference(s)') can be provided, as well as the associated materials.

In line with GVP module VI, namely Chapter **VI.App.2.11. Examples for the submission as ICSRs of suspected adverse reactions described in the medical literature and referring to more than one patient**, if a literature article refers to more than one ICSR, then the literature article should **only** be attached to the first created ICSR and all the other associated ICSRs should be linked to the first ICSR through the linked report number C.1.10.r 'Identification number of the report which is linked to this report' data element.

In line with ICH-E2B(R3) the following applies:

Table 9 – ICH E2B(R3) requirements

Reference	E2B(R3) requirements
ICH E2B(R3)	• Data element C.4.r.1 'Literature Reference(s)' should be populated with the literature reference. The Digital Object Identifier (DOI) for the article should be included where available e.g.: International Committee of Medical Journal

Editors. Uniform requirements for manuscripts submitted to biomedical journals. N Engl J Med 1997; 336:309-15. doi:10.1056/NEJM199701233360422.

- A comprehensive English summary of the article shall be provided in the ICH E2B data element H.1 'Case narrative including clinical course, therapeutic measures, outcome and additional relevant information'.
- Upon request by the receiver, a full translation in English and a copy of the relevant literature article shall be provided by the MAH that transmitted the initial report, taking into account copyright restrictions, by attaching it to the ICSR, in data element C.4.r.2 'Included Documents'. In this situation, the original ICSR along with all the same medical information captured in the E2B(R3) data elements should be retransmitted as an 'amendment' report.
- However, if new additional information is provided directly by the Primary Source, then the ICSR with the attachment should be submitted as a follow-up report and not as an 'amendment'.

3.2.2.2. Additional (non-literature) document(s) held by sender

If the sender of the ICSR holds additional (non-literature) documents, the data element C.1.6.1 'Are additional documents available?' should be entered as 'true' and a description of the document should be provided in the data element C.1.6.1.r.1 'Documents held by sender'.

As already explained above, attachments should **not** be routinely added to ICSRs. However, and whenever the transmission is required, the electronic version of the clinical document(s) can be provided as attachments in the data element C.1.6.1.r.2 'Included documents'. If the receiver of the ICSR does not receive additional documents held by the sender and needs to subsequently forward the ICSR to another receiver, the data element C.1.6.1 (ICH E2B(R3)) should be amended on upon retransmission to indicate that the organisation does not hold additional documents.

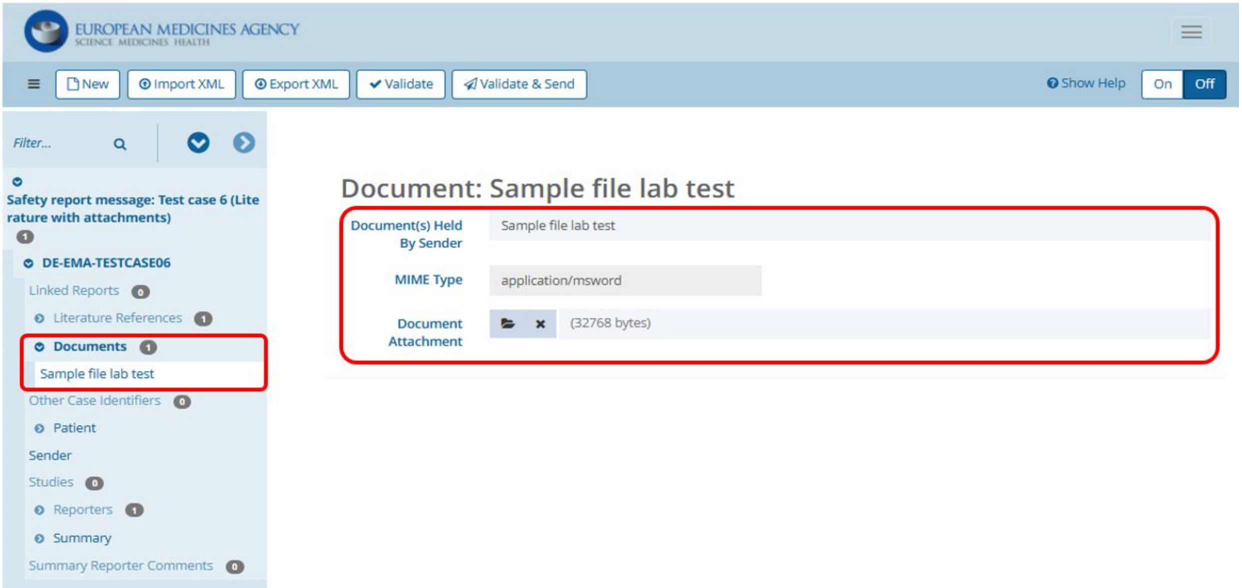


Figure 78 - EVWEB snippet showing the documents-related fields populated

In line with ICH-E2B the following applies:

Table 10 – ICH E2B(R3) requirements

Reference	E2B(R3) requirements
ICH-E2B(R3)	• Data element C.1.6.1 'Are Additional Documents Available' should be completed. • Section C.1.6.1.r 'Documents Held by Sender' should be completed as applicable, where the data element C.1.6.1.r.1 'Documents Held by Sender' should provide a description of the nature of documents (e.g. clinical records, hospital records, autopsy reports) • Whenever the document(s) is/are requested by the Receiver, section C.1.6.1.r.2 'Included Documents' should contain the actual attached document, if the sender chooses to send the document or is required to do so. The processing of personal data should be done in accordance with local data protection law (see VI.C.6.2.2.10. for guidance on the processing of personal data in the EU).

3.3. Sending a Safety Message

To send a completed Safety message you need to click on the "Validate & Send" button which is located in the dynamic buttons set.

EVWEB will then proceed to validate the message first on the client-side. If the validation is successful, EVWEB will proceed and apply the server-side validation process. If any of these validation checks is unsuccessful, you will be presented with the validation result window which will contain the errors that need correction.

If both validation steps are successful, EVWEB will send the Safety message to the EVDBMS and place a copy of the message in the "Outbox" view area of the **WEB Trader** screen (see **section 3.4. WEB Trader Screen Functions** of this manual). After processing, the user will obtain the corresponding **Acknowledgement (ACK)** for the case submitted via the "Inbox" area (see **section 3.4. WEB Trader Screen Functions**).

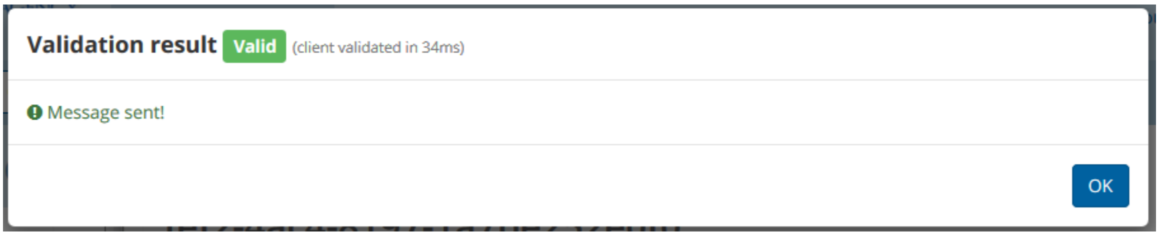


Figure 79 - Validation result window of successfully sent Safety message

Attention: The "Validate & Send" button is only available to WEB Trader users. Only WEB Trader users are allowed to send messages via EVWEB. If you are a Gateway user you may use EVWEB to create a Safety message, but you can only send it through your local Gateway.

Note: to view the EMA's official gateway date for an ICSR, please refer to section **3.5.2.3. Viewing the EMA's official receipt date (gateway** date**) for a** *case in EVWEB***.**

3.4. WEB Trader Screen Functions

Some of these functions will only be available to WEB Trader users

The **WEB Trader** screen of the EVWEB application allows WEB Trader users to keep track of sent and received Safety and Acknowledgement messages.

To access the **WEB Trader** screen click on the **WEB Trader** link in the main menu.

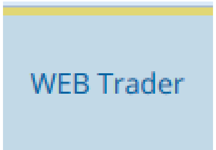


Figure 80 - WEB Trader screen link

The following screen will be displayed once you enter this link:

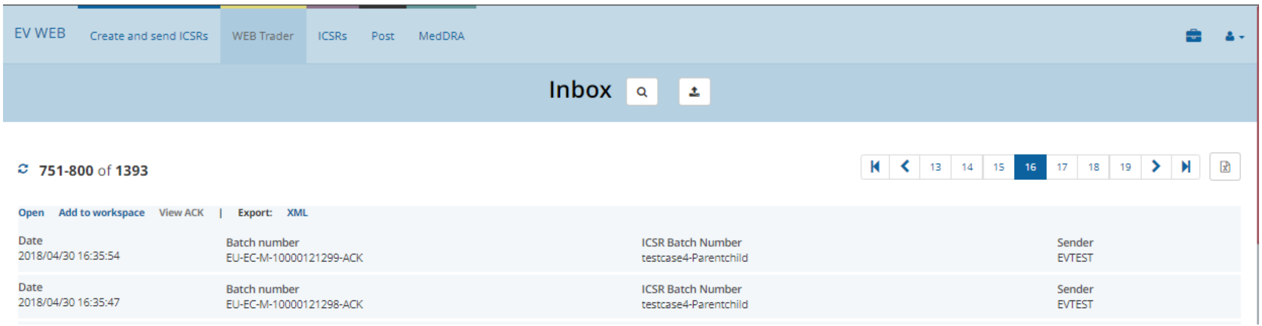
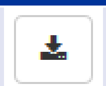
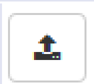


Figure 81 - WEB Trader "Inbox" screen

Directly under EVWEB's main menu are the "Inbox", "Search" and "Outbox" view options. By default, when you enter this screen you will be presented with the "Inbox" view.

Here is a brief description of the WEB Trader view options:

Table 11 – Description of the WEB Trader view options

WEB Trader View Option	Description
	"Inbox" view option. Enabled by default, allows the user to view all Safety and Acknowledgement messages sent to the user's organisation.
	"Search" view option. Allows the user to perform queries based on user-defined criteria to all WEB Trader messages.
	"Outbox" view option. Allows the user to view all Safety and Acknowledgement messages sent by the user's organisation.

Below these WEB Trader view options, and residing in the active area, is the messages list view.

If the "Inbox" view option is active, you will find Safety and Acknowledgement messages displayed in the list view. These are messages that other organisations have sent to you by specifying your organisation as the receiver. All received messages, regardless of type, will be displayed in your “Inbox” view.

If the “Outbox” view option is active, you will find Safety and Acknowledgement messages displayed in the list view. These are messages that you have sent to other organisations. All sent messages, regardless of type, will be displayed in your “Outbox” view.

3.4.1. Handling Messages in WEB Trader

Besides viewing sent/received Safety and Acknowledgement messages, the **WEB Trader** screen also allows you to manage these messages. This is possible through the contextual actions menu that appears once you click on a WEB Trader message.

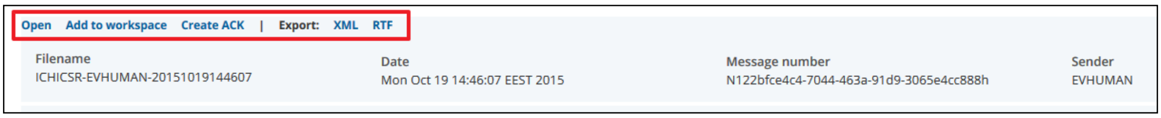


Figure 82 - WEB Trader message handling

The available options in the contextual actions menu will adapt according to the type of the selected message (Safety or Acknowledgement). In general, the available options will include all or a subset of the following:

Table 12 – Description of the options in the Contextual Actions Menu

Contextual Actions Menu Option	Description
Open	Loads the selected message and displays it in a typical, read-only, tree view and active area layout. See **section 2.8.1.3. WEB Trader Screen** for further information regarding this option.
Add to workspace	Adds the selected message to the **Workspace** screen for later viewing or handling. You can add multiple messages, in the same manner, allowing you to concentrate specifically on those items. You can find more information about the **Workspace** screen and its functions in section **3.7. Workspace Screen Functions** of this manual.
Create ACK	Creates an Acknowledgement message from the selected Safety message and auto-completes all common fields between the newly created Acknowledgement message and the selected Safety message. If required, you can edit any of these auto-completed fields in the Acknowledgement message before validating and sending it. See **section 3.4.3. Creating an Acknowledgement Message** and **section 3.4.4. Sending an Acknowledgement Message** for further information regarding the creation and sending of Acknowledgement messages.
Export	Exports the selected message into an XML file (which is the typical format for a message), or a RTF file (which is the typical "text" document format). See **section 3.9. Export Functions** for more information regarding EVWEB’s export features.

3.4.2. Searching Messages in WEB Trader

The "Search" view option allows the execution of queries based on user-defined criteria to all WEB Trader messages. To enter the "Search" view mode, click on the magnifying glass icon ( ) which is located between the "Inbox" and "Outbox" view options.

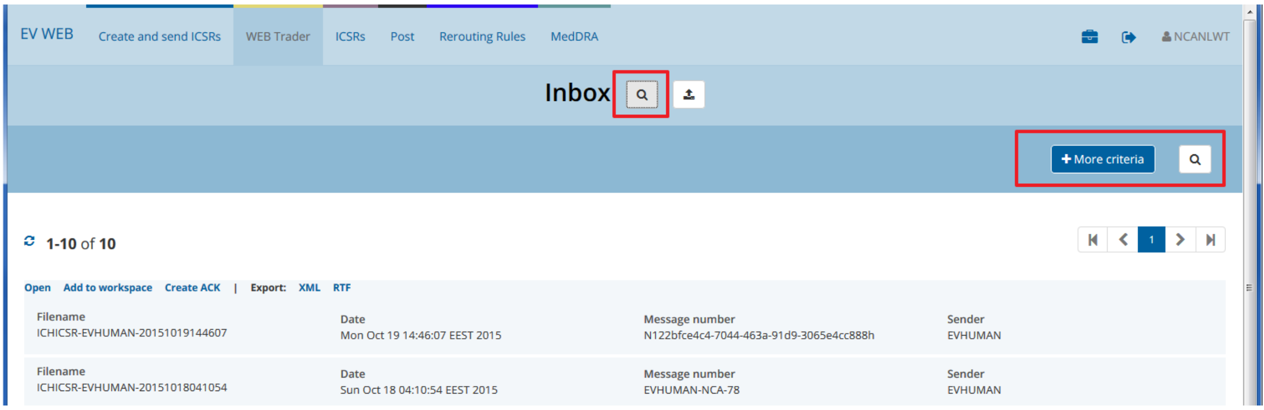


Figure 83 - WEB Trader "Search" view mode

After clicking on the "Search" view icon, a criteria ribbon will appear below the "Inbox", "Search" and "Outbox" view options.

The criteria ribbon is used to define the conditions of a WEB Trader query. This area allows you to select one or more items and define their value. These items are then used as criteria to filter the results of the query.

To add a criterion item you need to click on the "+More criteria" button that is located in the criteria ribbon. This will produce a drop-down list from which you can select the desired criteria item. You can repeat this process as many times as necessary to obtain all required criteria items required for your query.

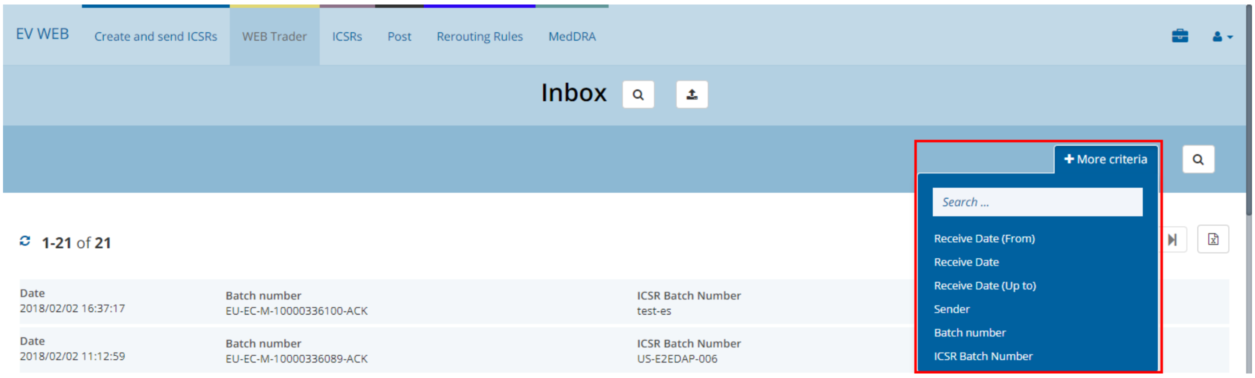


Figure 84 - Adding a search criteria item

Tip: The WEB Trader criteria ribbon appears only when clicking on the "Search" view option which appears as a magnifying glass icon ( ). By default, it will not be displayed when entering the **WEB Trader** screen.

Once you have selected your criteria items, and before you perform the query, you should define their values. This is accomplished by clicking on each criteria item that you have inserted in the criteria ribbon, and defining their value using the available options presented.

Depending on criteria type, when you click on an inserted criteria item you will be presented with a text field, or a calendar in the case of date criteria items, in which you can insert or choose the required values.

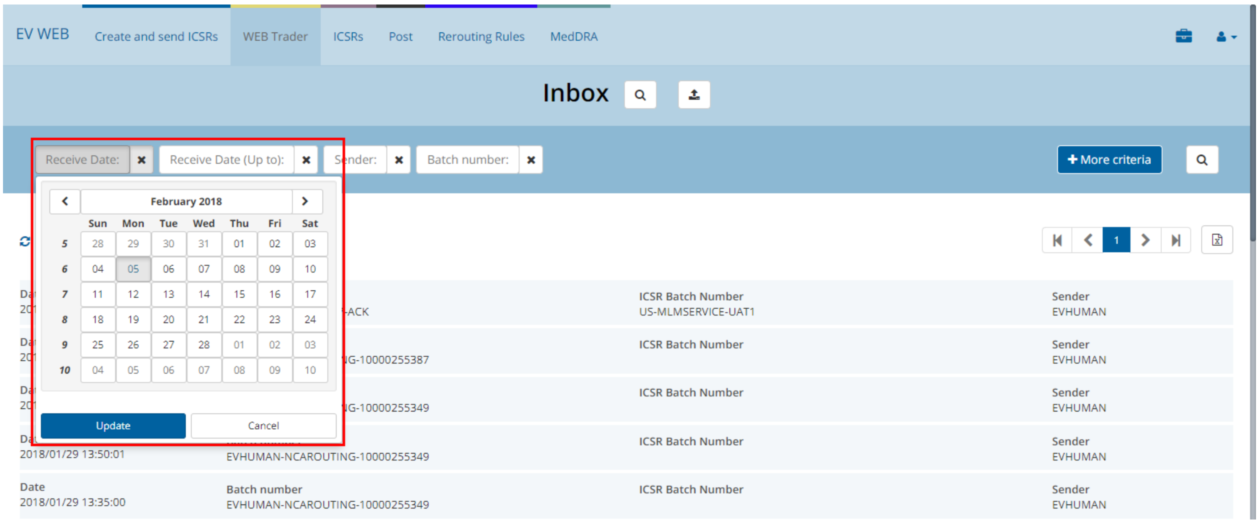


Figure 85 - Defining criteria item values

To remove a criteria item you simply need to click on the ✖ icon located on the right side of the item.

To initiate the search, after having specified the criteria items, you need to click on the magnifying glass icon ( ) in the criteria ribbon. The results of the search will be displayed in the active area of the **WEB Trader** screen in a list view layout.

You can now manage the search result messages as any other WEB trader message by clicking on each one and utilizing the contextual actions menu. See **section 3.4.1. Handling Messages in WEB Trader** for more information.

3.4.3. Creating an Acknowledgement Message

EVWEB allows the creation of a manual Acknowledgement message. If you are a WEB Trader user, you may also use EVWEB to send the created Acknowledgement message.

Acknowledgement messages are used to inform other users that a Safety message has been received and processed. They also report the outcome of the validation (at the receiver's end) of that Safety message and the ICSR(s) it contains.

Creating an Acknowledgement message is available in the following EVWEB screens:

- WEB Trader
- Workspace

Note: You can create an Acknowledgement message in the **Workspace** screen only from Safety messages that have been added from the **WEB Trader** screen (using the "Add to workspace" option from the contextual actions menu), or that have been imported using the **Workspace** screen's "Import" function.

The following example uses the **WEB Trader** screen to create an Acknowledgement message (see **section 3.4. WEB Trader Screen Functions** for more information regarding WEB Trader functions).

Click on the **WEB Trader** link in the main menu.

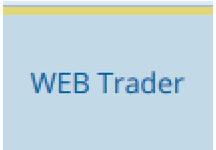


Figure 86 - WEB Trader screen link

In the "Inbox" view area click on a Safety message.

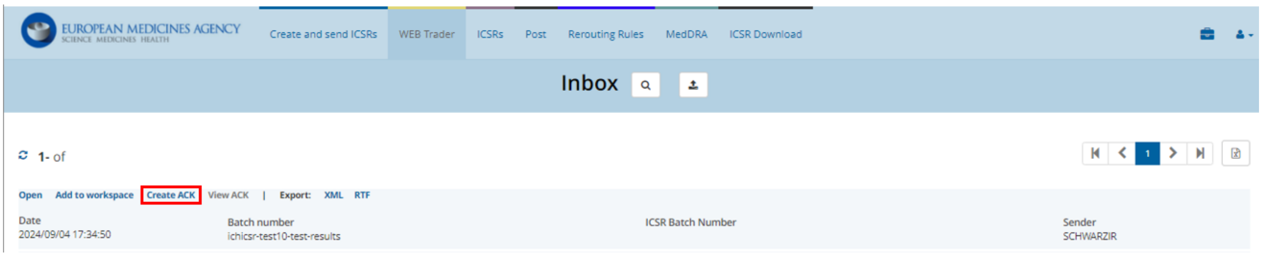


Figure 87 - WEB Trader: Creating an Acknowledgement message

A contextual actions menu will appear above the Safety message, providing various options applicable to the selected message. One of these options is the "Create ACK" which, once clicked, initiates the process of creating an Acknowledgement message.

Note: EVWEB will require the user to select the validation target type before allowing him/her to proceed with the server-side validation process. In this case, the user should choose between "PM" (Post-authorisation Module; default for submissions to EVHUMAN or EVTEST), and "CT" (Clinical Trial Module; default for submissions to EVCTMPROD or EVCTMTEST), then click on the "Proceed to server side validation" button, as shown in the dialog box below:

Figure 88 - Validation target selection for non-EMA receiver

The user is then presented with the following screen, in which the required fields should be completed for the process to continue:

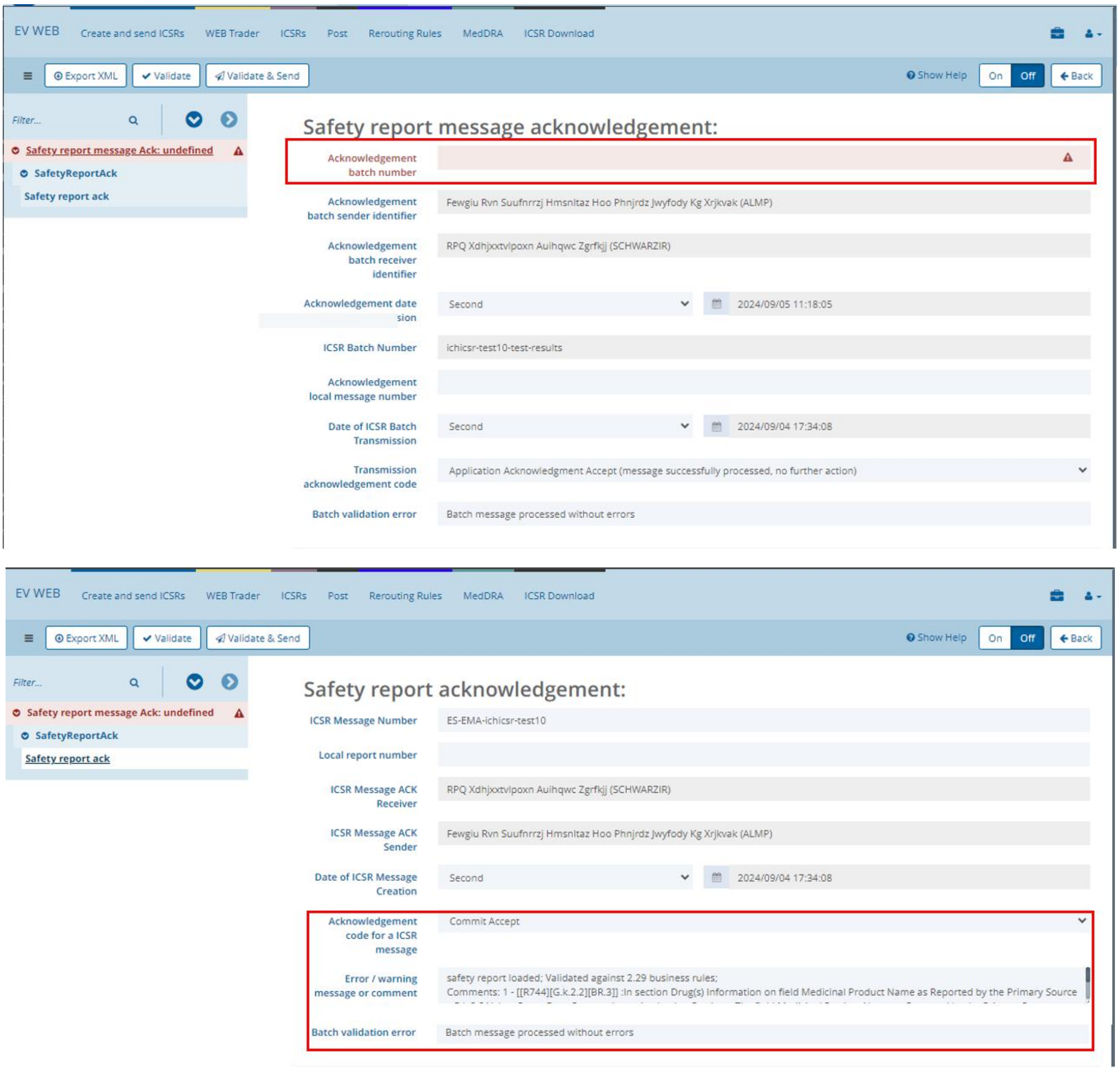


Figure 89 - Creating an Acknowledgement message

Since this process involves data entry, please refer to Chapter 1 for a detailed description on how to manage the different types of fields when creating an Acknowledgement message.

Clicking on any section in the tree view area will display the corresponding fields available for data entry in the active area.

For a detailed guide of all the fields and sections of an Acknowledgement message see the ICH E2B(R3) Implementation Guide that is available from the following ICH website: https://www.ich.org/page/electronic-standards-estri.

Since an Acknowledgement message is a receipt confirmation (including validation) of a Safety message, it should be addressed to the sender of that Safety message.

Note: If you are creating an Acknowledgement message from the **WEB Trader** or **Workspace** screens, EVWEB will auto-complete all common fields between the newly created Acknowledgement message and the received Safety message. However, it will still be possible to edit any of these auto-completed fields in the Acknowledgement message.

By default, any mandatory fields in the active area will be highlighted in red denoting that they are invalid or incomplete. This is also the case for sections in the tree view area, which will appear in red text and background (this indicates that these invalid tree view sections contain invalid active area fields).

