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eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD) Data-Entry Tool (EVWEB) user manual

Version 5.8

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Summary of changes

Following the publication of version 5.7 in June 2022, the links to the EMA Service Desk were amended through-out the document.

Editorial changes in this document are not described in the summary of changes.

Table of Content

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 marketing authorisation holders (MAHs) and sponsors of clinical trials using the eXtended EudraVigilance Medicinal Product Dictionary data-entry tool (EVWEB) and focuses on EVWEB functionalities based on the **XEVPRM format published by the Agency on 31 January 2014 and available in the EVWEB production environment as of 16 June 2014.**

For marketing authorisation holders, related documents to be read in conjunction with this user manual include:

- Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance of the Detailed guidance on the electronic submission of information on medicinal products for human use by marketing authorisation holders to the European to the European Medicines Agency in accordance with Article 57(2) of Regulation (EC) No. 726/2004;
- Legal Notice on the Implementation of Article 57(2) of Regulation (EC) No. 726/2004;
- Electronic submission of Article 57(2) data: Questions & Answers (Q&As) document.

Further information related to the electronic submission of authorised medicines can be found on the Reporting requirements for marketing-authorisation holders webpage of the Agency's website.

For sponsors of clinical trials, related documents to be read in conjunction with this user manual include:

- Guidance on the electronic submission of information on investigational medicinal products for human use in the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): eXtended EudraVigilance Medicinal Product Report (XEVPRM) user guidance;
- Electronic submission of investigational medicinal product (IMP) data to the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): Frequently asked questions & answers (FAQs).

Case and medicinal product examples used in this manual to describe the functionalities and rules of the system are intended for demonstration purposes only.

1.2. About EudraVigilance

EudraVigilance is the European Union pharmacovigilance database and data-processing network (the 'EudraVigilance database').

It supports the:

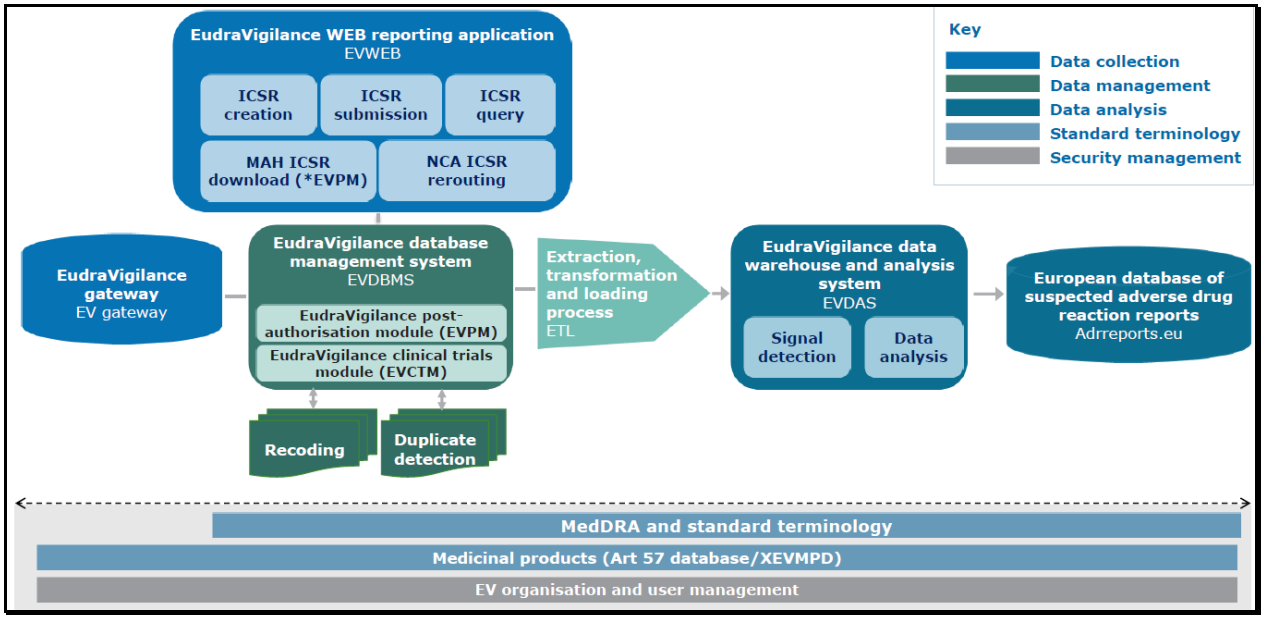
- secure exchange, processing and evaluation of Individual case safety reports (ICSRs) related to medicinal products authorised in the European Union (EU) and investigational medicinal products (IMPs) studied in clinical trials authorised in the EU;
- signal detection, evaluation and management;
- proactive release of information on adverse reactions in compliance with personal data protection legislation in the EU;
- electronic submission of information of medicinal products authorised in the EU;
- provision of information on IMPs by the sponsor before completing a clinical trials application in the EU.

Main components are:

- **EudraVigilance (EV) gateway**: a data-processing solution for the secure electronic exchange of adverse reaction data;
- **EudraVigilance Post-Authorisation Module (EVPM):** dedicated to the collection of ICSRs related to all medicinal products authorised in the EEA in line with Regulation (EC) No 726/2004 and Directive 2001/83/EC;
- **EudraVigilance Clinical Trial Module (EVCTM)**: dedicated to the collection of ICSRs of Suspected Unexpected Serious Adverse Reactions (SUSARs) in accordance with Directive 2001/20/EC and Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC;
- **eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD)**: a reference source for the coding of substances and medicinal products reported in ICSRs based on the information provided by MAHs in line with Article 57(2), second subparagraph of Regulation (EC) No 726/2004.
- **EudraVigilance Data Analysis System (EVDAS):** supporting the EU pharmacovigilance safety monitoring activities with the main focus on signal detection and evaluation of ICSRs;
- **Adrreports.eu portal**: allowing to search and view data on suspected adverse reactions for authorised medicinal products in the EEA and provides general information to aid the understanding of the reports.

The EMA launched a new EudraVigilance system with enhanced functionalities for reporting and analysing suspected adverse reactions in November 2017. For more information, see the EudraVigilance change management webpage.

1.3. EudraVigilance system overview



For further information related to the EudraVigilance system overview please refer to the dedicated EMA webpage.

1.4. EudraVigilance ESTRI gateway

The EudraVigilance gateway is a data-processing network which follows the ICH M2 gateway recommendation for the electronic standards (for the) transmission (of) regulatory information (ESTRI) for the secure electronic exchange of data.

The purpose of the EudraVigilance gateway is to operate a single common gateway for receiving regulatory submissions in a fully automated and secure way.

The EudraVigilance gateway allows MAHs, applicants and sponsors of clinical trials (sponsors) to report to a common reporting point within the EEA from where the transactions are re-routed to the addressed competent authorities, the EMA and the WHO.

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 fully ICH E2B(M) compliant pharmacovigilance database available, which permits the generation, receipt and transmission of ICSRs and via a local gateway solution that meets the ICH M2 standards, and that 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 facilitate electronic submissions by small and medium size enterprises (SMEs) or regional Pharmacovigilance centres in a secure way.

The Web Trader transmission mode is applicable to organisations that do not have a local gateway solution that allows connecting to the EudraVigilance gateway.

! Only registered organisations are permitted to exchange safety, product, and acknowledgement messages by means of the EudraVigilance gateway. Please see the EudraVigilance registration webpages for information on how to register.

1.5. EVWEB

In addition to the automated message generation and processing, the EudraVigilance database management system also provides interactive tools to allow for a 'manual' safety and acknowledgement message, as well as medicinal product report generation and administration by a user via a web interface called EVWEB.

EVWEB can be used by any marketing authorisation holder or sponsor of a clinical trial with reporting or submission obligations in the EU but has been specifically designed for small and medium size enterprises (SMEs), which do not have the necessary IT in-house tools available.

EVWEB requires an internet connection, and the application is supported by Internet Explorer 8 and above. EVWEB may require, depending on the software available on the Windows Client, to install an **ActiveX Component for the User Interface** (Setup ZIP Package available in Production and in XCOMP). For versions of IE 9 and above, users also need to set their IE browser to compatibility view. Article 57 User Interface (UI) Installation Guide is available to registered users (i.e., users with XEVMPD login credentials) in the EV restricted area, in the **'User Support**' section, under **'XEVMPD Support'**.

Following Microsoft's announcement that IE11 will be retired from 15 June 2022, the EMA investigated various alternatives and identified IE Tab extension for Google Chrome and Microsoft Edge as the best alternative to access EVWEB. EMA validated that there is no loss of functionality nor changes in behaviour of EVWEB when accessed via IE Tab.

To access EVWEB using Microsoft Edge or Google Chrome, registered users should log on to the EV restricted area and follow the steps described in the **'User Support**' section, under **'XEVMPD Support'**.

For further technical information, please refer to the information available on the 'How to submit information' webpage.

A version of EVWEB with an XHTML Active Area is available to allow the visualisation and input of the full Unicode Character Set (Production and XCOMP).

The electronic submission of information on medicinal products is secure. Security is achieved in a first instance by a username/password combination to access the registered user restricted area of the EudraVigilance website, and in a second instance using a HTTPS (SSL) protocol. Secure sockets layer (SSL) provides security using a public key to encrypt data that is then transferred over the SSL connection. In HTTP (S-HTTP), 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 are therefore complementary technologies.

Access to EVWEB is personal and non-transferable for each user of each organisation. It is achieved through personal login and password access keys. The registration process is outlined on the EudraVigilance registration webpage.

The main functionalities of EVWEB are to:

- **Create and send eXtended EudraVigilance Product Report Messages (XEVPRMs)** in relation to authorised medicinal products as per Article 57(2) of Regulation (EC) 726/2004 requirements,

and investigational medicinal products in accordance with the Commission's detailed guidance CT-3 requirements.

Only Web Trader users can send XEVPRMs via EVWEB. Gateway users may use the application to create XEVPRMs but messages can only be sent via their local gateway or via EV Post functionality (see section *4.9. Use EV Post*), which is available in the restricted area of the EudraVigilance website (accessible by registered users only).

EVWEB automatically displays the complete sections of the hierarchical structure of a typical XEVPRM, giving the user an opportunity to insert the information on medicinal products in the various fields as necessary. The application displays mandatory fields and allows detecting errors in complying with business rules before sending the message.

- **Receive XEVPRM Acknowledgment messages (XEVPRM ACKs)**

  XEVPRM acknowledgement messages are used to inform a marketing authorisation holder or a sponsor of a clinical trial that the XEVPRM has been received and processed by the EMA and of the outcome of validation of an authorised medicinal product entity performed by the Agency. See Chapter 5: eXtended EudraVigilance Product Report Acknowledgement Message for further information.

  Only Web Trader users can receive XEVPRM ACKs via EVWEB. Gateway users will receive their XEVPRM ACKs via their local gateway.

- **Keep track of sent XEVPRMs and received XEVPRM ACKs**, as well as **rejected XEVPRMs** (e.g. due to non-conformity with the XEVPRM schema or non-adherence with the XEVPRM business rules).

  Only Web Trader users can use the Web Trader Inbox and Outbox (current and archived) sections of EVWEB. Gateway users will store their sent and received messages via their local gateway.

- **Export XEVPRMs**

  After an XEVPRM has been created, it can be exported in different formats: XML (which is the typical format for electronic submissions of information on medicinal products) and RTF (which are typical 'text' document formats).

  This is to enable the user to maintain a copy of the XEVPRM submissions locally.

- **Navigate, browse, and perform queries throughout the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD)**

  EVWEB users are able to insert specific key words and/or combinations of search criteria to run complex queries in the XEVMPD. Results will be displayed on screen.

- **Browse and query MedDRA terminology** in its latest version in use. MedDRA is fully integrated in the EVWEB application.

1.6. eXtended EudraVigilance Medicinal Product Report Message (XEVPRM)

An XEVPRM is an XML file used to insert and maintain information in the XEVMPD. It consists of a set of controlled vocabularies covering a set of codified data elements required from companies submitting information.

An XEVPRM can contain:

- product(s): authorised or development;
- approved substance[1];
- source(s);
- organisation(s): MAH or sponsor;
- ATC Code(s);
- pharmaceutical form(s);
- administration route(s);
- attachment(s);
- master file location(s).

When creating an XEVPRM message using EVWEB, the **'XEVPRM Message' section** allows specifying the message header, which is a mandatory section in the XEVPRM. Please note that for the 'message header' section, you only have to specify the 'Message Number', since the system will automatically complete the other message header information which is not displayed (i.e. sender ID, receiver ID, etc.).

The **'Medicinal Products' section** is the main section and allows users to create product reports both for authorised and development medicinal products that need to be added or maintained in the XEVMPD.

Users can add more than one product report in the same XEVPRM, but for each product report, the operation type and the medicinal product type ('Authorised' or 'Development') must be specified.

The **'Substances' section** allows users to create substance reports for substances that need to be added, updated, or deleted in the substance lookup table.

EMA users can add more than one substance report in the same XEVPRM, but for each substance, the operation type, and the substance type (i.e., 'Approved') must be specified.

! MAHs and/or sponsor users can no longer insert or maintain substance information in the XEVMPD. Substance information is inserted and maintained in the XEVMPD by the EMA. Please refer to the changes related to submission of approved substance information described in the document Changes to some business rules of the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): Submission of substance information or see section *1.7.2.3. Approved substance (AS)* for further information.

The **'Sources' section** allows users to create reference sources that need to be added, updated, or deleted in the Source lookup table.

Users can add more than one source in the same XEVPRM, but for each source the operation type must be specified.

The '**Organisations' section** allows users to create organisations for marketing authorisation holders and sponsors that need to be added, updated or deleted in the MAH and sponsor lookup tables.

[1] Substance information is inserted and maintained in the XEVMPD by the EMA.

Users can add more than one organisation in the same XEVPRM but for each organisation the operation type and the organisation type ('MAH' or 'sponsor') must be specified.

Marketing authorisation holders/sponsors are not allowed to send medicinal products for which they do not hold a marketing authorisation or for which they are not the sponsors. Users are only allowed to specify MAHs/sponsors/affiliate/subordinates that belong to their organisation hierarchy (e.g. the headquarter organisation and its affiliates). The organisations users can specify must be registered in the EudraVigilance system; their 'Organisation Sender ID' must be reported in the 'Sender ID' field. Please refer to the Registration with EudraVigilance webpages for further information.

The '**ATC Codes' section** allows users to create ATC Codes for proposed or development ATC Codes that need to be added, updated or deleted in the ATC Code lookup table. Standard ATC Codes are entered and maintained in the XEVMPD by the EMA.

Users can add more than one ATC Code in the same XEVPRM but for each ATC Code the operation type and the term type ('Proposed' or 'Development') must be specified. Development terms can only be referenced in development medicinal products.

The '**Pharmaceutical Forms' section** allows users to create pharmaceutical forms for proposed or development pharmaceutical forms that need to be added, updated, or deleted in the pharmaceutical dose form lookup table. Standard ATC Codes are entered and maintained in the XEVMPD by the EMA. Users can add more than one pharmaceutical dose form in the same XEVPRM, but for each pharmaceutical dose form the operation type and the term type ('Proposed' or 'Development') must be specified. Development terms can only be referenced in development medicinal products.

The '**Administration Routes' section** allows users to create administration routes for proposed or development routes of administration that need to be added, updated, or deleted in the administration route lookup table. Standard routes of administration are entered and maintained in the XEVMPD by the EMA. Users can add more than one administration route in the same XEVPRM but for each administration route the operation type and the term type ('Proposed' or 'Development') must be specified. Development terms can only be referenced in development medicinal products.

The '**Attachments**' **section** allows users to create a reference to a printed product information (PPI) and/or printed substance information (PSI) [PSI is currently not in use]. This information will be attached to the message when sending. Users need to specify the file type and name, as well as the language of the file, the version number and version date of the file to be attached.

The '**Master File Location**' **section** allows users to provide information about the physical location of the pharmacovigilance master file.

For a complete description of the XML schema and the structure of the XEVPRM please refer to the XEVPRM and XEVPRM acknowledgement documentation available on the Guidance Documents webpage:

- Extended EudraVigilance product report message (XEVPRM) schema;
- Chapter 3.I: Extended EudraVigilance product report message (XEVPRM) technical specifications;
- Chapter 5: Extended EudraVigilance product report acknowledgement message.

1.7. eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD)

eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD) is a database designed to support the collection, reporting, coding, and evaluation of medicinal product data in a standardised and structured way.

The main objective of the XEVMPD is to assist the pharmacovigilance activities in the European Economic Area (EEA), enabling the Agency to:

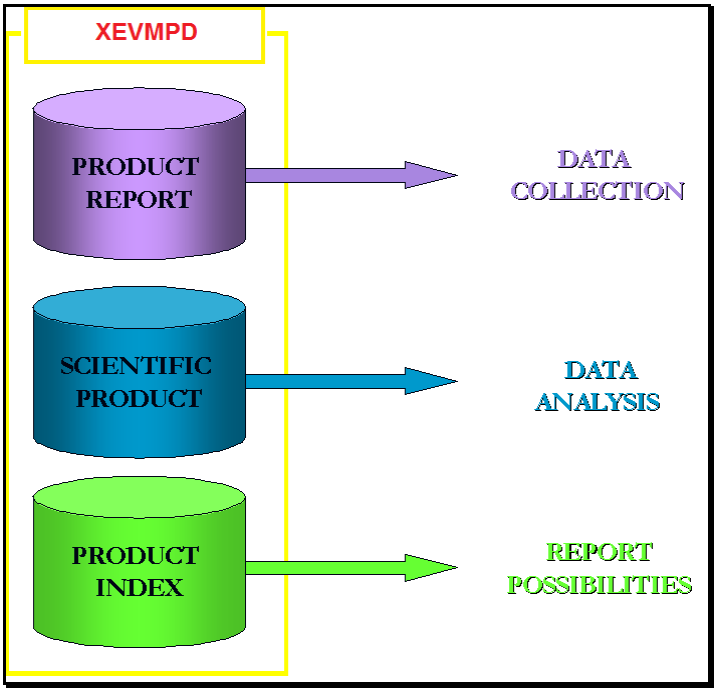
- create a list of all medicines authorised in the EEA;
- accurately identify medicines, especially medicines included in reports of suspected adverse reactions;
- co-ordinate the regulation and safety monitoring of medicines across the EU and EEA.

The XEVMPD consists of three different databases designed to support the collection, scientific evaluation and coding of medicinal products authorised worldwide.

Investigational medicinal products, which are subject to a clinical trial in the EEA, are also integrated with the necessary security level to ensure data confidentiality.

The three different databases are:

1. product report database (product report);
2. scientific product database (scientific product); and
3. product index database (product index).



The **product report database** is designed to support data collection and contains a key set of information about authorised and development medicinal products, for which the information is provided by MAHs and sponsors of clinical trials.

The **scientific product database** is designed to support data analysis and implements a hierarchy allowing a classification of all medicinal products available in the XEVMPD on the basis of the active ingredient, the concentration and the pharmaceutical form. It allows grouping of medicinal products solely based on their composition, regardless of their different trade names, or their MAHs or sponsors.

The hierarchy within the scientific product consists of the following levels:

- abstract composition: each abstract composition represents the set of pharmaceutical products containing the same active ingredient(s);

- abstract strength: each abstract strength represents the set of pharmaceutical products containing the same active ingredient(s) in the same strength(s);
- abstract formulation: each abstract formulation represents the set of pharmaceutical products containing the same active ingredient(s) and the same pharmaceutical dose form;
- abstract pharmaceutical product: each abstract pharmaceutical product represents the set of pharmaceutical products with the same active ingredient(s) in the same strength(s) and the same pharmaceutical dose form.

The product index database and the scientific product database are two data structures maintained by entering or updating medicinal product information in the XEVMPD through data from the product report database.

The product reports database collects information on authorised medicinal products and development medicinal products.

The **product index (PI) database** is designed to provide various reporting possibilities on the same medicinal product. It is very important to consider the possible vagueness of the reported medicinal product information provided by the original reporting source, which is especially common in spontaneous adverse reaction reporting. It is very important to standardise this information to allow accurate data analysis by scientific experts.

The product index database provides a reference lookup list containing various reporting possibilities generated from the full presentation name of a medicinal product (i.e. the medicinal product name as it has been authorised). Each reporting possibility is generated from the data available in both, the product report database and in the scientific product database.

The combination of the following fields (all part of the full medicinal product presentation name) of the product report database provides the reporting possibilities in the product index database:

- 'Product Short Name';
- 'Product INN/Common Name';
- 'Product Company Name';
- 'Product Strength Name';
- 'Product Form Name'.

It is therefore very important that the authorised medicinal product name information provided in the 'Full Presentation Name' field is correctly entered in the relevant fields (i.e. 'Product Short Name' field, 'Product INN/Common Name' field, 'Product Company Name' field, 'Product Strength Name' field and 'Product Form Name' field). For related information please refer to Chapter 3.II: XEVPRM User Guidance, section *1.2.13. AMP - Presentation Name element structure (AP.13).*

The document 'European Medicines Agency splitting of the full presentation name of the medicinal product best practice: procedure and principles to handle product name in the EudraVigilance Medicinal Product Dictionary (XEVMPD)' also provides further information and additional examples.

The reporting possibilities are also generated using the development medicinal product and development substance information collected in the product report DB for IMPs. These entries consider the confidentiality of the information related to IMPs.

The reporting possibilities in the product index database are also generated using the scientific database. These reporting possibilities enable the system to maintain a valid list of substances, and combination of substances, for the mapping process of equivalent 'generic products'.

1.7.1. Data submission in the XEVMPD

The XEVMPD contains information provided by sponsors and marketing authorisation holders.

1.7.1.1. Marketing authorisation holders (MAHs)

As per Article 57(2) of Regulation (EC) No 726/2004 as amended by Regulation (EU) 1235/2010 and Regulation (EU) 1027/2012, marketing authorisation holders are required to submit to the EMA information on all medicinal products for which they hold a marketing authorisation in the European Union, i.e. information on:

- nationally authorised medicinal products (NAPs);
- centrally authorised medicinal products (CAPs);
- mutually recognised medicinal products (MRPs);
- de-centrally authorised medicinal products (DCPs).

MAHs are also required to submit to the EMA information on all medicinal products for which they hold a marketing authorisation in the EEA countries outside the European Union since the Pharmacovigilance legislation has been incorporated into the EEA agreement.

Full details on the legal provisions and requirements for marketing authorisation holders are available in the Legal Notice on the Implementation of Article 57(2) of Regulation (EC) No. 726/2004 - Electronic Submission of Information on Medicinal Products for Human Use by Marketing Authorisation Holders to the European Medicines Agency.

Medicinal product data shall be submitted to XEVMPD via the eXtended EudraVigilance Medicinal Product Report Message (XEVPRM). EMA first published the data format in July 2011 and the XML schema definition (XSD) for the individual data elements in September 2011. This was followed by updated requirements in March 2012, with fewer mandatory data fields to reduce the administrative burden on marketing authorisation holders submitting medicinal product information in the context of Art 57(2) of Regulation (EC) No 726/2004.

The XSD schema was amended and published on 31 January 2014, including additional information on medicines required to fulfil new legal obligations. The new XSD schema is available in the EVWEB production environment as of 16 June 2014 and in XCOMP (i.e. the EudraVigilance External Compliance Testing Environment) from 17 June 2014.

From 16 June 2014, the required data elements for authorised medicinal product information increased, and the following new required fields must be included in the data submission format:

- the details of the legal basis of the marketing authorisation;
- description of the medicinal product type;
- information on the authorised pharmaceutical form and, where applicable, before reconstitution into the administered pharmaceutical form;
- description of the size of the organisation (i.e. the SME status information).

For detailed information please refer to the Reporting requirements for marketing-authorisation holders webpage.

If your organisation is a headquarter organisation, you have the option to send all medicinal products for which you and your affiliates hold the marketing authorisation. Alternatively, you may delegate the sending of the medicinal product information to your affiliates, i.e. for those medicinal products for which they hold the local marketing authorisation. For information how to register, please see the EudraVigilance registration webpage.

1.7.1.2. Sponsors

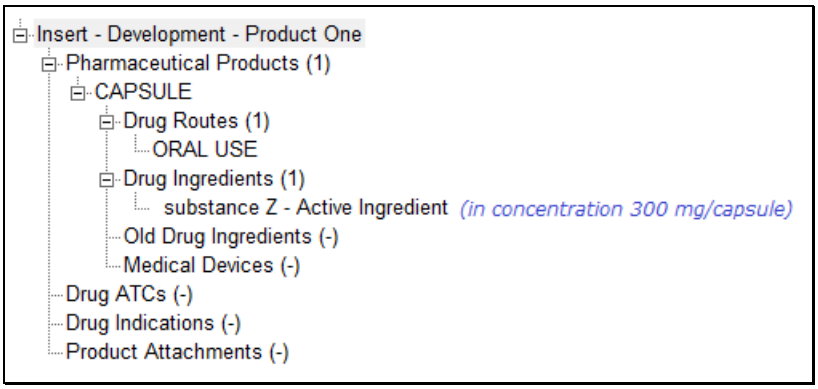
Directive 2001/20/EC, Article 2 (d), provides the following definition of an IMP: *'a pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial, including products already with a marketing authorisation but used or assembled (formulated or packaged) in a way different from the authorised form, or when used for an unauthorised indication, or when used to gain further information about the authorised form.'*

For a clinical trial application to be completed, the study drug(s) must be entered in the XEVMPD. As stated in the Detailed guidance on the collection, verification and presentation of adverse event/reaction reports arising from clinical trials on medicinal products for human use ('CT-3') (OJ 2011/C 172/01) published by the Commission on 11 June 2001 paragraph 7.9. Format of report, section 104: *'- the Sponsor should provide, before completing the clinical trials application form, information on the IMP in the EudraVigilance Medicinal Product Dictionary ('EVMPD')'.*

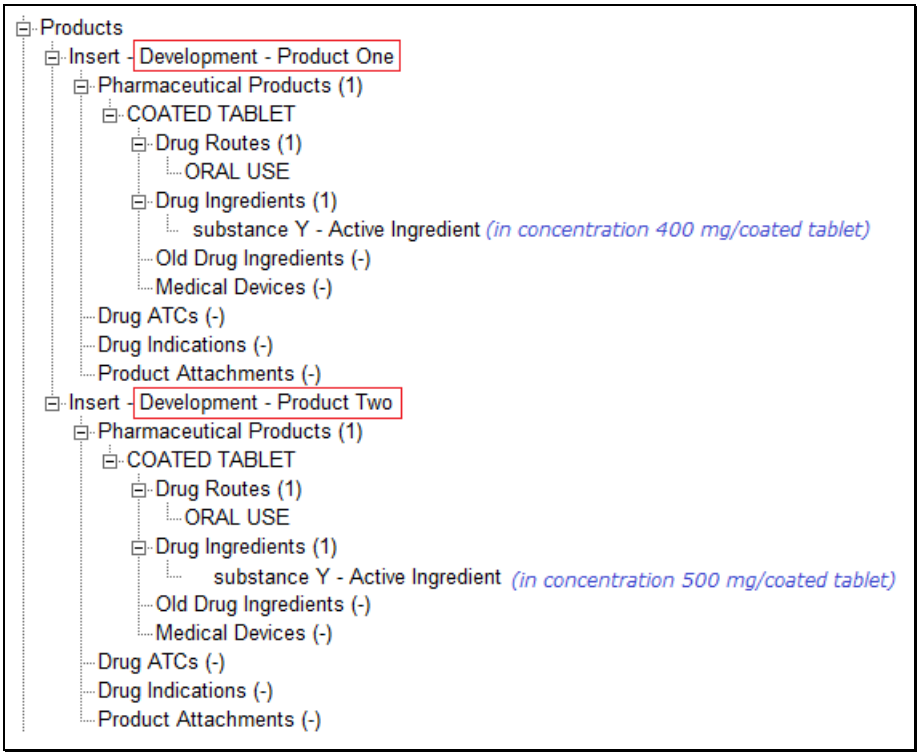
To simplify the process of IMP information submissions in the XEVMPD for sponsors, the following guidance should be used:

- If an active substance (approved or development) is used in a clinical trial in a **new pharmaceutical dose form and/or new strength**, a new DMP must be entered in the XEVMPD.
  - In the CTA form, the sponsor makes a reference to the DMP entered in the XEVMPD by their sponsor organisation.

    Example 1: Sponsor A studies in their clinical trial 300 mg of substance Z in a capsule which is administered orally to the subjects. The sponsor submits one DMP referencing one pharmaceutical product in the XEVMPD:



    Example 2: Sponsor B runs two clinical trials. In one trial, 400 mg of substance Y is given to the subjects orally in coated tablets. In the other trial, 500 mg of substance Y is given to the subjects orally in coated tablets. The sponsor submits two DMPs, each referencing one pharmaceutical product, in the XEVMPD:

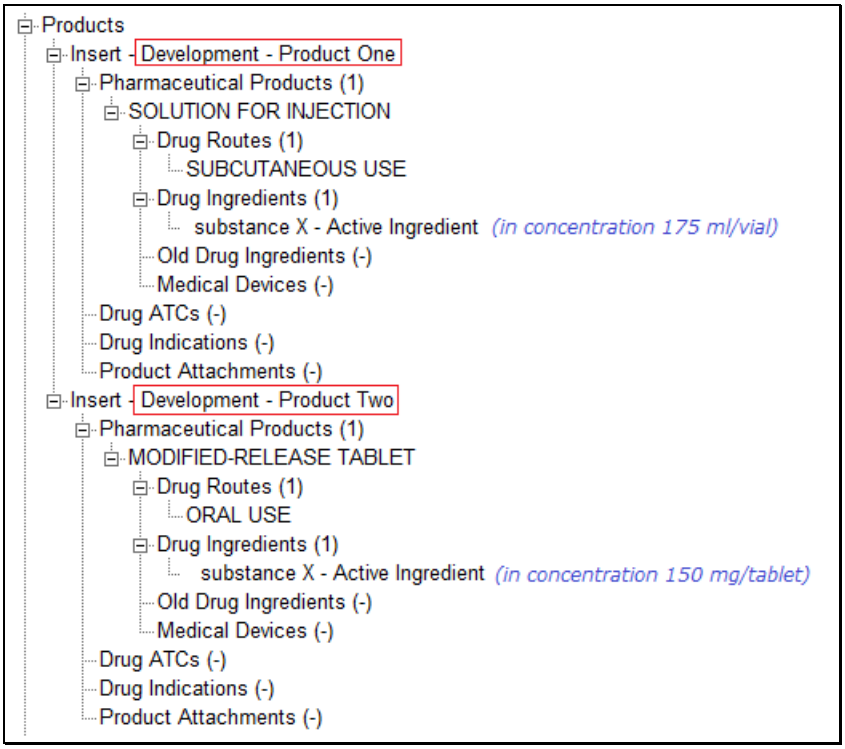


Example 3: Sponsor C studies in two separate clinical trials:

- 175 ml of substance X in a solution for injection, which is administered subcutaneously; and

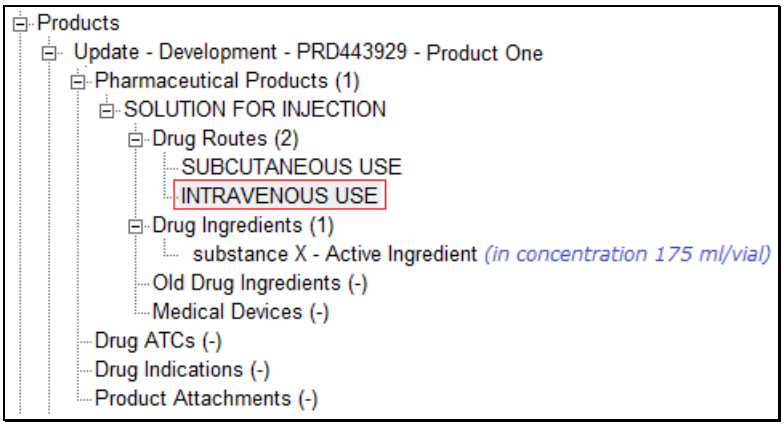
- 150 mg of the same substance in a modified-release tablet administered orally.

The sponsor submits two DMPs in the XEVMPD, each referencing one pharmaceutical product:



- If a medicinal product authorised in the EEA is used in a clinical trial in its authorised form (i.e. the pharmaceutical dose form, active ingredient and its concentration remain unchanged) **for authorised or unauthorised indications and/or route of administration(s)** different to those described in the SmPC, no DMP needs to be submitted in the XEVMPD by the sponsor.
  - In the Clinical Trial Application (CTA) form, the sponsor makes a reference to the AMP entered in the XEVMPD by the marketing authorisation holder.
- If a medicinal product not yet authorised in the EEA is used in a clinical trial **for new authorised or unauthorised indications and/or route of administration(s)**, the sponsor can update the existing DMP with the new indication/route of administration.
  - In the Clinical Trial Application (CTA) form, the sponsor makes a reference to the existing DMP entered in the XEVMPD by the sponsor.

    Example 4: As described in Example 3, Sponsor C submitted a development 'Product One' in the XEVMPD referencing a solution for injection containing 175 ml of substance X, which is administered subcutaneously. Sponsor C conducted another trial using the same pharmaceutical product that was now administered intravenously. New DMP should therefore be entered by the sponsor; the sponsor can update the existing DMP entity to add a new route of administration:



- If various sponsors use a in their clinical trial the same substance that is not yet approved, each of the sponsors must enter the pharmaceutical product information (the pharmaceutical form, its active ingredient and concentration and the route of administration) as a DMP in the XEVMPD.
  - In the CTA form, the sponsor makes a reference to the DMP entered in the XEVMPD by their sponsor organisation.

    E.g. Sponsor A and Sponsor B use in their clinical trial 200 ml of development substance Y in a coated tablet which is administered orally. Each sponsor submits one DMP referencing one pharmaceutical product in the XEVMPD:
- If various sponsors are testing the same development product in their clinical trials, multiple development products must be entered in the XEVMPD; each DMP will reference the respective sponsor organisation.

Furthermore, regarding the submission of comparators and placebos, as stated in the Detailed guidance on the collection, verification and presentation of adverse event/reaction reports arising from clinical trials on medicinal products for human use ('CT-3') (OJ 2011/C 172/01): '*Comparators and placebos are IMPs. Therefore, SUSARs associated with a comparator product follow the same reporting requirements as for the test IMP. Events associated with placebo will usually not satisfy the criteria for*

a SUSAR and therefore for expedited reporting. However, where SUSARs are associated with placebo (e.g. reaction due to an excipient or impurity), the sponsor should report such cases'.

Also, as stated in section D.8 Reporting of the 'Placebo of the Note for guidance – EudraVigilance Human – Processing of safety messages and individual case safety reports (ICSRs)' document:

" If relevant, placebos can be reported in the ICSRs in the following data elements:

- *medicinalproduct (ICH E2B(R2) B.4.k.2.1)*
- *patientdrugname (ICH E2B(R2) B.1.8a)*
- *parentdrugname (ICH E2B(R2) B.1.10.8a)*

Placebos reported in ICSRs are recoded against the entry 'PLACEBO' in the Product Index Database. Placebos do not need to be entered in EVMPD. However, when a placebo is reported in the data element medicinalproduct (ICH E2B(R2) B.4.k.2.1) as 'SUSPECT' or 'INTERACTING', the suspected ingredient(s) of the placebo has/have to be specified in the data element activesubstancename (ICH E2B(R2) B.4.k.2.2).

In conclusion, sponsors do not need to submit information on placebo in XEVMPD. Only information on the active ingredient of the investigational medicinal product is required.

Historically, substances could be entered in the XEVMPD as 'approved' or 'development' by MAHs and sponsors. This is no longer applicable; all new substances are entered in the dictionary by the EMA as 'approved substances' based on SMS requests received via the EMA Service Desk portal. The 'development substance' section continues to exist and store legacy information, but it is not updated with any new entries. For further information please refer to the 'Changes to some business rules of the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): Submission of substance information' document.

Sponsor organisations and their affiliates/subordinates (e.g., clinical research departments) must be registered with the EudraVigilance system. Registration is a prerequisite to enable the submission of investigational medicinal product information to the XEVMPD. Please see the EudraVigilance registration webpages for information on how to register.

Sponsors may delegate the sending of medicinal product information to clinical research organisations (CROs) or IT vendors. CROs and IT vendors may be registered by a marketing authorisation holder, applicant, commercial or non-commercial sponsor as a **third-party service provider** acting on behalf of these organisations by providing services related to EudraVigilance. See the EudraVigilance registration webpage for further information.

1.7.2. Data collected in the XEVMPD

The information collected in the XEVMPD concerns:

- authorised medicinal products (AMPs); and
- development medicinal products (DMPs).

Many fields related to authorised or development medicinal products are coded in lookup tables in the XEVMPD.

Some lookup tables are maintained by the EMA, whilst other lookup tables can be maintained directly by the XEVMPD user (updatable lookup tables).

The lookup tables present in the XEVMPD are:

Lookup	Maintained by	Reference
MAH organisation list	User	
SME status list	EMA	
QPPV list	User (via EV Registration process)	
MFL list	User	
Country code list	EMA	ISO
Authorisation procedures	EMA	
Authorisation status	EMA	
Legal basis list	EMA	
Orphan drug designation	EMA	
Additional monitoring designation	EMA	
Medicinal product type	EMA	
Standard pharmaceutical form list	EMA	EDQM
Proposed pharmaceutical form list	User	
Development pharmaceutical form list	User	
Standard administration route list	EMA	EDQM
Proposed administration route list	User	
Development administration route list	User	
Approved substance list	EMA	
Development substance list	EMA	
Substance class list	EMA	ISO
Reference source list	EMA and User	
Role of the Ingredient list	EMA	
Amount value type (i.e. concentration type) list	EMA	UCUM
Concentration unit list	EMA	UCUM
Unit or presentation list	EMA	UCUM
Unit of measure list	EMA	UCUM
Numerator/Denominator prefix list	EMA	
Medical Device list	EMA	
Standard ATC Code list	EMA	WHO
Proposed ATC Code list	User	
Development ATC Code list	User	
MedDRA version	EMA	MSSO
MedDRA level	EMA	MSSO
MedDRA term	EMA	MSSO
Attachments list	User	
Attachment type list	EMA	
Attachment file type list	EMA	
EEA Language list	EMA	ISO

When a new entity is added (e.g., medicinal product, organisation, term) in the XEVMPD, a set of data/information must be provided, depending on the type of entity.

For list of data fields collected for entities in the XEVMPD and business rules on the information that needs to be provided for these fields and under which condition please refer to:

- Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance of the Detailed guidance on the electronic submission of information on medicinal products for human use by marketing authorisation holders to the European to the European Medicines Agency in accordance with Article 57(2) of Regulation (EC) No. 726/2004; and
- Guidance on the electronic submission of information on investigational medicinal products for human use in the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): eXtended EudraVigilance Medicinal Product Report (XEVPRM) user guidance.

For technical specifications, please see Chapter 3.I: Extended EudraVigilance product report message (XEVPRM) technical specifications.

1.7.2.1. Authorised medicinal product (AMP)

The information regarding an authorised medicinal product includes the below information [the symbol (*) means mandatory]:

- (*) Marketing authorisation holder (MAH) of the AMP
- (*) Qualified Person responsible for Pharmacovigilance (QPPV)
- (*) Master File Location
- (*) PhV enquiry e-mail and Phone number
- Sender Local Code
- (*) Info Date - the date of lifting of suspension (as applicable per the relevant business rules)
- (*) Authorisation Country Code
- (*) Authorisation Procedure
- (*) Authorisation Status
- (*) Authorisation Number
- (*) Authorisation/Renewal Date
- (*) MRP/DCP/EMEA Number (as applicable per the relevant business rules)
- (*) EU Number (as applicable per the relevant business rules)
- (*) Legal basis
- (*) Orphan drug designation
- (*) Additional Monitoring
- (*) Invalidated MA date (as applicable per the relevant business rules)
- (*) Product Name information
- Package description
- (*) Pharmaceutical Dose Form(s)
- (*) Route of Administration(s)
- Ingredients:
  - (*) Active Ingredient(s)
  - (*) Strength of the Active Ingredient(s)
  - (*) Excipient(s)
  - Strength of the Excipient(s)
  - (*) Adjuvant(s)
  - (*) Strength of the Adjuvant(s)
- Old Drug Ingredient(s)
- Medical Devices
- (*) Product ATC Code(s)
- (*) Product Indication(s) (using MedDRA coding)
- (*) Previous EV Code(s) (as applicable per the relevant business rules)

- (*) Product Attachment(s) including validity declaration (as applicable per the relevant business rules)
- (*) Legal Basis
- (*) Medicinal Product Type
- (*) Authorised Pharmaceutical Form

For details on which information should be provided in the individual fields of an *authorised medicinal product (AMP) entity* please refer to Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance.

1.7.2.2. Development medicinal product (DMP)

The information regarding a development medicinal product includes the below information [the symbol (*) means mandatory]:

- Sender Local Code
- (*) Sponsor of the DMP
- (*) Sponsor's Product Code may be provided if available.

  ❗If no Product Name is included Product code must be provided as mandatory information as per relevant business rules.
- (*) Sponsor's Product Name may be provided if available.

  ❗If no Product Code is included then the Product Name must be provided as mandatory information, as per relevant business rules.
- Product's Other Name, if applicable
- Comment
- (*) Pharmaceutical Dose Form(s)
- (*) Route of Administration(s)
- Ingredients:
  - (*) Active Ingredient(s)
  - (*) Strength of the Active Ingredient(s)
  - Excipient(s)
  - Strength of the Excipient(s)
  - (*) Adjuvant(s)
  - (*) Strength of the Adjuvant(s)
- Old Drug Ingredient(s)
- Medical Devices
- Product ATC Code(s)
- Product Indication(s) (using MedDRA coding)
- Product Attachment(s) including validity declaration (if applicable and as per relevant business rules)

For details on which information should be provided in the individual fields of a *development medicinal product (DMP) entity* please refer to the Guidance on the electronic submission of information on investigational medicinal products for human use in the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): eXtended EudraVigilance Medicinal Product Report (XEVPRM) user guidance document.

1.7.2.3. Approved substance (AS)

The information collected regarding an approved substance (AS) includes the below information [the symbol (*) means mandatory]:

- (*) English Name
- (*) The Substance Class and the reference source for the Substance (e.g. INN, EU Pharmacopoeia)
- CAS[2] Number / CBD[3] / Molecular Formula
- Alias/ Translation(s)
- Substance International Code (including the Source)
- Substance Parent Code (including the Substance Type)
- Previous EV Code(s)
- Substance Attachment(s)

Please note that substance information can be inserted and/or updated by the EMA only. Please refer to the information available in the 'Changes to some business rules of the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): Submission of substance information' document.

1.7.2.4. Source

The information collected regarding a source includes the below information [the symbol (*) means mandatory]:

- (*) Source Name
- Comment

For details on what information should be provided in the individual fields of *a reference source entity* please refer to Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance or Guidance on the electronic submission of information on investigational medicinal products for human use in the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): eXtended EudraVigilance Medicinal Product Report (XEVPRM) user guidance.

1.7.2.5. MAH organisation

The information collected regarding a marketing authorisation holder organisation includes the below information [the symbol (*) means mandatory]:

- (*) MAH Name
- (*) SME status
- SME number (if applicable)
- MAH Sender ID
- (*) Address
- (*) City

2 CAS = Chemical Abstract Service

3 CBD = Chemical/Biological Description

- Region
- (*) Post Code
- (*) Country Code
- Tel Number
- Tel Extension
- Tel Country Code
- E-mail Address
- Comment

For details on what information should be provided in the individual fields of *MAH* entity please refer to Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance.

1.7.2.6. Sponsor organisation

The information collected regarding a sponsor organisation includes the below information [the symbol (*) means mandatory]:

- (*) Sponsor Name
- Sponsor Sender ID
- (*) Address
- (*) City
- Region
- (*) Postcode
- (*) Country Code
- Tel Number
- Tel Extension
- Fax Number
- Fax Extension
- Fax Country Code
- E-mail Address
- Comment

1.7.2.7. Development/proposed ATC Code

The information collected regarding a development/proposed ATC Code includes the below information [the symbol (*) means mandatory]:

- (*) ATC Code
- (*) ATC Code Description
- Version Date
- Comment

For details on what information should be provided in the individual fields of *a proposed ATC Code entity* please refer to Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance or Guidance on the electronic submission of information on investigational medicinal products for human use in the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): eXtended EudraVigilance Medicinal Product Report (XEVPRM) user guidance.

The same rules are applicable to a *development ATC Code entry* - the type of the term is however to be specified as 'Development Term (1)'.

1.7.2.8. Development/proposed pharmaceutical form

The information collected regarding a development/proposed pharmaceutical form includes the below information [the symbol (*) means mandatory]:

- (*) Pharmaceutical dose form
- Version Date
- Previous EVCODE
- Comment

For details on what information should be provided in the individual fields of *a proposed pharmaceutical form entity* please refer to Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance or Guidance on the electronic submission of information on investigational medicinal products for human use in the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): eXtended EudraVigilance Medicinal Product Report (XEVPRM) user guidance.

The same rules are applicable to a *development pharmaceutical entity* - the type of the term is however to be specified as 'Development Term (1)'.

1.7.2.9. Development/proposed route of administration

The information collected regarding a development/proposed route of administration includes the below information [the symbol (*) means mandatory]:

- (*) Administration Route Name
- Version Date
- Previous EVCODE
- Comment

For details on what information should be provided in the individual fields of *a proposed route of administration entry,* please refer to Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance or Guidance on the electronic submission of information on investigational medicinal products for human use in the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): eXtended EudraVigilance Medicinal Product Report (XEVPRM) user guidance.

The same rules are applicable to a *development route of administration entry* - the type of the term is however to be specified as 'Development Term (1)'.

Pharmaceutical forms, routes of administration and ATC Codes will be referred to as 'Term' in this session. The reference to 'Development Term' indicates either 'Development ATC Code' or 'Development Pharmaceutical Form' or 'Development Route of Administration'.

1.7.2.10. Printed product information (PPI)/printed substance information (PSI)

The information collected regarding the attachment for the printed product information (PPI) includes the below information [the symbol (*) means mandatory]:

- (*) File Type
- (*) Name
- (*) Type (PPI or PSI)
- (*) Language
- (*) Version Number
- (*) Version Date

For details on what information should be provided in the individual fields of *a Printed Product Information (PPI) entity* please refer to Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance or Guidance on the electronic submission of information on investigational medicinal products for human use in the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): eXtended EudraVigilance Medicinal Product Report (XEVPRM) user guidance.

The same rules are applicable to a *printed substance information (PSI)* - the attachment type is however to be specified as 'PSI' (2). Please note that currently, PSI is not in use.

1.7.2.11. Pharmacovigilance System Master File Location (PSMFL)

The information collected regarding the **master file location** includes the below information [the symbol (*) means mandatory]:

- Company
- Department
- Building
- (*) Street
- (*) City
- Region
- (*) Post Code
- (*) Country
- (*) Comment (as per applicable business rules)

For details on what information should be provided in the individual fields of *a PSMFL entity,* please refer to Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance or Guidance on the electronic submission of information on investigational medicinal products for human use in the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): eXtended EudraVigilance Medicinal Product Report (XEVPRM) user guidance.

The provision of medicinal product information can be accomplished via one of the following procedures:

- exchanging XML files through an ESTRI gateway or the EV Post function; or
- using EVWEB.

At the end of each procedure, the EudraVigilance system handles and processes the XEVPRM.

Before explaining how to use EVWEB for creating and sending an XEVPRM, it is important to briefly describe:

- XEVMPD terminologies;
- data ownership and maintenance rules;
- data quality;
- data access policy.

1.7.3. XEVMPD terminologies

The following terminologies and definitions apply for the XEVMPD:

- **medicinal product (MP):** any substance or combination of substances presented as having properties for treating or preventing disease in human beings; or any substance or combination of substances, which may be used in or administered to human beings either with the view to restoring, correcting or modifying physiological functions by exerting a pharmacological, immunological or metabolic action, or to making a medical diagnosis (Directive 2004/27/EC).
- **authorised medicinal product (AMP):** a medicinal product authorised either within or outside the EEA.
- **investigational medicinal product (IMP):** a pharmaceutical form of an active substance or placebo being tested or used as a reference in a clinical trial, including products already with a marketing authorisation but used or assembled (formulated or packaged) in a way different from the authorised form, or when used for an unauthorised indication, or when used to gain further information about the authorised form (Directive 2001/20/EC).
- **development medicinal product (DMP):** a medicinal product under investigation in a clinical trial in the EEA which does not have a marketing authorisation in the EEA and to which special confidentiality arrangements need to be applied.
- **approved substance:** any substance as defined in Directive 2004/27/EC, which is an ingredient of a medicinal product for which a marketing authorisation was granted.
- **term:** pharmaceutical dose form, administration route, or an ATC Code.
- **standard term:** term published as a term of standard terminology by an official maintenance body [e.g. European Directorate for the Quality of Medicines (EDQM)] used in the XEVMPD. This information is entered and maintained in the XEVMPD by the European Medicines Agency (EMA). Standard terms can be used either in development medicinal products or authorised medicinal products.
- **development term:** confidential term used in a clinical trial. These terms are entered and maintained in the XEVMPD by sponsors. Development terms can only be referenced in development medicinal products.
- **proposed term:** term for which there is an application to the maintenance organisation, but the term is not yet approved or published. These terms are entered and maintained in the XEVMPD by sponsors or MAHs. Proposed terms can be used either in development medicinal products or authorised medicinal products.

1.7.4. Data ownership and maintenance

Medicinal product information provided via the XEVPRM is 'owned' by the **headquarter (HQ) ID** of the sender organisation that submitted the information. For each submitted entity the XEVMPD stores the **sender organisation ID** and checks this field before allowing the modification of such entity.

! Only the owner organisation of the data is authorised to maintain the submitted information.

Duplicated or obsolete entities can only be nullified by the owner organisation and/or the EMA if they are **not** referenced in any other current (i.e., not nullified) entities. With the exception of development medicinal products, which can be nullified even if flagged as validated in the XEVMPD, validated entities can only be nullified by the EMA upon a request received via the EMA Service Desk portal:

- Substance related requests: https://support.ema.europa.eu/esc?id=sc_cat_item&sys_id=6fac4352c3195d10e68bf1f4e40131a5
- XEVMPD product data related request: https://support.ema.europa.eu/esc?id=sc_cat_item&sys_id=5cd0ff1ec3995d10e68bf1f4e40131bb

! MAH or sponsors cannot perform maintenance related operation types on substances; these will lead to a negative XEVPRM ACK. Please refer to the information available in Changes to some business rules of the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): Submission of substance information for further details.

The operation types that a sender organisation can perform by sending an XEVPRM are described in Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance or Guidance on the electronic submission of information on investigational medicinal products for human use in the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): eXtended EudraVigilance Medicinal Product Report (XEVPRM) user guidance.

1.7.5. Data quality

During the creation and sending of an XEVPRM there are technical business rules where the system automatically checks if mandatory information has been provided or cross-referenced for a medicinal product submission.

If the validation reports no errors, the information is sent and loaded in the XEVMPD.

Users will receive an XEVPRM acknowledgement for every XEVPRM sent to the XEVMPD. The acknowledgement informs the sender organisation whether the information contained in the XEVPRM and sent to the XEVMPD has been loaded successfully, or if some reports contained in the XEVPRM have not been loaded. In the latter case, the acknowledgement will display the list of errors found in the unloaded reports.

Detailed information related to an XEVPRM Acknowledgement can be found in Chapter 5: Extended EudraVigilance product report acknowledgement message and *Appendix 5 – Element Acknowledgement Codes* of Chapter 3.I: Extended EudraVigilance product report message (XEVPRM) technical specifications.

In July 2014, the Agency began the review of quality and integrity of authorised medicinal product information submitted in line with the amended XEVPRM format and specifications effective as of 16

June 2014. The EMA performs data integrity assessments and, where necessary, revisions in accordance with the principles outlined in the published Data Quality Control methodology. Systematic assessment of the latest version of the received medicinal product data is performed by checking each data element against the information stated in the provided summary of product characteristics (SmPCs) or equivalent document that facilitates the data quality assurance process by the EMA. For further information please see the Agency's document Quality control of medicinal-product data submitted as per the legal requirement introduced by Article 57(2) of Regulation (EC) No 726/2004.

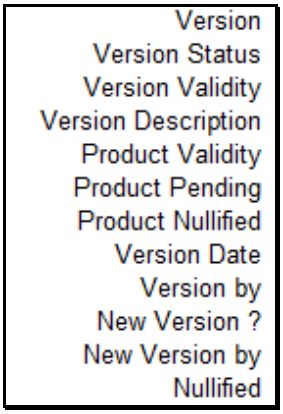
The EMA does not perform dedicated validation of development product information in the XEVMPD; DMP entities are automatically flagged as valid (i.e., the 'Product Validity' field in EVWEB displays 'Valid') upon their initial submission by the sponsor organisation. This is to allow for the DMP to be available for the recoding of suspected unexpected serious adverse reactions reports (SUSARs).

1.7.6. Product status fields

Following a successful submission of a medicinal product entity in the XEVMPD, a version number is assigned (i.e. if a new AMP/DMP is submitted via an operation type 'Insert', the version number will be '1').

When maintenance related operation(s) are applied to this entity, subsequent version numbers will be assigned (e.g., if an 'Update' is performed following the 'Insert', the version number will be '2' and any other subsequent updates will be assigned version numbers '3', '4' etc.).

The following fields are available in EVWEB to provide information on the history and status of the product entity:



- **Version**

This field indicates the number of the displayed version and the total number of versions for this product (e.g. 1/1).

- **Version Status**

This field indicates whether the displayed version of the product was:

- Accepted (i.e. it is a correct version of this product),
- Nullified (i.e. it is a nullification version - the last correct data is the previous version),
- Rejected (i.e. the update by an MAH is an identical copy of the version created before the validation by the EMA),

- Unassessed (i.e. the version was incorrectly processed; there were issues in the loading process. This would be an exceptional situation).

- **Version Validity**

This field indicates whether the displayed version of the product:

- Need MAH follow-up (i.e. this version of the product has been assessed by EMA and MAH follow-up is needed); the status is currently not used, MAHs are contacted directly when needed,
- Unassessed (i.e. this version of the product has not been assessed by EMA),
- Valid (i.e. this version of the product has been assessed by EMA as valid).

- **Version Description**

A one-line description of the status of this product version is included in this field (e.g., 'Current valid version') and it is a concatenation of the above-described terms.

- **Product Validity**

This field indicates whether the product entity was flagged as:

- Not Assessed (i.e., no version of this product has been assessed by EMA),
- Valid (i.e., a version of this product has been assessed as 'Valid' by EMA),
- Need MAH follow-up (i.e., this version of the product has been assessed by EMA and MAH follow-up is needed); the status is currently not used, MAHs are contacted directly as an when needed.

- **Product Pending**

This field indicates whether the product version was flagged as:

- Not Assessed (i.e., this version has not been assessed by EMA),
- Pending Update (i.e., this Version is an update of a version assessed by EMA),
- Assessed (i.e., this version has been assessed by EMA).

- **Product Nullified**

This field indicates whether the product entity has been nullified. The following field values are available:

- Yes,
- No.

- **Version Date**

The date and time of the receipt of the message containing this product version is included (e.g., '09/07/2015 13:19:32'.

- **Version By**

The sender ID (organisation routing ID) of the sender of the message containing this product version is included (e.g., 'EVHUMANWT').

- **New Version ?**

This field indicates whether there is a newer (more recent) version of this product (e.g., following an update, nullification etc.). The available values are:

- Yes,
- No.

- **New Version By**

The sender ID (organisation routing ID) of the sender of the message containing a newer version of this product (e.g., update, nullification, etc.) is included ((e.g. 'EVHUMANWT').

- **Nullified**

This field indicates whether this version of the product is a version that nullifies the product entity. The available values are:

- Yes
- No

To compare the current versus the previous version of the same AMP record (excluding nullified products) please refer to section *4.15. Comparing individual versions of a medicinal product entity*.

1.7.7. Data access policy

An organisation registered with the EudraVigilance system and that is not a national competent authority (NCA) can read:

- data for which they are the owners (product data, substance data etc.);
- authorised medicinal products, approved substances and proposed terms that have been checked by the EMA;
- all standard terms present in the lookup tables and maintained by the EMA.

Some information collected in the XEVMPD is however strictly confidential.

Development substances, development products and development terms not owned by the organisation, even if flagged as 'Valid' by the EMA, remain strictly confidential and cannot be accessed by other applicants, MAHs or sponsors.

The general rules applicable to any MAH/sponsor/applicant registered with the EudraVigilance system are summarised in the following table:

Sponsor, MAH or APPLICANT	Entities Owned		Entities NOT Owned	
Read access	**Not validated**	**Flagged as "Valid"**	**Not validated**	**Flagged as "Valid"**
Authorised or Approved*	√	√	X	√
Development CONFIDENTIAL	√	√	X	X
Proposed	√	√	X	√
Standard	*Not applicable*	*Not applicable*	*Not applicable*	√

* Approved substances are visible whether or not they are flagged as "Valid" by the EMA

National competent authority registered with the EudraVigilance system can read every entity that has been validated by the EMA. The general rules applicable to any national competent authority registered with the EudraVigilance System are summarised in the following table:

NATIONAL COMPETENT AUTHORITIES	Entities Owned		Entities NOT Owned	
Read access	**Not validated**	**Flagged as "Valid"**	**Not validated**	**Flagged as "Valid"**
Authorised or Approved*	*Not applicable*	*Not applicable*	X	√
Development CONFIDENTIAL	*Not applicable*	*Not applicable*	X	√
Proposed	*Not applicable*	*Not applicable*	X	√
Standard	*Not applicable*	*Not applicable*	*Not applicable*	√

* Approved substances are visible whether or not they are flagged as "Valid" by the EMA

1.7.8. Controlled vocabularies and terminologies

Terminologies and Controlled Vocabularies (CVs) are integrated in EudraVigilance, the below CVs are available on the Agency's website, section 'Controlled vocabularies':

- EudraVigilance eXtended Medicinal Product Dictionary (XEVMPD) Anatomical Therapeutic Chemical (ATC) code;
- EudraVigilance eXtended Medicinal Product Dictionary (XEVMPD) authorisation procedures;
- EudraVigilance eXtended Medicinal Product Dictionary (XEVMPD) - authorisation status;
- EudraVigilance eXtended Medicinal Product Dictionary (XEVMPD) concentration types;
- EudraVigilance eXtended Medicinal Product Dictionary (XEVMPD) medical devices;
- EudraVigilance eXtended Medicinal Product Dictionary (XEVMPD) organisations;
- EudraVigilance eXtended Medicinal Product Dictionary (XEVMPD) pharmaceutical dose forms;
- EudraVigilance eXtended Medicinal Product Dictionary (XEVMPD) reference sources;
- EudraVigilance eXtended Medicinal Product Dictionary (XEVMPD) routes of administration;
- EudraVigilance eXtended Medicinal Product Dictionary (XEVMPD) substance classes;
- EudraVigilance eXtended Medicinal Product Dictionary (XEVMPD) substances;
- EudraVigilance eXtended Medicinal Product Dictionary (XEVMPD) units of measurement;
- EudraVigilance eXtended Medicinal Product Dictionary (XEVMPD) units of presentation;
- EudraVigilance eXtended Medicinal Product Dictionary (XEVMPD) - Legal basis;

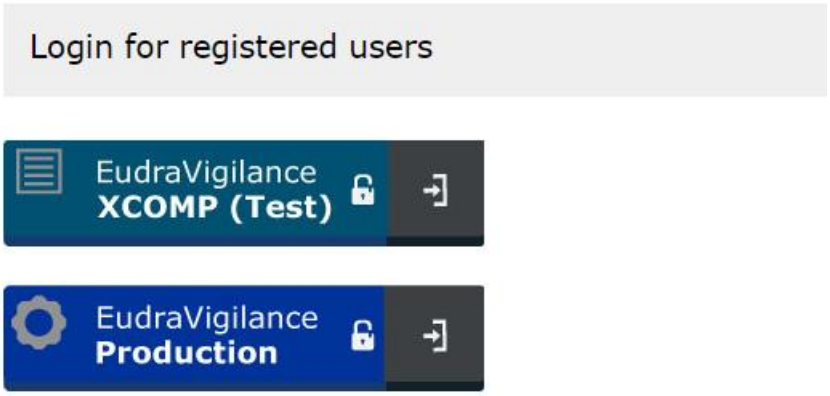
- EudraVigilance eXtended Medicinal Product Dictionary (XEVMPD) - Medicinal product types.

In addition to the CVs maintained by the Agency, further information on terminologies and controlled vocabularies integrated in EudraVigilance, which are maintained by external providers, can be obtained from the following websites:

- A MedDRA license can be obtained (purchased) from the MSSO;
- ATC Codes need be obtained from the WHO Collaborating Centre for Drug Statistics Methodology;
- Pharmaceutical forms and routes of administration are based on the standard terms published by the European Directorate for the Quality of Medicines & HealthCare (EDQM);
- The Unified Code for Units of Measure (UCUM) is maintained by the Regenstrief institute;
- The official list of ISO 3166-1 country codes is maintained by the International Organization for Standardization (ISO);
- The official list of ISO 639-1:2002 codes for the representation of names of languages: Part 1: Alpha-2 code is maintained by the International Organization for Standardization (ISO).

2. Accessing EVWEB

To access EVWEB for XEVPRM production or XCOMP (test) environment, go to the 'EudraVigilance' webpage and select the required environment:

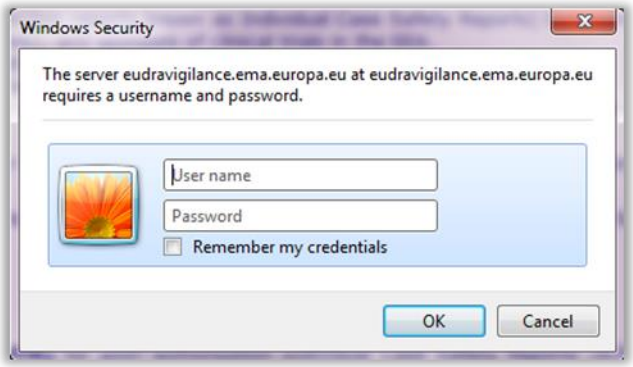


Alternatively, you can click on the below links:

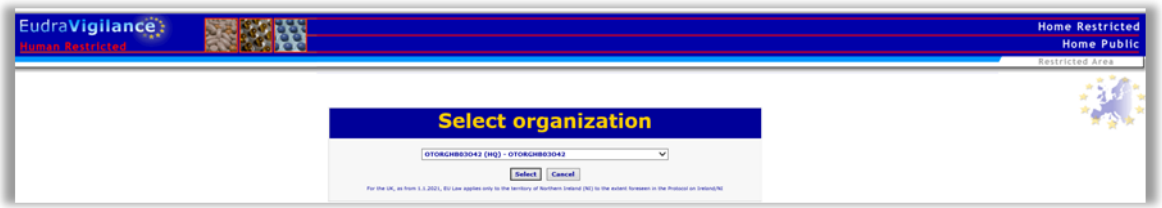
EVWEB production: https://eudravigilance.ema.europa.eu/x

XCOMP (test) environment: https://evtest.ema.europa.eu/x

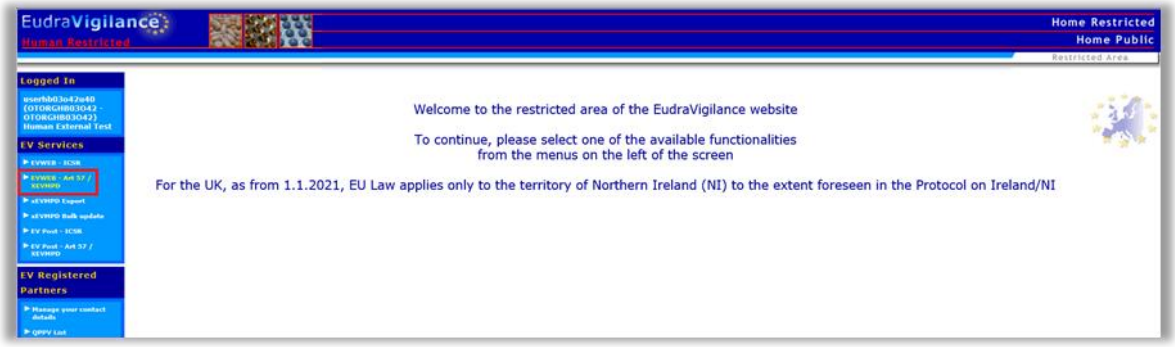
Enter your username and password:



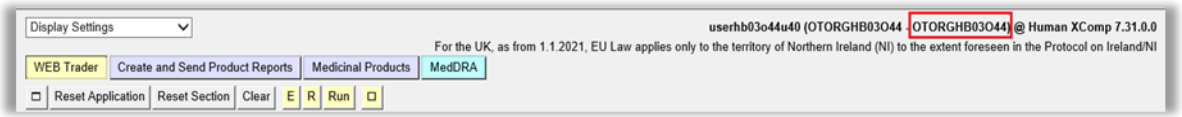
Select the organisation under which you wish to log in:



In the restricted area, click on 'EVWEB - Art 57 / XEVMPD':

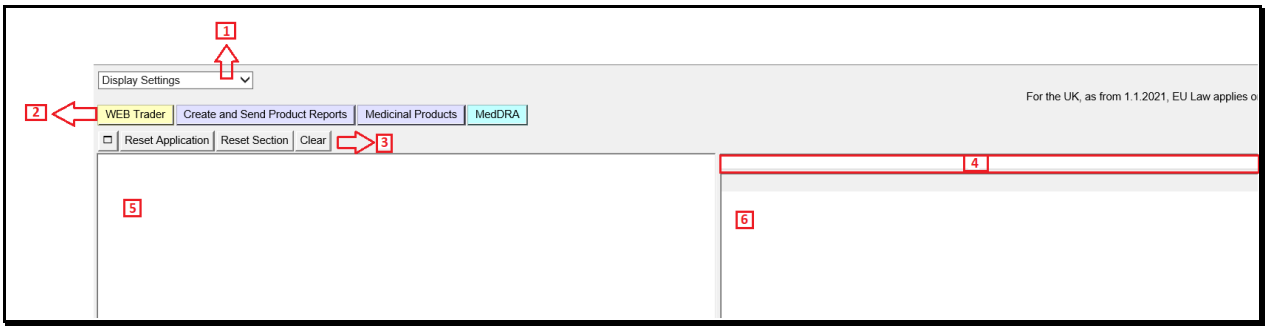


You are now logged in EVWEB; the organisation ID under which you are logged in is shown in the top right corner:



The main menu is located at the top of your screen and consists of two sets of buttons: the default buttons and the dynamic sets.

Below the main menu, the screen is divided vertically into two parts: on the left side is the tree-view area and on the right is the active area.



1. This drop-down menu allows the user to select the font size to visualize the information on the screen and to customize the screen to the best individual working conditions.

   It also allows changing the active area from ActiveX (default set up) to XHTML and vice versa.

2. Main menu: The EVWEB-section navigator menu, with the **default button set**, is always present in every section of the application. EVWEB is divided into different sections according to the kind of information you are going to operate with and your organisation's profile set-up during the registration process.

3. Main menu: This area represents the **dynamic button set**. It will change according to the EVWEB-section of the application you are using.

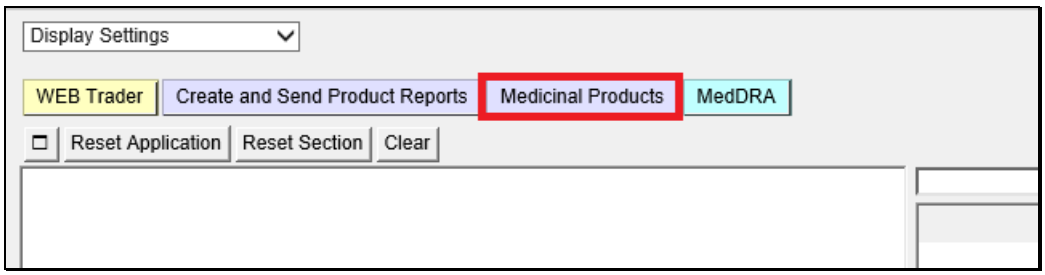
4. The simple query field.

5. The tree-view area.

6. The active area.

3. Accessing medicinal product section in EVWEB

To access the 'Medicinal Products' section, click on the 'Medicinal Products' or 'Products' button (depending on your screen set up) on the main menu:



The Medicinal Products section displays a tree-view area on the left side of your screen, and an active area on the right side of the screen.

3.1. The main menu

3.1.1. Sections navigator menu

Depending on your screen settings and EVWEB chosen font size, the menu is displayed in the 'full' version:

or in the 'short' version:

To expand the menu, click on the square button highlighted above.

WEB Trader Allows users access to review their own XEVPRMs, both sent and received. Users will be able to see messages sent to them and by them, in the Inbox and Outbox folders (the last 50 received during the day reference for message archive). The Inbox and Outbox folders are only available to Web Trader users. Users sending information via their locally established Gateway will not see these folders.

When in this section, users will also be able to import Messages located on their computer.

Create and Send Product Reports Allows users to create and send an XEVPRM.

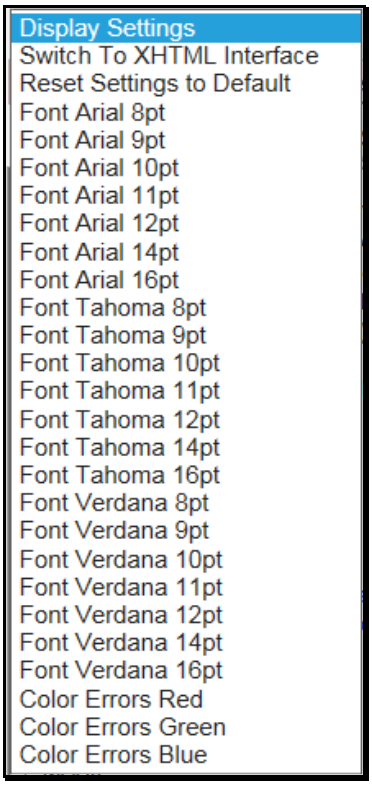
Medicinal Products Allows users to browse and perform searches at all levels of the XEVMPD.

MedDRA This area of the application allows users to browse and perform searches at all levels of MedDRA.

3.1.2. Default buttons set

This pop-down menu allows a user to select the type and size of the font used to display the information on the screen, and to customize the interface to individual working conditions.

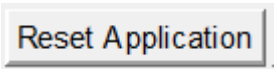
You can choose the interface of the EVWEB application through an option of this pop-up menu:



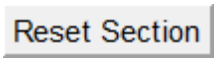
ActiveX Interface (default set up) means that the Active Area is an ActiveX, which allows fast operations but doesn't allow the data entry and display of special Unicode characters.

XHTML Interface means that the Active Area is made of standard HTML components, which allows the data entry and display of any Unicode character, but it can be slower than the ActiveX Interface. Use this interface when you need to enter Greek or Bulgarian characters (they will be displayed in the active area, but not on the tree view).

 Maximize: The screen is resizable allowing the interface to be adapted to the user screen size by clicking twice on the button pictured above. The application interface can also be resized by dragging its bottom right corner.



Resets the application, affects all its sections. You will lose all locally entered data up to that point.

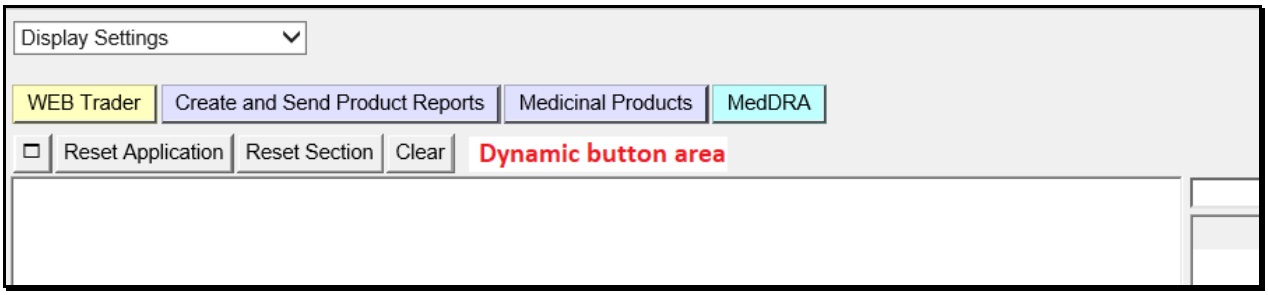


Resets only the specific section of the application currently in use. Data entered in that section will be lost if you use the 'Reset Section' button.

Removes all items marked for deletion in the section of EVWEB currently in use (also unchecked items)

The button corresponding to the currently active section of EVWEB will have the appearance of being pressed in.

3.1.3. Dynamic buttons set



This set of buttons is located on the lower right corner of the main navigation menu and displays a variable number of buttons that changes according to:

- the section of the application in which you are working, and the related item(s) selected in the tree-view area; and

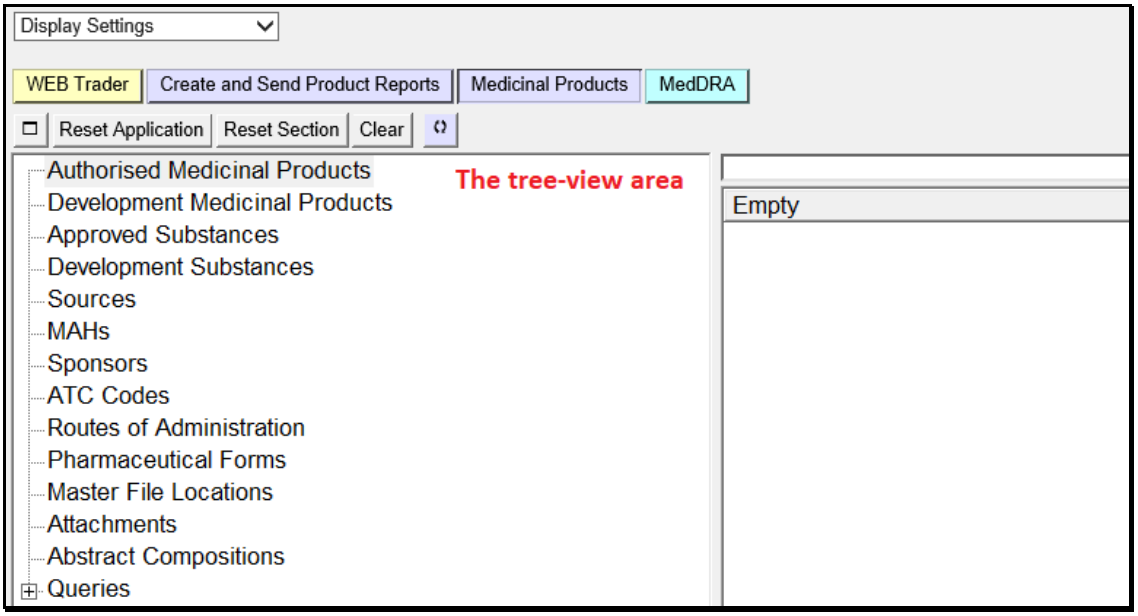
- the applicable visibility and ownership rules in place.

For example, it can display the following buttons:

These buttons will be described in the various sections and functions of EVWEB.

3.2. The tree-view

The tree-view area is located on the left side of the application, below the main navigation menu. It shows elements in a tree-view menu style (similar to Windows Explorer).



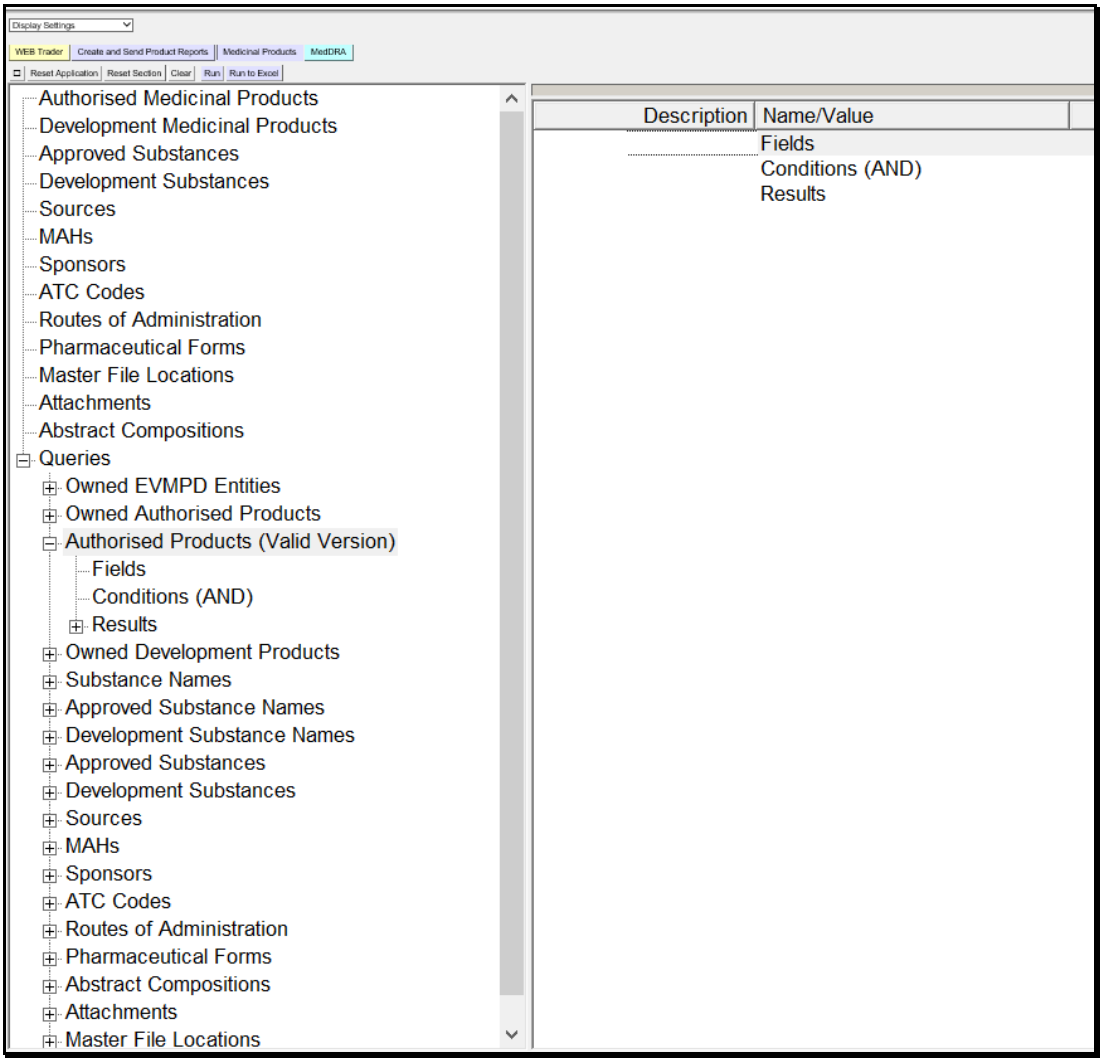
To select an item in the tree-view, click on the textual description of the item with your mouse. The selected item will be displayed with a dark background.

When the '+' sign appears on the left of the tree-view menu, that item contains a sub-menu that can be expanded by clicking (once) on the little '+'.

After a menu is expanded the '+' changes into a '-' sign.

To collapse a menu, just click once on the '-'.

Elements in the tree-view area can also be expanded by hitting the 'Enter' key on the keyboard after they have been selected by clicking once on them with the mouse. To select an item the user must click once on the text, rather than on the '+' sign. Selected items are always displayed with a dark background.



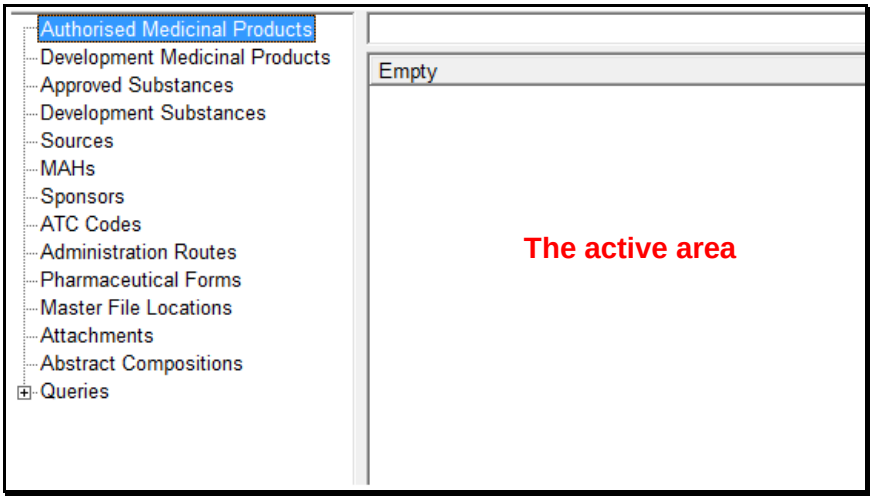
The tree-view can grow, expand, and become extensive while using the application. The active area of the tree-view area is always marked with a dark background.