Note: EVWEB uses an internal auto-validation process that determines whether a field contains the correct input or not. This process is also responsible for providing a descriptive error message when hovering your mouse pointer over the icon that appears on the right edge of the field.

Thus, at this stage, you should correctly complete all invalid/incomplete fields and fill in any other necessary ones before proceeding with the Acknowledgement message creation process. When successfully done, all sections in the tree view and active area should appear in blue text, indicating that no errors are present in the Acknowledgement message.

The next step involves validating the entire Acknowledgement message which, in turn, will validate all included ICSR Acknowledgements. EVWEB provides two methods for this function:

- Validate
- Validate & Send

These two methods appear in the dynamic buttons set when creating the Acknowledgement message.

While the “Validate” button might seem redundant, since it is already part of the “Validate & Send” method, it has been included for specific validation scenarios. One such scenario is the importing of a local XML file which only needs to be validated and not sent to any receiver. For all other regular Acknowledgement message creation cases, you can choose “Validate & Send”.

If there are errors when running the validation process on the created Acknowledgement message, you will be presented with a validation result window in which all invalid fields will be listed, along with a description of their errors.

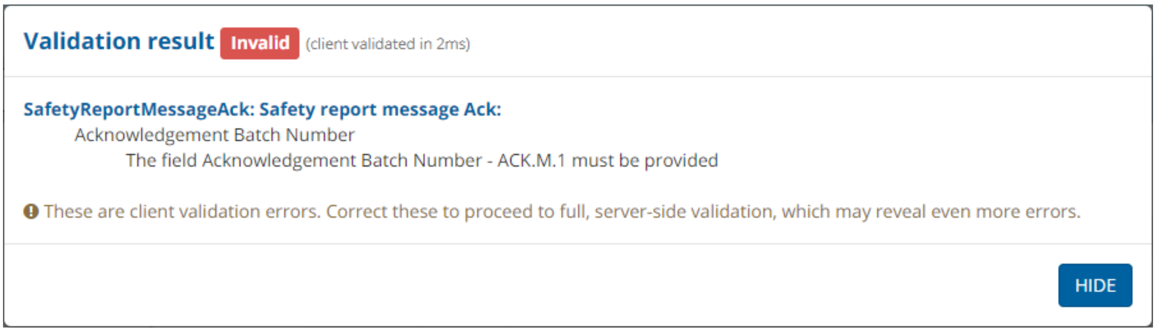


Figure 90 - Validation result window with errors (Acknowledgement message)

The errors displayed in the validation result window are grouped per tree view section of the validated Acknowledgement message. To correct a reported validation error you can either close the validation result window (by clicking on the “HIDE” button) and fix the issue in the data entry form, or click on a tree view section error from within the validation result window; this will take you directly to the invalid fields of that tree view section. If there are no errors, the "HIDE" button will be replaced by an "OK" button.

Once you have validated your ACK(s), if it contains errors then the dynamic buttons set will have a new button added to it: "Errors". You can use this button to remind yourself of which errors were reported on validation and go directly to them.

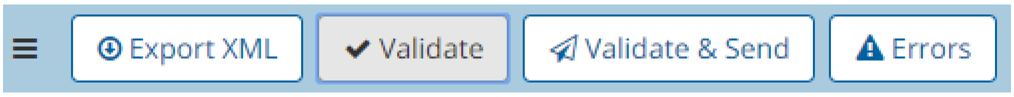


Figure 91 - Dynamic buttons showing "Errors" button

Note: The validation process applied by "Validate" or "Validate & Send" occurs locally (client-side validation) without the involvement of the remote EVDBMS. Only when an Acknowledgement message validates without errors in EVWEB will it be submitted for final validation to the EVDBMS (server-side validation). The server-side validation may reveal additional errors, even if the client-side validation was error-free.

For a more detailed description of the validation process and other related information, you can refer to the EU Individual Case Safety Report (ICSR) Implementation Guide (EMA/51938/2013) for E2B(R3) messages.

3.4.4. Sending an Acknowledgement Message

To send a completed Acknowledgement message you need to click on the "Validate & Send" button which is located in the dynamic buttons set.

EVWEB will then proceed to validate the message first on the client-side. If the validation is successful, EVWEB will proceed and apply the server-side validation process. If any of these validation checks are unsuccessful, you will be presented with the validation result window which will contain the errors that need correction.

If both validation steps are successful, EVWEB will send the Acknowledgement message to the EVDBMS and place a copy of the message in the "Outbox" view area of the **WEB Trader** screen (see **section 3.4. WEB Trader Screen Functions** of this manual).

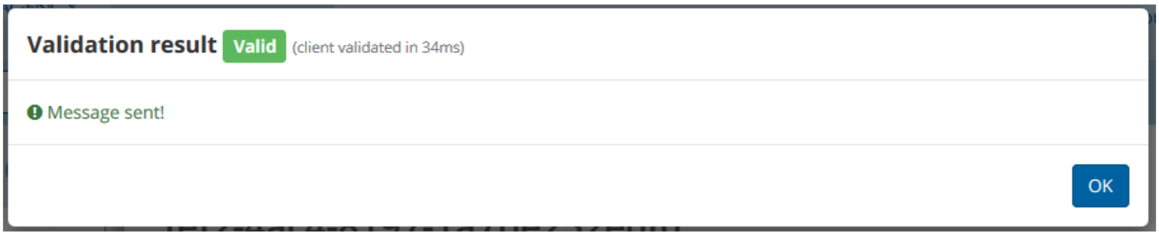


Figure 92 - Validation result window of successfully sent Acknowledgement message

Attention: The "Validate & Send" button is only available to WEB Trader users. Only WEB Trader users are allowed to send messages via EVWEB. If you are a Gateway user you may use EVWEB to create an Acknowledgement message, but you can only send it through your local Gateway.

3.5. ICSRs Screen Functions

The **ICSRs** screen allows users to browse and perform searches at all levels of the EVDBMS. It also provides ICSR and Safety message handling through the contextual actions menu, allowing the user to apply various processes to items stored in the EVDBMS. These functions are performed taking into account the general access rights of the users.

To access the **ICSRs** screen click on the **ICSRs** link in the main menu.

Figure 93 - ICSRs screen link

Note: The **ICSRs** screen gives access to all (EEA and non-EEA) ICSRs at either level 1 (public), level 2A (if the ICSR is associated with your organisation's XEVMPD data – see **section 1.7. Classification of product information and Level 2A/B access**) or level 3 (if your organisation sent the case or if it was sent by MLM). However, organisations should **NOT** use the **ICSRs** search function to fulfil their pharmacovigilance obligations (L2A ICSR download). Instead, the **ICSR Download** functionality (see **section** ICSR Download**3.9.3. ICSR Download**) should be used. The search criteria for **ICSRs** screen searches are different to the **ICSR Download** function and using the **ICSRs** screen search may lead to an organisation missing cases for downloading.

The following screen will be displayed once you enter this link:

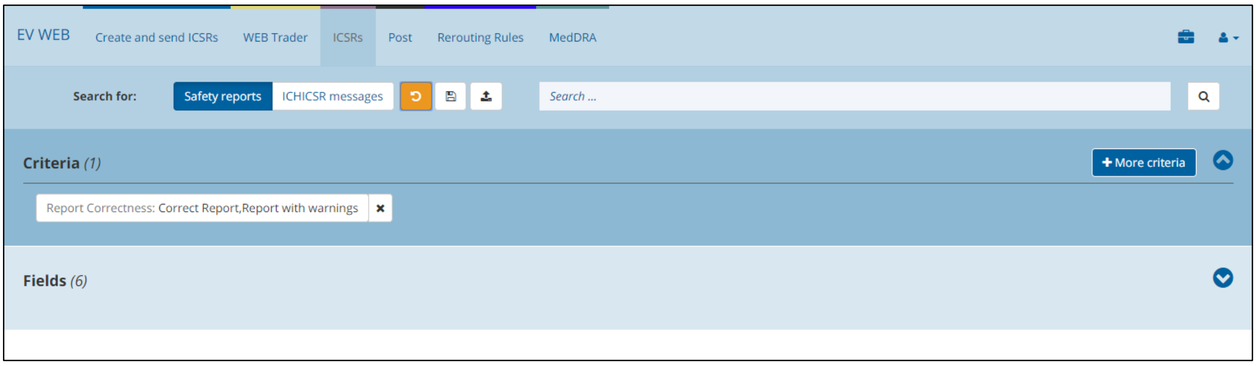


Figure 94 - ICSRs screen

3.5.1. Handling ICSRs & Safety Messages in the ICSRs Screen

Besides browsing and searching ICSRs and Safety messages, the **ICSRs** screen also allows you to manage these items. This is possible through the contextual actions menu that appears once you click on a **ICSRs** screen item.

Figure 95 - ICSRs screen item handling

The available options in the contextual actions menu will adapt according to the type of the selected item (ICSR or Safety message).

If the selected item is an ICSR, the available contextual actions menu options will be as follows:

Table 13 – Description of the options in the Contextual Actions Menu

Contextual Actions Menu Option	Description
Open	Loads the selected ICSR and displays it in a typical, read-only, tree view and active area format. See **section 2.8.1.1. ICSRs Screen** for further information regarding this option.
Follow-up	Creates a copy of the selected ICSR, adding it to the current Safety message in the **Create and send ICSRs** screen, and navigates you to that screen for modification of the ICSR content. Note that the created follow-up ICSR is populated with all values from the selected ICSR. See **section 0** **Create** a case Follow-up, Amendment or Nullification **Case Follow-Up** for more information regarding the "Follow-up" option.
Add to follow-ups	Creates a copy of the selected ICSR, adding it to the current Safety message in the **Create and send ICSRs** screen, but does not navigate you to that screen. You remain in the **ICSRs** screen to perform other actions (i.e. initiate more "Add to follow-ups"). See **section 0** **Create** a case Follow-up, Amendment or Nullification **Case Follow-Up** for more information regarding the "Add to follow-ups" option.
Add to workspace	Adds the selected ICSR to the **Workspace** screen for later viewing or handling. You can add multiple ICSRs, in the same manner, allowing you to concentrate specifically on those items. You can find more information about the **Workspace** screen and its functions in section **3.7. Workspace Screen Functions** of this manual.
Export	Exports the selected ICSR into the following formats: ICSR Form, XML, RTF and HTML. See **section 3.9.2. Single-Item Export** for more information regarding EVWEB's export features and the differences between the export formats.

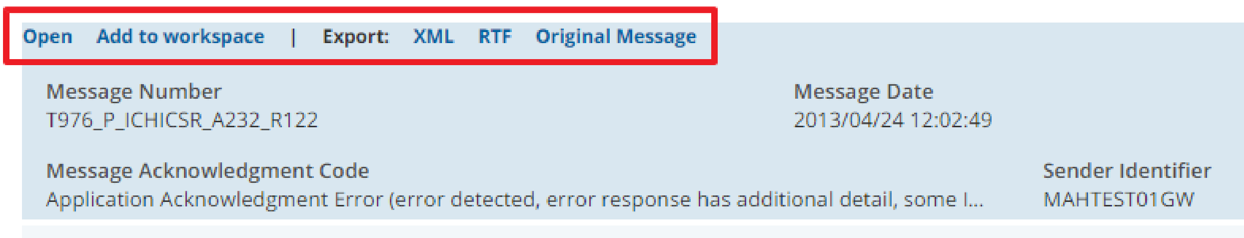


Figure 96 - Safety Messages screen item handling

If the selected item is a Safety message, the available contextual actions menu options will be as follows:

Table 14 – Description of the options in the Contextual Actions Menu

Contextual Actions Menu Option	Description
Open	Loads the selected Safety message and displays it in a typical, read-only, tree view and active area format. See **section 2.8.1.1. ICSRs Screen** for further information regarding this option.
Add to workspace	Adds the selected Safety message to the **Workspace** screen for later viewing or handling. You can add multiple Safety messages, in the same manner, allowing you to concentrate specifically on those items. You can find more information about the **Workspace** screen and its functions in **section 3.7. Workspace Screen Functions** of this manual.
Export	Exports the selected Safety message into an XML file (which is the typical format for a Safety message), a RTF file (which is the typical "text" document format), or as the Original Message that was sent to/received from the system. See **section 3.9. Export Functions** for more information regarding EVWEB's export features.

3.5.2. Searching ICSRs & Safety Messages in the ICSRs Screen

A core function of the **ICSRs** screen is to allow users to perform searches at all levels of the EVDBMS. This is possible through two search methods. Depending on your search requirements, you can use any of these search methods interchangeably to obtain the desired search results.

1. Simple query
2. Advanced query

Note: The **ICSRs** screen gives access to all (EEA and non-EEA) ICSRs at either level 1 (public), level 2A (if the suspect/interacting products in the ICSR are associated with your organisation's XEVMPD data) or level 3 (if your organisation sent the case or if it was sent by MLM). However, organisations should **NOT** use the **ICSRs** search function to fulfil their pharmacovigilance obligations (L2A ICSR download). Instead, the **ICSR Download** functionality (see **section** ICSR Download**3.9.3. ICSR Download**) should be used as the search criteria for **ICSRs** screen searches are different to the **ICSR Download** function and using the **ICSRs** screen search may lead to an organisation missing cases for downloading.

3.5.2.1. Simple Query in the ICSRs Screen

The simple query process is covered in section **2.7.1. Simple Query** of this manual. Please refer to that part of the manual for further information regarding this process.

3.5.2.2. Advanced Query in the ICSRs Screen

The advanced query process is covered in section **2.7.2. Advanced Query** of this manual. Please refer to that part of the manual for further information regarding this process.

3.5.2.3. Viewing the EMA's official receipt date (gateway date) for a case in EVWEB

To view the EMA's official receipt date (gateway date) of a given ICSR with the EVWEB tool, go to the **ICSRs** screen and on the "Search for" field, click on "ICHICSR messages" and then search for the case. Once a case is retrieved, the official gateway date can be viewed under the "Message Received Date".

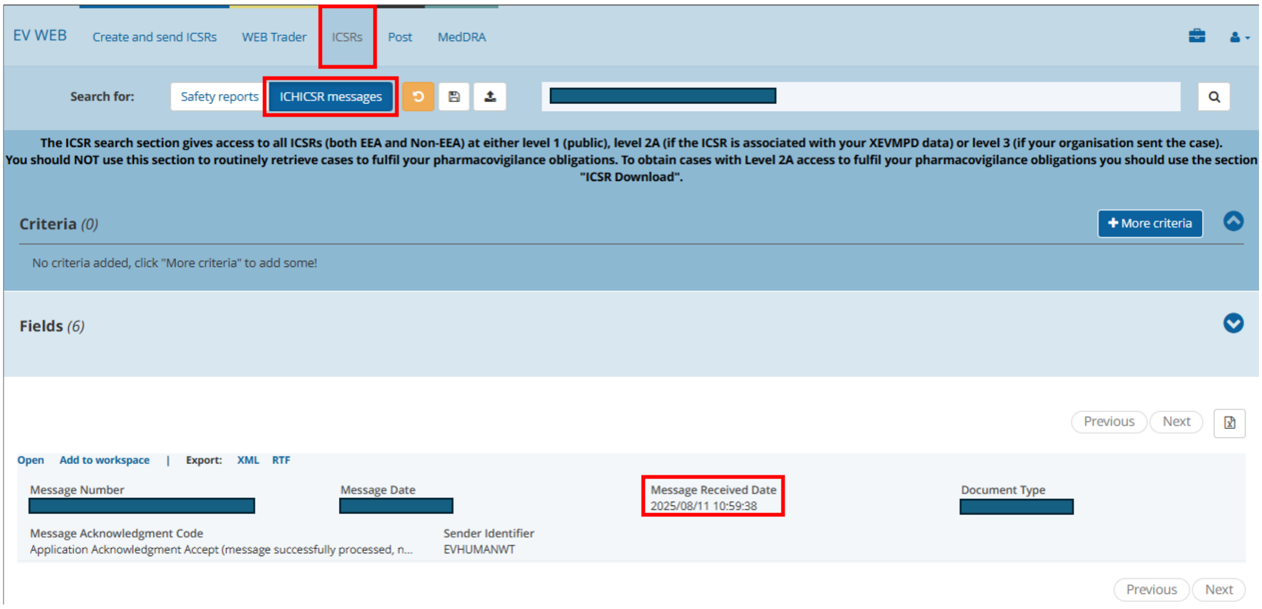


Figure 97 – Viewing the official gateway date in EVWEB

3.5.2.3.1. Reporting compliance calculation

As explained in the EMA document Compliance notifications explanation and Q&A, the reporting compliance is calculated between the official receipt date (Gateway or MDN date) and receipt of the latest information about the case (C.1.5 "Date of most recent information for this report").

The ICH E2B(R3) field C.1.5 "Date of Most Recent Information for this Report" captures the date each time significant information (whether initial or follow-up) on a given case is directly reported by the primary source to the sender organisation.

The EudraVigilance Gateway Date is the date of the ICSR-MDN, which is returned to sender organisation by the EV Gateway for each safety report message successfully transmitted; for WebTrader users, the gateway date is visible in the ICHICSR messages area of the **ICSRs** section of EVWEB – see **section 3.5.2.3. Viewing the EMA's official receipt date (gateway date) for a case in EVWEB**).

As detailed in the EU Individual Case Safety Report (ICSR) Implementation Guide, Chapter **I.C.2.1.8 Processing and Acknowledgement of Receipt of Safety Messages**:

> *(…) the date of the ICSR-MDN will serve as the official receipt date of the transmission of the Safety Message by the Gateway and it documents the fulfilment of the reporting timelines as defined in EU legislation. (…)*

Notes:

1. When a case is transmitted to EV and the Acknowledgment (ACK) message is received, this confirms that the transmission was successful. Still, the organisation should review the ACK

codes included in the message, explained further below, to determine whether additional action is required.

2. If an ACK message is **not** received within a few minutes, the transmission has likely **failed**. However, in certain situations – such as during system maintenance or for submissions done outside the EMA business hours – the processing may take up to 48 hours. For this reason, organisations should wait, ideally and if feasible, approximately 24 hours to confirm whether it is received. If the ACK is still not available after this period, the organisations should contact the EMA's Gateway team to request clarification.

   Organisations should **not** submit multiple copies of the same case during the 24-hour waiting period as doing so would result in duplicate reports being created in EV, creating unnecessary burden with no added value.

   Note: If a case is transmitted to EV but **no ACK is returned, then the regulatory clock has not stopped**. The clock will only stop once a positive ACK is received, as explained further below.

3. When a transmission has occurred, the message is **only** considered as having been successfully delivered to EudraVigilance if the corresponding message ACK contains the code "**AA**" [Application Acknowledgement Accept]. This code denotes that all ICSRs included in the message were successfully loaded into the EV database and, therefore, each case received a positive ACK at report level ("**CA**" [Commit Accept] acknowledgement).

   However, if the message ACK contains the code "**AE**" [Application Acknowledgement Error] this indicates that at least one of the ICSRs was **not** successfully processed in EV and, as such, it received negative ACK at report level ("**CR**" [Commit Reject] acknowledgement). When receiving an "**AE**" acknowledgement, the user should check which ICSR(s) contained errors, correct them and resend those ICSRs to EudraVigilance.

   Finally, if the message ACK contains the code "**AR**" [Application Acknowledgement Reject], then there was a parsing error and no data was extracted, requiring correction and resubmission of the entire message.

   Please refer to section **I.C.2.1.8 Processing and Acknowledgement of Receipt of Safety Messages** of the EU Individual Case Safety Report (ICSR) Implementation Guide, for further guidance on these codes.

   Note: For cases that received a "**CR**" acknowledgement, **the regulatory timeline clock has not stopped** – the clock will only stop once a positive ACK ("**CA**" acknowledgement) is received. Therefore, those cases should be corrected and resubmitted to EudraVigilance.

4. Given the considerations above, organisations should plan their submissions to EV in order to have enough time to accommodate any potential delays.

5. If a case was successfully transmitted and a Positive (**AA**-**CA**) ACK returned, then the regulatory clock has stopped.

6. The EMA's official receipt date of the ICSRs is reflected in the E2B(R3) field "ACK.M.4 Acknowledgement date of batch transmission" of the ACK message. Organisations can view it also in EVWEB – please refer to **section 3.5.2.3. Viewing the EMA's official receipt date (gateway date) for a case in EVWEB**.

3.6. Post Screen Functions

The **Post** screen provides a quick method to import and send a Safety message to the EVDBMS. It accepts only XML files that are compliant with the ICH E2B(R3) standard. To access the **Post** screen click on the **Post** link in the main menu.

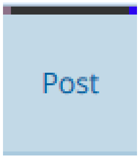


Figure 98 - The Post screen link

The following screen will be displayed once you enter this link:

Figure 99 - Post screen

The process is quite straightforward. The user needs to click on the "Import XML" button that appears at the top left of the **Post** screen. This action will display a file selection window in which the user can locate and select a local XML file.

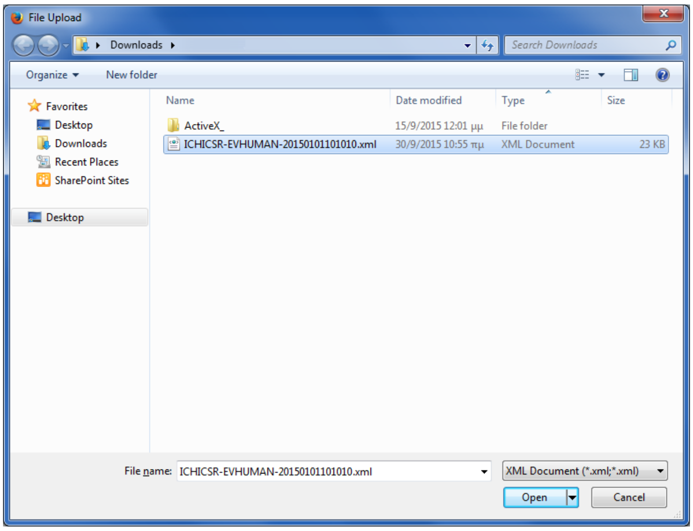


Figure 100 - Post screen file selection window

Once the file is selected and uploaded, EVWEB initiates a series of validation checks to make sure that the message is eligible, and then proceeds to submit it to the EVDBMS.

Note: The maximum XML file size allowed to be submitted via the **Post** screen is 20 MB.

Upon successful submission of the XML file, EVWEB will place a copy of it in your WEB Trader "Outbox" view area for future reference.

3.7. Workspace Screen Functions

The **Workspace** screen acts as a temporary, centralised, area where multiple EVWEB items (ICSRs, Safety messages, Acknowledgement messages) can be added for better review and management.

Attention: The **Workspace** screen retains the added EVWEB items only during an active EVWEB session. If a user logs out or terminates the session (i.e. closes the web browser window), the **Workspace** screen will clear all previously added items. The cleared items are not actually deleted since they reside on the remote EVDBMS. Items added to the **Workspace** screen are copies that are loaded from the remote system.

To access the **Workspace** screen click on the suitcase icon () in the main menu.

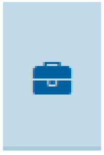


Figure 101 - Workspace screen link

The following screen will be displayed once you enter this link:

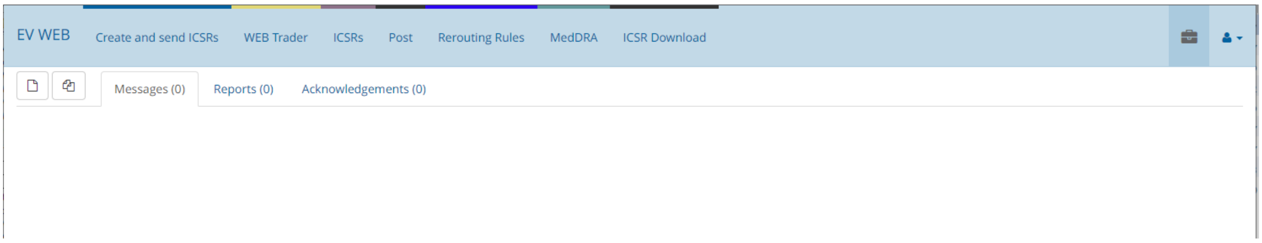
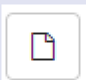


Figure 102 - Workspace screen

The main options available to the user are located at the top left of the **Workspace** screen. Their purpose is described in the following table:

Table 15 – Workspace Screen options

Workspace Screen Option	Description
	This is the **Workspace** import function of a single ICH E2B(R3) or ICH E2B(R2) compliant XML file (Safety message) in the **Workspace** screen. With this function, it is possible to import (upload) only 1 XML file at a time.
	This is the **Workspace** import function of multiple ICH E2B(R3) and/or ICH E2B(R2) compliant XML files (Safety message) in the **Workspace** screen. With this function, it is possible to import (upload) more than 1 XML files at the same time.

Workspace Screen Option	Description
Messages	This tab contains the Safety messages that have been imported or added to the **Workspace** screen from direct import (ICSR uploaded) into the **Workspace** area or via local import (ICSR added) from the **WEB Trader** screen.
Reports	This tab contains the ICSRs that have been added using the "Add to workspace" option from the **ICSRs** screen.
Acknowledgements	This tab contains the Acknowledgement messages that have been added using the "Add to workspace" option from the **WEB Trader** screen.

Note: The option "Add to workspace", which is available through the contextual actions menu and allows the addition of an EVWEB item in the **Workspace** screen, will appear only in the **WEB Trader** and **ICSRs** screens' contextual actions menu.

3.7.1. Import Function

The **Workspace** import function allows importing an ICH E2B(R3) or ICH E2B(R2) compliant XML file (Safety message) in the **Workspace** screen. The imported file is placed in the "Messages" tab and is available for further handling. Note that this function is only available when the user is in the "Messages" tab.

Note: ICH E2B(R2) compliant XML files can **only** be imported into EVWEB through the **Workspace** import function. In other words, the ICH E2B(R2) XML file **cannot** be uploaded via the **Create and send ICSRs** screen.

3.7.1.1. Import of a single XML file

The user needs to click on the single XML file import icon () that appears at the top left of the **Workspace** screen. This action will display a file selection window in which the user can locate and select a local XML file.

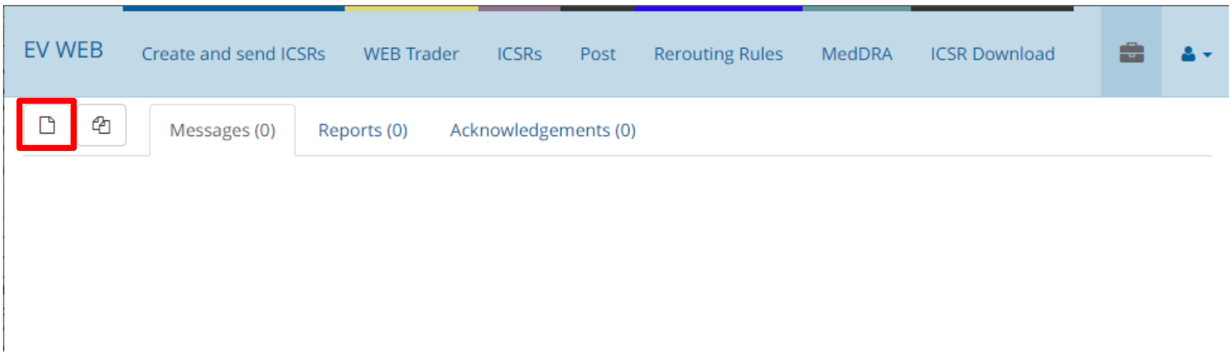


Figure 103 - Workspace import function

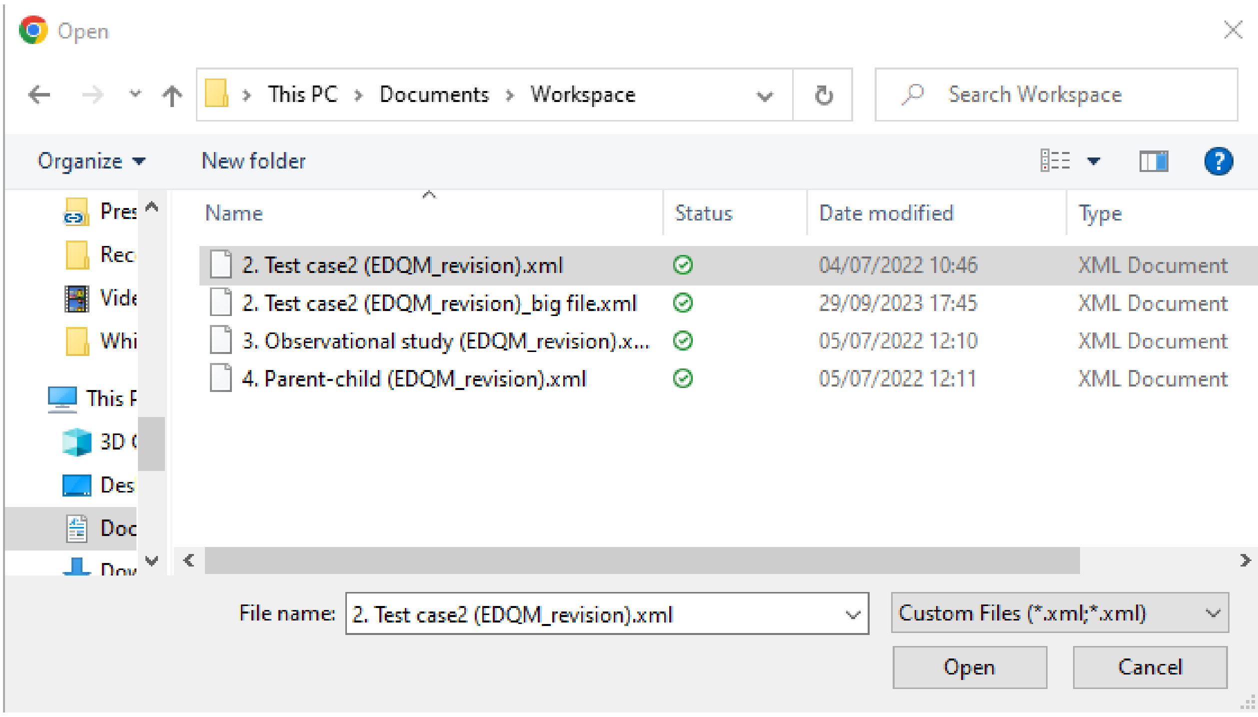


Figure 104 - Workspace screen: Importing an XML file

If there is a problem with a file (for example, the file size exceeds the maximum allowed size), an error message is returned.

Figure 105 - Error message

Once the XML file is imported, it is placed in the “Messages” tab for further handling (see **section 3.7.2. Messages Tab** for more information).

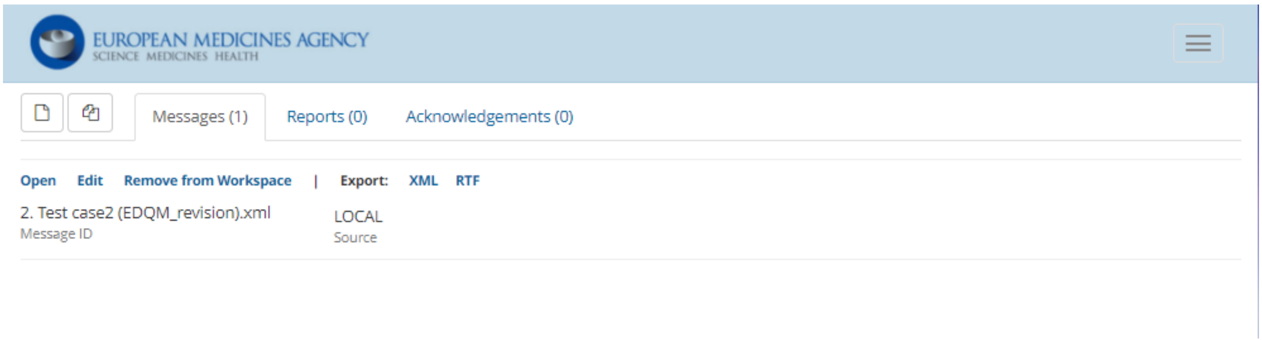


Figure 106 - Workspace screen: 1 XML file imported

It is possible to repeat this operation to add another XML file. The imported XML files will be placed in the “Messages” tab for further handling (see **section 3.7.2. Messages Tab** for more information).

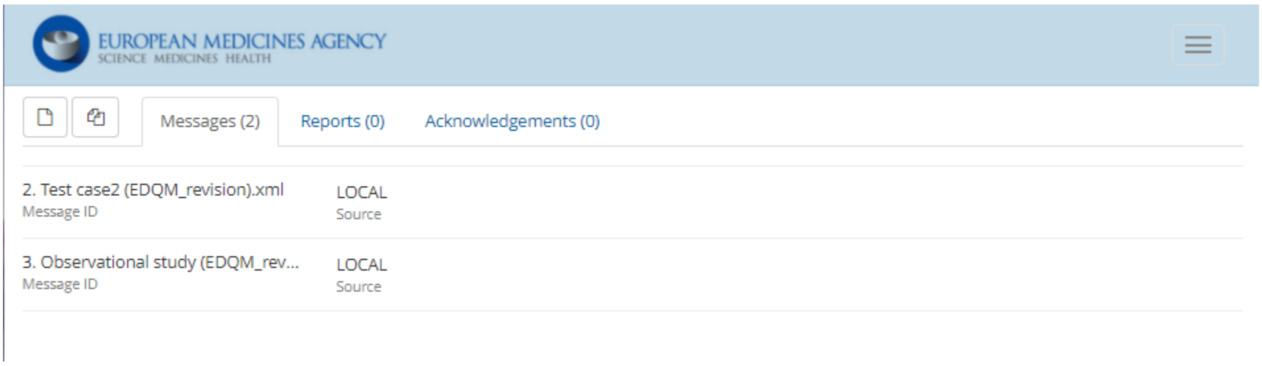


Figure 107 - Workspace screen: 2 XML files imported

3.7.1.2. Import of multiple XML files

The user needs to click on the multiple XML file import icon ( ) that appears at the top left of the **Workspace** screen. This action will display a new window in which the user can use to locate and select multiple local XML files.

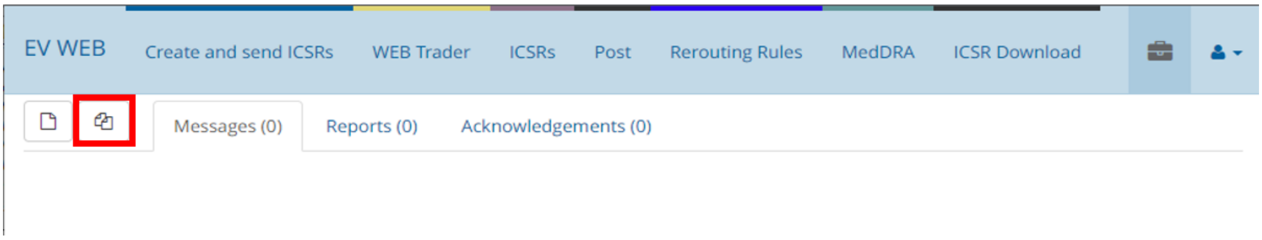


Figure 108 - Workspace import function

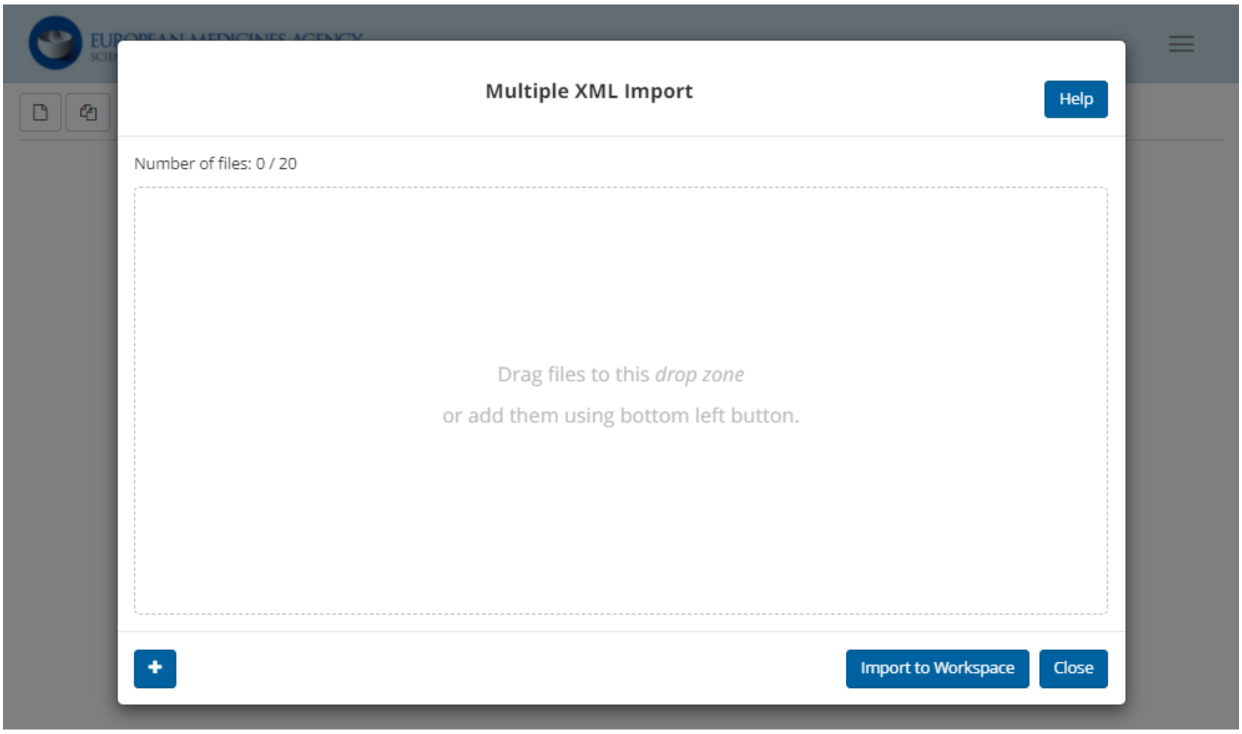


Figure 109 - Workspace screen: Importing multiple XML files

To select the XML files, you can click on the "+" button (+). This action will display a file selection window in which the user can locate and select the local XML files.

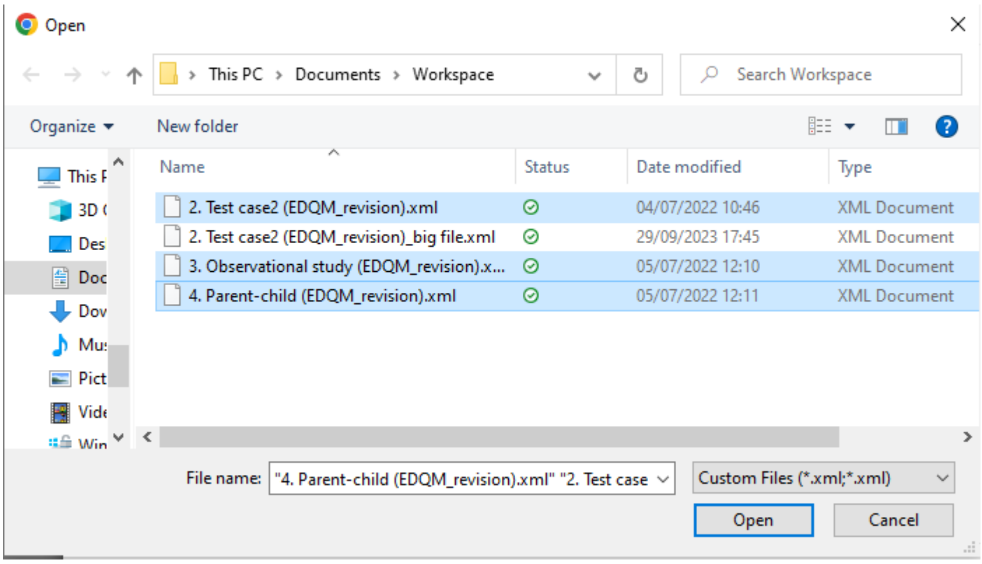


Figure 110 - Workspace screen: Importing multiple XML files

Once the intended files are selected, just click on "Open" and the files will be loaded into the "Multiple XML Import" window. If there is a problem with a file (for example, the file size exceeds the maximum allowed size), the problematic file will have the colour **red** assigned, instead of **green**.

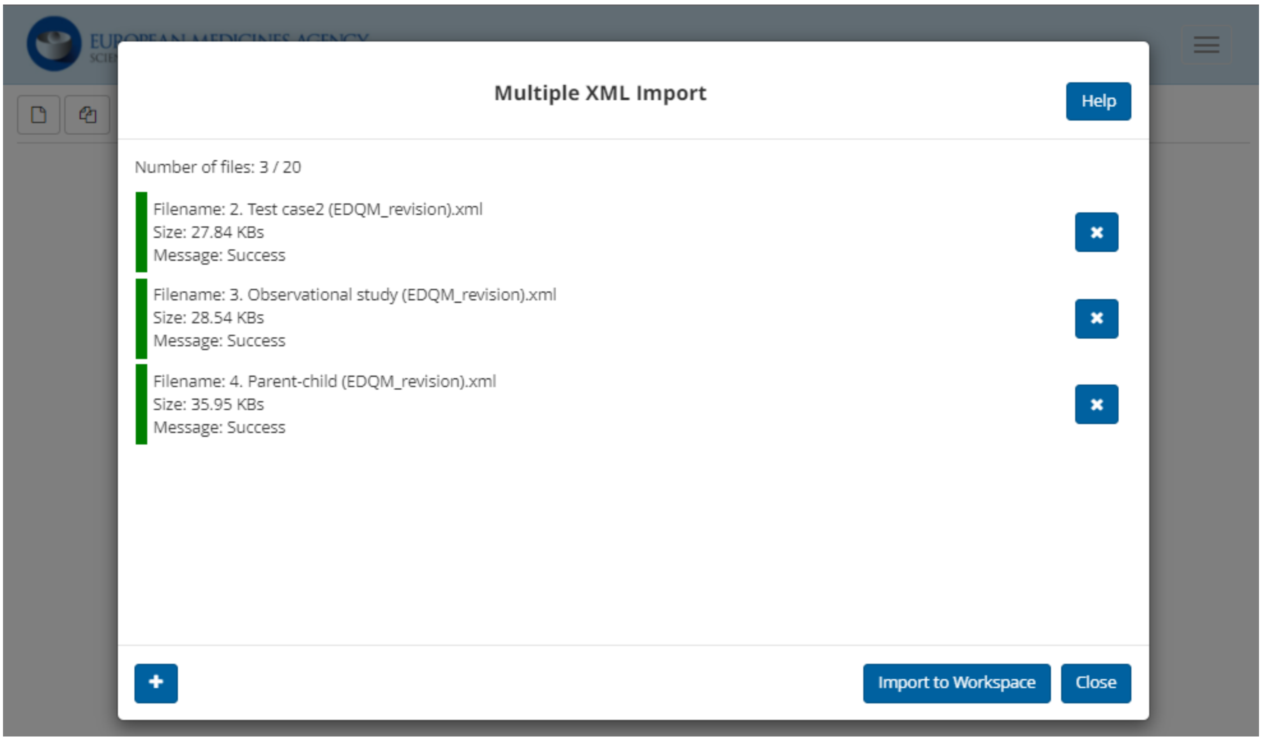


Figure 111 - Multiple XML Imported – all files are ok

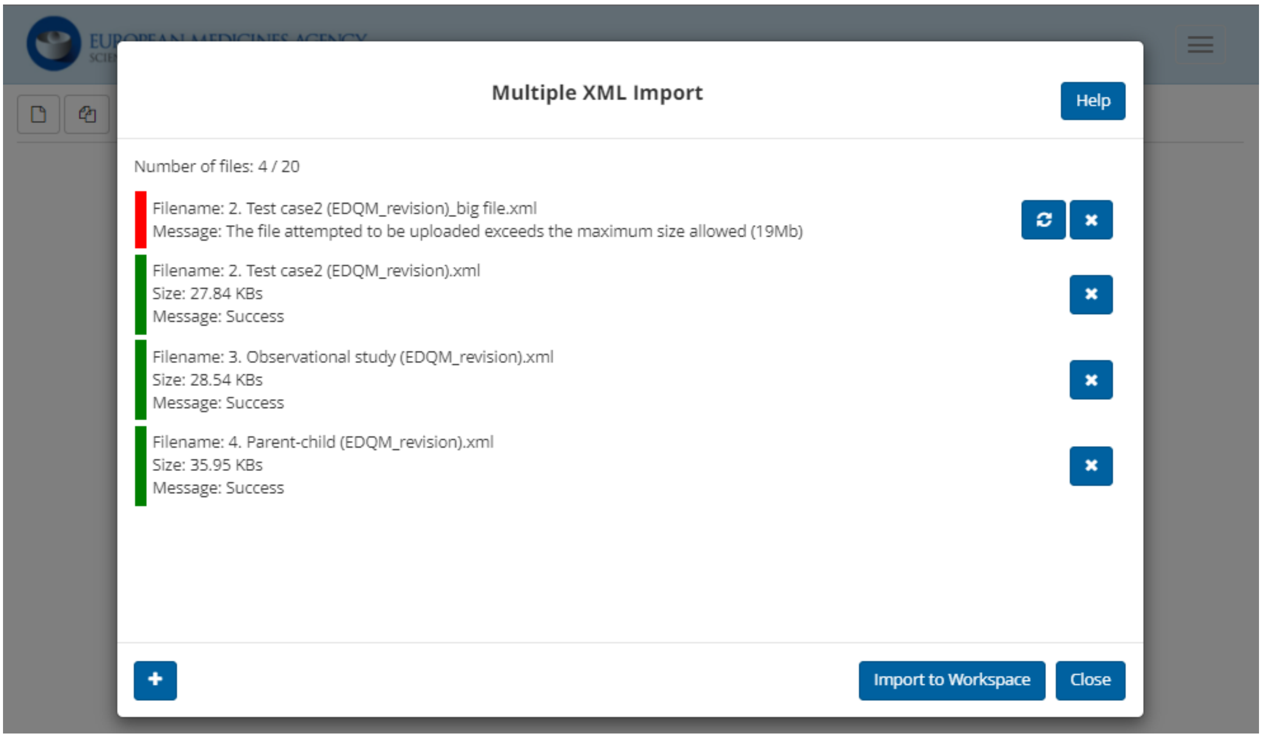


Figure 112 - Multiple XML Imported – not all files are ok

In this situation, you can either repeat the upload process by clicking on the "Reload" button ( ) or delete the XML file by clicking on the "Remove file" button ( ).

The Help (Help) button prompts the user to refer to the EVWEB User Manual, where additional guidance is available.

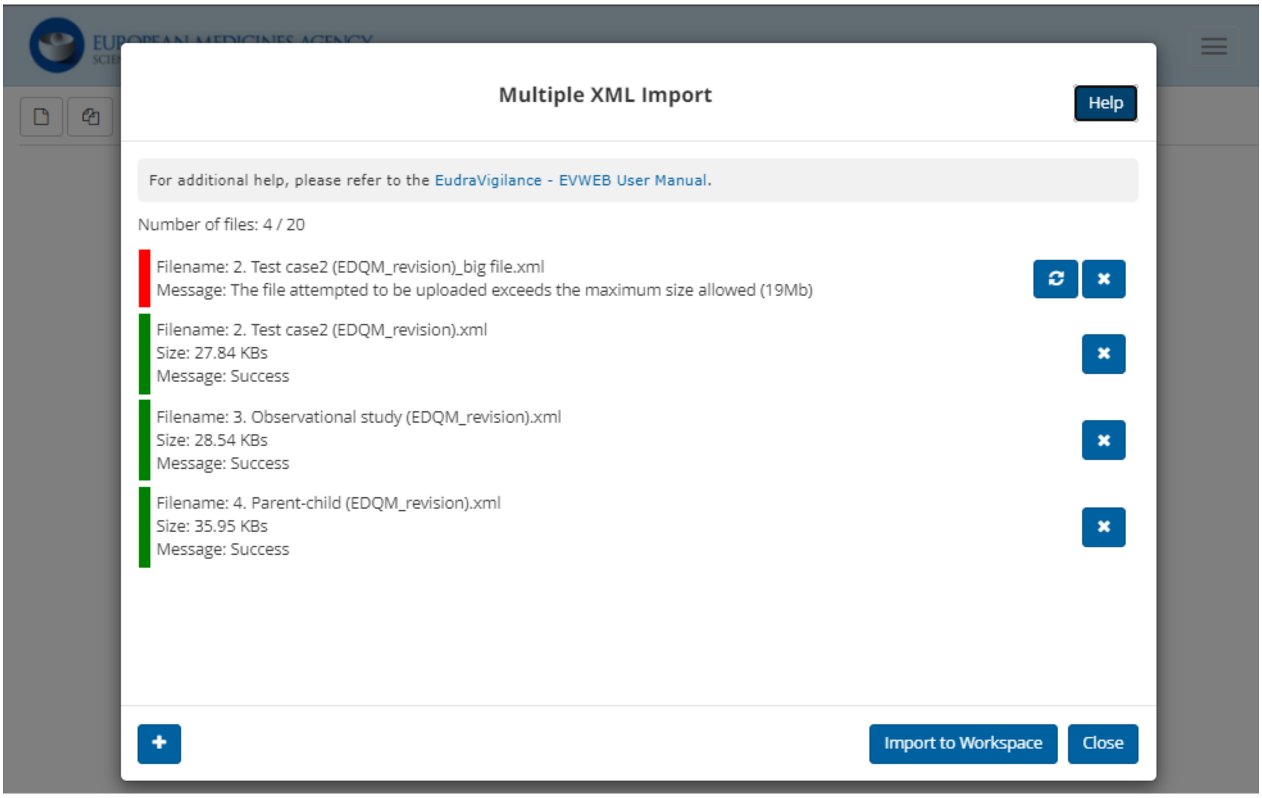


Figure 113 - Help message displayed when the Help button is clicked

Regardless of the XML files being ok or not, the "Import to Workspace" ( ) button finishes the upload process by importing only the XML files that are error free. Once the XML files are imported, they are placed in the "Messages" tab for further handling (see **section 3.7.2. Messages Tab** for more information).

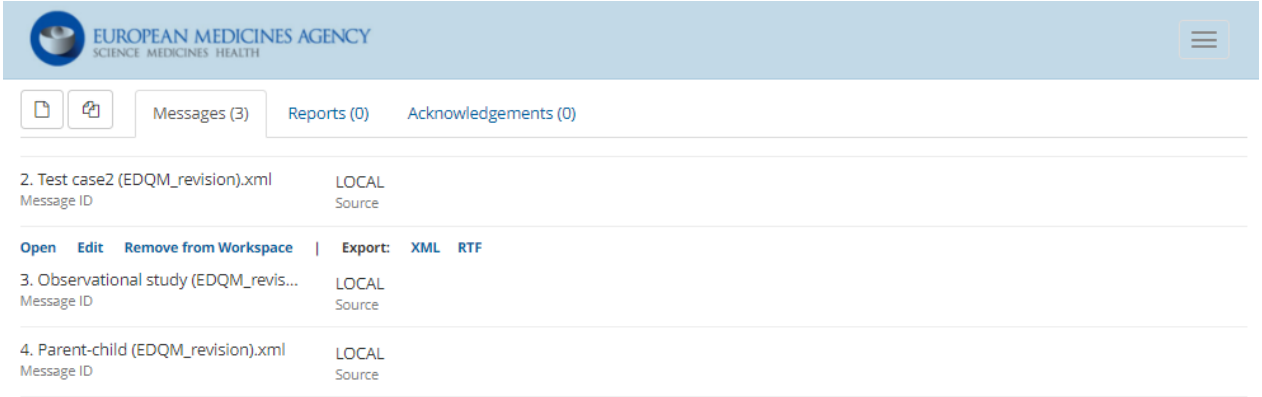


Figure 114 - Workspace screen: 1 XML file (containing only 1 case) imported

3.7.2. Messages Tab

The "Messages" tab contains Safety messages that have been imported using the import function of the **Workspace** screen, or have been added using the "Add to workspace" option (found in the contextual actions menu) from the **WEB Trader** or **ISCRs** screens.

Tip: The value in the parentheses following the tab's title indicates the number of messages available in the tab.

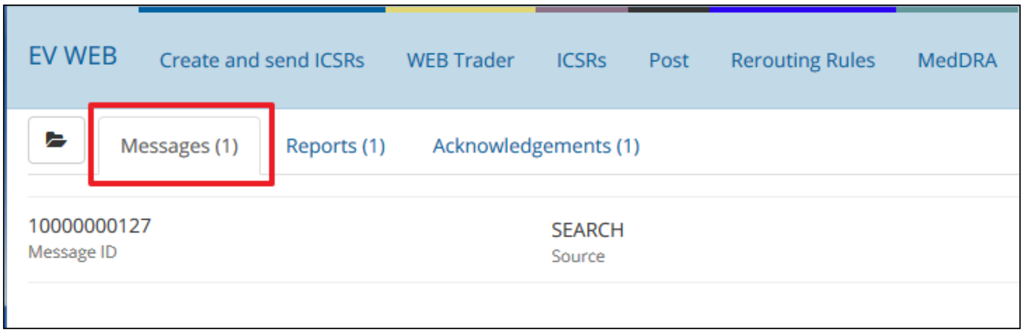


Figure 115 - Workspace screen: The "Messages" tab

The available Safety messages in the "Messages" tab are displayed in a list view layout.

The description fields per message are:

- **Message ID:** This is the message's identification number. It is a unique code that distinguishes it from other messages.
- **Source:** This discloses the origin of the message. It could include entries such as:
  - SEARCH
  - WEBTRADER

– LOCAL

The "SEARCH" source descriptor denotes that the message was added to the **Workspace** screen from a search process. This search process could have been initiated by a simple or advanced query in the **ICSRs** screen.

The "WEBTRADER" source descriptor denotes that the message was added to the Workspace screen from the WEB Trader screen.

The "LOCAL" source descriptor denotes that the message was added to the Workspace screen by importing an XML file using the Workspace screen's import function (see **section 3.7.1. Import Function** for further details).

Besides browsing the Safety messages that have been added to the **Workspace** screen, the "Messages" tab also allows you to manage these items. This is possible through the contextual actions menu that appears once you click on a Safety message.