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 to reach any part of the tree.

3.3. The active area

The active area shows the content of the currently selected item in the tree-view.

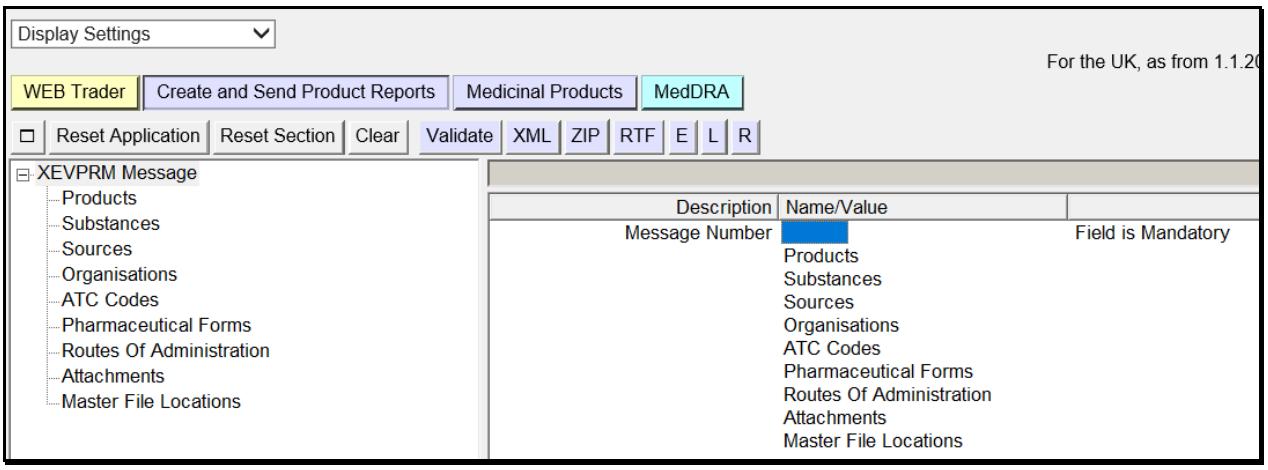
The active area is located on the right side of the application, below the main navigation menu.



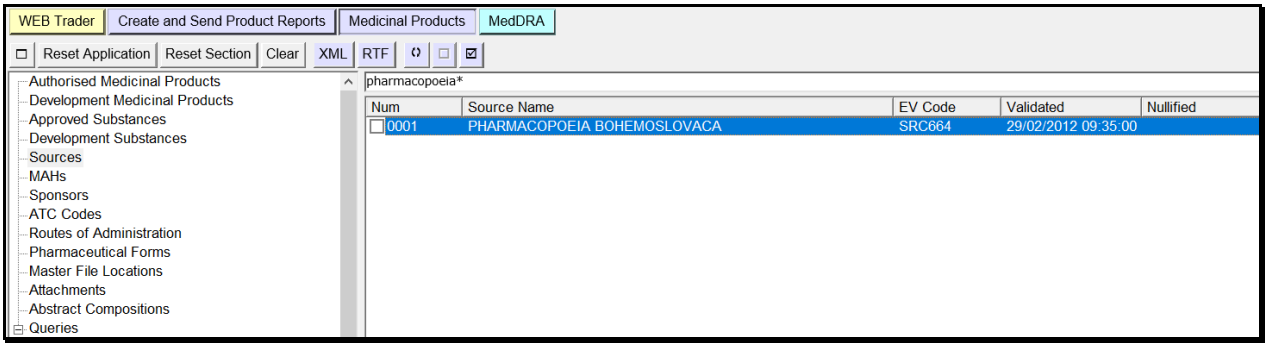
The main difference between the tree-view area and the active area is that the active area is interactive and displays information that can be edited and modified by the user whilst the tree-view area only displays available items from the XEVPRM (see section *3.5. Data entry*).

The active area displays the information in two different ways:

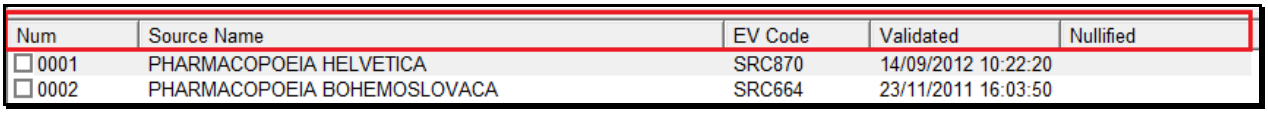
- **Section view** (which usually displays fields and/or subsections) is used to display information and/or for data entry. A typical example of a section view is the editing of a new XEVPRM:

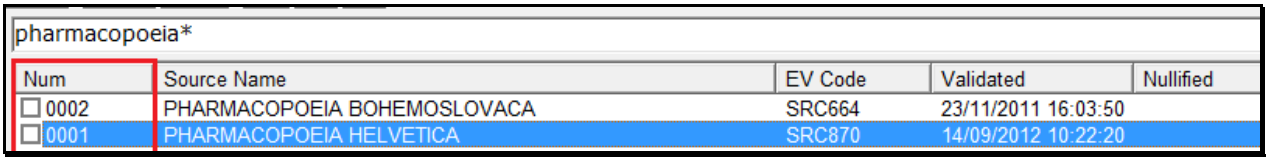


- **List view** (a detailed list of items of the same kind) is used to display items that can be selected, loaded, or just analysed. A typical example of list view is the result of a query.

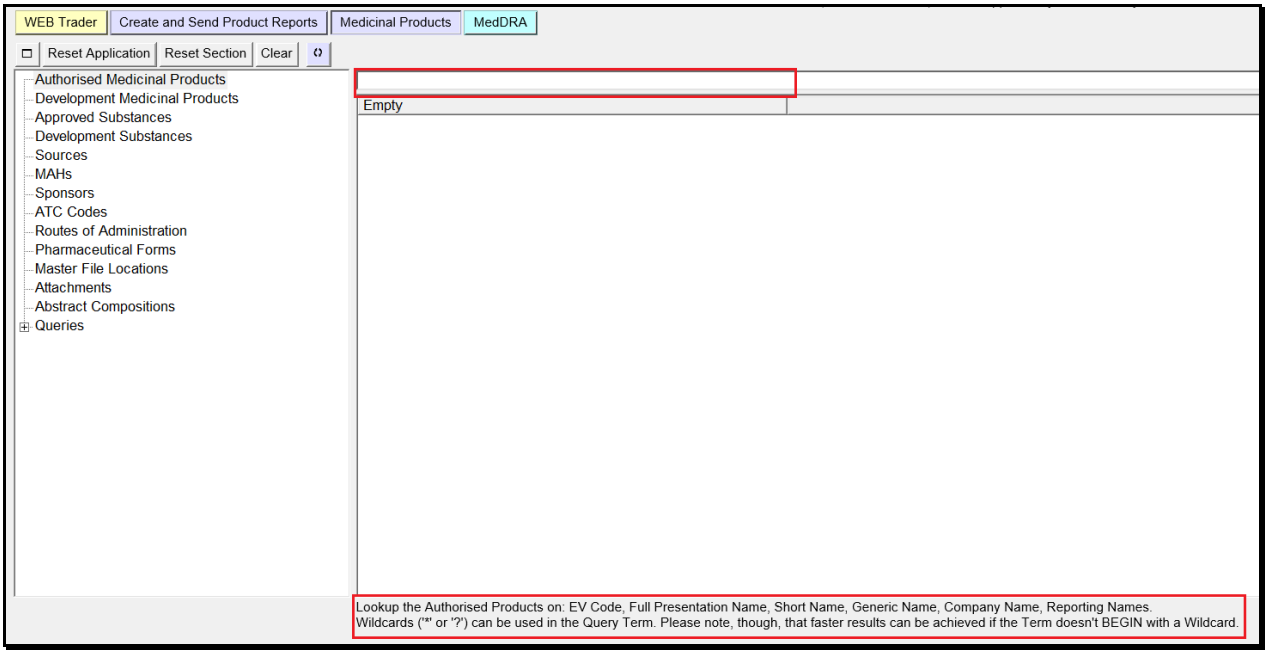


You can re-arrange the order of presentation of items in the active area by clicking on the header of each column (a click will switch from ascending to descending order and vice versa):





On top of the active area, but still below the main menu, you will find the simple query field (see section *3.6.1. Simple query*).



This search field is not always active. When the search field is locked, the field will appear in grey, indicating that the search is not allowed.

When the simple query is available and selected (clicking inside it), the bottom of the screen will display how the query will work (i.e., on which fields the query will be executed).

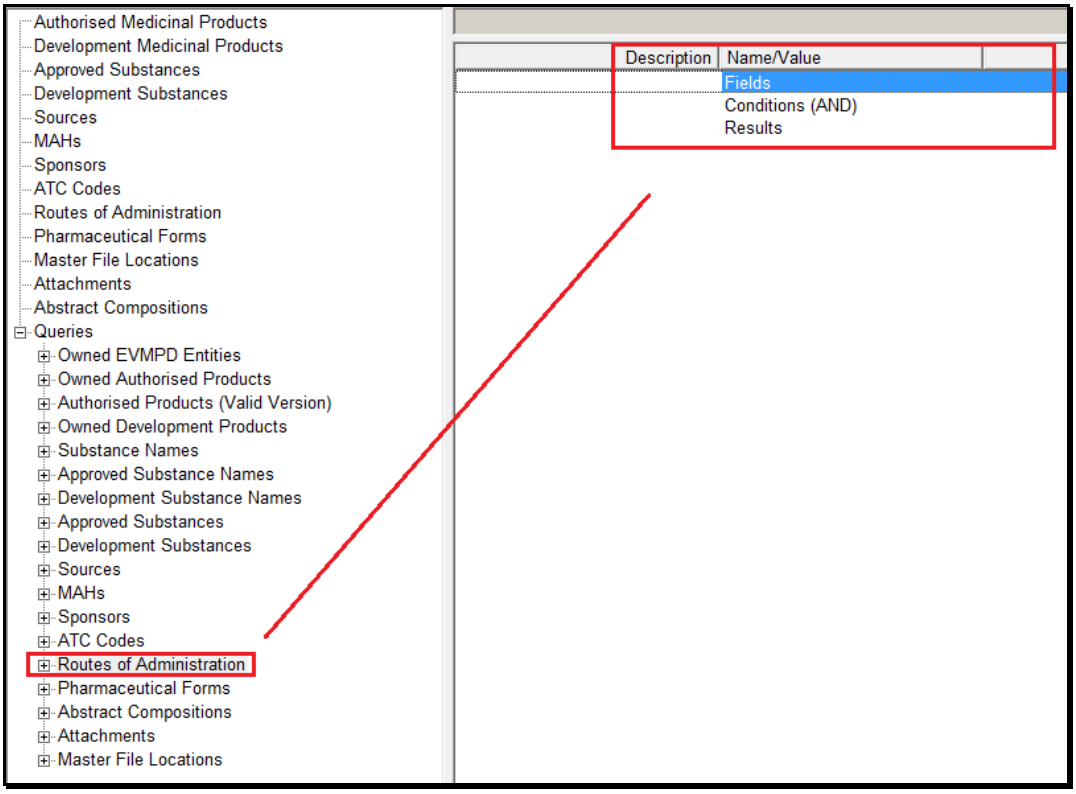
The main body of the active area may display editable or non-editable information.

Sometimes it shows information to the users, other times it requests information or an action from the user.

3.4. Interaction between the tree-view area and active area

The tree-view area enables you to browse items by selecting them, and by expanding or closing menus. Functionally, the tree-view can be considered as a navigation system.

The active area displays the content of the selected item in the tree-view, and allows the user to view, input, amend, modify, and nullify information.

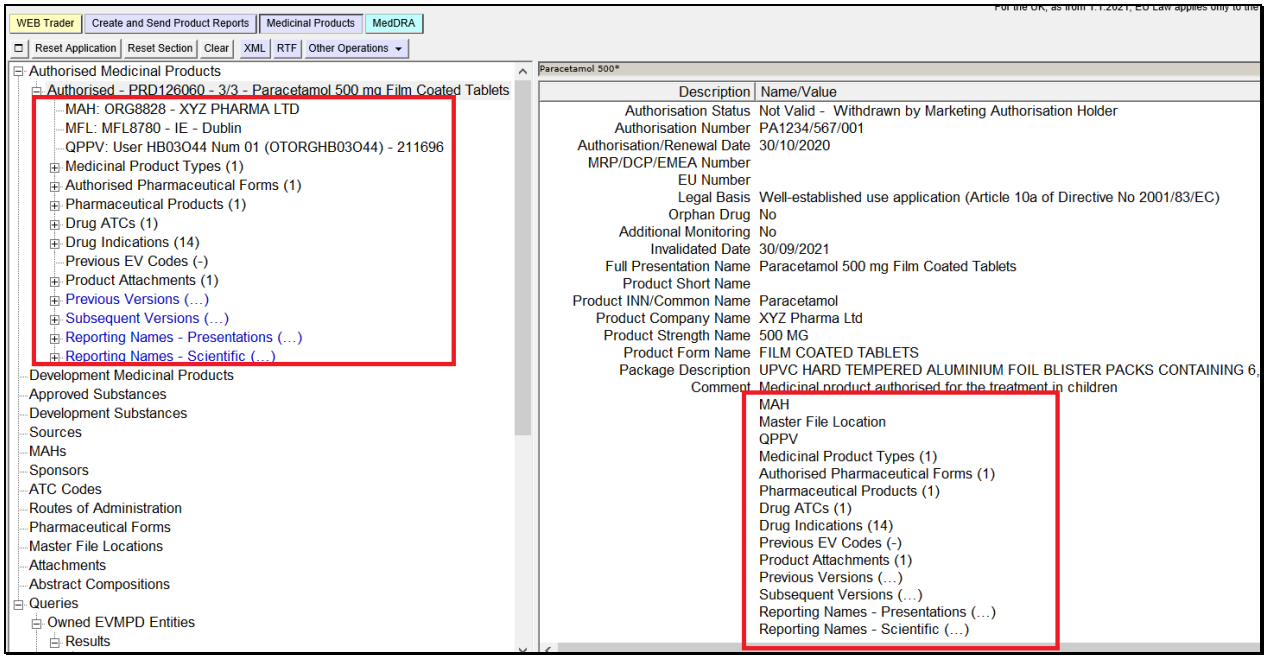


The information displayed in the active area can be presented in two different formats: section view or a list view, depending on the section selected. To display the details of any of your items you have two options:

- double click on the name of the item in the active area; or
- click once on the name of the item in the tree-view area.

In both cases you will be presented with the same screen.

Please note that the subsections of the item currently selected will be displayed in both screens (in the tree-view and at the bottom of the active area).



When a field is selected, a longer description, giving a better indication of the information required, will appear at the bottom of the active area.

3.5. Data entry

This section contains information on all the specific actions that you can perform to insert data in the EVWEB application.

3.5.1. Input field types

EVWEB contains four different types of fields for the user to input information into the system. These are: **text fields, date/time fields, look-up fields and query fields**. They are explained in detail below. You do not necessarily need to know what type of fields it is when you enter information. The system will take you through the necessary stages for each field type. In some specific situations, a field can be filled in different ways (i.e., a text field that can also be filled as a look-up field).

During the input phase, the application performs a real-time validation of the inserted data.

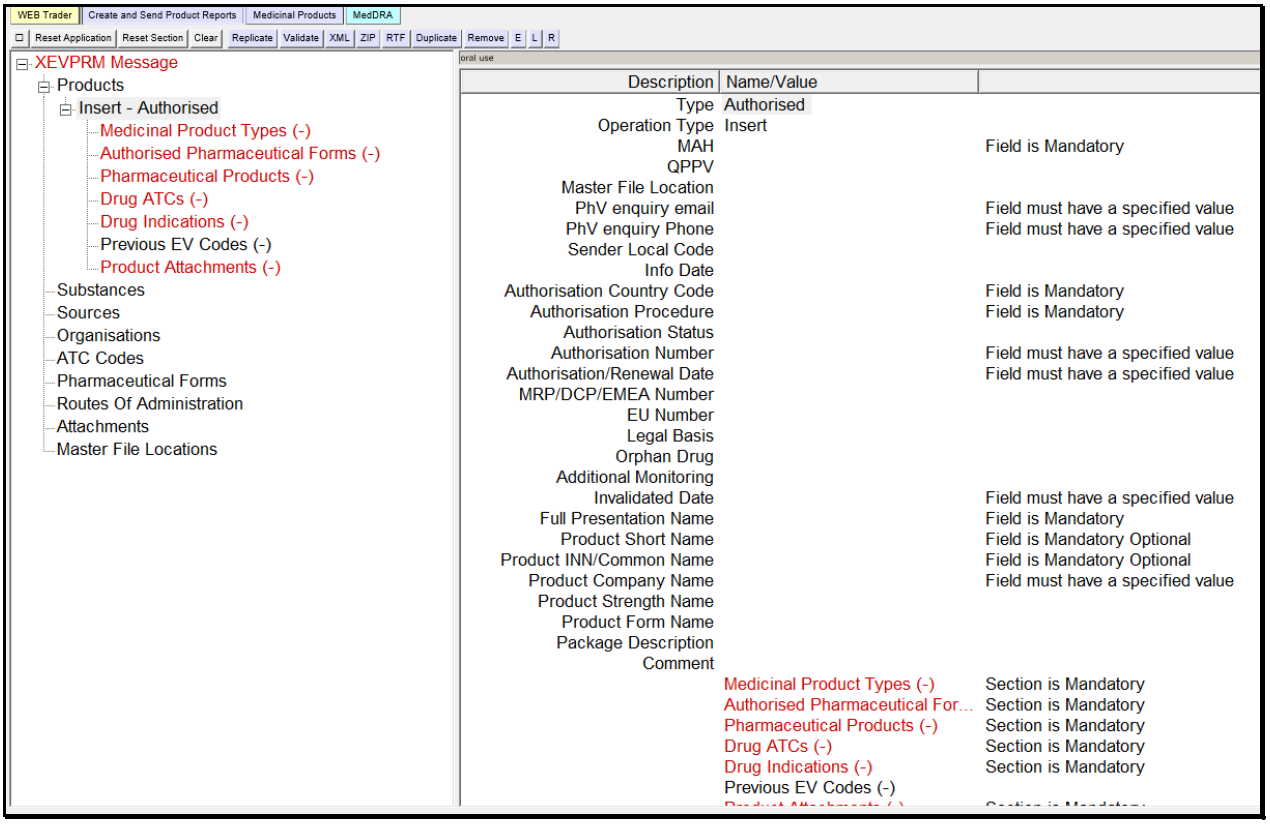
Fields that contain erroneous or incomplete information have their value (if present) displayed in red, and the relative error message is displayed in the third column of the active area. In addition to that, the section that contains errors is also displayed in red, both in the tree-view and the active area.

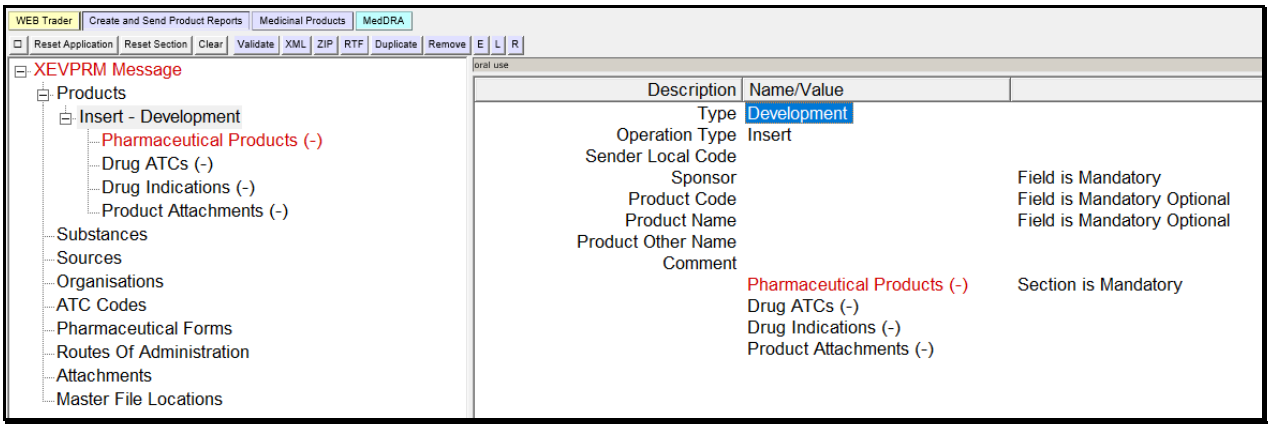
The most common error message is 'Field is mandatory' or 'Field must have a specified value'. Mandatory fields require essential information, which needs to be provided to complete the data entry operation successfully.

Some fields are flagged as 'Mandatory Optional' which means that they must/may be completed depending on the applicable business rules.

Mandatory sections must be competed[4].

[4] In case of 'Invalidated date', the 'Field is mandatory' will continue to appear until some further sections are completed.

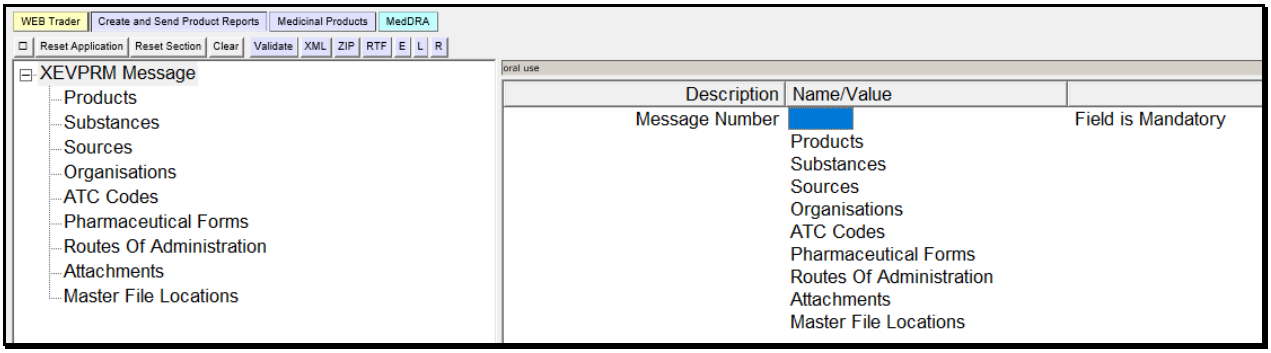




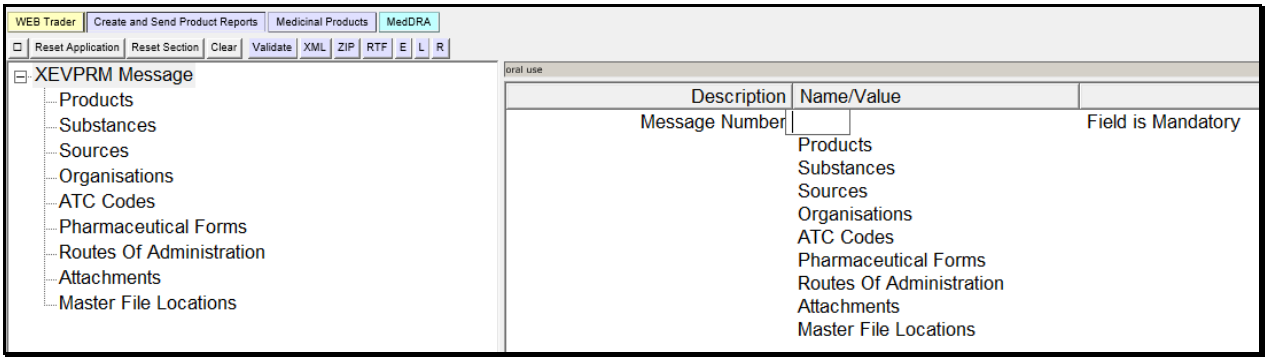
3.5.1.1. Text field

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

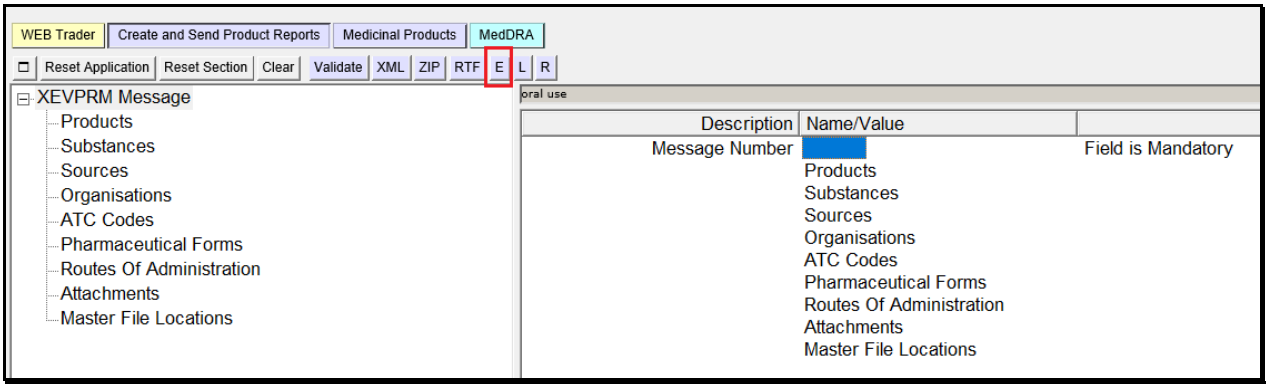
To enter information in a field text, you must first select it by clicking once on the field space:



and then press 'Enter' on your keyboard:



You can also use the 'E' button on the dynamic section of the main menu to enter this type of field.

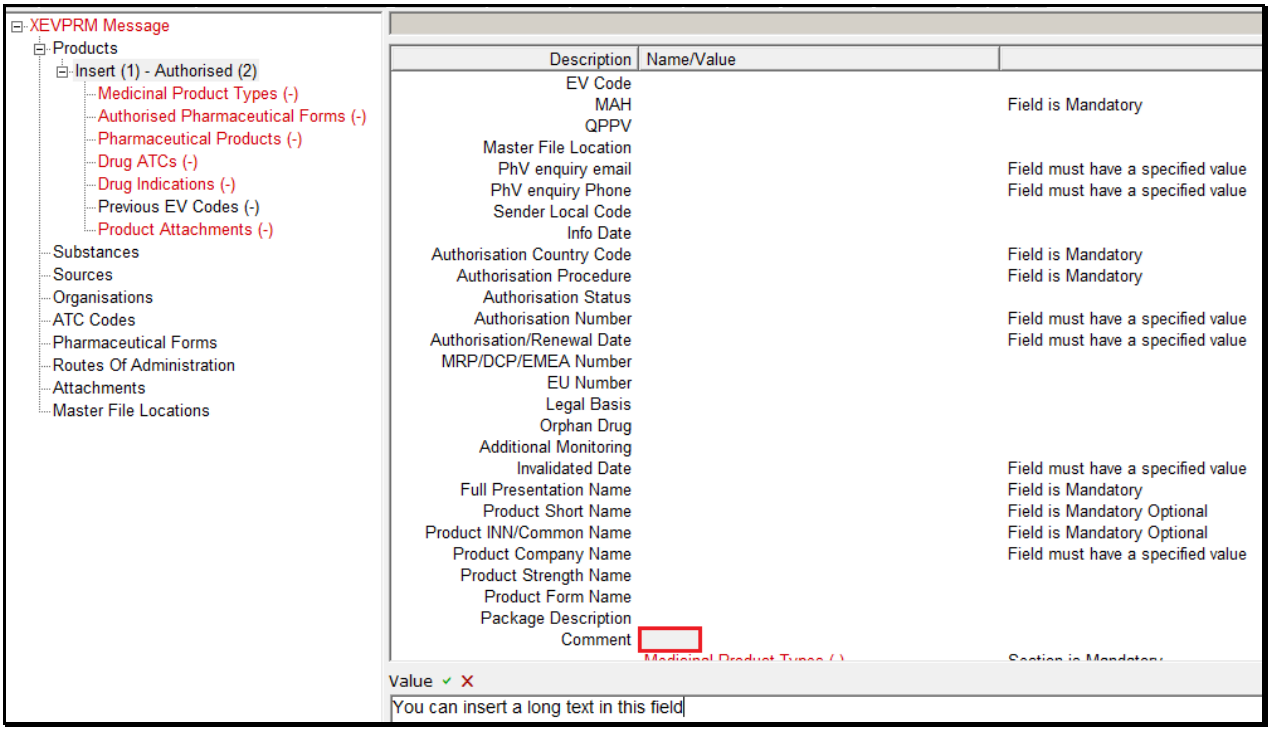


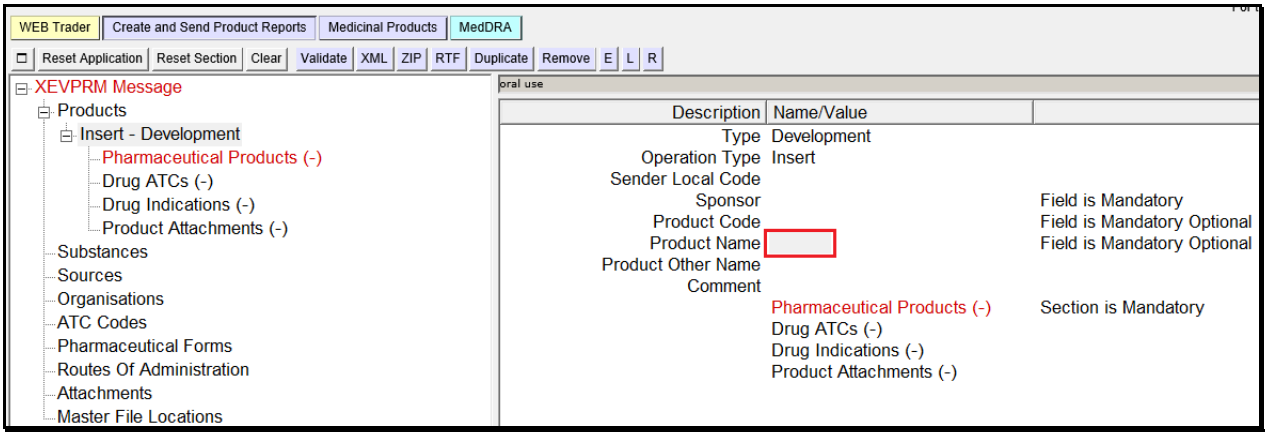
A blank text box appears in the field for you to enter the necessary data. Press 'Enter' again when you have finished. Press 'Esc' on your keyboard if you wish to cancel the input and press the 'Delete' key on your keyboard to delete the data (not backspace).

You can copy and paste information from/to text fields.

A particular type of text field is the large text field.

This type of field allows you to insert a long text with the help of a specific text area that will be displayed when you activate the editing of this type of field.





In this special text area, you are also allowed to enter line breaks. You can do that by pressing, 'Shift' + 'Enter' on your keyboard (just pressing 'Enter' will end the editing process and confirm the text entered).

On top of the text area, two buttons are visible. The first one (Green tick) ends the edit and confirms the text entered. The second one cancels the edit (Red cross).

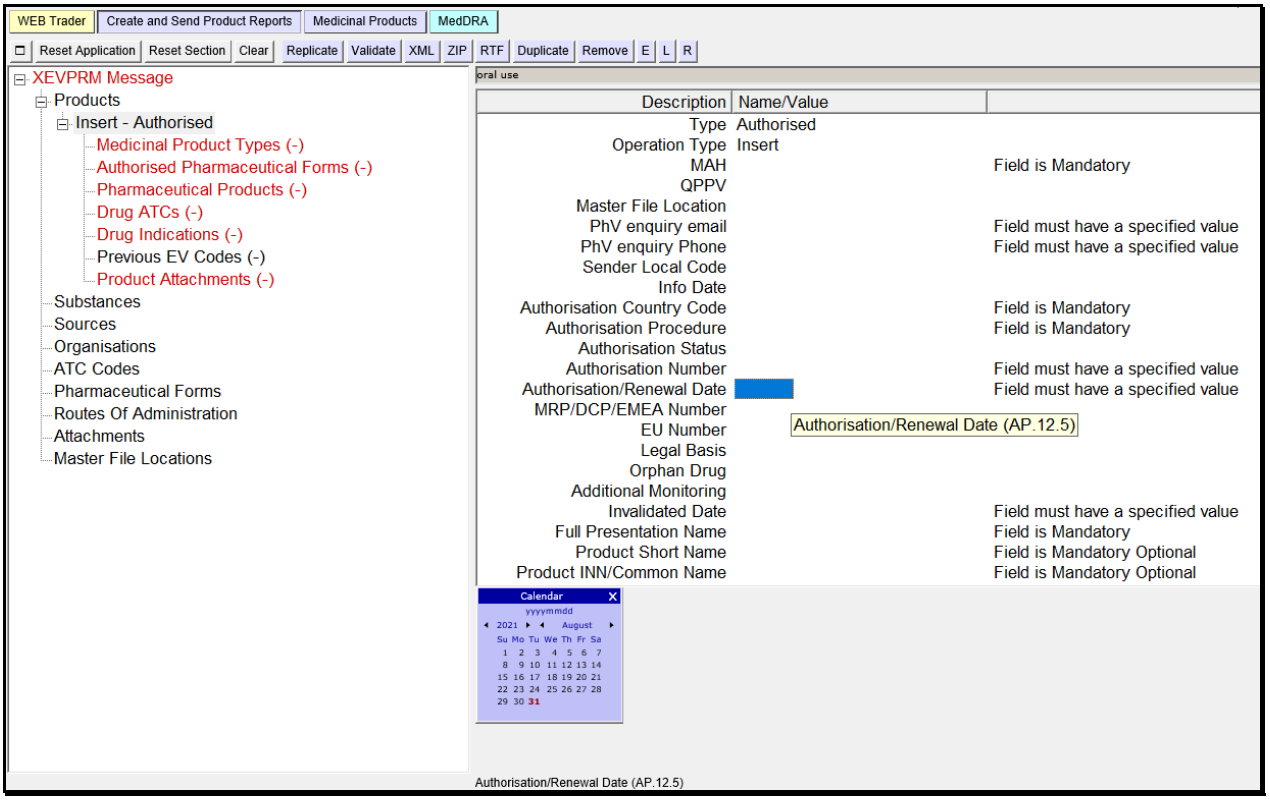
The large text field is the only one that has a special viewing mode when you are not in a data entry session.

Since this field can contain a very large amount of text (also allowing for line breaks), it can be useful to display the entire content of it. To do so, you can double click on it, and the same text area used for the editing will be displayed. The difference is that in this case, you cannot edit the text.

3.5.1.2. Date/time field

This type of field is used in EVWEB to enter the date information in different formats. The information is entered using a graphical interface that recalls a calendar.

To enter information in a date field, you first need to select it by double clicking on the field or by pressing 'Enter' on your keyboard after having selected it.

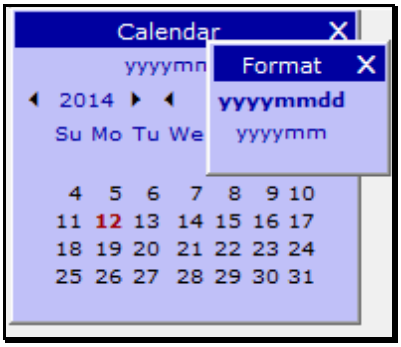


Many fields in EVWEB can accept the date/time information in different formats:

Year/month/day

Year/month/

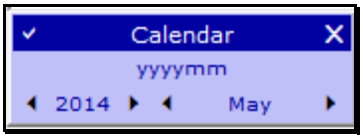
The formats can be selected by clicking on the format button at the top of the calendar. The available formats are based on the business rules.



Depending on the format selected, the calendar interface will change accordingly:

- If yyyymmdd is selected, the calendar will appear in the following format:

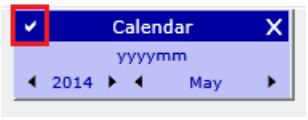
- If yyymm is selected, the calendar will appear in the following format:



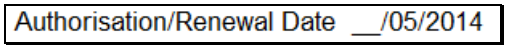
If you wish to change the date, just click on a specific date. If you require a change of the month or the year, use the side arrows flanking the month and year or click on the year and month to allow faster navigation.

Please note that the day selection confirms and enters the date and closes the calendar screen. Therefore, make sure that the year and the month are correct before you select the day.

To exit the calendar without selecting a date, click on the  sign located on the top left corner of the calendar screen.



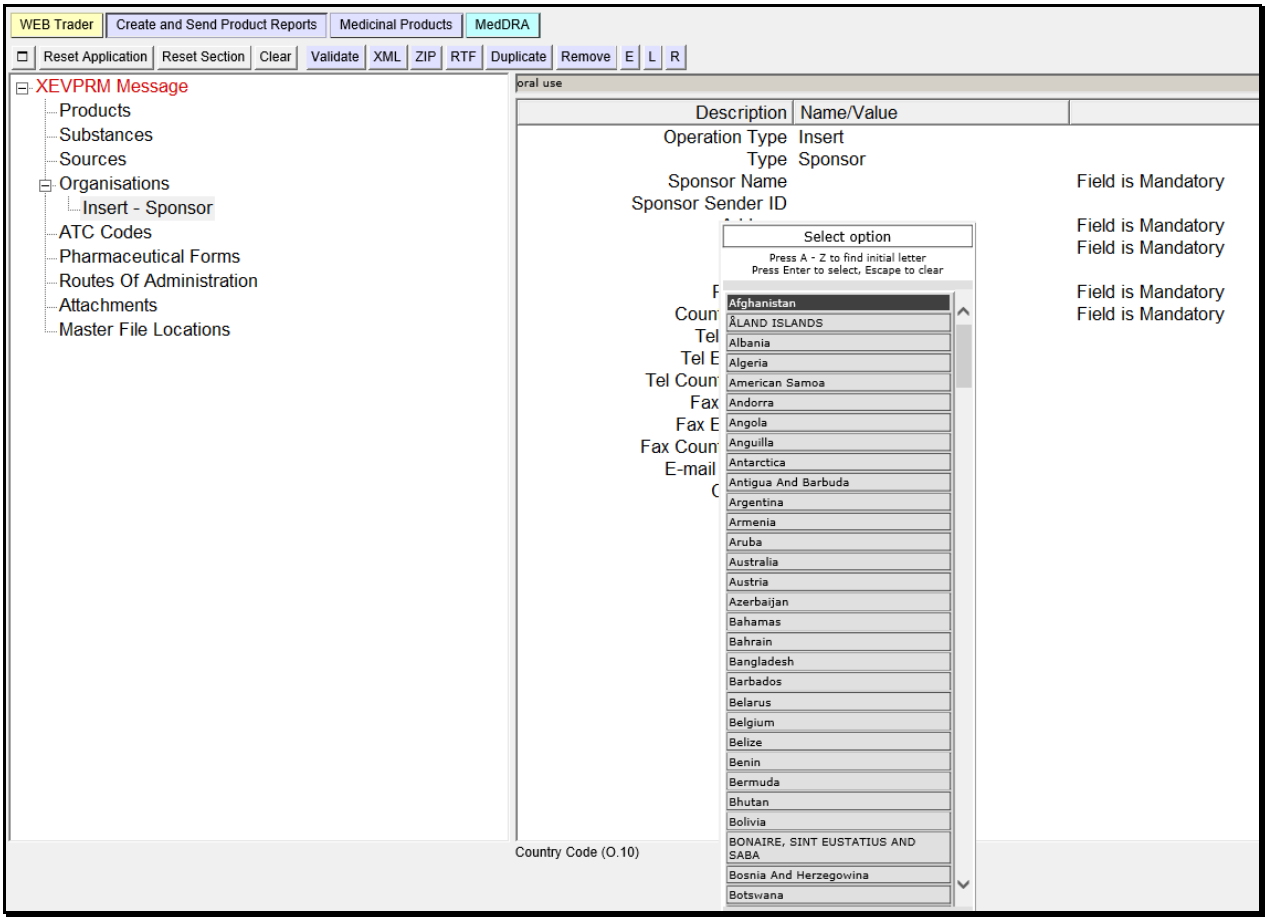
By doing so, the date will reference only the month and year:



3.5.1.3. Look-up fields/tables

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

By positioning your cursor on the selected field and pressing 'Enter' or by double clicking on the field, a list of pre-defined values will be displayed:



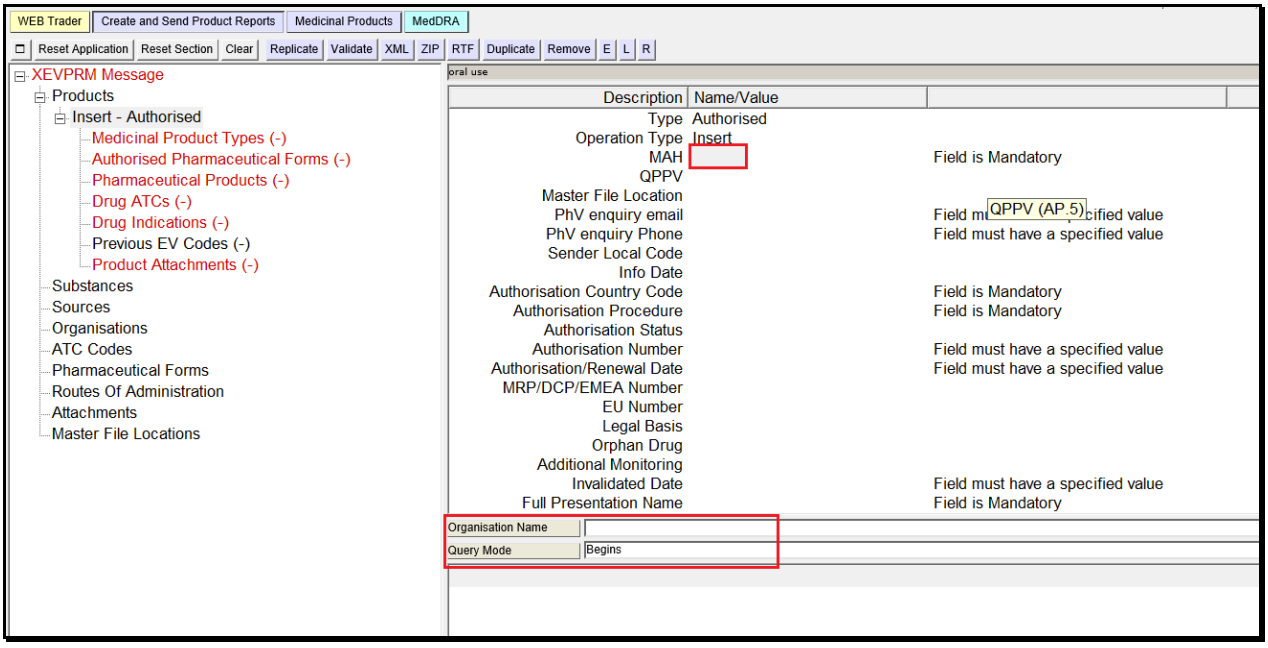
3.5.1.4. Remote database look-up tables

This type of field requires data that needs to be selected from a predefined list, generated as a result of a query.

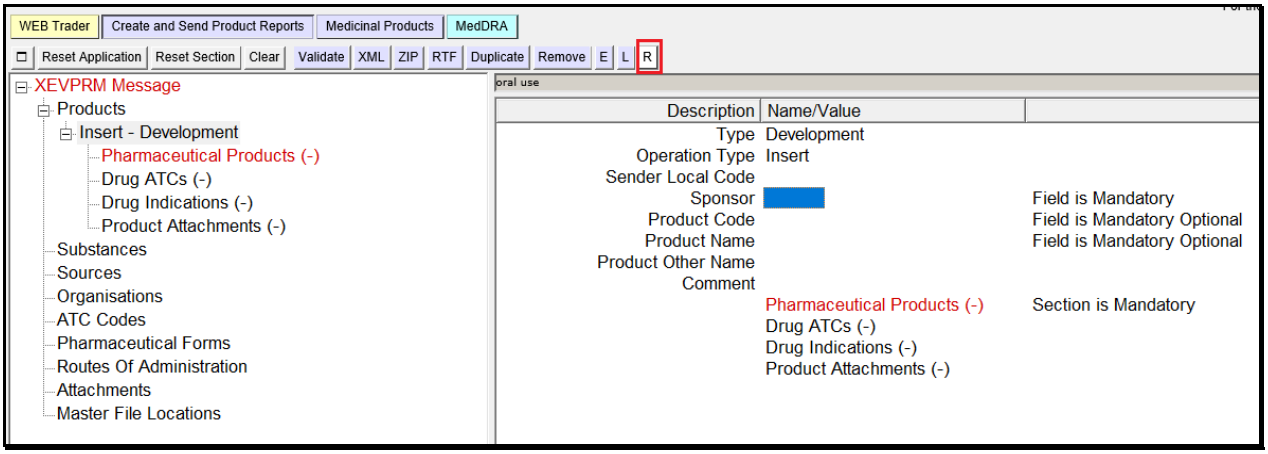
A query is a search performed in the XEVMPD (for this reason, a query operation always requires an active internet connection).

A 'query area' will appear in the lower section of the active area. This 'query area' always contains at least one search field, one or more 'parameter' fields (in this example the one labelled 'Query Mode') and an area to display the results.

You can select the field with your cursor and press '**Enter**' on the keyboard:



You can also select the field with your cursor and press the '**R**' (**Remote Database Look-up**) button:

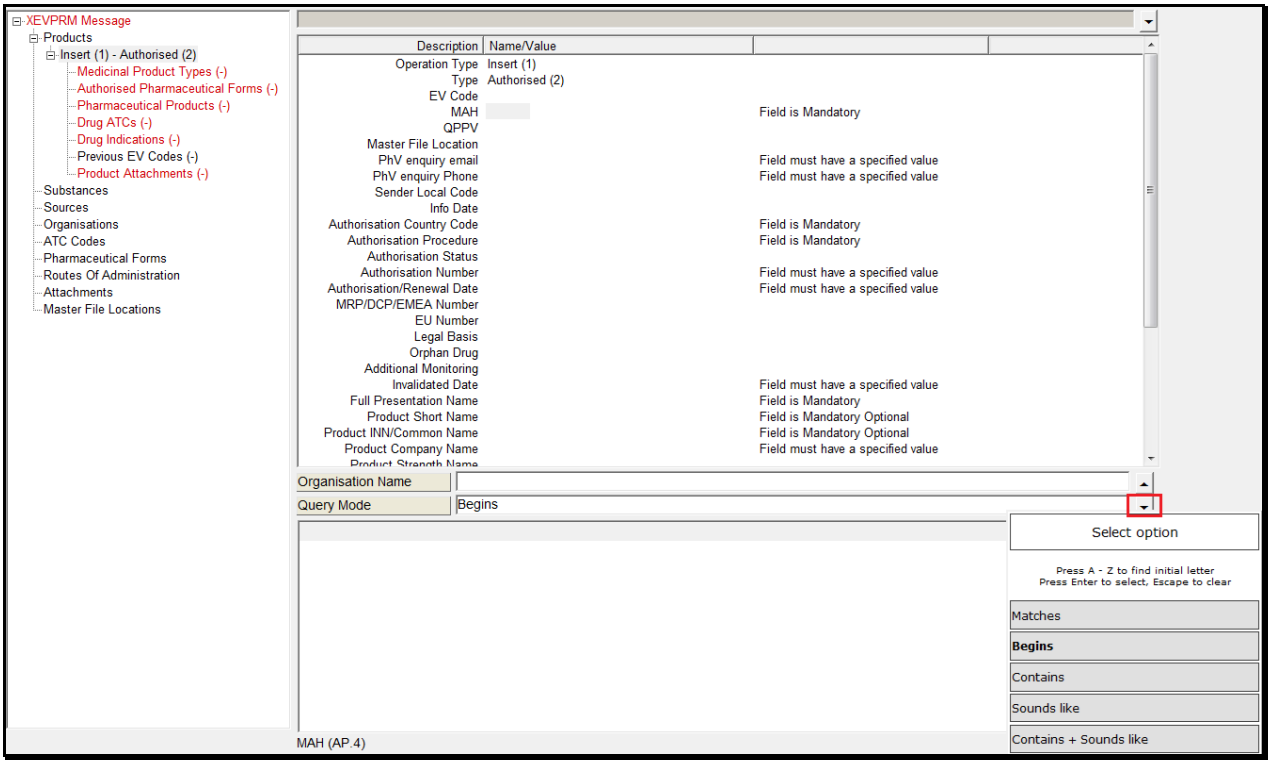


In both cases, a search window will be displayed.

You need to search the correct information by typing keywords in the search field. In our example, we are searching for a marketing authorisation holder name. We may know part of the name or be unsure about the correct spelling. Using the wildcards (e.g.? and *) we can search the system. In our example, we typed 'Nobel' in the search field of the 'query area'.

The 'query mode' field allows us to perform a more restricted search by applying one condition in the query.

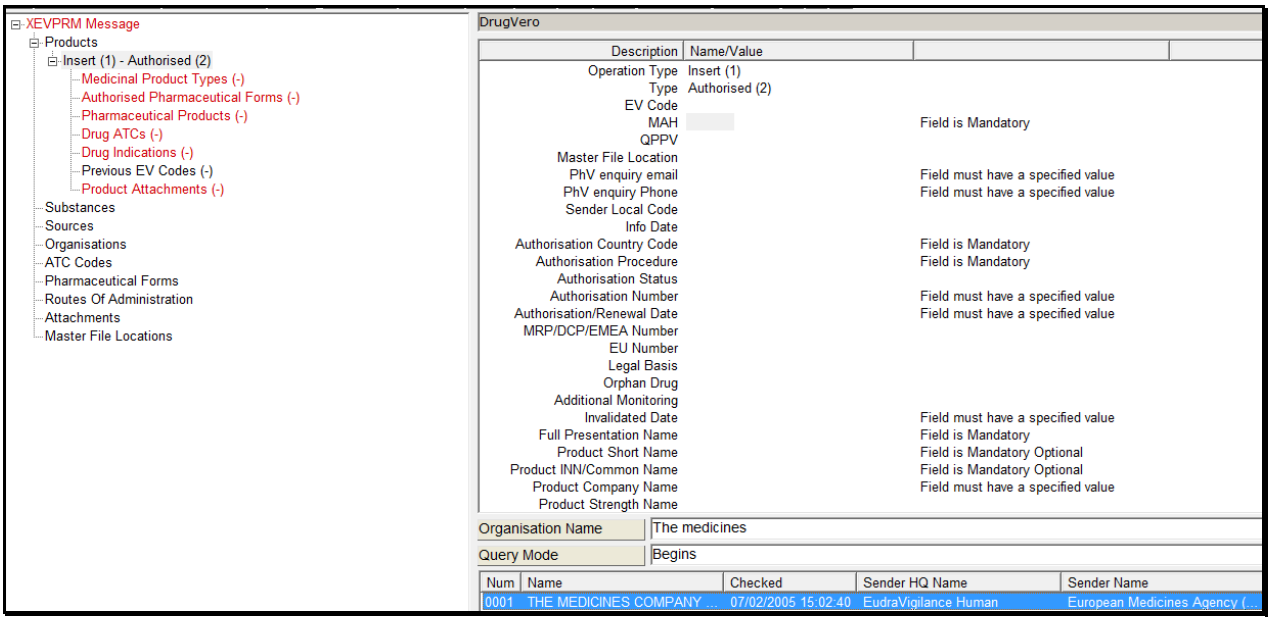
You can choose to apply the following conditions in your search: 'Matches', 'Begins', 'Contains', 'Sounds like' and 'Contains + sounds like' by pressing on the arrow on the right:



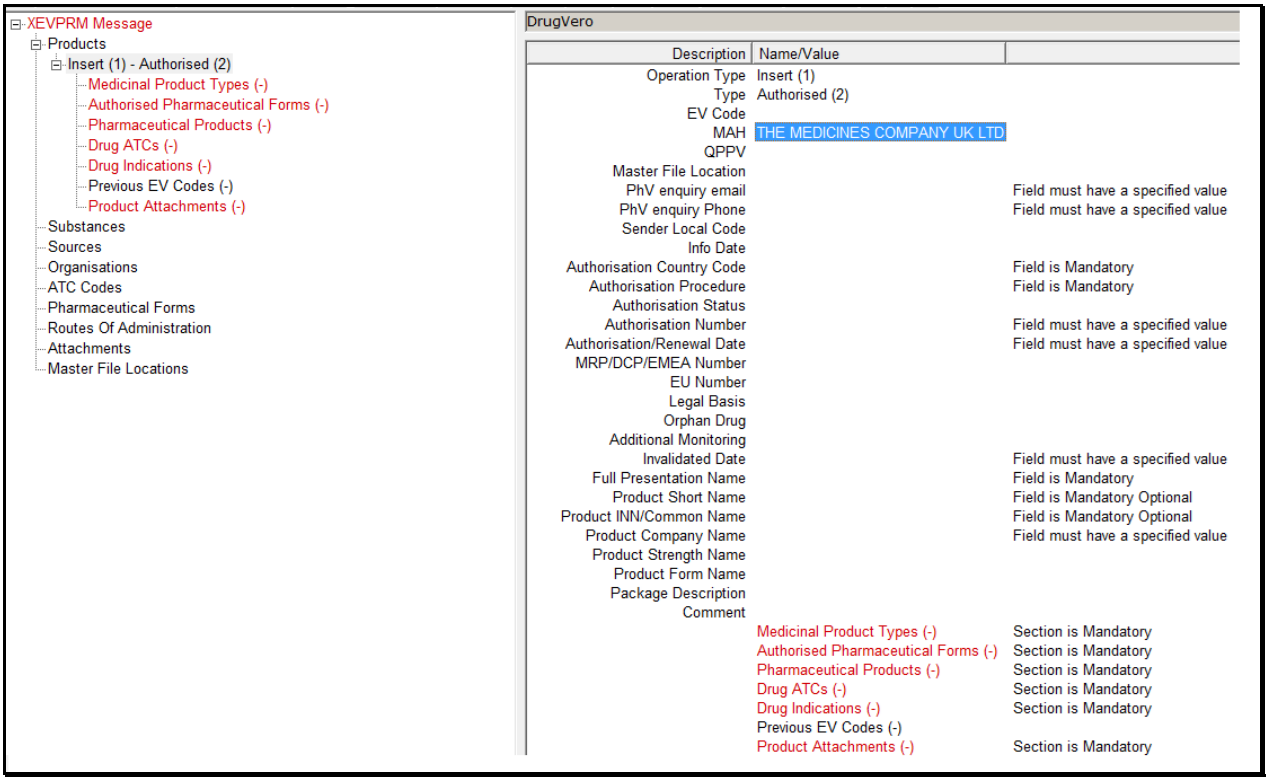
Press 'Enter' on your keyboard to run the search. The search (or query) results will be displayed in the result screen below the search field.

! When clicking on this arrow and it does not work, it is a sign that EVWEB is about to crash. Save your work, reset the application, and delete the temporary internet files from the internet options in the 'Tools' menu of the browser. Then reload your file to continue data entry.

You now must select one of the items displayed in this list by either pressing 'Enter' or by double-clicking on the selected value:



The selected value will be automatically inserted in the relevant (in this case MAH) field:



3.5.1.5. Local database look-up tables

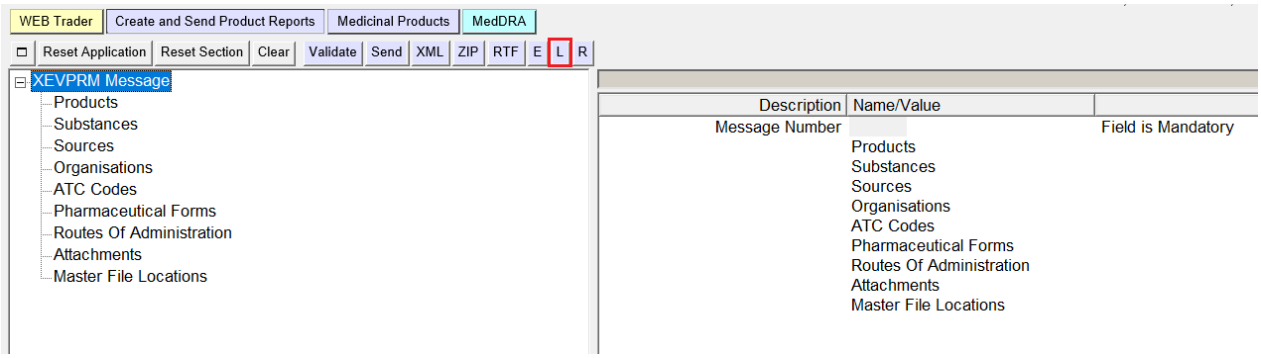
When an entity that you need to reference in your product report is not included in the lookup tables, you must add this new information in the same XEVPRM.

You may add information regarding new organisations, reference sources, ATC codes (proposed or development), routes of administration (proposed or development), pharmaceutical forms (proposed or development), MFLs and attachments.

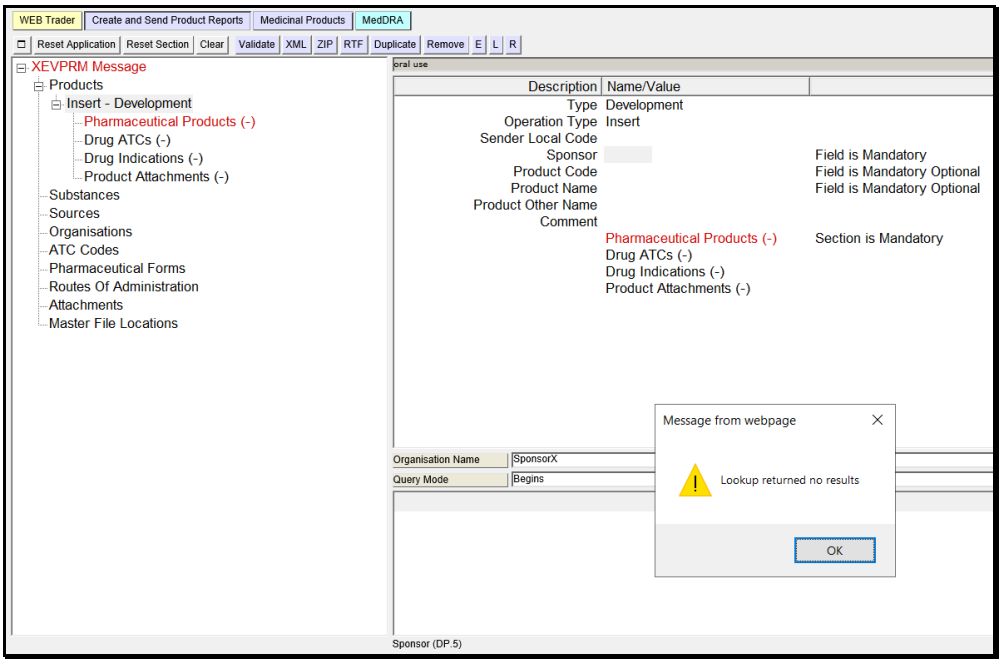
! Technically, you can also add approved and development substance in your XEVPRM and reference it in your product entry in the same XEVPRM. However, if you do so, upon submission, **your XEVPRM will be rejected**. The submission of substance information can only be performed in the XEVMPD by the EMA. If you require new substance information to be entered in the XEVMPD, you should follow the process described in the document Changes to some business rules of the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): Submission of substance information

To reference an entity not yet present in the XEVMPD (i.e., an EV Code is not assigned to the entity and the entity is not available in the remote look-up table), you must add the entity in the relevant section of the XEVPRM.

Once this entity is added, you can retrieve it from the **Local ('L') look-up table**:



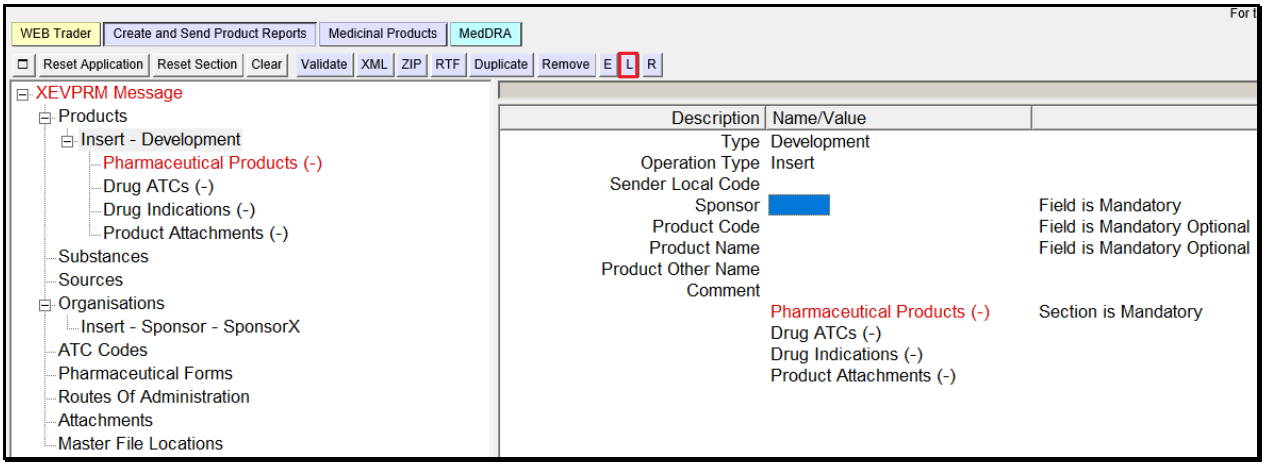
As an example, we wish to enter a DMP entity in an XEVPRM and reference the sponsor 'SponsorX' in the data field 'Sponsor'. However, the sponsor does not seem to be available in the Sponsor look-up table:



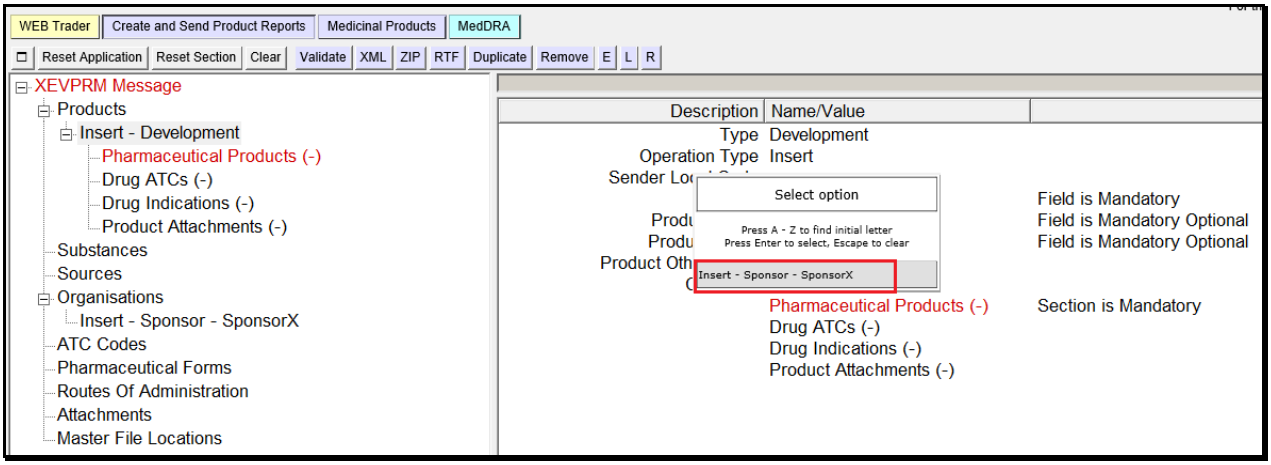
We should therefore add the sponsor information in the same XEVPRM and reference the newly added sponsor 'SponsorX' in the DMP using the 'L' (Local Data Lookup) feature.

You will therefore need to create a new sponsor entity in the same XEVPRM. Please refer to section *4.2.6. Insert of a Sponsor organisation* for related information.

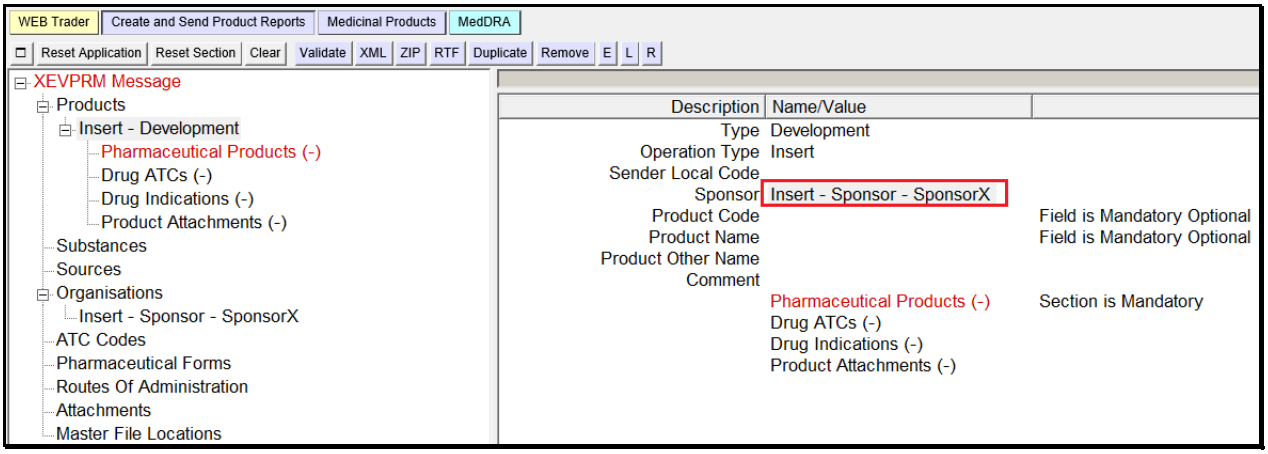
Once you have created the new sponsor organisation, go to the DMP entity section that you started to create, click in the area next to the field 'Sponsor' and then on the button L (Local data lookup):



From the pop-up menu, select the new sponsor present in your XEVPRM:



The sponsor will then be referenced in your DMP entity:



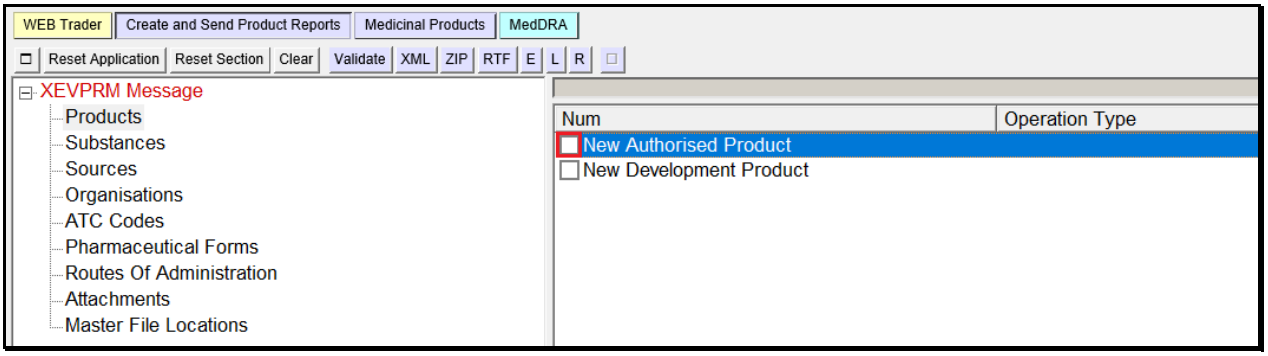
The same process can be used to add information regarding new organisations, reference sources, ATC codes (proposed or development), routes of administration (proposed or development), pharmaceutical forms (proposed or development), MFLs and attachments.

3.5.2. Adding and removing items

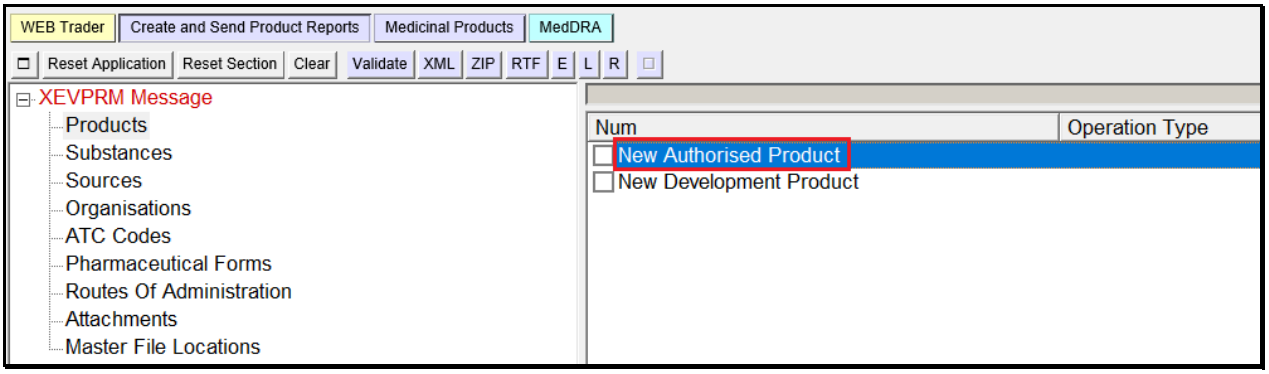
During the data entry process, you may be required to add a new section to the tree-view.

This can be done in two different ways:

- in a checklist (see section *3.5.3. Checklists*) by clicking on the special item called 'New …', or



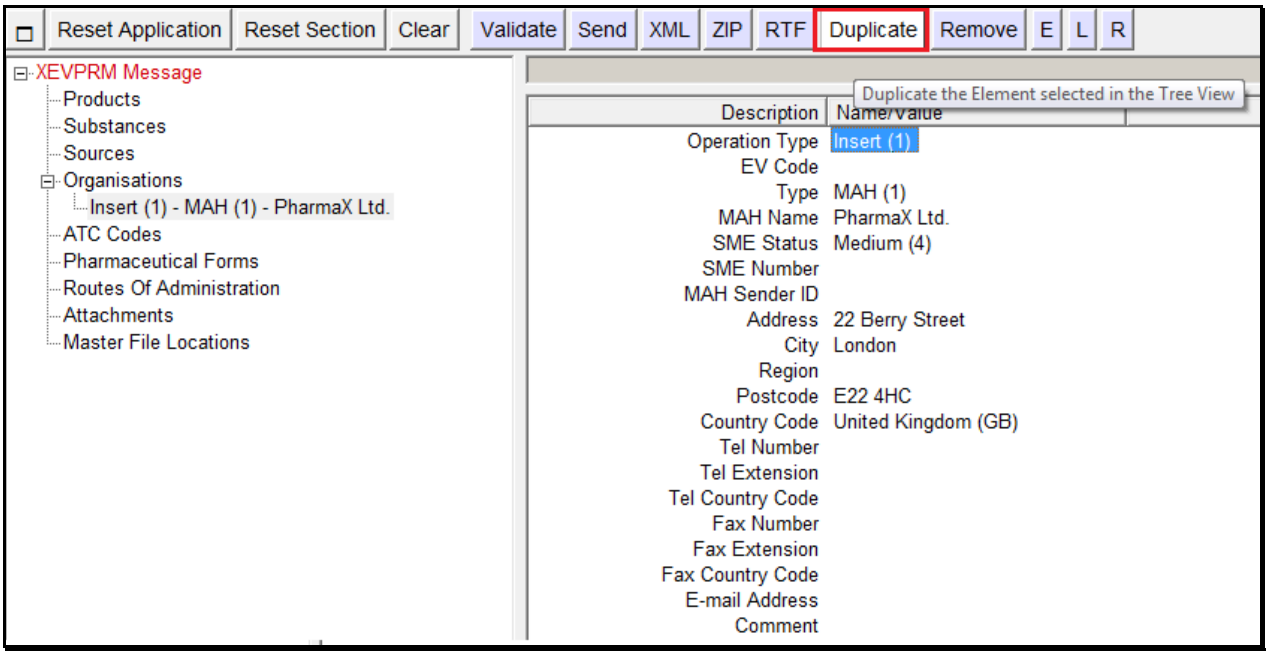
- by double clicking on the item in the list view in the active area.



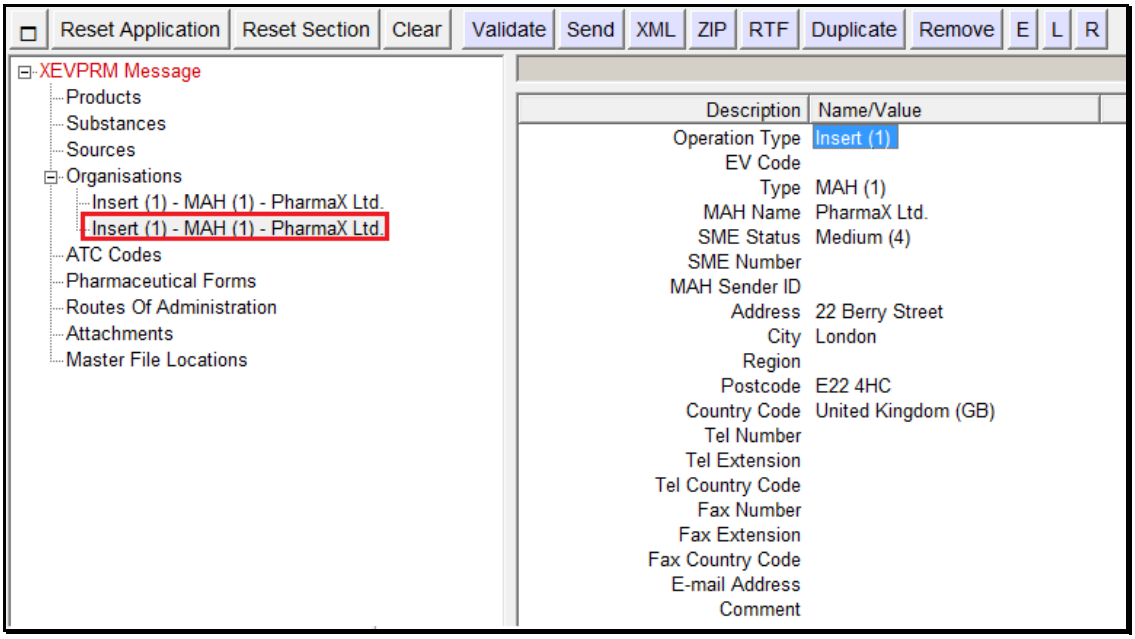
Some of the sections that you can add are repeatable, which means that you can add several of them. To do that, you can click on the 'New …' item more than once. You can also duplicate an already existing item.

Duplicate

To do this, in the tree-view, you must select the section you wish to duplicate and then click on the 'Duplicate button' that becomes available only in these situations:

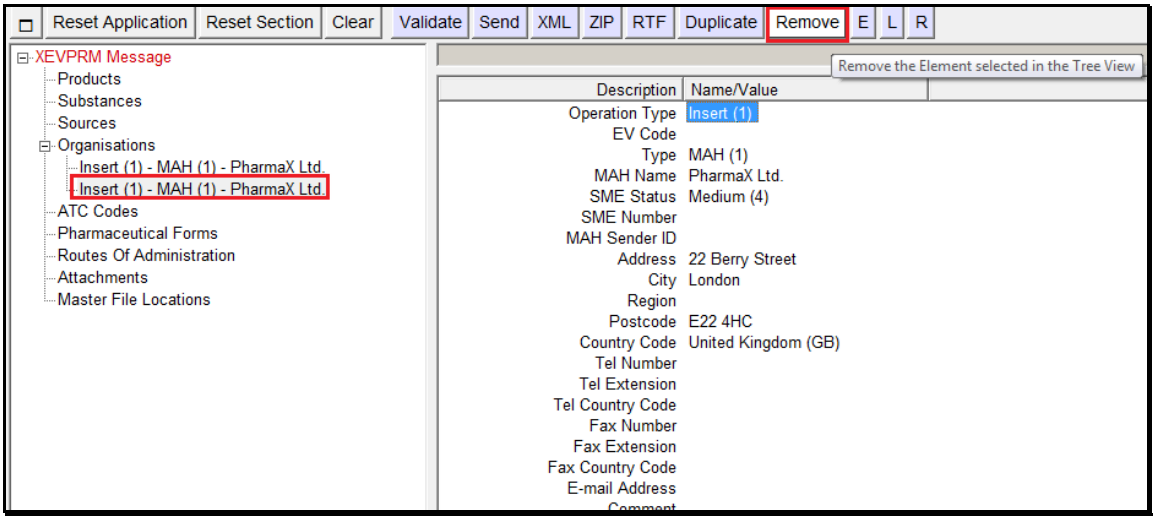


The duplicated entity will appear in the tree-view area:

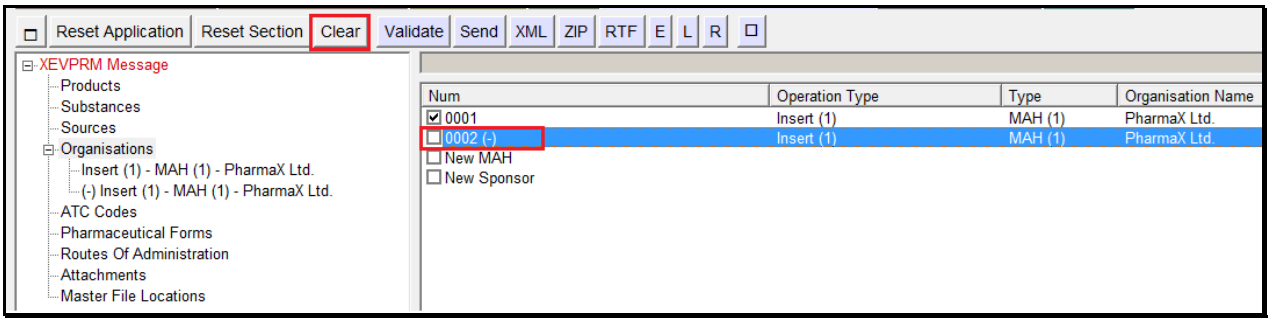


The sections you added can also be removed; to do this, you have two different options:

- you can select in the tree-view area the section you want to remove and click on the 'Remove' button that becomes available only in these situations:



- or, in case of multiple sections, un-check the section you want to remove (see section *3.5.3. Checklists*) and press the 'Clear' button:



3.5.3. Checklists

A checklist is a specific type of **list view** (see section *3.3. The active area* for related information) displayed in the active area, allowing the user to perform specific actions on the displayed items.

A checklist always displays a list of items with a white check box beside it. You can check/uncheck one or more items by clicking on the checkboxes with your mouse, or by pressing the 'Space' key on your keyboard when the item is selected (dark background).

When dealing with a checklist, you may see two standard buttons in the dynamic buttons area on the main menu:

Deselect all: The button on the left is used to automatically uncheck all the checked items in the checklist. You can use this button instead of manually unchecking all the single items.

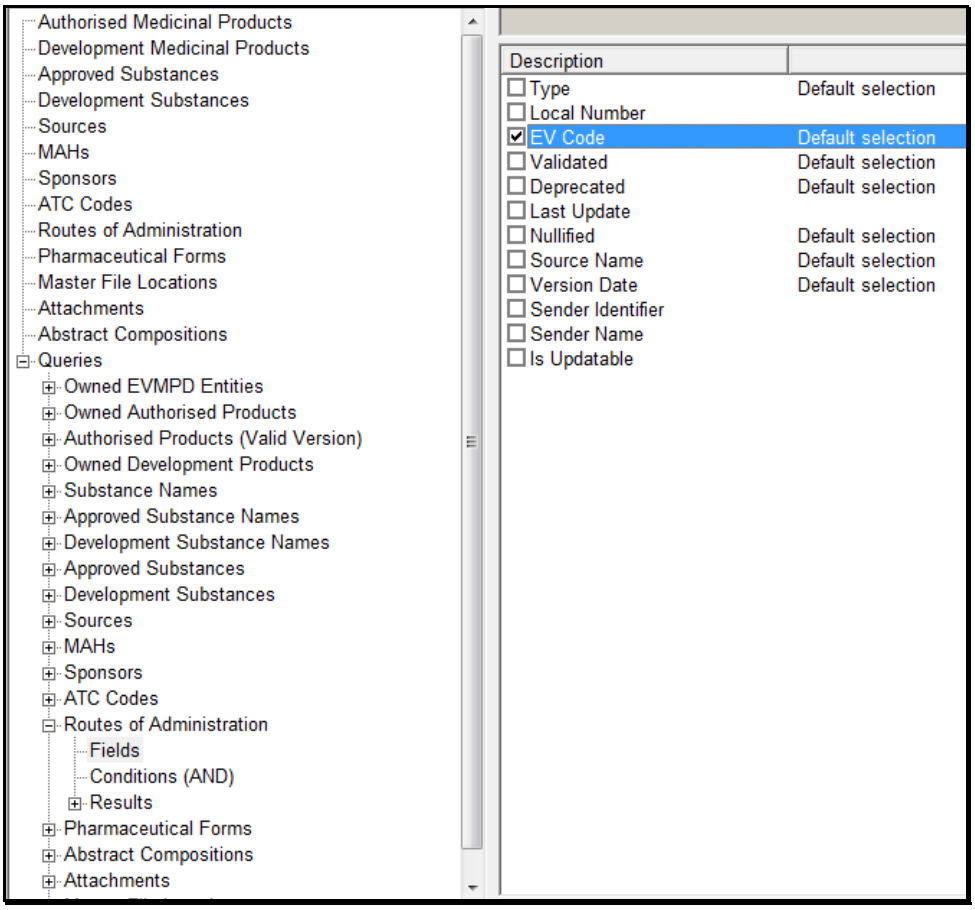
Select all: The button on the right (which is not always displayed) has different functions depending on the operations allowed in each section. These functions will be explained in detail when the EVWEB-sections will be described in the following sessions of the manual (load/unload checklists, fields of a query search, message receivers).

There are three types of checklists, depending on the actions you can perform on the list of items:

- Select/Deselect
- Load/Delete
- Add/Delete

3.5.4. Select/Deselect checklist

This type of checklist allows you to select and deselect one or more items from the list displayed on the screen in the active area. It is used for the 'Fields', 'Conditions' and 'Results' sections of a query search.



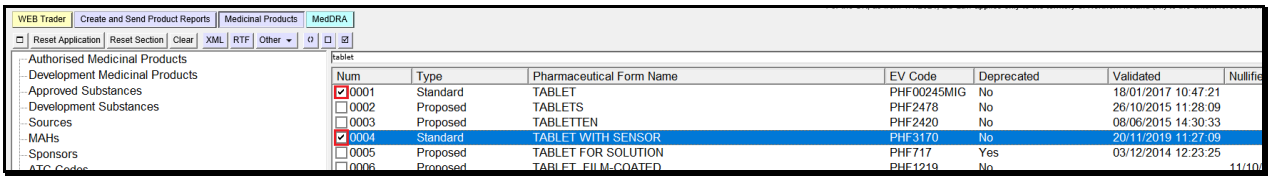
In this type of checklist, the selected items are displayed only in the active area; nothing changes in the tree-view area when you select or deselect an item.

For the 'Results' sections, the purpose of the selection is to mark the entities on which to perform commands.

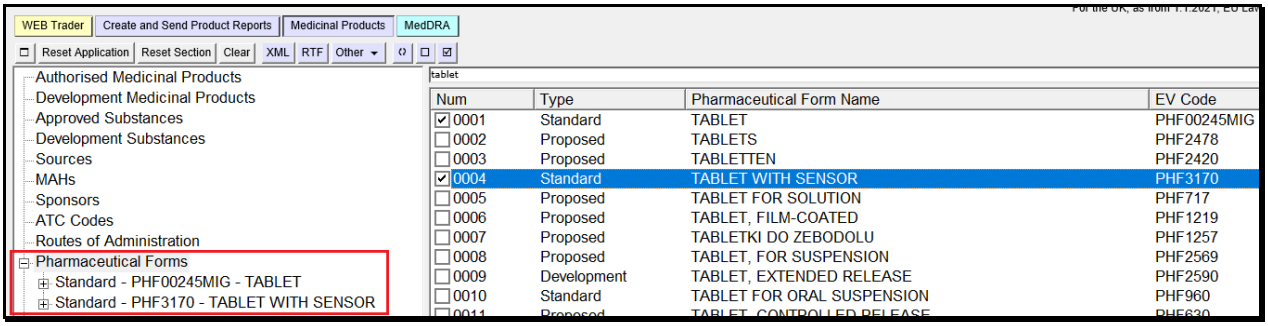
3.5.5. Load/Delete checklist

This type of checklist allows the user to load one or more of the items displayed on the list from the remote system. This type of checklist is used to display the results of a **simple query** and an **advanced query** (see section *3.6. Search methods*).

By marking one or more of the checkboxes, EVWEB will load the data from the remote system. This operation may take a few moments to be performed. This means that the result of the operation is not immediate.



The loaded data will appear in the appropriate section of the tree-view area :



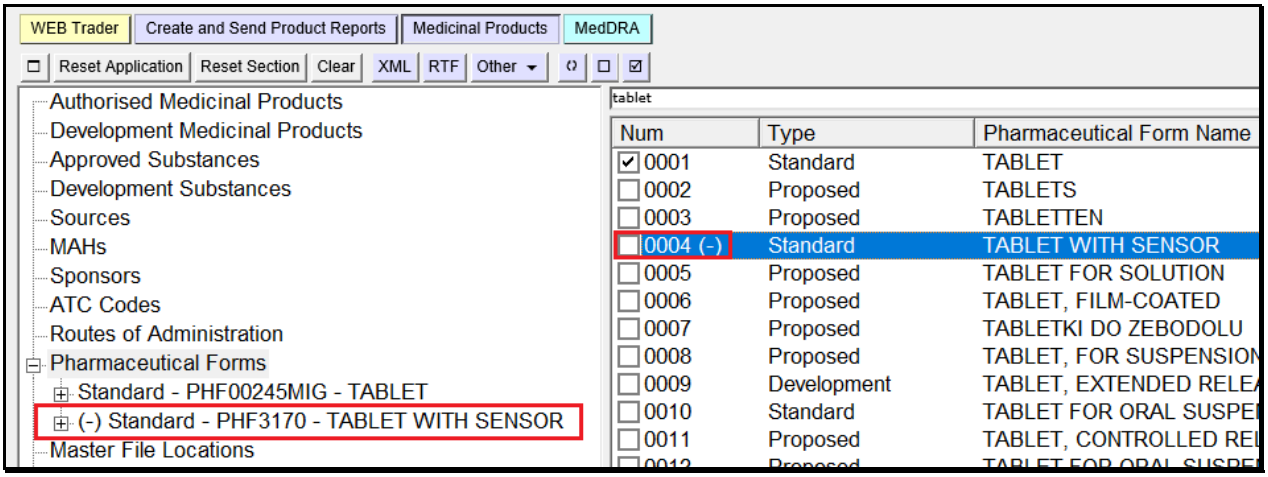
The section currently selected in the tree-view area may not be related to the section where the loaded items will be added.

As an example, when you are positioned on the results of an advanced query, the selected item in the tree-view area is the result of the query itself. The loaded items will be loaded to a different section, depending on the main subject of the query (see section *3.4. Interaction between the tree-view area and active* area and section *3.7. Loading data*).

In case of failure of the loading process, an error message box will be displayed.

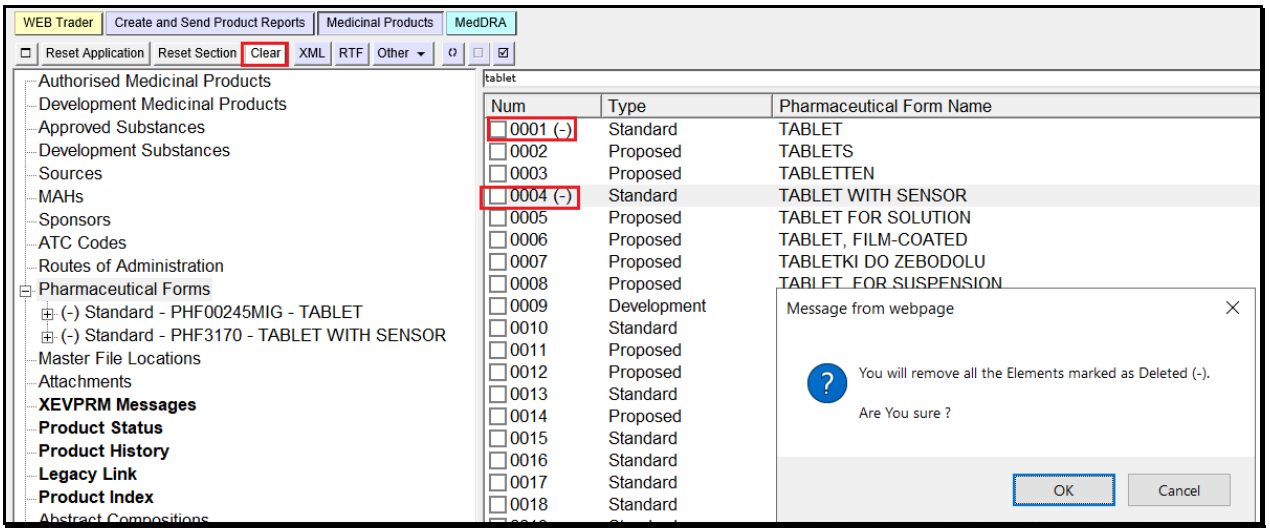
The opposite action is to remove one or more of the loaded items. If you unmark one of the items displayed in the list, a negative (-) sign will be displayed in both, the tree-view area and in the active area. This indicates that that specific item has been marked for deletion and therefore will be no longer considered in the active data.

As an example, we unmark 'capsule, soft':



To **permanently delete an unmarked item,** click on the 'Clear' button on the main menu dynamic section.

The 'Clear' button will remove **all the items unmarked this way**:



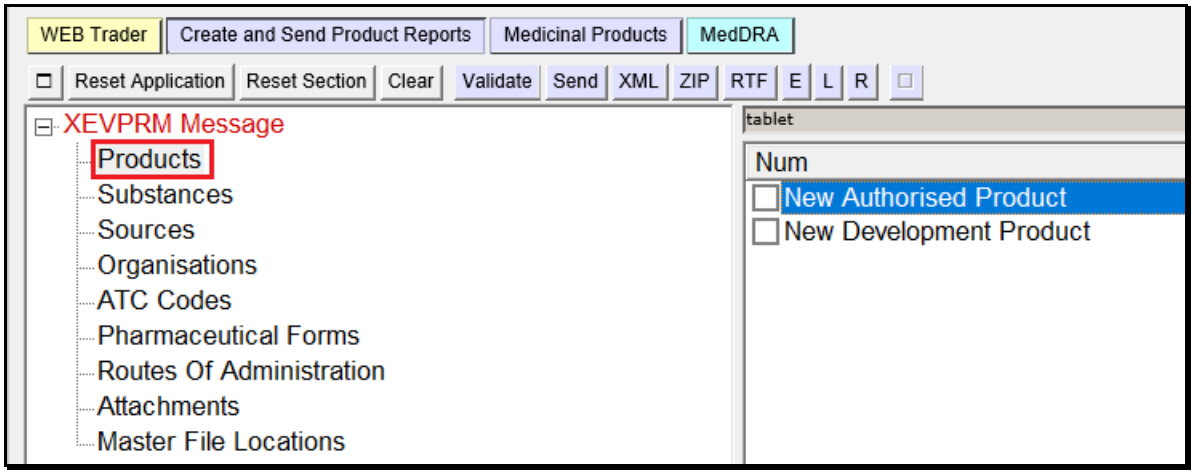
When using EVWEB, keep in mind that there **is no way to directly delete or modify the data present in the EVDBMS**. All actions performed here only affect the current data present in your personal EVWEB session.

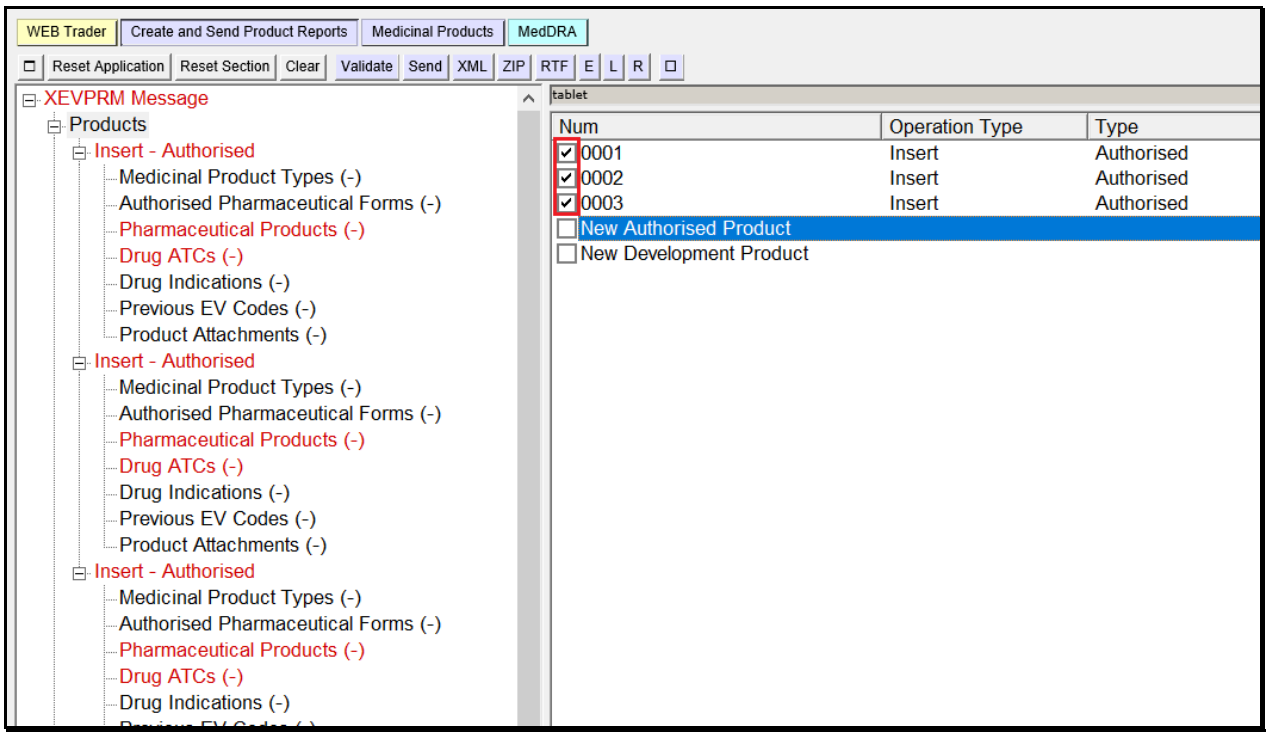
In this particular type of checklist, this button allows you to load all items displayed in the active area with a single click. The loading operation may take some time since the result of a query could be very long. For this reason, when you click on this button, the system will ask you to confirm your choice, and will also give you the possibility to stop the loading sequence.

3.5.6. Add/Delete checklist

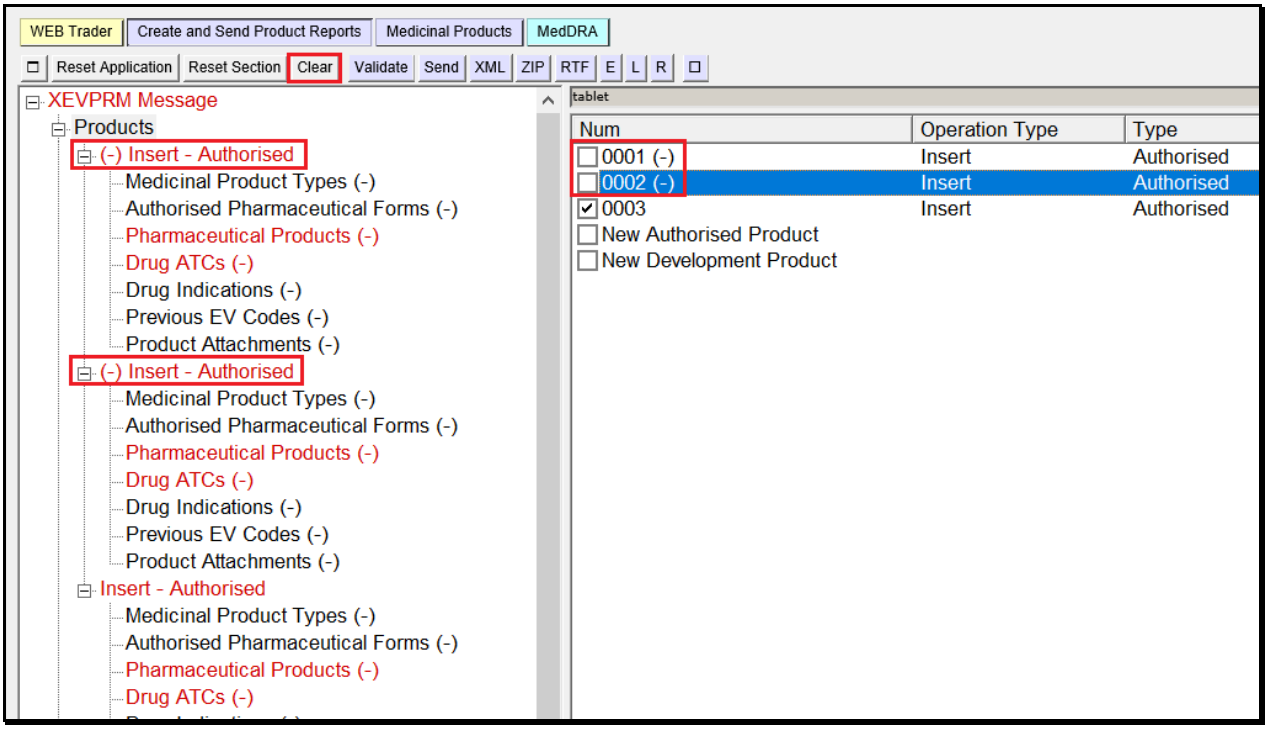
This type of checklist allows the user to add one or more new items during a data entry procedure (e.g., creating a new Authorised Product).

This can be used to display the content of a multiple section. A multiple section is a container of one or more items of the same category. This means that whenever it is possible to insert one or more items of the same category, there is always a section container. As an example, an XEVPRM can contain one or more Authorised Products; to handle this situation in EVWEB, there is a section container called 'Products' that contains all the Product Report items.

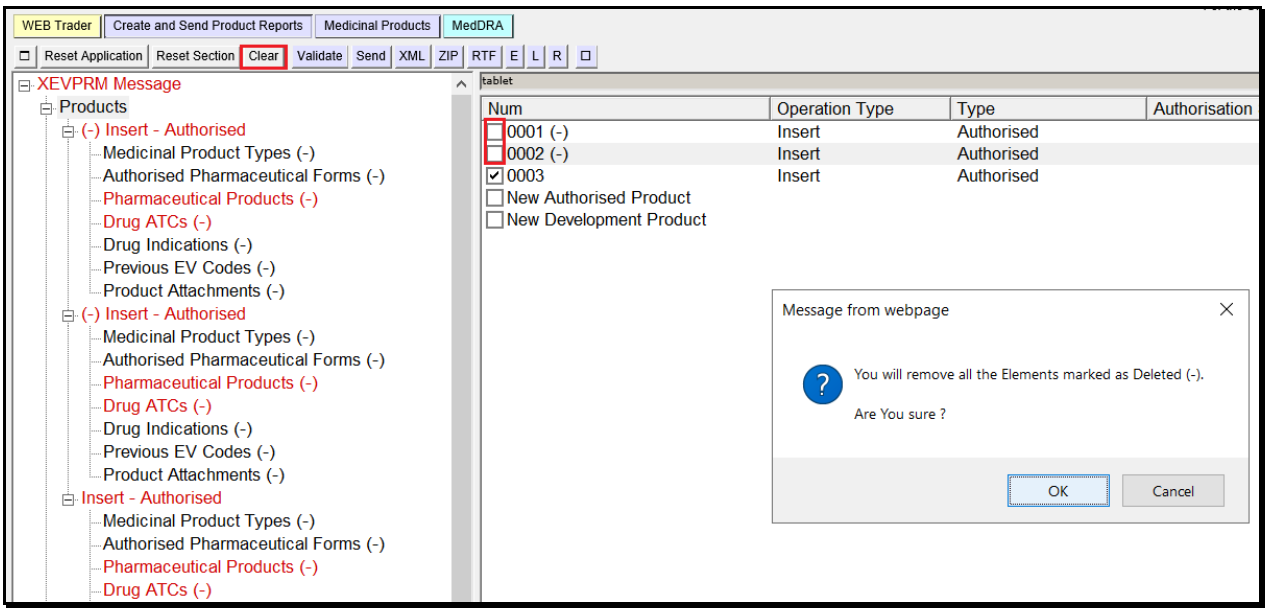


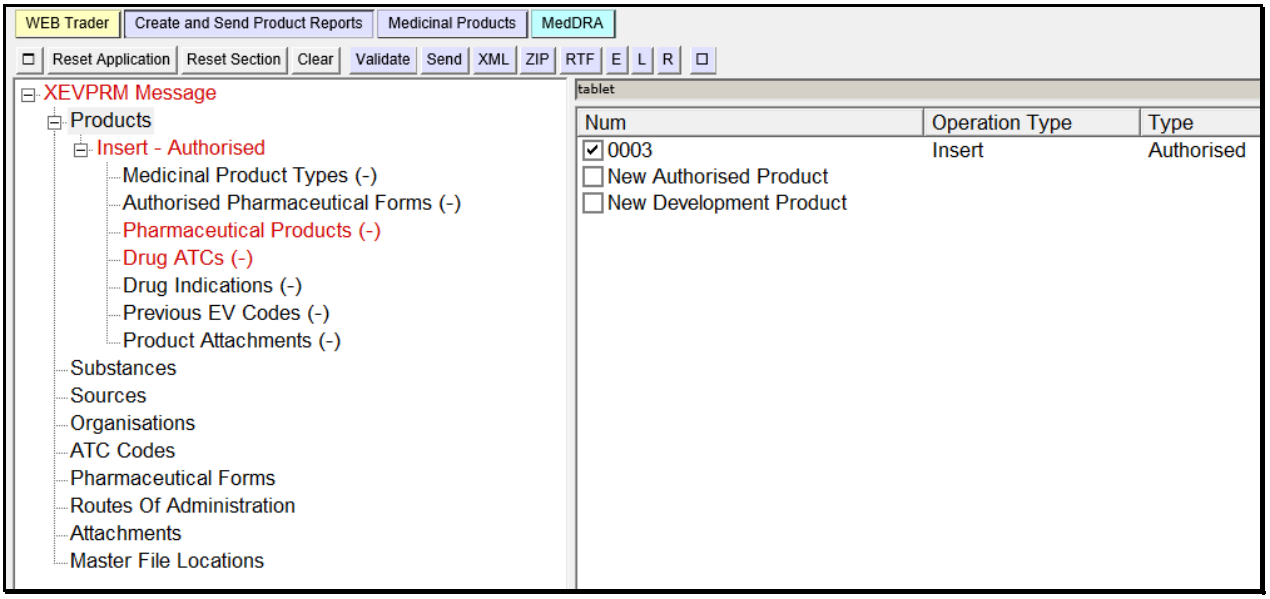


The delete function of this type of checklist works exactly as the one for the Load/delete checklist:



Once you deselect your items and click on 'Clear', the deselected entities will be removed from your tree-view area:





3.6. Search methods

To navigate through the information available in the Product Report Database and in the Scientific Product Database, you need to load the product data in EVWEB.

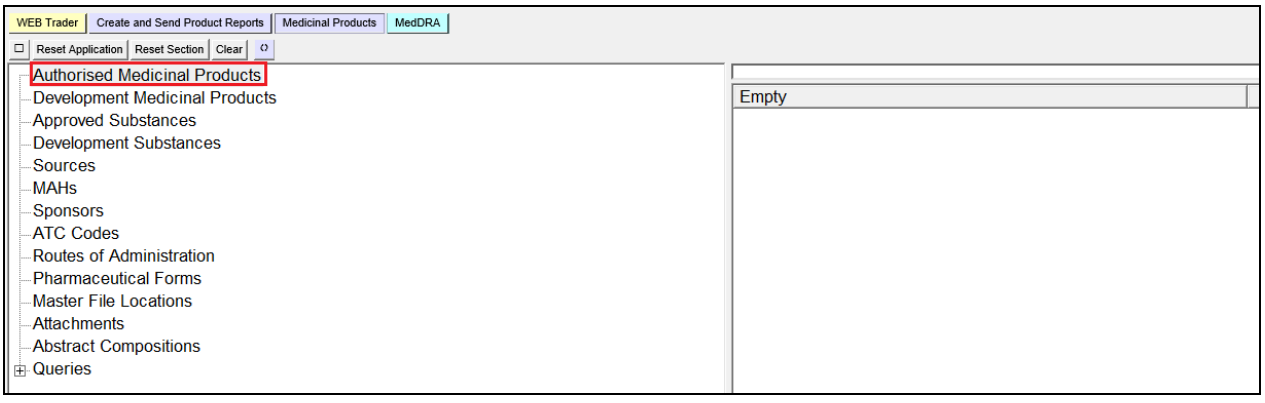
The starting point to load data in EVWEB is always a query (simple or advanced).

3.6.1. Simple query

The simple query field is located at the top of the active area as shown below. Here you can enter key words and activate the search by pressing 'Enter' on the keyboard. A pull-down menu on the right of the search field allows you to see a list of previous searches.

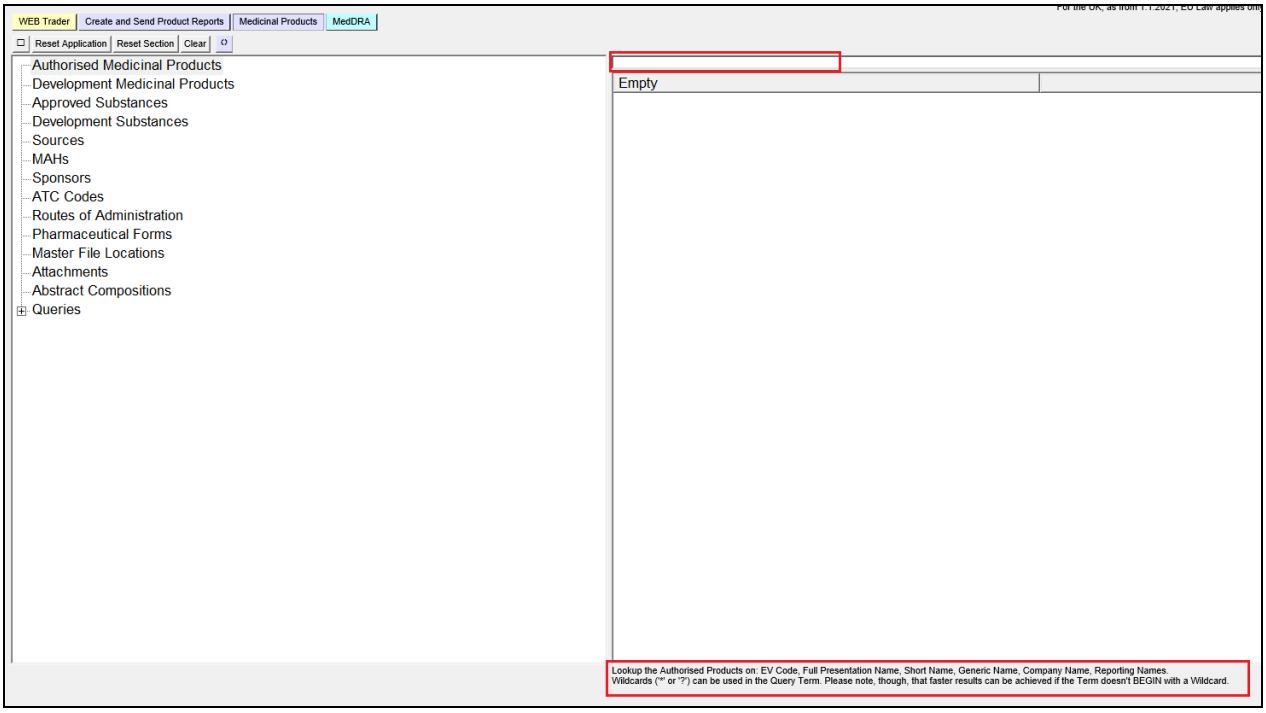
The simple query is available for specific items displayed in the tree-view area. Selecting one of these items will activate the simple query field.

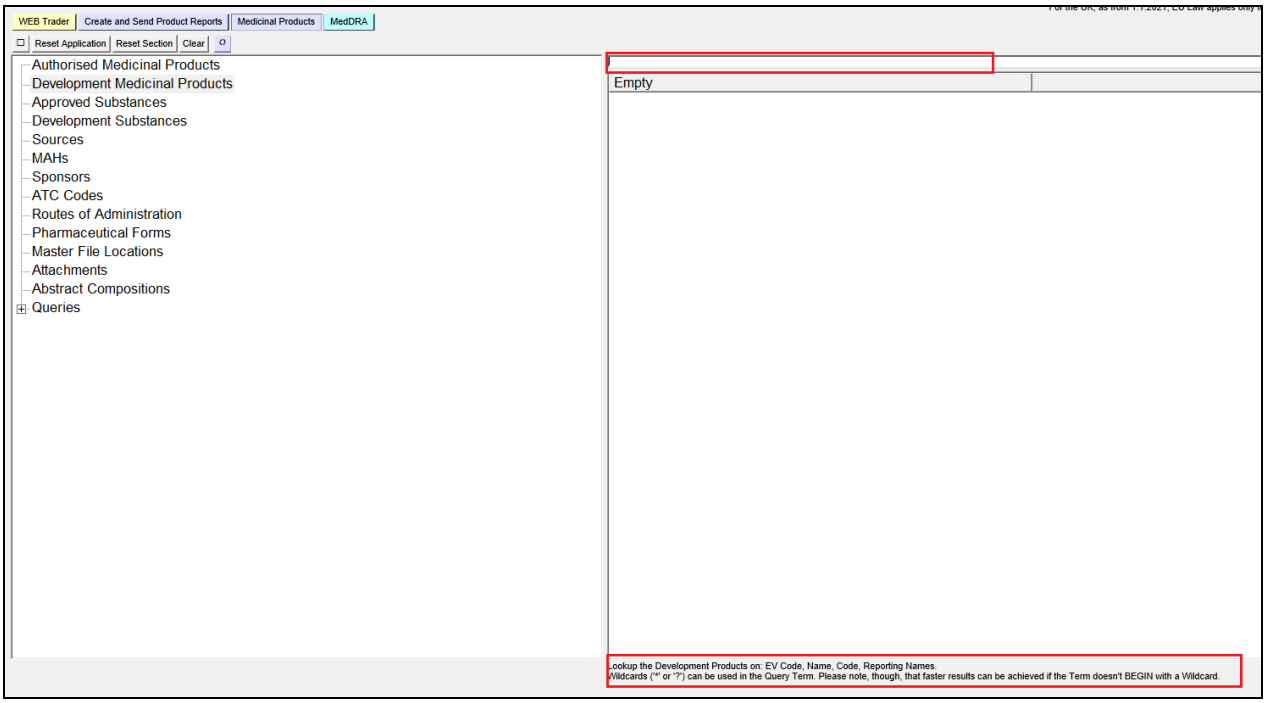
To search for an AMP, you must click on the 'Authorised Medicinal Products' section in the tree-view area:



To search for a DMP, you must click on the 'Development Medicinal Products' section in the tree-view area:

Clicking inside the simple query field will display the description of the simple query (on which fields the query will be executed):





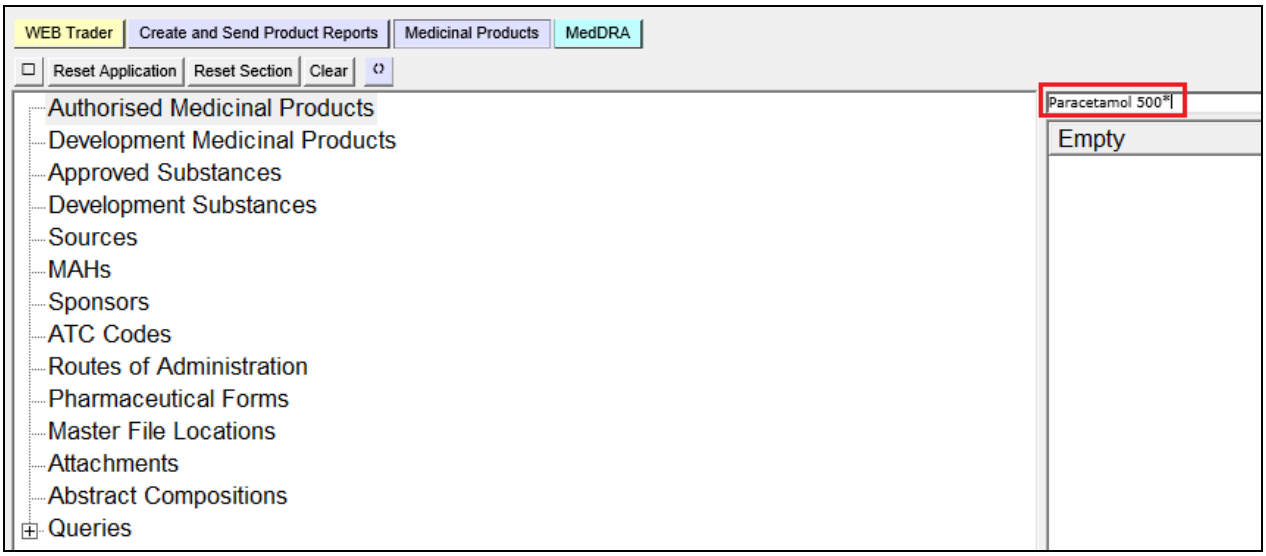
A simple query is carried out with the simple 'contains' clause. You can also use the following wildcards to extend your queries:

- A question mark (?) is a special character that matches any character (but only one): T?ST will match: TEST, TAST, but not TEEST
- Asterix (*) is a special character that matches any set of characters of any length: T*ST will match: TEST, TAST, TST, TEEST

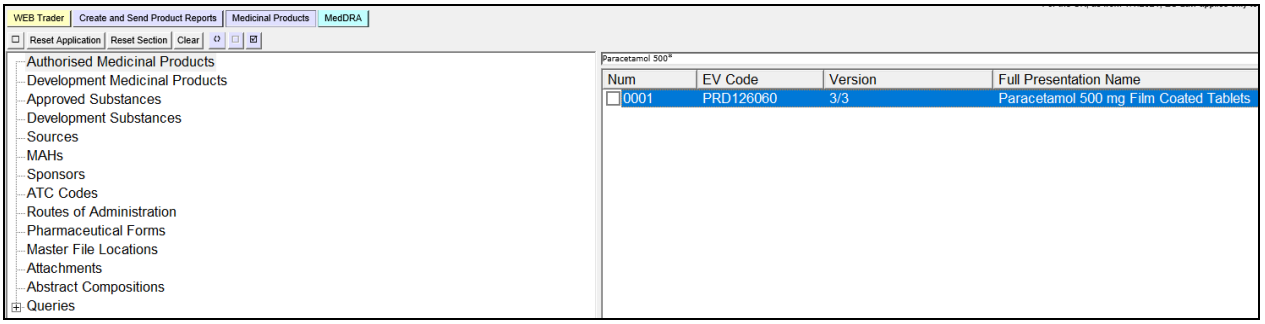
Combined examples for the use of both wildcards: T?ST*TERM will return: TEST TERM, TEST of the TERM, TAST – TEARM, TESTTERM

To perform a search in the simple query filed, you can enter the EV Code of the entity you are searching for or part of the name of the entity.

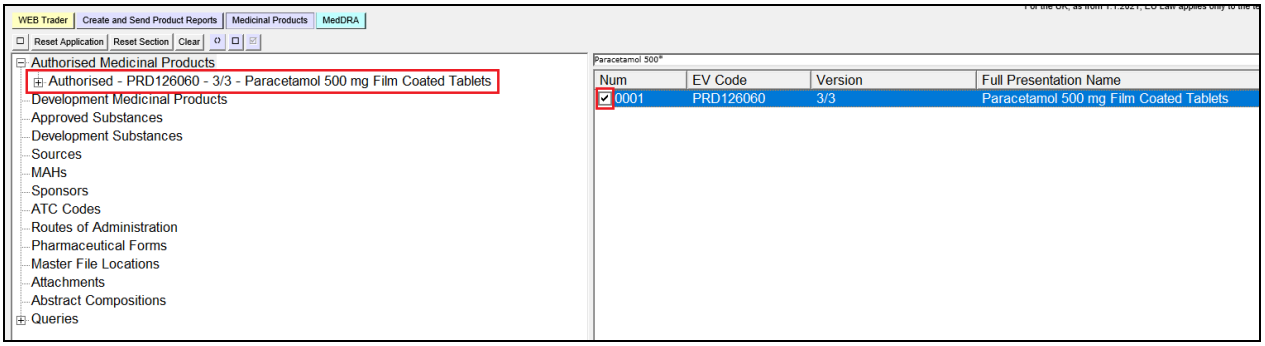
In the below example, the search is performed for an AMP with part of the name 'Paracetamol 500'. To Widen our search, * is also added at the end of the text:



Once you press 'Enter' on your keyboard to execute the search, the result(s) of your simple query will be displayed:



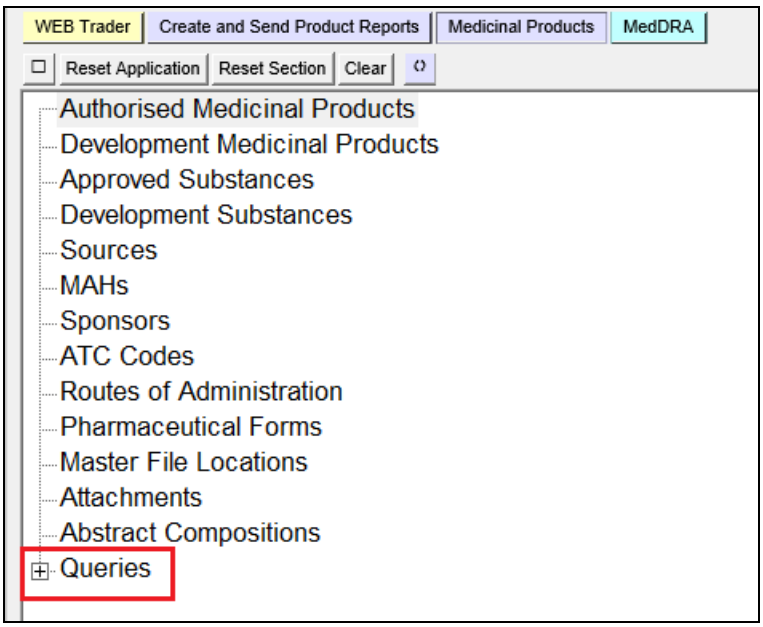
The result(s) of the query will be displayed in the active area, as a Select/Deselect checklist (see section *3.5.3. Checklists*). Once you select the entity in the active area, in the tree-view area, a new element will appear under the relevant section, containing the results of the query:



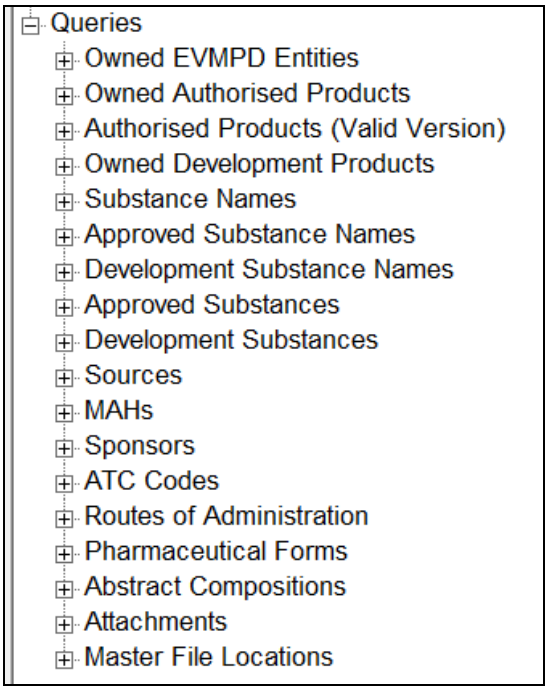
3.6.2. Advanced Query

EVWEB allows you to perform elaborate queries in the EVDBMS (e.g. Medicinal Products, MedDRA, terms etc.).

The query items in the 'Medicinal product' section of EVWEB are available as selectable items in the tree-view area under 'Queries':

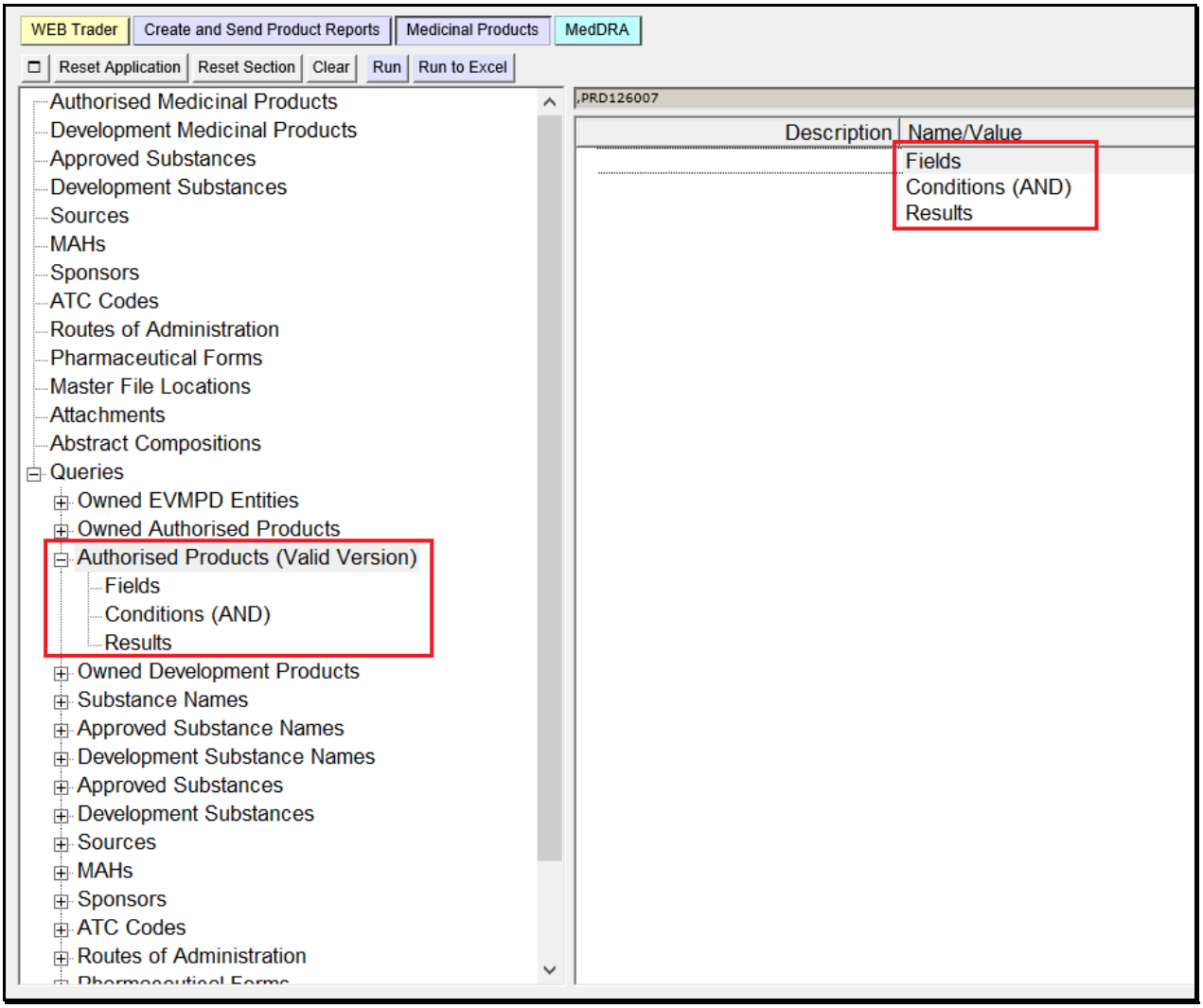


You can perform queries on the following entities:



Every query is divided in 3 different sections:

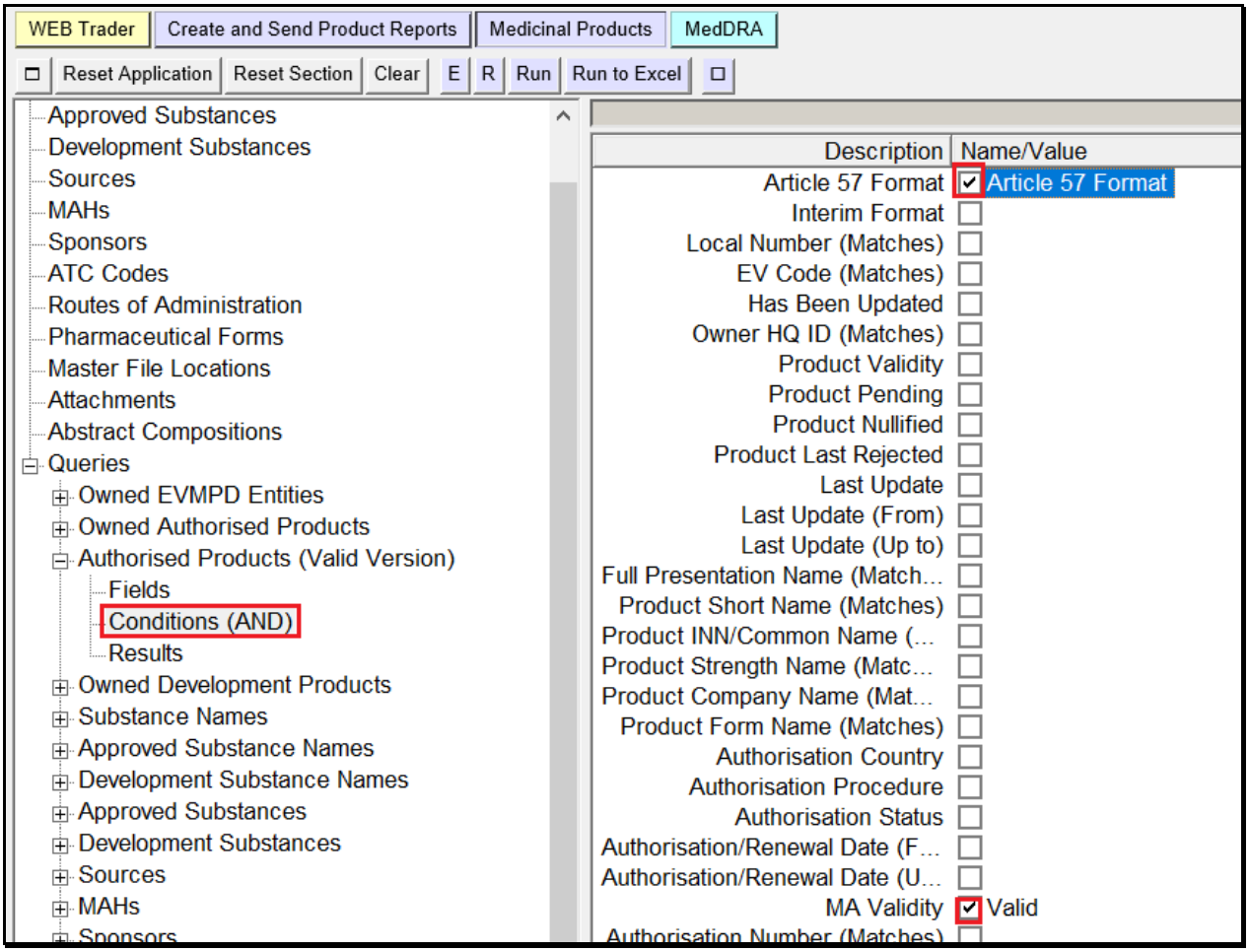
- Fields
- Conditions (AND)
- Results



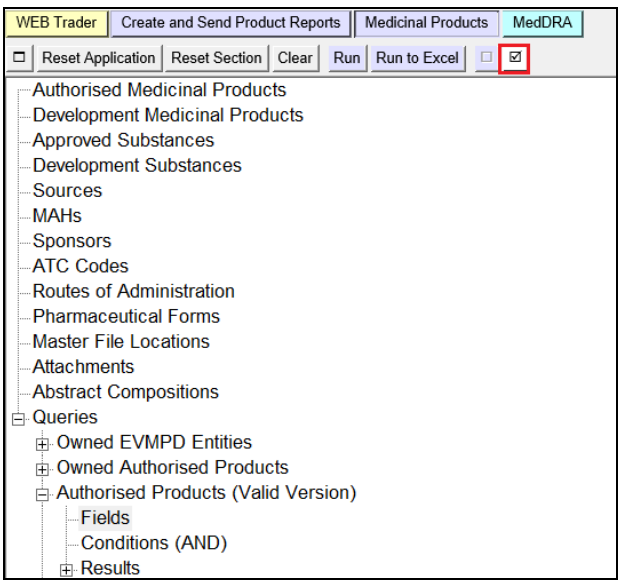
3.6.2.1. Fields section

The 'Fields' section is used to define the output of an advanced query. That means that the items displayed in the result checklist will contain only the fields selected in this section.

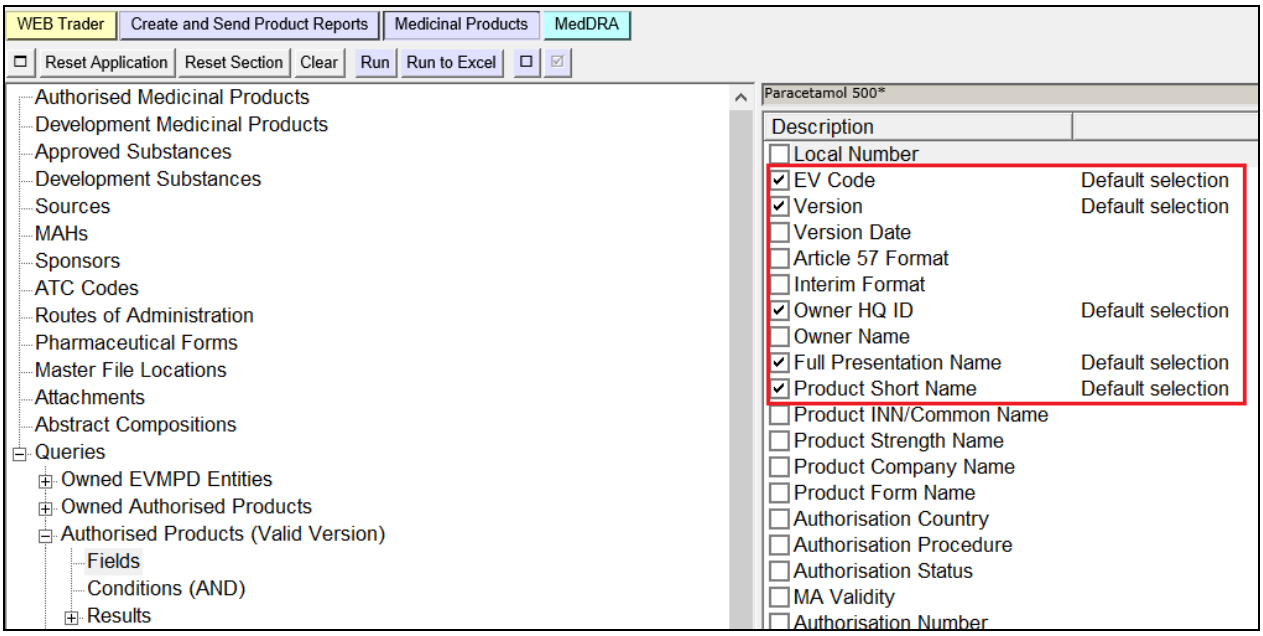
Usually, some of the items displayed in the 'Fields' section are marked as 'Default selection'. This means that if you run the query without selecting any of the items in the 'Fields' section, the default ones will be considered as selected.



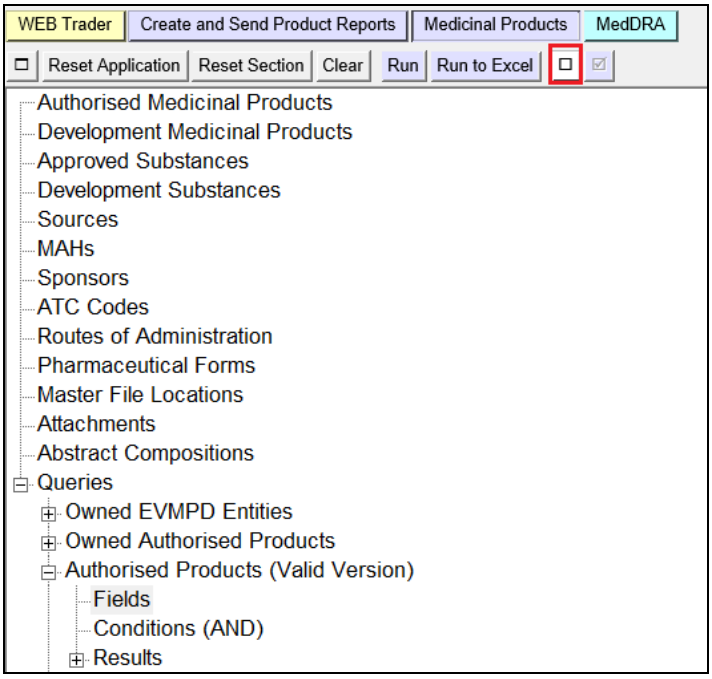
To select all items marked as 'Default selection' (or 'Last selection') by the application, select the below highlighted button in the main area:



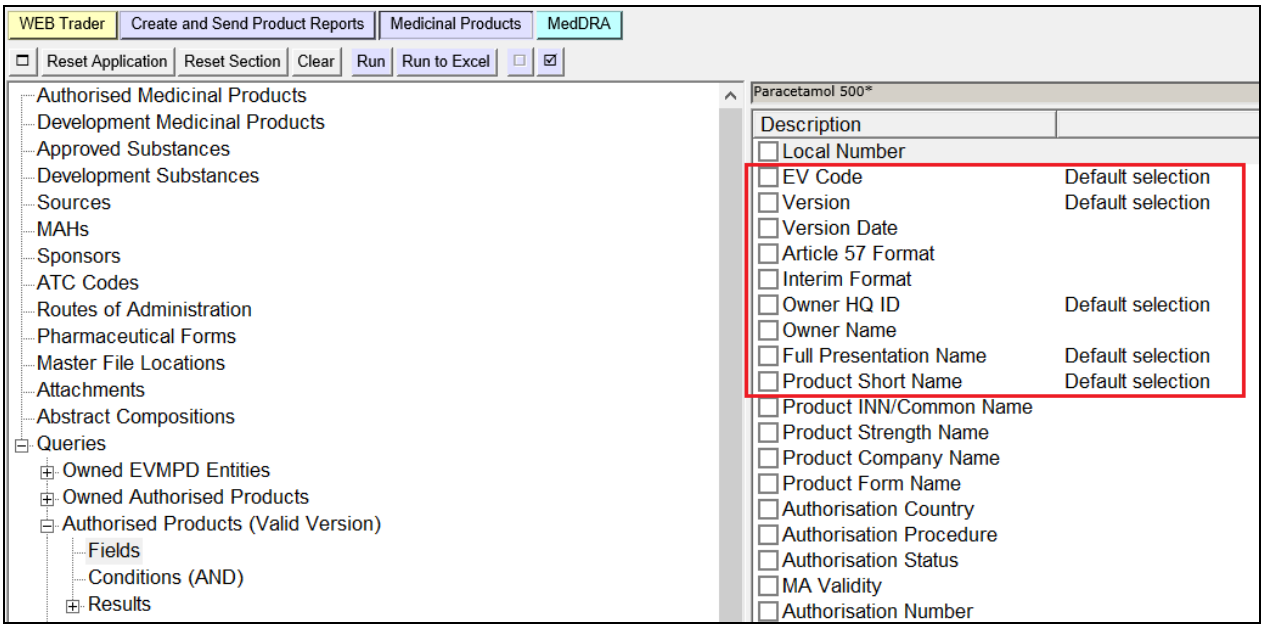
All fields marked as 'default' will become selected:



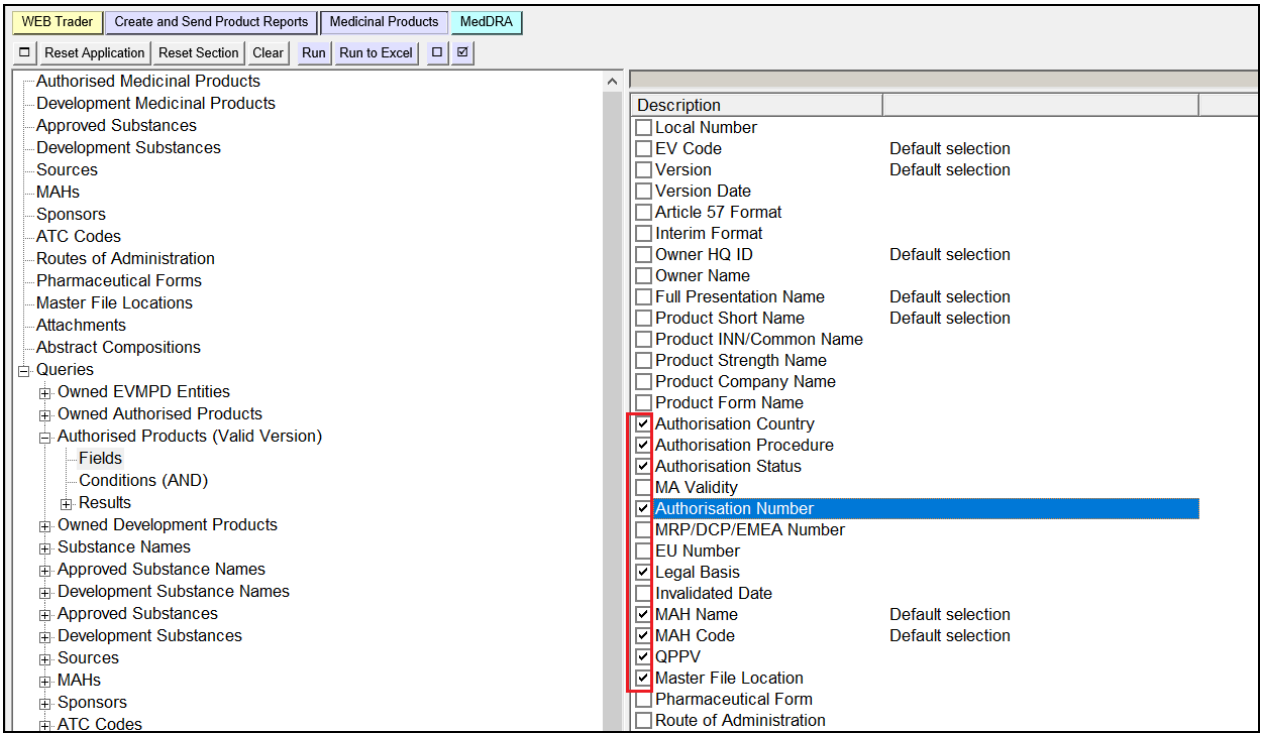
To deselect all items marked as 'Default selection' (or 'Last selection') by the application, select the below highlighted button in the main area:



All fields marked as 'default' will become deselected:

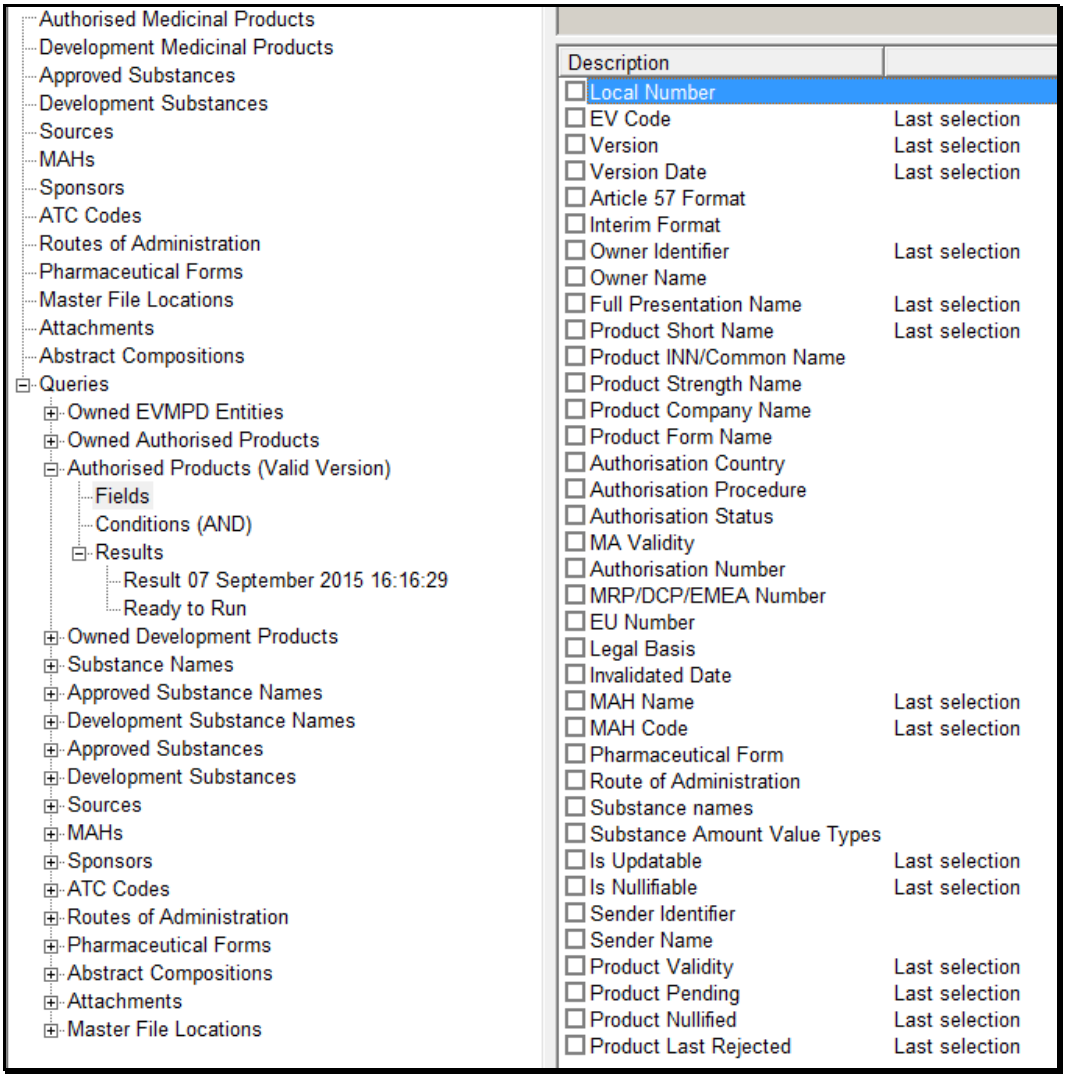


Aside from the fields selected by default, you can make your own selection by ticking the required fields:



NOTE: When performing a query on authorised medicinal products, whilst it is possible to select all the 'Fields', not all of them will be displayed in the results of your query.

If you use your own selection, after having run the query at least once, the 'Default selection' will be no longer visible. Instead, the last selection used to run the query will be visible. These items will be labelled as 'Last selection'.



It is not possible to select all the fields, the system will display an error message if you try to do that.

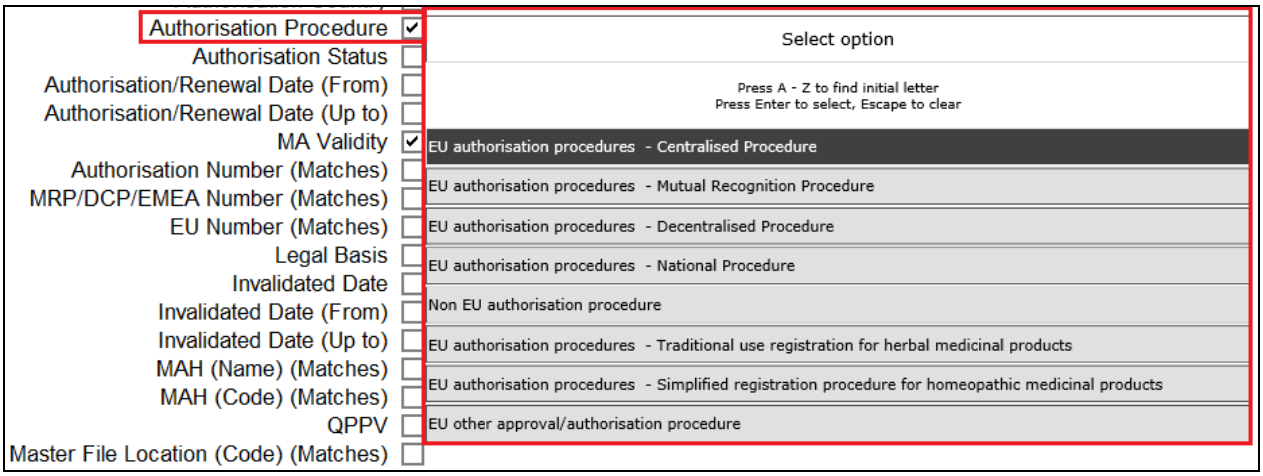
3.6.2.2. Conditions (AND) section

The 'Conditions' section is used to define the criteria of an advanced query. This section 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.

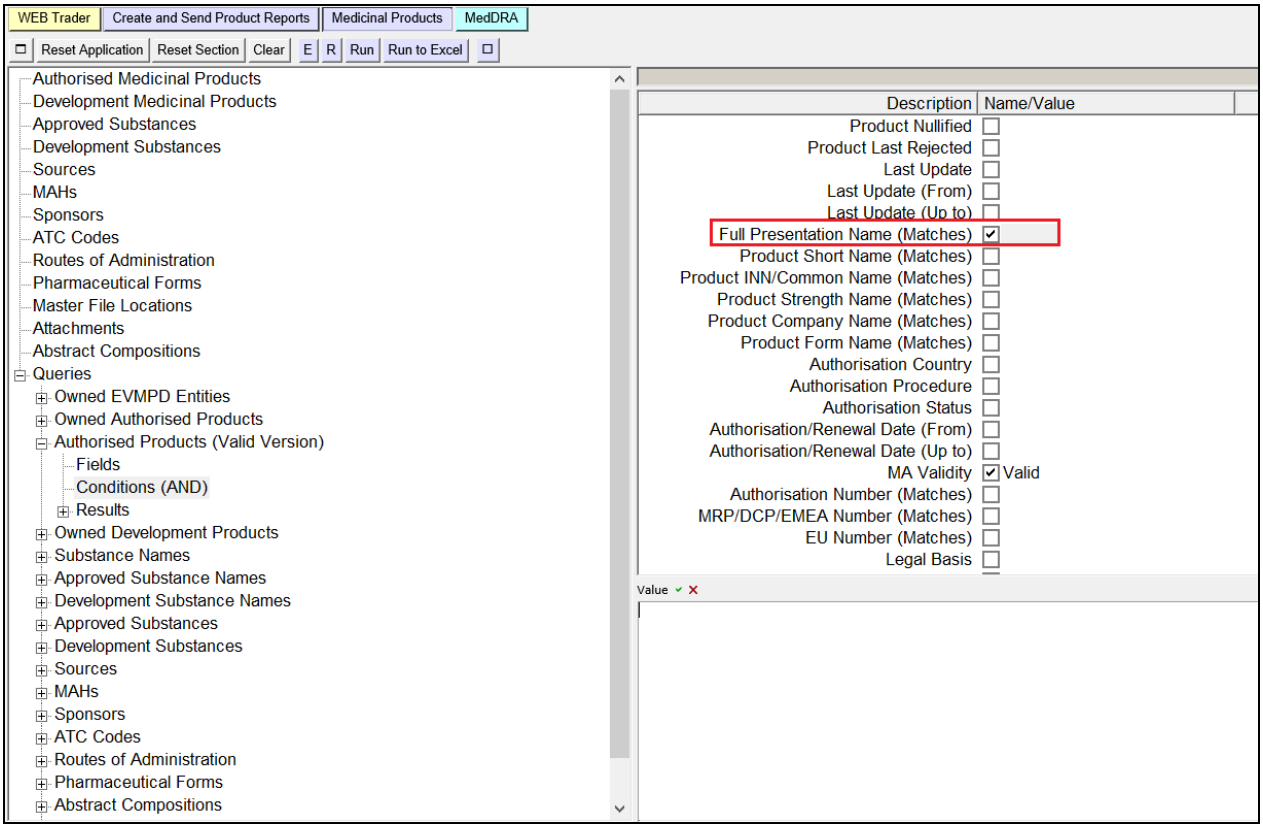
The conditions section works exactly as a data entry section. The only difference is the checkbox beside the field name. This is because you can define the value of the criteria, as well as which criteria you want to use (selecting it with the checkbox).

Each item will become active and editable only if it is selected (marked checkbox):

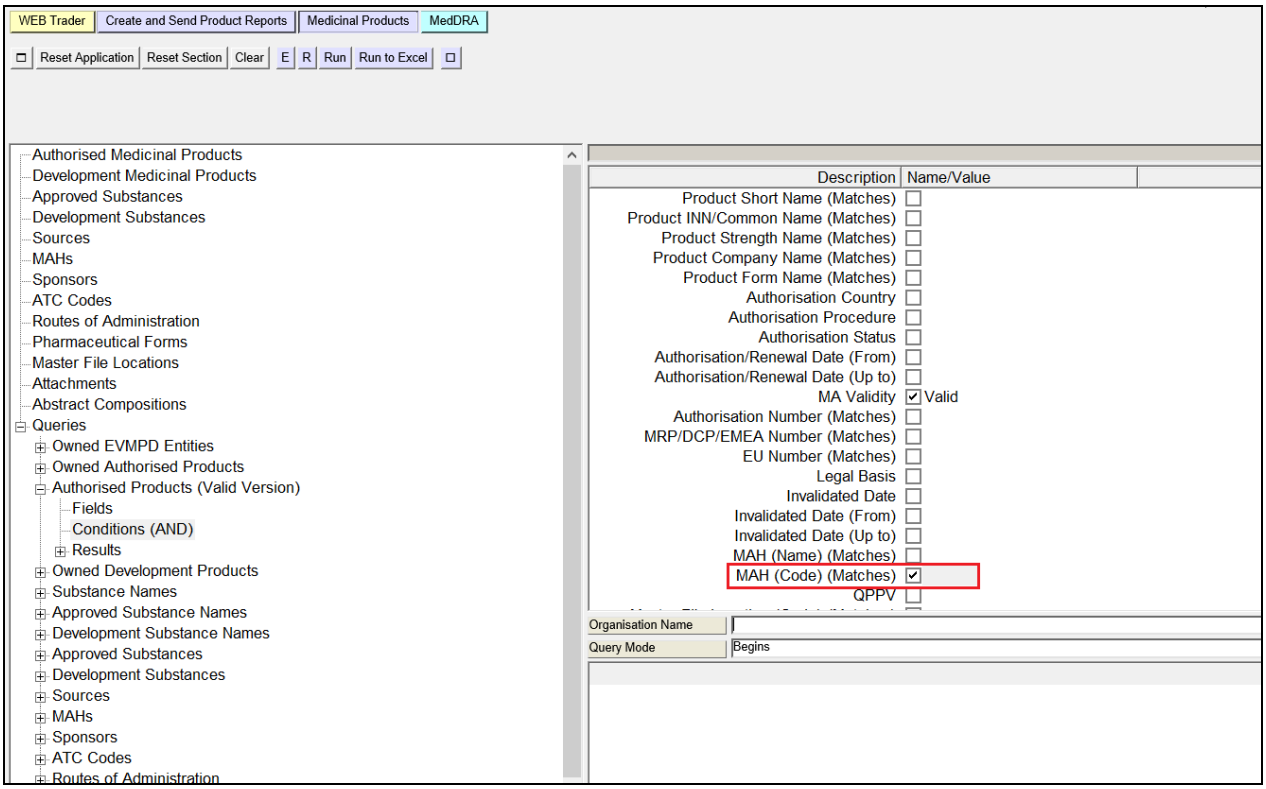
- Some fields have their values available as a pre-defined list, e.g.:



- Others are free-text fields, e.g.:



- You can also search for the required value using the remote look-up tables:



If a criterion contains a value, but it is not selected (checkbox not marked), then it will not be considered when running the query.

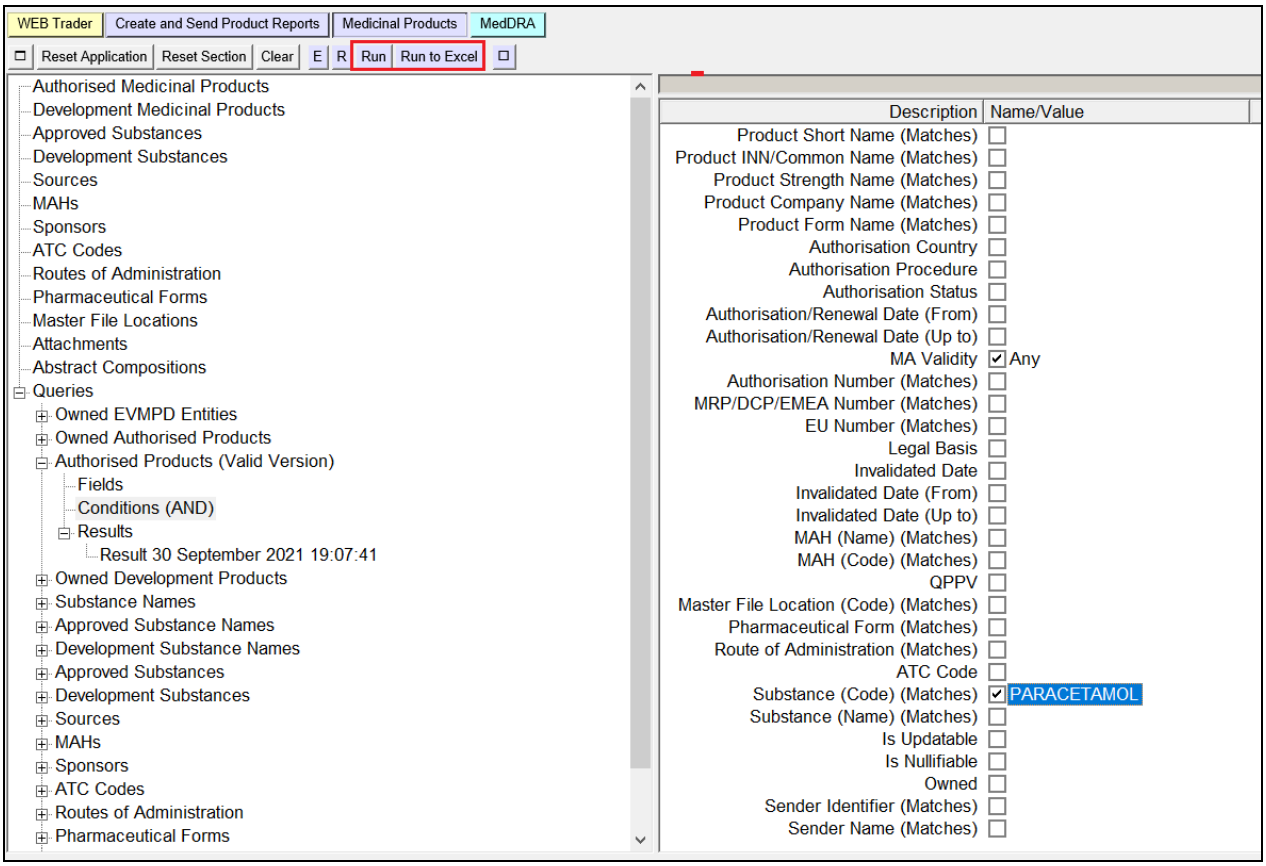
For details about the possibilities in dealing with different kind of fields, please refer to section *3.5. Data entry*).

3.6.2.3. Results section

To launch a query after specifying the fields and conditions:

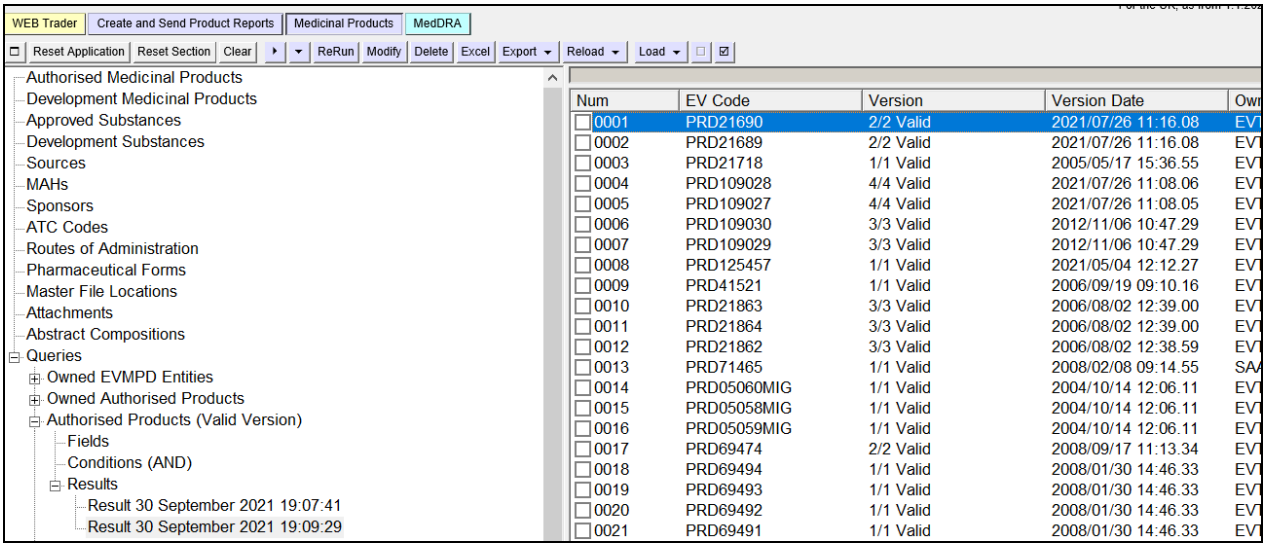
- press the 'Run' button in the dynamic section of the main menu to view the results in the active area; or
- press 'Run to Excel' to view the results in an Excel file[5].

[5] For AMPs, this only works if the condition "Owned" is selected.