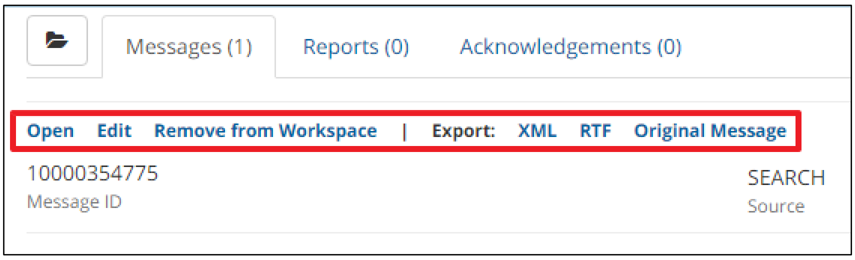


Figure 116 - Contextual actions menu in "Messages" tab

The available contextual actions menu options that appear in this case are the following:

Table 16 – Description of the options in the Contextual Actions Menu

Contextual Actions Menu Option	Description
Open	Loads the selected Safety message and displays it in a typical, read-only, tree view and active area format, within the **Workspace** screen. **Note:** After clicking the "Open" option, it will be substituted by the option "Close" which, when clicked, unloads the opened Safety message and returns you back to the regular list view layout.
Edit	Opens the selected Safety message in the **Create and send ICSRs** screen and allows the modification of its content.
Remove from Workspace	Removes the selected Safety message item from the **Workspace** screen.
Export	Exports the selected Safety message into an XML file (which is the typical format for a Safety message), a RTF file (which is the typical "text" document format), or as the Original Message that was sent to/received from the system. See **section 3.9. Export Functions** for more information regarding EVWEB's export features.

3.7.3. Reports Tab

The "Reports" tab contains ICSRs that have been added using the "Add to workspace" option (found in the contextual actions menu) from the **ICSRs** screen.

Tip: The value in the parentheses following the tab's title indicates the number of reports available in the tab.

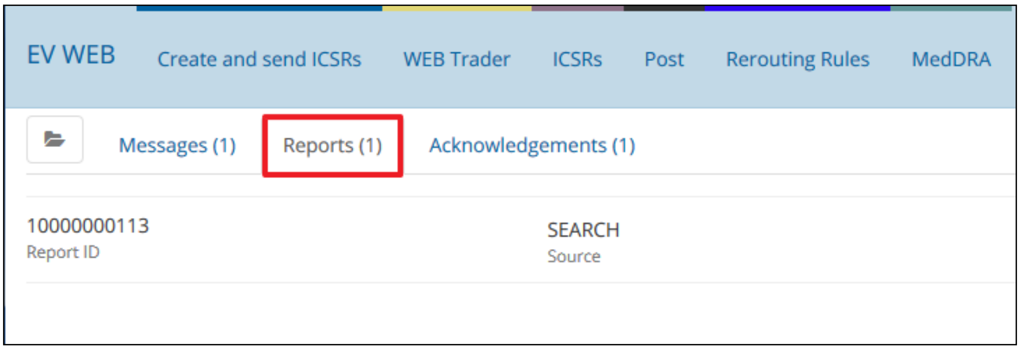


Figure 117 - Workspace screen: The "Reports" tab

The available ICSRs in the "Reports" tab are displayed in a list view layout.

The description fields per ICSR are:

- **Report ID:** This is the ICSR's identification number. It is a unique code that distinguishes it from other ICSRs.
- **Source:** This discloses the origin of the ICSR. It usually will include the entry "SEARCH", which denotes that the ICSR was added to the **Workspace** screen from a search process. This search process could have been initiated by a simple or advanced query in the **ICSRs** screen.

Besides browsing the ICSRs that have been added to the **Workspace** screen, the "Reports" tab also allows you to manage these items. This is possible through the contextual actions menu that appears once you click on an ICSR.

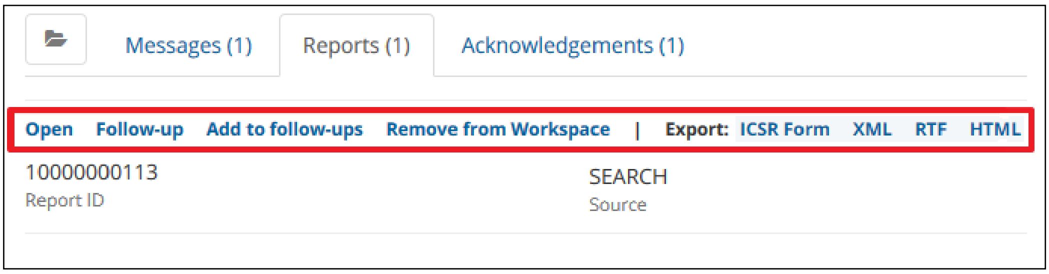


Figure 118 - Contextual actions menu in "Reports" tab

The available contextual actions menu options that appear in this case are the following:

Table 17 – Description of the options in the Contextual Actions Menu

Contextual Actions Menu Option	Description
Open	Loads the selected ICSR and displays it in a typical, read-only, tree view and active area format, within the **Workspace** screen. **Note:** After clicking the "Open" option, it will be substituted by the option "Close" which, when clicked, unloads the opened ICSR and returns you back to the regular list view layout.
Follow-up	Creates a copy of the selected ICSR, adding it to the current Safety message in the **Create and send ICSRs** screen, and navigates you to that screen for modification of the ICSR content. Note that the created follow-up ICSR is populated with all values from the selected ICSR. See **section 0** **Create** a case Follow-up, Amendment or Nullification **Case Follow-Up** for more information regarding the "Follow-up" option.
Add to follow-ups	Creates a copy of the selected ICSR, adding it to the current Safety message in the **Create and send ICSRs** screen, but does not navigate you to that screen. You remain in the "Reports" tab of the **Workspace** screen to perform other actions (i.e. initiate more "Add to follow-ups"). See **section 0** **Create** a case Follow-up, Amendment or Nullification for more information regarding the "Add to follow-ups" option.
Remove from Workspace	Removes the selected ICSR item from the **Workspace** screen.
Export	Exports the selected ICSR into the following formats: ICSR Form, XML, RTF and HTML. See **section 3.9. Export Functions** for more information regarding EVWEB's export features.

3.7.4. Acknowledgements Tab

The "Acknowledgements" tab contains Acknowledgement messages that have been added using the "Add to workspace" option (found in the contextual actions menu) from the **WEB Trader** screen.

Tip: The value in the parentheses following the tab's title indicates the number of Acknowledgement messages available in the tab.

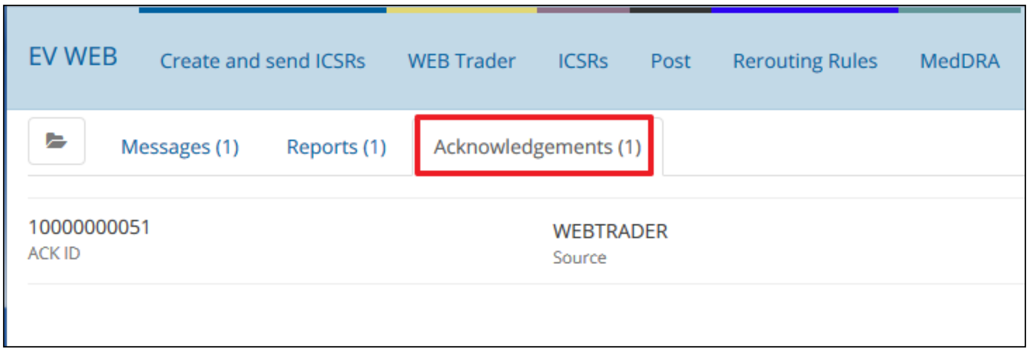


Figure 119 - Workspace screen: The "Acknowledgements" tab

The available Acknowledgement messages in the "Acknowledgements" tab are displayed in a list view layout.

The description fields per Acknowledgement message are:

- **ACK ID:** This is the Acknowledgement message's identification number. It is a unique code that distinguishes it from other Acknowledgement messages.
- **Source:** This discloses the origin of the Acknowledgement message. It usually will include the entry "WEBTRADER", which denotes that the Acknowledgement message was added from the **WEB Trader** screen.

Besides browsing the Acknowledgement messages that have been added to the **Workspace** screen, the "Acknowledgements" tab also allows you to manage these items. This is possible through the contextual actions menu that appears once you click on an Acknowledgement message.

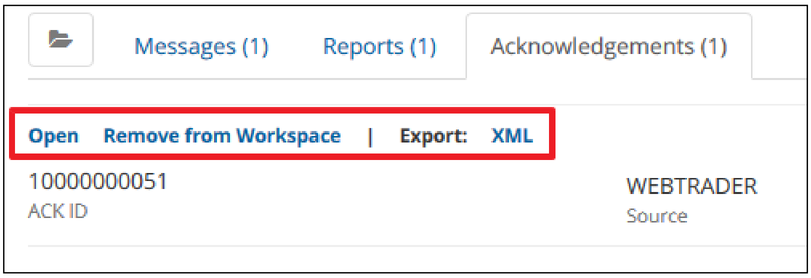


Figure 120 - Contextual actions menu in "Acknowledgements" tab

The available contextual actions menu options that appear in this case are the following:

Table 18 – Description of the options in the Contextual Actions Menu

Contextual Actions Menu Option	Description
Open	Loads the selected Acknowledgement message and displays it in a typical, read-only, tree view and active area format, within the **Workspace** screen. **Note:** After clicking the "Open" option, it will be substituted by the option "Close" which, when clicked, unloads the opened Acknowledgement message and returns you back to the regular list view layout.
Remove from Workspace	Removes the selected Acknowledgement message item from the **Workspace** screen.

Contextual Actions Menu Option	Description
Export	Exports the selected Acknowledgement message into an XML file (which is the typical format for an Acknowledgement message). See **section 3.9. Export Functions** for more information regarding EVWEB's export features.

3.8. Create a case Follow-up, Amendment or Nullification

3.8.1. Case Follow-Up

During routine case processing activities, additional information may be received by the case sender directly from the Reporter/Primary Source. That new information is regarded as follow-up information and can be classified as Significant or as non-significant information and this will dictate if a new report for the case needs to be submitted or not.

Significant information:

Senders of cases should submit follow-up ICSRs if significant new medical information has been received directly from the Primary Source. Significant new information relates to, for example, a new suspected adverse reaction, a change in the causality assessment, and any new or updated information on a case that impacts on its medical interpretation. Medical judgement should therefore be applied for the identification of significant new information requiring to be submitted as follow-up ICSR.

Situations where the seriousness criteria and/or the causality assessment are downgraded (e.g. the follow-up information leads to a change of the seriousness criteria from serious to non-serious, or the causality assessment is changed from related to non-related) should also be considered as significant changes and thus submitted as ICSR.

In addition, the competent authority in a Member State or the marketing authorisation holder should also submit a new version of an ICSR, when new administrative information is available, that could impact on the case management. For example, if new case identifiers have become known to the sender, which may have been used in previous submissions. This information may be specifically relevant to manage potential duplicates. In this context, the following sections should be completed in line with ICH-E2B:

Table 19 – ICH E2B(R3) requirements

Reference	E2B(R3) requirements
ICH-E2B(R3)	• Section C.1.9.1 'Other case identifiers in previous transmissions'.

Another example refers to additional documents held by sender, whereby new documents that have become available to the sender may be relevant for the medical assessment of the case. In this regard, the following sections should be completed in line with ICH-E2B:

Table 20 – ICH E2B(R3) requirements

Reference	E2B(R3) requirements
ICH-E2B(R3)	• Section C.1.6 'Additional Available Documents Held by Sender'.

New follow-up information should be clearly identifiable in the case narrative and the corresponding data should also be captured in structured fields, as applicable.

In line with ICH-E2B the following data elements/sections should always be completed for follow-up ICSRs submission:

Table 21 – ICH E2B(R3) requirements

Reference	E2B(R3) requirements
ICH-E2B(R3)	• Data element C.1.1 'Sender's (case) Safety Report Unique Identifier'. • Data element C.1.4 'Date Report Was First Received from Source' (which should remain unchanged). • Data element C.1.5 'Date of Most Recent Information for this Report'. • Section C.1.8 'Worldwide Unique Case Identification' (which should remain unchanged). • Data element C.3.2 'Sender's organisation'. • Data element H.1 'Case narrative including clinical course, therapeutic measures, outcome and additional relevant information' (for serious reports of suspected adverse reactions).

Non-significant information:

In contrast, a follow-up report which contains non-significant information does not require to be submitted as ICSR. This may refer, for example, to minor changes to some dates with no implication for the evaluation or submission of the case, or to some corrections of typographical errors in the previous case version. Medical judgement should be applied since a change to the birth date may constitute a significant modification (e.g. with implications on the age information of the patient). Similarly, a change of the status of a MedDRA code/term from current to noncurrent, due to a version change of MedDRA, can be considered as a non-significant change as long as this change has no impact on the medical content of a case.

The "Follow-up" and "Add to follow-ups" options allow you to edit, update and resend existing ICSRs. These two options appear in the contextual actions menu of the following EVWEB screens:

- **ICSRs** screen (when displaying Safety reports):

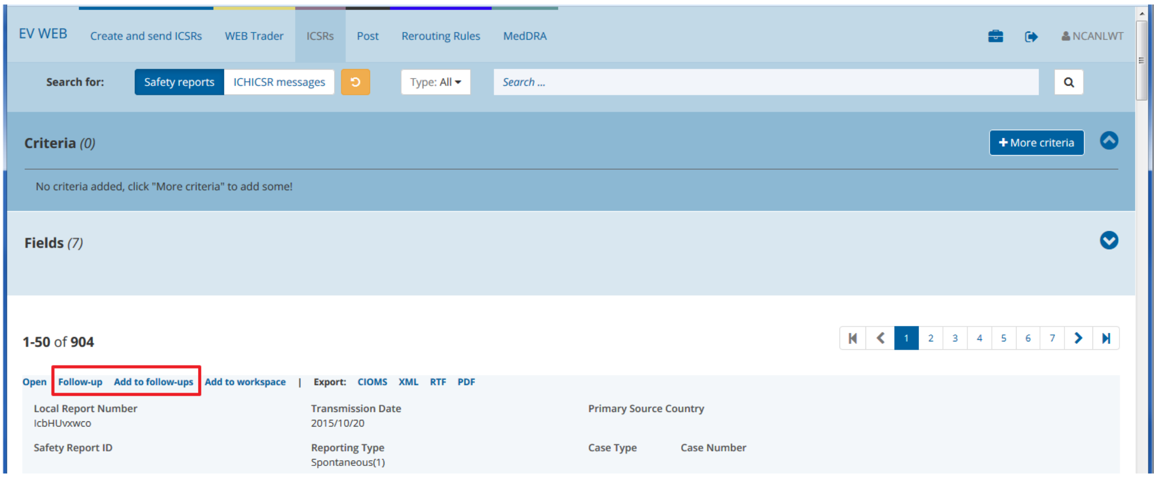


Figure 121 - "Follow-up" & "Add to follow-ups" options in the ICSRs screen

- **Workspace** screen (in the "Reports" tab):

Figure 122 - "Follow-up" & "Add to follow-ups" options in the Workspace screen

The "Follow-up" option creates a copy of the selected ICSR, adding it to the current Safety message in the **Create and send ICSRs** screen. You are then directed to that screen to modify the specific ICSR content (see **section 3.2. Creating Safety Messages & ICSRs** of this manual). The created follow-up ICSR is populated with all values from the selected ICSR, allowing you to locate and modify only the fields that require changing.

The "Add to follow-ups" option creates a copy of the selected ICSR, adding it to the current Safety message in the **Create and send ICSRs** screen, but does not navigate you to that screen. You remain in the current screen (**ICSR** or **Workspace**) to perform additional actions (i.e. initiate more "Add to follow-ups"). This provides a type of batch processing, in which you can add multiple follow-up ICSRs and then proceed to modify them based on your requirements.

3.8.2. Case Amendment

Serious and non-serious cases which have already been submitted to EudraVigilance may need to be amended when, for example, after an internal review or according to an expert opinion some items have been corrected (such as adverse event/reaction terms, seriousness, seriousness criteria or causality assessment) but **without** receipt of new information that would warrant for the submission of a follow-up report. The same would apply to situations where documentations mentioned in an ICSR, translations or literature articles are requested by competent authorities and are further sent as attachments in line with ICH E2B(R3). These submissions are considered as **amendment** reports.

Notes:

- For clarity, **new information** received from directly the primary source (significant or non-significant) should **always** be regarded as **follow-up** information. Hence, if the information fulfils the criteria for expedited reporting, i.e., is considered medically significant, then the report should be submitted to EudraVigilance as a **follow-up** and thus **never** as an amendment report.

- Where the additional information has **not** been received from the primary source but rather results from an internal revision of the case and significantly impacts on its medical evaluation, the ICSR should be resubmitted and amended information should be explained in the case narrative. For example, an amendment of the MedDRA coding due to a change in the interpretation of a previously submitted ICSR may constitute a significant change and therefore should be resubmitted as amendment report.
- If a report referring to a valid case was erroneously sent to the **incorrect EV Module** (for example: a SUSAR report sent to EVPM instead of EVCTM), the correct procedure is to send an **Amendment report** to the correct EV Module. The sender should **NOT** submit a nullification report as doing so would nullify the entire valid case in EudraVigilance, thereby preventing the organisation from submitting any further follow-ups for that case.

Users should note that if the organisation's HQ EV profile is set up to make submissions as a **gateway trader** (i.e. via a gateway connection) and they wish to amend a case in EV, then the amendment report can be submitted via the organisation's local Gateway. Alternatively, and in order to use the **EVWEB application** to amend their cases, they should use a separate 'Affiliate' or 'Virtual Affiliate' profile that has been set up as a WebTrader (more information is available in the EudraVigilance Registration Manual, under section 6.2). Organisations registered as Gateway trader do **not** have the "Validate & Send" button available to them (available only to WebTrader organisations) and thus will **not** be able to use the EVWEB tool to submit their amendment reports to EV.

The following principles should be followed when case amendment is required:

- The amendment reason should be **clear enough** and concise to explain **why** this case is being amended. For example, an amendment reason stating, 'corrections' or 'case being corrected following Health Authority request' are **not detailed enough explanations**;
- An individual case can only be amended by the original sending organisation.

In line with ICH-E2B the following applies for the submission of amendment ICSRs:

Table 22 – ICH E2B(R3) requirements

Reference	E2B(R3) requirements
ICH-E2B(R3)	• Data element C.1.1 'Sender's (case) Safety Report Unique Identifier' should remain unchanged. • Data element C.1.4 'Date Report Was First Received from Source' should remain unchanged. • Data element C.1.5 'Date of Most Recent Information for This Report' should remain unchanged. • Section C.1.8 'Worldwide Unique Identifier' should remain unchanged. • Data element C.1.11.1 'Report Nullification/Amendment' should be set to '2=Amendment'. • Data element C.1.11.2 'Reason for Nullification/Amendment' should be completed to indicate clearly the reason why a previously transmitted ICSR is amended.

Note: Please also refer to the EudraVigilance Training Module [EV Reporting for users: Create and send ICSRs using EVWEB part II (EV-M3e)](), namely to the video recording where it is shown the step-by-step on how to amend a case in EVWEB.

The case should first be loaded (see **section 3.8.1. Case Follow-Up**) and, next, the information in the case should be amended as needed (**please ensure that you also take into consideration the information from the table above**). For example, if the patient sex previously coded in the previous report was incorrect, it should be corrected to the intended value in the amendment report.

Also, in line with best practices, the organisation should add a note in the case narrative stating that the case is being amended, why it is being amended and what changes were made.

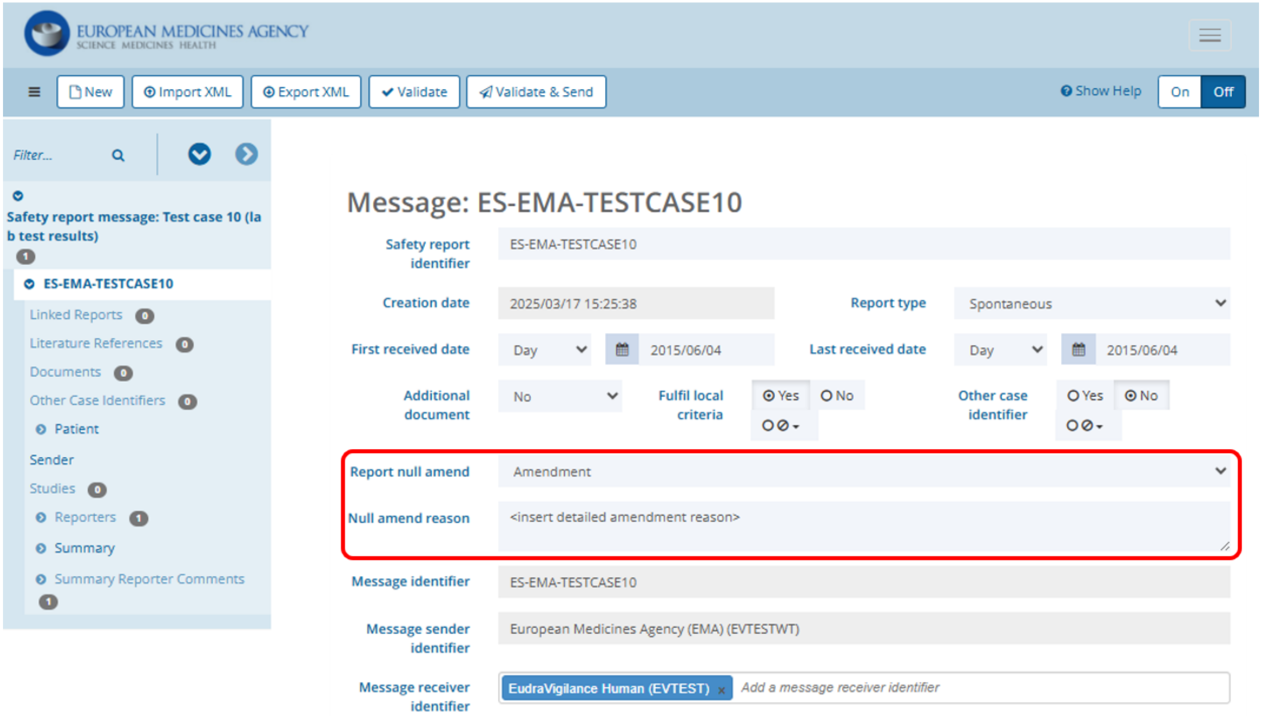


Figure 123- EVWEB snippet showing the fields populated

Finally, and to send the amendment report, you'll need to click on the "Validate & Send" button (see **section 3.3. Sending a Safety Message**). EVWEB will then proceed to validate the message first on the client-side. If the validation is successful, EVWEB will proceed and apply the server-side validation process. If any of these validation checks is unsuccessful, you will be presented with the validation result window which will contain the errors that need correction.

If both validation steps are successful, EVWEB will send the Safety message to the EVDBMS and place a copy of the message in the "Outbox" view area of the **WEB Trader** screen (see **section 3.4. WEB Trader Screen Functions** of this manual).

3.8.3. Case Nullification

The nullification of a case should be used to indicate that a previously transmitted ICSR is considered completely void (nullified), for example when the whole case was found to be erroneous.

Notes:

- If a report referring to a valid case was erroneously sent to the **incorrect EV Module** (for example: a SUSAR report sent to EVPM instead of EVCTM), the correct procedure is to send an **Amendment report** to the correct EV Module. The sender should **NOT** submit a nullification report as doing so would nullify the entire valid case in EudraVigilance, thereby preventing the organisation from submitting any further follow-ups for that case.
- For **SUSAR 'downgrade'** reports (i.e., a case previously submitted as a SUSAR that is later confirmed not to be serious or unexpected or related, and therefore no longer qualifies as a SUSAR), it is **NOT** appropriate to submit the downgrade as a nullification report. Doing so would nullify the entire case in EudraVigilance, preventing the sender from submitting any further follow-up reports. Therefore, SUSAR 'downgrade' reports should be submitted to EVCTM as a follow-up, within 15 calendar days, with the downgraded information is clearly explained in the narrative and the relevant E2B fields updated accordingly.
- GVP Module VI lists in **Table VI.11** of **Appendix 5** the most common scenarios where it is appropriate to send a nullification report to EV. Despite this document focusing on post-marketing reports, **the core principles on case nullification can still be applied, with the necessary adaptations, to SUSAR reports**.
- Similarly, GVP Module VI **Table VI.12** of **Appendix 5** contains a list of scenarios where the cases should **NOT** be nullified. Again, **most of those core principles can still be applied, with the necessary adaptations, to SUSAR reports** (i.e., to situations where the SUSAR should **NOT** be nullified).

Users should note that if the organisation's HQ EV profile is set up to make submissions as a **gateway trader** (i.e. via a gateway connection) and they wish to nullify a case in EV, then the nullification report can be submitted via the organisation's local Gateway. Alternatively, and in order to use the **EVWEB application** to nullify their cases, they should use a separate 'Affiliate' or 'Virtual Affiliate' profile that has been set up as a WebTrader (more information is available in the EudraVigilance Registration Manual, under section 6.2). Organisations registered as Gateway trader do **not** have the "Validate & Send" button available to them (available only to WebTrader organisations) and thus will **not** be able to use the EVWEB tool to submit their nullification reports to EV.

The following principles should be followed when case nullification is required:

- The nullification reason should be **clear enough** and concise to explain **why** this case is no longer considered to be a valid report. For example, a nullification reason stating, 'the report no longer meets the criteria for submission' or 'report sent previously in error' are **not detailed enough explanations**;
- An individual case can only be nullified by the original sending organisation;
- Once an individual case has been nullified, the case **cannot** be reactivated;
- **Individual versions (i.e. follow-up reports) of a case cannot be nullified. When a given report is nullified the entire individual case to which it refers to is nullified**;

- A nullified case is one that should no longer be considered for scientific evaluation. The process of nullification of a case is by means of a notification by the sender to the receiver that this is no longer a valid case. **However, the case should be retained in the sender's and receiver's pharmacovigilance database for auditing purposes**.

In line with ICH-E2B the following applies for nullified ICSRs submission:

Table 23 – ICH E2B(R3) requirements

Reference	E2B(R3) requirements
ICH-E2B(R3)	• Data element C.1.1 'Sender's (case) Safety Report Unique Identifier' (should remain unchanged. • Data element C.1.4 'Date Report Was First Received from Source' should remain unchanged. • The data element C.1.5 'Date of Most Recent Information for This Report' should either reflect the date when information was received that warrants the nullification of the report or otherwise should remain unchanged. • Data element C.1.8 'Worldwide Unique Identifier' should remain unchanged. • Data element C.1.11.1 'Report Nullification/Amendment' should be set to: 1=Nullification. • Data element C.1.11.2 'Reason for Nullification/Amendment' should be completed to indicate clearly the reason why a previously transmitted ICSR is considered completely void. • Data element C.3.2 'Sender's organisation' should remain unchanged.

Note: Please also refer to the EudraVigilance Training Module EV Reporting for users: Create and send ICSRs using EVWEB part II (EV-M3e), namely to the video recording where it is shown the step-by-step on how to nullify a case in EVWEB.

The case should first be loaded (see **section 3.8.1. Case Follow-Up**) and, next, the information in the case should be changed as needed so as to create a Nullification report (**see the information from the table above**).

In EVWEB, once the field C.1.11.1 "Report Nullification/Amendment" is set to: 1=Nullification, an automatic pop-up confirmation message appears, prompting the user to confirm that the nullification is required.