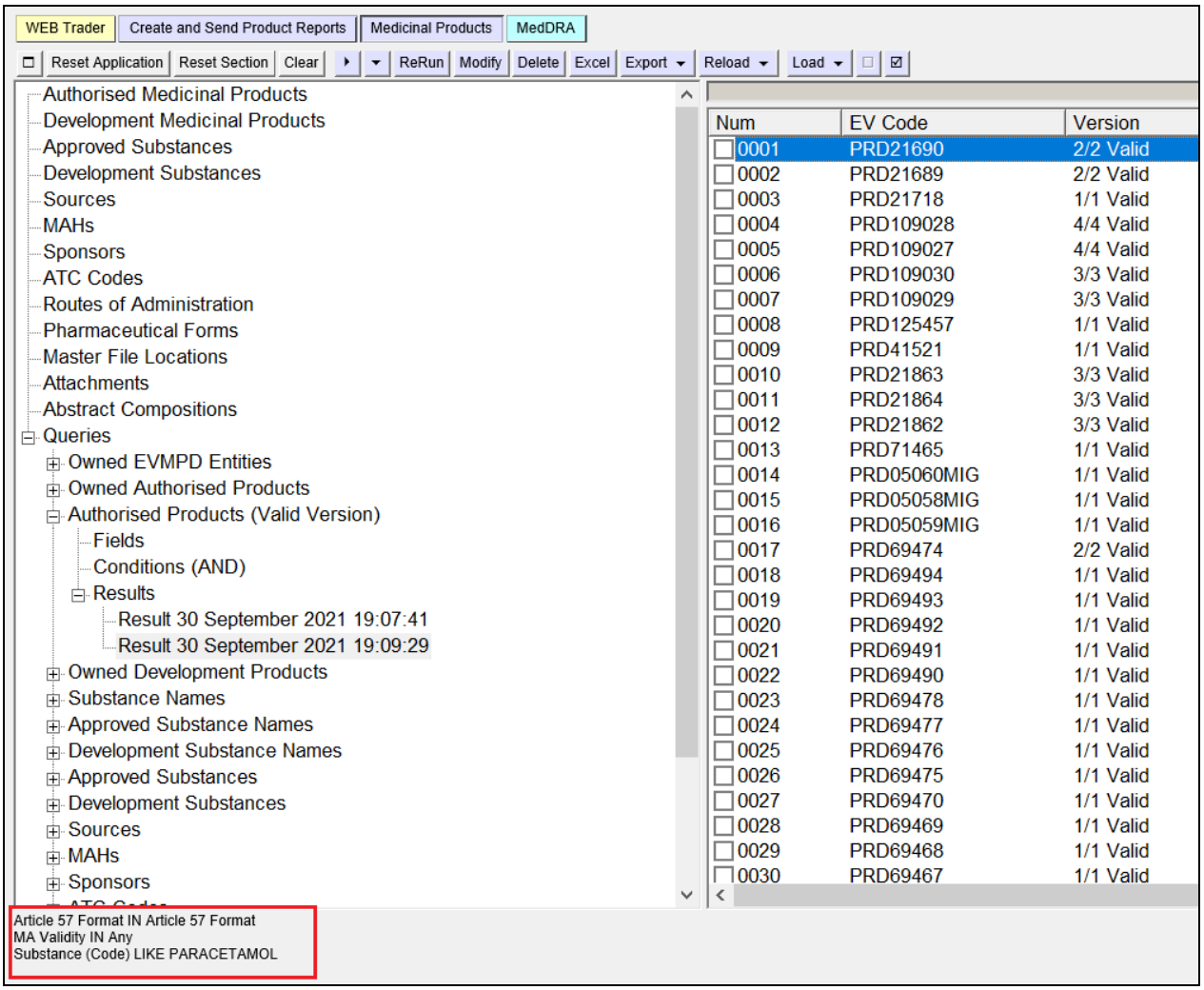


3.6.2.3.1. 'Run' functionality

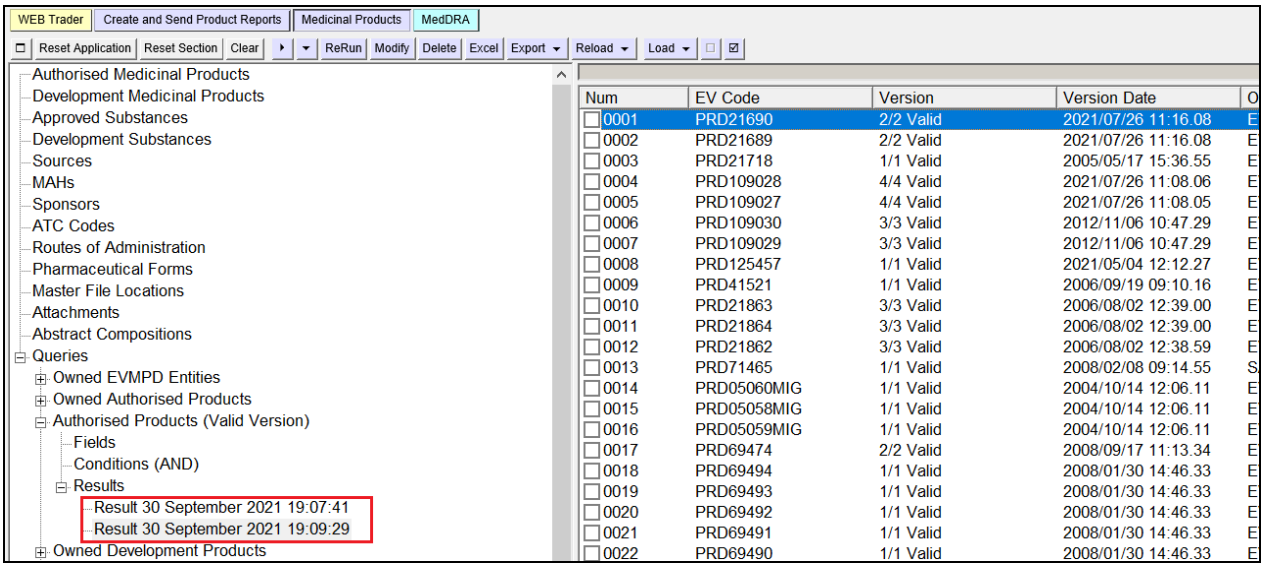
Once you select the fields that you wish to see as the results of your query and specify the conditions of your advanced query, if you click on the **'Run'** button, the results of the query will be displayed in the active area, as a Select/Deselect checklist (see section *3.5.3. Checklists*):



When a result set is selected in the tree-view area, the lower part of the left side of the EVWEB screen will display a summary of the conditions used to obtain this result set. This way, when you have different result sets, you can easily understand how the query has been run:

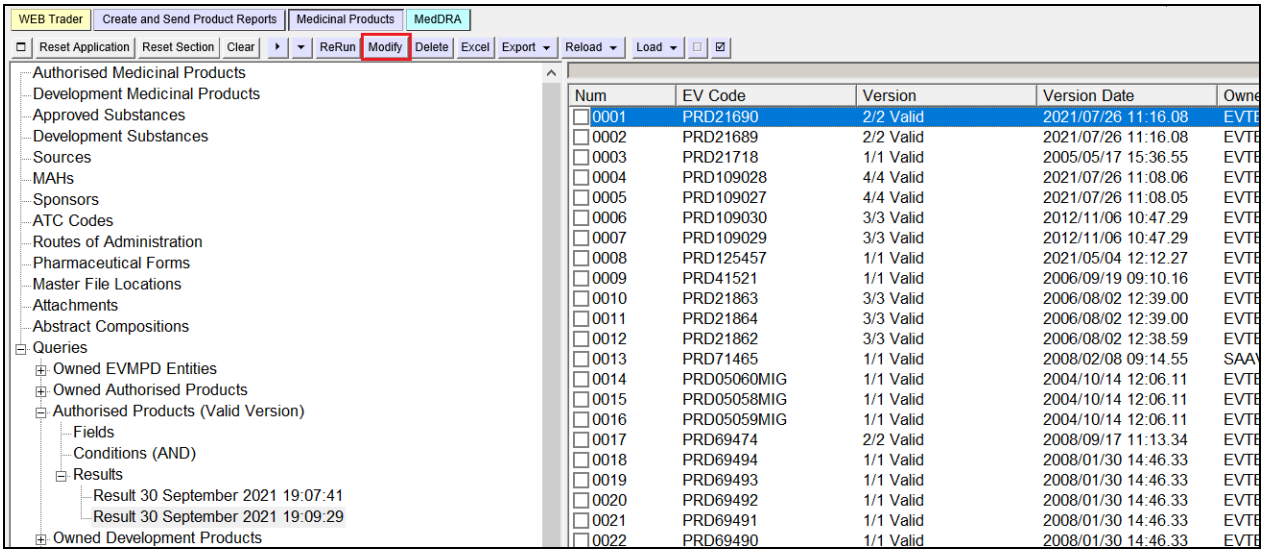


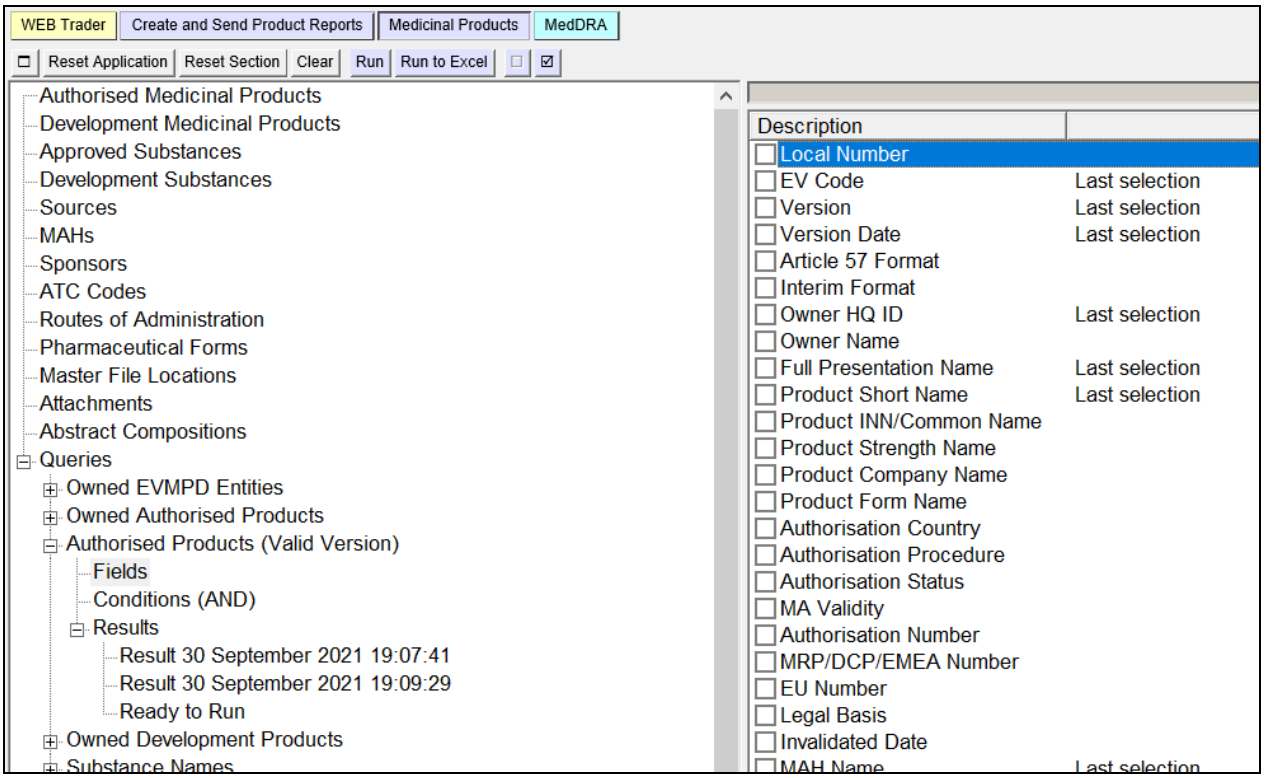
In the tree-view area, a new element will appear under the 'Results' section, containing the information on the date and time when the query was launched:



If you then want to modify one of these results without having to set all the fields and conditions again, you can create a new query based on the result set that you want to modify.

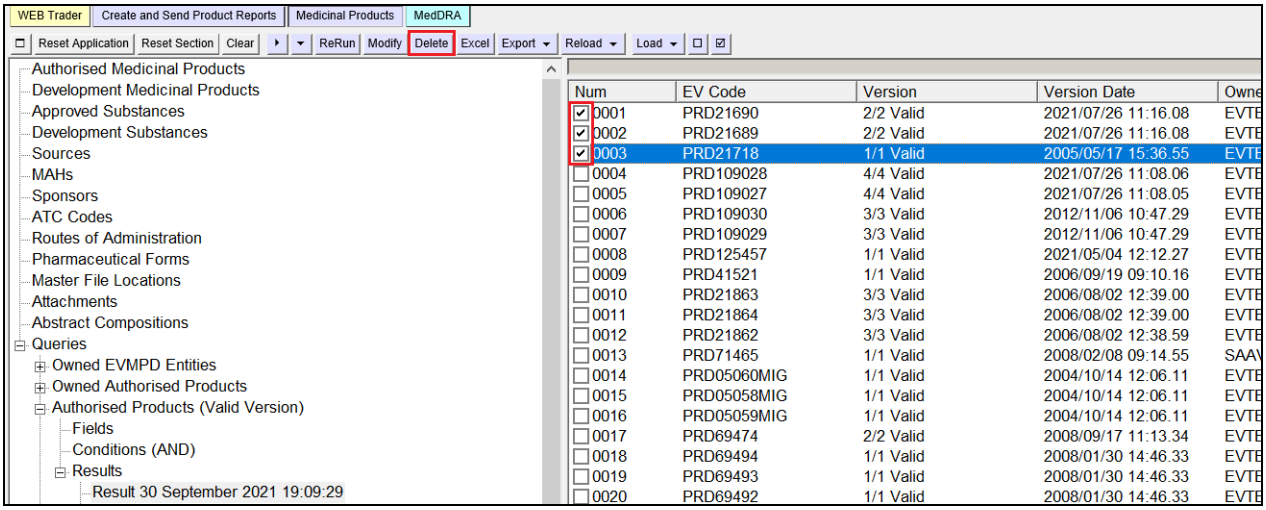
To modify a result set, you must select it from the tree-view area and click on the 'Modify' button. Then you will be brought directly to the fields screen already compiled with the previous query criteria so that you can modify them and run a new query. Alternatively, you can select fields or conditions from the tree-view with your mouse.



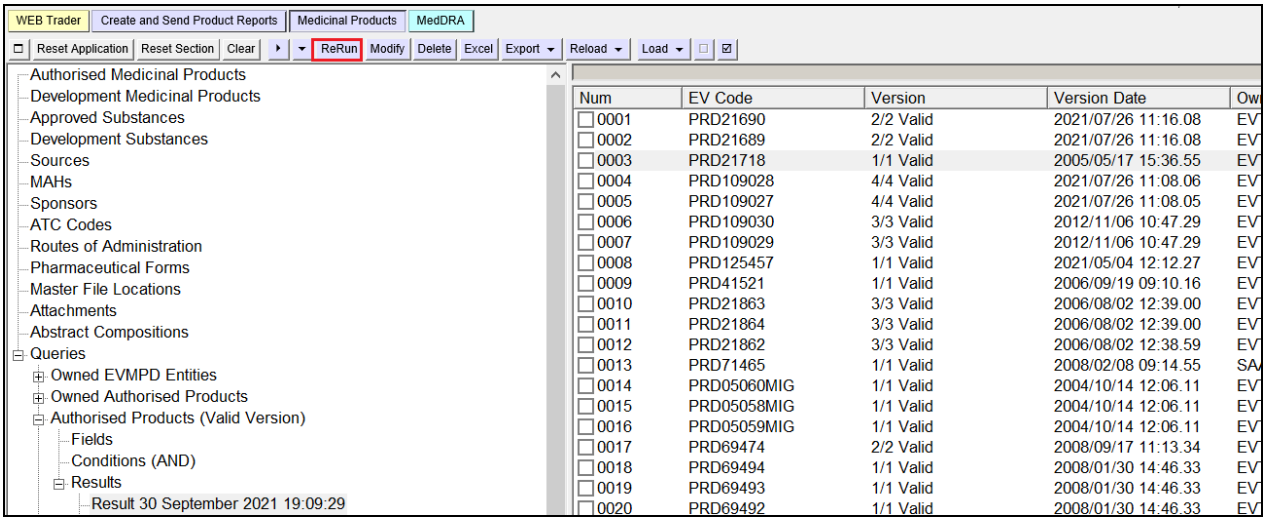


All the results of the different executions of the query in an active session will be stored until you delete them.

Delete To delete a result set, select it in the tree-view area and then click the 'Delete' button on the main menu in the dynamic section.

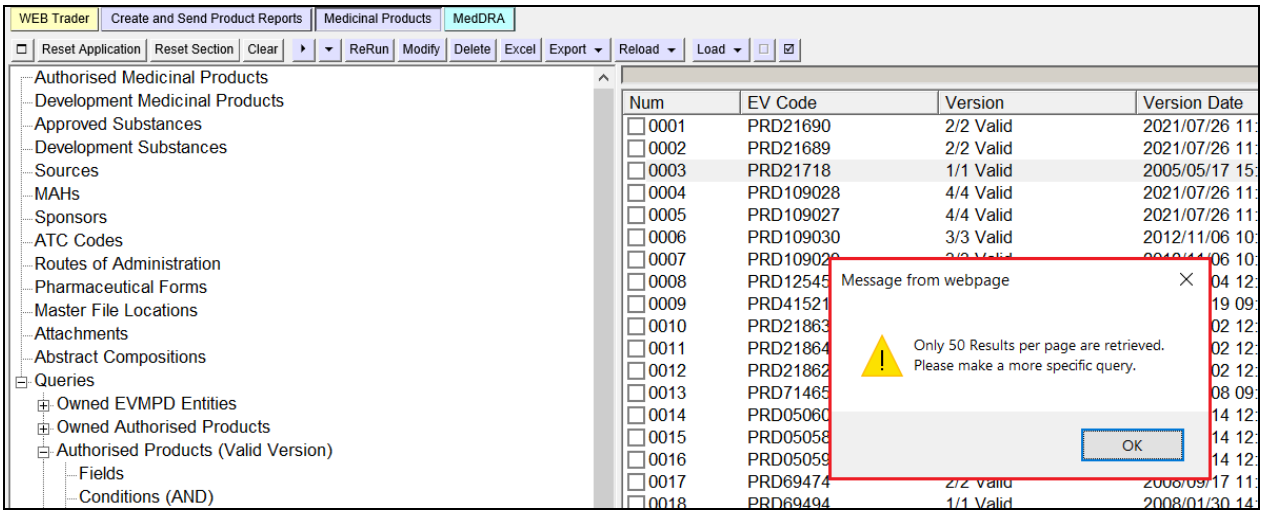


ReRun Another option available within the result set is to launch the same query again. To do that, click on the 'ReRun' button after selecting the result set.

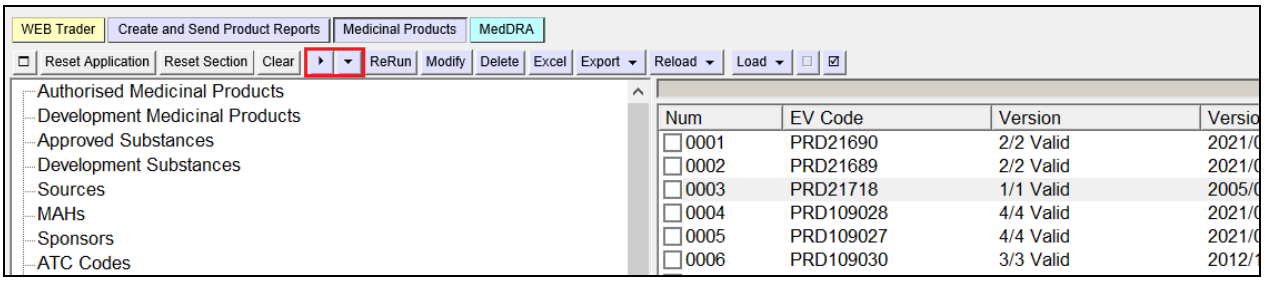


When running a query, the system will always return a maximum of 50 rows as a result.

When the number of results exceeds that limit, a message box is displayed.

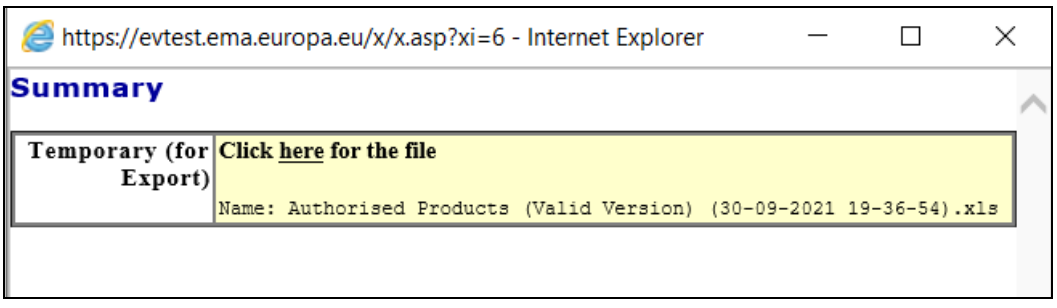


When making a more general query, where many results are displayed, this set of buttons is available to navigate among the complete results of an advanced query. They take you 'backwards' and 'forwards' on the results already displayed in your screen. The first two buttons replace the 50 rows displayed with the Previous/Next 50. The third button, with the arrow facing down, adds a new page of results to the results already displayed in your screen without removing them.



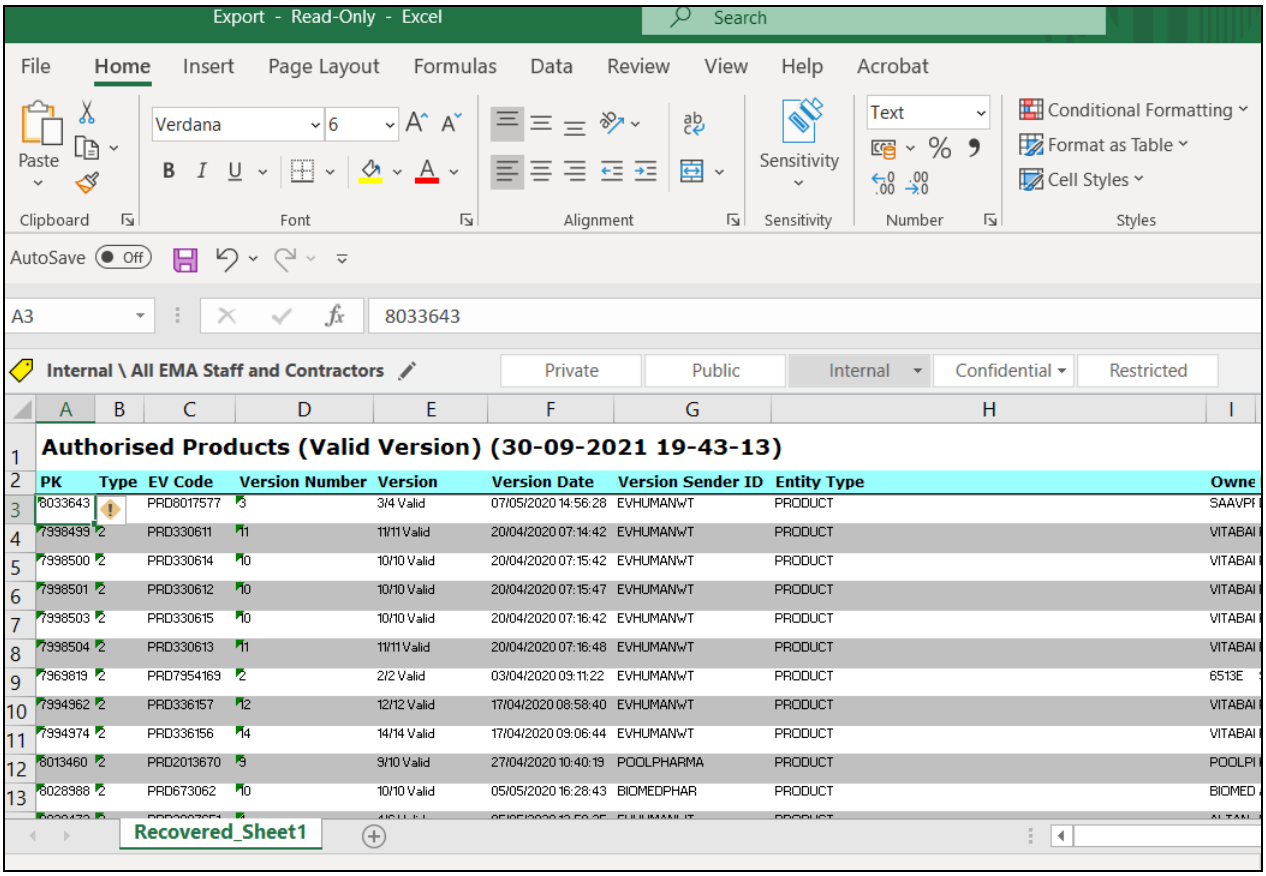
3.6.2.3.2. 'Run to Excel' functionality

Once you select the fields that you wish to see as the results of your query and specify the conditions of your advanced query, if you click on the **'Run to Excel'** button, a new window will open:



By clicking on 'here', another window will pop-up, allowing you to open or save the file.

Before the Excel file opens, you might be prompted to re-enter your login credentials.

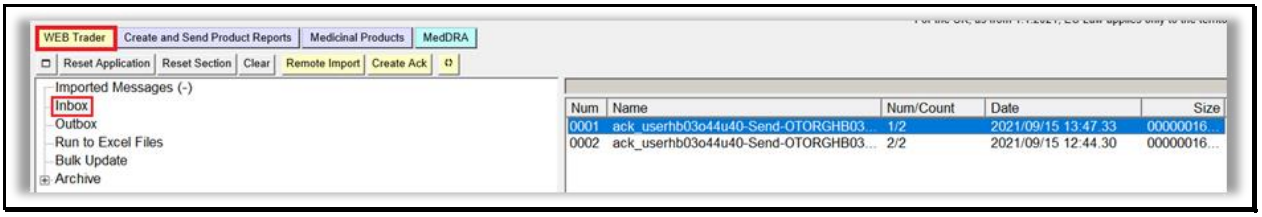


3.6.3. Immediate Query

An immediate query is a simple query performed automatically by EVWEB without the user's input when needed.

As any other query in the system, this will require EVWEB to connect to the remote system to retrieve the data. The difference is that in this situation, the query will be launched simply by selecting the item (no 'Run' buttons or specific user input).

This type of query is used for example in the 'Inbox' and 'Outbox' folders in the Web Trader section:



This type of query is loaded by EVWEB only once and then it is retained in the system's memory. If you believe that any change may have occurred in this section, you can tell EVWEB to reload the content of the list by clicking the refresh button.

The refresh button will be available on the dynamic section of the main menu.

3.7. Loading data

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

There are 4 different loading processes available:

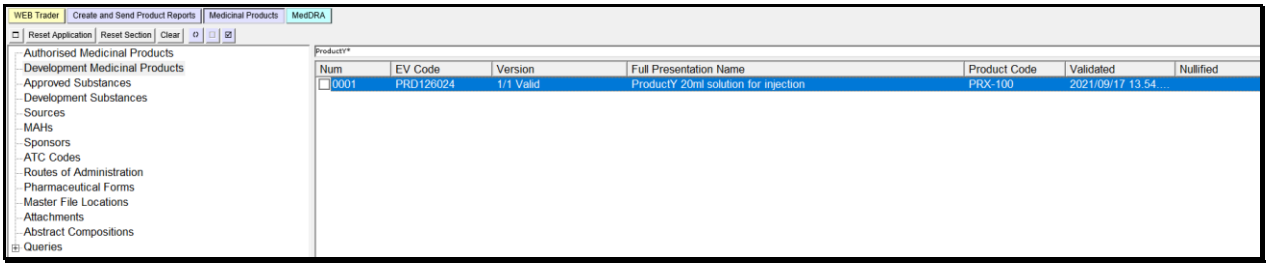
- load from the EVDBMS;
- load from a remote file;
- load from a local file;
- load from inside the EVWEB.

3.7.1. Load from the EVDBMS

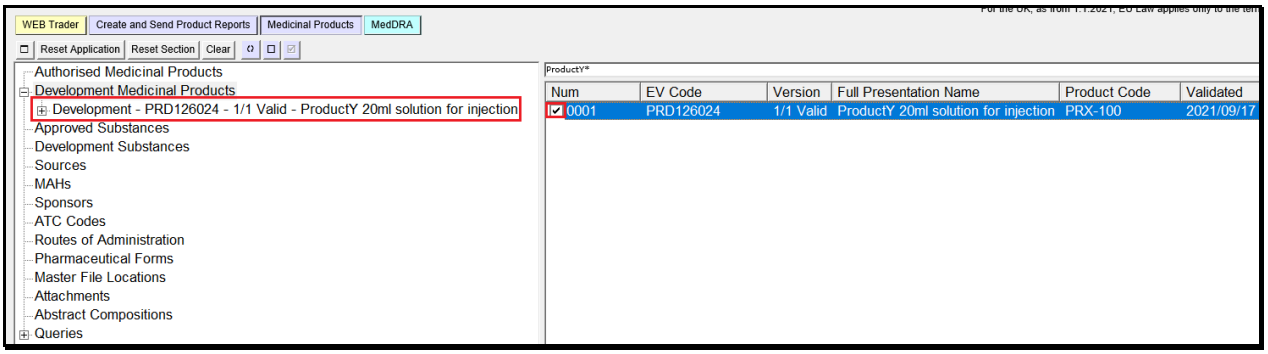
The load from the EVDBMS is available from the Load/Delete and the Select/Deselect checklists (see section *3.5.3. Checklists*).

3.7.1.1. Load/Delete checklist

As an example, you will see the checklist result of a simple query for a DMP with part of the name 'ProductY':



By selecting one or more of the checkboxes, the EVWEB will load the data from the remote system. This operation may take a while to be performed. This means that the result of the operation is not immediate. The data loaded will appear in the appropriate section of the tree-view area:



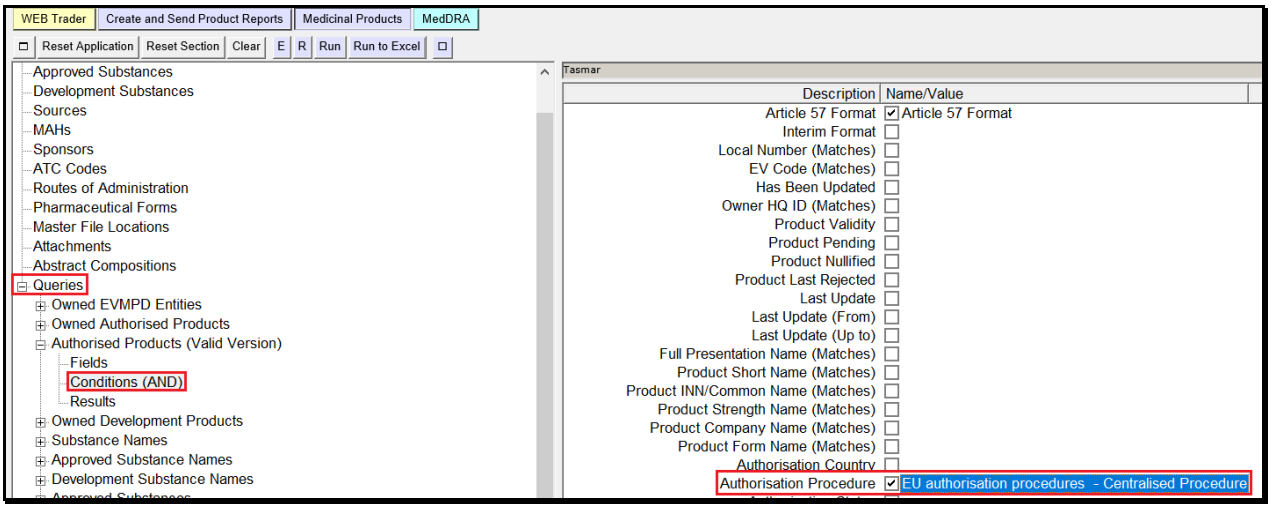
The section currently selected in the tree-view area may not be related to the section where the loaded items will be added.

As an example, when you have the results of an advanced query, the selected item in the tree-view area is the query result set itself. The loaded items will be loaded to a different section, depending on the main subject of the query (see section *3.4. Interaction between the tree-view area and active* area).

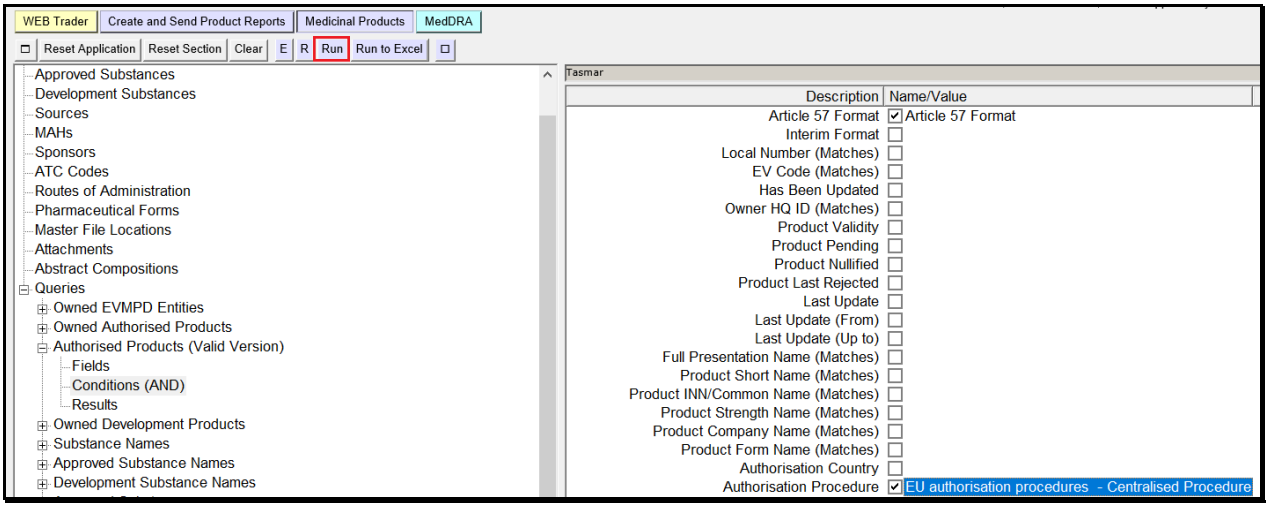
In case of failure of the load process, an error message box will be displayed.

3.7.1.2. Select/Deselect checklist

As an example, you will see the checklist result of an advanced query for AMPs authorised via the centralise procedure:

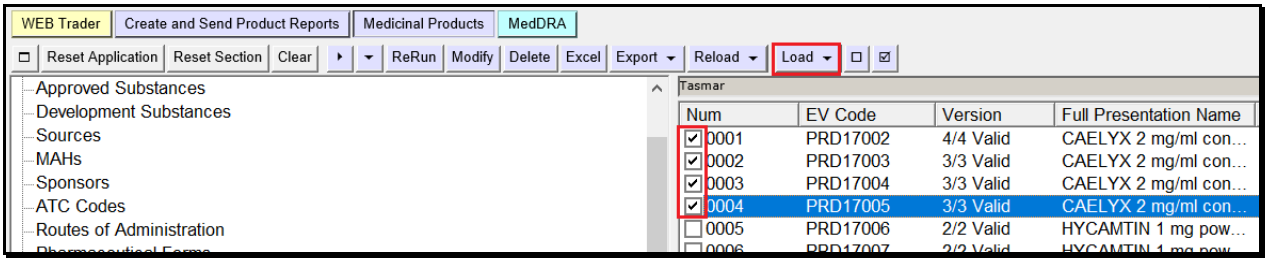


Once you select your condition(s), 'RUN' the query:

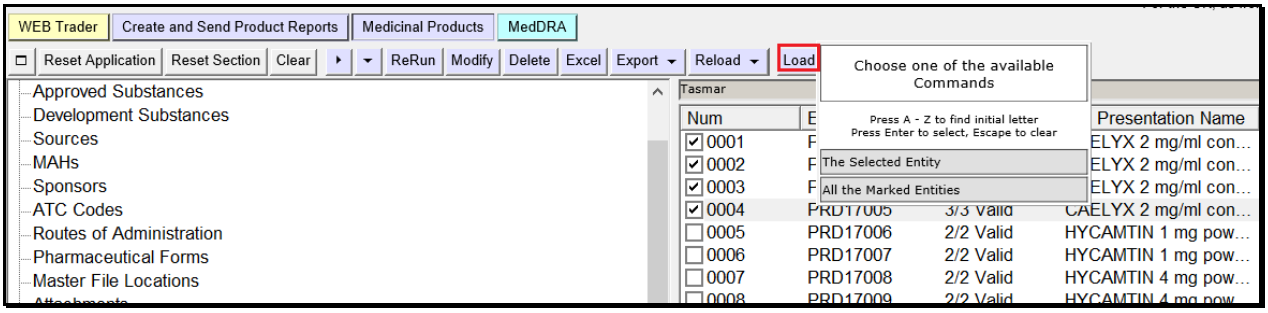


The results of your query will be displayed.

By selecting one or more of the checkboxes, you are indicating for which entries you want to perform a specific command. In this case, we wish to load the products in the tree-view area. We therefore need to use the 'Load' button:

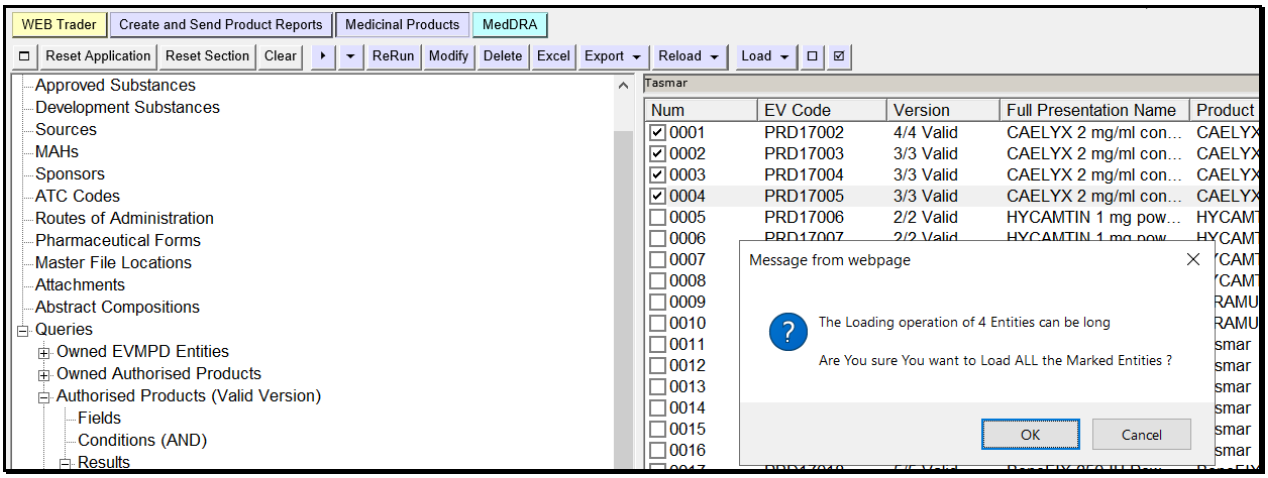


A pop-up menu will be displayed allowing you to choose which entries to load:

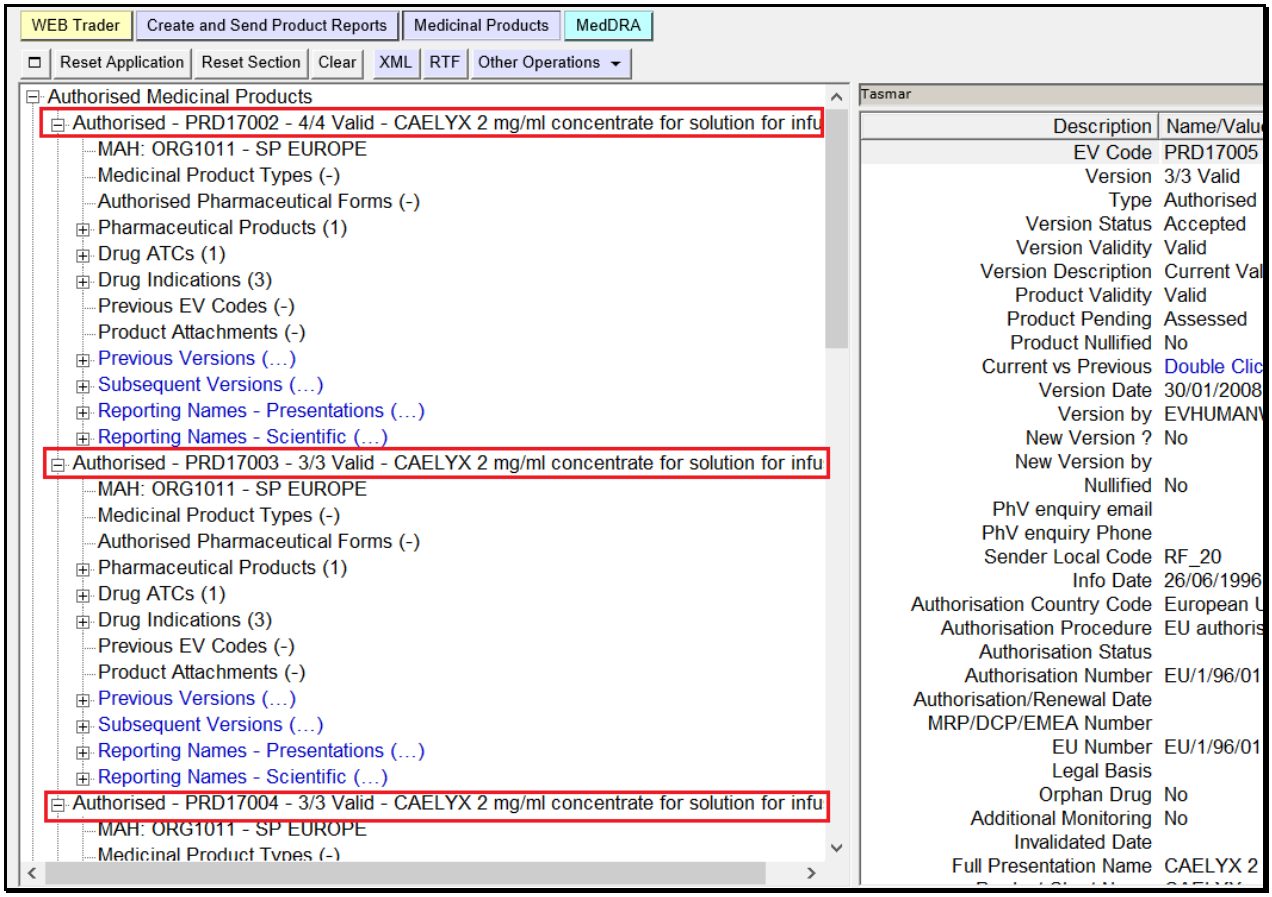


- All the Marked Entities (the ones marked with the checkbox)
- The Selected Entity (the last one selected before pressing the button, which is highlighted with a darker background colour)

In this case, we chose to load 'All the Marked Entities':



After selecting the two options, EVWEB will load the data from the remote system in exactly the same way as for the Load/Delete checklist (see section *3.5.5. Load/Delete checklist*).



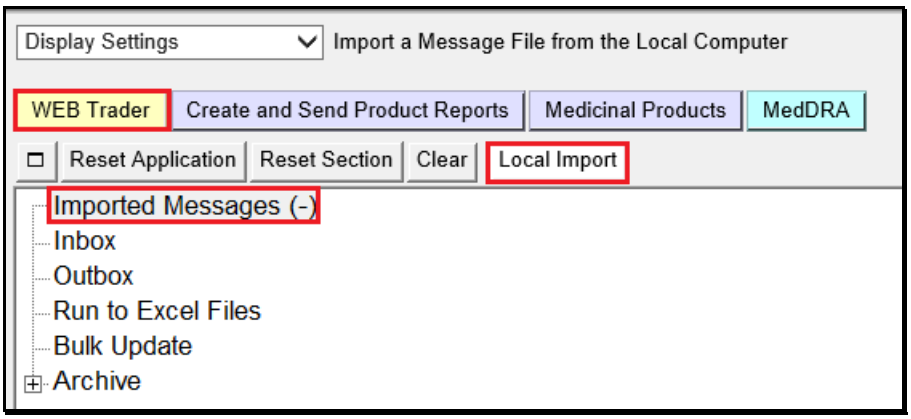
3.7.2. Load from a local file

This loading process is used to import data from an XML file available locally (your computer or your local network) into the EVWEB application. It is possible to load any kind of message (product or acknowledgement) handled by the EVWEB from a remote file.

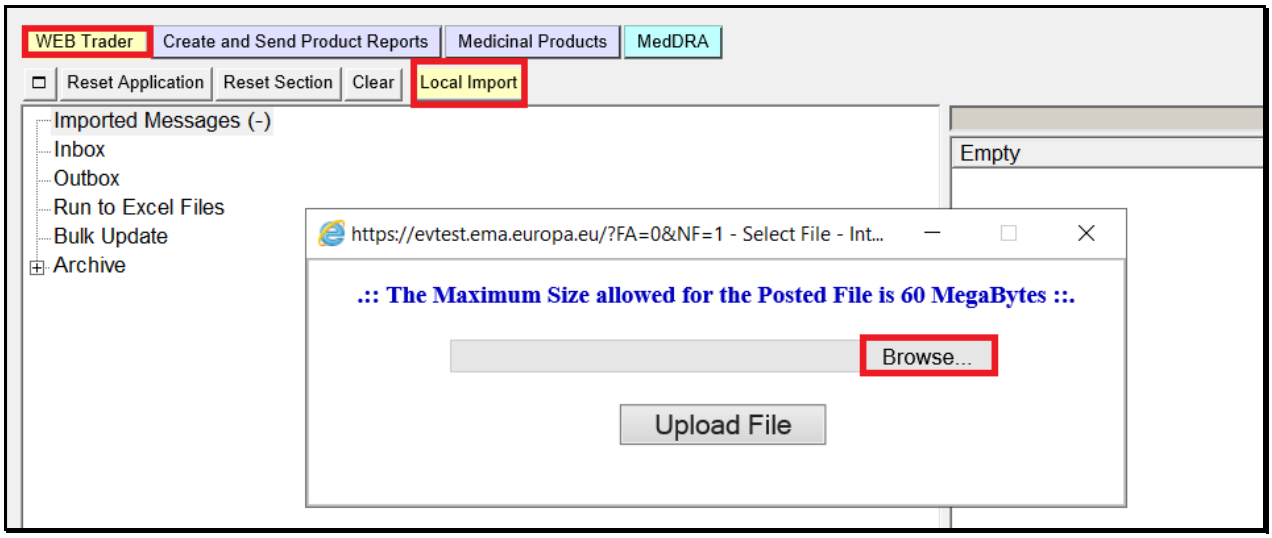
Load from a local file is available in different sections.

As an example, we wish to upload an XML file of an XEVPRM previously saved on our desktop.

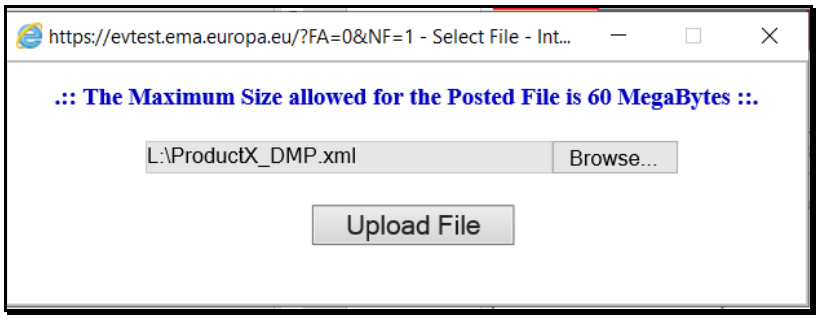
In the 'WEB Trader', click on 'Imported Messages' and then 'Local Import':

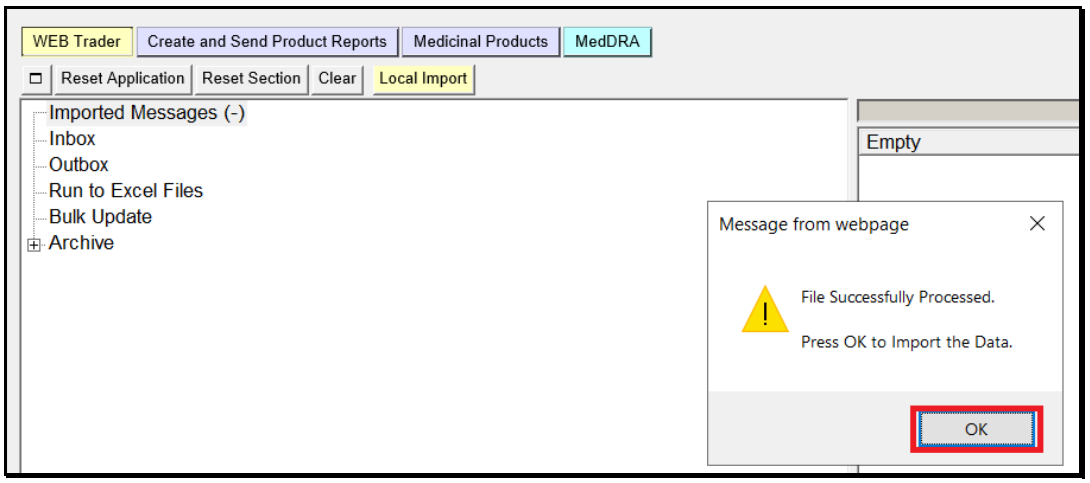


Local Import Clicking this button will open a pop-up new window that will allow you to browse and select a local file.



Once you have browsed and selected the file you want to import, click on the 'Upload File' button to activate the import process:

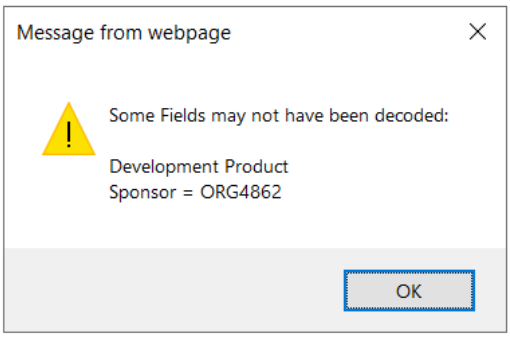




At the end of the import process, you will be prompted with a pop-up window allowing you to view the original file that has been imported.

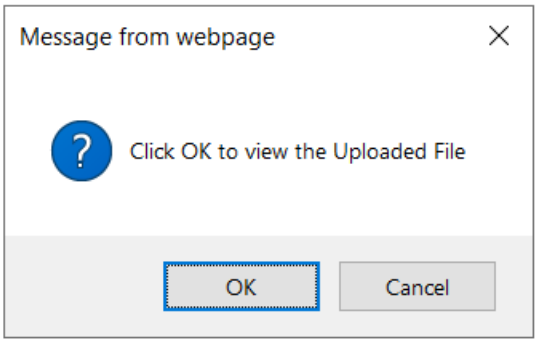
In case that some of the information in your XML file has not been decoded properly (for example the information referenced in the product entity could not be found in the environment where the XML file

is uploaded), a pop-up message will be displayed. In our case, the sponsor organisation EV code referenced in the product entity in our XML file does not exist:

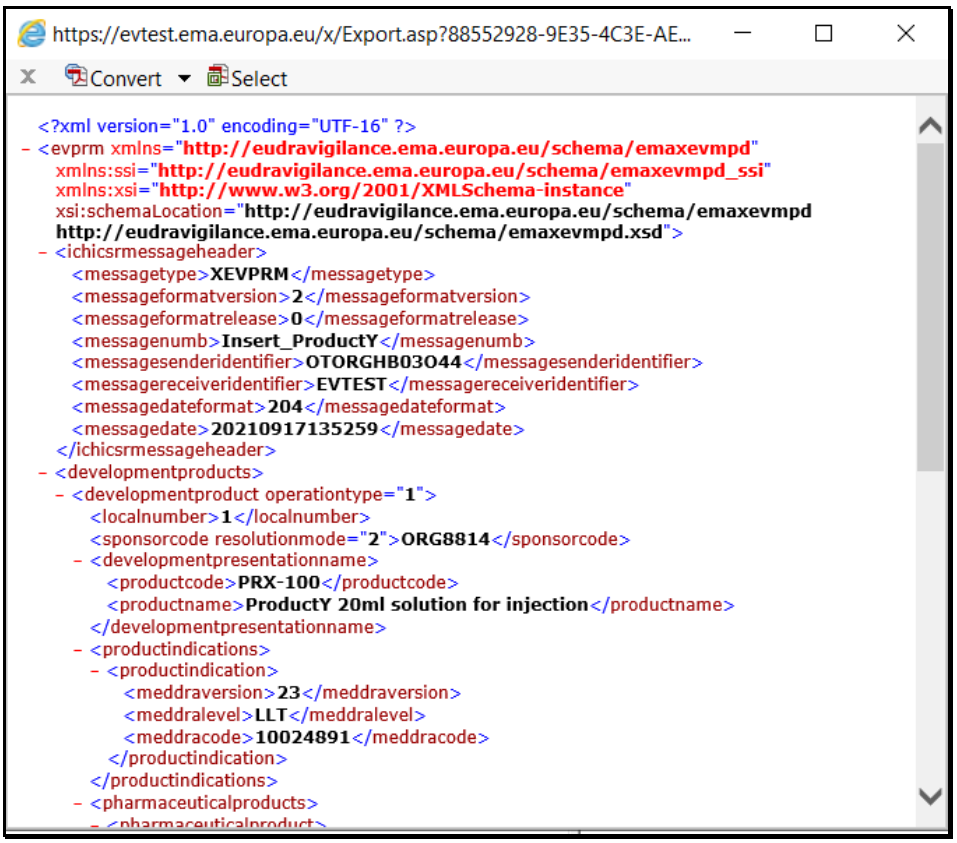


You can dismiss the message by clicking on 'OK' or the 'x' in the right-hand corner.

You will be presented with the below message:

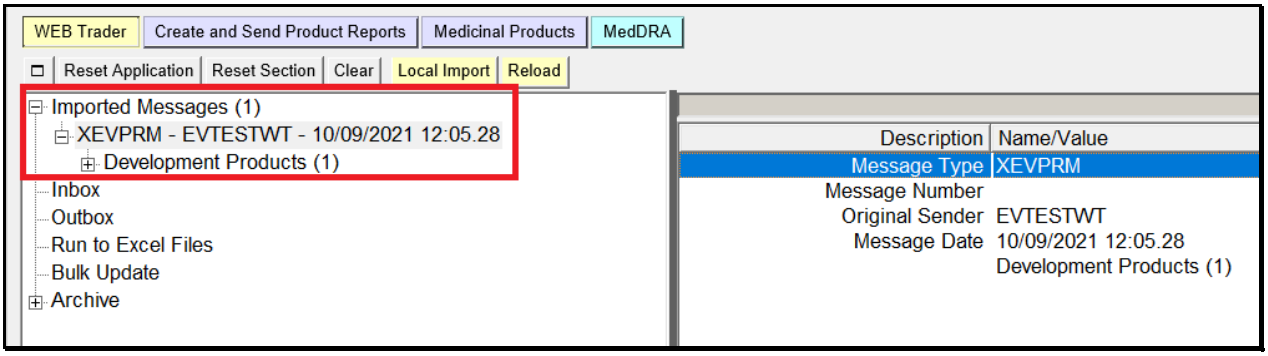


By clicking on 'OK', you will be able to view the file in the XML format:



The imported data are displayed in a specific section of the tree-view area.

In our example, the data are displayed under 'Imported Message (s)':



See section *3.4. Interaction between the tree-view area and active area* and *3.10.1.1. Reloading an XEVPRM* for reloading an imported XEVPRM.

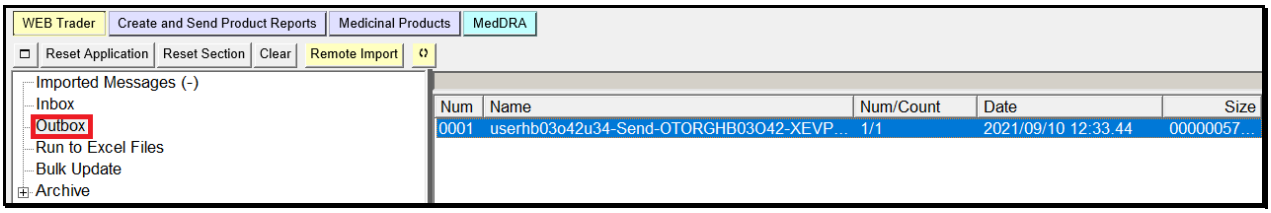
3.7.3. Load from a remote file

This loading process is used to import data from an XML file from a remote system into the EVWEB application. It is possible to load any kind of message (product or acknowledgement) handled by the EVWEB from a remote file.

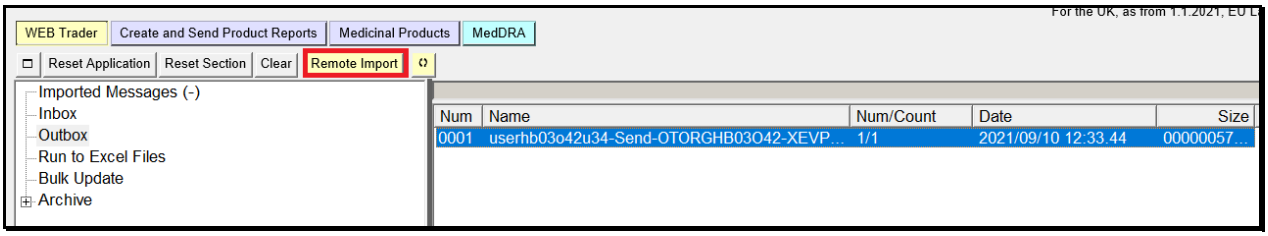
Loading from a remote file does not have a standard procedure to be performed. This depends on the section where this function is available.

As an example, the below screenshots demonstrate the import function available in the **'Outbox'** section. This functionality will allow us to retrieve an XEVPRM already submitted.

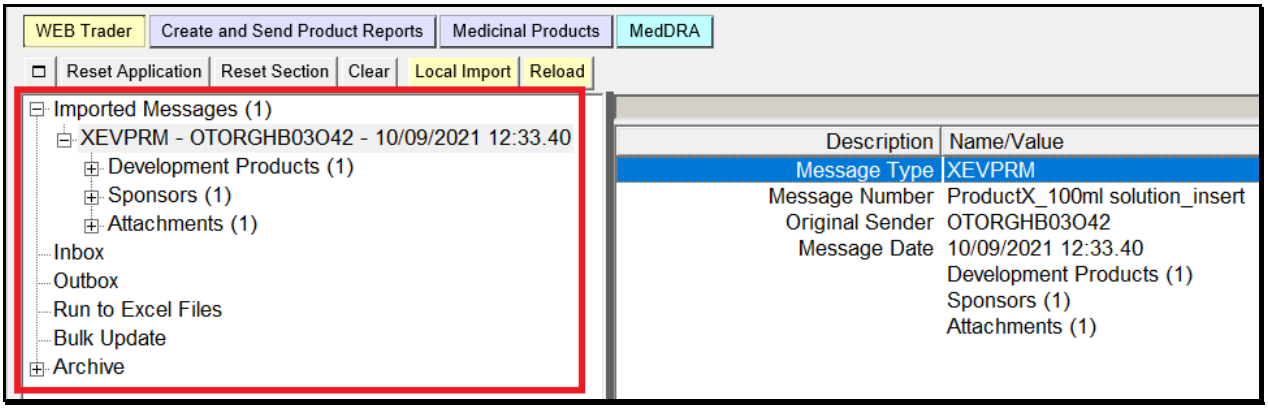
In the 'WEB Trader' section, click on 'Outbox'; the list of XEVPRMs submitted from your organisation ID will be displayed:



By selecting one of the file items in the list view of the active area, you will be able to import it in EVWEB by pressing the 'Remote Import' button available on the dynamic section of the main menu:



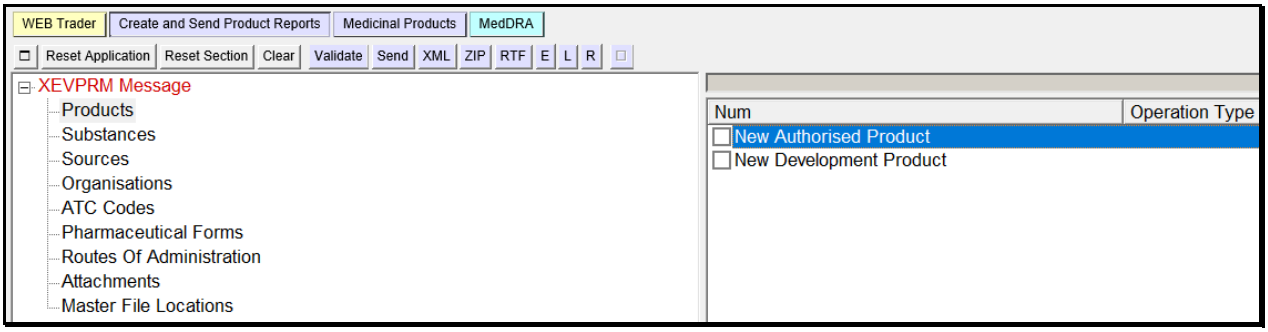
The imported data is displayed in the relevant section of the tree-view area:



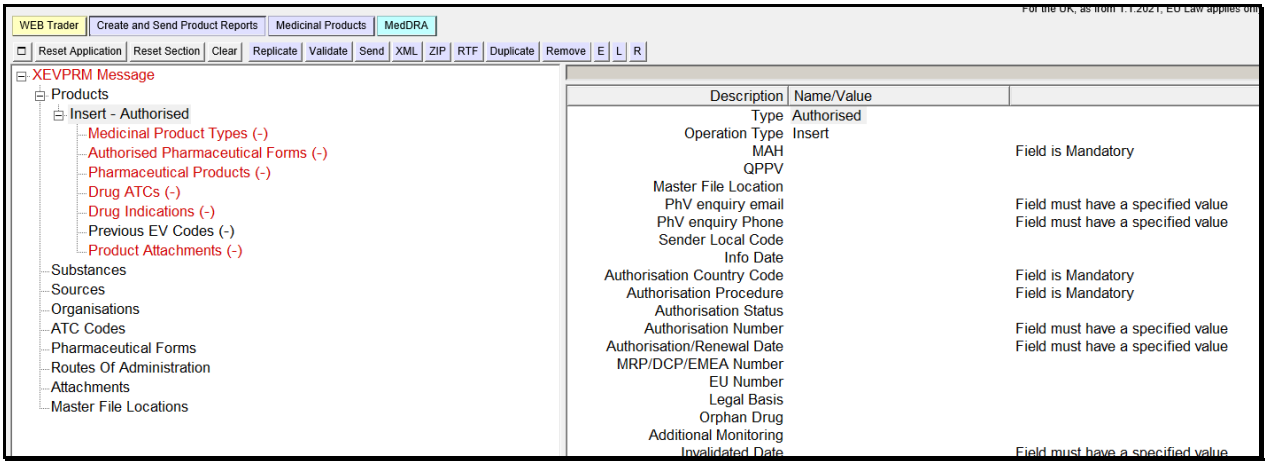
3.7.4. Load from inside the EVWEB

This operation does not actually load any external data. It creates new items in a data entry section (i.e., 'Create and Send Products') and eventually completes the newly created items with data taken from others section (i.e. 'Medicinal Products' – Update operation).

As an example of this loading process, we will see the creation of a New Authorised Product in the 'Create and Send Products' section.



Clicking on the checkbox will create the Authorised Product in the section currently selected in the tree-view area:



As you can see, all the fields are empty because in this case, the newly created section is a new Authorised Product (which is supposed to be completed by the user).

In other situations (e.g., when using the 'Update'(2)' operation type), you may find that some fields are already completed.

3.8. Pop-up Commands

In certain sections, commands are grouped together as a single pop-up menu.

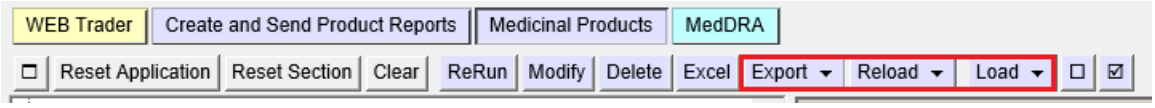
In these cases, the command, which triggers the pop-up has a small arrow to the right of the button description name.

By clicking on the button, the pop-up appears, and displays the commands available.

After selecting one of the commands available, the behaviour of the application is the same as any other normal command.

The pop-up can be closed by clicking the escape (ESC) key or by clicking anywhere outside the pop-up.

As an example, some of the commands available on the result of the products queries are grouped in three pop-up menus:

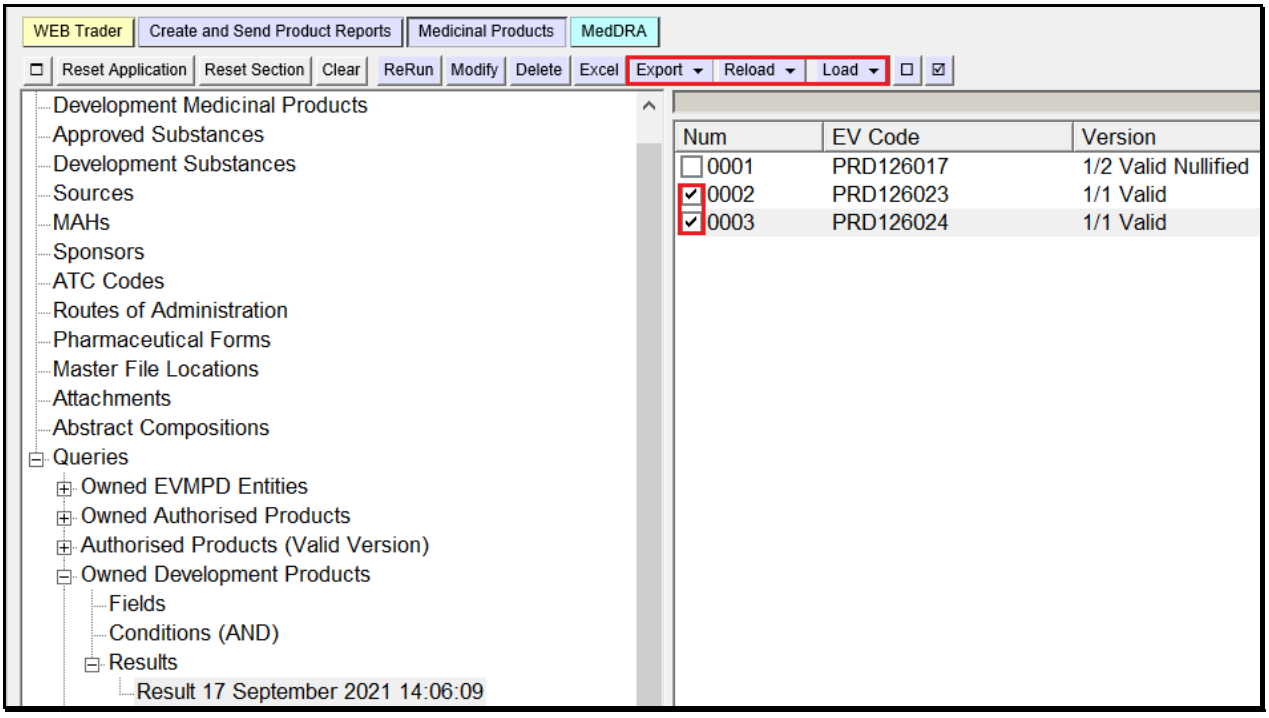


3.9. Batch Commands

When a Select/Deselect checklist is displayed (for example as a result of a query), the commands available to interact with the entities displayed in the checklist have a special behaviour.

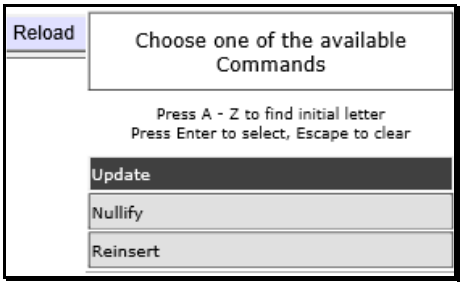
The underlying action, instead of being performed on a single entity (the selected one), is performed as a 'batch' on all the entities marked with the checkbox.

As an example, the commands available on the result of the products query are grouped in three pop-up menus:

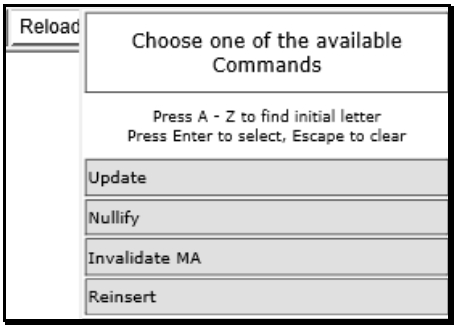


After the required product entities, clicking on the 'Reload' button will show the possible commands.

The following commands are available for owned development product entities:



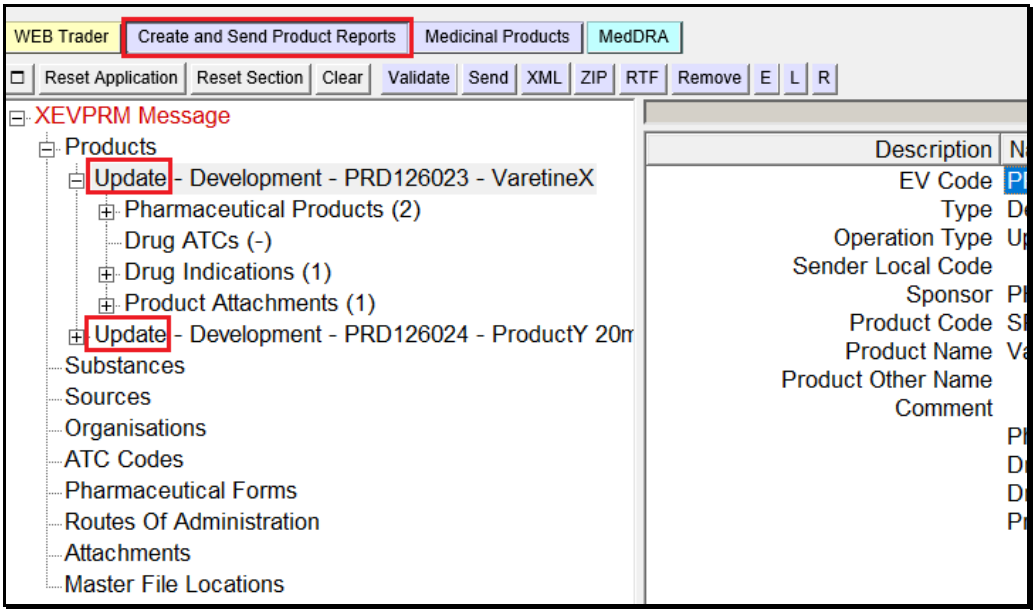
The following commands are available for owned authorised product entities:



If some of these commands are not available for the products selected as a result of your advanced query, this may be due to the fact that you are not logged on to EVWEB under the ID of the organisation that owns the product entries. You cannot update/nullify DMPs and update/nullify/invalidate AMPs that your organisation does not own in the XEVMPD. In such case, usually only the 'Reinsert' command will be available.

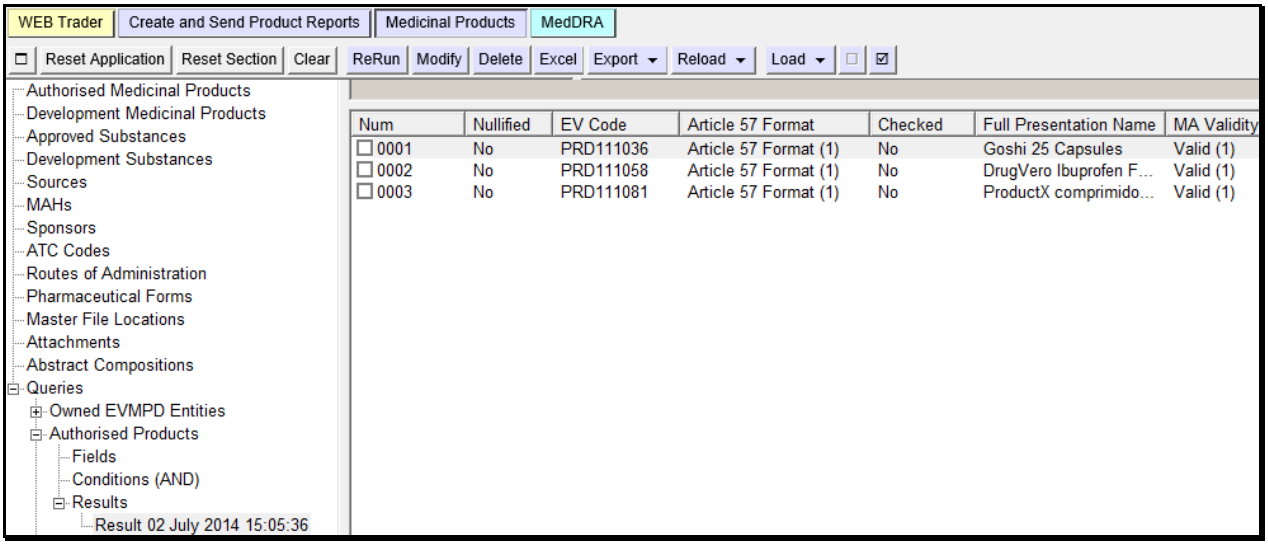
By clicking on the selected command/operation type, the application will load all the selected (marked with the checkbox) entities and then create an XEVPRM for each one of them in the 'Create and Send Products' section. The operation type assigned to the entities will correspond to the command selected.

In the below example, the command 'Update (2)' was used for the selected development medicinal products:w @q



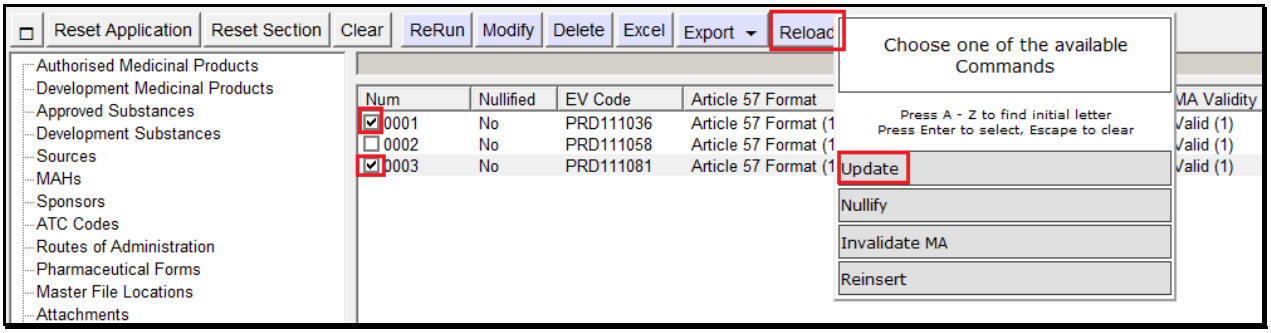
3.9.1. Create an XEVPRM with various commands - practical example

In this example, we performed an advanced query on all AMP entries referencing MAH 'PharmaX' as the MAH with the following result:

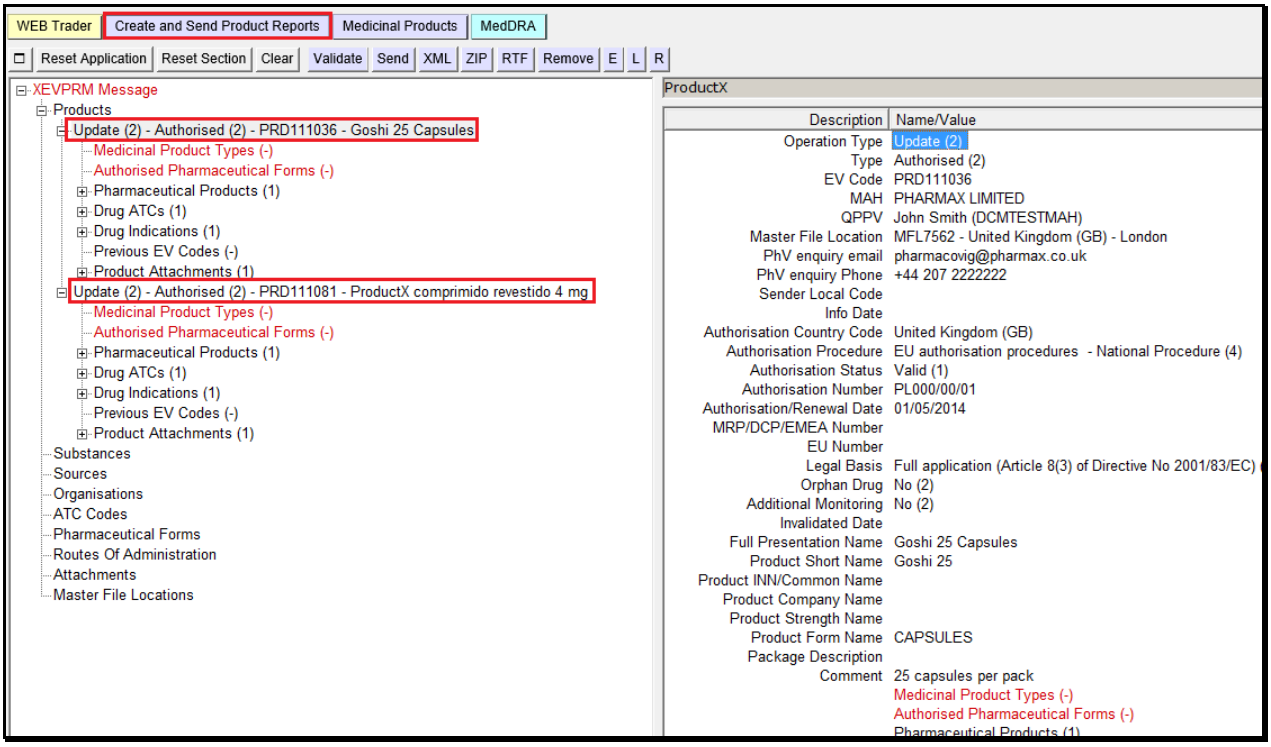


Two of the AMP entries need to be amended using the command/operation type 'Update (2)' and one will need to be invalidated using command/operation type 'Invalidate MA (6)'.

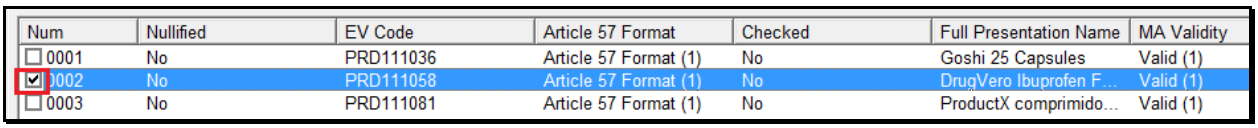
We select the two AMP entries which need to be updated and select the applicable command under 'Reload':



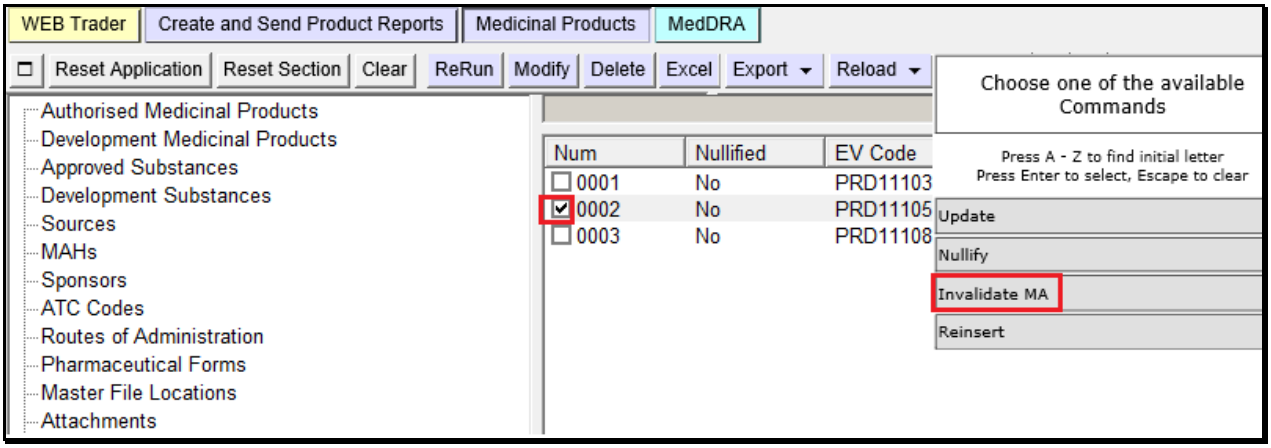
Those two AMPs are now available in the 'Create and Send Product Reports' with the command/operation type 'Update (2)':



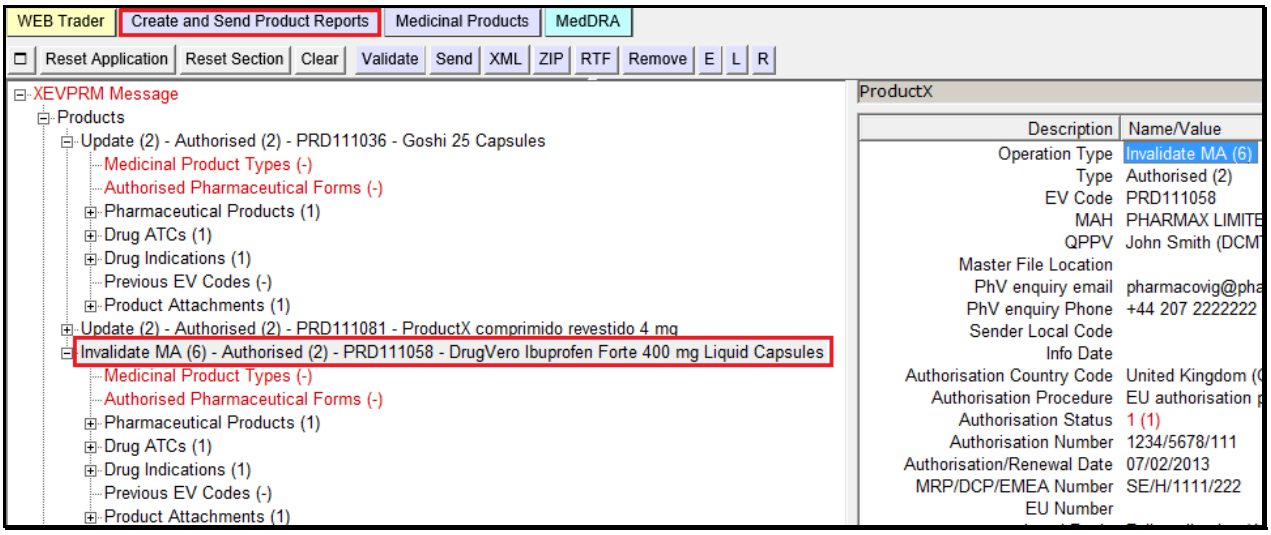
To add the AMP to be invalidated in the same XEVPRM, we must go back to the 'Medicinal Products' section and select the product to be invalidated:



Then select the applicable command under 'Reload':



This AMPs is now available in the 'Create and Send Product Reports' with the command/operation type 'Invalidate MA (6)', together with the two AMPs with the assigned command/operation type 'Update (2)':



We can now amend all the AMP entries as applicable, validate and send the XEVPRM.

3.10. WEB Trader Functions

Please note that some of these functions will only be available to WEB Trader users.

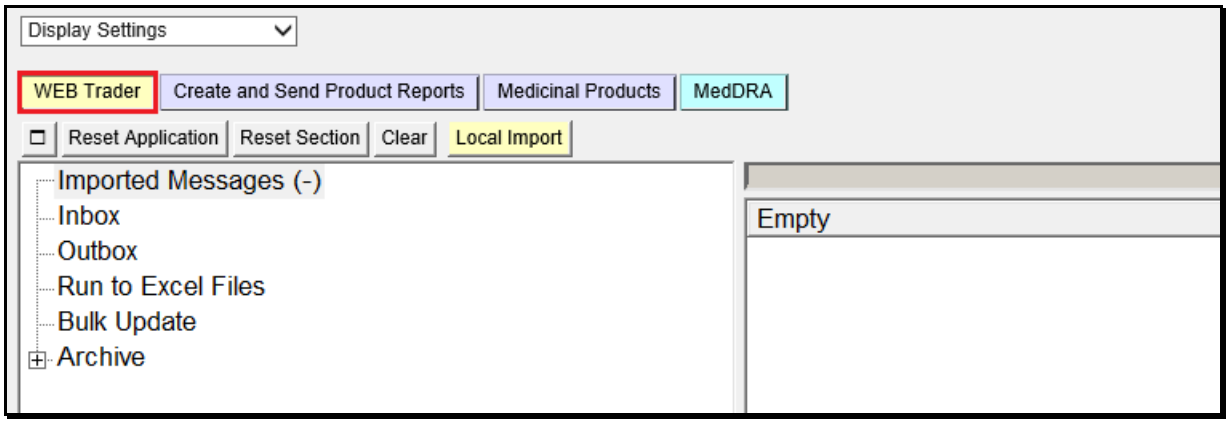
The WEB Trader section of the application will allow WEB Trader users to keep track of sent product messages and received acknowledgement messages and also to retrieve XML files created as a result of changes performed via the XEVMPD Bulk Update Manager tool (see section *3.10.4. Bulk Update)*.

The WEB Trader section of the application will also allow any user to import in the EVWEB product and acknowledgement messages from his/her local computer.

The tree-view area displays three different sections:

- Imported Message (s)
- Inbox
- Outbox

- Run to Excel Files
- Bulk Update
- Archive



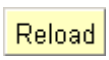
3.10.1. Imported messages

The section 'Imported Messages' will display the message(s) that you imported from your local computer or from EVWEB.

For information how to import messages, see sections and *3.7.2. Load from a local file* and *3.7.3. Load from a remote file*.

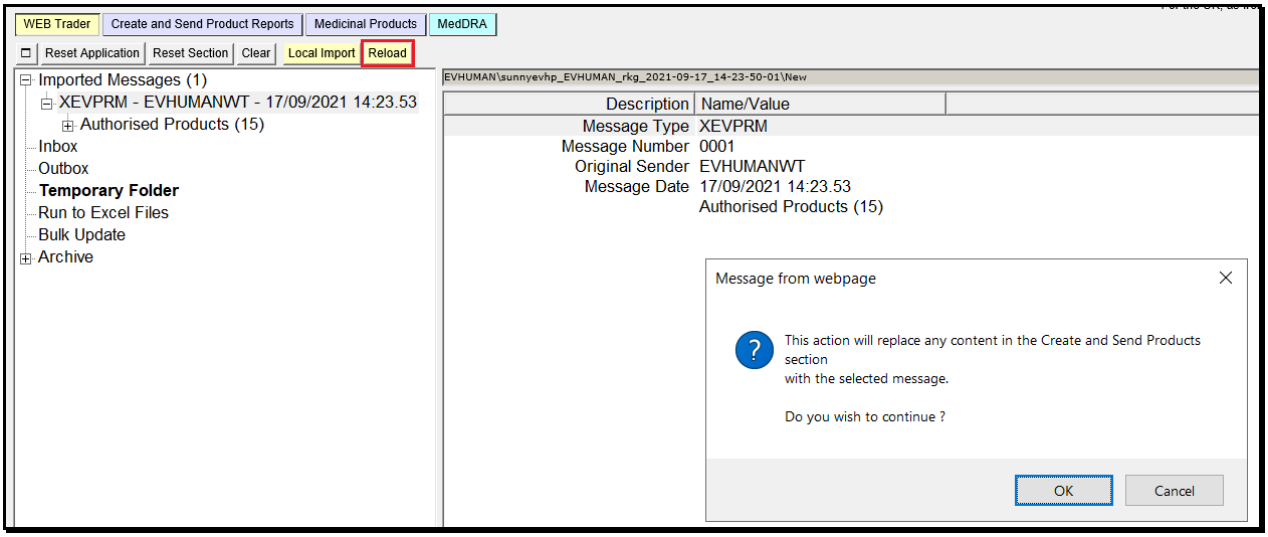
When you click on the imported file, the 'Reload' button becomes available in the dynamic area of the main menu:

3.10.1.1. Reloading an XEVPRM in the 'Create and Send product reports' section

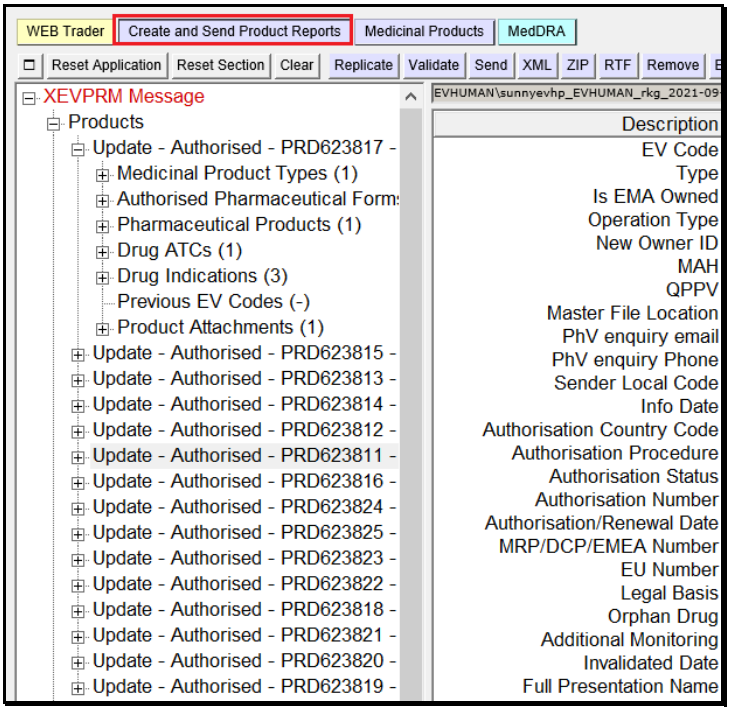


This button will enable you to reload the content of an XEVPRM in the 'Create and Send Products' section, allowing you to continue and/or complete, validate and send the XEVPRM.

When you click on the 'Reload' button a new window will open informing you that performing this action will replace any content you may have in the 'Create and Send Product Reports' section:



Once you confirm that you wish to continue by clicking on 'OK', the products with the applied changes will be displayed in the 'Create and Send Product Reports' section for your review:



Please note that any products that you may have had in this section prior to re-uploading the imported file will be deleted!

You will be able to review the information in your XEVPRM, assign the XEVPRM Message number (it is not reloaded from the original file), validate and send the XEVPRM.

3.10.2. Inbox and Outbox

The Inbox and Outbox sections are two immediate query items that will display respectively the content of the Inbox and Outbox folder associated to the Web Trader.

These folders work in a similar way to the Inbox and Outbox folder of almost every email software (such as Microsoft Outlook®).

In the **Inbox**, you will find:

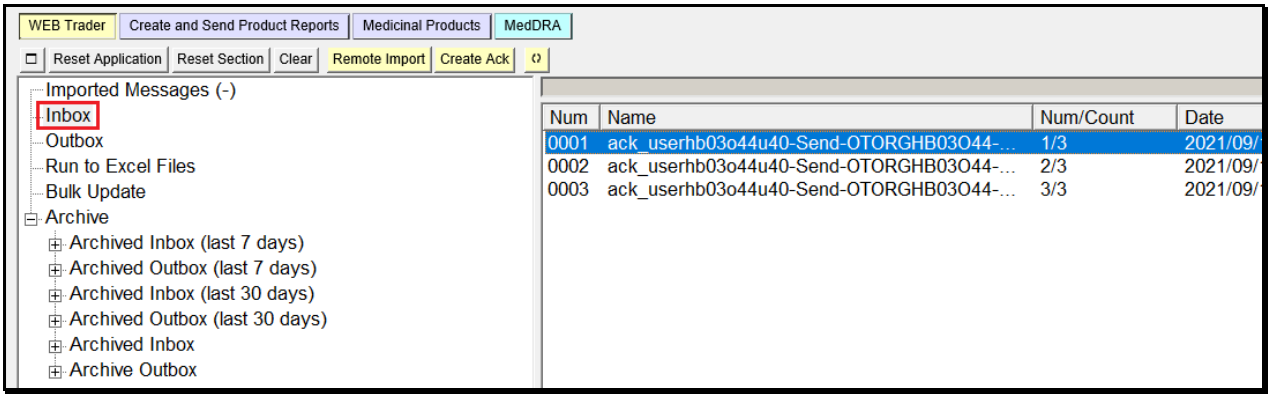
- Acknowledgement messages sent to your organisation's ID specified as a receiver. All messages received, regardless of the type, will be displayed in your Inbox.
- Acknowledgement messages that the XEVMPD has sent to you after submitting an XEVPRM.

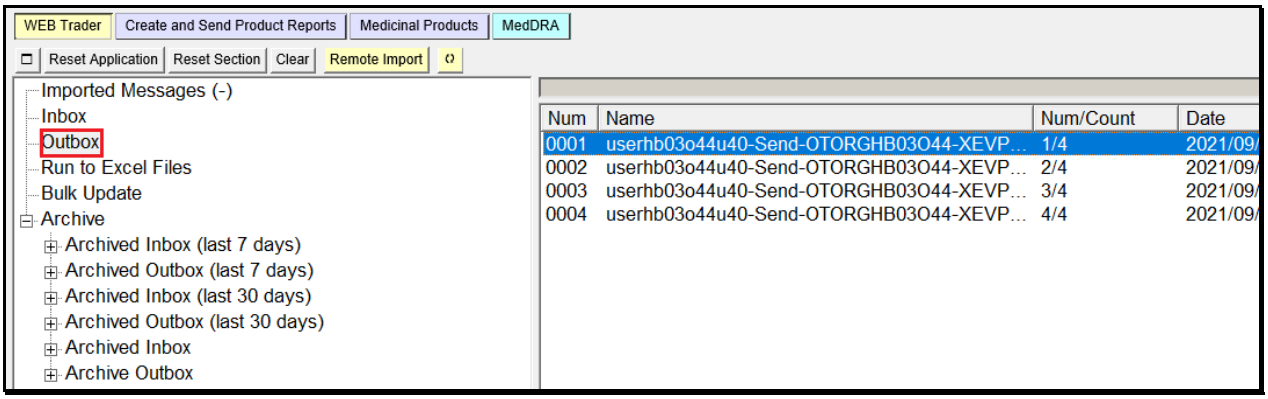
The **Outbox** will display the XEVPRMs sent by your organisation to the XEVMPD.

Please note that you **are not able to modify the content of your Inbox/Outbox**.

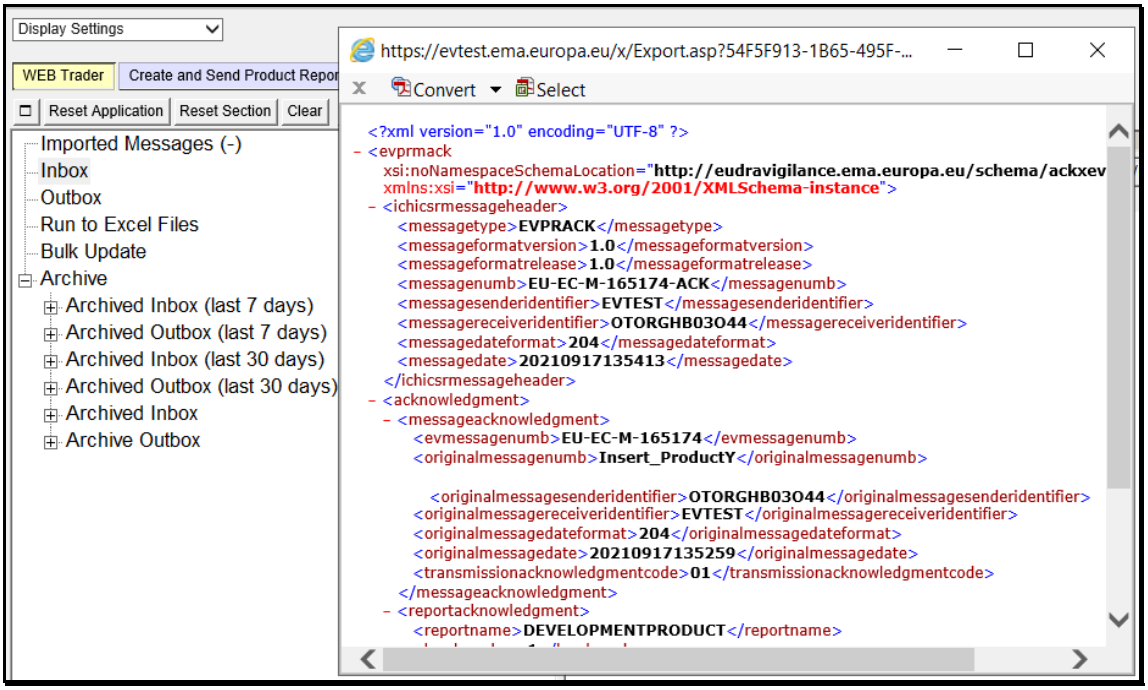
The system automatically archives messages in your Inbox and Outbox **on daily basis.**

To see the content of your Inbox or Outbox, just select these items in the tree-view area. Their content will be displayed in the Active area:





To open the individual XEVPRM/XEVPRM ACK, just double click on each item. A new pop-up window will be displayed showing the content of the XEVPRM/XEVPRM ACK:



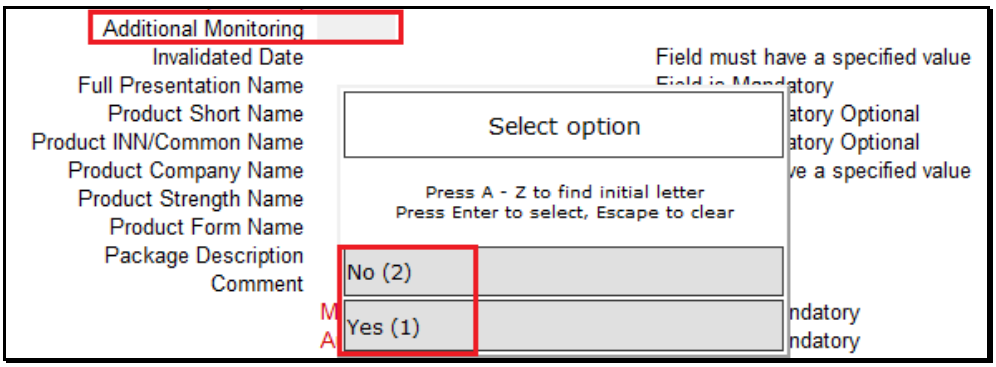
In some browsers, the XML file is displayed directly.

You can perform different actions on these files:

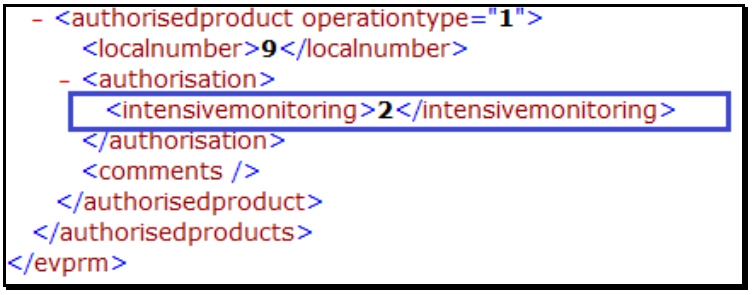
- show their content in Internet Explorer without any transformation, or
- import them in to EVWEB and decode the content in a user-friendly way.

A Product Message (or Acknowledgement Message) in the XML format contains information in a coded form (fields requiring MedDRA terms, pharmaceutical forms, lookup fields, etc.), therefore, when you see the message in its original format, you see the coded information instead of the descriptions used in EVWEB (i.e. 1/2 instead of 'Yes'/'No'):

For example, the values for 'Additional monitoring' field in EVWEB are displayed as Yes/No:



The values in an XML format are shown as 1 or 2, depending on which value is selected (in our case, the value 'No' was selected in EVWEB:



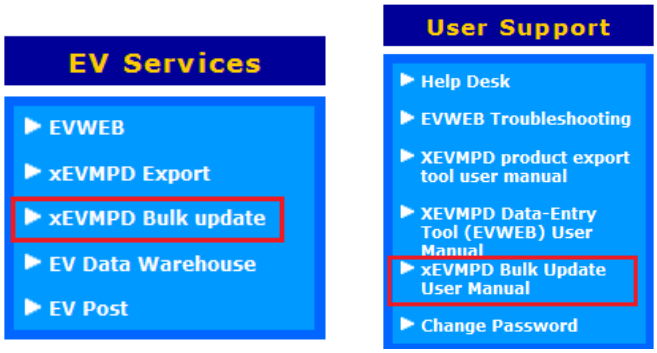
3.10.3. Run to Excel Files

When you export results in Excel using the 'Run to Excel' button during an advanced query, and the condition selected as "owned", the result of the query will be displayed in this section:

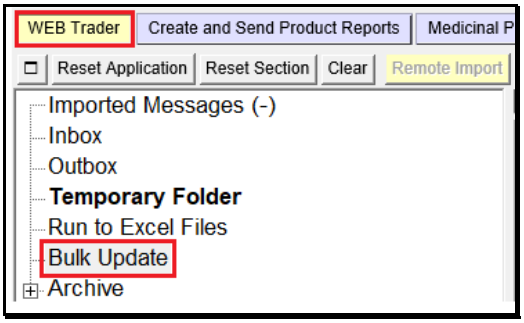
3.10.4. Bulk Update

EVWEB users can use the XEVMPD Bulk update Manager tool to perform bulk data operations on multiple products owned in the XEVMPD by their organisation. The tool facilitates editing key data fields and supports the re-submission of this data to the XEVMPD.

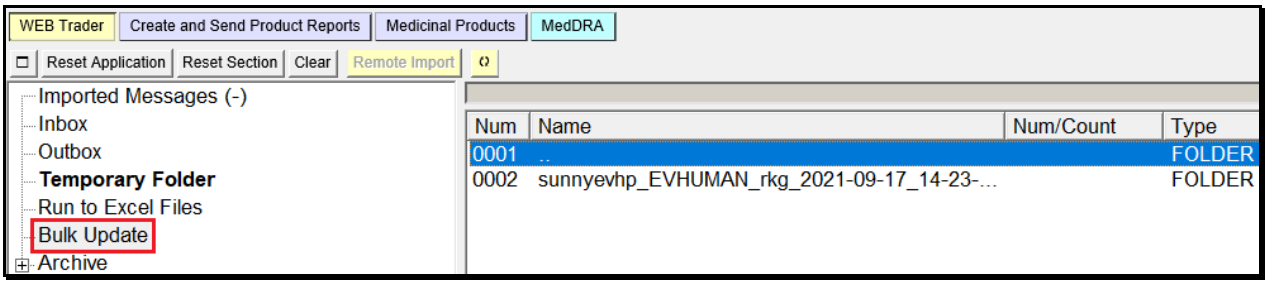
The tool, together with the corresponding XEVMPD bulk update manager user guide, is available in the restricted area of the EudraVigilance website.



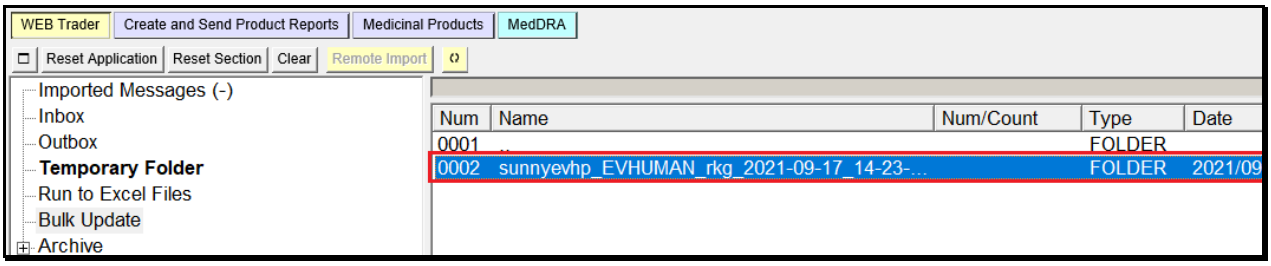
Once a user has generated the updated product set using the Bulk Update Manager tool, a series of files will then become available in the 'Bulk Update' sub-section of the Web Trader section of EVWEB:



To retrieve the files in the 'Bulk Update' section, click on 'Bulk Update'. The available files will become visible in the active area:

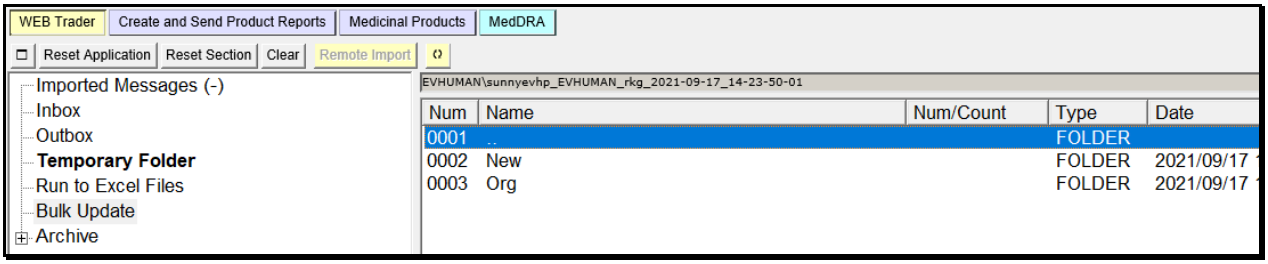


Select the file you created so it is highlighted in blue:

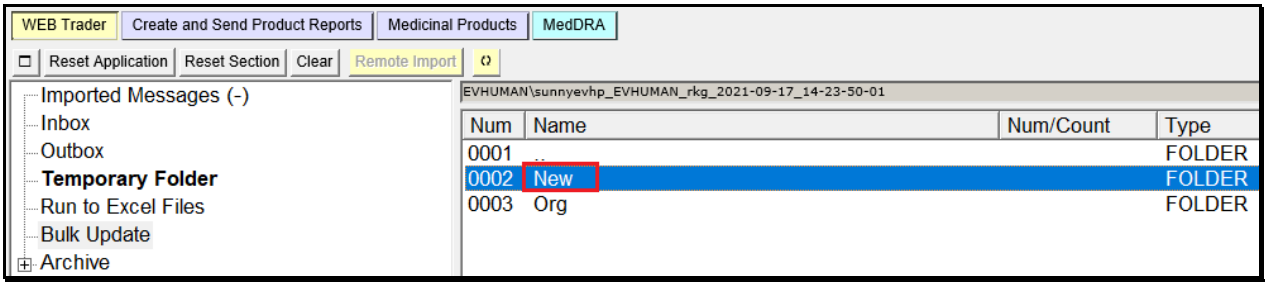


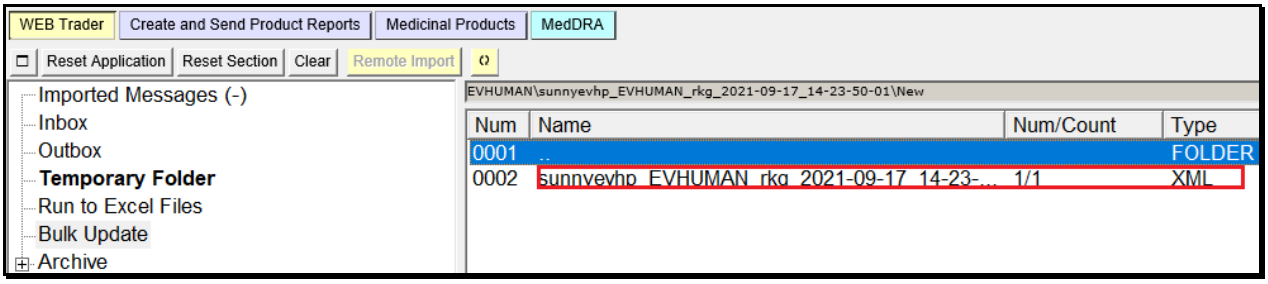
Double-clicking on the file; two folders will be displayed in the active area:

- The new file ('New'), generated as a result of the bulk update operations/changes you applied to the selected products;
- The original ('Org') file, containing the product set prior to performing the bulk update operations/changes:

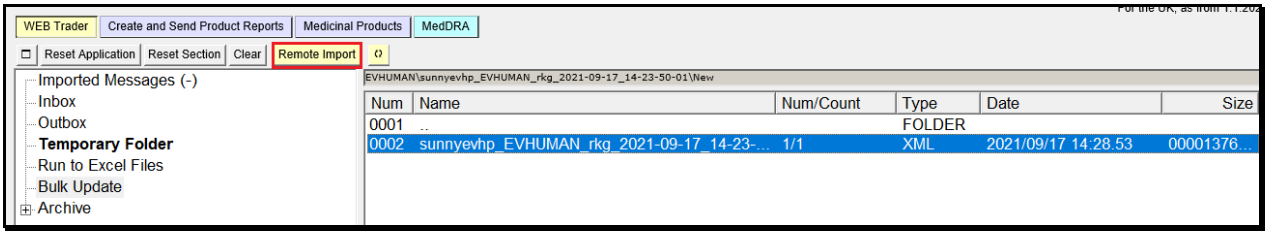


Double-click on the 'New' folder and the XML file will be displayed:

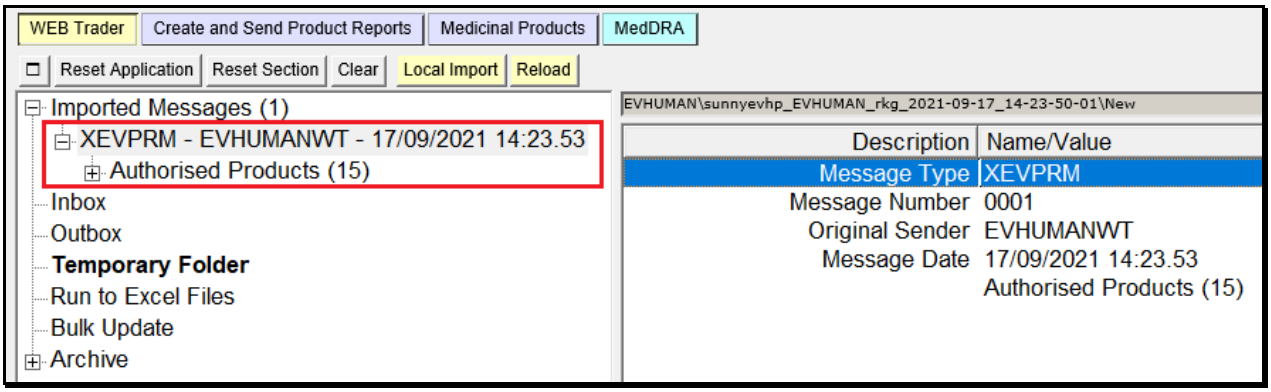




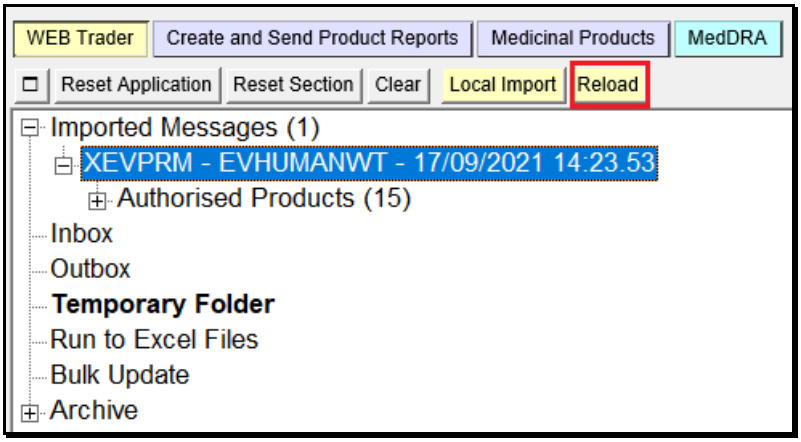
Click on the XML file (so it is highlighted in blue) and the 'Remote Import' functionality will become available:



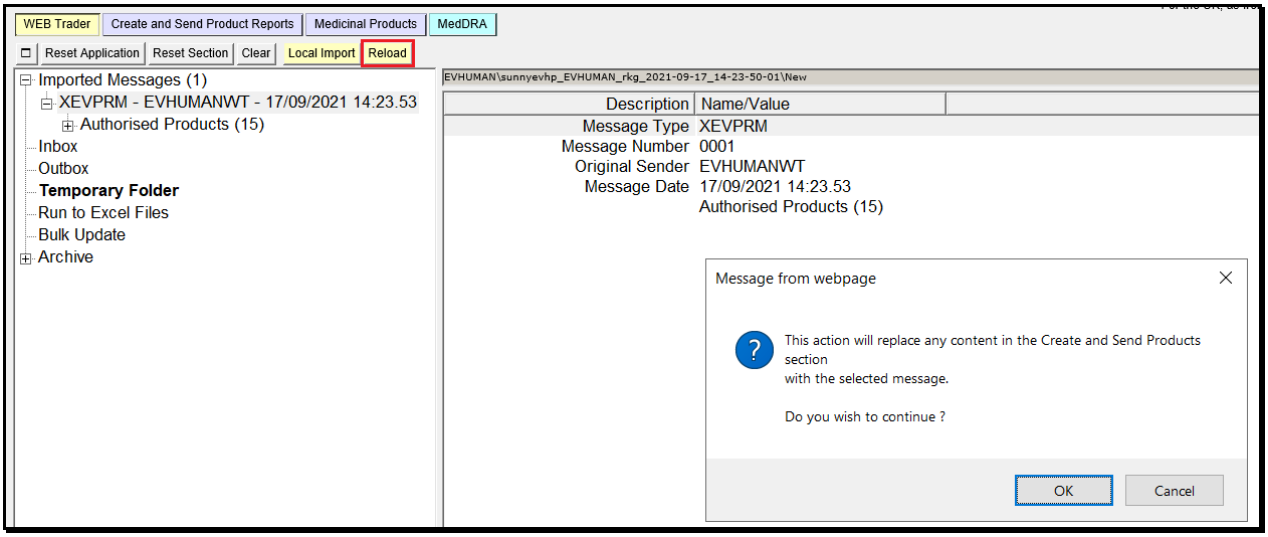
Once you click on the 'Remote Import', the file will become available in the tree-view area:



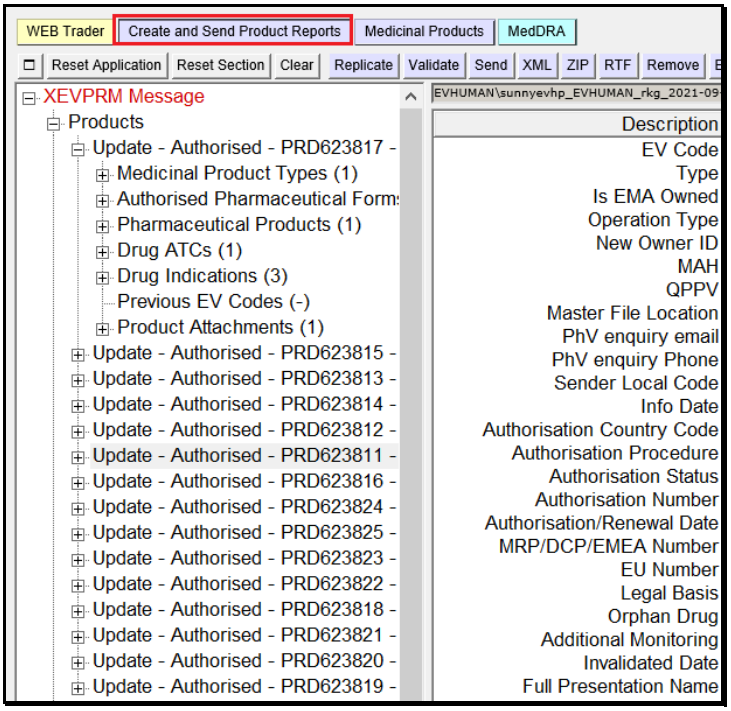
To import the products in the 'Create and Send Product Reports' section, click on 'Reload':



A new window will pop-up asking for confirmation that you wish to re-load the content of the XEVPRM in the 'Create and Send product reports' section:



Once you confirm by clicking on 'OK', the products with the applied changes will be displayed in the 'Create and Send Product Reports' section for your review:

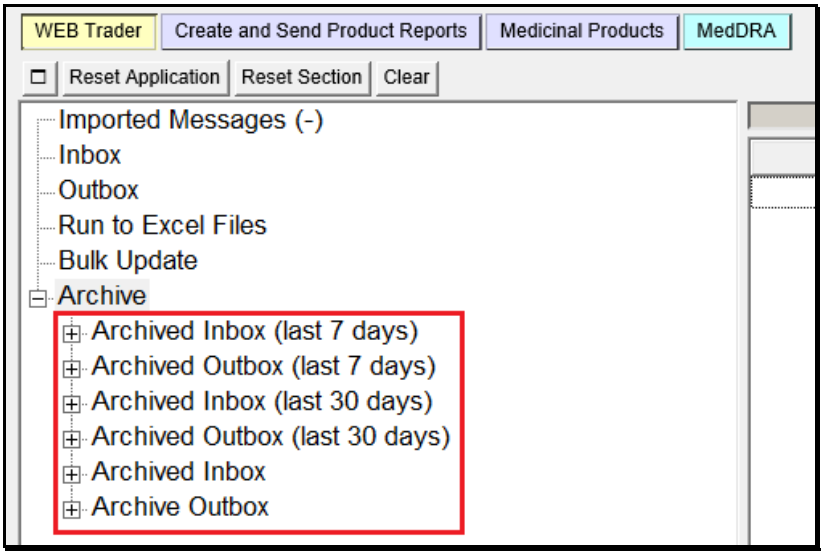


Once you perform the review, assign the XEVPRM Message number to your XEVPRM, validate, and send the XEVPRM.

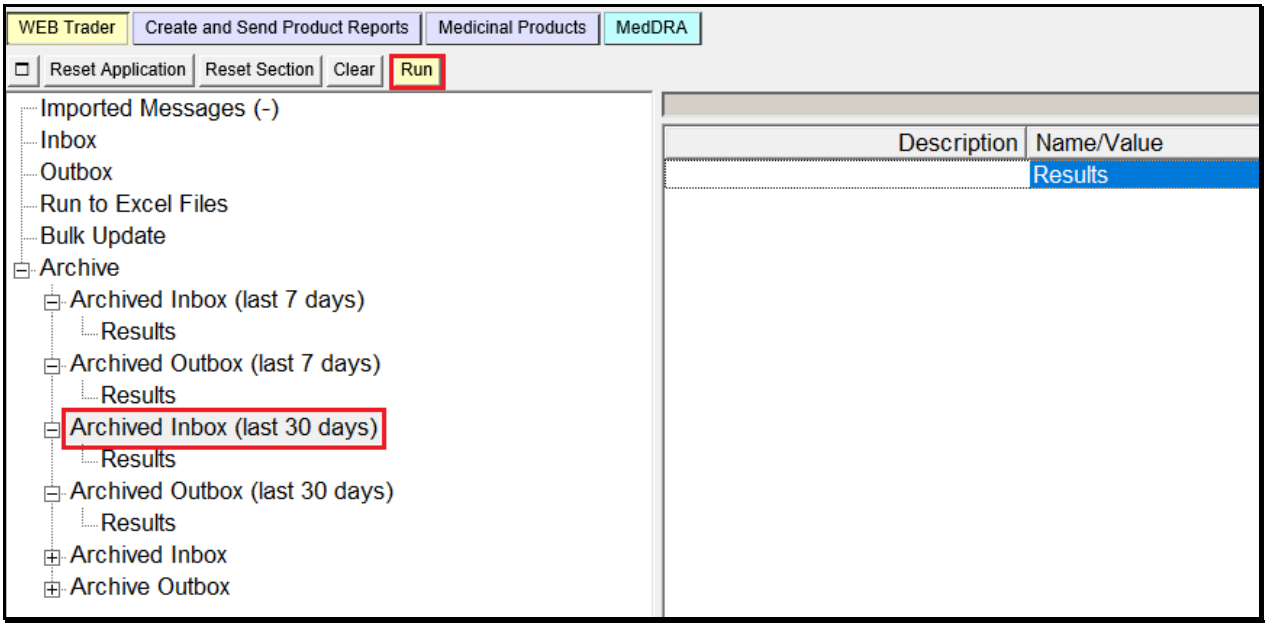
3.10.5. Archive

To find messages that have been archived, you will need to **run** queries in the **Archive section** of EVWEB.

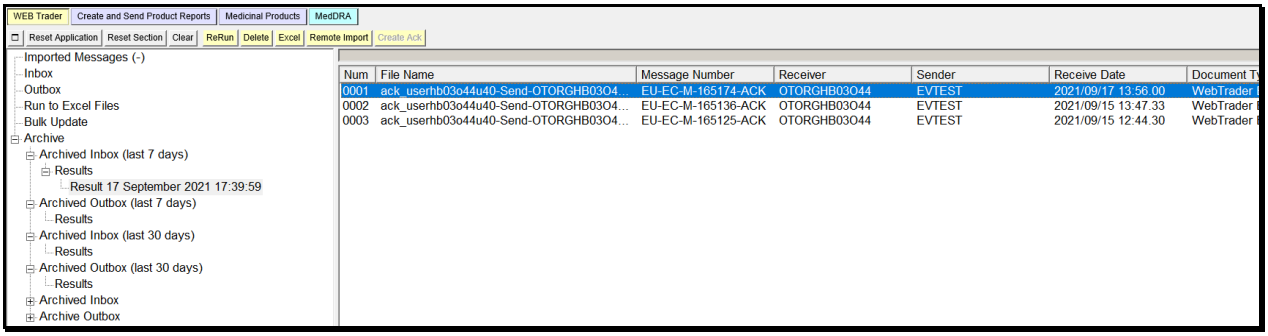
You will need to select the applicable period for which you wish to retrieve your submission of acknowledgement messages:



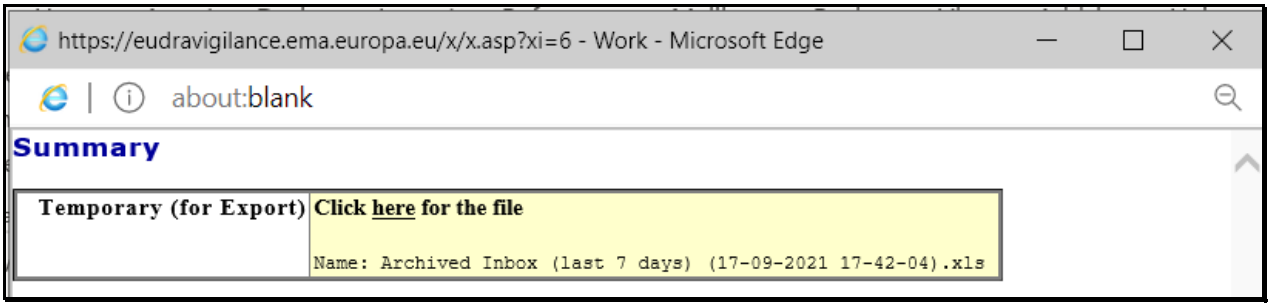
Once you click on the required folder (it will become highlighted in light grey), either 'Run' **and/or** 'Run to Excel' buttons will become available in the dynamic button area, depending on the number of messages in that folder:



If you select **'Run'**, the results will be displayed in the active area:



If **'Run to Excel'** is available and you select this option, a new window will open:



Once you click on 'here', you will retrieve the results in an Excel file.

3.10.6. Data-export functionality

XEVMPD Export functionality is available to enable organisations to export their own data from EVWEB.

The export tool can be accessed directly via an IE browser at the URL https://eudravigilance.ema.europa.eu/evmpdex/ExportManager.asp.

Alternatively, the application may be accessed via the main EudraVigilance secure home page where a link will be found in the 'EV Services' section.

For all related information see the XEVMPD product export tool: user manual, which is also available in the EudraVigilance secure area, under 'User Support'.

3.11. Export functions and available formats

EVWEB allows several ways to export the loaded information. Each of these buttons will be available on the dynamic section of the main menu, **depending on the section, in which you are working in, and on the item(s) selected.**

Data can be exported in the following formats:

Every set of results of every advanced query available in EVWEB may be exported as an Excel spread sheet. To do this, click on the 'Excel' button when a result set is selected in the tree-view area.

This button allows you to generate an XML version of the message selected in EVWEB.

This button allows you to generate an RTF (which is a typical cross-platform document format) version of the message selected in EVWEB.

Please note that Internet Explorer may handle the RTF format in different ways, depending on the settings of your Windows system (e.g., opening this document inside the browser, launching an external application, or asking you to save the document).

This button allows you to generate a ZIP file also containing the attachment (if present).

Once exported, the document in any of these formats (except for a ZIP file) can be printed or saved like any other document on your computer.

See section *4.8. Save, Reload and Send an XEVPRM* for information.

4. Create and Send XEVPRMs

4.1. Commands/operation types to be used in an XEVPRM

You can create a single XEVPRM that contains more than one report for a product (approved or development), a source, an organisation (MAH or sponsor), an ATC code (proposed or development), a route of administration (proposed or development) and for a pharmaceutical form (proposed or development). Moreover, for each report, you can specify different operation types.

Via an XEVPRM, users can:

- Add new information in the XEVMPD;
- Update information already present in the XEVMPD;
- Nullify information already present in the XEVMPD;
- Notify the EMA of extensions of marketing authorisations;
- Notify the EMA of variations to the terms of marketing authorisations;
- Notify the EMA of any changes to the name and the contact details of the qualified person responsible for pharmacovigilance (QPPV);
- Notify the EMA of any changes in the location of the Pharmacovigilance system master file (PSMF);
- Notify the EMA of any changes to the contact information for Pharmacovigilance enquiries;
- Notify the EMA of transfers of marketing authorisations;
- Notify the EMA of any suspension/lifting of the suspension, revocation or withdrawal of a marketing authorisation granted in the Union;
- Notify the EMA of any suspension/lifting of the suspension, revocation or withdrawal of a marketing authorisation granted in the Union;
- Notify the EMA of renewal of the marketing authorisation;
- Notify the EMA of the electronic copy of the latest approved Summary of Product Characteristics (SmPC) where any variations lead to a significant revision of the content.

The below overview provides a description of the available operation types/commands to be used in an XEVPRM:

- '**Insert' (1)**: allows the sender organisation to insert medicinal product information in the XEVMPD.

  For EVWEB users, a '**Reinsert**' button is also available, allowing users to re-insert an existing medicinal product in the XEVMPD whilst retaining the previous information. Following the modification of the required data elements, the XEVPRM is then submitted in the XEVMPD with the operation type 'Insert' (1).

- **'Update' (2)**: allows the sender organisation to correct erroneous information previously submitted. Also, as per specific guidance provided in section *2. Maintenance of medicinal product data* of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance,

this operation type shall be used to maintain some of the authorised medicinal product information.

- '**Nullification' (4)**: allows users to flag incorrectly submitted information (including duplicated information) as 'non-current'.
- **'Invalidate MA' (6):** This operation allows the sender organisation to submit a notification about the withdrawal of an authorised medicinal product from the market via an XEVPRM. The 'Invalidate MA' operation covers a number of scenarios including the transfer of an authorised medicinal product to a third party, and a renewal of the marketing authorisation by the marketing authorisation holder if the marketing authorisation number changes.

  See the relevant sections of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance for further information and processes.

  Operation type **'Variation' (3)**: is no longer available in EVWEB as it should not be used to notify the EMA of a variation procedure of an authorised medicinal product in the context of maintenance of medicinal product data during the transition maintenance phase. Gateway users, who will submit an XEVPRM containing an authorised medicinal product assigned with operation type 'Variation' (3) will receive a negative XEVPRM acknowledgement as the entire XEVPRM will be rejected.

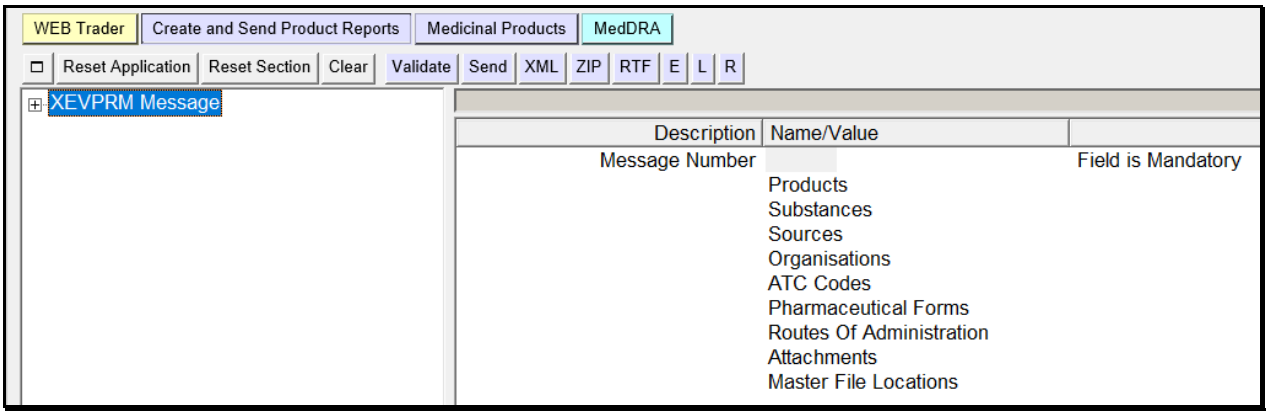
  The process to be followed to amend an authorised medicinal product entity following a variation procedure is described in section *2.2.3.1. Variations of marketing authorisation* of Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance.

4.2. Create an XEVPRM with operation type Insert

To insert new information in the XEVMPD, you must create and send an XEVPRM.

To create an XEVPRM, open EVWEB and go to the 'Create and Send Product Reports' section:

EVWEB will display the sections present in the XEVPRM:

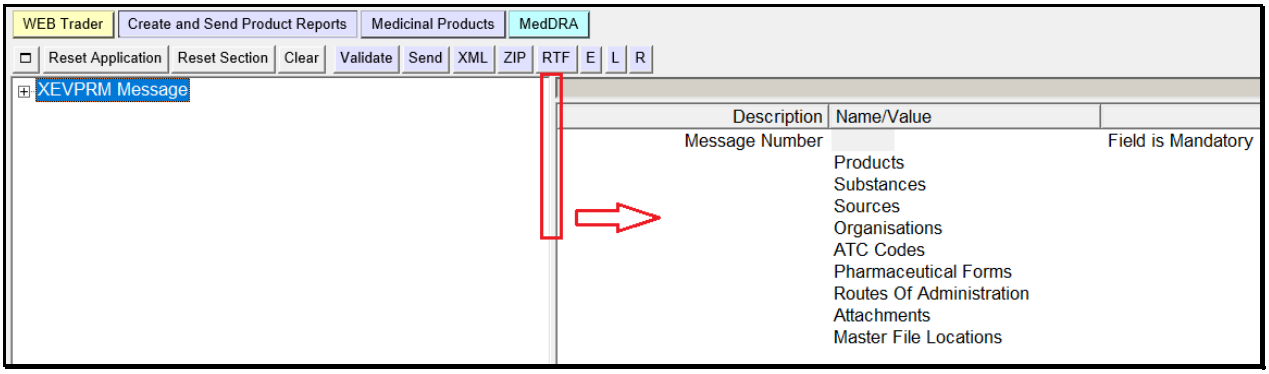


The XEVPRM contains a mandatory section named 'message header' (shown in the below screenshot as present in XML file of the XEVPRM):

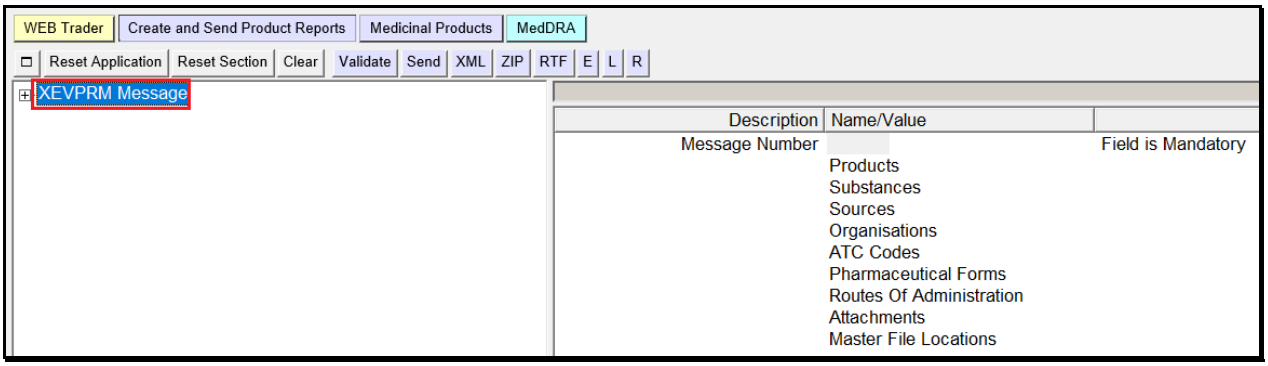
```
<?xml version="1.0" encoding="UTF-16" ?>
- <evprm xmlns="http://eudravigilance.ema.europa.eu/schema/emaxevmpd"
    xmlns:ssi="http://eudravigilance.ema.europa.eu/schema/emaxevmpd_ssi"
    xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"
    xsi:schemaLocation="http://eudravigilance.ema.europa.eu/schema/emaxevmpd
    http://eudravigilance.ema.europa.eu/schema/emaxevmpd.xsd">
  - <ichicsrmessageheader>
      <messagetype>XEVPRM</messagetype>
      <messageformatversion>2</messageformatversion>
      <messageformatrelease>0</messageformatrelease>
      <messagenumb />
      <messagesenderidentifier>OTORGHB03044</messagesenderidentifier>
      <messagereceiveridentifier>EVTEST</messagereceiveridentifier>
      <messagedateformat>204</messagedateformat>
      <messagedate>20210922181311</messagedate>
    </ichicsrmessageheader>
  </evprm>
```

EVWEB completes automatically the 'message header' section except from the 'Message number' field. Therefore, you must type in the message number that you wish to assign to your message.

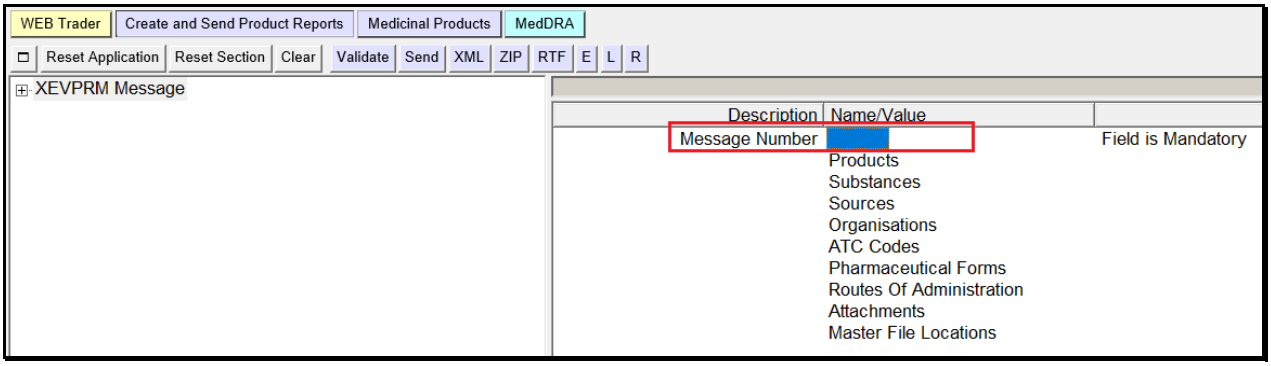
You can expand the tree-view area to display the sections of the XEVPRM by moving the separation line to the right:



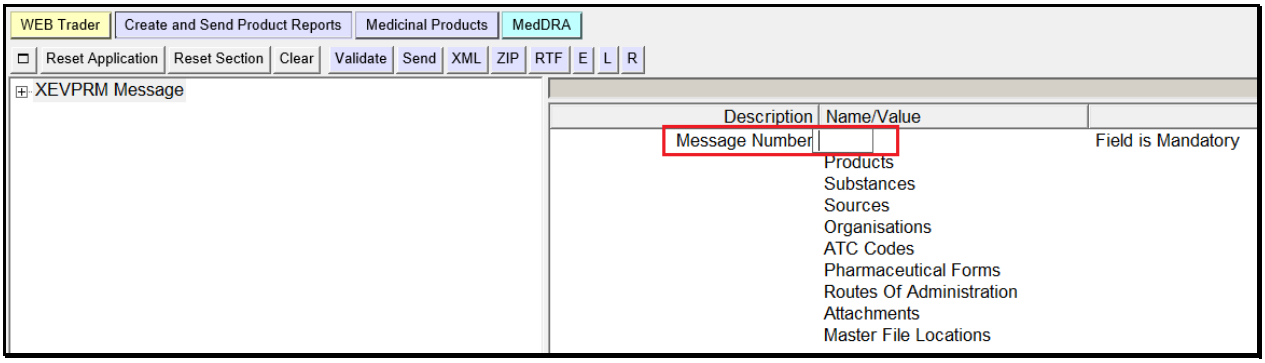
You must enter a message name of number in the 'Message Number' field, to do so, click on the 'XEVPRM Message' text in your tree-view area:



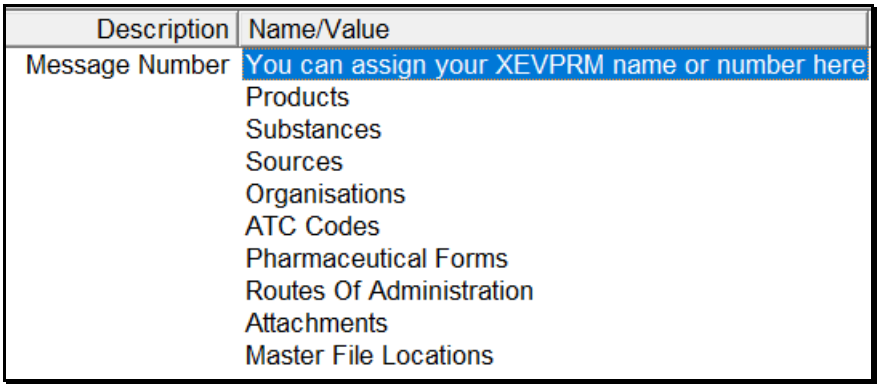
The active area will show the 'XEVPRM Number' field; the area next to the 'Message Number' will be highlighted in blue:



Click on the 'E' (Text Edit) button or use 'Enter' on your keyboard to activate the field, and you will be able to write the name/number that you wish to assign to you XEVPRM:

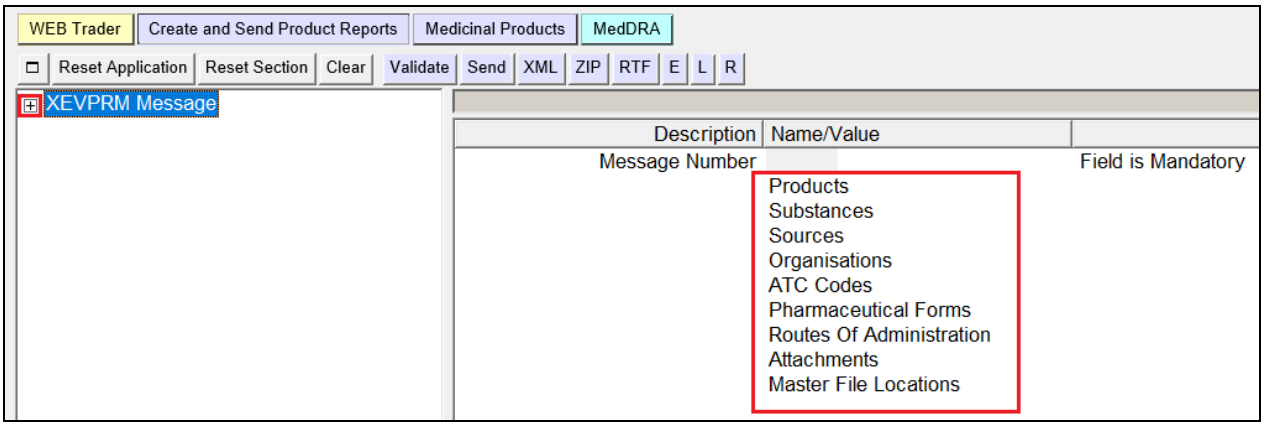


Enter the required message number or name and press 'Enter'; the text that you entered will appear in blue:



To add a new entity in the XEVMPD, you must add the required entity in the XEVPRM with the operation type 'Insert (1)'.

To do so, you must select the relevant section of the XEVPRM. You can double click on the required section in the active area, or expand the menu (by clicking on the + sign) in the tree-view area:



The active area allows you to create the required report by clicking in the check box next to the entity that you wish to insert.

The principle of clicking in the checkbox to create a new element in the tree-view is the same in all parts of the XEVPRM where applicable, e.g., administration route, pharmaceutical form, ATCs etc.

You can also insert new reference sources, new organisations (MAH or Sponsor), new ATC codes (proposed or development), routes of administration (proposed or development), new pharmaceutical forms (proposed or development), attachments and Master File Locations when this information is not present in the relevant lookup tables.

Please note that whilst you can also add new approved and development substances in your XEVPRM, once you send the XEVPRM, the submission will be rejected. This is because substance information can be inserted and/or updated by the EMA only. Please refer to the information available in the 'Changes to some business rules of the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): Submission of substance information' document.

The below examples describe how to create and add a report with the operation type 'Insert' to the XEVPRM.

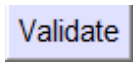
Each report (Product Report, Master File Location Report, etc.) contains different fields, but the process for inserting the information does not change.

Please refer to Chapter 3.I: Extended EudraVigilance product report message (XEVPRM) technical specifications for a complete list of the fields present in each section and their definition.

For list of data fields collected for entities in the XEVMPD and the applicable business rules please refer to:

- Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance of the Detailed guidance on the electronic submission of information on medicinal products for human use by marketing authorisation holders to the European to the European Medicines Agency in accordance with Article 57(2) of Regulation (EC) No. 726/2004; and
- Guidance on the electronic submission of information on investigational medicinal products for human use in the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): eXtended EudraVigilance Medicinal Product Report (XEVPRM) user guidance.

Once you create your report, you can validate, save, and send the XEVPRM:



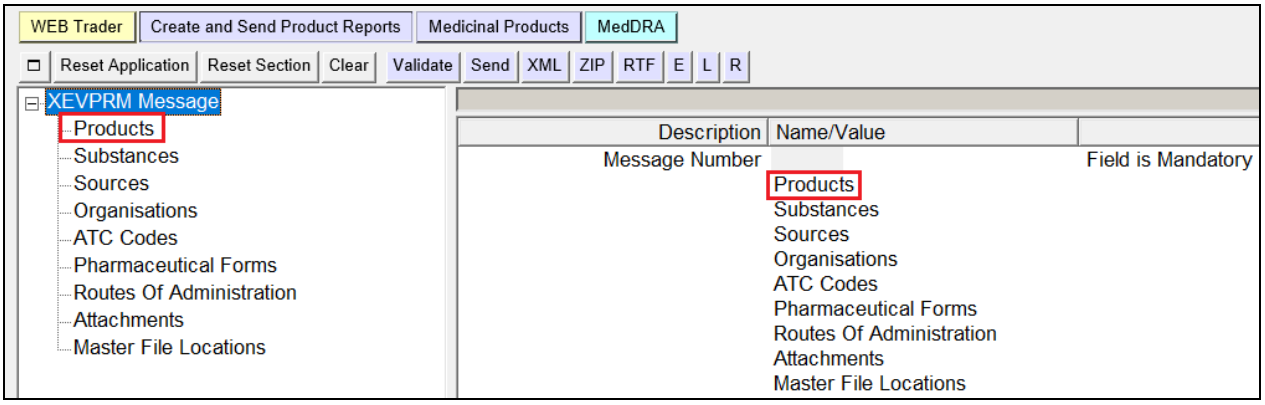
When you have entered all the necessary information, click on the 'Validate' button from the dynamic button set. The system will check the data you have entered and inform you of any missing mandatory information.

To save the XEVPRM you have created, either in 'XML' format, 'RTF' format, or as a zip file, click on the buttons from the dynamic button set.

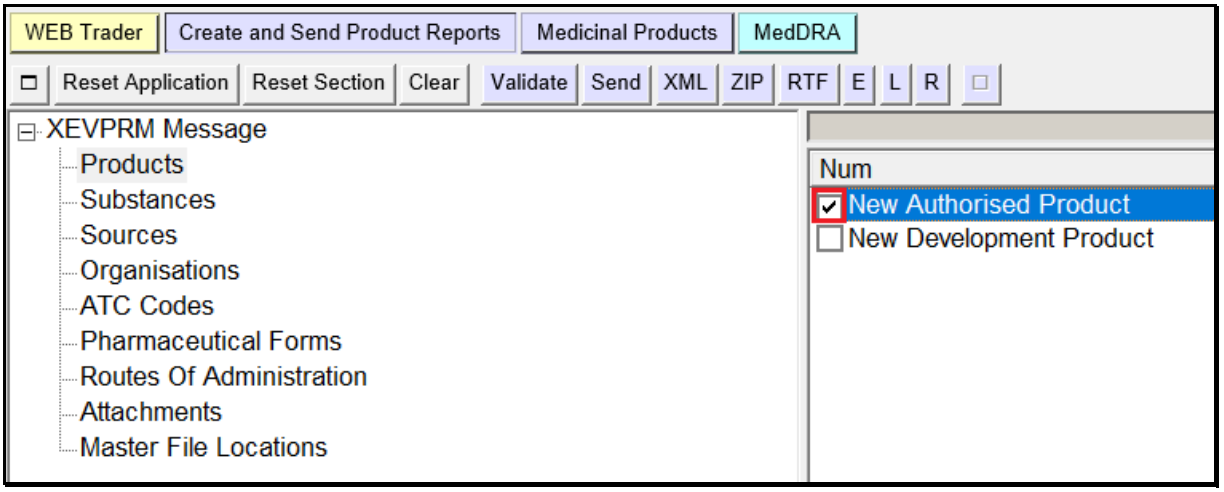
After validating the message click on the 'Send' button from the dynamic button set to transmit the message to the XEVMPD.

4.2.1. Insert of an authorised medicinal product (AMP)

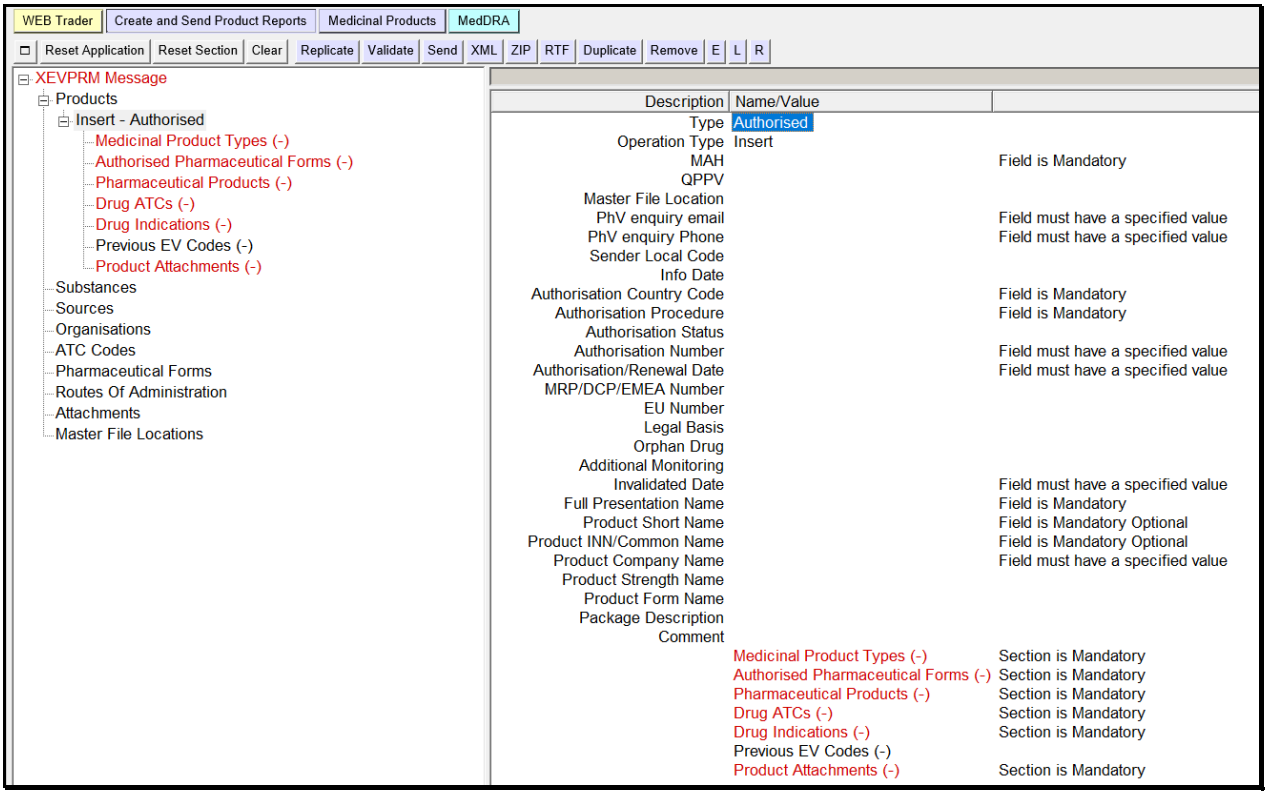
To create a 'Product Report', you must select 'Products' in the tree-view area or in the active area:



You must select the type of product you wish to create by ticking the relevant box in the active area; to create a product report for an authorised product, you must select **'New Authorised Product'** in the active area:



Once you have selected 'New Authorised Product', the tree-view area and the active area will display the fields that need to be completed for the relevant section of the XEVPRM:



The 'Type' field displays 'Authorised' as default.

The 'Operation Type' field displays 'Insert' as default.

Information to be provided as mandatory is highlighted as 'Field is Mandatory'/'Field is Mandatory Optional' and/or in red in the tree-view area.

Complete the fields as required.

For the complete list of data fields collected for an AMP entity in the XEVMPD and the applicable business rules please refer to Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance; section *1.1. Initial Submission of an Authorised Medicinal Product (AMP)*.

Validate and send the XEVPRM.

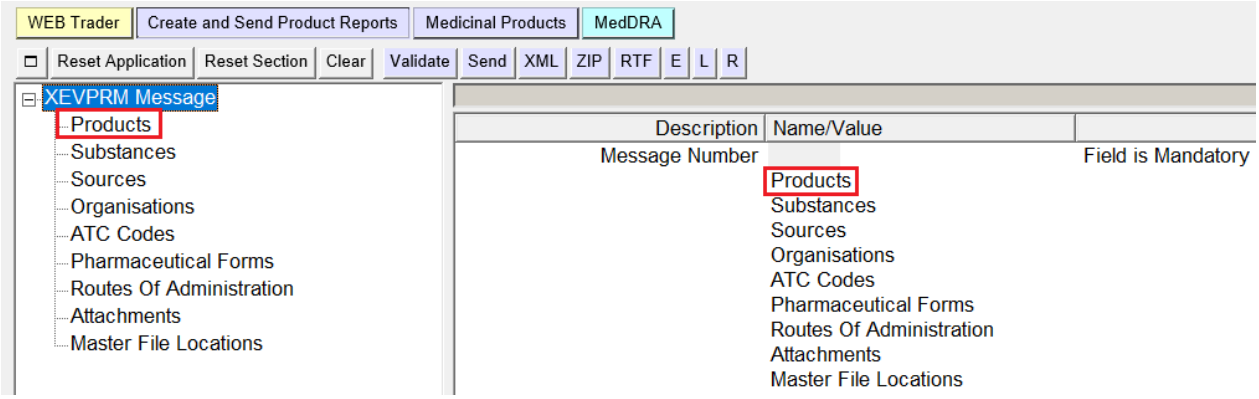
The XEVPRM acknowledgement will be sent to the sender organisation ID; if the submission was successful, the EV code assigned to the AMP will be provided:

```
- <reportacknowledgment>
    <reportname>AUTHORISEDPRODUCT</reportname>
    <localnumber>1</localnumber>
    <ev_code>PRD371943</ev_code>
    <operationtype>1</operationtype>
    <operationresult>2</operationresult>
    <operationresultdesc>Entity inserted succesfully</operationresultdesc>
  </reportacknowledgment>
</acknowledgment>
</evprmack>
```

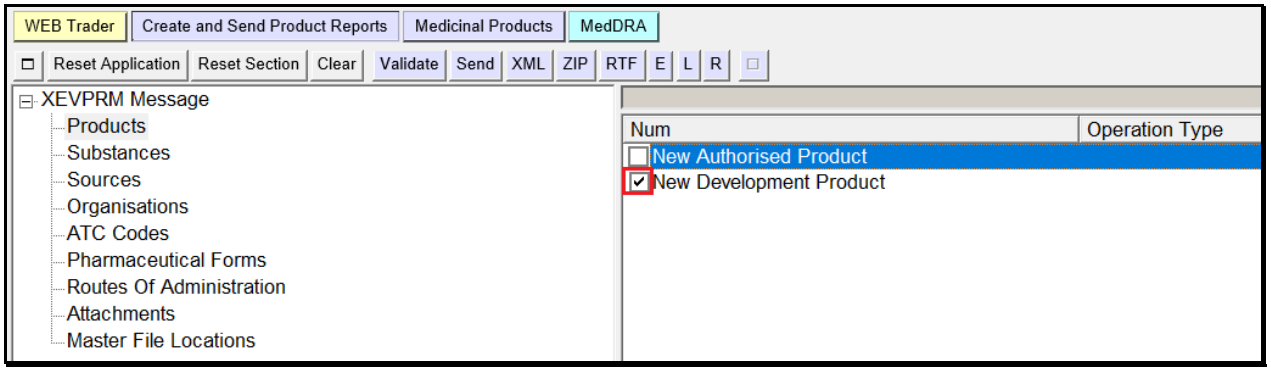
See also Extended EudraVigilance Medicinal Product Report Message step-by-step guide: **Insert of an authorised medicinal product** step-by-step document available on the 'Training' webpage for more details.

4.2.2. Insert of a development medicinal product (DMP)

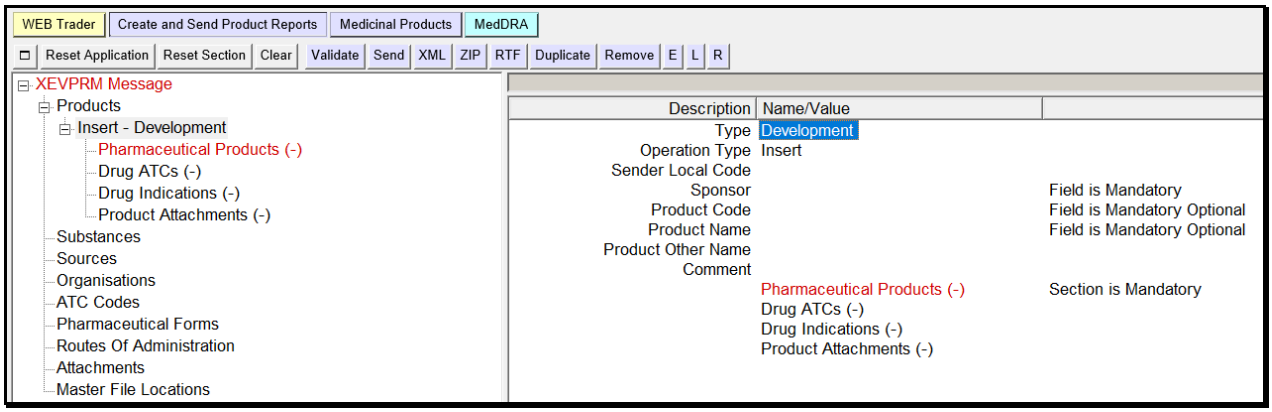
To create a 'Product Report', you must select 'Products' in the tree-view area or in the active area:



To create a product report for a development product, you must select **'New Development Product'** in the active area:



Once you have selected 'New Development Product', the tree-view area and the active area will display the fields that need to be completed in the product report for the relevant section of the XEVPRM:



The 'Type' field displays 'Development' as default.

The 'Operation Type' field displays 'Insert' as default.

Information to be provided as mandatory is highlighted as 'Field is Mandatory'/'Field is Mandatory Optional' and/or in red in the tree-view area.

Complete the fields as required.

For the complete list of data fields collected for a DMP entity in the XEVMPD and the applicable business rules please refer to the 'Guidance on the electronic submission of information on investigational medicinal products for human use in the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): eXtended EudraVigilance Medicinal Product Report (XEVPRM) user guidance' document, section *1. Initial submission of a development medicinal product.*

Validate and send the XEVPRM.

The XEVPRM acknowledgement will be sent to the sender organisation ID; if the submission was successful, the EV code assigned to the DMP will be provided:

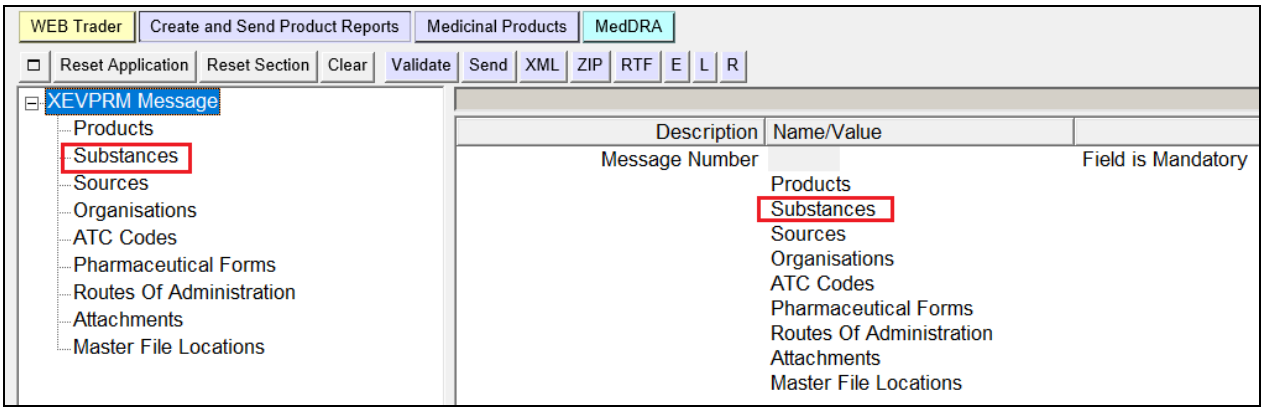
```
- <reportacknowledgment>
    <reportname>DEVELOPMENTPRODUCT</reportname>
    <localnumber>1</localnumber>
    <ev_code>PRD126024</ev_code>
    <operationtype>1</operationtype>
    <operationresult>2</operationresult>
    <operationresultdesc>Entity inserted successfully Version 1</operationresultdesc>
  </reportacknowledgment>
</acknowledgment>
</evprmack>
```

See also Extended EudraVigilance Medicinal Product Report Message step-by-step guide: **Insert of a development medicinal product** step-by-step document available on the 'Training' webpage for more details.

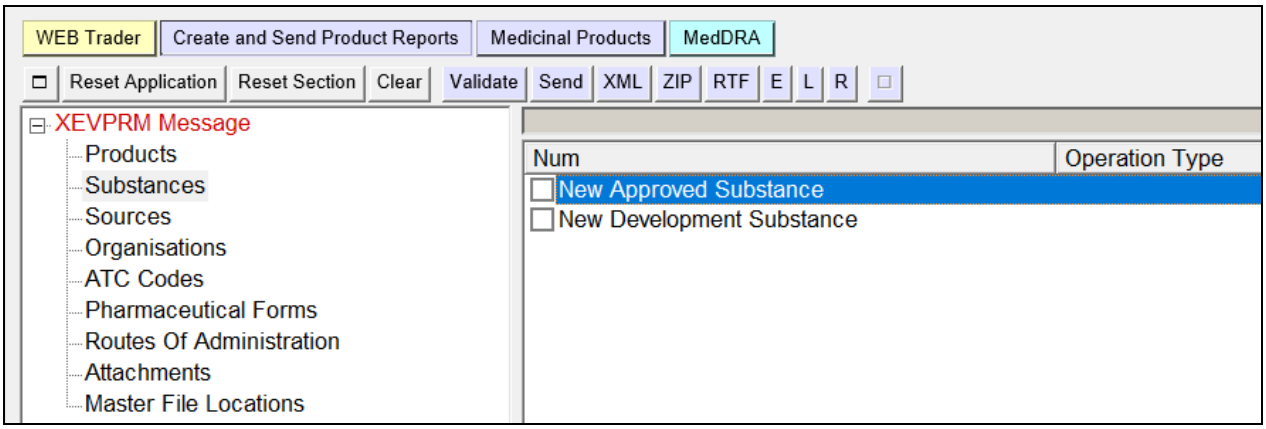
4.2.3. Insert of an approved substance

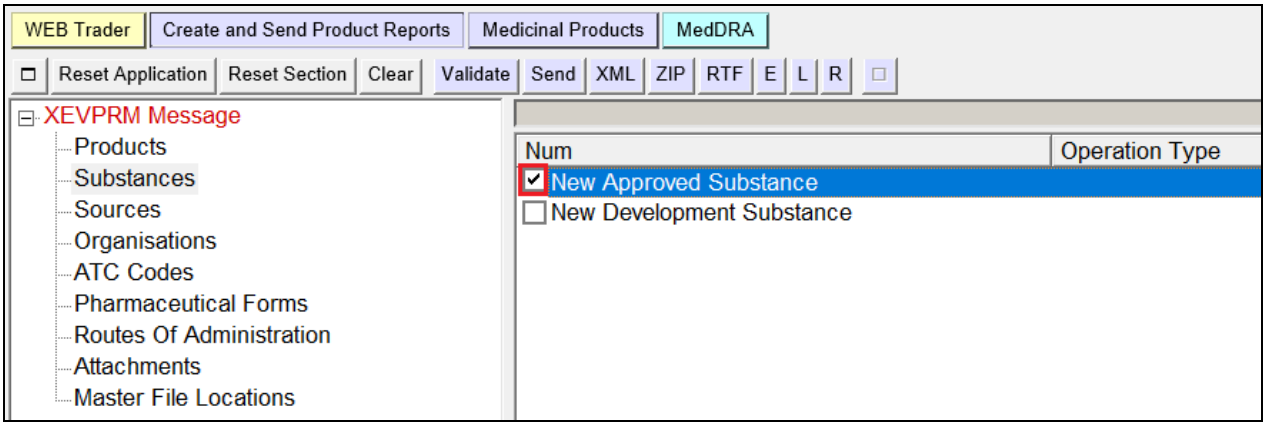
Please note that the below screenshots and guidance are for training purposes and for EMA users only. Only the EMA can insert, update, or nullify substance information in the XEVMPD. The submission of substance information in an XEVPRM by a user from an MAH or sponsor organisation will result in the receipt of a negative ACK. If an MAH or sponsor users requires new substance information to be entered in the XEVMPD, the user should follow the process described in the document Changes to some business rules of the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): Submission of substance information.