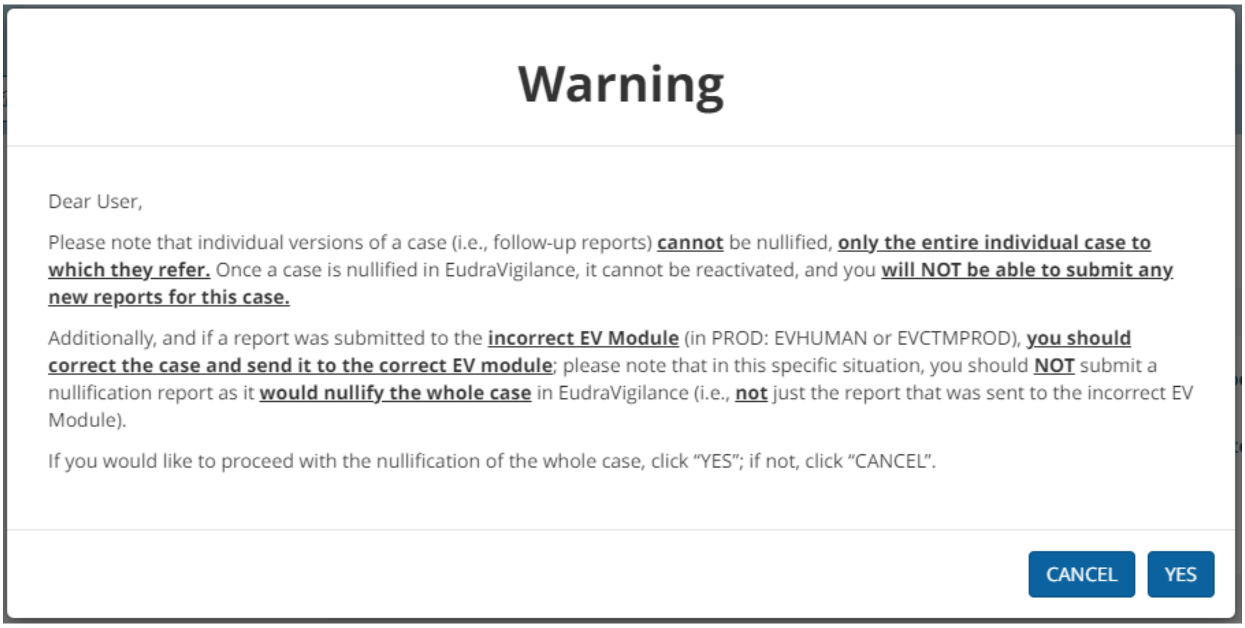


Figure 124- EVWEB snippet showing the warning message

Once the action is confirmed, the fields should appear as follows:

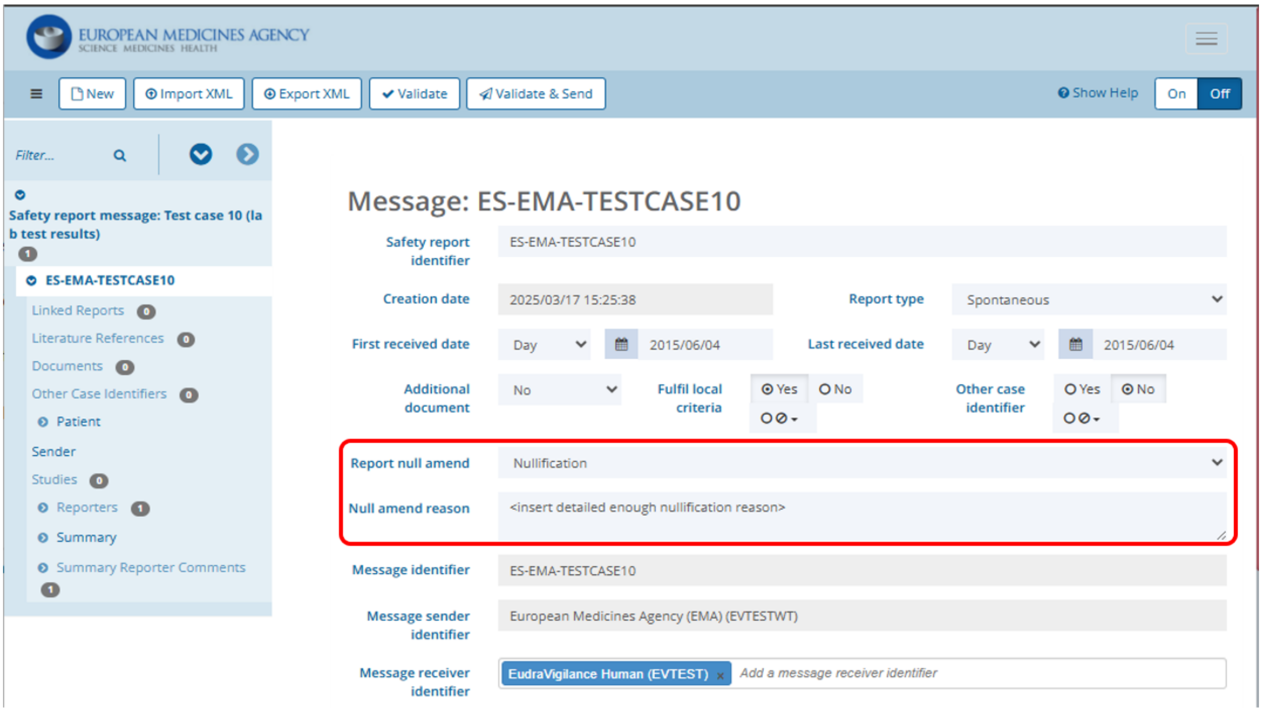


Figure 125 - EVWEB snippet showing the fields populated

To send the nullification report, you'll then need to click on the "Validate & Send" button (see **section 3.3. Sending a Safety Message**). EVWEB will then proceed to validate the message first on the client-side. If the validation is successful, EVWEB will proceed and apply the server-side validation process. If any of these validation checks is unsuccessful, you will be presented with the validation result window which will contain the errors that need correction.

If both validation steps are successful, EVWEB will send the Safety message to the EVDBMS and place a copy of the message in the "Outbox" view area of the **WEB Trader screen** (see **section 3.4. WEB Trader Screen Functions**).

3.9. Export Functions

EVWEB provides a framework to export ICSRs, Safety and Acknowledgement messages as electronic files enabling, thus, the distribution and storing of such items outside the EVDBMS. These export functions are available as selectable options in various locations in the application, and offer Excel list export, single-item export or bulk export features.

3.9.1. Excel List Export

In contrast to the other export functions featured in this section, this one does not export actual items (i.e. ICSRs or Safety messages) but only a list that references them. The Excel list export feature is available in most EVWEB screens that support list view in the active area, and is signified by the icon.

This type of export process is quite straightforward. For example:

- Set and run your ICSR or Safety message query in the ICSRs screen.
- Click on the Excel list export button to generate the list.
- Download and save locally the resulting Excel file.

The Excel list export button ( ) is located next to the page navigation buttons, at the top right corner of the query results area.

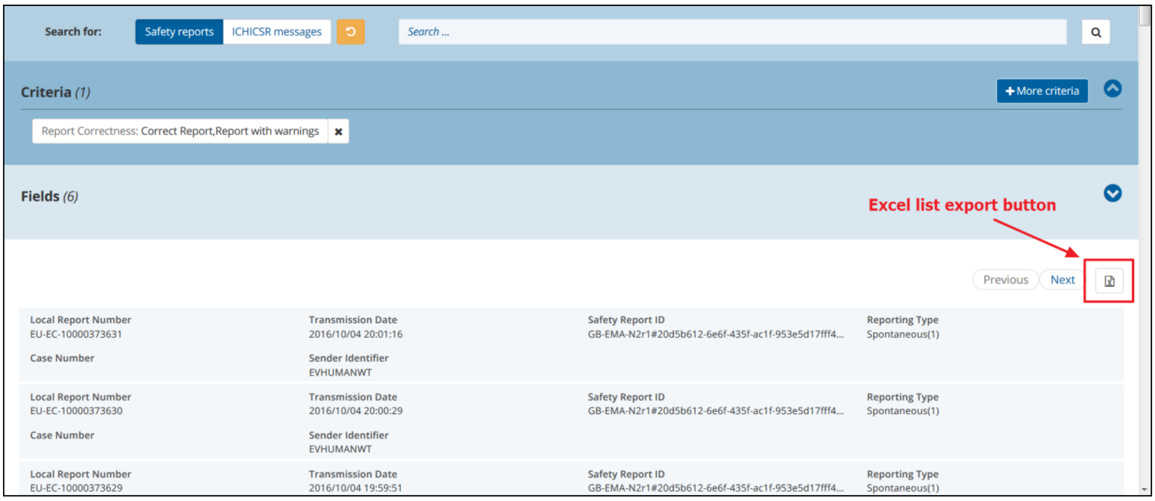


Figure 126 - Excel list export button location

The exported list contains any information that appears under the headers of each query result item's row. For example, the screenshot below has such ICSR headers highlighted (same applies to Safety messages):

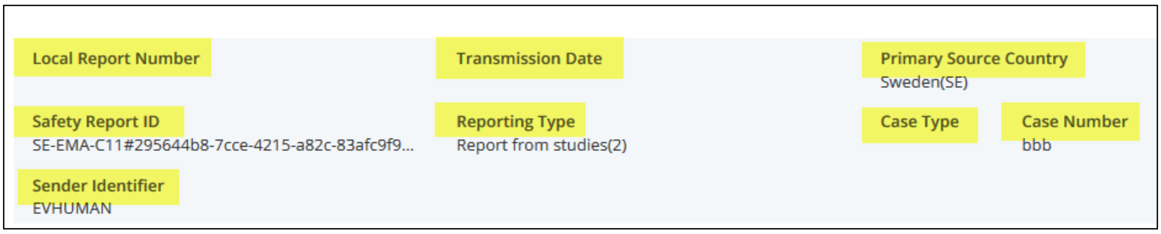


Figure 127 - ICSR headers included in Excel list export

If you open the exported Excel file, you can see the identical headers with all relevant information under them:

	A	B	C	D	E	F	G	H	I
1	Row #	Local Report Number	Transmission Date	Primary Source Country	Safety Report ID	Reporting Type	Case Type	Case Number	Sender Identifier
2	1	cnCzWtANNH	2015-08-15T00:00:00.000Z		SE-EMA-KK2108	Spontaneous(1)		SE-EMA-KK2108	EVHUMAN
3									
4									

Figure 128 - Excel list export file contents

3.9.2. Single-Item Export

To export single EV items you can use any 2 of the following EVWEB locations:

- In the dynamic buttons set of the following screens (as XML only export):
  - Create and send ICSRs
  - WEB Trader (when creating an Acknowledgement message)

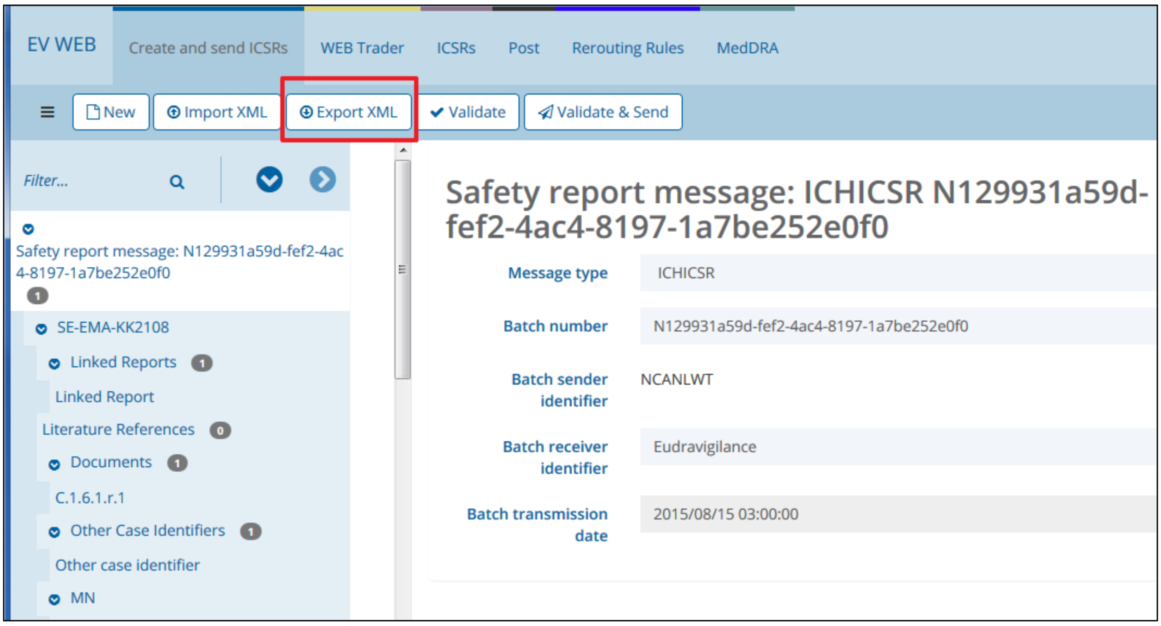


Figure 129 - Export function in the dynamic buttons set

- In the contextual actions menu of the following screens:
  - WEB Trader
  - ICSRs
  - Workspace

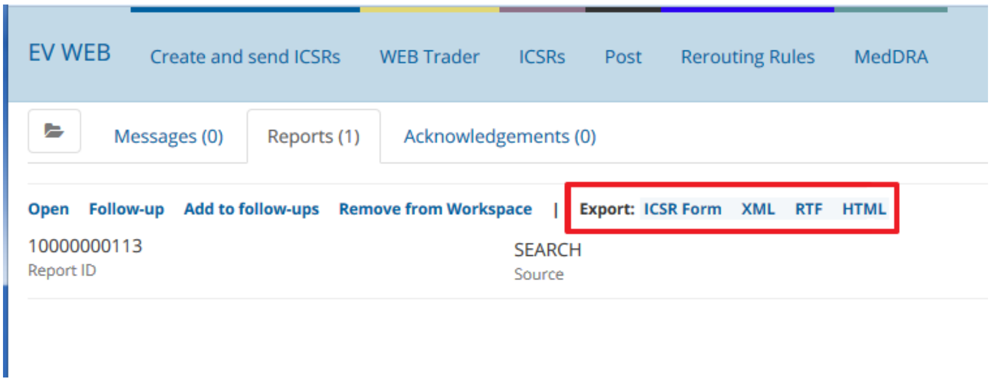


Figure 130 - Export function in the contextual actions menu (Reports tab)

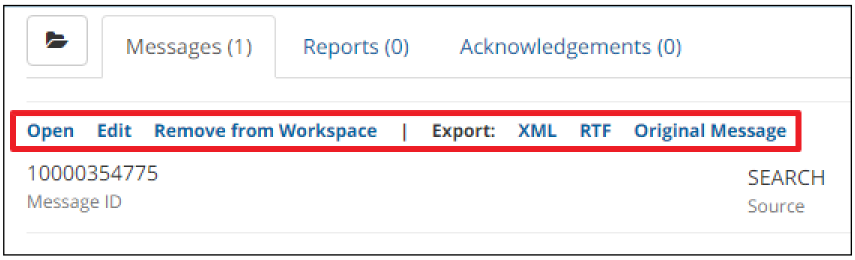


Figure 131 - Export function in the contextual actions menu (Messages tab)

Once you initiate the export function, and regardless of the function's location (i.e. dynamic buttons set or contextual actions menu), a window will appear requesting you to download the generated file.

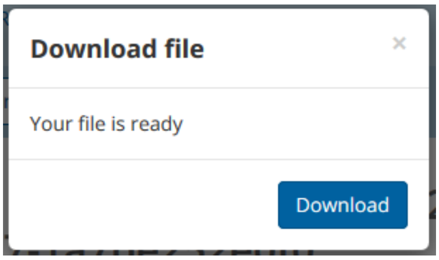


Figure 132 - Export function: Downloading the generated file

By clicking on the "Download" button you can save the exported file to your local computer or network.

The available export file formats vary per EVDBMS item. The below matrix outlines the supported export file formats per these items:

Table 24 – EVDBMS Item matrix

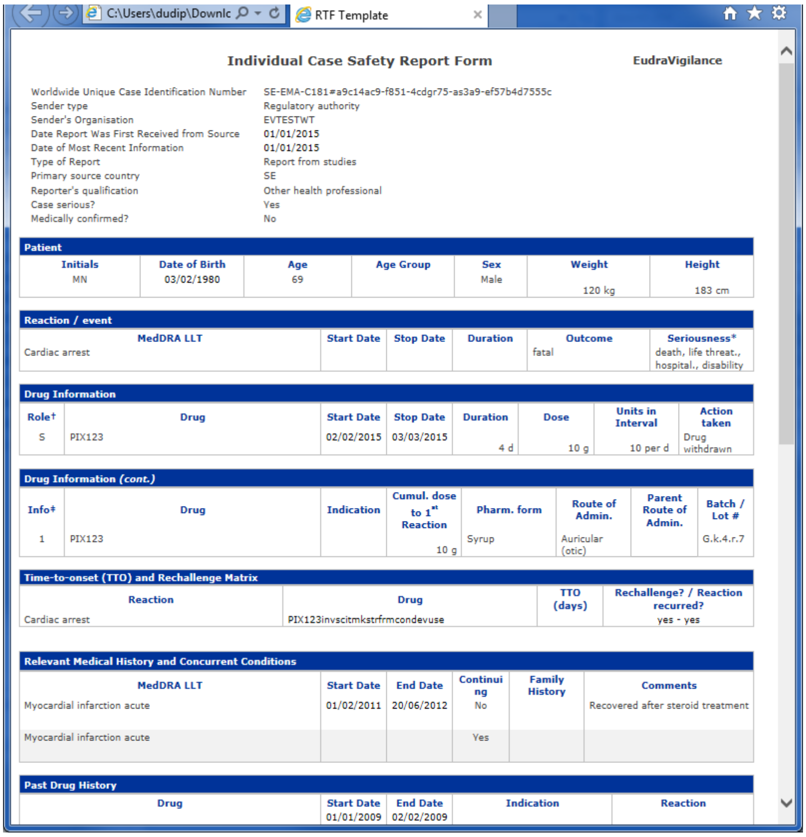
EVDBMS Item	XML	RTF	ICSR Form	HTML	Original Message
ICSR	✓	✓	✓	✓	
Safety message	✓	✓			✓
Acknowledgement message	✓				✓

The following table provides a description of all available export file formats:

Table 25 – Description of the export file formats

Export File	Description
XML	EVWEB exports ICH E2B(R3) compliant XML (eXtensible Markup Language) files. **Note:** The markup language defines a set of rules for encoding documents in a format which is both human-readable and machine-readable.
RTF	The RTF (Rich Text Format) export format is the most complete human-readable export document users can obtain from the cases in the ICSRs tab in EVWEB. **Note:** It presents data in a structured way that replicates the fields of EVWEB. As a result, <u>this format is more comprehensive when compared to the ICSR form</u>.
ICSR Form	The ICSR form is a PDF document of an ICH E2B(R3)-based adaptation of the legacy CIOMS form. As such, it is the most user-friendly format users can obtain from EV as the data is presented in an easy-to-follow CIOMS-like format. **Note:** Because of this adaptation, some information that is present in the RTF document is not shown in the ICSR form, which makes this format <u>less detailed when compared to the RTF format</u>.
HTML	The HTML (HyperText Markup Language) export file is the HTML version of the ICSR Form.

The below screenshots provide visual examples of the supported export file formats:



C:\Users\dudip\Downlc RTF Template

Individual Case Safety Report Form EudraVigilance

Worldwide Unique Case Identification Number	SE-EMA-C181#a9c14ac9-f851-4cdgr75-as3a9-ef57b4d7555c
Sender type	Regulatory authority
Sender's Organisation	EVTESTWT
Date Report Was First Received from Source	01/01/2015
Date of Most Recent Information	01/01/2015
Type of Report	Report from studies
Primary source country	SE
Reporter's qualification	Other health professional
Case serious?	Yes
Medically confirmed?	No

Patient

Initials	Date of Birth	Age	Age Group	Sex	Weight	Height
MN	03/02/1980	69		Male	120 kg	183 cm

Reaction / event

MedDRA LLT	Start Date	Stop Date	Duration	Outcome	Seriousness*
Cardiac arrest				fatal	death, life threat., hospital., disability

Drug Information

Role†	Drug	Start Date	Stop Date	Duration	Dose	Units in Interval	Action taken
S	PIX123	02/02/2015	03/03/2015	4 d	10 g	10 per d	Drug withdrawn

Drug Information *(cont.)*

Info‡	Drug	Indication	Cumul. dose to 1st Reaction	Pharm. form	Route of Admin.	Parent Route of Admin.	Batch / Lot #
1	PIX123		10 g	Syrup	Auricular (otic)		G.k.4.r.7

Time-to-onset (TTO) and Rechallenge Matrix

Reaction	Drug	TTO (days)	Rechallenge? / Reaction recurred?
Cardiac arrest	PIX123invscitmkstrfrmcondevuse		yes - yes

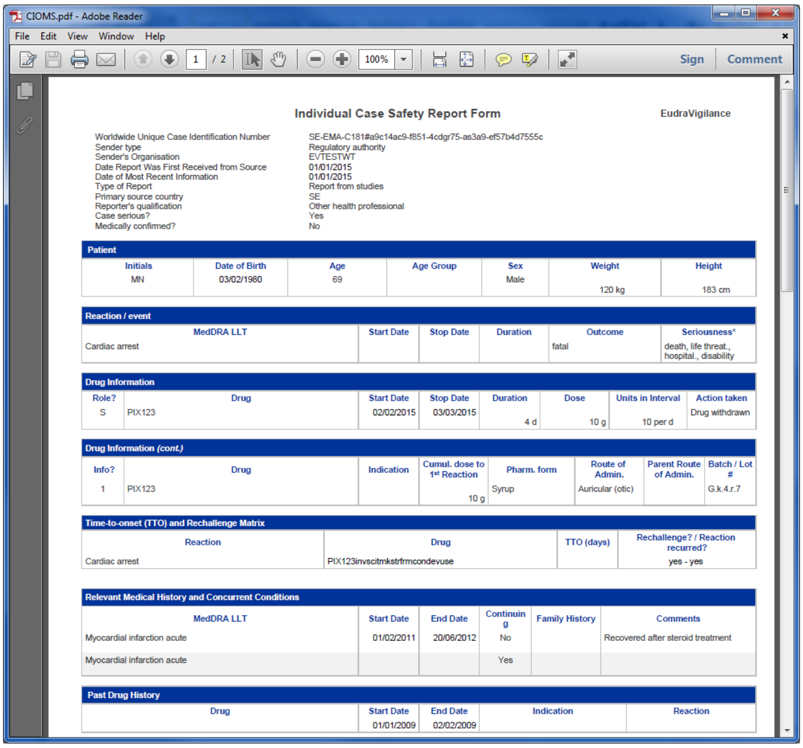
Relevant Medical History and Concurrent Conditions

MedDRA LLT	Start Date	End Date	Continuing	Family History	Comments
Myocardial infarction acute	01/02/2011	20/06/2012	No		Recovered after steroid treatment
Myocardial infarction acute			Yes		

Past Drug History

Drug	Start Date	End Date	Indication	Reaction
	01/01/2009	02/02/2009		

Figure 133 - ICSR Form (HTML) export file format



CIOMS.pdf - Adobe Reader

File Edit View Window Help

Sign Comment

Individual Case Safety Report Form EudraVigilance

Worldwide Unique Case Identification Number	SE-EMA-C181#a9c14ac9-f851-4cdgr75-as3a9-ef57b4d7555c
Sender type	Regulatory authority
Sender's Organisation	EVTESTWT
Date Report Was First Received from Source	01/01/2015
Date of Most Recent Information	01/01/2015
Type of Report	Report from studies
Primary source country	SE
Reporter's qualification	Other health professional
Case serious?	Yes
Medically confirmed?	No

Patient

Initials	Date of Birth	Age	Age Group	Sex	Weight	Height
MN	03/02/1980	69		Male	120 kg	183 cm

Reaction / event

MedDRA LLT	Start Date	Stop Date	Duration	Outcome	Seriousness*
Cardiac arrest				fatal	death, life threat., hospital., disability

Drug Information

Role?	Drug	Start Date	Stop Date	Duration	Dose	Units in Interval	Action taken
S	PIX123	02/02/2015	03/03/2015	4 d	10 g	10 per d	Drug withdrawn

Drug Information *(cont.)*

Info?	Drug	Indication	Cumul. dose to 1st Reaction	Pharm. form	Route of Admin.	Parent Route of Admin.	Batch / Lot #
1	PIX123		10 g	Syrup	Auricular (otic)		G.k.4.r.7

Time-to-onset (TTO) and Rechallenge Matrix

Reaction	Drug	TTO (days)	Rechallenge? / Reaction recurred?
Cardiac arrest	PIX123invscitmkstrfrmcondevuse		yes - yes

Relevant Medical History and Concurrent Conditions

MedDRA LLT	Start Date	End Date	Continuing	Family History	Comments
Myocardial infarction acute	01/02/2011	20/06/2012	No		Recovered after steroid treatment
Myocardial infarction acute			Yes		

Past Drug History

Drug	Start Date	End Date	Indication	Reaction
	01/01/2009	02/02/2009		

Figure 134 - ICSR Form (PDF) export file format

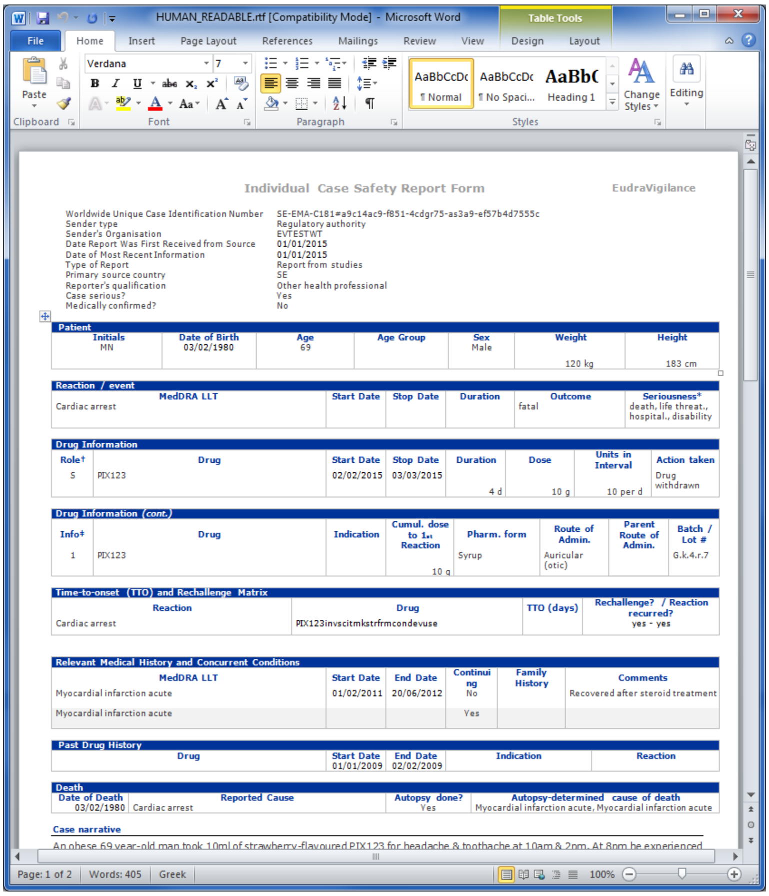


Figure 135 – ICSR Form (RTF) export file format

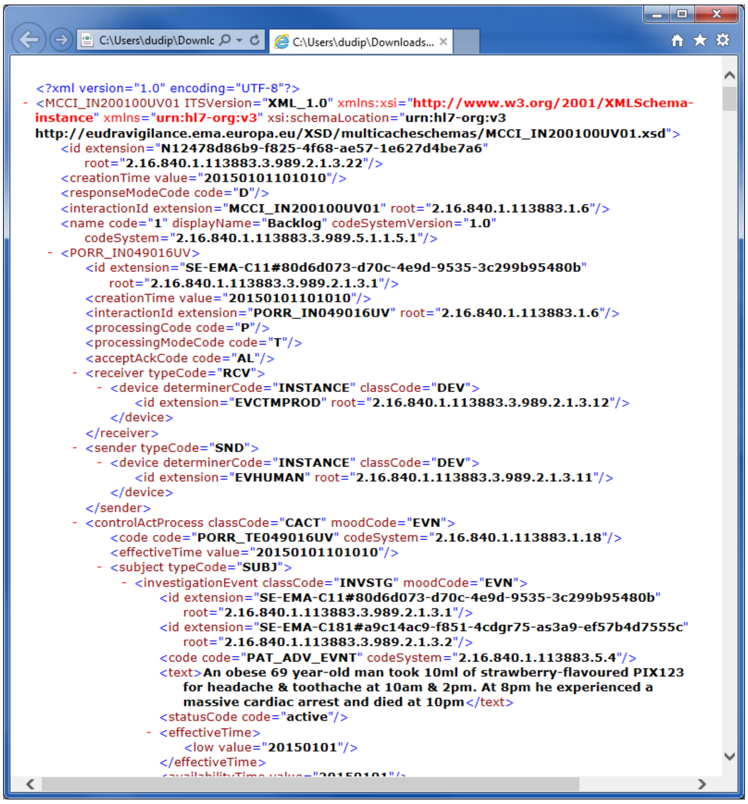


Figure 136 - XML export file format

Note: If you are exporting ICSRs from other senders as XML files using the contextual actions menu in the ICSR screen, then you will receive a redacted version of the case and the message will not have all the mandatory message headers. This means that you might need to amend the downloaded file before loading it into a pharmacovigilance database.