To create a 'Substance Report' for a new substance, you must select 'Substances' in the tree-view area or in the active area:

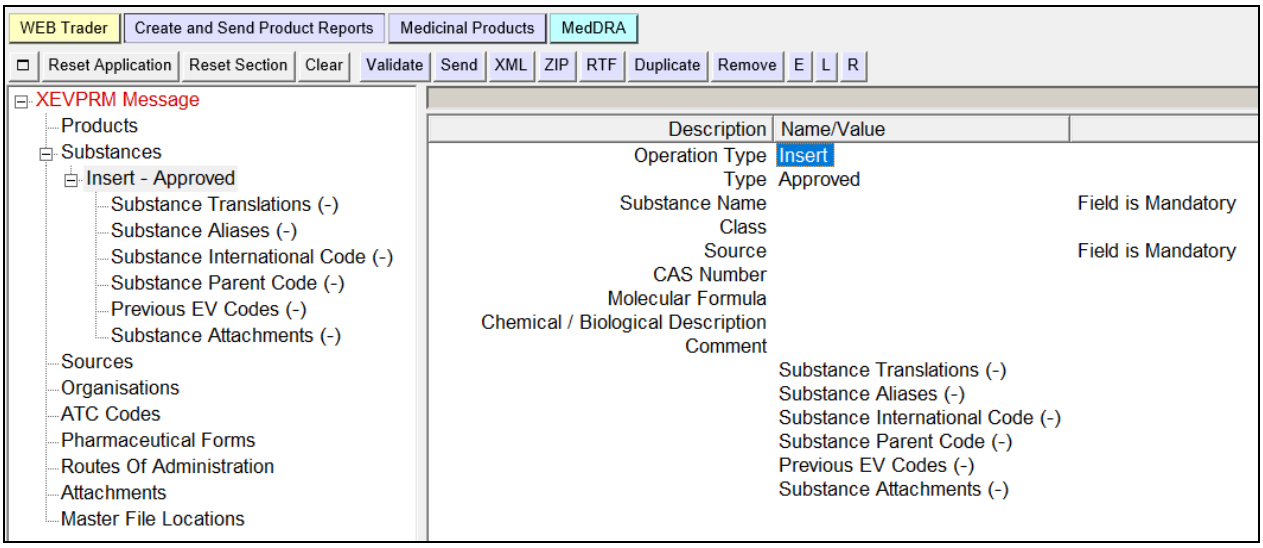


You must select 'New Approved Substance' by ticking the relevant box in the active area:





Once you selected the required type of substance entity, the tree-view area and the active area will display the fields that need to be completed for the relevant section of the XEVPRM:



The 'Operation Type' field displays 'Insert' as default.

The 'Type' field displays 'Proposed' or 'Development', depending on your selection, as default.

Information to be provided as mandatory is highlighted as 'Field is Mandatory'.

Complete the fields as required.

For the complete list of data fields collected for an approved substnce entity in the XEVMPD and the applicable business rules please refer to Chapter 3.I: Technical specifications, section *3.I.b.9 Approved Substance (AS)*.

Validate and send the XEVPRM.

The XEVPRM acknowledgement will be sent to the sender organisation ID; if the submission was successful, the EV code assigned to the approved substance will be provided:

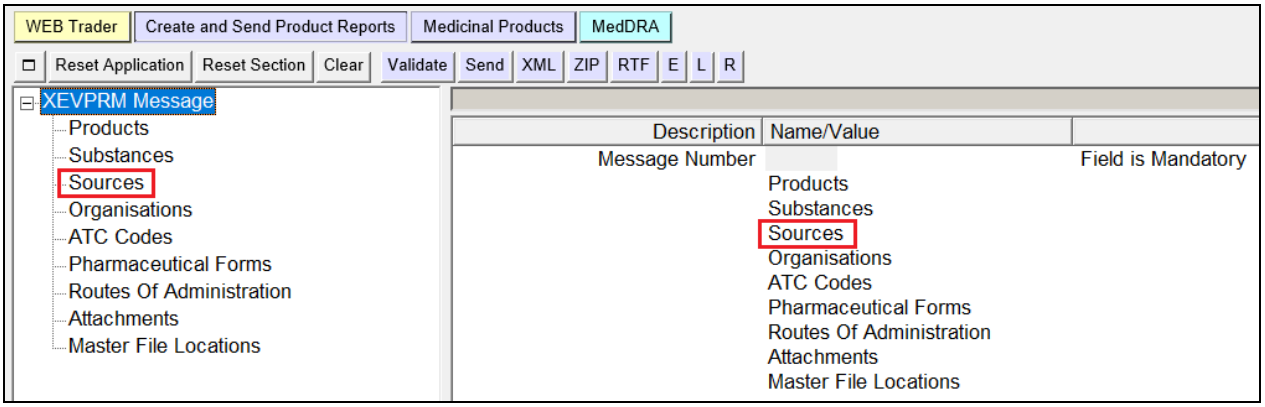
```
- <reportacknowledgment>
    <reportname>APPROVEDSUBSTANCE</reportname>
    <localnumber>1</localnumber>
    <ev_code>SUB166236</ev_code>
    <operationtype>1</operationtype>
    <operationresult>2</operationresult>
    <operationresultdesc>Entity inserted successfully</operationresultdesc>
  </reportacknowledgment>
</acknowledgment>
```

Since users from MAHs/Sponsor organisations are not allowed to insert, update, or nullify substance information in the XEVMPD production environment, the XEVPRM ACK received by the MAH/Sponsor organisation will the following message:

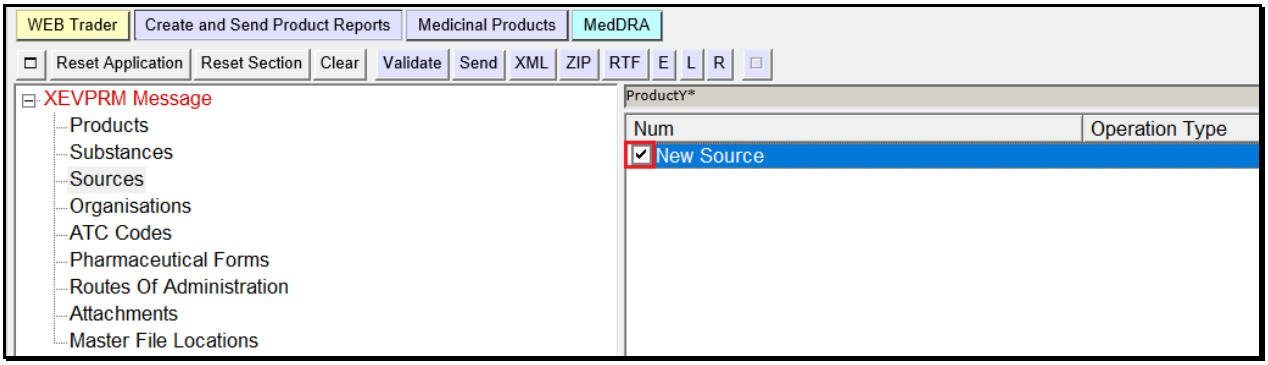
```
- <reportacknowledgment>
    <reportname>APPROVEDSUBSTANCE</reportname>
    <localnumber>15</localnumber>
    <ev_code />
    <operationtype>1</operationtype>
    <operationresult>74</operationresult>
    <operationresultdesc>Please note that it is not possible to perform
      any operations on substances. If you need to insert substances
      or update substance names or translations, please send a ticket
      to the EMA Service Desk portal with the title "Request for a
      substance to be registered" and providing the relevant substance
      details to be entered or amended</operationresultdesc>
  </reportacknowledgment>
 </acknowledgment>
</evprmack>
```

4.2.4. Insert of a reference source

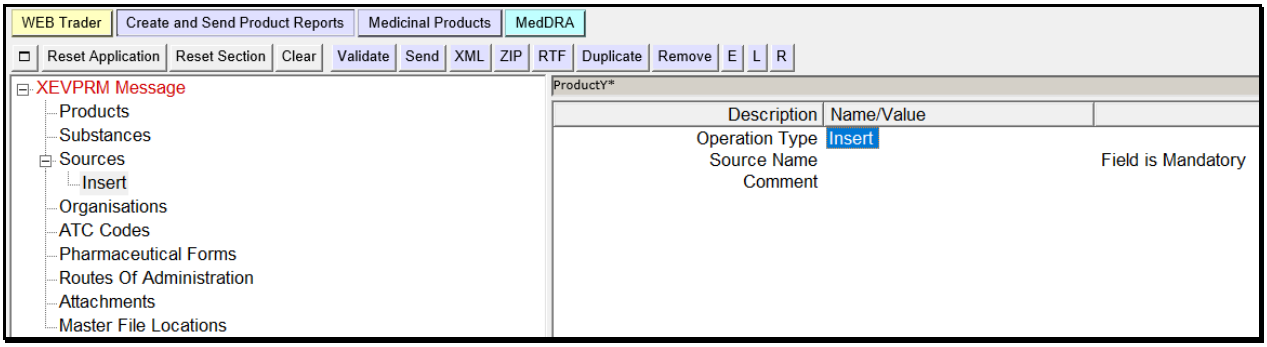
To create a 'Source Report', you must select 'Sources' in the tree-view area or in the active area:



You must select 'New Source ' in the active area by ticking the relevant box:



Once you have selected 'New Source', the tree-view area and the active area will display the fields that need to be completed for the relevant section of the XEVPRM:



The 'Operation Type' field displays 'Insert' as default.

Information to be provided as mandatory is highlighted as 'Field is Mandatory'.

Complete the fields as required.

For the complete list of data fields collected for reference source entity in the XEVMPD and the applicable business rules please refer to:

- Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance; section *1.5. Initial submission of a reference source*, or
- the Guidance on the electronic submission of information on investigational medicinal products for human use in the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): eXtended EudraVigilance Medicinal Product Report (XEVPRM) user guidance document, section *2. Initial submission of a reference source*.

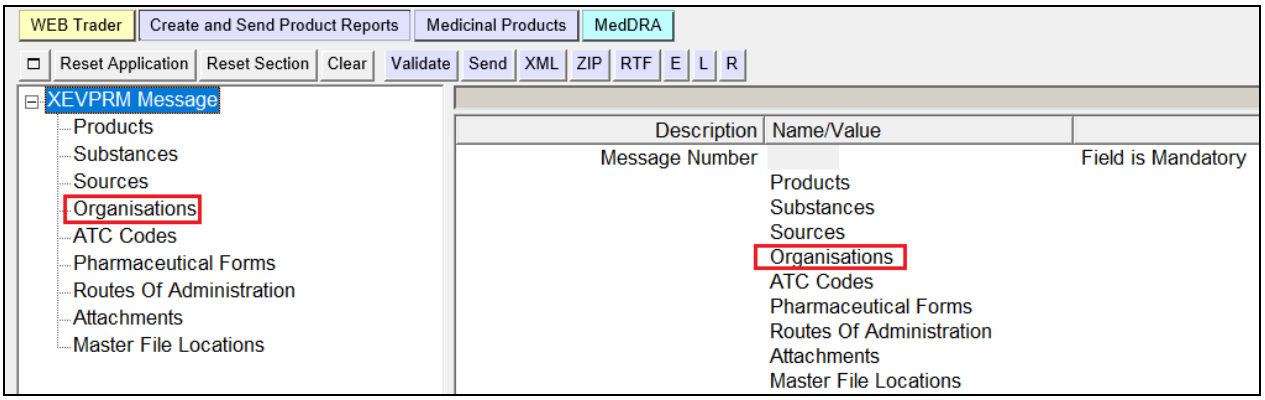
Validate and send the XEVPRM.

The XEVPRM acknowledgement will be sent to the sender organisation ID; if the submission was successful, the EV code assigned to the reference source will be provided:

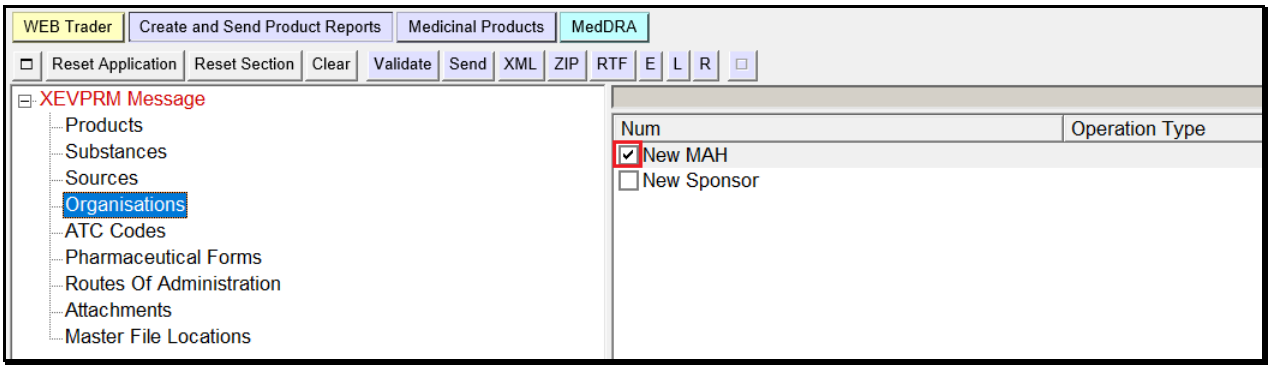
```
- <reportacknowledgment>
    <reportname>SOURCE</reportname>
    <localnumber>6</localnumber>
    <ev_code>SRC870</ev_code>
    <operationtype>1</operationtype>
    <operationresult>2</operationresult>
    <operationresultdesc>Entity inserted succesfully</operationresultdesc>
  </reportacknowledgment>
```

4.2.5. Insert of a marketing authorisation holder organisation

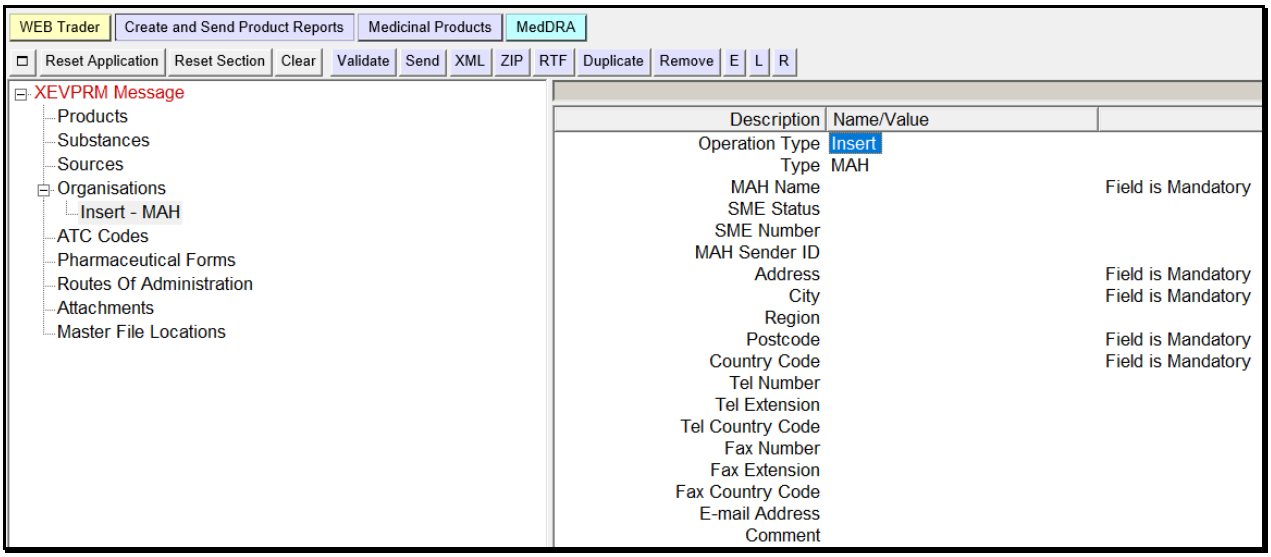
To create an 'Organisation Report', you must select 'Organisations' in the tree-view area or in the active area:



To create an organisation report for an MAH organisation, you must select 'New MAH' in the active area by ticking the relevant box:



Once you have selected 'New MAH', the tree-view area and the active area will display the fields that need to be completed for the relevant section of the XEVPRM:



The 'Operation Type' field displays 'Insert' as default.

The 'Type' field displays 'MAH' as default.

Information to be provided as mandatory is highlighted as 'Field is Mandatory'.

Complete the fields as required.

For the complete list of data fields collected for an MAH organisation entity in the XEVMPD and the applicable business rules please refer to Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance; section *1.6. Initial submission of a marketing authorisation holder (MAH) organisation*.

Validate and send the XEVPRM.

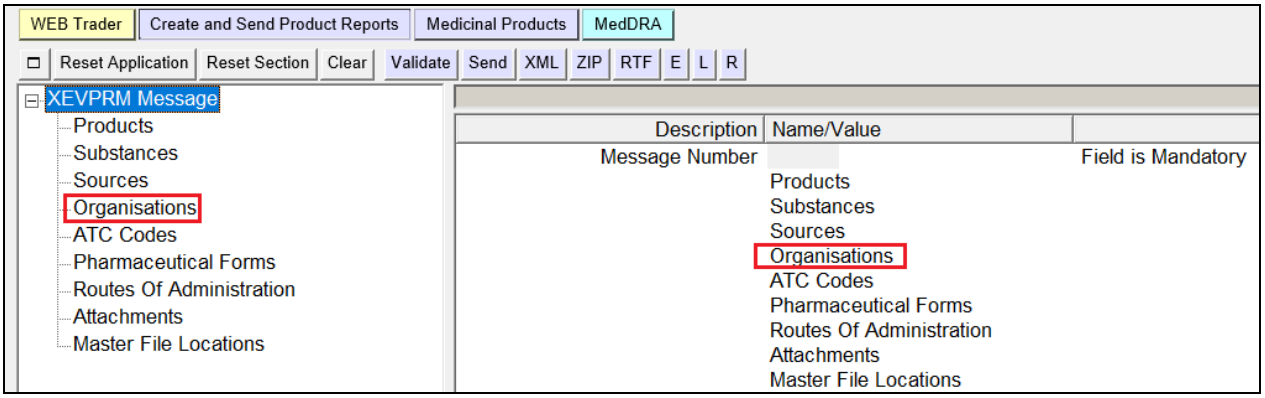
The XEVPRM acknowledgement will be sent to the sender organisation ID; if the submission was successful, the EV code assigned to the organisation will be provided:

```
- <reportacknowledgment>
    <reportname>ORGANISATION</reportname>
    <localnumber>1</localnumber>
    <ev_code>ORG40544</ev_code>
    <operationtype>1</operationtype>
    <operationresult>2</operationresult>
    <operationresultdesc>Entity inserted successfully</operationresultdesc>
  </reportacknowledgment>
</acknowledgment>
</evprmack>
```

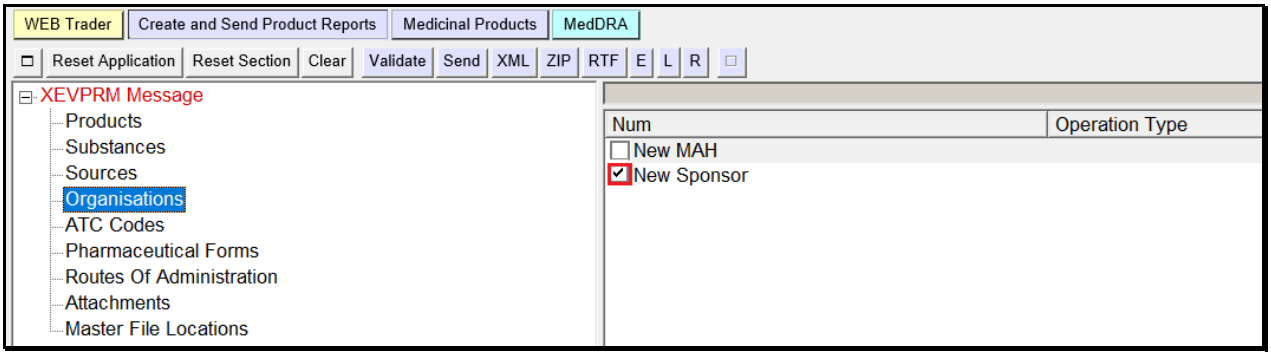
See also Extended EudraVigilance Medicinal Product Report Message step-by-step guide: **Insert of an organisation** step-by-step document available on the 'Training' webpage for more details.

4.2.6. Insert of a Sponsor organisation

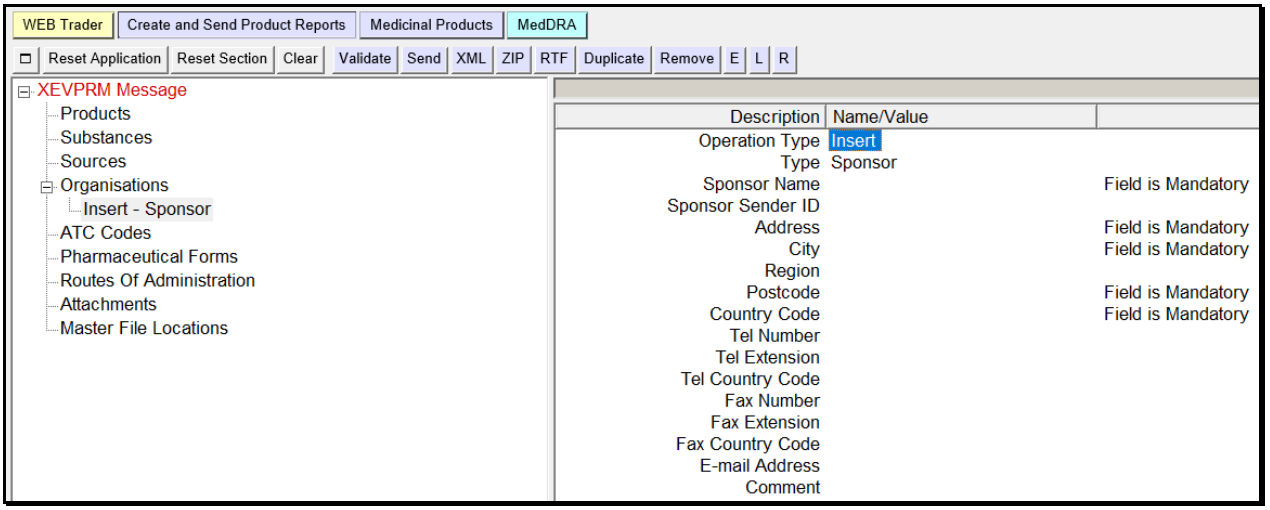
To create an 'Organisation Report', you must select 'Organisations' in the tree-view area or in the active area:



To create a report for a sponsor organisation, you must select 'New Sponsor' in the active area by ticking the relevant box:



Once you have selected 'New Sponsor', the tree-view area and the active area will display the fields that need to be completed for the relevant section of the XEVPRM:



The 'Operation Type' field displays 'Insert' as default.

The 'Type' field displays 'Sponsor' as default.

Information to be provided as mandatory is highlighted as 'Field is Mandatory'.

Complete the fields as required.

For the complete list of data fields collected for a sponsor entity in the XEVMPD and the applicable business rules please refer to the Guidance on the electronic submission of information on investigational medicinal products for human use in the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): eXtended EudraVigilance Medicinal Product Report (XEVPRM) user guidance document, section *3. Initial submission of a sponsor information*.

Validate and send the XEVPRM.

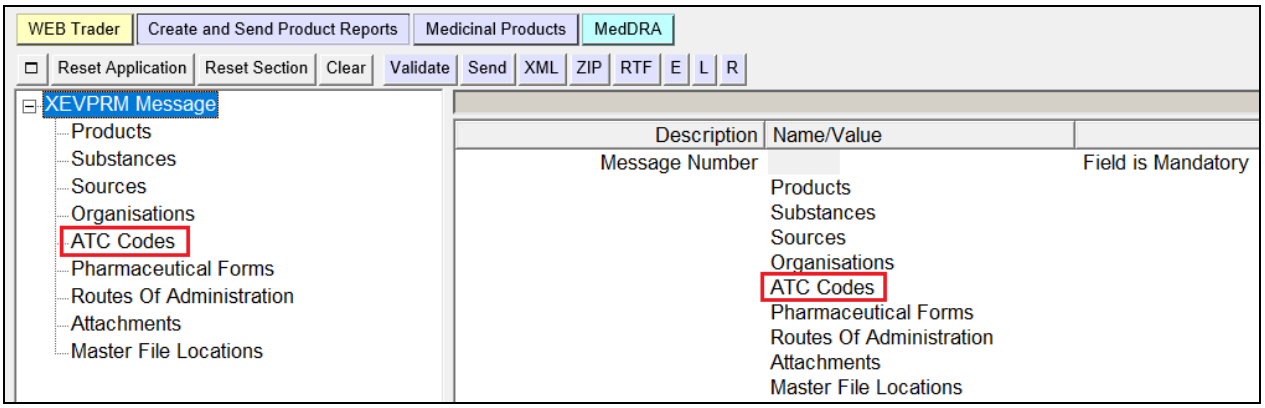
The XEVPRM acknowledgement will be sent to the sender organisation ID; if the submission was successful, the EV code assigned to the sponsor organisation will be provided:

```
- <reportacknowledgment>
    <reportname>ORGANISATION</reportname>
    <localnumber>1</localnumber>
    <ev_code>ORG40544</ev_code>
    <operationtype>1</operationtype>
    <operationresult>2</operationresult>
    <operationresultdesc>Entity inserted successfully</operationresultdesc>
  </reportacknowledgment>
 </acknowledgment>
</evprmack>
```

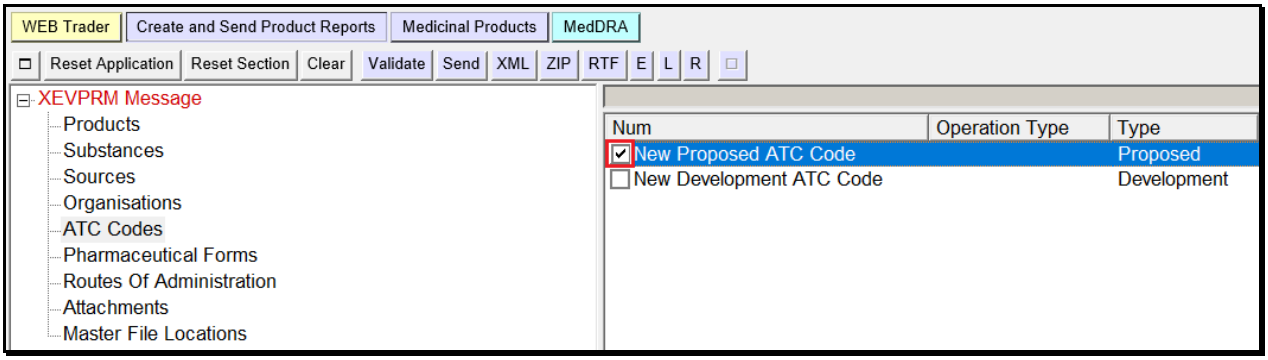
See also Extended EudraVigilance Medicinal Product Report Message step-by-step guide: **Insert of an organisation** step-by-step document available on the 'Training' webpage for more details.

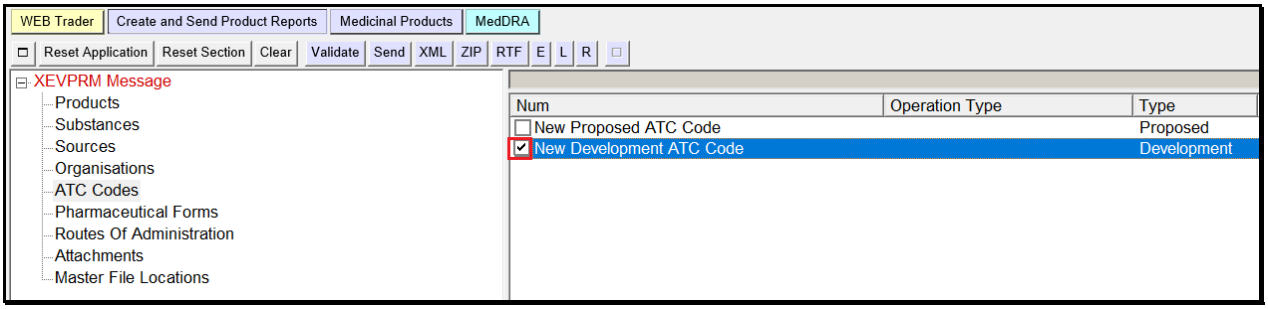
4.2.7. Insert of a proposed or development ATC Code

To create an 'ATC Code Report', you must select 'ATC Codes' in the tree-view area or in the active area:

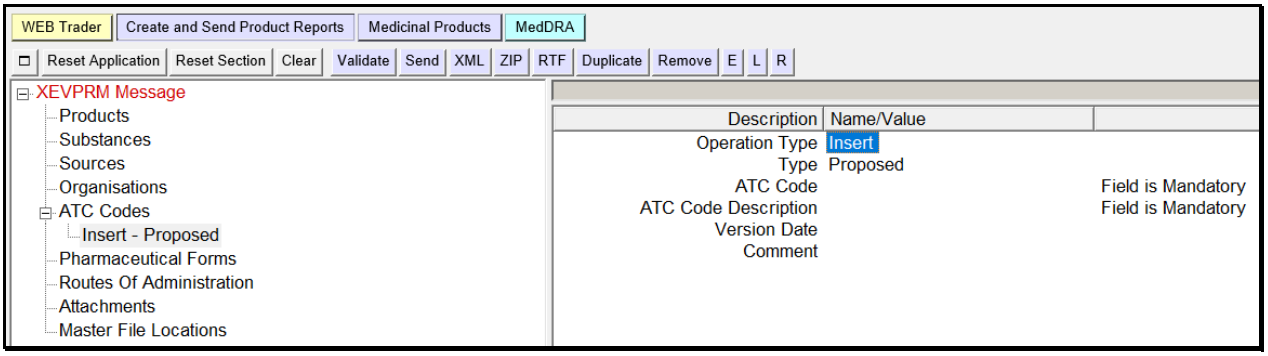


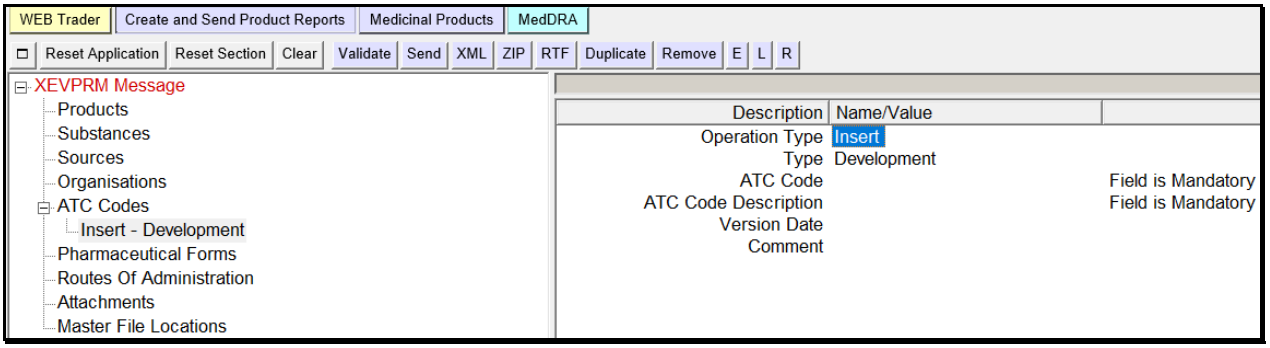
You must select 'New Proposed ATC Code', or 'New Development ATC Code', as required, in the active area by ticking the relevant box:





Once you selected the required type of ATC Code, the tree-view area and the active area will display the fields that need to be completed for the relevant section of the XEVPRM:





The 'Operation Type' field displays 'Insert' as default.

The 'Type' field displays 'Proposed' or 'Development', depending on your selection, as default.

Information to be provided as mandatory is highlighted as 'Field is Mandatory'.

Complete the fields as required.

For the complete list of data fields collected for an ATC Code entity in the XEVMPD and the applicable business rules please refer to:

- Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance; section *1.7. Initial submission of an ATC Code*, or
- the Guidance on the electronic submission of information on investigational medicinal products for human use in the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): eXtended

EudraVigilance Medicinal Product Report (XEVPRM) user guidance document, section *4. Initial submission of an ATC Code*.

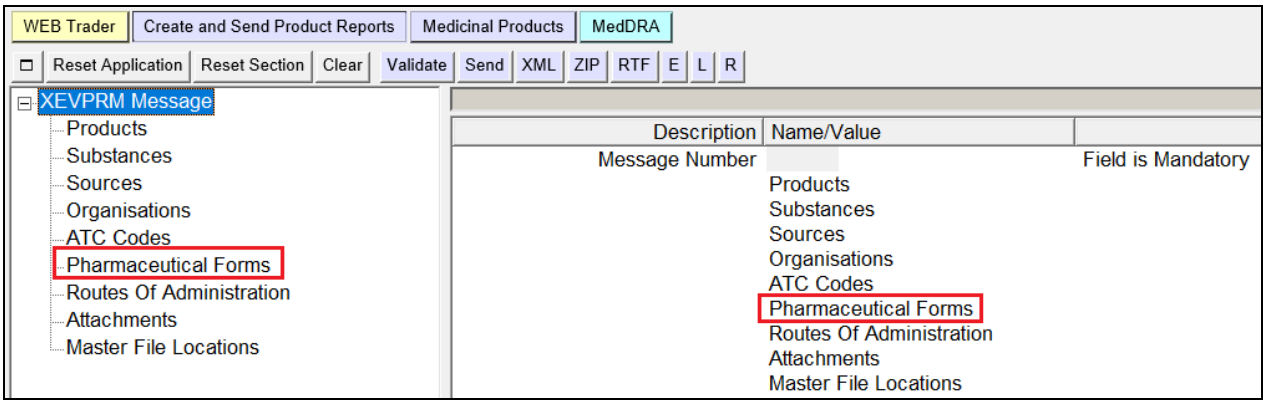
Validate and send the XEVPRM.

The XEVPRM acknowledgement will be sent to the sender organisation ID; if the submission was successful, the EV code assigned to the ATC Code will be provided:

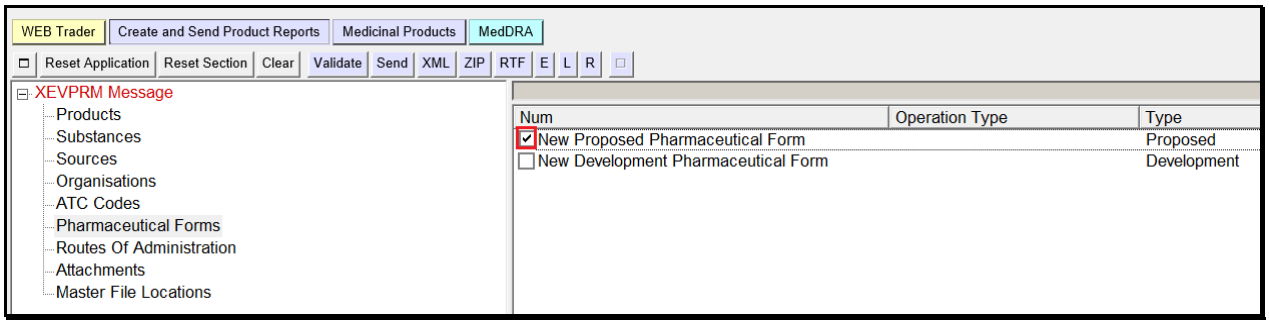
```
- <reportacknowledgment>
    <reportname>ATCCODE</reportname>
    <localnumber>L04AA34</localnumber>
    <ev_code>L04AA34</ev_code>
    <operationtype>1</operationtype>
    <operationresult>2</operationresult>
    <operationresultdesc>Entity inserted successfully</operationresultdesc>
  </reportacknowledgment>
```

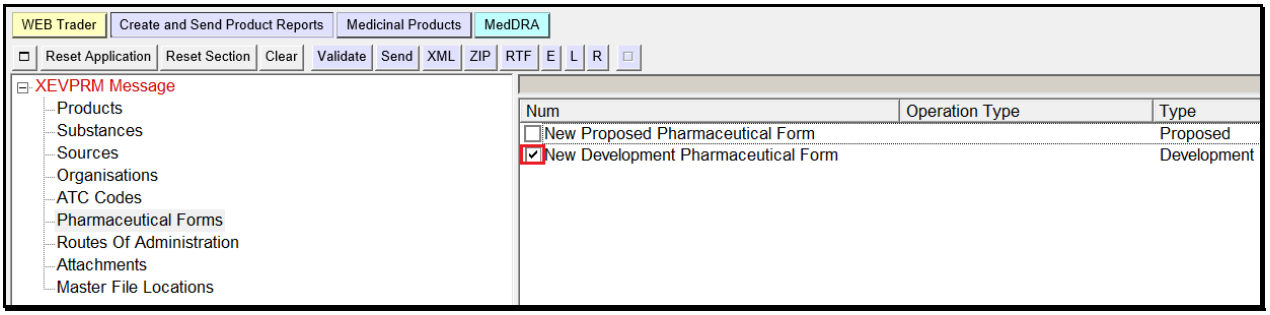
4.2.8. Insert of a proposed or development pharmaceutical form

To create a 'Pharmaceutical Form Report', you must select 'Pharmaceutical Forms' in the tree-view area or in the active area:

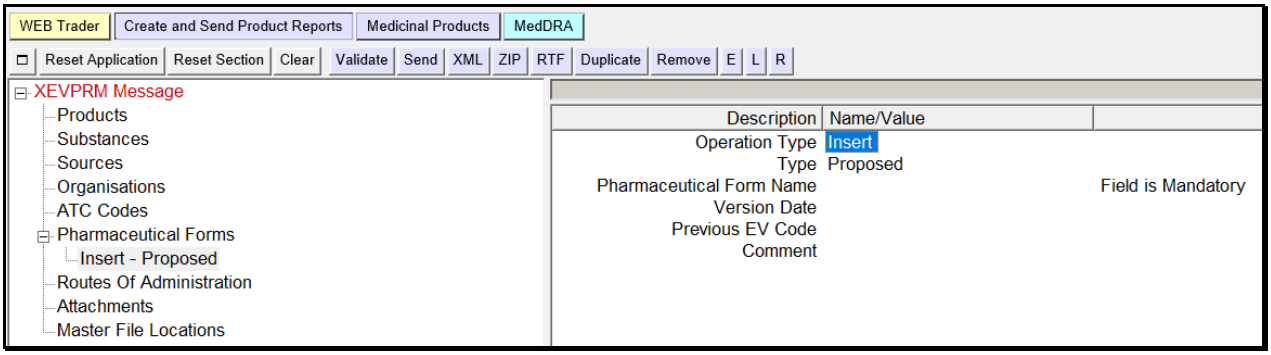


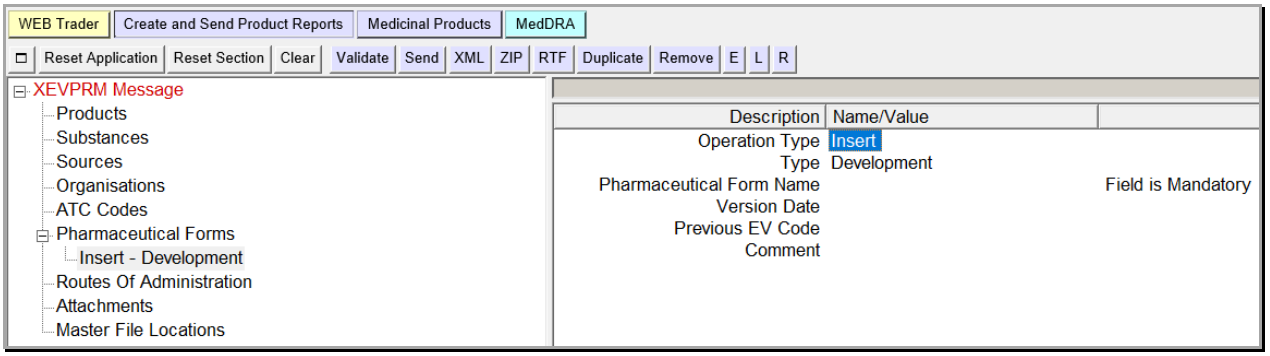
You must select 'New Proposed Pharmaceutical Form' or 'New Development Pharmaceutical Form', as required, in the active area:





Once you selected the required type of pharmaceutical form, the tree-view area and the active area will display the fields that need to be completed for the relevant section of the XEVPRM:





The 'Operation Type' field displays 'Insert' as default.

The 'Type' field displays 'Proposed' or 'Development', depending on your selection, as default.

Information to be provided as mandatory is highlighted as 'Field is Mandatory'.

Complete the fields as required.

For the complete list of data fields collected for a pharmaceutical form entity in the XEVMPD and the applicable business rules please refer to:

- Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance; section *1.8. Initial submission of an authorised/administrable pharmaceutical form*, or
- the Guidance on the electronic submission of information on investigational medicinal products for human use in the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): eXtended EudraVigilance Medicinal Product Report (XEVPRM) user guidance document, section *5. Initial submission of a pharmaceutical form*.

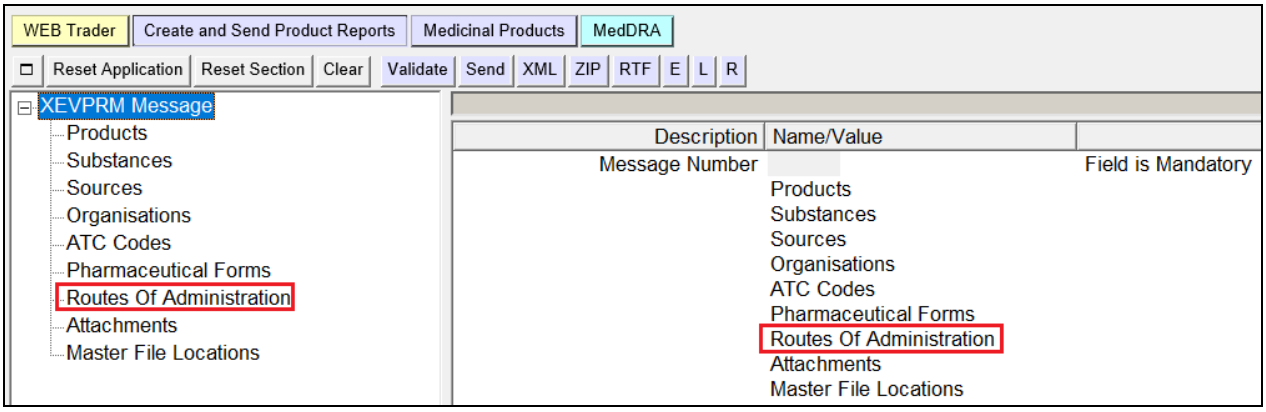
Validate and send the XEVPRM.

The XEVPRM acknowledgement will be sent to the sender organisation ID; if the submission was successful, the EV code assigned to the pharmaceutical form will be provided:

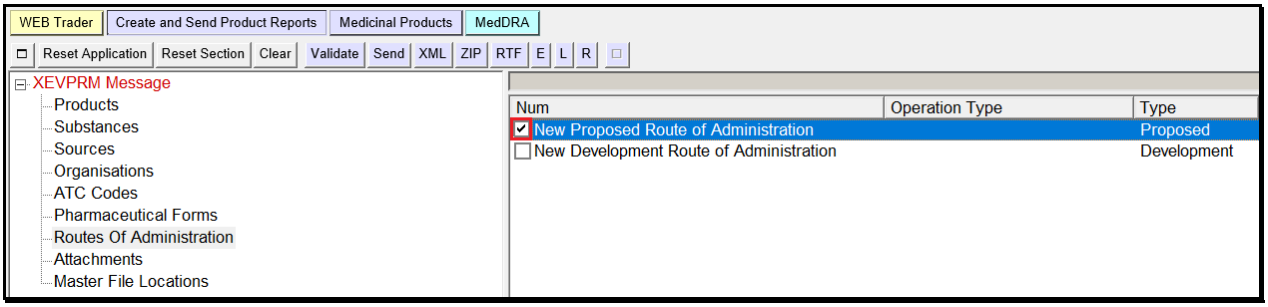
```
- <reportacknowledgment>
    <reportname>PHARMACEUTICALFORM</reportname>
    <localnumber>1</localnumber>
    <ev_code>PHF3162</ev_code>
    <operationtype>1</operationtype>
    <operationresult>2</operationresult>
    <operationresultdesc>Entity inserted successfully</operationresultdesc>
  </reportacknowledgment>
```

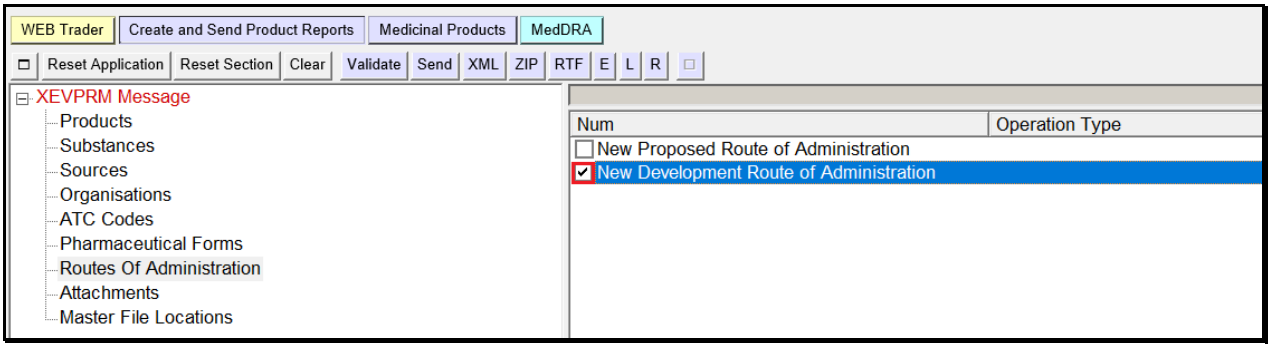
4.2.9. Insert of a proposed or development route of administration

To create a 'Route of Administration Report', you must select 'Routes of Administration' in the tree-view area or in the active area:

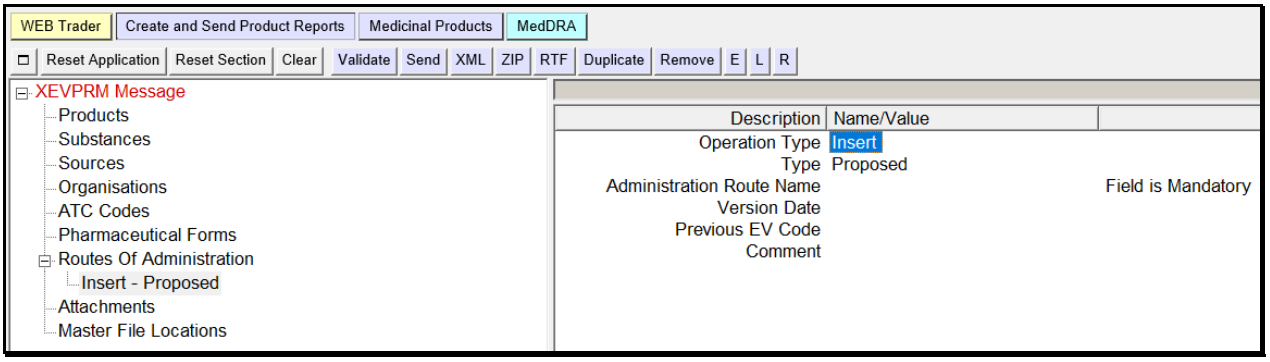


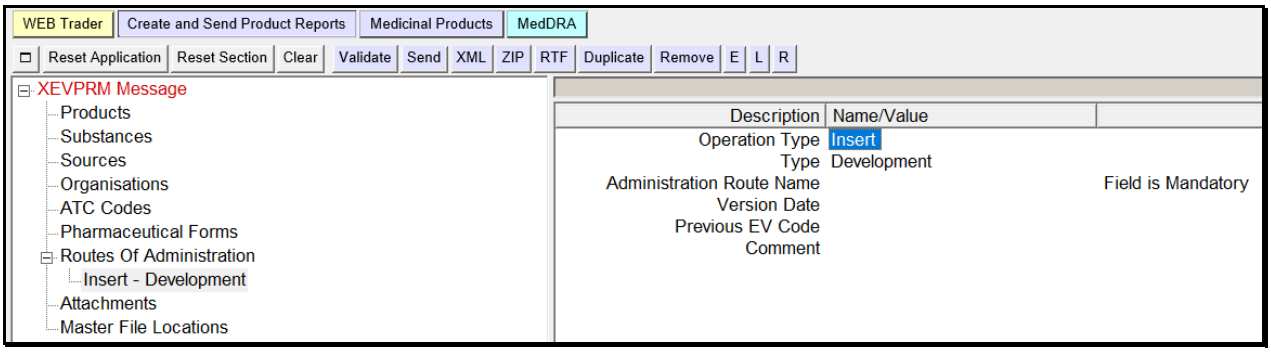
You must select 'New Proposed Route of Administration', or 'New Development Route of Administration', as required, in the active area:





Once you selected the required type of pharmaceutical form, the tree-view area and the active area will display the fields that need to be completed for the relevant section of the XEVPRM:





The 'Operation Type' field displays 'Insert' as default.

The 'Type' field displays 'Proposed' or 'Development', depending on your selection, as default.

Information to be provided as mandatory is highlighted as 'Field is Mandatory'.

Complete the fields as required.

For the complete list of data fields collected for a route of administration entity in the XEVMPD and the applicable business rules please refer to:

- Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance; section *1.9. Initial Submission of a route of administration (RoA)*, or
- the Guidance on the electronic submission of information on investigational medicinal products for human use in the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): eXtended

EudraVigilance Medicinal Product Report (XEVPRM) user guidance document, section *6. Initial submission of a route of administration*.

Validate and send the XEVPRM.

The XEVPRM acknowledgement will be sent to the sender organisation ID; if the submission was successful, the EV code assigned to the route of administration will be provided:

```
- <reportacknowledgment>
    <reportname>ADMINISTRATIONROUTE</reportname>
    <localnumber>3</localnumber>
    <ev_code>ADR775</ev_code>
    <operationtype>1</operationtype>
    <operationresult>2</operationresult>
    <operationresultdesc>Entity inserted successfully</operationresultdesc>
  </reportacknowledgment>
```

4.2.10. Insert of an attachment

Printed Product Information (**PPI**) is an attachment to be referenced in a produt entity.

Printed Substance Information (**PSI**) is an attachment to be referenced in a substance entity; the submission of PSI is currently not in use.

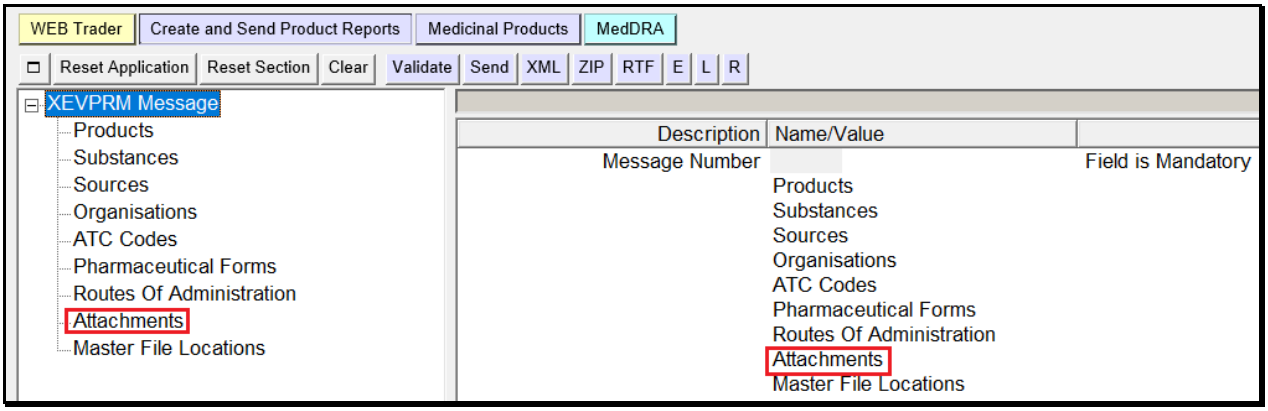
To create a PPI Attachment Report, you must select 'New PPI Attachment' in the active area:

To insert an attachment in the XEVMPD, you must follow the below described steps:

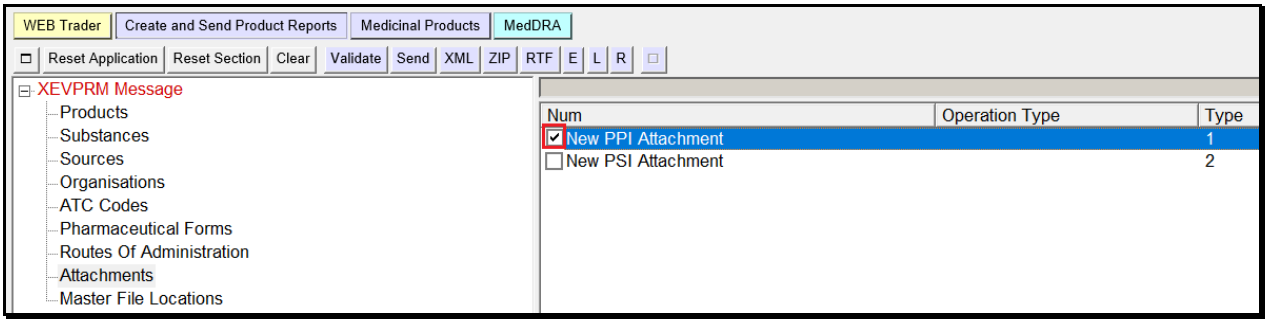
1. Provide the information of the file to be attached in the 'Attachments' section of the XEVPRM;
2. Reference the attachment information in the relevant product or substance entity;
3. Attach the file at the time of submission of the XEVPRM.

4.2.10.1. Create an Attachment Report

To create an 'Attachment Report', you must select 'Attachments' in the tree-view area or in the active area:



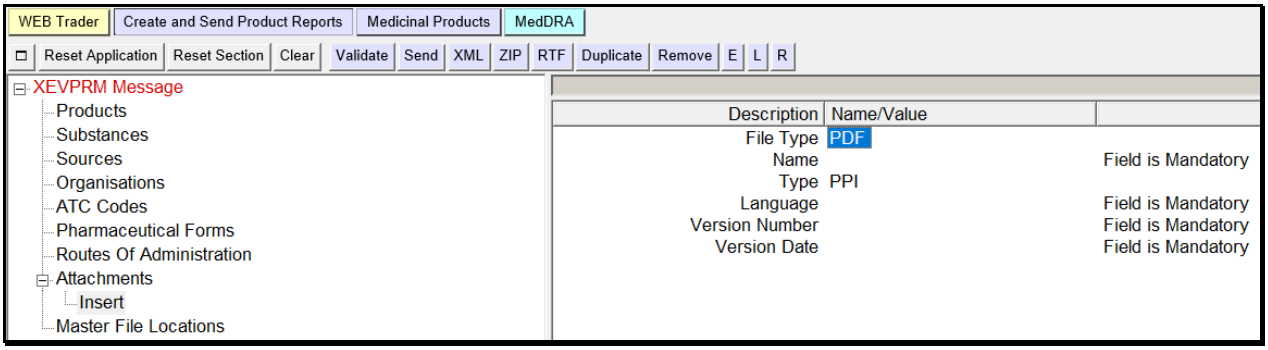
You must select 'New PPI Attachment' in the active area:



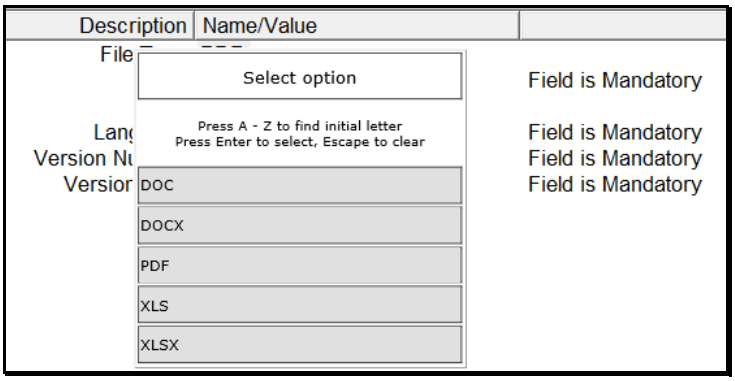
Once you selected the required type of attachment, the tree-view area and the active area will display the fields that need to be completed for the relevant section of the XEVPRM.

For a PPI:

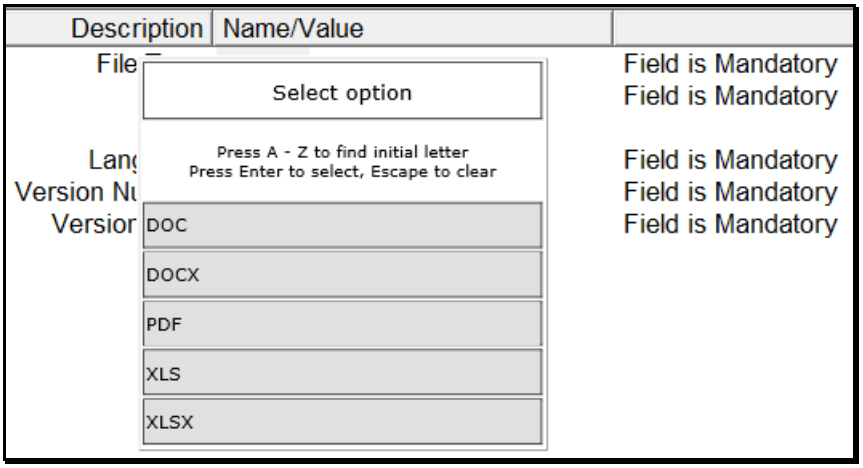
- the 'Type' displays 'PPI' by default;



- the 'File Type' displays 'PDF' by default; you can change this predefined value by double-clicking on the text in blue, or by using 'Enter' on your keyboard, to view the list of all values available for this field:



- the 'File Type' does not display any value; you must select the required value by double-clicking on the text in blue, or by using 'Enter' on your keyboard, to view the list of all values available for this field:



With regards to PDF attachments, only 'genuine' PDF documents should be attached (not scanned documents). PDF file version 1.4 or 1.7 should be used, as these are the only two versions that are ISO standards compliant. They are used for long term preservation of information and therefore the EMA/MAHs will have the assurance that we will be able to open them for many years.

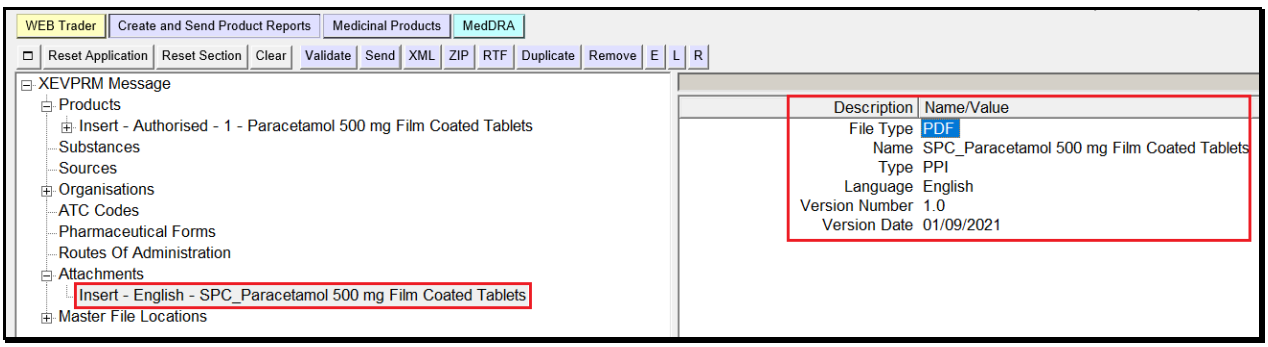
Once you selected the required format of your PPI, complete the fields as required.

Information to be provided as mandatory is highlighted as 'Field is Mandatory'.

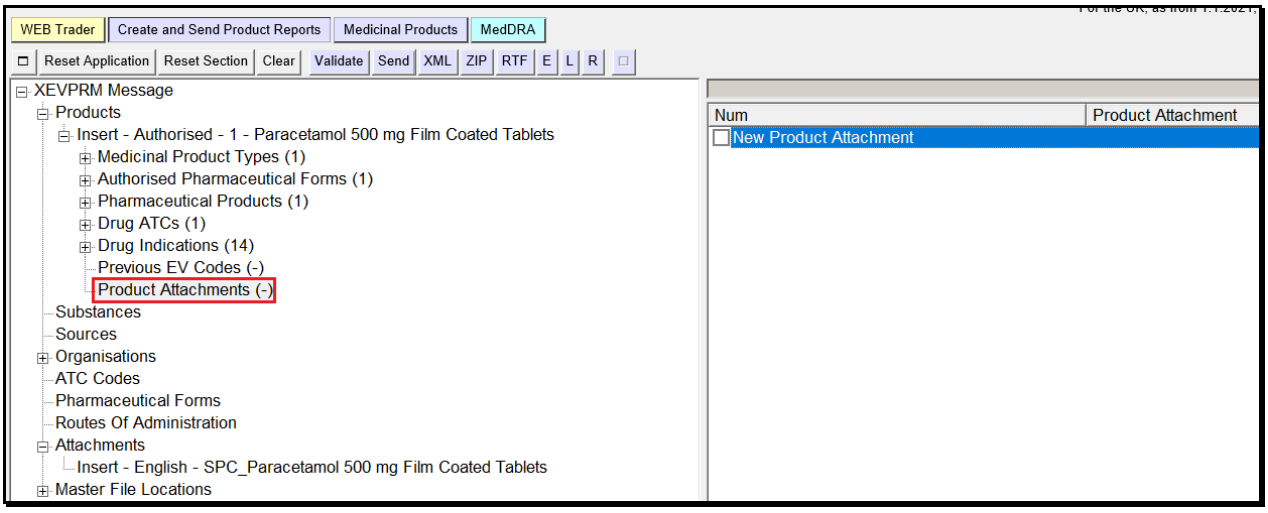
- For the complete list of data fields collected for a **PPI attachment entity** in the XEVMPD and the applicable business rules please refer to:
  - Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance; section *1.10. Submission of an attachment*, or
  - the Guidance on the electronic submission of information on investigational medicinal products for human use in the eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD): eXtended EudraVigilance Medicinal Product Report (XEVPRM) user guidance document, section *7. Initial submission of an attachment*.

4.2.10.2. Reference an attachment in a product entity

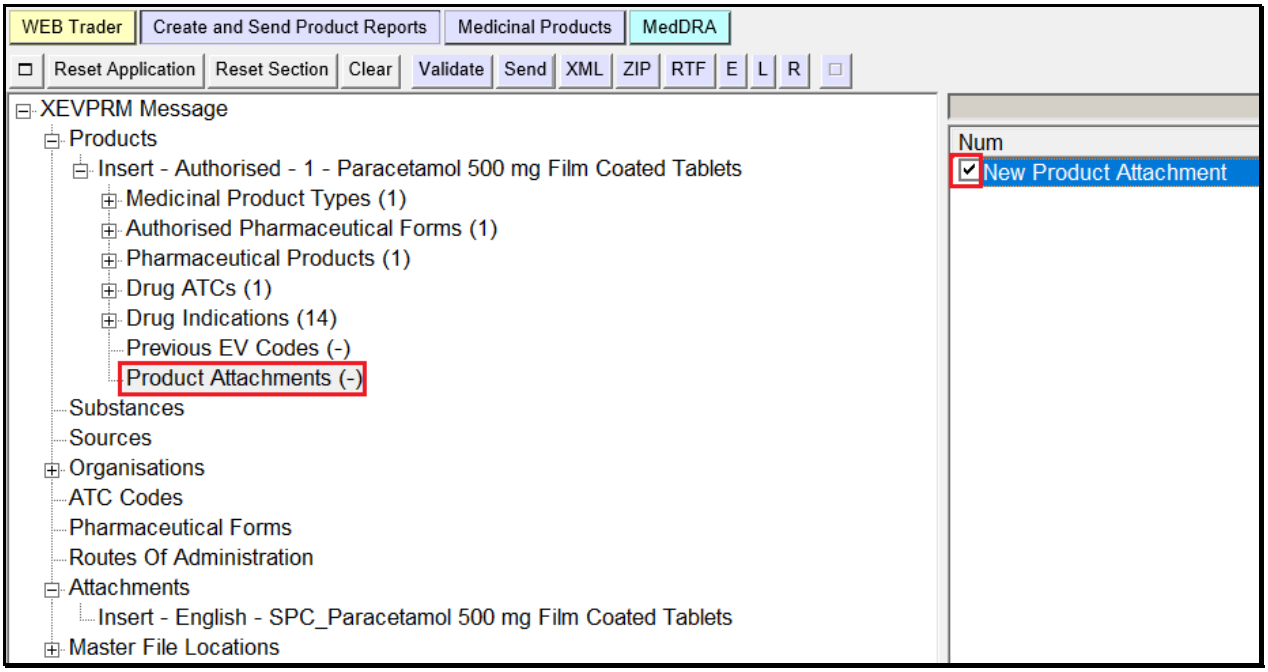
Once you enter all the required information for your attachment in the 'Attachment' section of your XEVPRM, you must reference the attachment in the product entity, for which the attachment is to be used as a supporting document.



To do so, go to the 'Attachment' section of your AMP and click on 'Product Attachments' in the tree-view area; 'New Product Attachment' will become available in the active area:

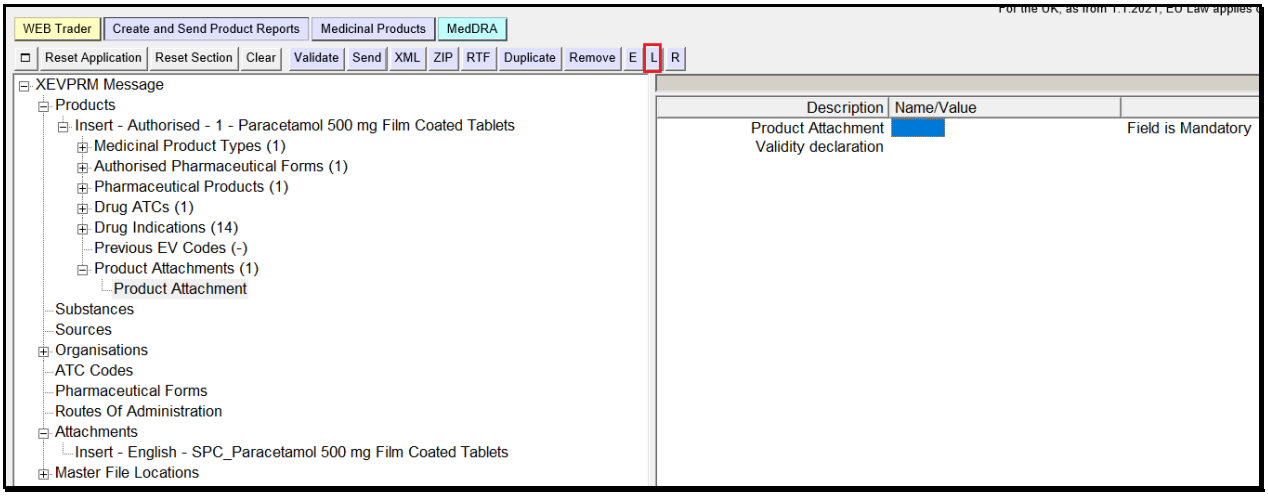


Tick the box next to 'New Product Attachment':

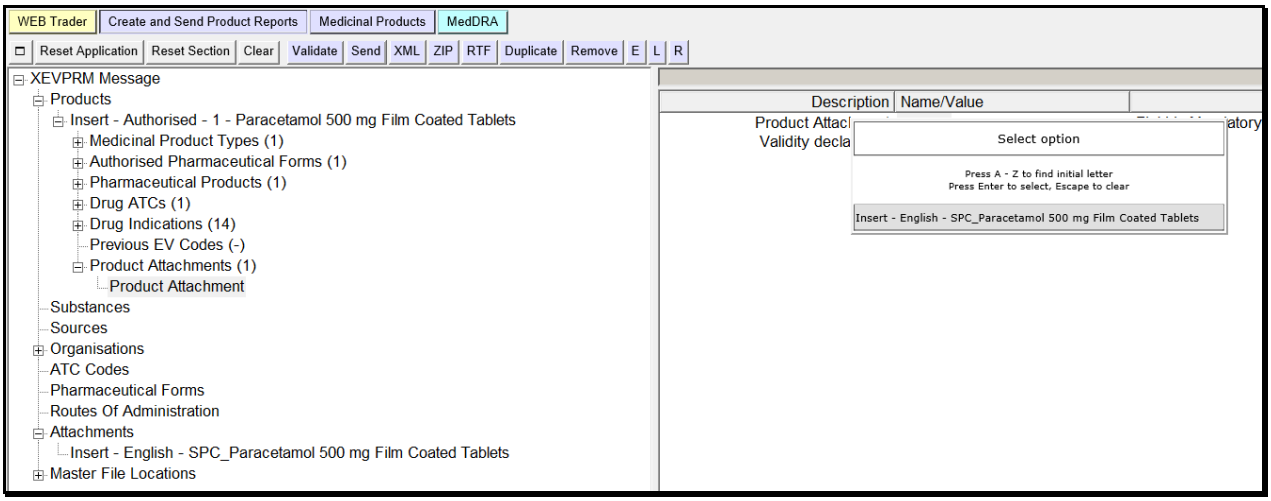


The active area will display the information that needs to be provided for the attachment that you wish to reference in your AMP. Since you are referencing a new attachment, which was not yet submitted in the XEVMPD and no attachment EV code is therefore available for the attachment, you must select the attachment from the local look-up table (L).

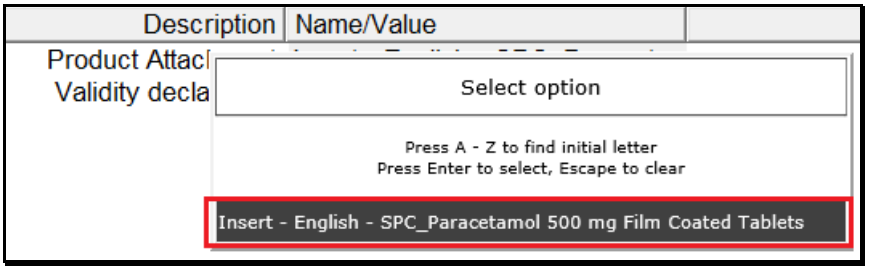
Click on the button  (Local data lookup) in the dynamic buttons section:



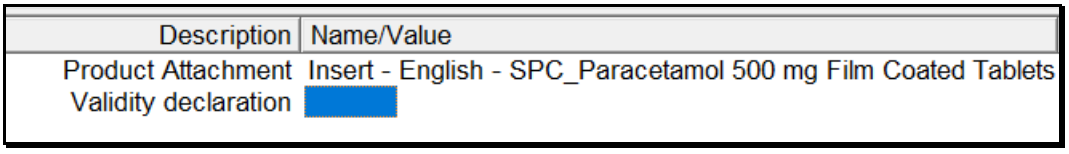
The available options will be displayed in the local look-up list of the 'Product Attachment field':



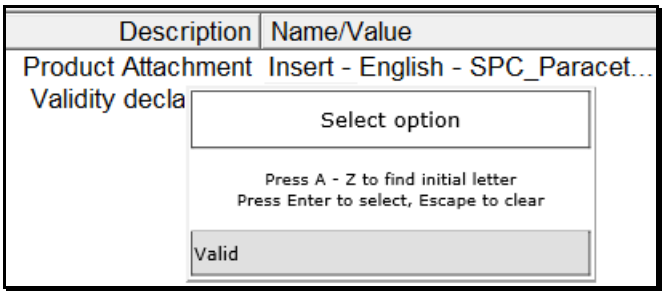
Using your mouse, select the required attachment:



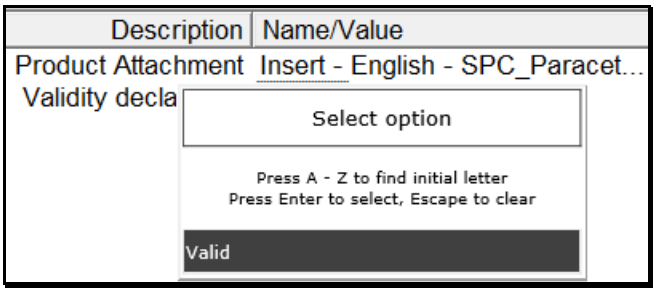
The attachment name will be displayed in the 'Product Attachment' field. The area next to 'Validity declaration' will be highlighted in blue:



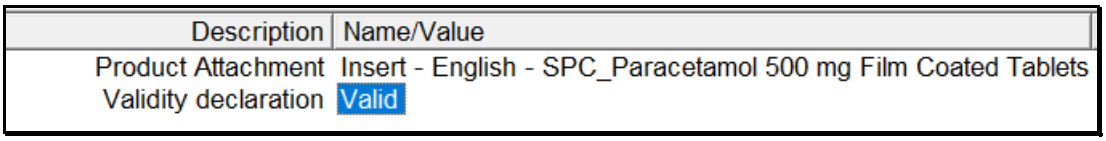
When you double-click on the area or use 'Enter' on your keyboard, you will be able to view the value applicable for this field:



Using your mouse or 'Enter' on your keyboard, select 'Valid':

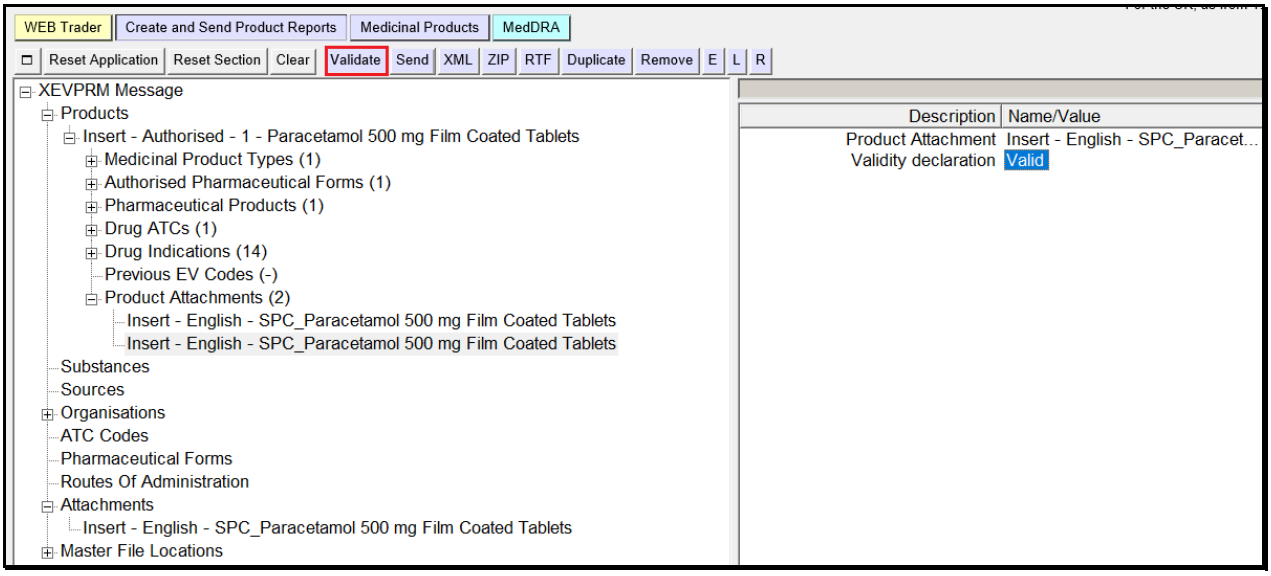


The value will be displayed in the 'Validity declaration' field:

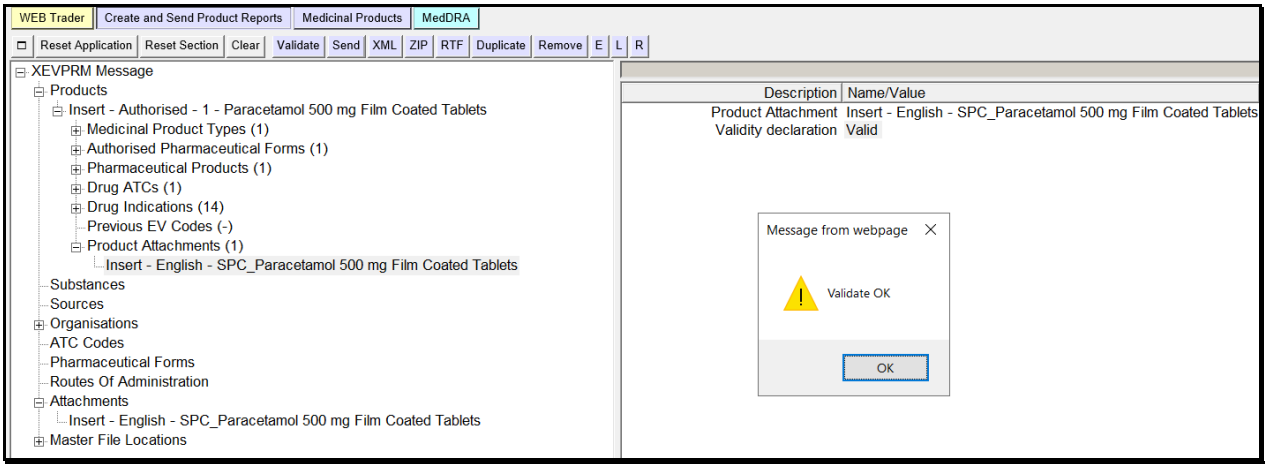


The validity declaration is only mandatory in case of maintenance operations, not for initial submissions of an attachment.

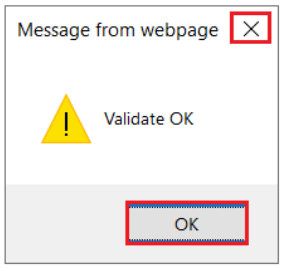
Validate your XEVPRM before proceeding with sending the attachment file and the XEVPRM:



New pop-up window will inform you of the validation status. If there are no errors in your XEVPRM, the below message will be displayed:

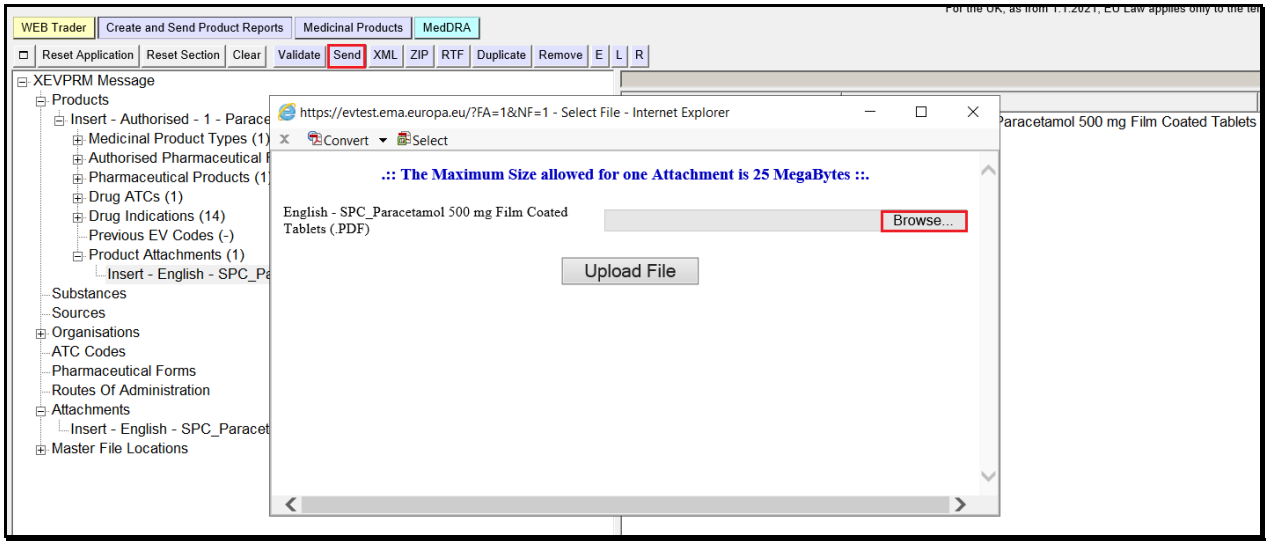


You can dismiss the message by clicking on 'OK' or 'x' in the right-hand corner of the window:



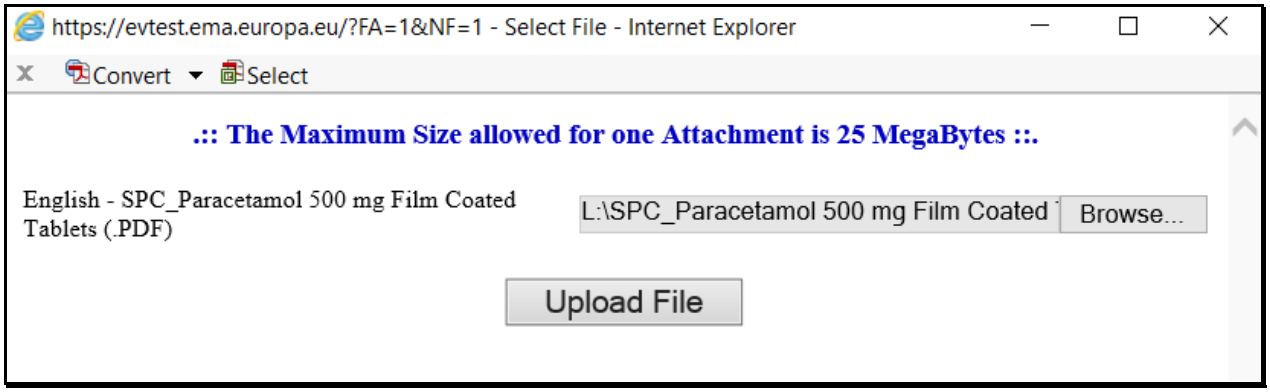
4.2.10.3. Submission of a file attachment at the time of XEVPRM submission

To send the XEVPRM, click on the 'Send' button:

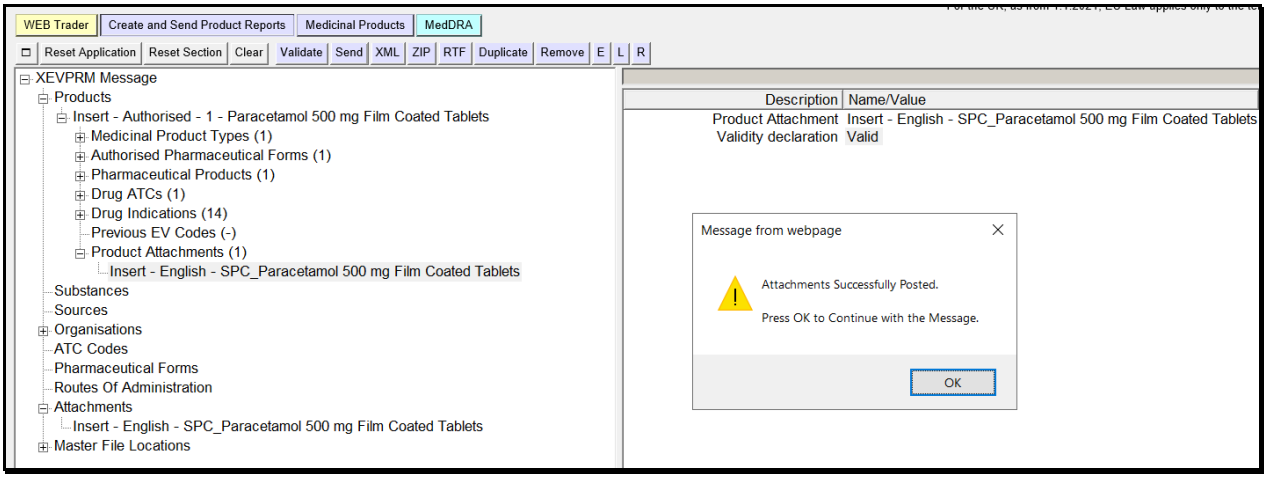


! The 'Send' button will only be available for users from organisations registered for product reporting via Web Trader. Whilst users from organisations registered for product submissions via Gateway can create XEVPRMs using EVWEB, the 'Send' button will not be available to them. Gateway organisation users can submit XEVPRMs as 'ZIP' files using EV Post. See section *4.9. Use EV Post* of this document for further information.

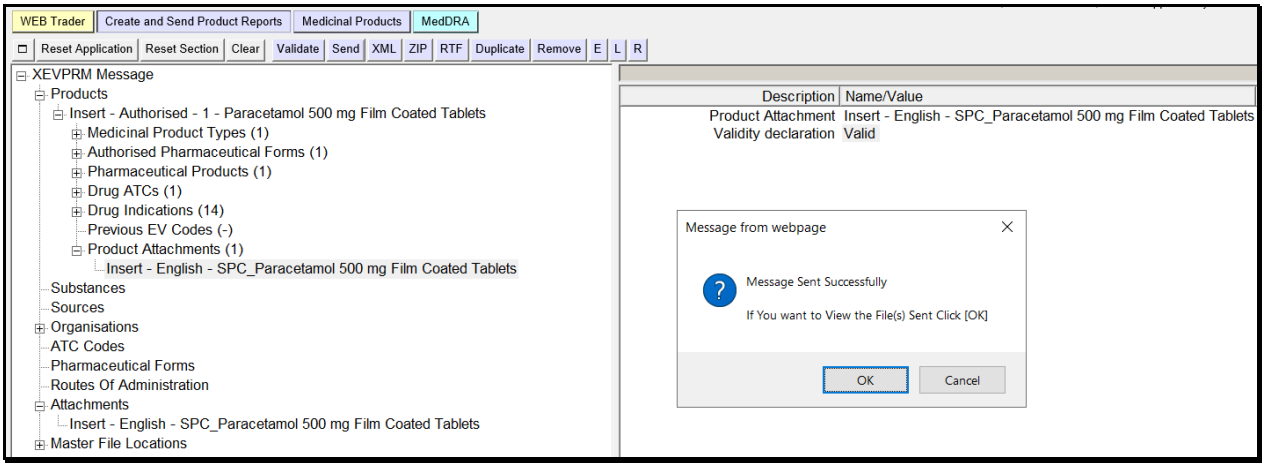
Once you click on the 'Send' button a new window will open, allowing you to browse your computer and select the file that you wish to submit in the XEVMPD. Once you make the selection, click on 'Upload File':



If the attachment was successfully posted, a new window will open confirming the result of your action:



Click 'OK' to dismiss the message; another pop-up window will open informing you that your XEVPRM was sent successfully:

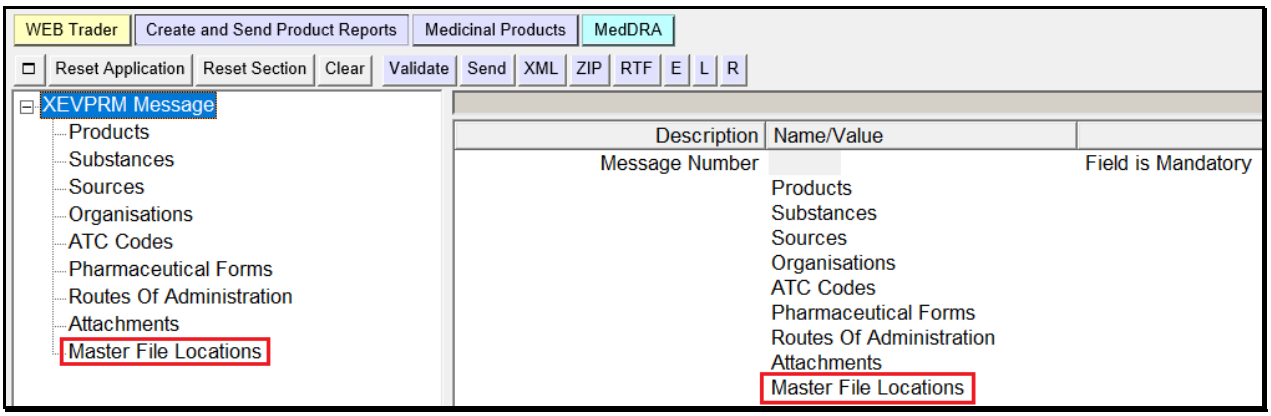


An XEVPRM acknowledgement will be sent to the sender organisation ID, and if the submission was successful, it will include the EV Codes assigned to the attachment, as well as to the product entity:

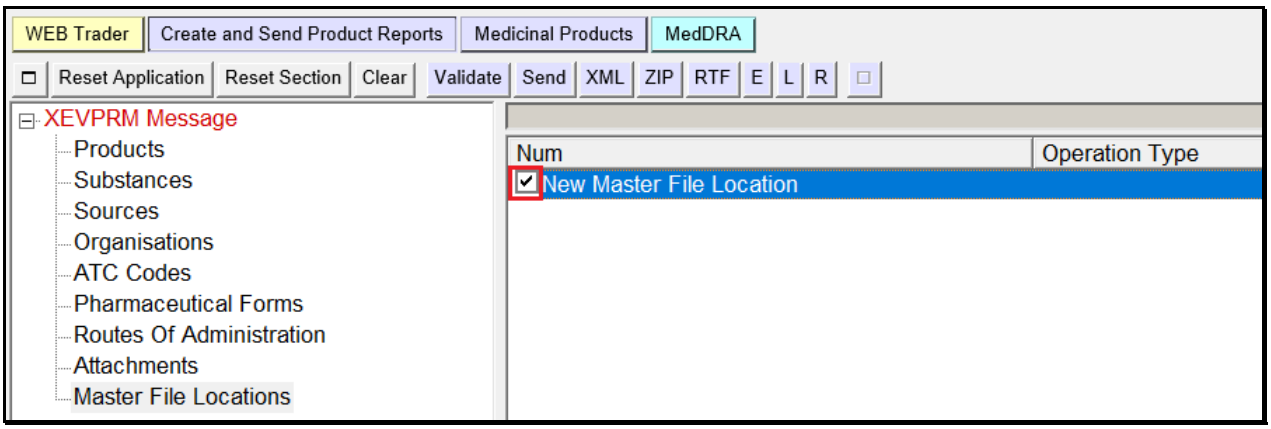
```
- <reportacknowledgment>
    <reportname>ATTACHMENT</reportname>
    <localnumber/>
    <ev_code>ATT1234567</ev_code>
    <operationtype>1</operationtype>
    <operationresult>2</operationresult>
    <operationresultdesc>Entity inserted successfully</operationresultdesc>
  </reportacknowledgment>
- <reportacknowledgment>
    <reportname>AUTHORISEDPRODUCT</reportname>
    <localnumber/>
    <ev_code>PRD8757963</ev_code>
    <operationtype>1</operationtype>
    <operationresult>2</operationresult>
    <operationresultdesc>Entity inserted successfully Version 1 The product will be validated by the
      EMA in due course. When validated you will receive a further acknowledgement with the
      message number: "Product Validated PRD8757963 Version [Version Number] / [Date and
      Time]". </operationresultdesc>
  </reportacknowledgment>
```

4.2.11. Insert of a Master File Location

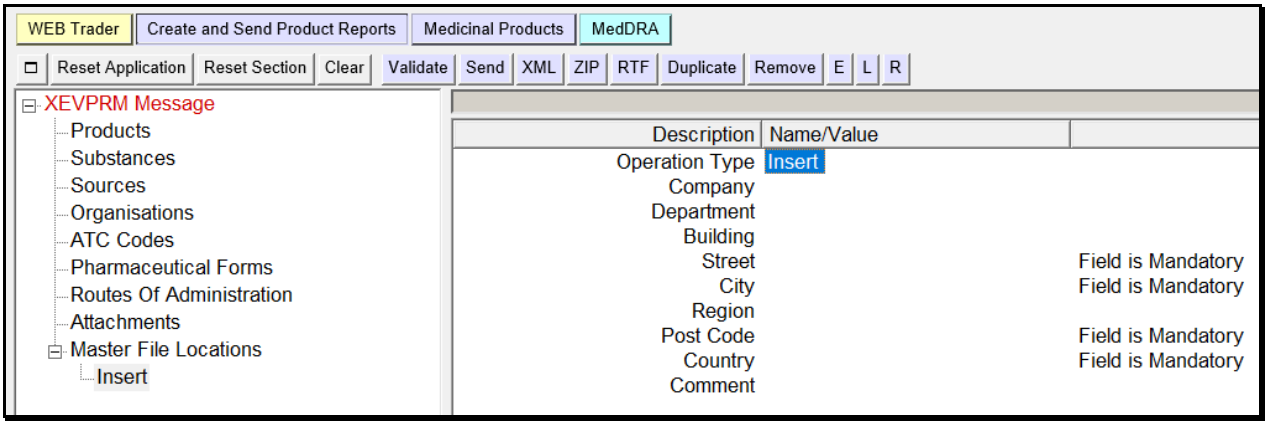
To create a 'Master File Location Report', you must select 'Master File Locations' in the tree-view area or in the active area:



You must select 'New Master File Location' in the active area by ticking the relevant box:



Once you have selected 'New Master File Location', the tree-view area and the active area will display the fields that need to be completed for the relevant section of the XEVPRM:



The 'Operation Type' field displays 'Insert' as default.

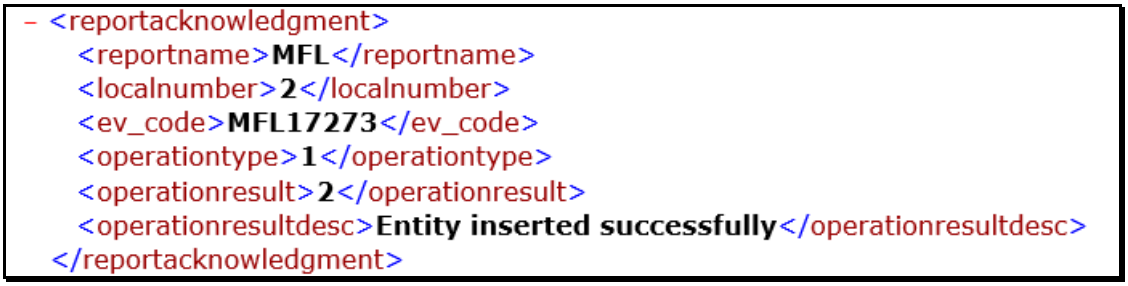
Information to be provided as mandatory is highlighted as 'Field is Mandatory'.

Complete the fields as required.

For the complete list of data fields collected for a Master File Location entity in the XEVMPD and the applicable business rules please refer to Chapter 3.II: Extended EudraVigilance product report message (XEVPRM) user guidance; section *1.11. Initial submission of a Pharmacovigilance System Master File (PSMF) information*.

Validate and send the XEVPRM.

The XEVPRM acknowledgement will be sent to the sender organisation ID; if the submission was successful, the EV code assigned to the MFL will be provided:



See also Extended EudraVigilance Medicinal Product Report Message step-by-step guide: **Insert of a pharmacovigilance master file location entity** step-by-step document available on the 'Training' webpage for more details.

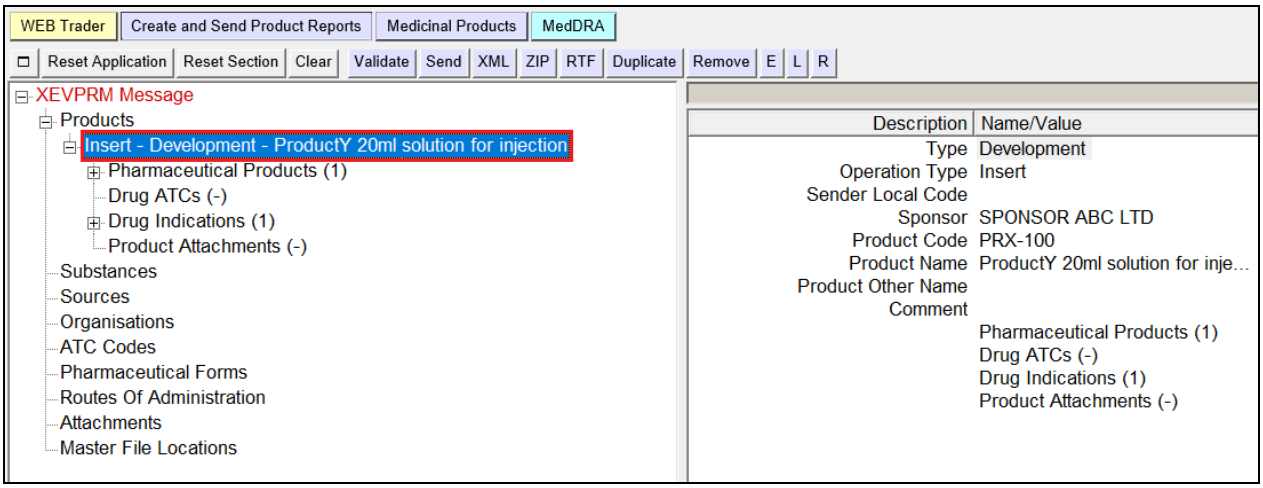
4.3. Duplicate an entity in an XEVPRM

To accelerate the data entry process during the creation of an XEVPRM in EVWEB, it is possible to duplicate any entity present in you XEVPRM and modify it as appropriate.

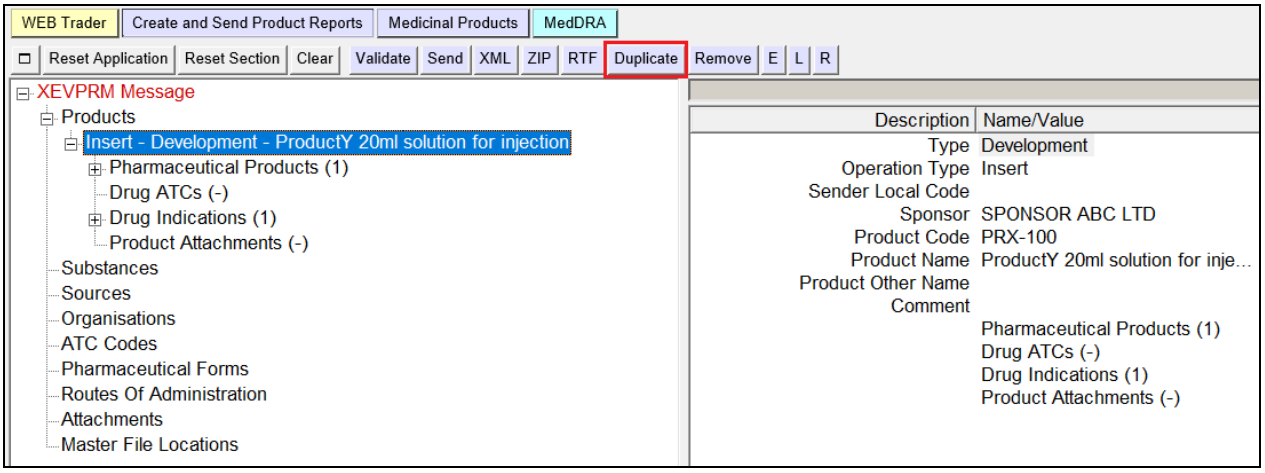
Once you have created an entity (e.g., a product, a source, an organisation, an ATC code, route of administration, pharmaceutical form etc.) with operation type 'Insert' in your XEVPRM, and you **select the item in the tree-view area**, the main menu will display the 'Duplicate' button:

4.3.1. Duplication of a product entity information in an XEVPRM

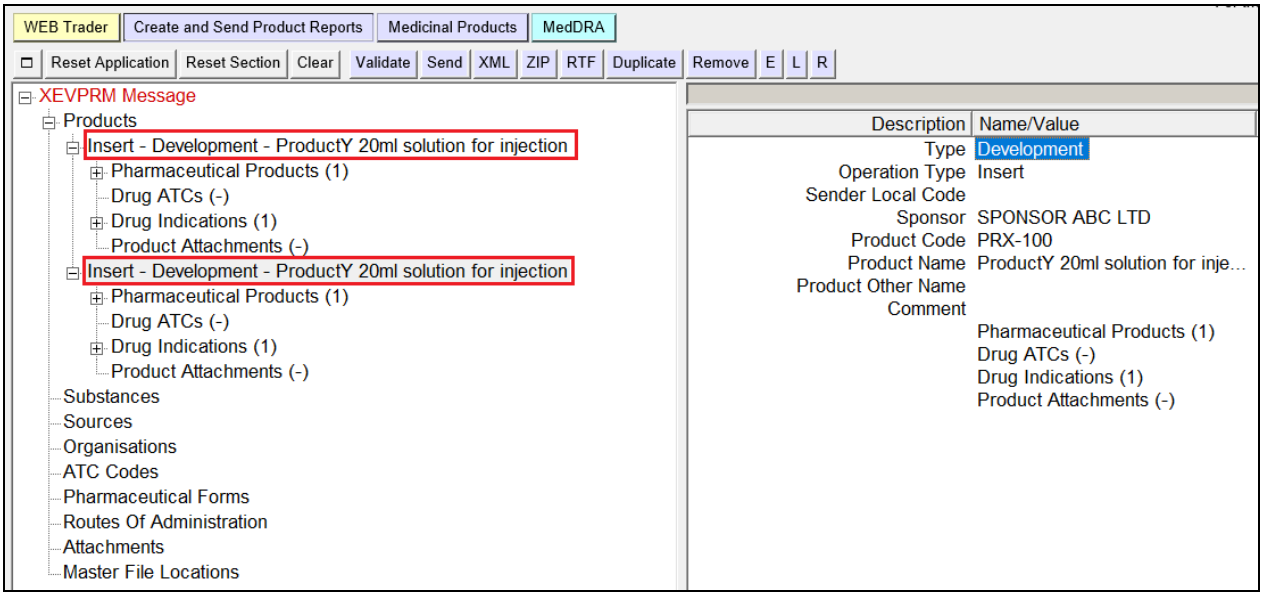
To duplicate a product entity in an XEVPRM, select the product entity in the tree-view area:



Click on the 'Duplicate' button:

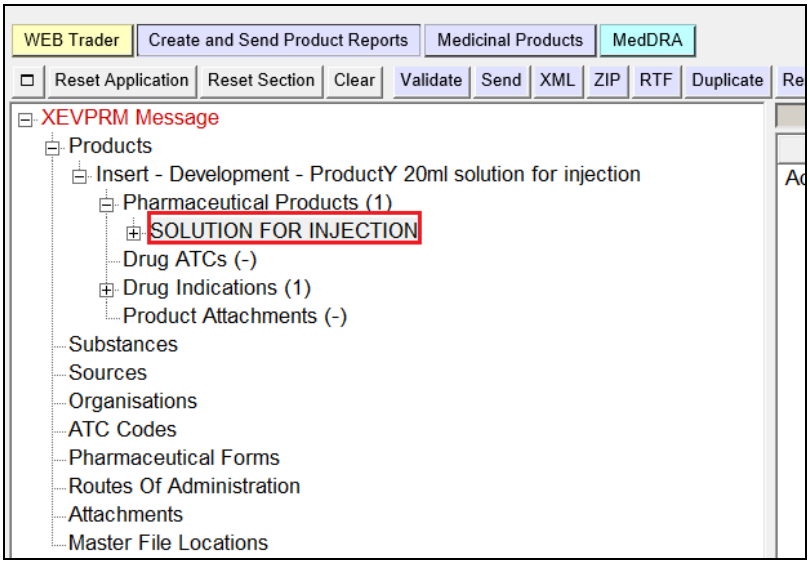


EVWEB automatically adds a copy of the previously entered item in the tree-view area; a new entity is displayed with the operation type assigned as 'Insert':

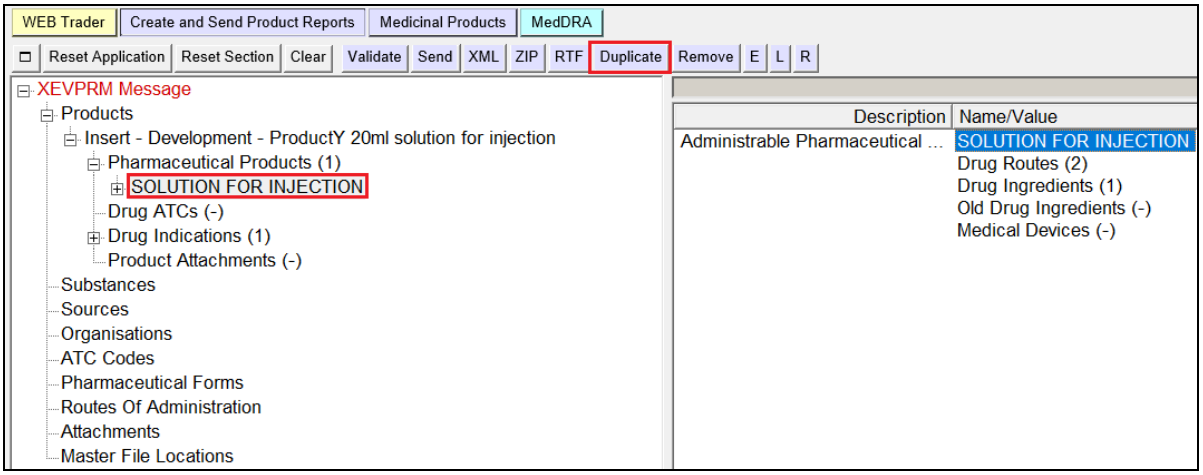


4.3.2. Duplication of a pharmaceutical product information of a product entity in an XEVPRM

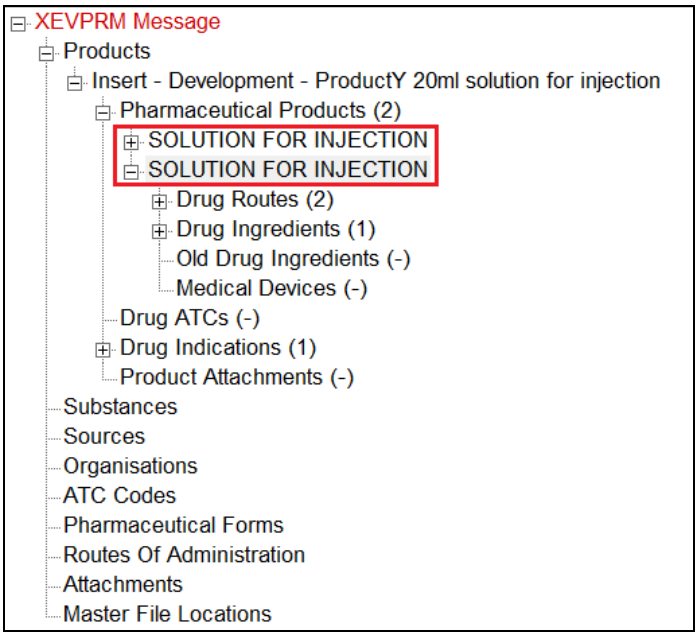
To duplicate pharmaceutical product information of a product entity in an XEVPRM, select the pharmaceutical product information in the tree-view area:



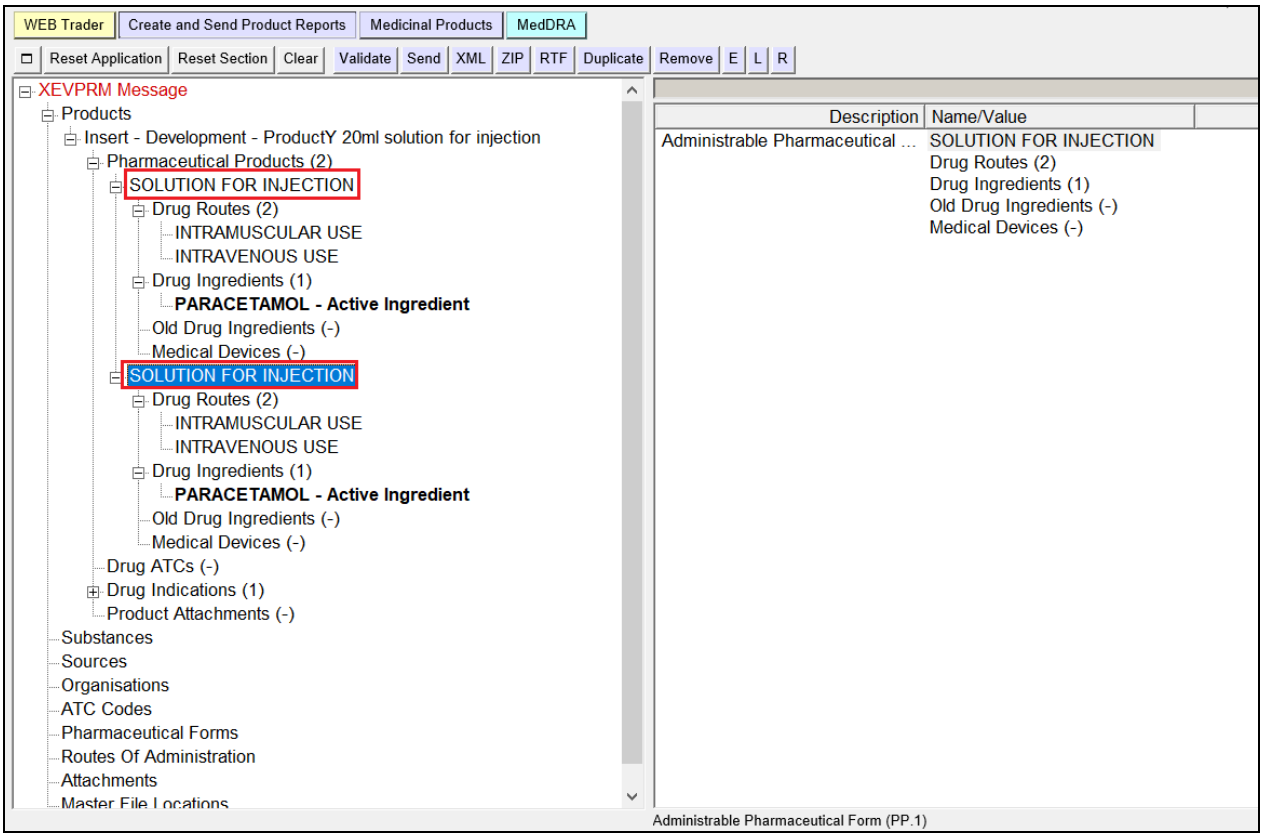
Click on the 'Duplicate' button:



EVWEB automatically adds a copy of the previously entered item in the tree-view area; a new entity is displayed with the operation type assigned as 'Insert':



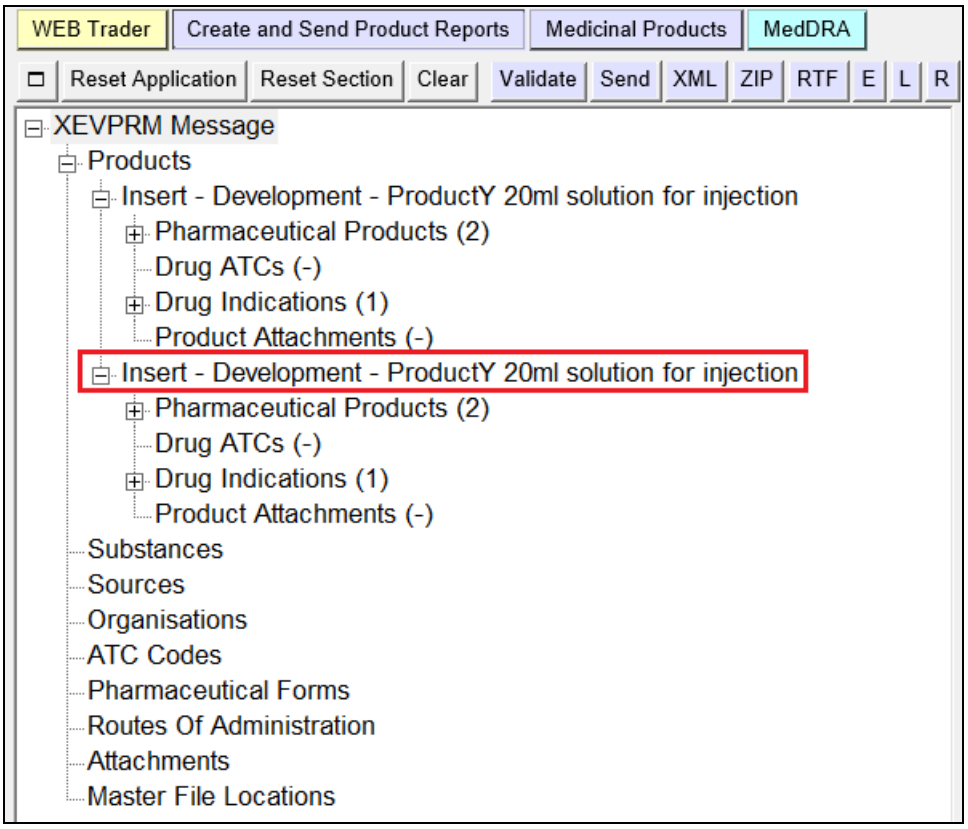
You can expand the items and modify the information of each of the items as required:



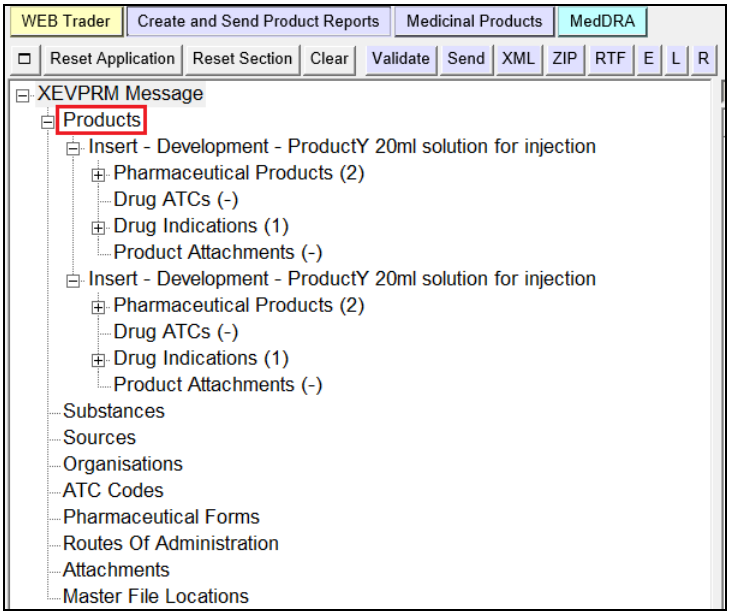
4.4. Remove an entity from an XEVPRM

To remove one or more items from your XEVPRM, you need to mark the item to be removed by unmarking the item in the list displayed in the active area.

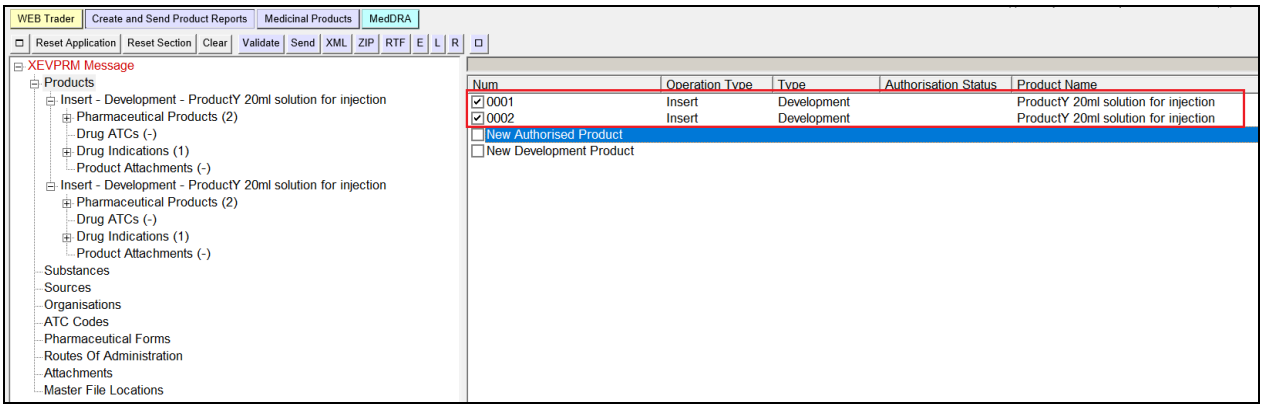
As an example, we wish to remove one of the DMP entities currently present in our XEVPRM:



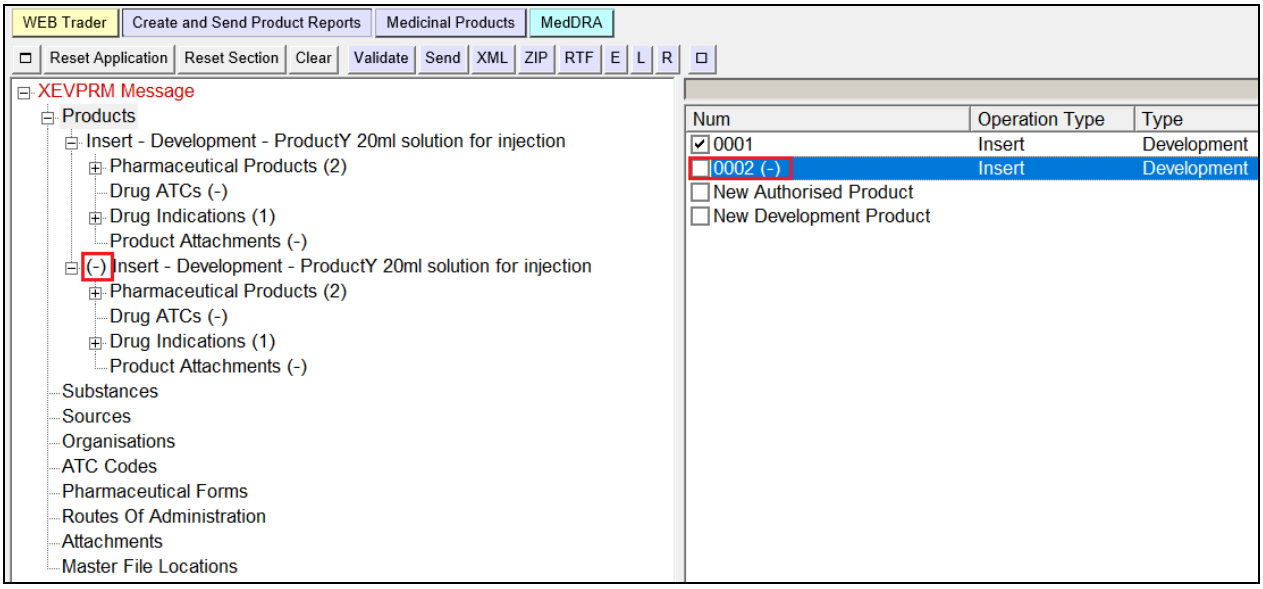
To do so, we must click on the 'Product' section in the tree-view area:



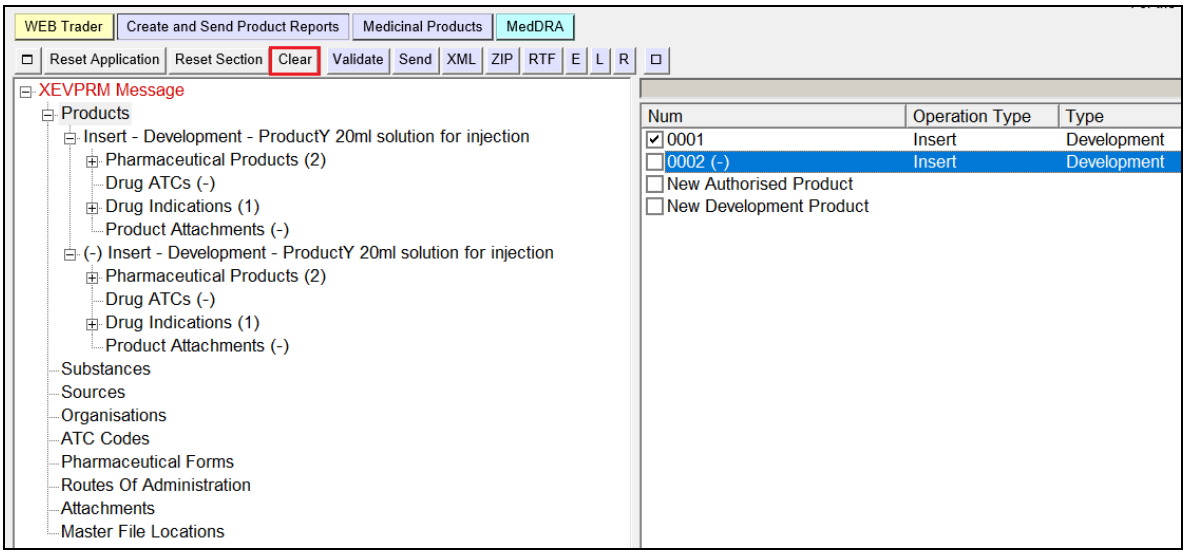
By doing so, the active area will display the list of entities present in our XEVPRM:



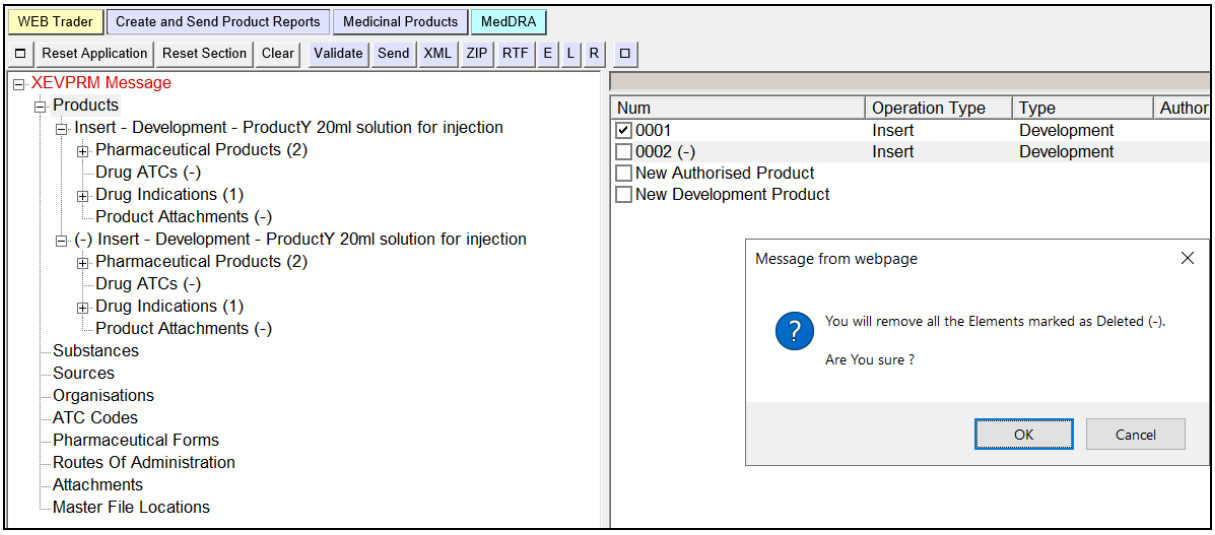
If you unmark one of the items displayed in the list, a negative (-) sign will be displayed in both, the tree-view area and in the active area. This indicates that that specific item has been marked for deletion and therefore will be no longer considered in the active data:



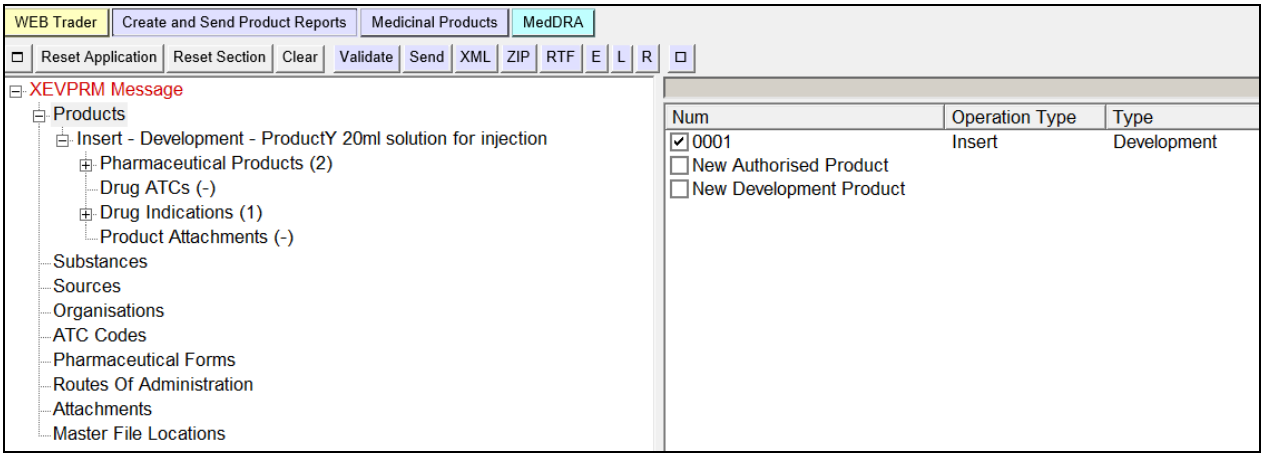
Once you unmark the item you wish to remove from your XEPRM, click on 'CLEAR' in the main menu:



The below message will be displayed:



By clicking on 'OK', you will confirm that you wish to remove the de-selected item(s); the item will be removed from the tree-view area:

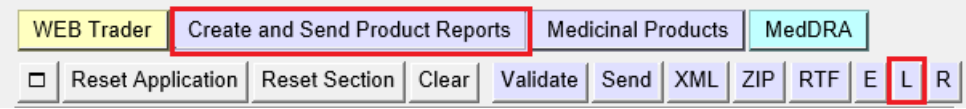


The same process described above can be used remove other entities from your XEVPRM (pharmaceutical products, organisations, attachments referenced in product entries etc.).

4.5. Reference information not yet present in the XEVMPD in a product entity in an XEVPRM

To reference an entity not yet present in the XEVMPD (i.e. an EV Code is not assigned to the entity and the entity is not available in the remote look-up table), you must add the entity in the relevant section of the XEVPRM.

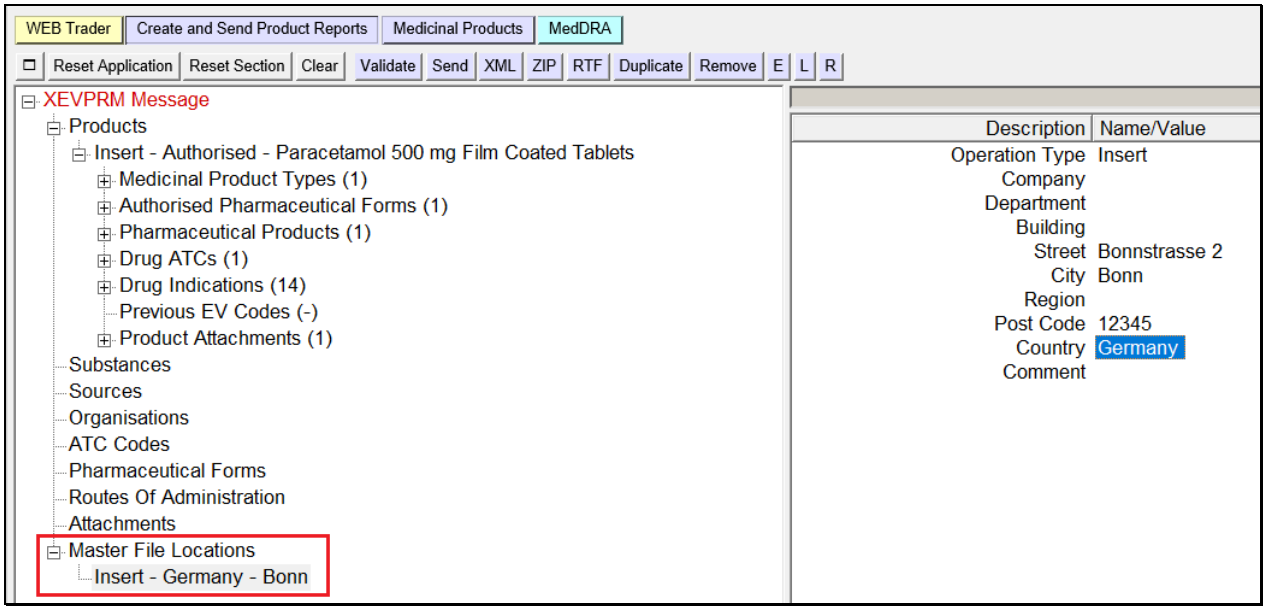
Once this entity is added, you can retrieve it from the Local ('L') look-up table:



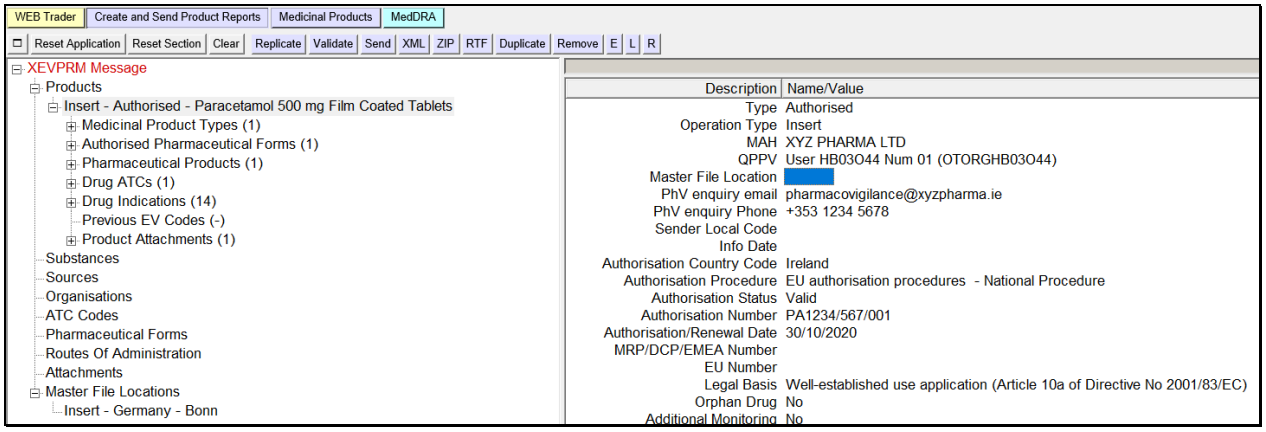
See section *3.5.1.5. Local database look-up tables* of this document for related information.

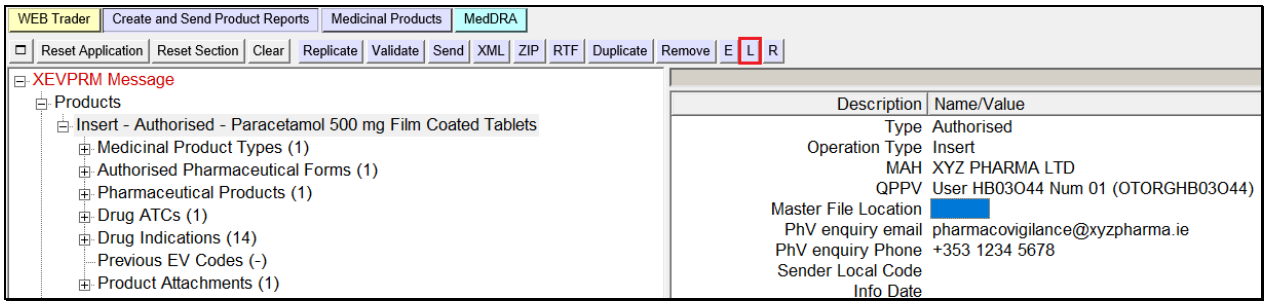
As an example, we wish to reference in an AMP entity, which is a subject to an insert, a new Master File location entity, which is not yet present in the XEVMPD.

First, we must enter the master file location information in the 'Master File Location' section of the XEVPRM:

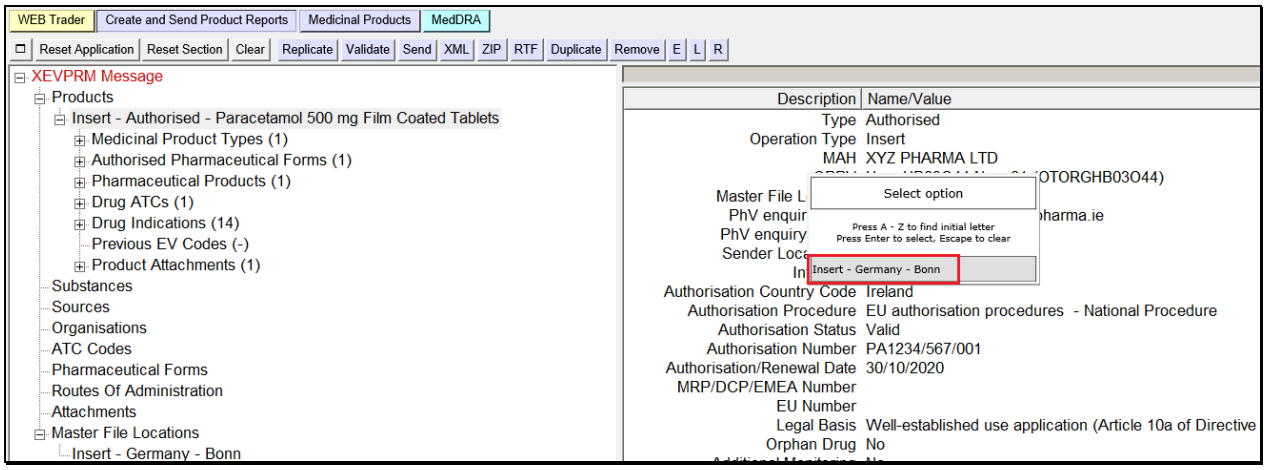


When done, go to your AMP entity, click in the area next to the field 'Master file location' (so it becomes highlighted in blue) and then on the button L (Local data lookup):

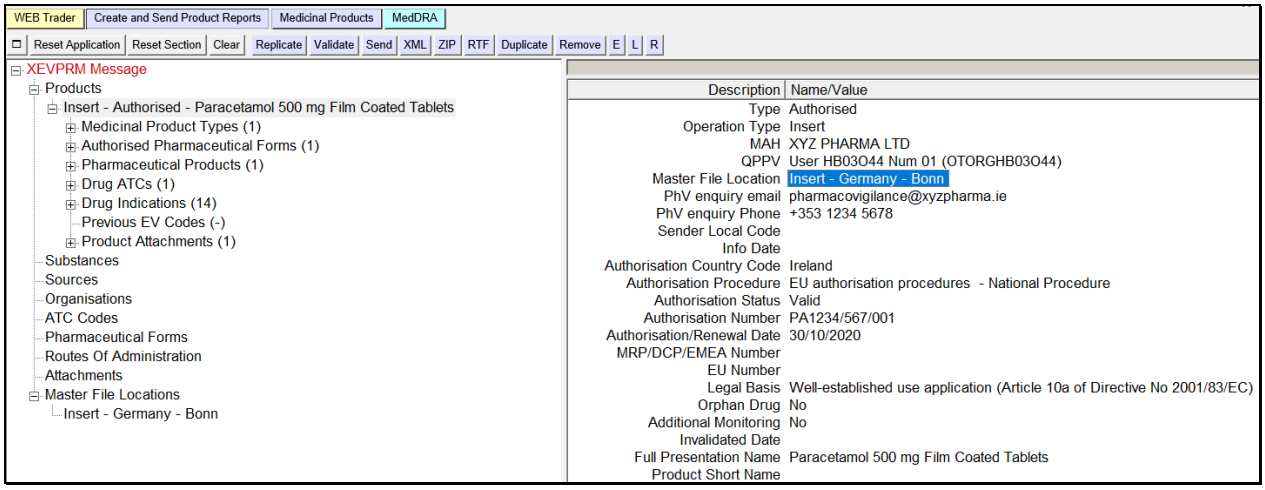




From the pop-up menu, select MFL location and click on the entity or press 'Enter' on your keyboard:



The MFL entity will then be referenced in your AMP entity:



The same process can be used to add information regarding new organisations, reference sources, ATC codes (proposed or development), routes of administration (proposed or development), pharmaceutical forms (proposed or development), MFLs and attachments.

4.6. Create an XEVPRM with maintenance related operation types/commands

4.6.1. Update of entities in the XEVMPD

The information concerning medicinal products (authorised or development), sources, organisations (MAH or sponsor), ATC codes (proposed or development), routes of administration (proposed or development), pharmaceutical forms (proposed or development), attachments and Master File Locations, can be modified only by the owner of the entity in the XEVMPD (i.e. the organisation that has provided the initial information) and the EMA.

XEVMPD will check the ownership of the information before allowing any modification to the information in the XEVMPD.

Information of substance entities can only be modified by the EMA.

Operation type 'Update (2)' shall be used cover several scenarios related to the maintenance of data submitted in the XEVMPD, for example:

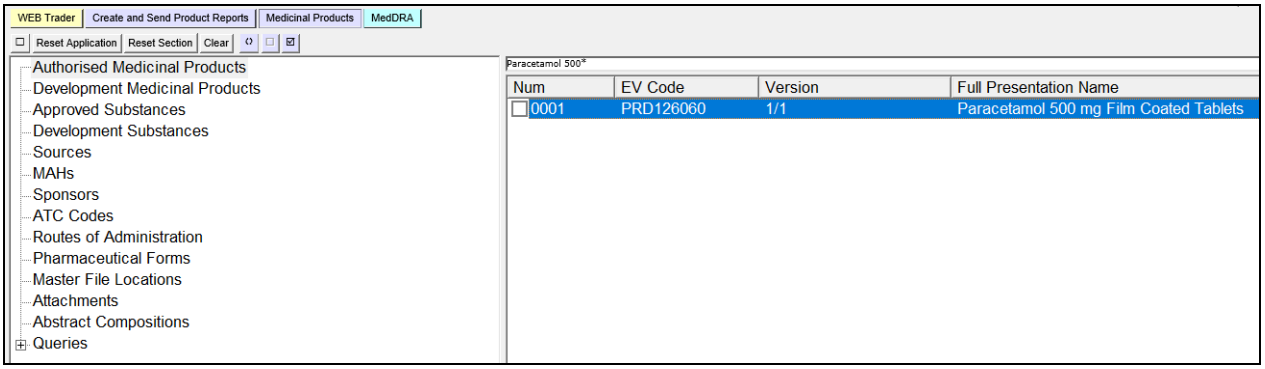
- To amend in an XEVMPD entity (e.g., medicinal products, organisations, MFLs, pharmaceutical forms; routes of administration, ATC Codes, sources etc.) information submitted incorrectly or by mistake (e.g. spelling mistake, incorrect information).
- To amend an AMP entry following a variation procedure, lifting of suspension of marketing authorisation or a renewal or marketing authorisation, extension to the terms of marketing authorisation changing the route of administration where the MA number doesn't change.
- To amend an AMP entry to reference a new QPPV, MAH organisation, SmPC, MFL etc.

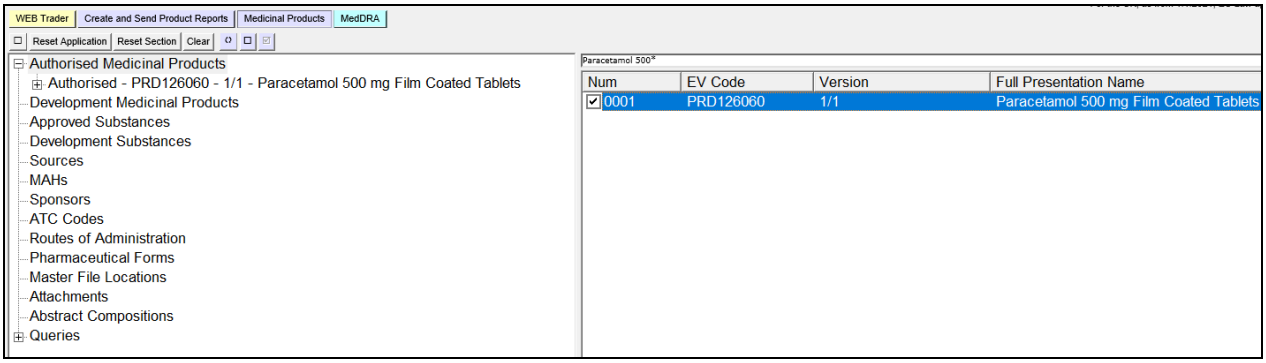
4.6.1.1. Create an XEVPRM with operation type 'Update (2)'

The update an entity, the entity:

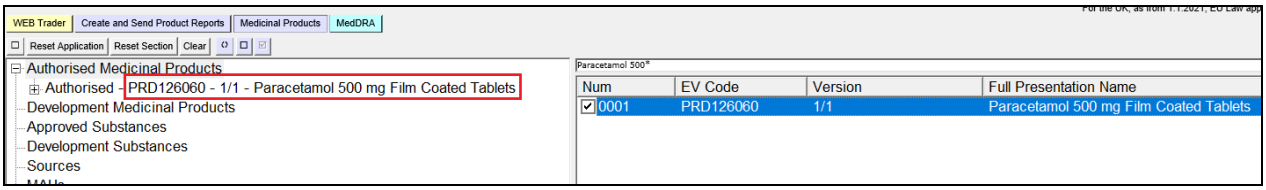
- must be already present in the XEVMPD (i.e., an EV Code has been assigned); and
- must not be nullified;
- must not be an invalidated entity.

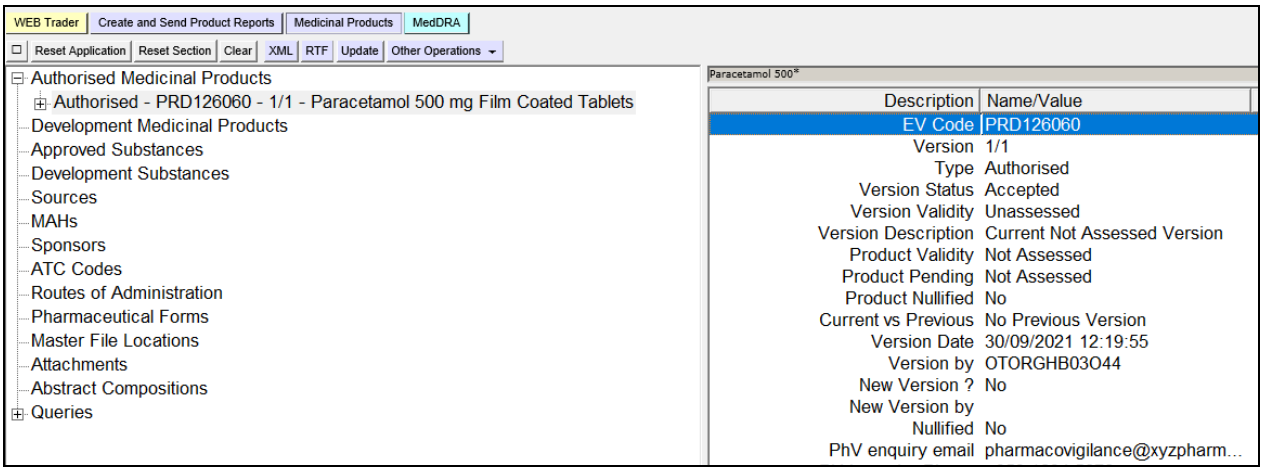
Retrieve the entity you need to update in the XEVMPD either using a simple or an advanced query and select the entity so that it is displayed in your tree-view area:



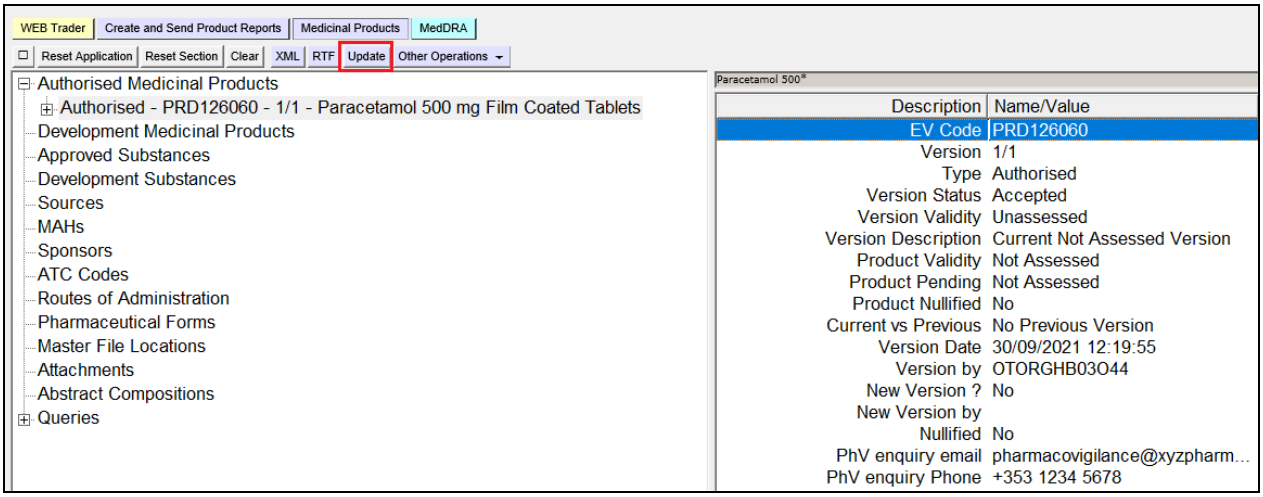


Click on the EV Code or name of the medicinal product entry in the tree-view area so the product information is visible in the active area:

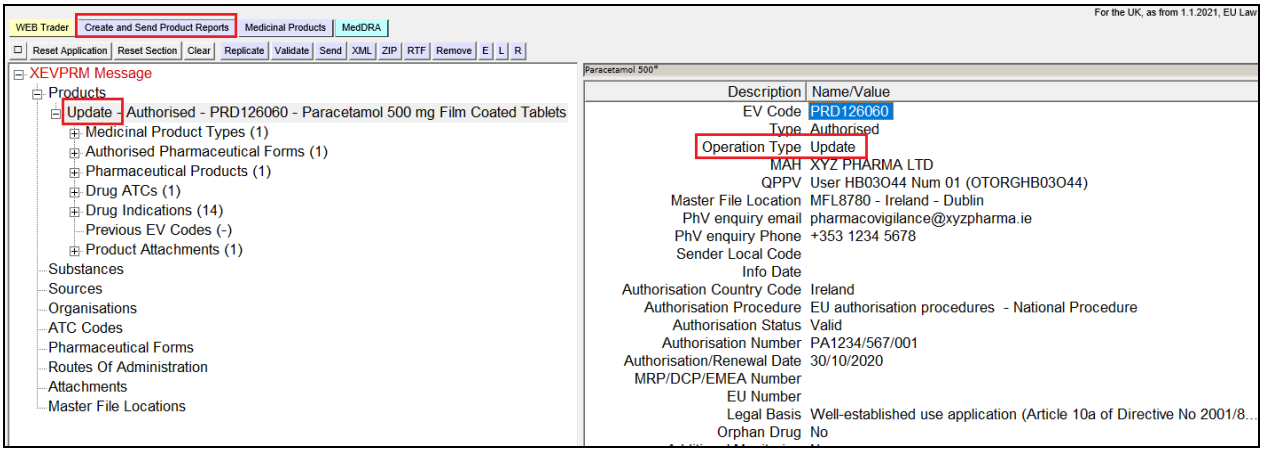




To perform and update, click on operation type 'Update' in the main menu:



Your product entity is moved from the 'Medicinal product' section to the 'Create and Send Product Reports' section. The operation type displayed is 'Update':



Modify the information within the entity as requested, enter the message number, validate, and send the XEVPRM.

The XEVPRM acknowledgement will be sent to the sender organisation ID and, if the update submission was successful, will display a message similar to the following message:

```
- <reportacknowledgment>
    <reportname>AUTHORISEDPRODUCT</reportname>
    <localnumber />
    <ev_code>PRD126060</ev_code>
    <operationtype>2</operationtype>
    <operationresult>4</operationresult>
    <operationresultdesc>Entity updated successfully Version 2 The
      product will be validated by the EMA in due course. When
      validated you will receive a further acknowledgement with the
      message number: "Product Validated PRD126060 Version
      [Version Number] / [Date and Time]".</operationresultdesc>
  </reportacknowledgment>
 </acknowledgment>
</evprmack>
```

! Please note that not every version of a medicinal product entity is validated by the EMA in the Article 57 database.

See also the Extended EudraVigilance Medicinal Product Report Message step-by-step guide: **Update of an authorised medicinal product** document available on the 'Training' webpage for more details.

4.6.2. Nullification of entities in the XEVMPD

Operation type 'Nullification (4)' should be used whenever an entity previously submitted, and for which an EV Code exists, needs to be nullified.

Operation type 'Nullification (4)' should be used when:

- an entity was submitted by mistake;
- an entity was identified as a duplicate;
- an entity is obsolete and will not be used in any future submissions.

The information concerning medicinal products (authorised or development), sources, organisations (MAH or sponsor), ATC codes (proposed or development), routes of administration (only development), pharmaceutical forms (only development) and master file locations, can be nullified by the owner organisation that has provided the initial information and the EMA. The XEVMPD will check the ownership of the information before allowing any modification in the dictionary.

Nullification of validated entities can only be performed by the EMA upon request submitted via the EMA Service Desk portal:

- Substance related requests: https://support.ema.europa.eu/esc?id=sc_cat_item&sys_id=6fac4352c3195d10e68bf1f4e40131a5

- XEVMPD product data related request: https://support.ema.europa.eu/esc?id=sc_cat_item&sys_id=5cd0ff1ec3995d10e68bf1f4e40131bb

The nullification of XEVMPD entities is not allowed in the XEVMPD if the entity is referenced in any other entry (e.g., AMP).

Please note that entries are never deleted from the XEVMPD, they are flagged as 'nullified', which means 'non-current'.

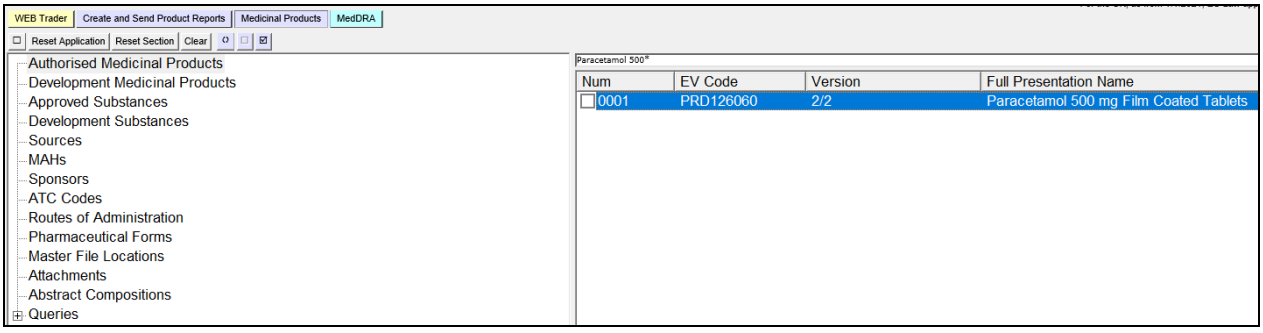
4.6.2.1. Create an XEVPRM with operation type 'Nullification (4)'

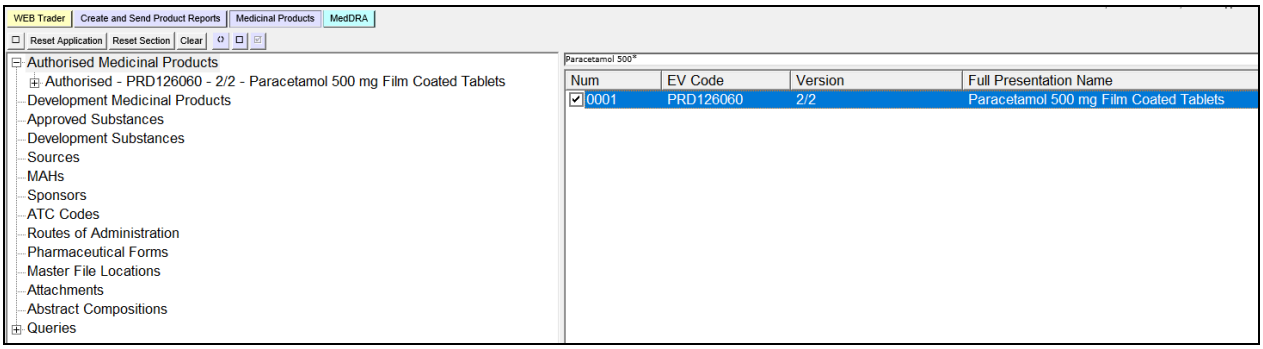
For an entity to be nullified by the MAH/Sponsor, the entity:

- must be already present in the XEVMPD (i.e., an EV Code has been assigned);
- must not be referenced in any other entity;
- must not be already nullified;
- must not be flagged as 'Valid' by the EMA. Nullification of validated entities can only be performed by the EMA upon request submitted via the EMA Service Desk portal:
  - Substance related requests: https://support.ema.europa.eu/esc?id=sc_cat_item&sys_id=6fac4352c3195d10e68bf1f4e40131a5
  - XEVMPD product data related request: https://support.ema.europa.eu/esc?id=sc_cat_item&sys_id=5cd0ff1ec3995d10e68bf1f4e40131bb

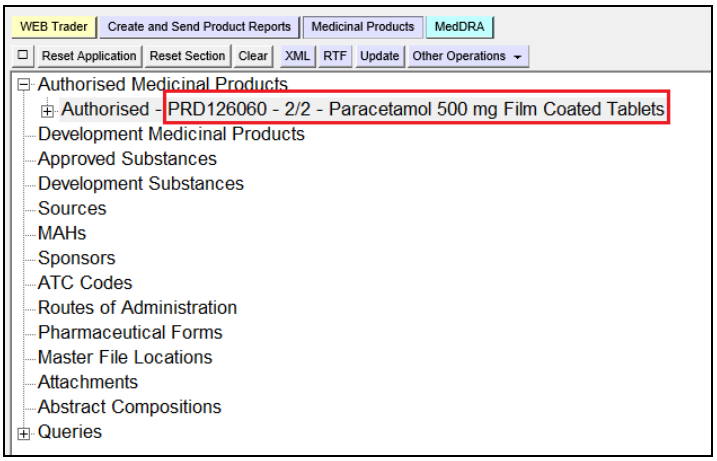
    and the reason for nullification must be provided.
- This rule is not applicable for development product entities; DMPs can be nullified by the owner organisation even if flagged as 'Valid' by the system.

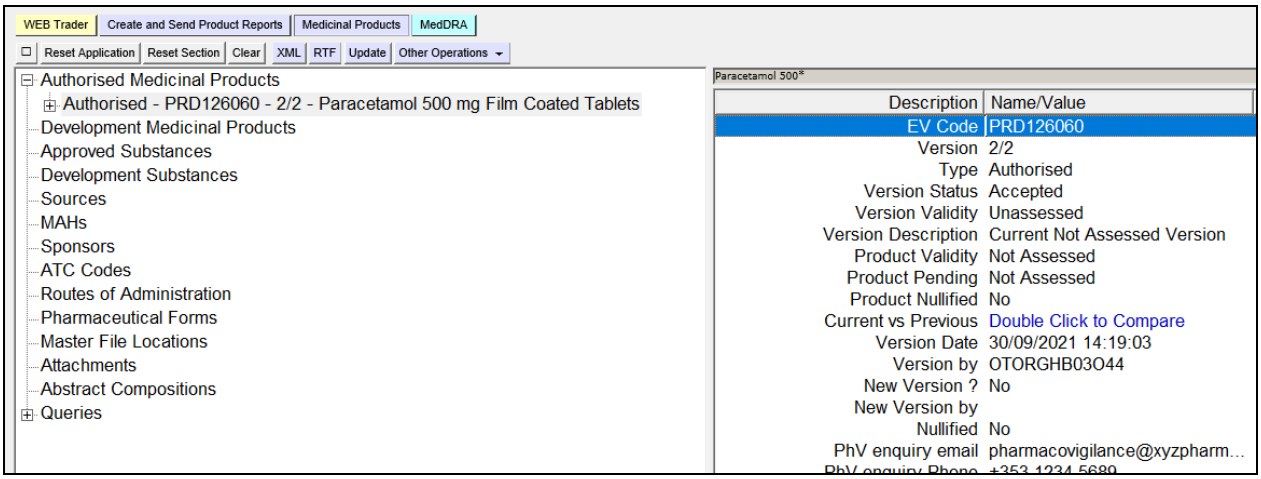
Retrieve the entity you need to nullify in the XEVMPD either using a simple or an advanced query and select the entity so that it is displayed in your tree-view area:



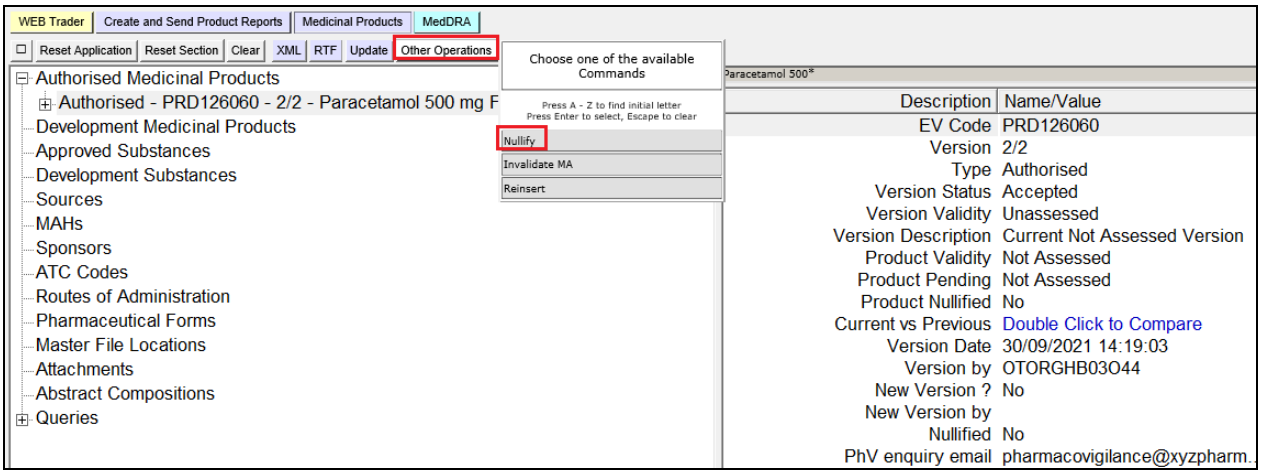


Click on the EV Code or name of the medicinal product entry in the tree-view area so the product information is visible in the active area:

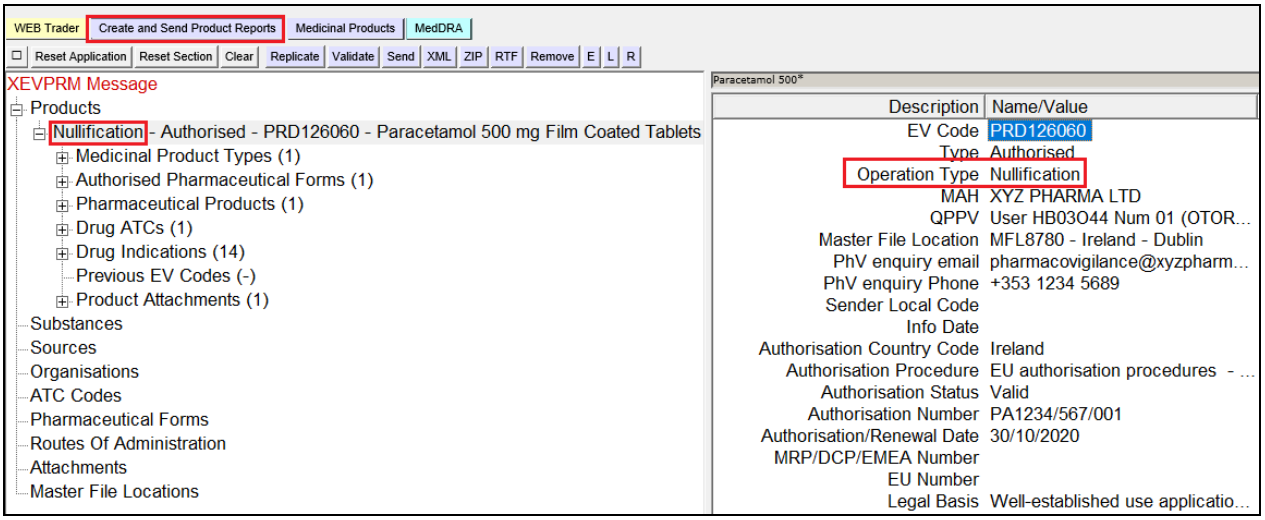




To perform the nullification, click on 'Other Operations' in the main menu and select 'Nullify':



Your product entity is moved from the 'Medicinal product' section to the 'Create and Send Product Reports' section. The operation type displayed is 'Nullification':



Enter the reason for nullification in the 'Comment' field of the entity, enter the message number, validate, and send the XEVPRM.