Tip: The ICSR download section (see below) is the best method for obtaining XML files of ICSRs.

3.9.3. 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.

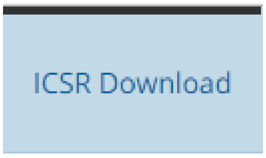


Figure 137 - ICSR Download screen link

For guidance on the recording of adverse drug reactions reported to EudraVigilance by marketing authorisation holders (MAHs), organisations should consult the document Recording by marketing authorisation holders of information on suspected adverse reactions held in EudraVigilance – Note for clarification, especially section 3.1.

Notes:

1. ICSR download requests – Level 2A (L2A), Level 2B (L2B) or MLM – can **only** be made between **6am & 6pm CET/CEST**. This changed introduced by EMA in January 2024 aims to ensure the system stability as outside of these times the EV system performs many automated updates to prepare the data for the next day. Download requests received whilst the EV system is performing these updates take longer to run and have a larger impact on the performance of the system with a risk that the overnight system updates do not finish before 6am. If these overnight processes do not finish in time, the previous day's set of ICSRs may not be available for all organisations.

2. Organisations should **never** send **acknowledgements (ACKs)** for any ICSR downloaded from EudraVigilance.

3. Organisations should **not** resubmit the case(s) downloaded to EudraVigilance, as explained in Questions 2.89, 2.123 and 2.115 of the document The launch of the new EudraVigilance System – Questions and answers (Q&A) from stakeholders. This would cause case duplication and subsequent new automatic master cases for you to download and process.

   The only exception to this provision is in the context of new and significant information obtained **directly** from the reporter/primary source by the MAH doing the ICSR download, in the context of follow-up as outlined in GVP Module VI. Therefore, please note the following:

   - If you believe information has been incorrectly captured the downloaded ICSR – e.g. incorrect MedDRA coding of the reaction(s), missing reaction(s), incorrect product name(s), suspect/interacting product(s) not marketed in that country, etc. –, then **please contact the organisation that has submitted that ICSR to EudraVigilance as only they have the source documents and can confirm the accuracy of the information or make corrections in the data if required** – please refer to Annex 4 of the document

Detailed guide regarding the EudraVigilance data management activities by the European Medicines Agency on how to contact the original case sender.

- It is for the organisation who downloaded the case(s) to determine how to process data obtained from EudraVigilance in accordance with their SOPs. This includes but is not limited to doing the MedDRA coding of possible missing reactions, adding the MAH's company/causality assessment, etc.

3.9.3.1. User access

L2A or L2B reports: Access (download) requests can **only** be made by MAH users registered at **headquarter** level.[3] MAH users registered at Affiliate- or Virtual Affiliate-level do **not** have permission to make such requests and thus the options "PV obligations reports (L2A)" and "Case narrative requests (L2B)" (mentioned in **section 3.9.3.3.1. "Reports" Criteria**) are not displayed in the Reports field of **ICSR Download** screen of EVWEB.

Note: Service Provider/CRO users working on behalf of a MAH need to be registered at MAH EV HQ level to be able to make those L2 ICSR download requests.

MLM reports: MAH/Sponsor users registered at either HQ-, Affiliate- or Virtual Affiliate-level can make MLM access (download) requests.

Note: Service Provider/CRO users working on behalf of a MAH/Sponsor can be registered at either MAH/Sponsor EV HQ-, Affiliate- or Virtual Affiliate-level to be able to make those MLM download requests.

3.9.3.2. Product classification and access to Level 2A/B ICSRs

Section 1.7. Classification of product information and Level 2A/B access explains how Level 2A (L2A) / Level 2B (L2B) access is provided and the difference between scientific groups and scientific products – please refer to it.

Organisations performing L2A and/or L2B ICSR download should be aware that access to ICSRs is granted upon the successful classification of suspect/interacting drugs within an ICSR against the MAH's validated[4] XEVMPD data.

Note: For MLM reports and in accordance with the EMA's EudraVigilance Access Policy, MAH and Sponsor organisations have Level 3 access to all MLM cases.

When a medicinal product within an ICSR is classified, the date of this classification is recorded in the database. This date is used for download date range calculation. As an ICSR can involve more than one medicinal product, the classification of this information can occur on subsequent days, leading to the update of the ICSR classification date. This is done to ensure that those organisations that did not previously have Level 2 access to the ICSR are able to download it once this new classification takes place.

However, the consequence of this change of the classification date will result in the ICSR being made available again for download on subsequent days, which may appear to organisations as duplicate downloads. Because most classification updates to an ICSR occur within the first three days after

[3] Please refer to Questions 2.6 and 2.59 of the document The launch of the new EudraVigilance System – Questions and answers (Q&A) from stakeholders.
[4] Please refer to Question 2.12 of the document The launch of the new EudraVigilance System – Questions and answers (Q&A) from stakeholders.

receipt, it is recommended that organisations using the download functionality set the date range for exporting cases to exclude the last three days.

3.9.3.3. Downloading of ICSRs

You will be presented with the **ICSR Download** interface as shown in the following screenshot, which is further explained in **Table 26 – Description of the options in the ICSR Download Screen**.

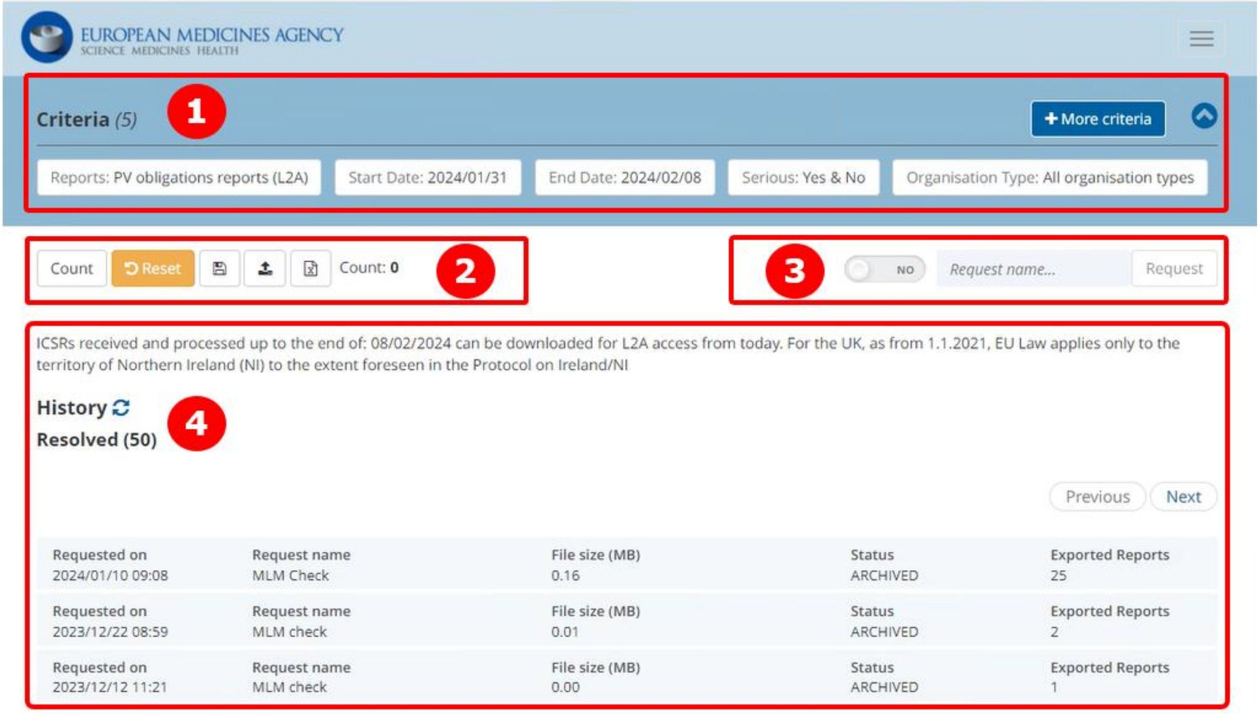


Figure 138 - ICSR Download screen

A bulk export procedure is quite similar to a query action: first you define a set of criteria which will return a set of matches but instead of acting on each single one of these matches, you export all of them in a single compressed (.zip) file. The exported items contained in that single compressed (.zip) file are in ICH E2B(R3) XML format.

Note: Organisations should **NOT** send **acknowledgements (ACKs)** for any ICSR downloaded from EudraVigilance.

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

Table 26 – Description of the options in the ICSR Download Screen

ICSR Download Screen Option	Description
(1) Criteria	Define the criteria that will narrow down the items you wish to bulk export (see **section 2.7.2.1. Criteria Ribbon** for more information on using criteria). The default, pre-selected criteria available in the ribbon are: • **Reports:** Filter mandatory for MAH users; select the type of report/request: "PV obligations reports (L2A)", "Case narrative requests (L2B)" or "MLM reports" (see **section 3.9.3.3.1. "Reports" Criteria** for more information). • **Start Date:** Select the start date of a date range on which a suspect/interacting drug in an ICSR has been classified against data in the XEVMPD. This date thus represents the time the products in the ICSR were classified or reclassified against XEVMPD data. • **End Date:** Select the end date of date range on which a suspect/interacting drug in an ICSR has been classified against data in the XEVMPD. This date thus represents the time the products in the ICSR were classified or reclassified against XEVMPD data. **Notes on the Start and End dates:** ○ The Start and End dates are related to the classification or reclassification dates of the products in the ICSR by EMA and **not** to the date of ICSR submission date to EV by the sender. ○ ICSRs may be reclassified (and thus appear again for download) if changes within XEVMPD are made by EMA or if product linkage is amended. ○ The maximum range (i.e., the time interval between the Start and End dates) **cannot** exceed 9 days. **Tip on the Start and End dates:** As mentioned above in **section 3.9.3.2. Product classification and access to Level 2A/B ICSRs**, although access to date from the day before maybe available for download, **it is recommended that you do not include the last 3 days in the time period**. This is to avoid downloading the same ICSR on subsequent days, during which most of the reclassification ICSRs against XEVMPD data occurs. • **Serious:** Select whether you wish to receive only serious ICSRs ("Yes"), non-serious ICSRs ("No") or all qualifying ICSRs regardless of their seriousness ("Yes & No"). • **Organisation Type:** Select the type of organisation that submitted the ICSR to EudraVigilance. The options are: "NCA" (National Competent Authorities), "Non-NCA" for all other organisations excluding NCAs, or "All organisation types".

ICSR Download Screen Option	Description
	Tip: If you wish to exclude ICSRs submitted by other MAHs please select the option "NCA". 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 match the verbatim text within the ICSR substance name field. **Tip:** You should only use this field if you are certain that you know precisely how the reported substance text was typed. Any misspellings or use of different languages used in the report sent to EudraVigilance (e.g. "paracetamolo" rather than "paracetamol") will result in you missing cases. **It is best practice to use the filter "Active Substance Group" (namely for combination products) to avoid any undue exclusion.** **Note:** This search does not use the drug information as reclassified against the XEVMPD. • **Primary Source Country:** selects all the reports for a given Reporter Country that contains the Boolean field "Primary Source for Regulatory Purposes" checked. • **Worldwide Case ID (WWID):** Insert the worldwide unique case identification number. • **Active Substance Group:** Select the active substance group (scientific group), high level search of substances and fixed combinations of substances, grouped by EMA for the purpose of pharmacovigilance activities e.g. IBUPROFEN, PARACETAMOL or the combination IBUPROFEN, CODEINE – see below **section 3.9.3.3.2. Considerations on the "Active Substance Group" and "Active Substance Combination" filters.** **Note:** This filter uses the XEVMPD classification of the reported product and substance information in the ICSR and includes all salts, grades and active moieties of the active substances. Being less specific when compared to the "**Active Substance Combination**", therefore it returns more results. **Tip: It is best practice to use this filter (namely for combination products) to avoid any undue exclusion that may occur with other filters**. • **Active Substance Combination:** Select the active substance combination (Scientific product). ICSR drugs as classified against the salts, moieties and grades of active substances and combinations of these terms. This filter allows for searches of specific salts, moieties and grades of active substances. Being more specific than the "**Active Substance Group**" filter, it returns fewer results (but more than the "**Active Substance**" free text search) – see, below, **section**

ICSR Download Screen Option	Description
	3.9.3.3.2. Considerations on the "Active Substance Group" and "Active Substance Combination" filters. **Note:** In spontaneous reporting and medical literature, substances are very often only described by the active moiety. Therefore, if your obligations concern a particular salt, searches for the moiety with that salt alone (by using this filter) may well result in undue exclusion. **Tip: It is best practice to use the filter "Active Substance Group" to avoid any undue exclusion.** If you use "**Active Substance Combination**" then best practice is to search for the salts or grades in your product AND the active moiety and then review the results obtained. • **Active Substance MLM Group:** Select the active substance MLM group. • **Active Substance MLM Combination:** Select the active substance MLM combination. • **Reporting type:** Select the type of report that has been specified in the ICSR. The options are "Spontaneous", "Report from studies", "Other" or "Not available to sender (unknown)". • **Current report only:** If selected ("Yes"), this filter will exclude older version(s) of a given case whenever a newer version of that case has been subsequently received from the same original sender organisation. **Note:** The newer version of the case will only become available after it has been classified against the XEVMPD data. Therefore, first access to an ICSR by an MAH may be delayed if several follow-up versions are received during the time of first receipt and XEVMPD classification.

ICSR Download Screen Option	Description
(2) "Count", "Reset", "Save Criteria" ( ), "Load Criteria" ( ) & "Excel list export ( )" Buttons	The buttons available in this area provide additional actions that help the user with the overall bulk export process. • **Count:** Click on this button to see the number of items that match the defined criteria. **Note:** Exports are limited to <10,000 results. If your count shows ≥10,000, then you should add further criteria to refine your results. • **Reset:** Clears all changes (including criteria options) and initiates a new count process. • **Save Criteria ( ):** Saves the applied criteria options as a .JSON file, allowing you to perform a future bulk export process reusing the same criteria settings once the JSON file is uploaded. • **Load Criteria ( ):** Loads criteria options that were saved using the "Save Criteria" button. • **Excel list export button ( ):** Exports the line listing of the cases returned into an Excel file.
(3) "Request" Field & "Request" toggle (NO) button	**"Request" Field:** Enter a 'request name' to distinguish the bulk export process that will initiate when clicking on the "Request" button – see **Figure 139 – Example of an L2A ICSR download request before being processed**. It also provides the filename to the compressed file that becomes available for download. **"Request" toggle:** By selecting YES on the toggle button, an Excel file with the list of results will also be included in the download folder.

ICSR Download Screen Option	Description

(4) ICSR Download Status	This area offers information regarding running ("Pending") and completed ("Resolved") bulk export processes – see **Figure 140 – Example of an L2A ICSR download request processing just started**.
	
	The common feedback fields are:
	
	• **Requested on:** Indicates the date on which the bulk export process was requested.
	• **Completion status:** Provides metrics on the succeeded (S) and total (T) number of matches processed for bulk exporting (S/T).
	• **Request name:** The name of the process and resulting compressed file. Originates from the "Request" field.
	• **File size:** The size of the resulting compressed file.
	• **Status:** Indicates the status of the bulk export process. The available conditions are:
	  – **NEW:** A bulk export request has just been initiated and is in queue.
	  – **STARTED:** A bulk export request has just been initiated and is in progress.
	  – **COMPLETED:** A bulk export request has been successfully processed and resolved.
	  – **COMPLETED_WITH_ERROR**: A bulk export request has been resolved but one or more reports failed to be exported.
	  – **ARCHIVED:** A resolved bulk export request that has passed the 30th day from its creation date.
	• **Exported Reports:** The number of exported reports originating from the resolved bulk export request.
	
	Notes:
	
	  ○ Exports are limited to <10,000 results. If the status is Completed and the number of Exported results is 9,999, then your export probably should have been larger and has cut off before truly completing.
	  ○ The rounded arrows icon ( ) next to "History", when clicked, refreshes the status area and displays the latest information updates.

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.

Notes:

- All bulk export processes which are not completed will be deleted after 2 days.
- Users performing downloads should avoid making repetitive requests for the same set of ICSR downloads and active requests should be allowed to complete before new ones are initiated. If multiple requests for the same set of ICSRs are made, that will cause a delay in completing all requests made in the system.

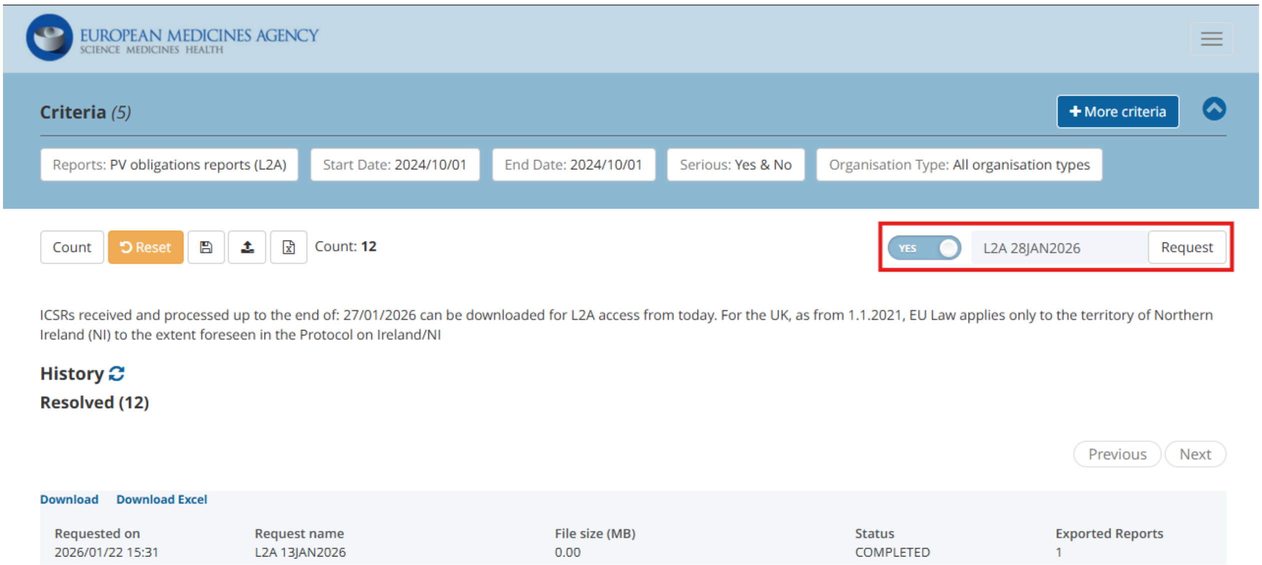


Figure 139 – Example of an L2A ICSR download request before being processed

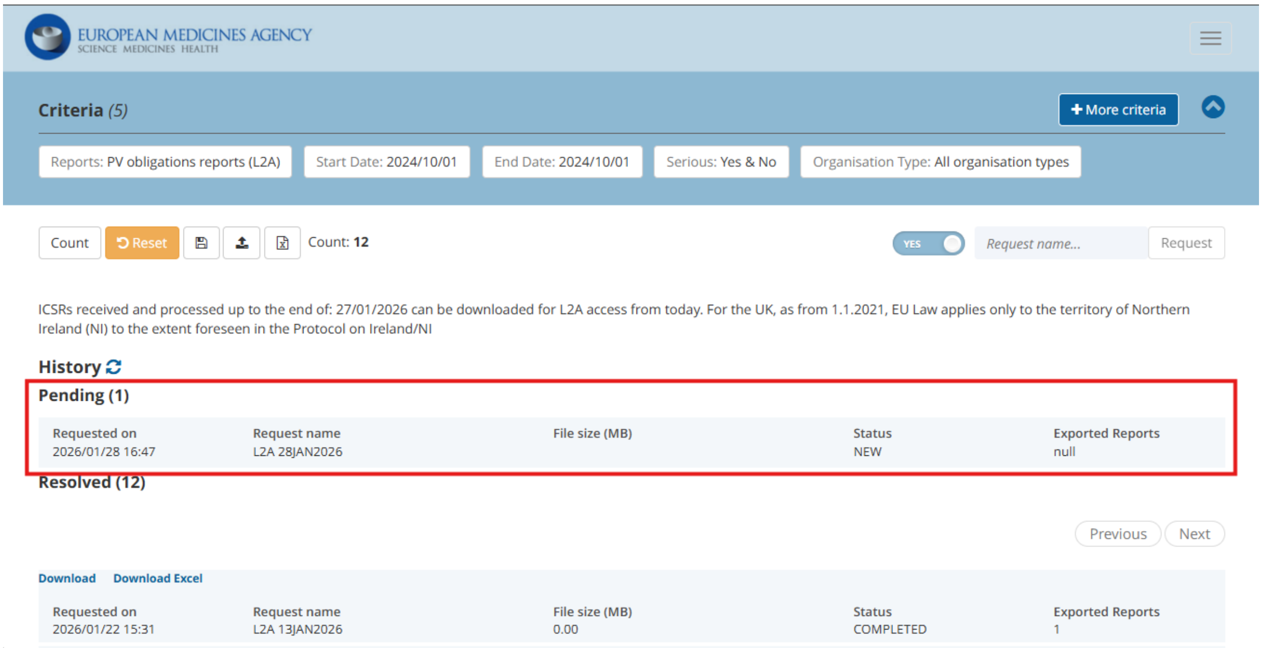


Figure 140 – Example of an L2A ICSR download request processing just started

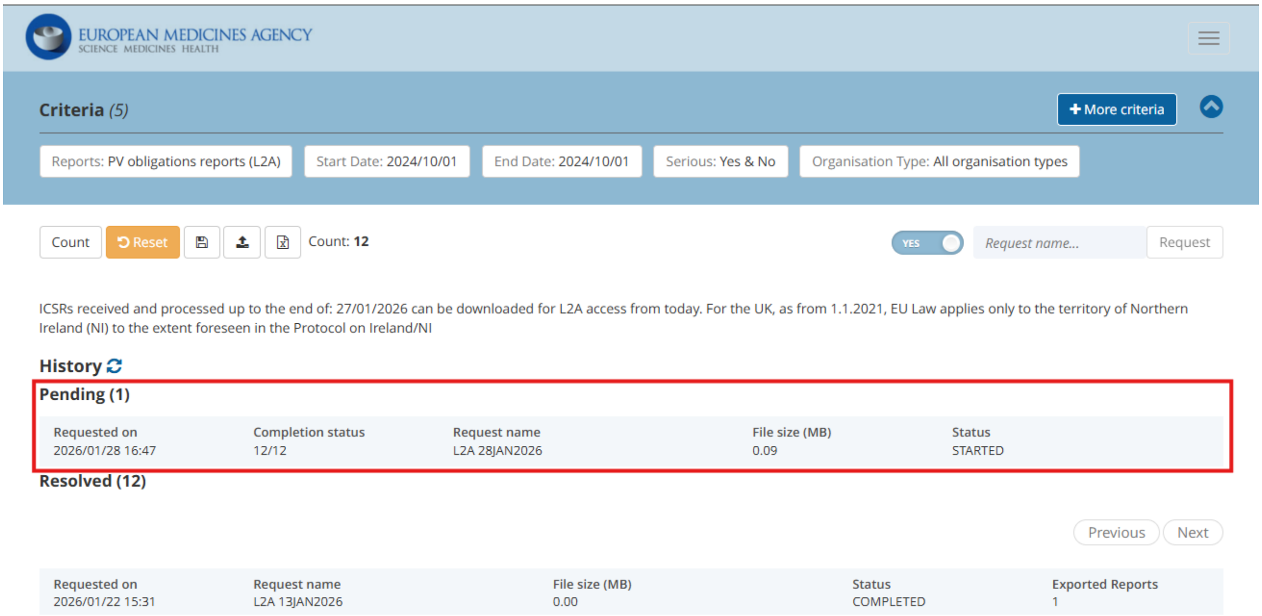


Figure 141 – Example of an L2A ICSR download request being processed

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.

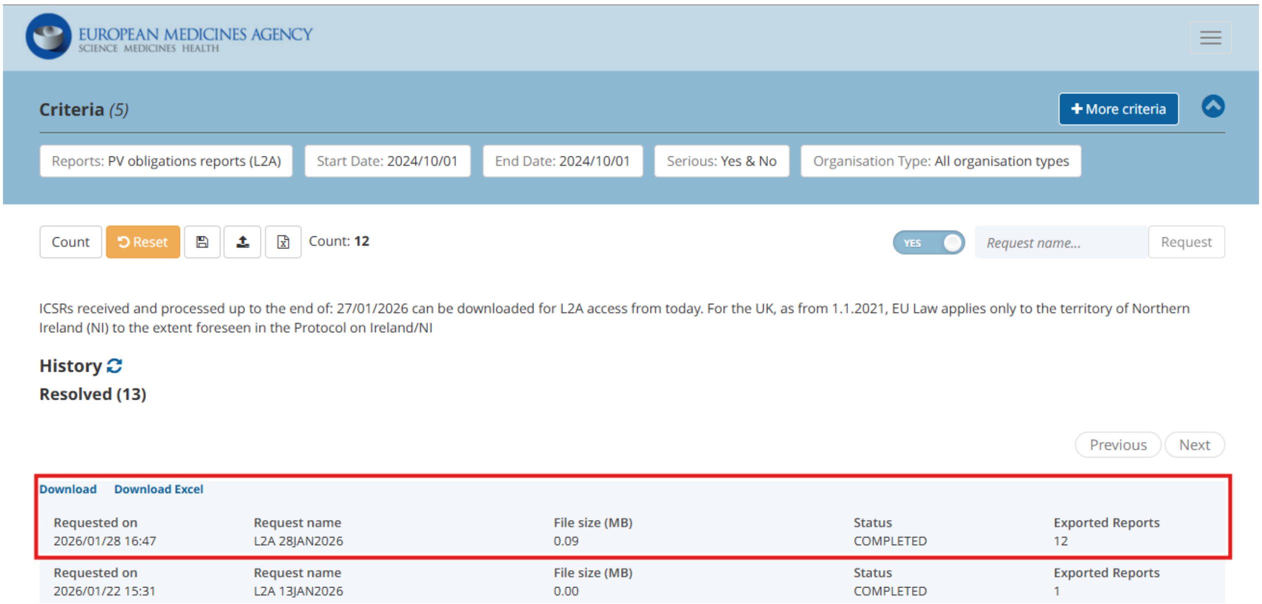


Figure 142 – Example of an L2A ICSR download request already processed

All completed bulk export processes remain in the "Resolved" group section. After 30 days from the date of their creation, they acquire the status of "ARCHIVED" and cannot be downloaded again. Therefore, if users need to retrieve the data again, they will have to rerun the query.

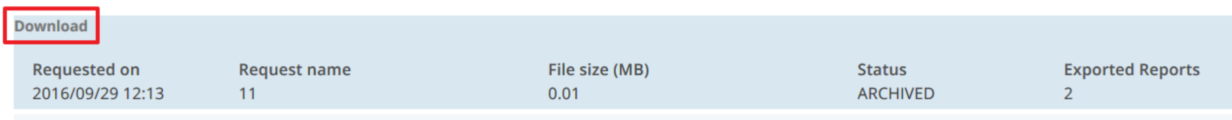


Figure 143 - Download bulk export file from "Resolved" section with Status "ARCHIVED"

3.9.3.3.1. "Reports" Criteria

The "Reports" criteria item is used to further 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 opposed to EMA/NCA users for whom it is optional.

MAH User "Report" Criteria Options

As mentioned above, the "Reports" criteria item is mandatory for MAH users and, thus, will always appear in the criteria ribbon.

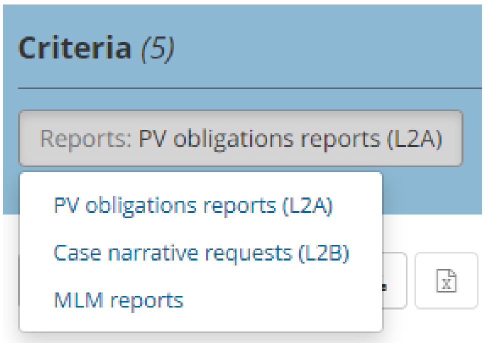


Figure 144 - "Reports" criteria options for MAH users

The above screenshot shows the available options for this criteria item.

Note: The option "Case narrative requests (L2B)" is available **only** to MAH users who are granted this function through the EudraVigilance registration system by the Qualified Persons for Pharmacovigilance (QPPV) or headquarter user administrator.

As previously mentioned in section **3.9.3. ICSR Download**, access to **Level 2B (L2B)** ICSRs is granted **only** in the context of signal evaluation and other activities for protecting public health; it should **not** be used for other purposes (such as deciding whether the ICSR should be entered into the MAH's own pharmacovigilance system or whether the case should be transmitted to 3rd country regulatory authorities).

When the user proceeds with this kind of export the system will display the following disclaimer:

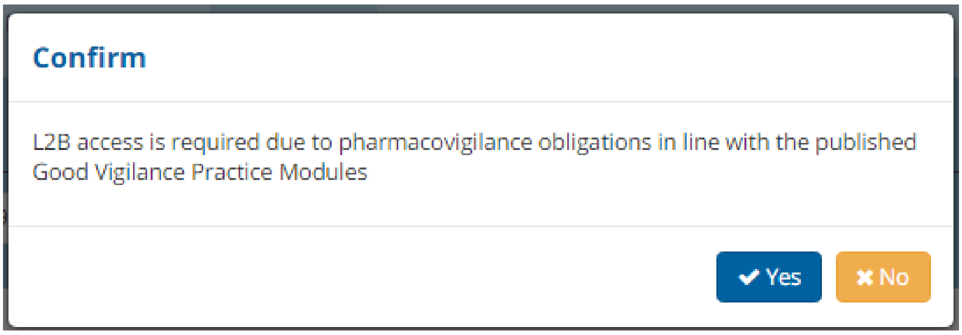


Figure 145 - "Confirm" dialog box for "Case narrative requests (L2B)" option

When the user clicks on the "Yes" button, a new dialog box will appear in which the reason for this export request should be provided:

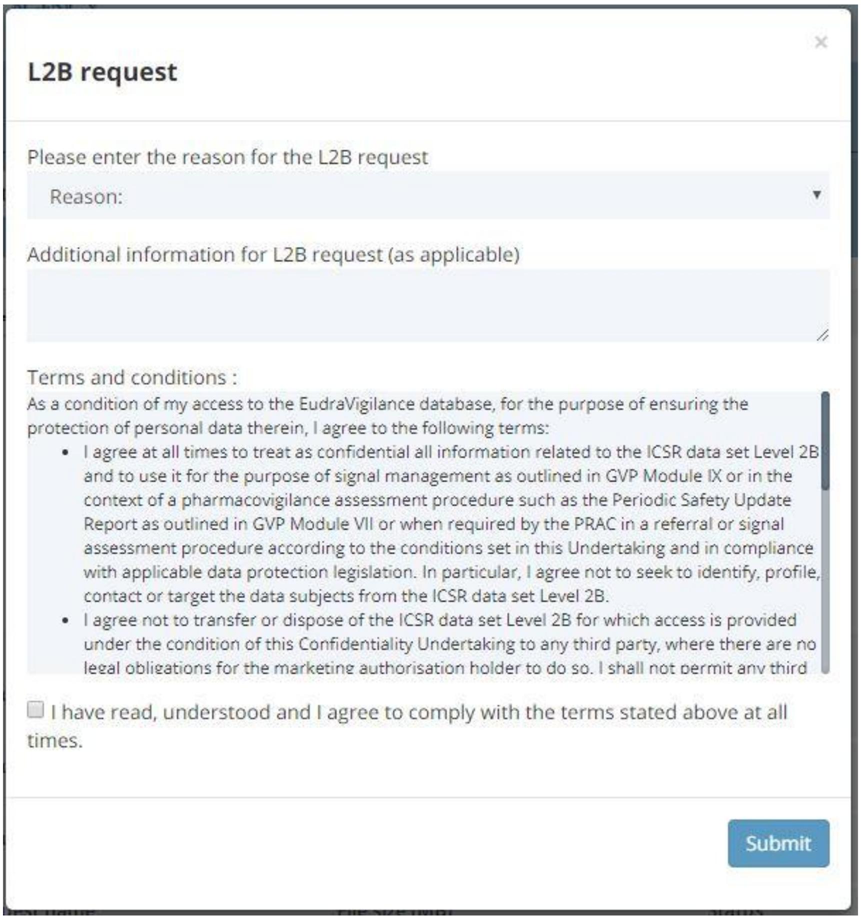


Figure 146 - L2B reason dialog box for "Case narrative requests (L2B)" option

EMA/NCA User "Report" Criteria Options

The "Reports" criteria item is optional for EMA/NCA users. Thus, it is left to the user's requirements to add this in the criteria ribbon.

3.9.3.3.2. Considerations on the "Active Substance Group" and "Active Substance Combination" filters

As explained in **section 1.7. Classification of product information and Level 2A/B access**, access to **L2A/B** ICSRs in EudraVigilance is based on the linkage of the suspect and/or interacting drug(s) within an ICSR and the data held in the XEVMPD for the MAH organisation accessing the system. This linkage is done at the level of the **Scientific product** or **Scientific group** (substance). The Level 2 search results returned will thus depend on which filter(s) are used which, in turn, are linked different clusters of data.

The "Active Substance Group" filter is linked to the Scientific Group cluster and thus yields more results than other substance filters as it encompasses all salts, grades and active moieties of each active substance. On the other hand, the "Active Substance Combination" filter is linked to the Scientific Product cluster, yielding fewer results but allowing for more focused searches (specific salts, moieties and grades) of active substances.

The table below illustrates these differences: by selecting 'IBUPROFEN' as the Scientific Group (via the "**Active Substance Group**" filter), the user retrieves 8 ICSRs whereas only 4 are returned if 'IBUPROFEN' is selected as the Scientific Product (via the "**Active Substance Combination**" filter).

Table 27 – Grouping of ICSRs in accordance with their Scientific Product or Scientific group

Case #	Reported terms in the ICSR	Scientific Product	Scientific Group
Case 1	NUROFEN	**IBUPROFEN**	**IBUPROFEN**
Case 2	NUROFEN 400 MG	**IBUPROFEN**	**IBUPROFEN**
Case 3	IBUPROFEN	**IBUPROFEN**	**IBUPROFEN**
Case 4	NUROFEN FOR CHILDREN	**IBUPROFEN**	**IBUPROFEN**
Case 5	SUBITENE 200 MG	IBUPROFEN SODIUM DIHYDRATE	**IBUPROFEN**
Case 6	IBUPROFEN SODIUM	IBUPROFEN SODIUM	**IBUPROFEN**
Case 7	5% STADERM CREAM	IBUPROFEN PICONOL	**IBUPROFEN**
Case 8	IBUPROFEN MEGLUMINE	IBUPROFEN MEGLUMIN	**IBUPROFEN**

Below are some figures illustrating the different filters being populated:

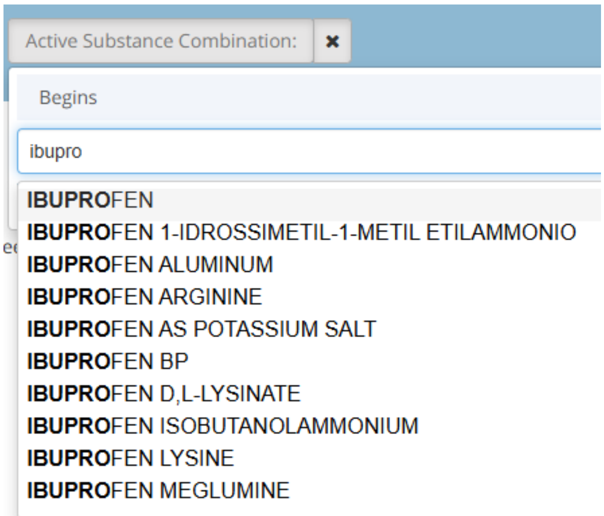


Figure 147 - "Active Substance Combination" filter being populated

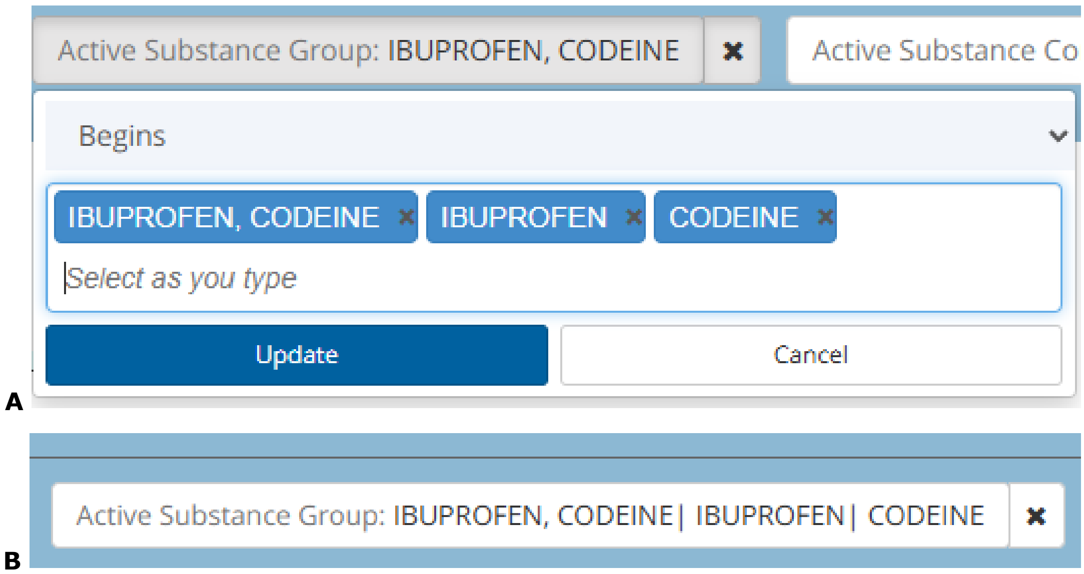


Figure 148 - "Active Substance Group" filter (A) being populated with 1 combination and 2 single substances and (B) after the 'Update' button was clicked

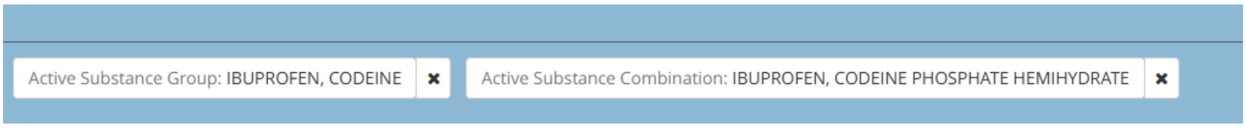


Figure 149 – Difference between the "Active Substance Group" and the "Active Substance Combination" filters when searching for a combination of substances

3.9.3.4. Use of Automation tools (API/RPA) in the Level 2A (L2A) ICSR download and Captcha control for Level 2B (L2B) download requests

The use of user accounts in automation tools, such as application programming interface (API) / Robotic process automation (RPA), by an organization is **not** permitted for **Level 2B (L2B)** case narrative download requests as this is not consistent with the EudraVigilance Access Policy and the Terms and Conditions of use. Therefore, the **Level 2B** download form has been updated and now includes a captcha (challenge-response test) control in order to prevent the automated downloading of case narratives.

For **Level 2A (L2A)** ICSR download request, the EMA does not actively support automation tools. However, their use will not be prevented on condition that they do not affect the performance and function of EMA systems such as making multiple requests within a short time frame.

The EudraVigilance system performs many overnight processes to prepare the data for the following day, data access requests made during these periods can have a negative effect on the completion of these processes. For this reason, and as detailed in section **3.9.3. ICSR Download**, it is only possible for perform ICSR download requests in EudraVigilance between **6am and 6pm CET/CEST**. Moreover, accounts identified as not respecting these conditions on the use of automation tools will receive an initial warning from the EMA and if problematic usage continues, the user access will be terminated.

MAHs should note that EMA takes accepts no responsibility or liability arising out of the use of Automation tools (API/RPA) in the L2A ICSR download, including, but not limiting to, any malfunction and/or missing case(s) that may derive from the use of these automated tools.

4. MedDRA

MedDRA is the Medicinal Dictionary for Regulatory Activities. It has been developed as a clinically validated international medical terminology for regulatory authorities and the pharmaceutical industry. MedDRA is intended to be used throughout the entire regulatory processes, from pre- to post-marketing phases, for data entry, retrieval, evaluation and presentation.

This chapter describes the principal aspects of MedDRA, its structure and how to access and use MedDRA in EVWEB. It also explains the process necessary to perform queries on MedDRA through EVWEB.

Every user of EVWEB should hold a valid MedDRA license. The license details should be provided as part of the registration process with EudraVigilance.

For further details about the MedDRA license policies, please refer to the official website of the MedDRA MSSO (http://www.meddra.org/) and the specific EudraVigilance license policy for SMEs published on the EMA's webpage Financial advantages of SME status.

4.1. Introduction

MedDRA encompasses a series of processes that allow data entry, retrieval, evaluation and presentation during all phases of the regulatory processes, from pre- to post-marketing phases. These processes consist of:

- Clinical studies
- Reports of spontaneous adverse reactions and events
- Regulatory submissions
- Regulated product information

The dictionary provides terminology intended to be used in the following areas:

- Diseases
- Diagnosis
- Signs
- Symptoms
- Therapeutic indications
- Investigations names and qualitative results
- Medical, social, family history

However, there are some areas excluded from MedDRA terminology:

- Population level qualifiers (e.g. "rare" and "frequent" fail to focus on the individual patient)
- Numerical values for results (numeric representations cannot be universalized, especially in terms of the measurement parameter)
- Severity descriptors (typically, terms such as "severe" or "mild" are not found in the terminology, with some exception when their presence is medically relevant, e.g., aggravated conditions are different than the condition itself)

- Patient demographics (aside from very few occasions where sex is a pertinent descriptor, terms like age, race and religion are not included in the terminology)
- Equipment, device and diagnostic product terms (e.g. the term "catheter" would not be include in the terminology whereas the failure and its health effects would be)
- Drug product terms
- Device failure terms
- Clinical trial study designs terms

4.2. MedDRA Structure

MedDRA is organized in a hierarchical structure. MedDRA terms are grouped at different levels allowing searches to be performed with several degrees of specificity.

The hierarchical structure provides vertical links between superordinate terms (broad grouping) and subordinate descriptors (higher level of specificity). This structure is characterised by the following levels:

- System Organ Class (SOC)
- High Level Group Term (HLGT)
- High Level Term (HLT)
- Preferred Term (PT)
- Lowest Level Term (LLT)

Here is a brief description of each level:

- **System Organ Class (SOC):** The highest level of the hierarchy that provides the broadest concepts for data retrieval.

  There are SOCs, representing parallel axes, which are not mutually exclusive. This allows terms to be represented in more than one SOC, and therefore grouped by different classifications.
- **High Level Group Term (HLGT):** A subordinate only to System Organ Classes (SOCs) and superordinate for one or more High Level Terms.
- **High Level Term (HLT):** A subordinate to High Level Group Terms and a superordinate for the Preferred Terms (PTs) linked to it.

  The specificity of HLTs is not uniform. HLT groupings reflect the relative importance of terms dependent on the individual SOC.
- **Preferred Term (PT):** A subordinate to High Level Terms and groups together the Lowest Level Terms (LLTs).

  There is no limit to the number of LLTs that can be linked to a single PT. For every new PT, an identical LLT is created for data entry purposes. A PT contained in a particular SOC can only be linked to that individual SOC via one route. PTs represent a single medical concept and are internationally agreed.

  Although a PT can be linked to more than one SOC, each PT is assigned to a Primary System Organ Class. The purpose for the Primary SOC is to determine which SOC will represent a PT during cumulative data output. This will prevent a PT from being represented more than once during data retrieval from all SOCs.

- **Lowest Level Term (LLT):** Constitutes the bottom level of the hierarchy and is linked to a PT.

  Culturally unique terms that have been internationally agreed upon are found at this level. LLTs facilitate the transfer of historical data; terms from other terminologies are also stored here.

  LLTs have one of the following three relationships to PTs:

  - Synonyms – different term for the same descriptor
  - Lexical variant – different word forms for same expression
  - Quasi-synonyms – terms with meanings generally regarded as different, but which in practice are treated as equivalent

4.3. MedDRA in EVWEB

You can access the **MedDRA** screen of EVWEB by clicking on the corresponding link in the main menu.

Figure 150 - MedDRA screen link

The following screen will be displayed once you enter this link:

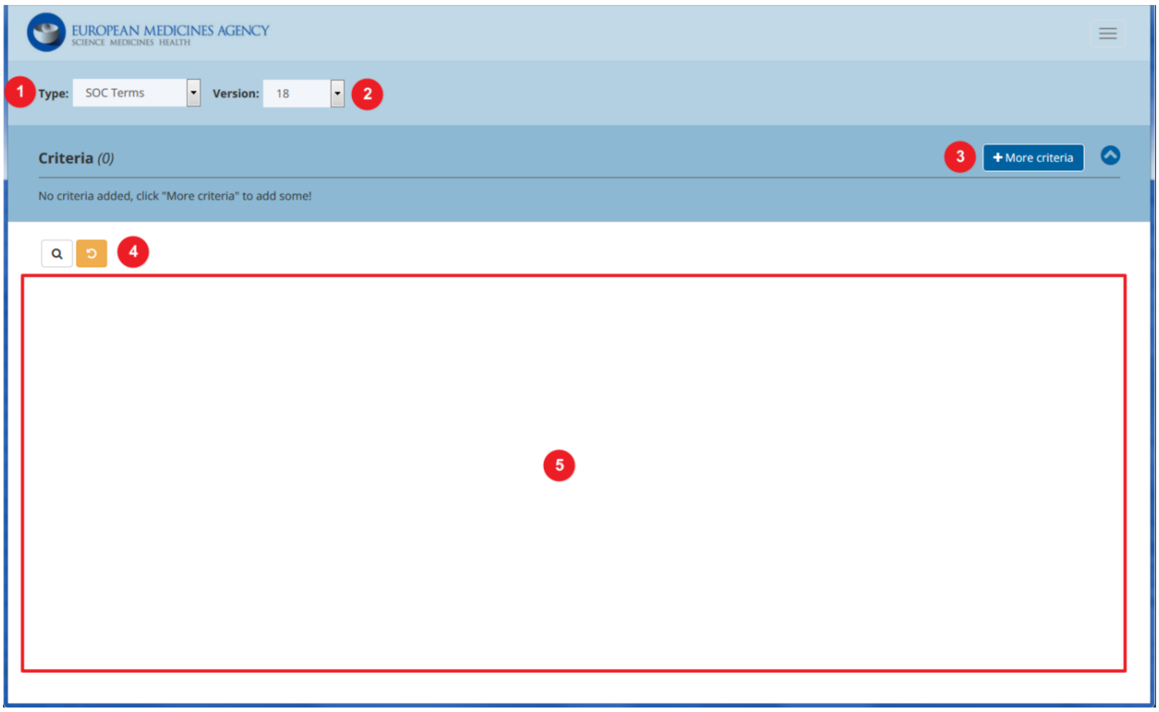


Figure 151 - MedDRA screen

The following table provides an overview of the **MedDRA** screen options:

Table 28 – Description of the options in the MedDRA screen

Screen Option	Description
(1) Type of term level query	Allows the selection of the MedDRA level query. The applicable values are: • SOC Terms • HLGT Terms • HLT Terms • Preferred Terms • Low Level Terms
(2) MedDRA version	Allows the selection of a specific MedDRA version on which to perform a query. The default value is the latest MedDRA version.
(3) Criteria button	Located in the MedDRA screen's criteria ribbon, this button defines the conditions of a query. See **section 2.7.2.1. Criteria Ribbon** for more information on using criteria.
(4) Initiate query/reset buttons	The magnifying glass button ( ) initiates the query, while the rounded arrow button ( ) resets the last query by removing the search results and inserted criteria.
(5) Results area	Displays the results of a query.

Note: When loading data in EVWEB (i.e. via Import XML and/or Follow-up functions), the MedDRA version of the loaded data will be automatically updated to the latest MedDRA version. This may lead to some terms being invalidated (due to terms following older MedDRA version naming schemes); in such cases, the user must correct them accordingly to be able to proceed with the intended process. When creating a Safety message, its MedDRA version will default to the latest MedDRA version available by the system and will not be editable by the user.

4.3.1. Performing a MedDRA Query

The following example describes how to perform a MedDRA query. We will search all Preferred Terms (with their relevant codes) linked to the High Level Terms containing the word "Glaucoma". The search is case sensitive so text at beginning of a term will need to be capitalised. Thus, the values we need to insert into the **MedDRA** screen are:

- **Type:** "Preferred Terms"
- **Criteria:** HLT Name (matches): Glaucoma

The steps to set up the above values and initiate the query are as follows:

- Click in the Type drop-box and select the option "Preferred Terms"

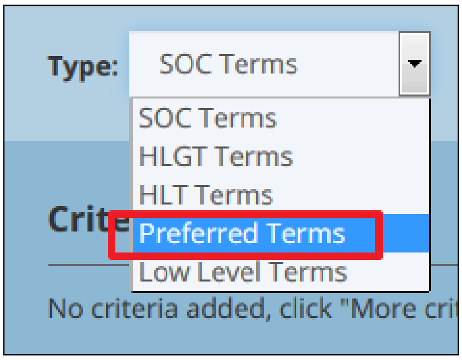


Figure 152 - MedDRA query type selection

- In the criteria ribbon, click on the "+More criteria" button and select the option "HLT Name (matches)"

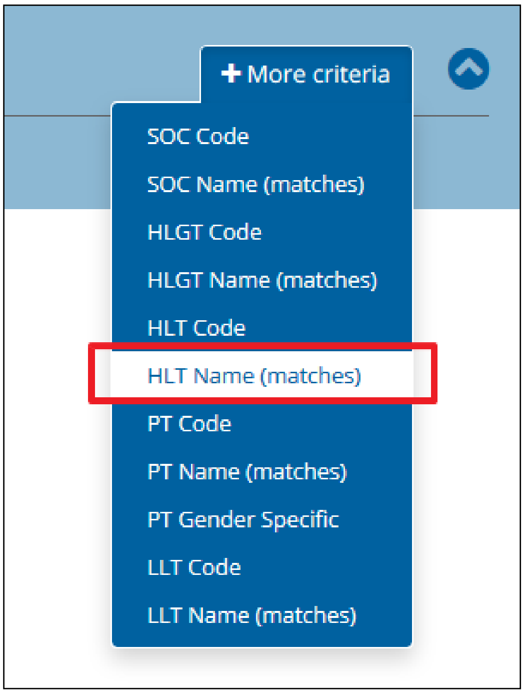


Figure 153 - MedDRA query criteria selection

- The selected criteria option will then appear in the criteria ribbon as a text box. Click on it to display a text field in which you should insert the text "Glaucoma" (without the quotes) and then click on the "Update" button

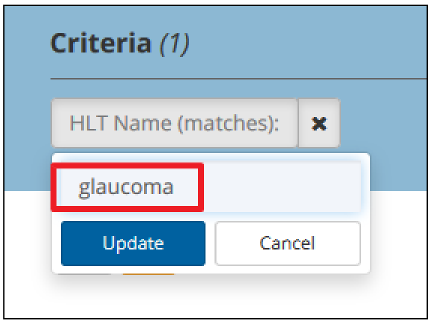


Figure 154 - MedDRA query criteria value

- With our values inserted in the **MedDRA** screen, we can now initiate the query process by clicking on the magnifying glass button ( )
  - **Note:** MedDRA searching is case-sensitive and all MedDRA terms start with a capital letter, so the search in the screenshot above would produce no results.

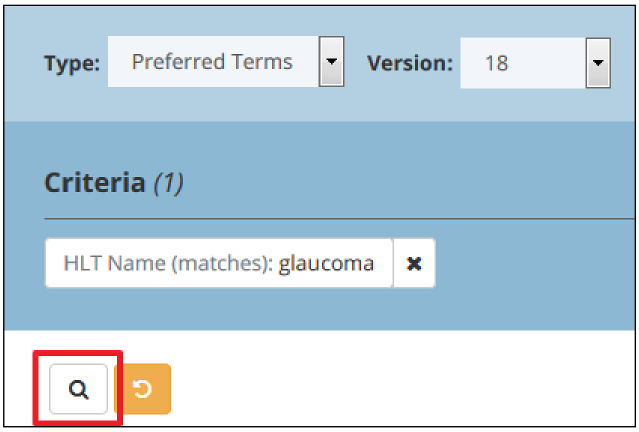


Figure 155 - MedDRA query initiation

The query results will be displayed in the results area of the **MedDRA** screen allowing, thus, further handling (see **section 4.3.2. MedDRA Query Results Management** on how to handle MedDRA query results).

Figure 156 - MedDRA query results

4.3.2. MedDRA Query Results Management

4.3.2.1. List View Layouts

By default, the query results will be displayed in a list view layout, the columns of which will adjust according to the MedDRA hierarchical structure level your query was based on. The table below outlines all possible list view layouts along with their corresponding columns:

Table 29 – Description of the possible list view layouts

MedDRA hierarchical structure level query	List view layout columns
SOC Terms	• SOC Code: A unique 8-digit number assigned to a term. • SOC Name: The full term name under this level. • SOC Abbreviation: The official abbreviation of a SOC name.

MedDRA hierarchical structure level query	List view layout columns
HLGT Terms	• HLGT Code: A unique 8-digit number assigned to a term. • HLGT Name: The full term name under this level.
HLT Terms	• HLT Code: A unique 8-digit number assigned to a term. • HLT Name: The full term name under this level.
Preferred Terms	• PT Code: A unique 8-digit number assigned to a term. • PT Name: The full term name under this level. • PT Gender Specific: Used for clinically distinct gender cases.
Low Level Terms	• LLT Code: A unique 8-digit number assigned to a term. • LLT Name: The full term name under this level. • LLT is current?: – true: The term is up-to-date. – false: The term is not up-to-date.

The following screenshot shows an example of a Preferred Terms query result. The red box shows the list view layout columns available for this type of query.

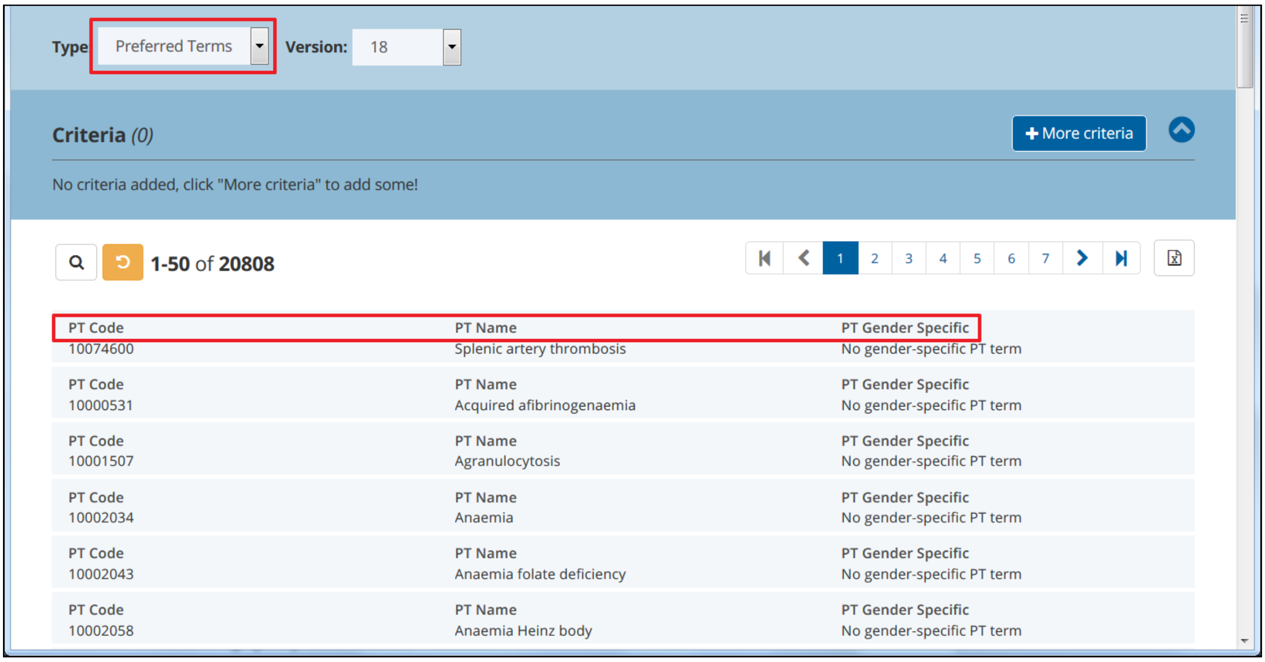


Figure 157 - MedDRA list view layout example

4.3.2.2. Accessing Query Information

With the MedDRA query completed and the results visible in the results area, you can now proceed with accessing the required information. Locate the result item you wish to further investigate and click on it. This action will reveal the "Open" option on the top left of the item's row.

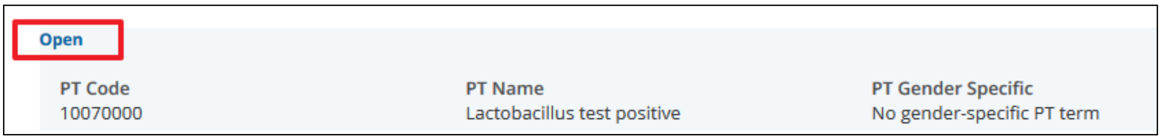


Figure 158 - MedDRA query result item's "Open" option

When the "Open" option is clicked, the result item's row expands to display the linked children and parent hierarchies that are applicable to the specific MedDRA term. Thus, to locate the MedDRA hierarchical structure level information you need for this term, you should expand its children or parent hierarchies sections accordingly, by clicking on the icon that appears under them (similarly, if you click on the icon it will collapse the corresponding hierarchy section).

Note: If a blank icon ( ) appears next to a hierarchy section's title, it means that this section has no further sub-sections to display.

To actually display the MedDRA hierarchical structure level information you should click on its linked title (appears underlined when hovering the mouse pointer over it). The information will appear at the bottom of the expanded result item's row, and will contain the necessary columns that are applicable to the specific structure level (see **section 4.3.2.1. List View Layouts** for more information regarding MedDRA hierarchical structure level columns).

The screenshot below provides a visual example of the children and parent hierarchies available in an opened MedDRA term query item. Also evident is the information displayed when selecting a MedDRA hierarchical structure level term (enclosed in red boxes).

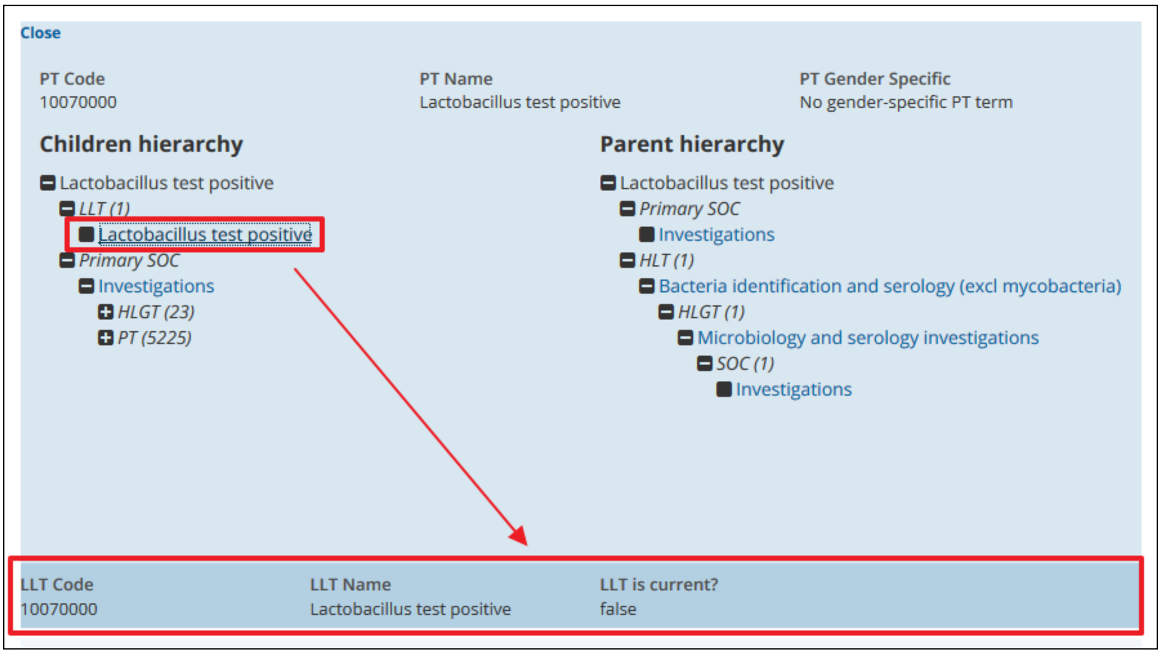


Figure 159 - Opened MedDRA term query item

To close an opened query result item click on the "Close" option that is located at the top left of the opened query item row.

4.3.3. Primary SOCs

As mentioned in **4.2. MedDRA Structure**, the purpose for the Primary SOC is to determine which SOC will represent a PT during cumulative data output. This prevents a PT from being represented more than once during data retrieval from all SOCs.

Specifically, a PT must be linked to at least one SOC but it is also allowed to be linked to as many SOCs as deemed appropriate. Furthermore, it can only be linked to each SOC via one hierarchical structure level route (i.e. HLT → HLGT → SOC).

EVWEB displays all linked SOCs and Primary SOCs under the children or parent hierarchies sections when accessing a MedDRA term.

4.3.4. LLT Current Status

LLTs carry a "true" (current) or "false" (non-current) flag status. Terms that are very vague, ambiguous, truncated, abbreviated, out-dated or misspelled carry the "false" (non-current) flag. These terms may derive from past terminology that was inserted into MedDRA. These LLTs with a "false" (non-current) flag are retained to preserve historical data for future retrieval and analysis. The flag also allows users to implement the terminology within other databases and prevent the inadvertent use of "false" (non-current) LLTs in post-implementation processes.

5. Administration Tools

EVWEB offers two administration tools that provide the ability to fine-tune certain aspects of the system. These tools are restricted to users with proper account permissions, thus will not be available to everyone accessing the application.

5.1. Rerouting Rules (NCA Users)

The re-routing rules administration tool is accessible to NCA user accounts with the role of "EV Human NCA Responsible" or "EV Human NCA Trusted Deputy" and appears as an option with the link **Rerouting Rules** in the main menu.

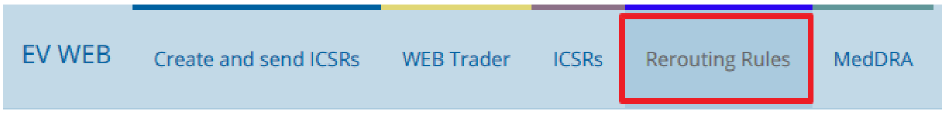


Figure 160 - Rerouting Rules screen link

The purpose of this tool is to allow interested NCAs to receive updated ICSRs and SUSARs for which they have legal responsibility to monitor.

By default, the updated EV items that will be re-routed concern serious cases only, meaning they must have at least one of the following fields filled-in or enabled:

- Results in Death
- Life Threatening
- Caused / Prolonged Hospitalisation
- Disabling / Incapacitating
- Congenital Anomaly / Birth Defect
- Other Medically Important Condition

Optionally, the user is allowed to include non-serious cases in addition to the default of serious cases, by enabling the corresponding checkbox as we will see below.

The creation of re-routing rules is straightforward and can be accomplished in the **Rerouting Rules** screen. The user first selects the countries from which they would like to receive the related updated ICSRs and SUSARs. Obviously, one of the entries should be the NCA user's country so that their organisation can keep track of modified EV items of interest to their locale or region. The next step involves enabling any extra settings related to the ICSRs/SUSARs and clicking on the "Save" button. From here on, the re-routing rules will be permanently active until they are amended or cleared.

The following screenshot and accompanying table provide a visual and descriptive overview of the process.

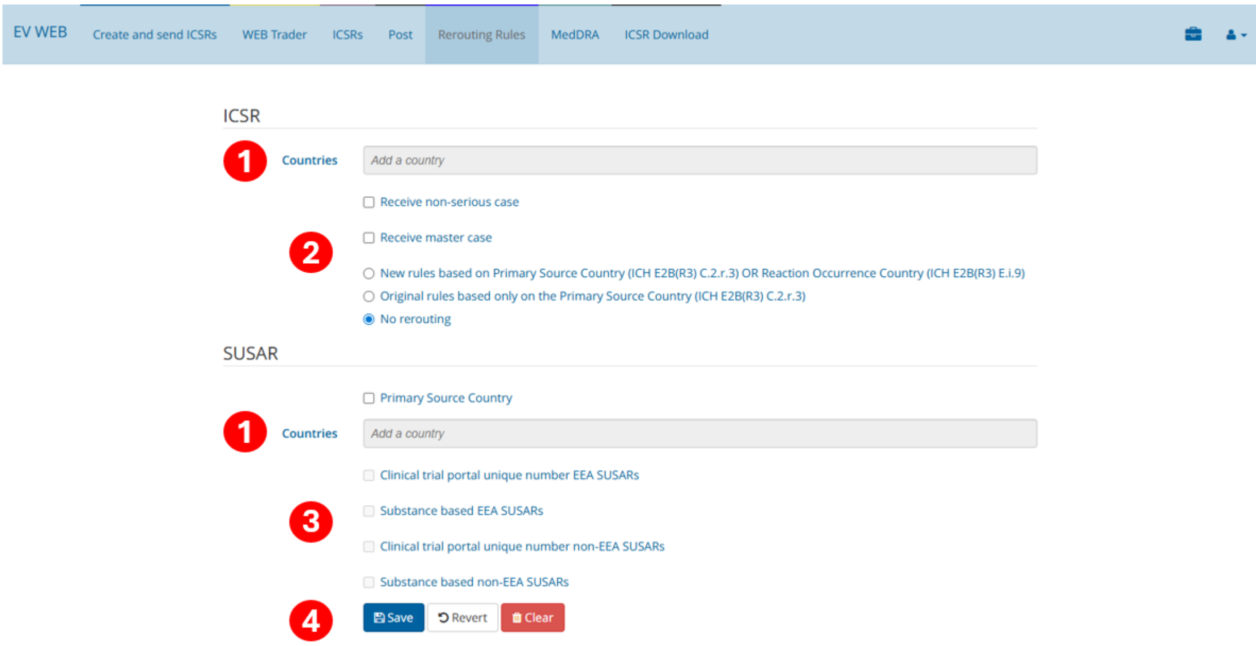


Figure 161 - Rerouting Rules screen

Table 30 – Description of the Rerouting Rules

Rerouting Rules Option	Description
(1) Countries Look-Up Field	This field allows the selection of one or more countries from which to receive and monitor updated ICSRs/SUSARs.
(2) ICSR Checkboxes	These checkboxes provide additional options for receiving updated ICSRs: • **Receive non-serious cases:** If enabled, allows the NCA to receive non-serious ICSRs in addition to serious cases. • **Receive master cases:** If enabled, allows the NCA to receive master cases, which are messages that contain the merged results of two or more duplicate ICSRs. ○ **New rules based on Primary Source Country (ICH E2B(R3) C.2.r.3) OR reaction occurrence country (ICH E2B(R3) E.i.9):** If selected, allows the NCA to receive reports where either the Primary Source Country OR the Reaction Occurrence Country matches the country selected in "Countries" field. ○ **Original rules based only on the Primary Source Country (ICH E2B(R3) C.2.r.3):** If selected, allows the NCA to receive reports where the Primary Source Country matches the country selected in "Countries" field. ○ **No rerouting:** If selected, it disables the ICSR rerouting to the NCA as none of the 2 radio buttons above are selected.

Rerouting Rules Option	Description
(3) SUSAR Checkbox	This checkbox provides the option for receiving SUSARs based on: • **Primary source country:** If enabled, allows the NCA to receive re-routed SUSAR reports based on the primary source country. In addition to the primary source country field, an NCA can also choose to receive SUSAR reports based on: • **Clinical trial portal unique number EEA SUSARs:** If enabled, allows the NCA to receive the re-routed EEA SUSAR reports based on clinical trial number (EudraCT number or EUCT number) matching a trial authorised in the Member State selected as country. • **Substance based EEA SUSARs:** If enabled, allows the NCA to receive the re-routed EEA SUSAR reports based on the suspected/interacting investigational medicinal product substance(s) matching a trial authorised in the Member State selected as country. • **Clinical trial portal unique number non-EEA SUSARs:** If enabled, allows the NCA to receive the re-routed non-EEA SUSAR reports based on the clinical trial number (EudraCT number or EUCT number) matching a trial authorised in the Member State selected as country. • **Substance based non-EEA SUSARs:** If enabled, allows the NCA to receive the re-routed non-EEA SUSAR reports based on the suspected/interacting investigational medicinal product substance(s) matching a trial authorised in the Member State selected as country.
(4) Buttons	These buttons allow the saving, undoing and resetting of applied options: • **Save:** Stores the currently applied settings. • **Revert:** Reverts all latest changes and returns to the previous saved state. • **Clear:** Clears (resets) all settings.

5.2. Rerouted ACKs (EMA Administrators)

The **Rerouted ACKs** screen allows EMA administrators to view basic details and results of Acknowledgement messages generated by NCAs. NCAs send ACKs to reply to rerouted messages they have received (according to their configured rerouting rules).

This screen is accessible to EMA administrators only and appears as an option in the main menu.

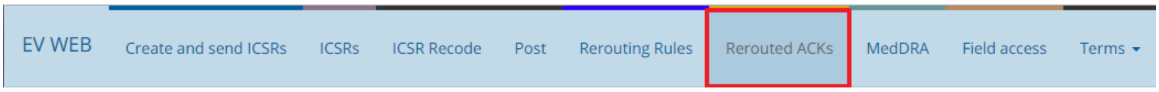


Figure 162 - Rerouted ACKs link

The rerouted Acknowledgement messages are displayed in the active area, in a list view layout. The information displayed per message is as follows:

- Sending NCA
- ACK Message number
- Message number
- Message receive date
- Message acknowledgement code

Figure 163 - Rerouted ACKs screen

Through the available contextual actions menu (which appears once an item in the active area is selected), EMA administrators have the option to download either the rerouted Acknowledgement or Safety message in XML format.

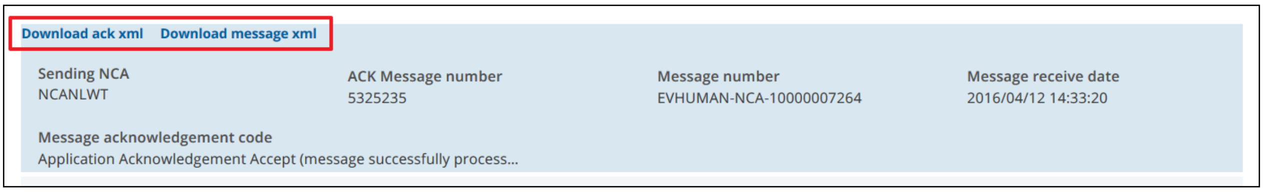


Figure 164 - Download rerouted Acknowledgement or Safety message

The **Rerouted ACKs** screen also provides advanced query functionality, which allows you to fine-tune the displayed items in the active area. This is possible through the use of the Criteria ribbon that can be activated when clicking on the magnifying glass icon ( ).

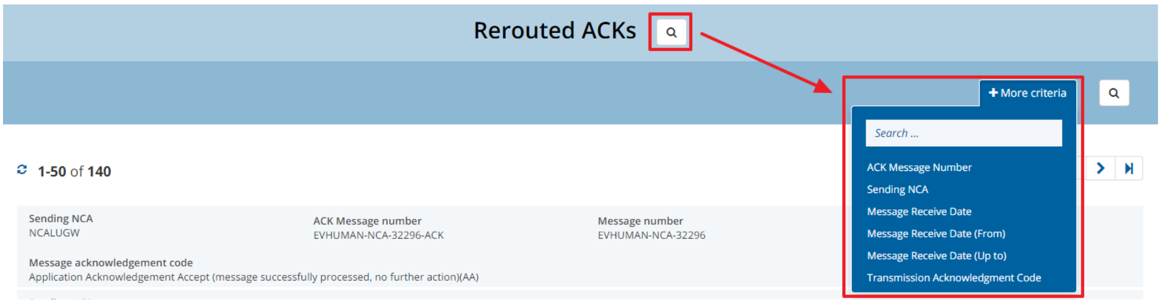


Figure 165 - Rerouted ACKs advanced query

For more information on performing advanced queries please check section **2.7.2. Advanced Query** of this manual.

5.3. Field-Level Access (EMA Administrators)

The field-level access administration tool is accessible to EMA administrators only, and appears as an option with the link **Field access** in the main menu.

Figure 166 - Field access screen link

The purpose of this tool is the management of permission levels for the following EVWEB account holders:

- EMA/NCAs
- MAHs
- WHO (World Health Organisation)

These permission levels define what each of the above EVWEB account holders can view, receive and download in terms of ICSR data. Specifically, these levels (which are also known as security permissions) concern the availability of ICSR E2B(R3) data fields, providing assignment rights for these fields to the affected abovementioned EVWEB account holders.

EMA administrators can define these security permissions by entering the **Field access** screen.

The below screenshot provides a visual overview of the tool's interface. The available labels and checkboxes are laid out in a table format view which permits quick navigation and activation/de-activation of each setting. Thus, applying security permissions consists of ticking (or unticking) the necessary checkboxes that relate to specific E2B(R3) data fields which, in turn, define their availability to the affected EVWEB account user.

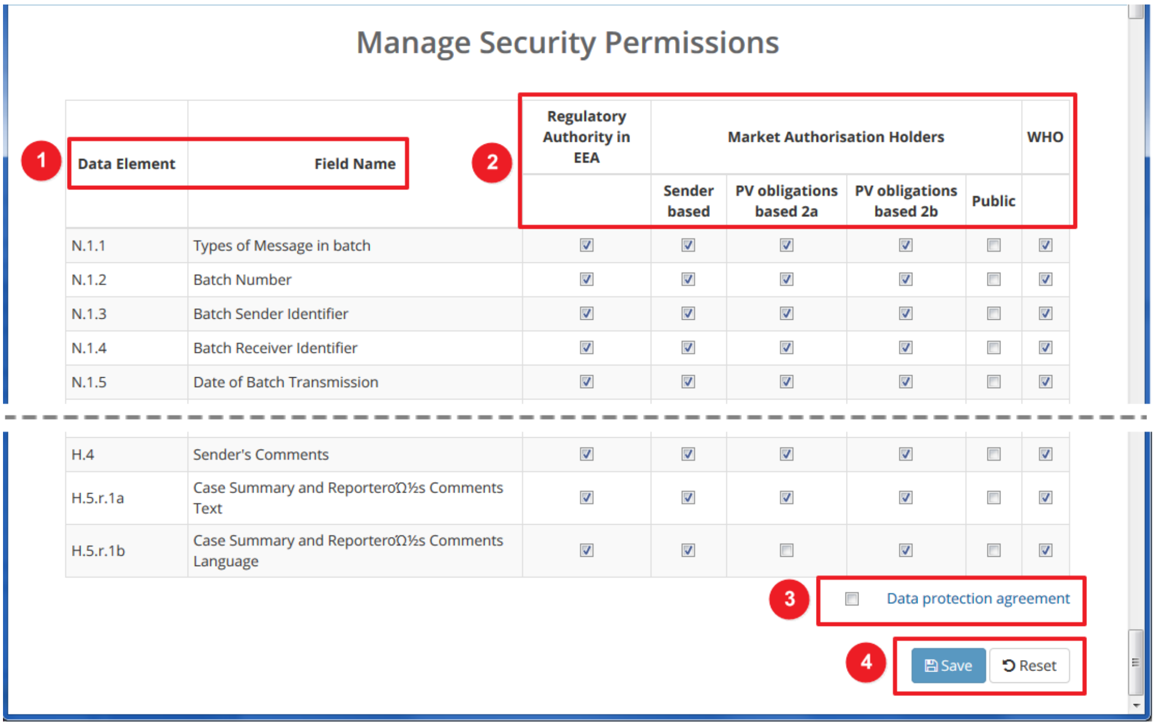


Figure 167 - Field access screen

Note: In order to save and apply the changes made to the security permissions, the EMA administrator must tick the "Data protection agreement" checkbox that is located at the bottom right of the screen. Only then will the "Save" button become active and allow the storing of the changes to the EV system.

Tip: By clicking on the "Data protection agreement" label (not its checkbox) you will be presented with the actual data protection agreement text which you should consent to (by clicking the checkbox), otherwise you will not be allowed to proceed and change any permissions.

The following table offers an overview of the screen's main features by referencing the previous screenshot.

Table 31 – Description of the Field Access Screen

Field Access Screen	Description
(1) Field Code & Name	Displays the ICSR E2B(R3) field codes and labels which can be enabled or disabled per EVWEB account holder.

Field Access Screen	Description

(2) EVWEB Account Holders	Presents the EVWEB account holders for which the permission levels can be set.
	• **Regulatory Authority in EEA** (EMA & NCAs)
	• **Market Authorisation Holders**
	  – **Sender based:** Grants the sender of the ICSR access to all E2B(R3) data fields within the ICSR, including any attachments.
	  – **PV obligations based 2a / 2b:** Grants access to specific E2B(R3) data fields concerning products referenced in an ICSR for which the MAH holds a marketing authorisation.
	  – **Public:** Grants access to E2B(R3) data fields that do not fit any of the above two categories.
	• **WHO**

(3) Data Protection Agreement	Requires the user to tick the checkbox to proceed and save any applied changes. The data protection agreement text can be viewed by clicking on the label.
(4) Buttons	These allow the saving and resetting of applied changes. • **Save:** Stores the currently applied settings. • **Revert:** Reverts all latest changes and returns to the previous saved state.

6. List of Abbreviations & Acronyms

The following table presents the abbreviations and acronyms introduced in this user manual.

Table 32 – Description of the Abbreviations and Acronyms

Abbreviation/Acronym	Description
CIOMS	Council for International Organizations of Medical Sciences
CT	Clinical Trial Module
DIA	Drug Information Association
EC	European Commission
EEA	European Economic Area
EMA	European Medicines Agency
ESTRI	Electronic Standards for the Transfer of Regulatory Information
EU	European Union
EV	EudraVigilance
EVCTM	EudraVigilance Clinical Trials Module
EVDBMS	EudraVigilance Database Management System
EVMPD	EudraVigilance Medicinal Product Dictionary
EVWEB	EudraVigilance WEB
HLGT	High Level Group Term (MedDRA)
HLT	High Level Term (MedDRA)
HTML	HyperText Markup Language
ICH	International Conference on Harmonisation of Technical Requirements for Registration of Pharmaceuticals for Human Use
ICSR	Individual Case Safety Report
ISO	International Organization for Standardization
LLT	Lowest Level Term (MedDRA)
MAH	Marketing Authorization Holder
MDN	Message Disposition Notification
MedDRA	Medical Dictionary for Regulatory Activities
MLM	Medical Literature Monitoring
MSSO	MedDRA Maintenance and Support Services Organisation
NCA	National Competent Authority

Abbreviation/Acronym	Description
NCS	Non-Commercial Sponsor
PDF	Portable Document Format
PM	Post-authorisation Module
PT	Preferred Term (MedDRA)
QPPV	Qualified Persons for Pharmacovigilance
RPC	Regional Pharmacovigilance Centre
RTF	Rich Text Format
SME	Small and Medium Size Enterprise
SOC	System Organ Class (MedDRA)
SSL	Secure Sockets Layer
SUSAR	Suspected Unexpected Serious Adverse Reaction
WHO	World Health Organisation
XML	eXtensible Markup Language