The XEVPRM acknowledgement will be sent to the sender organisation ID and, if the update submission was successful, will display a message similar to the following message:

```
- <reportacknowledgment>
    <reportname>AUTHORISEDPRODUCT</reportname>
    <localnumber/>
    <ev_code>PRD126060</ev_code>
    <operationtype>4</operationtype>
    <operationresult>3</operationresult>
    <operationresultdesc>Entity nullified successfully </operationresultdesc>
  </reportacknowledgment>
</acknowledgment>
</evprmack>
```

See also Extended EudraVigilance Medicinal Product Report Message step-by-step guide: Maintenance operations: **Nullification of development medicinal product (DMP) entity** in the XEVMPD available on the 'Training' webpage for more details.

4.6.3. Invalidation of an AMP entity in the XEVMPD

Invalidation can only be performed on Authorised Medicinal Products.

This function should be used when a marketing authorisation of an authorised medicinal product was revoked, withdrawn, transferred, or expired, and this change must be reflected in the Article 57 database. You can provide the information on the revocation/withdrawal/transfer/expiry of the AMP by sending an XEVPRM with the operation type 'Invalidate MA (6)'.

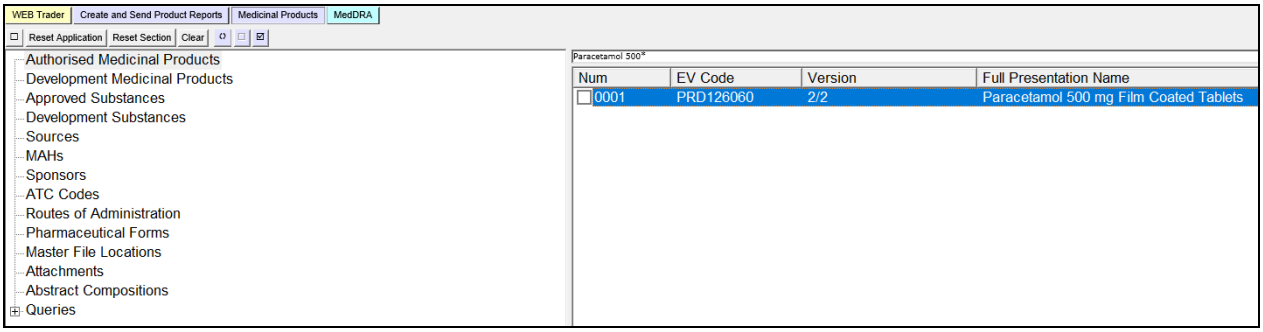
AMPs can be invalidated by the owner organisation that has provided the initial information and the EMA. The XEVMPD will check the ownership of the information before allowing any modification in the dictionary.

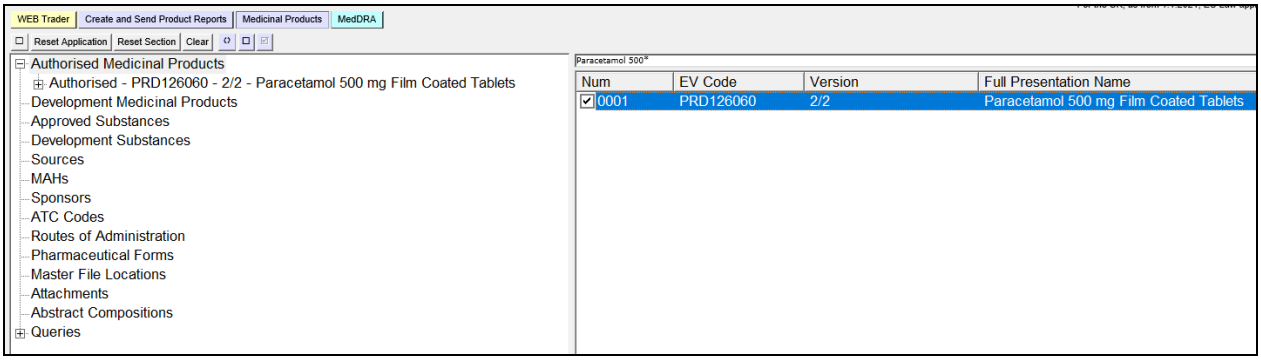
Please note that invalidated AMP entities are never deleted from the XEVMPD; their authorisation status is set as 'Not valid'.

4.6.3.1. Create an XEVPRM with Operation Type 'Invalidate MA (6)'

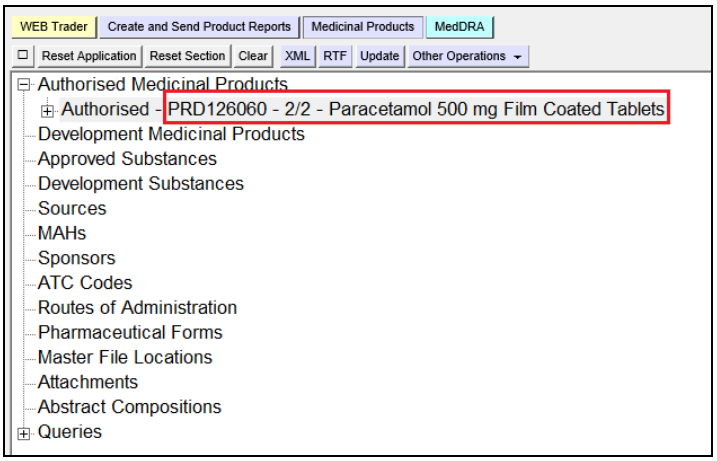
In the below example, we will modify an AMP to flag that the medicinal product was withdrawn from the market by the marketing authorisation holder.

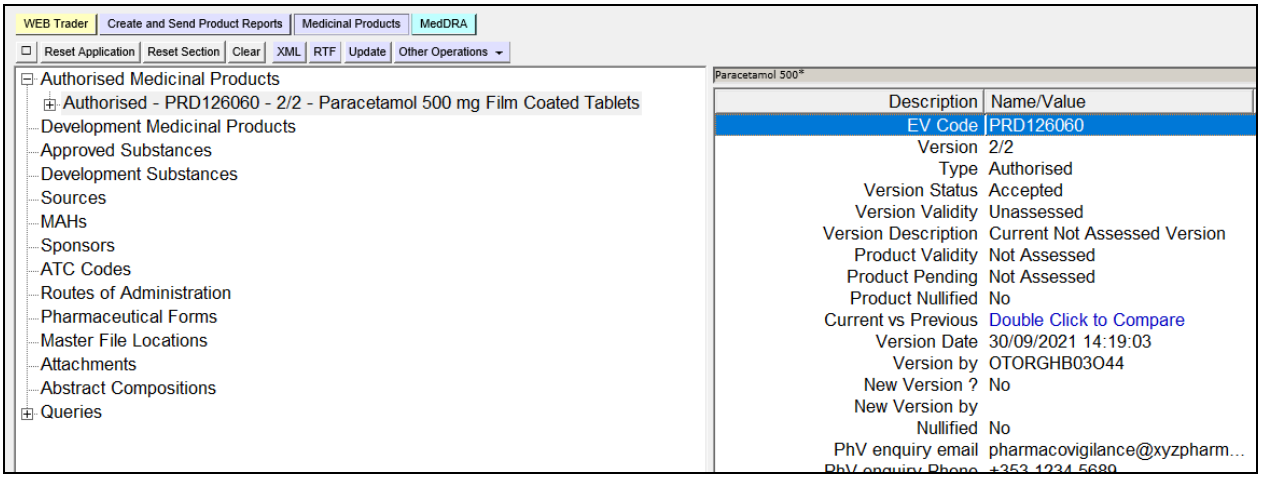
Retrieve the entity you need to flag as 'withdrawn' in the XEVMPD either using a simple or an advanced query and select the entity so that it is displayed in your tree-view area:



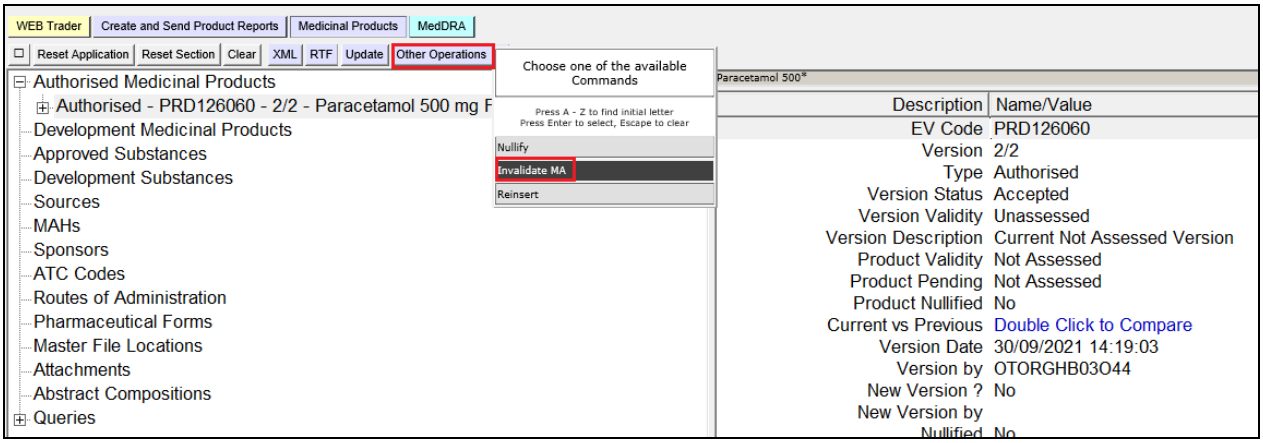


Click on the EV Code or name of the medicinal product entry in the tree-view area so the product information is visible in the active area:

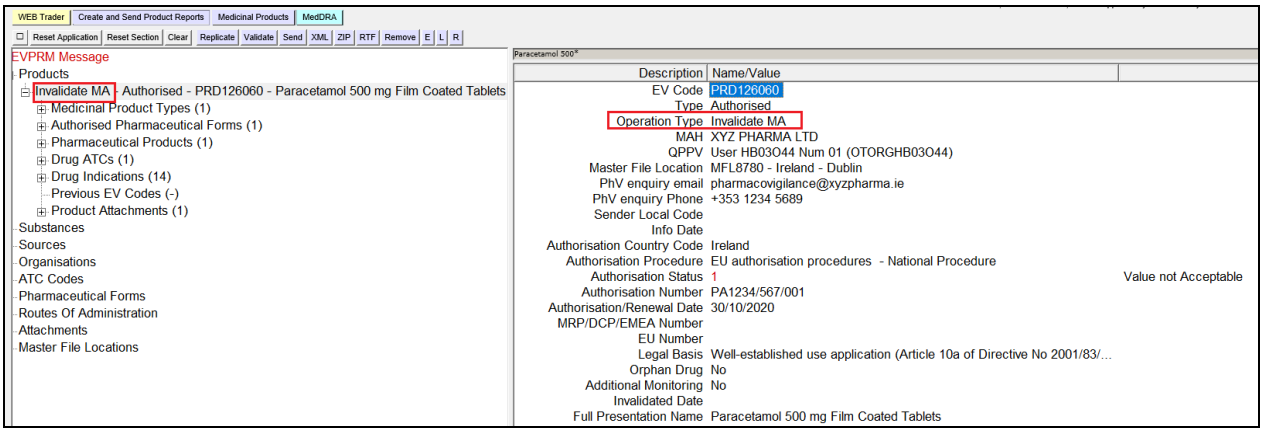




To perform the invalidation, click on 'Other Operations' in the main menu and select 'Invalidate MA':



Your product entity is moved from the 'Medicinal product' section to the 'Create and Send Product Reports' section. The operation type displayed is 'Invalidate MA':



Enter the required authorisation status and the invalidated date, assign the message number, validate, and send the XEVPRM.

The XEVPRM acknowledgement will be sent to the sender organisation ID and, if the update submission was successful, will display a message similar to the following message:

```
- <reportacknowledgment>
    <reportname>AUTHORISEDPRODUCT</reportname>
    <localnumber />
    <ev_code>PRD126060</ev_code>
    <operationtype>6</operationtype>
    <operationresult>29</operationresult>
    <operationresultdesc>Entity withdrawn/Invalidate MA successfully
      Version 3 The product will be validated by the EMA in due
      course. When validated you will receive a further
      acknowledgement with the message number: "Product
      Validated PRD126060 Version [Version Number] / [Date and
      Time]".</operationresultdesc>
  </reportacknowledgment>
 </acknowledgment>
</evprmack>
```

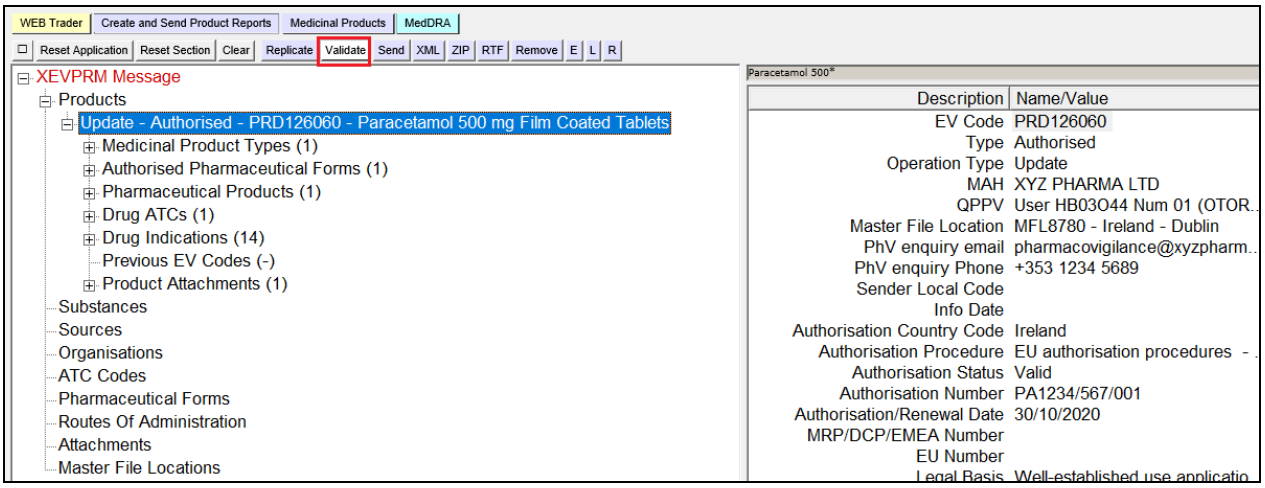
! Please note that no further validation is performed by the EMA on AMPs that are invalidated in the Article 57 database.

See also Extended EudraVigilance Medicinal Product Report Message step-by-step guide: Maintenance operations - **Invalidation of an authorised medicinal product (AMP) entity** in the XEVMPD available on the 'Training' webpage for more details.

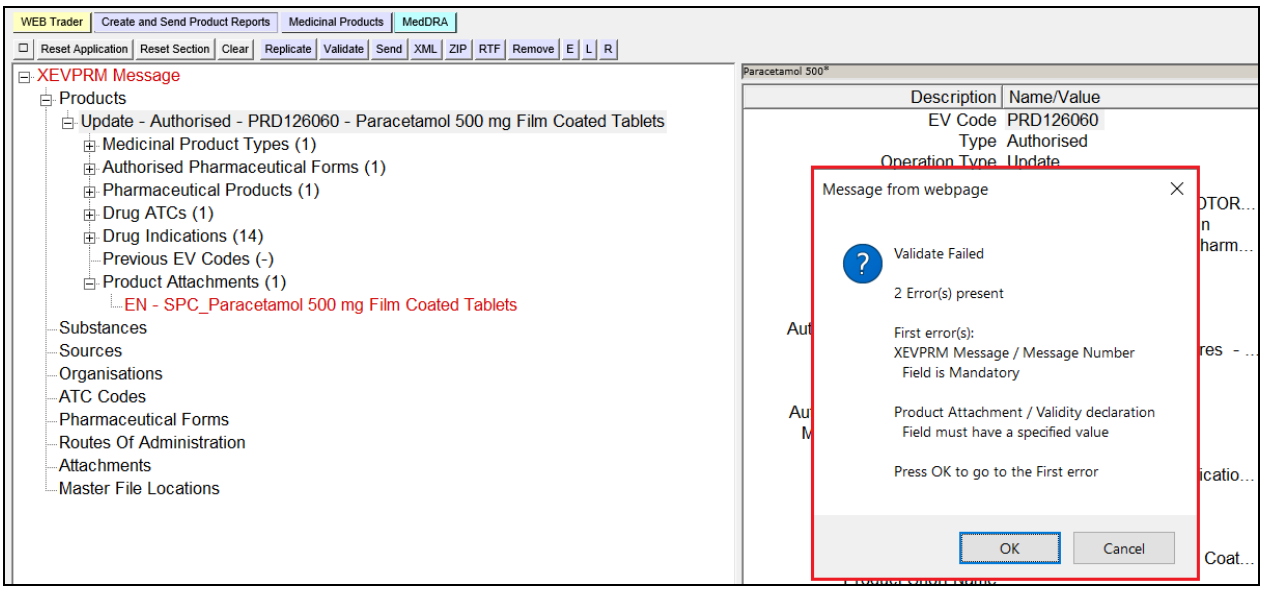
4.7. Validation of an XEVPRM

Once you have created an XEVPRM containing all the information that you wish to send, you should validate the information.

Click on the 'Validate' button from the dynamic button set. The system automatically checks all the information in the message.

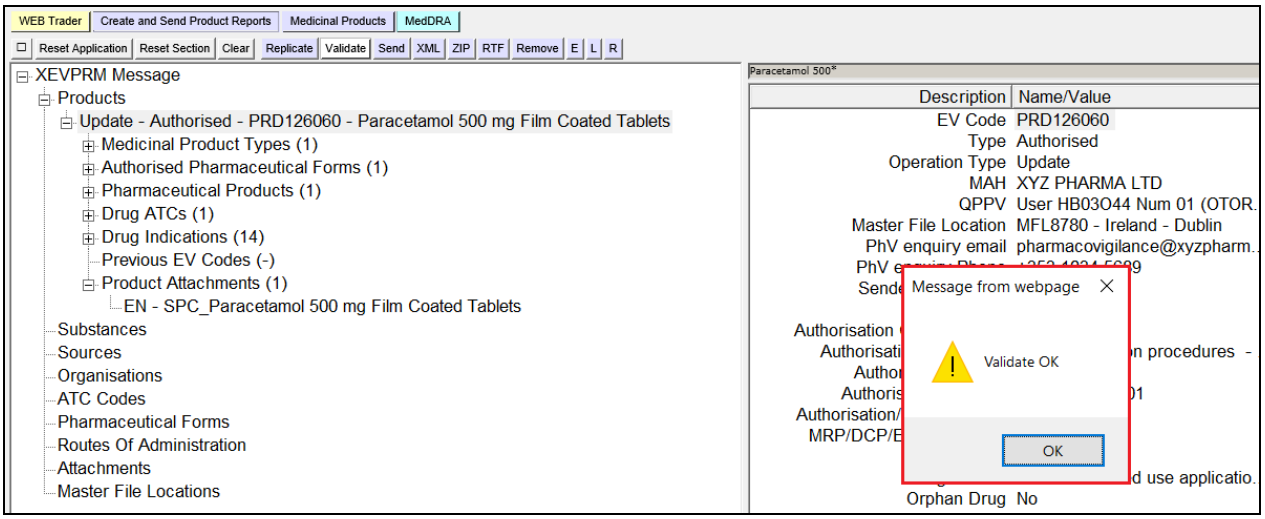


A pop-up window will confirm if the XEVPRM contains any error; if so, the errors or missing information will be highlighted. The pop-up window will describe the total number of errors detected and the description of the first error encountered:



After the correction of the error(s), 'Validate' the XEVPRM again.

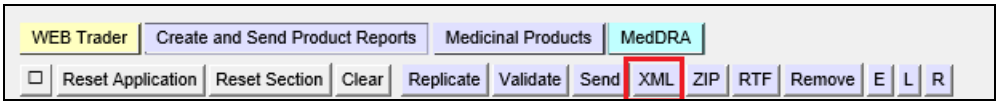
When the XEVPRM does not contain any errors and all the mandatory fields have been specified, the validation will be declared successful:



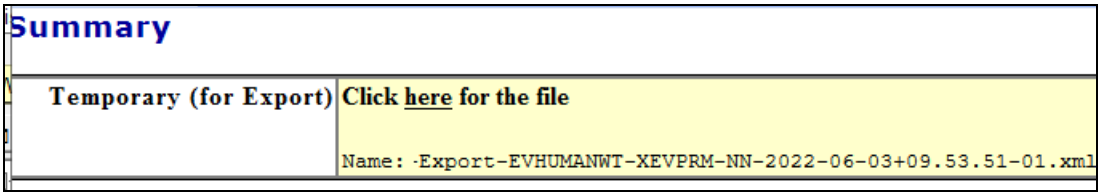
4.8. Save, Reload and Send an XEVPRM

Once you created and validated your XEVPRM, you have the possibility to save the XEVPRM as an **XML file**, **RTF file** or a **ZIP file**.

- To save the XEVPRM as an **XML file**, click on 'XML' button from the dynamic button set:

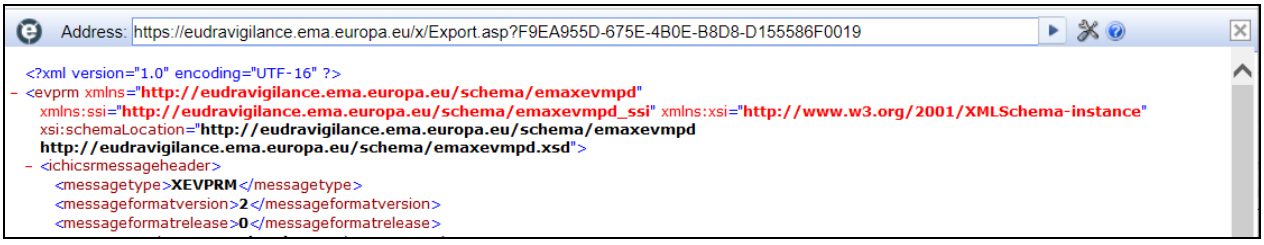


Once you click on the 'XML' button a new window will open:

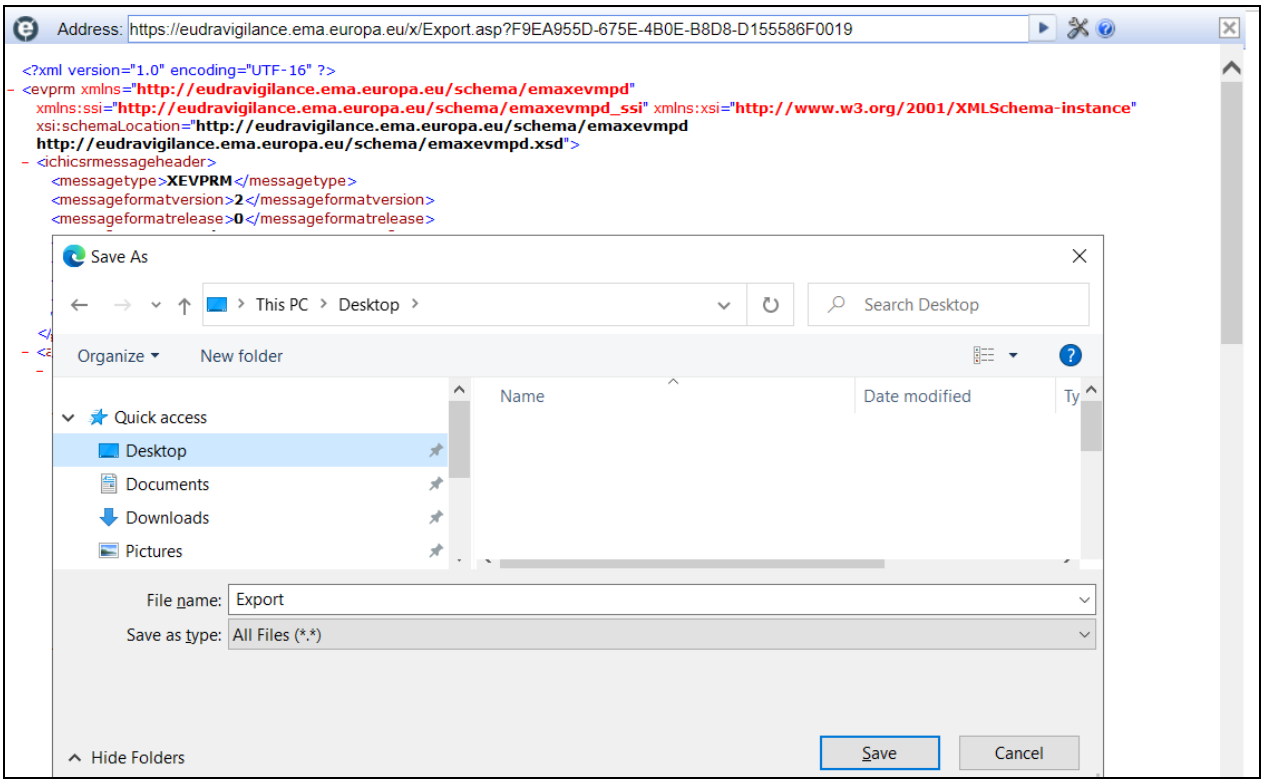


After clicking on 'here', the 'Save' options will become available to you.

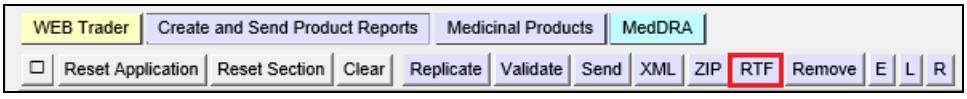
If you are accessing EVWEB via Edge or Chrome using the IE Tab, once you click on 'here', a new window will open, displaying the content of your XEVPRM.



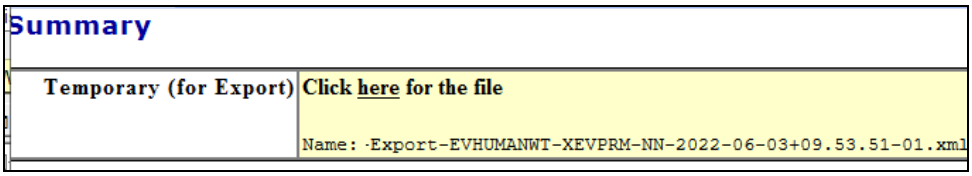
To save the file, you must select '**Ctrl**+**S**' on your keyboard, which will then allow you to save the file on your computer:



- Alternatively, you can save the XEVPRM as an **RTF file** by clicking on the 'RTF' button from the dynamic button set:

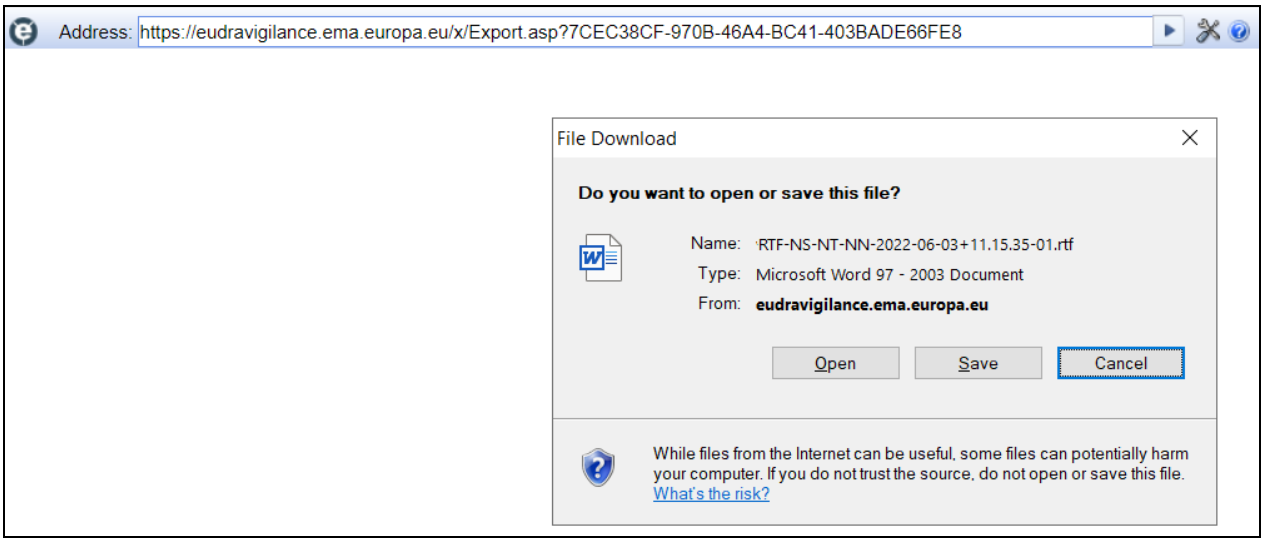


Once you click on the 'RTF' button a new window will open:

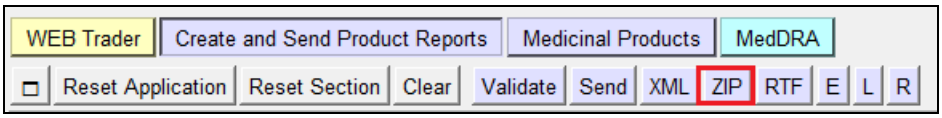


Once you click on 'here', the 'Open' and 'Save' options will become available to you.

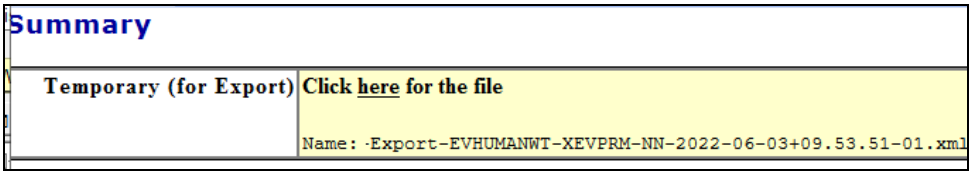
If you are accessing EVWEB via Edge or Chrome using the IE Tab, once you click on 'here', a new window will open, prompting you to open or save the file:



- To save the file as a **ZIP file**, click on the 'ZIP' button from the dynamic button set:

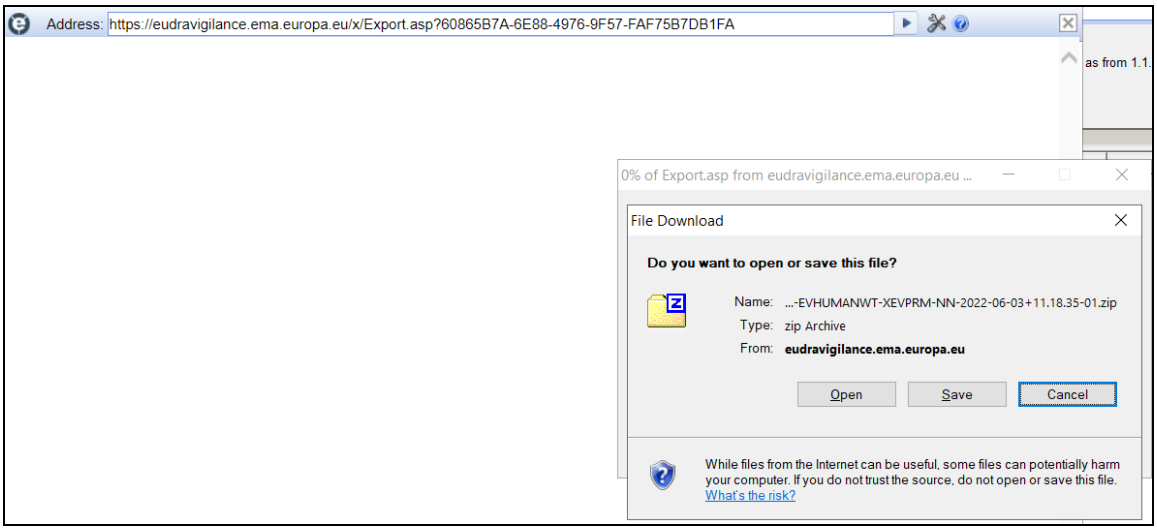


Once you click on the 'ZIP' button a new window will open:



Once you click on 'here', the 'Open' and 'Save' options will become available to you.

If you are accessing EVWEB via Edge or Chrome using the IE Tab, once you click on 'here', a new window will open, promting you to open or save the file:

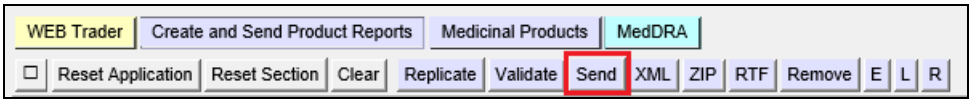


If you created but not completed an XEVPRM and you have saved the XML file locally, you can reload the incomplete XEVPRM and then continue with the completion of the data.

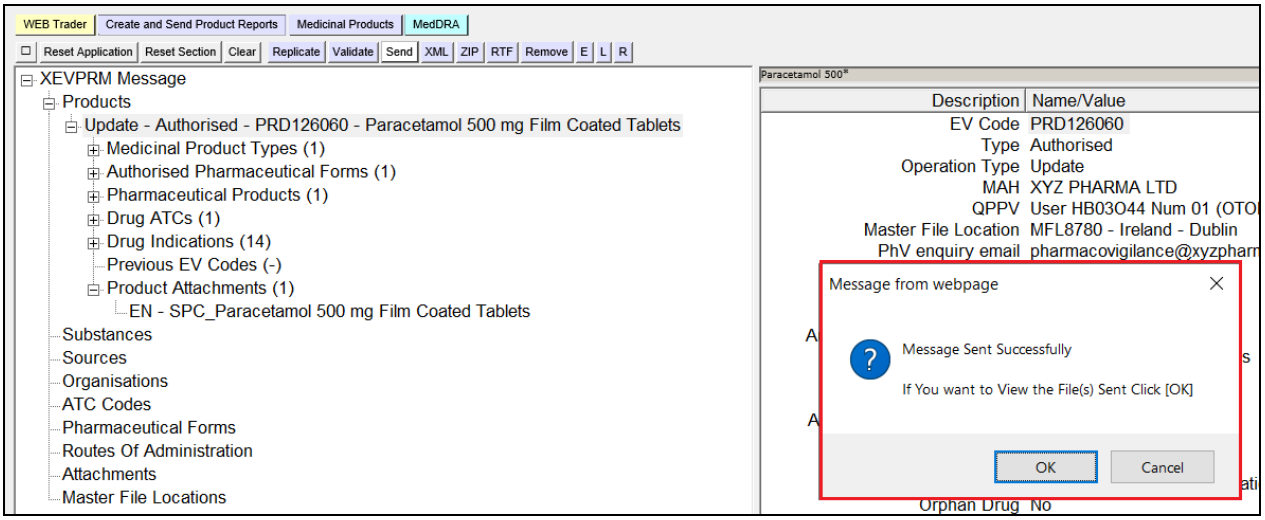
Please refer to *3.10.1.1. Reloading an XEVPRM*, for a detailed description on how you can reload an incomplete XEVPRM in the 'Send Product' section.

Once you have completed the XEVPRM you can submit it to the XEVMPD.

To send the XEVPRM in the XEVMPD, click on the 'Send' button from the dynamic button set:



The below message will be displayed on your screen:



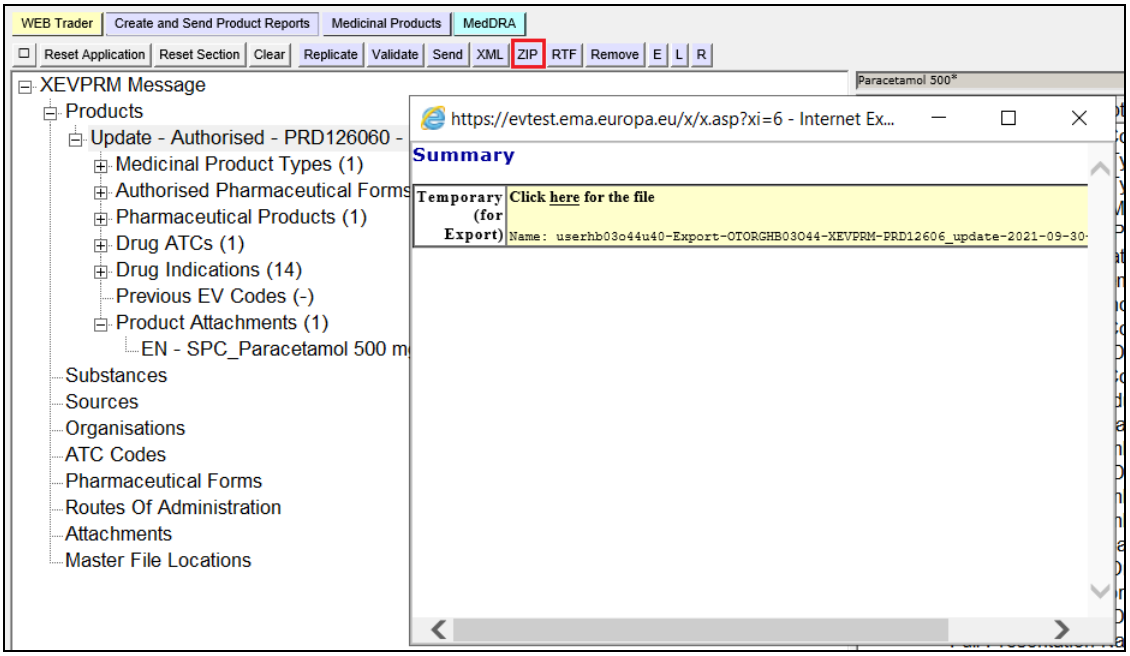
The 'Send' button will only be available for users from organisations registered for product reporting via Web Trader. Whilst users from organisations registered for product submissions via Gateway can create XEVPRMs using EVWEB, the 'Send' button will not be available to them. Gateway organisation users can submit XEVPRMs as 'ZIP' files using EV Post. See section *4.9. Use EV Post functionality* of this document for further information.

4.9. Use EV Post functionality

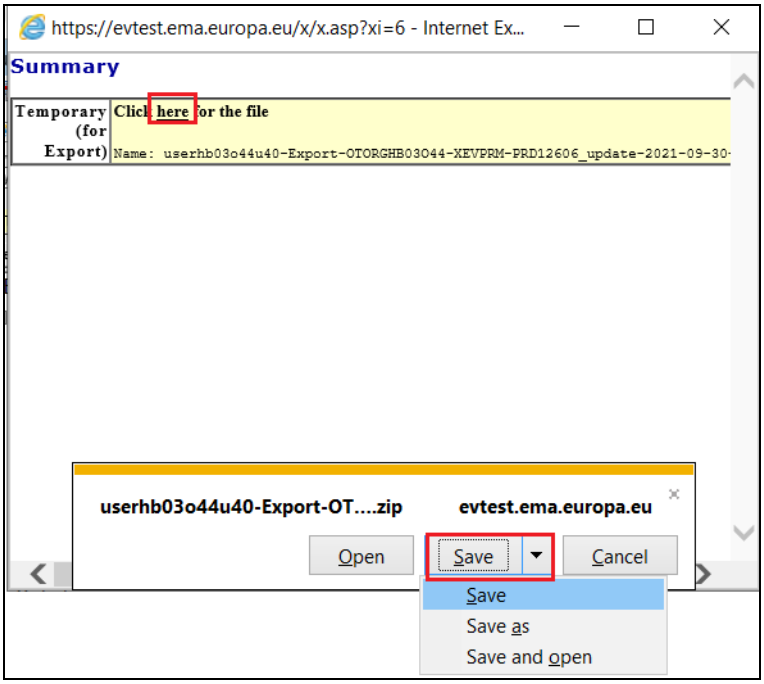
- If you are a Web Trader user, you can send XEVPRMs either from the 'Create and Send Product Reports' section of EVWEB, or by using the EV Post function.
- Gateway users can send XEVPRMs via their Gateway or by using the EV Post function.
  - Gateway organisation users can also create XEVPRMs using EVWEB (you may need to check that your organisation's profile in the EV registration system is set-up to allow this), however, since no 'Send' button is available to them in the 'Create and Send Product Reports' section, these XEVPRMs can only be submitted via EV Post.

XEVPRMs must be submitted via EV Post as a ZIP file.

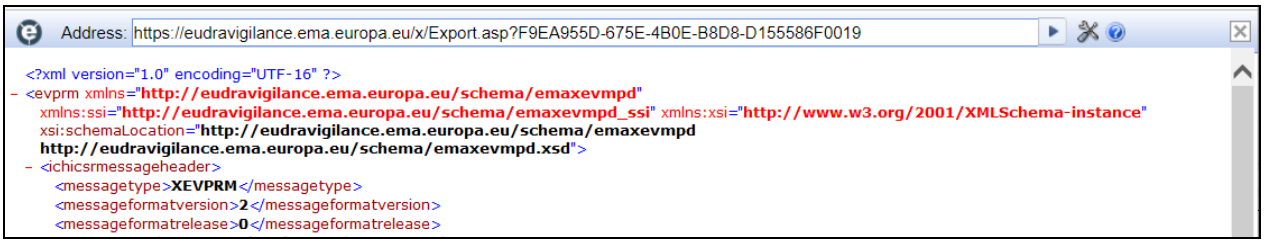
Create your XEVPRM in the 'Create and Send' product report section of EVWEB and click on 'ZIP' in the main menu; a new window will open:



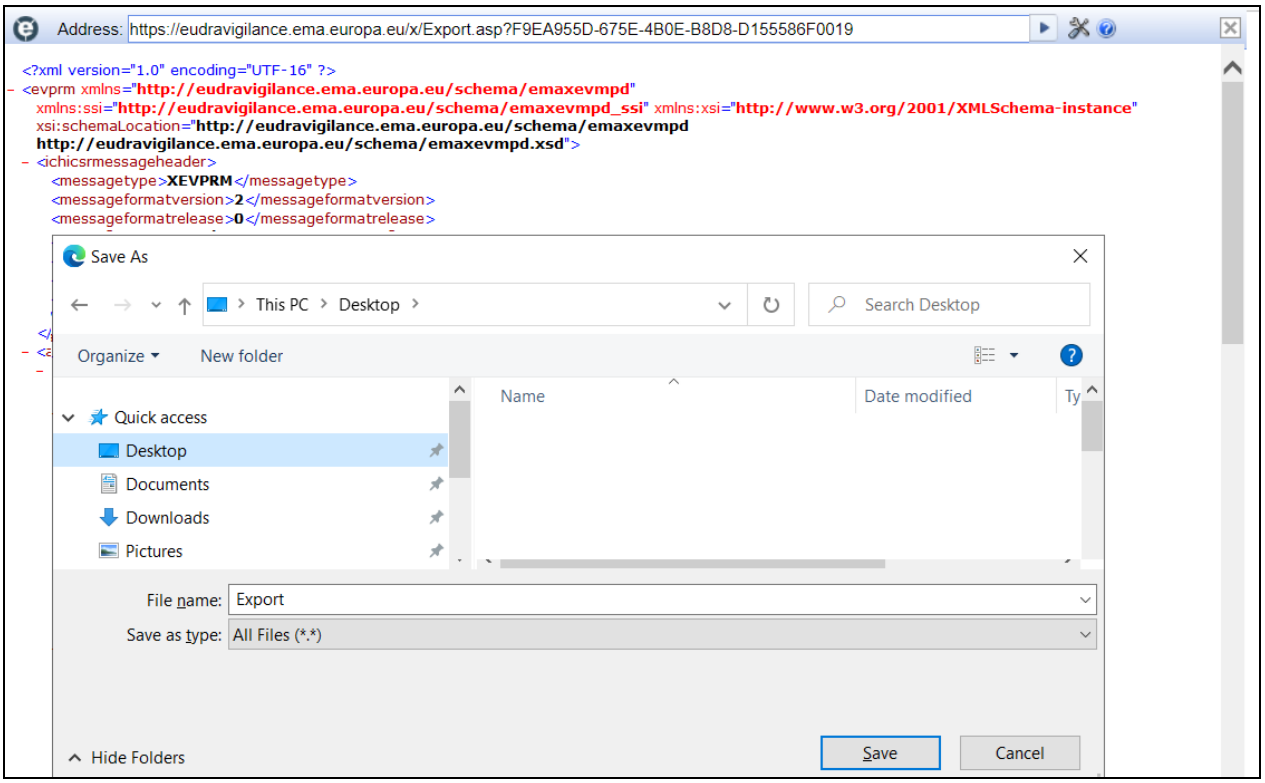
Click on 'here' and save your file on your computer:



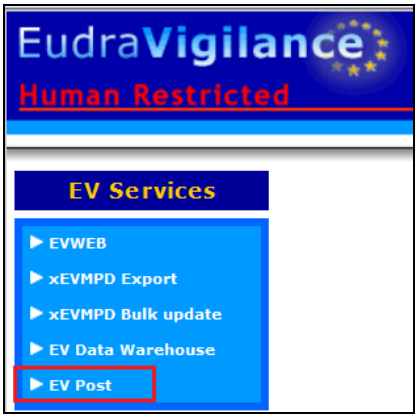
If you are accessing EVWEB via Edge or Chrome using the IE Tab, once you click on 'here', a new window will open, displaying the content of your XEVPRM.



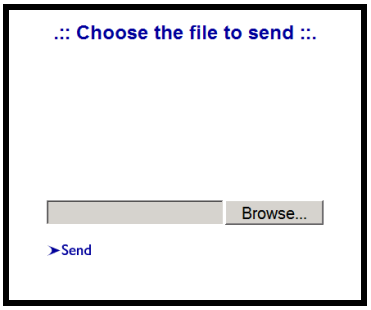
To save the file, you must select '**Ctrl**+**S**' on your keyboard, which will then allow you to save the file on your computer:



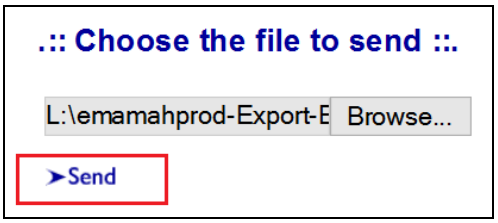
In the secure area of the EudraVigilance website click on EV Post:



Select the ZIP file from your computer:



Press 'Send':



The below message will be displayed if the file was successfully posted:

4.10. Export functions

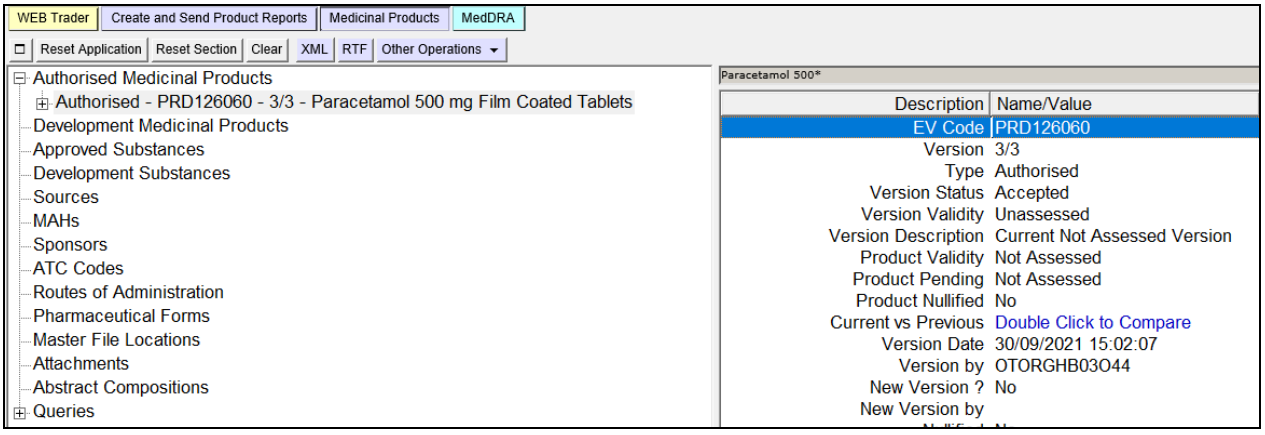
4.10.1. Exporting results of a simple query

The result of your query may be exported as an Excel spread sheet, XML file(s) or RTF file(s).

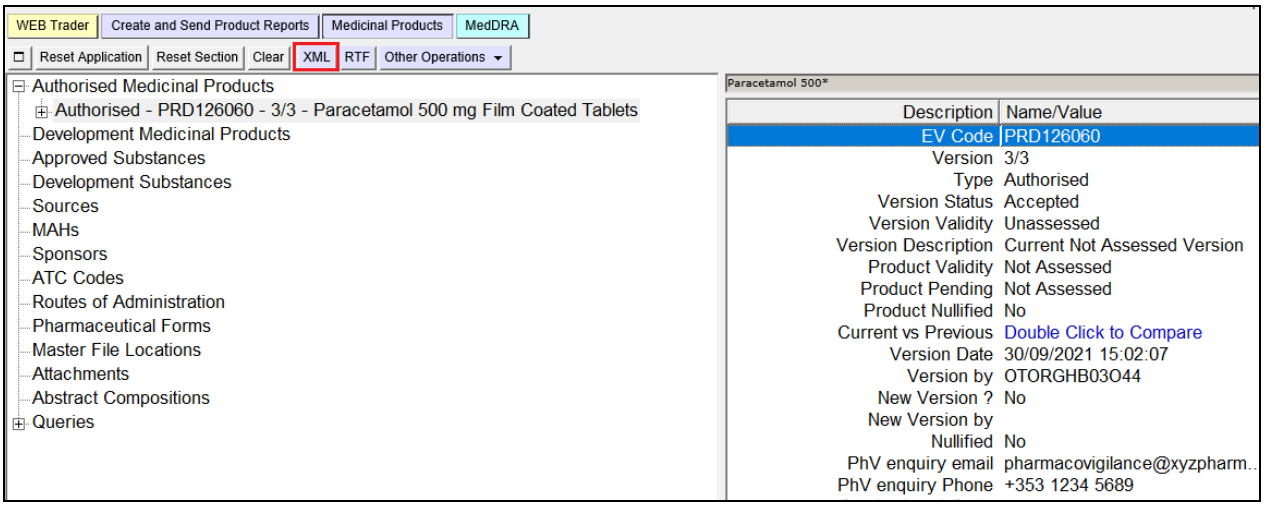
There are two options how to export entities displayed as a result of a simple query:

- XML file
- RTF file

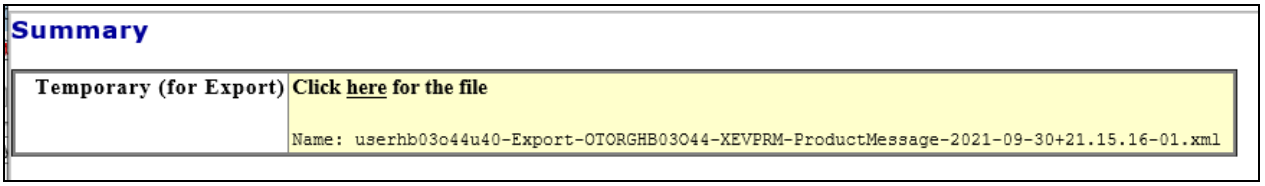
As an example, following a simple query, our AMP is displayed in the tree-view area:



To export the AMP as an **XML file**, select the 'XML' from the main menu:



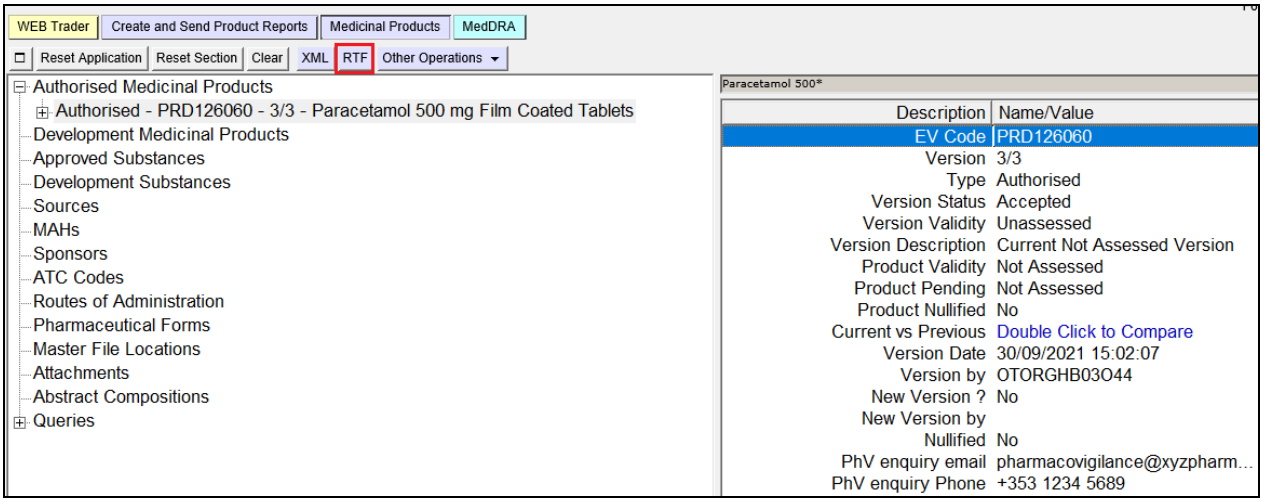
A pop-up window will be displayed:



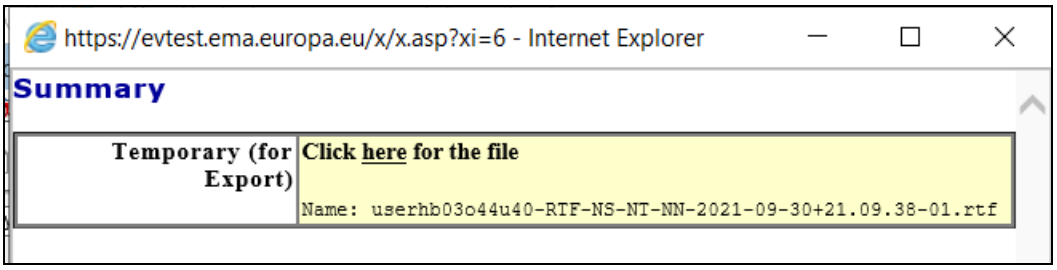
Clicking on 'here' will enable you to view and save the file on your computer in an XML format.

If you are accessing EVWEB via Edge or Chrome using the IE Tab, once you click on 'here', a new window will open, displaying the content of your XEVPRM. To save the file, you must select '**Ctrl**+**S**' on your keyboard, which will then allow you to save the file on your computer.

To export the AMP retrieved as a result of a simple query in an **RTF format**, select the 'RTF' from the main menu.



A pop-up window will be displayed:



After clicking on 'here', another window will open enabling you to open or save the file on your computer.

If you choose to open the file, the file will be displayed in an RTF format. You can then save the file, if required.

EudraVigilance

Authorised Product

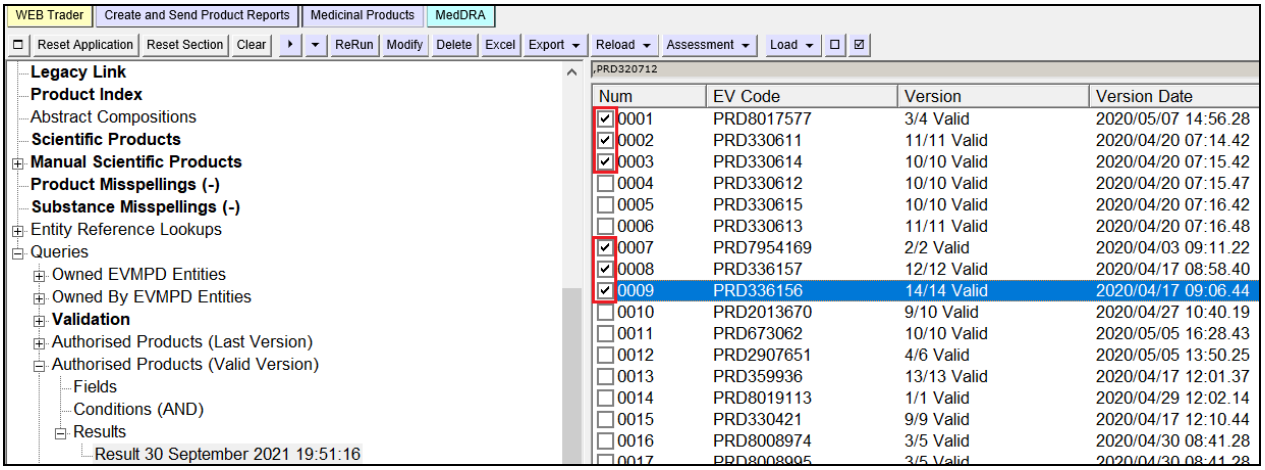
EV Code	**PRD126060**
Version	**3/3**
Type	**Authorised**
Version Status	**Accepted**
Version Validity	**Unassessed**
Version Description	**Current Not Assessed Version**
Product Validity	**Not Assessed**
Product Pending	**Not Assessed**
Product Nullified	**No**
Current vs Previous	**126061-126062**
Version Date	**30/09/2021 15:02:07**
Version by	**OTORGHB03O44**
New Version ?	**No**
Nullified	**No**
PhV enquiry email	**pharmacovigilance@xyzpharma.ie**
PhV enquiry Phone	**+353 1234 5689**
Authorisation Country Code	**Ireland**
Authorisation Procedure	**EU authorisation procedures - National Procedure**
Authorisation Status	**Not Valid - Withdrawn by Marketing Authorisation Holder**
Authorisation Number	**PA1234/567/001**
Authorisation/Renewal Date	**30/10/2020**
Legal Basis	**Well-established use application (Article 10a of**

4.10.2. Exporting results of an advanced query

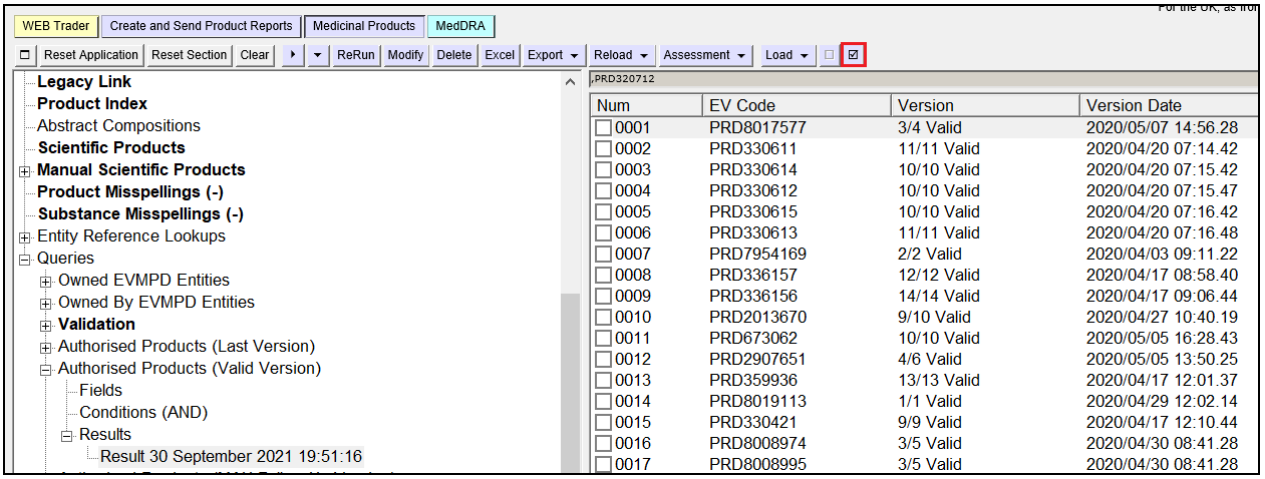
Results of an advanced query, which are available in the active area, may be exported as:

- an Excel spread sheet;
- one or multiple XML file(s);
- one or multiple RTF file(s).

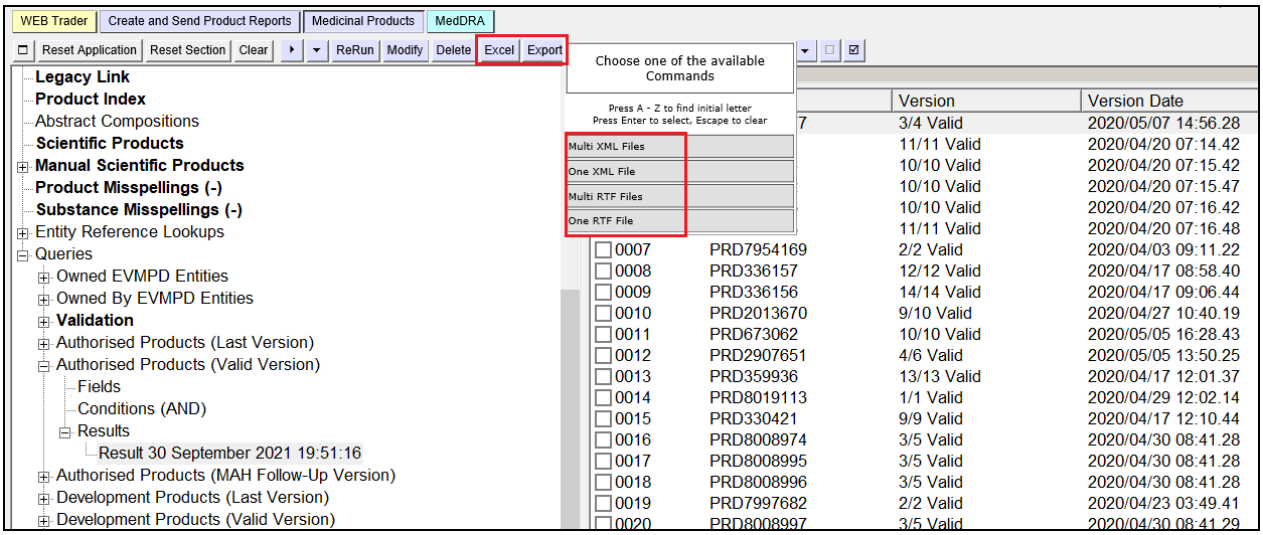
The results to be exported must be selected by ticking the check box next to the result. You can select each product manually:



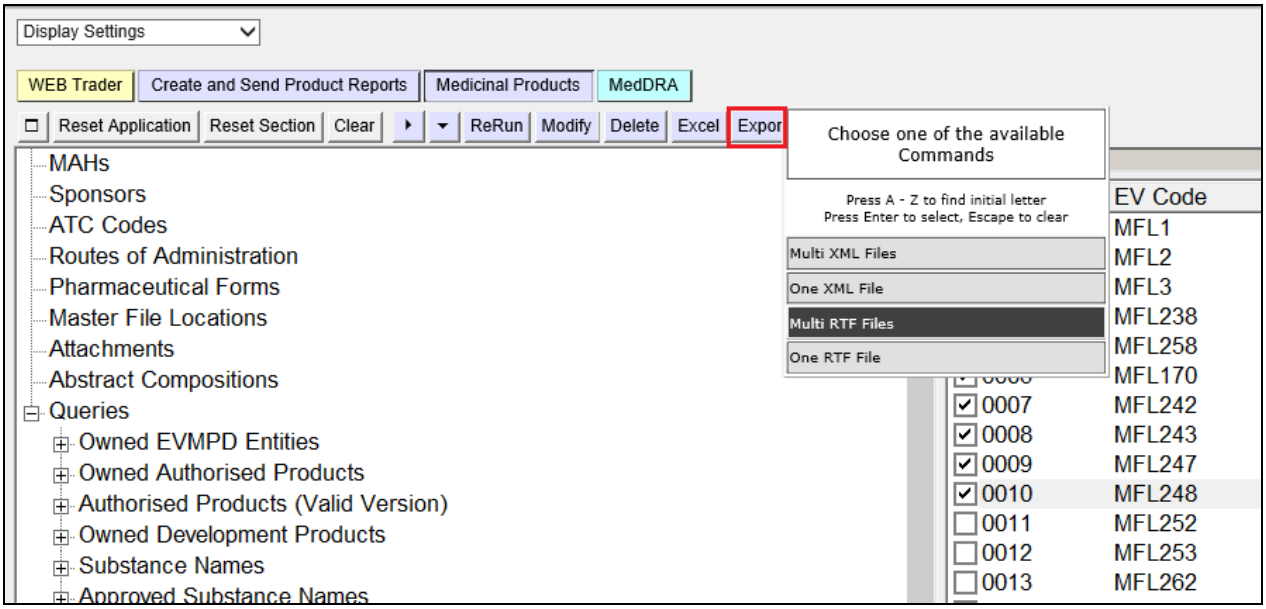
Or you can select all products by clicking on the checked box highlighted in the below screenshot in red:



The required format in which you wish to export you results can be selected from the main menu by clicking on the 'Excel' button or on 'Export':

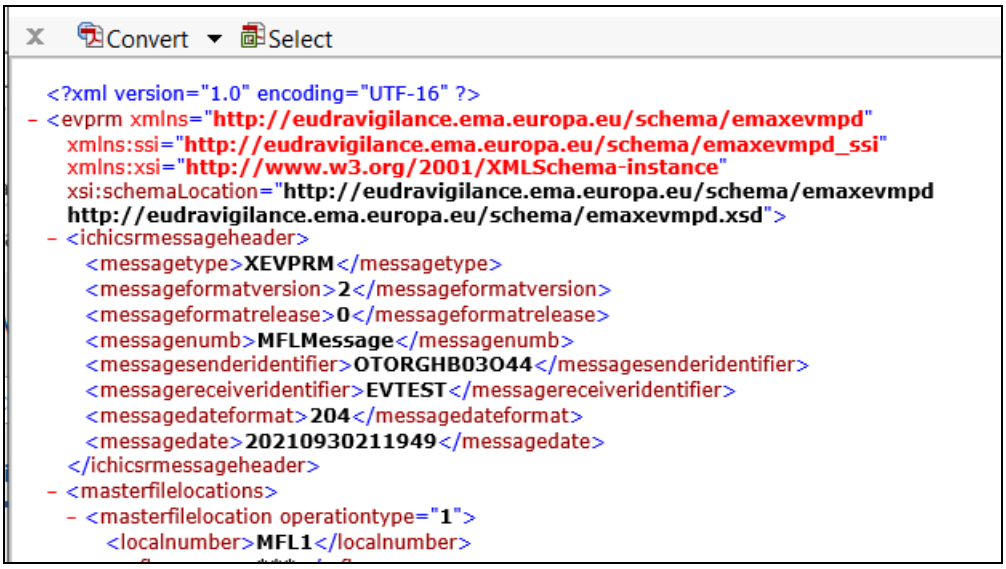


To export the selected results as an **RTF file,** select **'One RTF File'** (one RTF file will be created for all selected entities) or **'Multi RTF Files'** (one RTF file will be created for each selected entity) from the main menu, under 'Export':

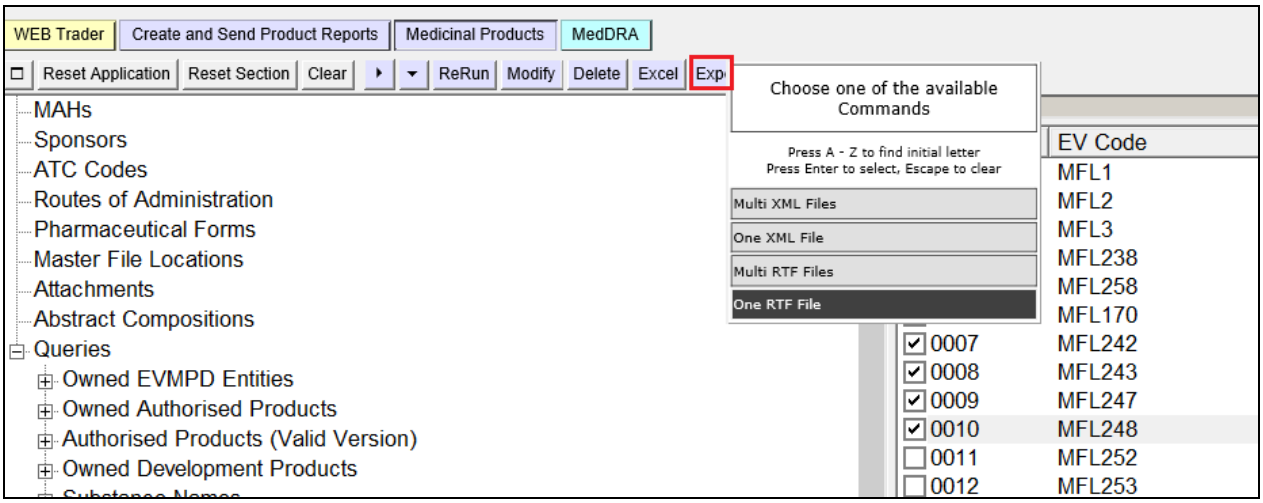


Depending on the selected option (we selected multiple RTF File), a pop-up window will be displayed:

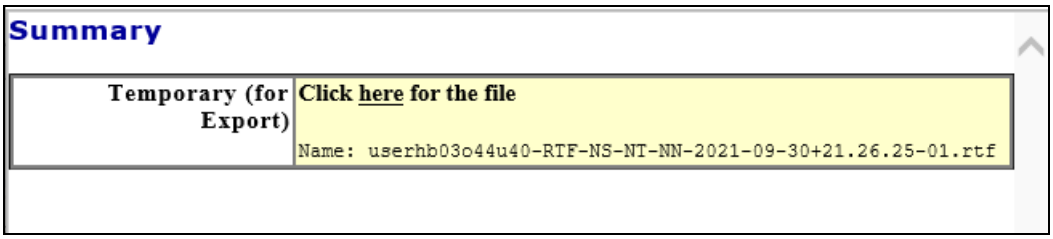
After clicking on 'here', another window will open enabling you to open or save the file on your computer, as required.



If you wish to view/save the file in an RTF format, select the 'RTF' from the main menu:

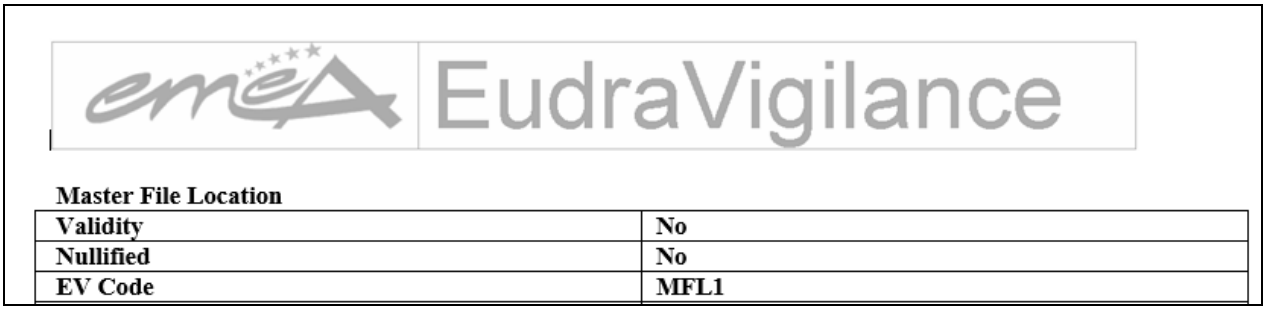


A pop-up window will be displayed:



After clicking on 'here', another window will open enabling you to open or save the file on your computer.

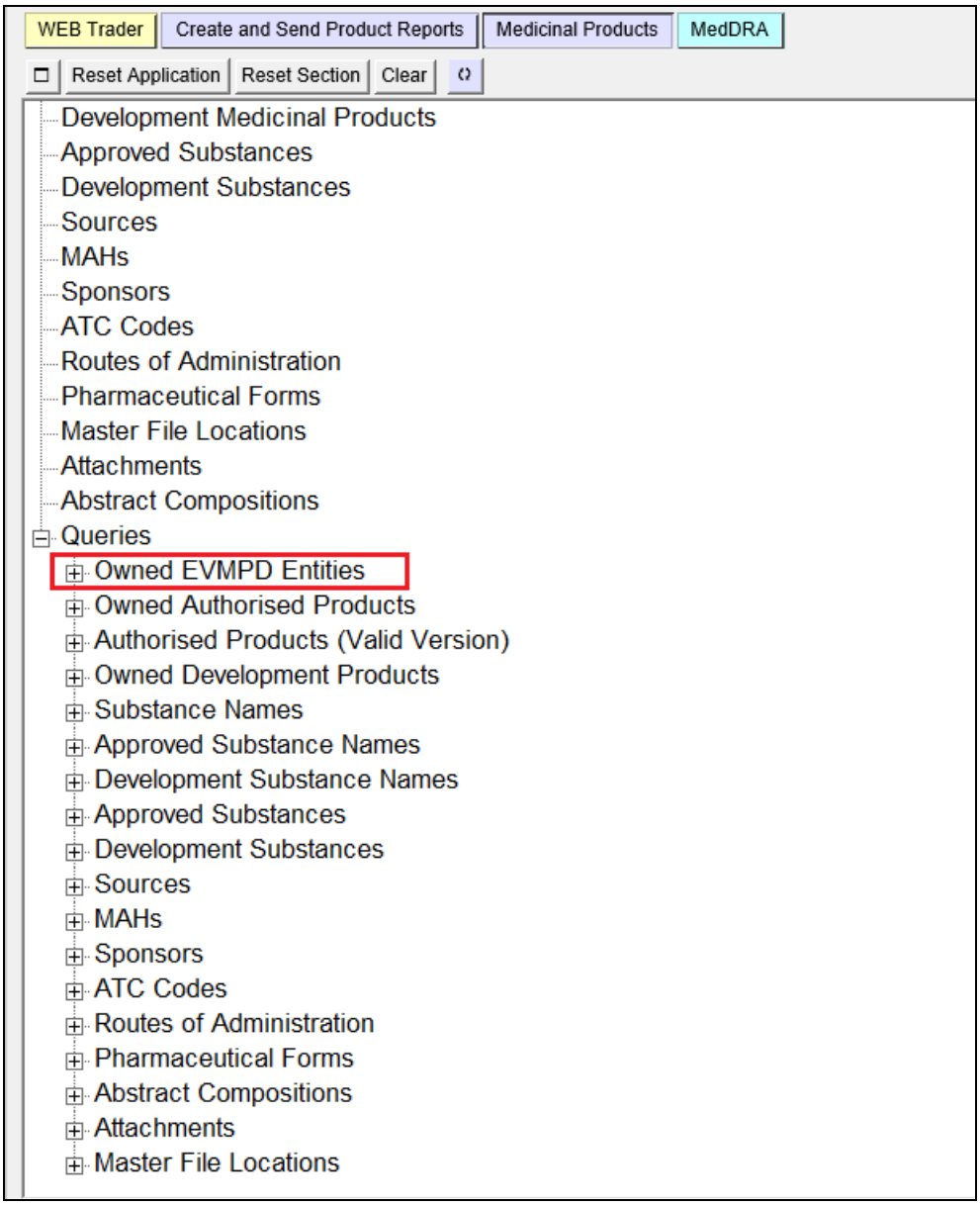
If you choose to open the file, the file will be displayed in an RTF format. You can then save the file, if required:



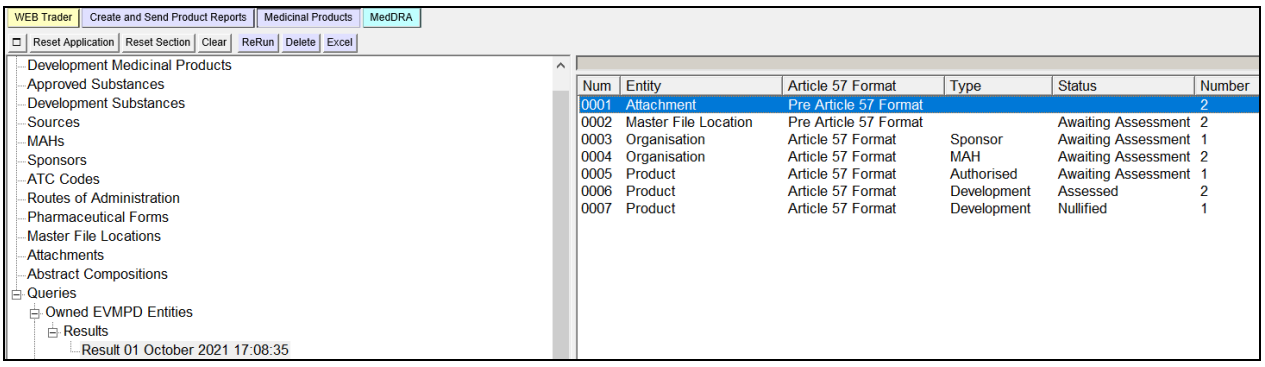
4.11. Export of owned entities to an Excel spread sheet

4.11.1. Exporting an overview of all owned entities to an Excel spread sheet

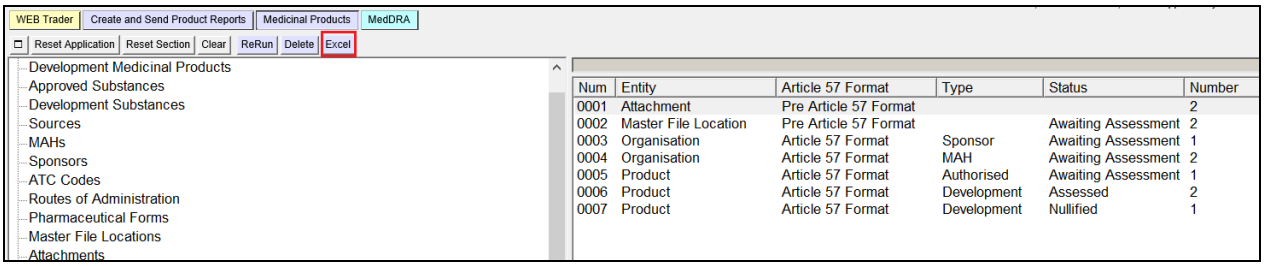
To view/save an overview of all owned entities in EVWEB, go to 'Queries' and click on 'Owned EVMPD entities':



An overview will be listed in the active area:



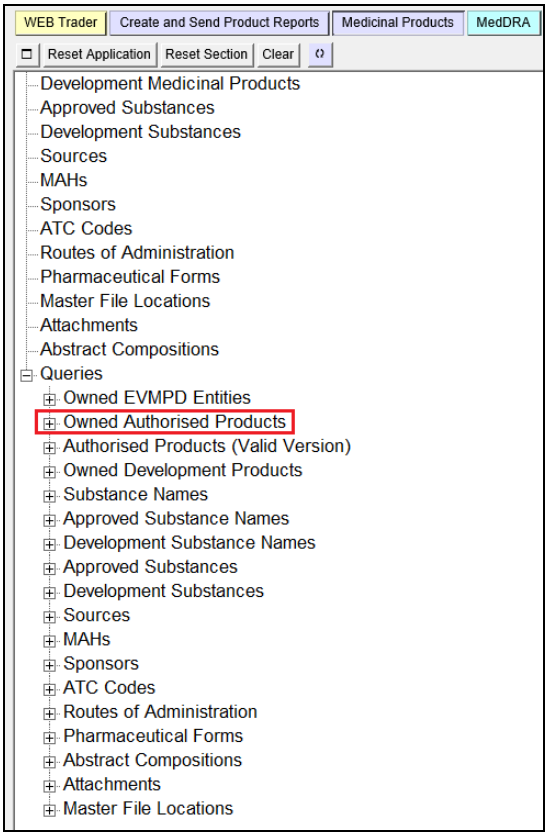
You can save this overview in Excel spread sheet by clicking on 'Excel':



4.11.2. Exporting an overview of all owned AMP or DMP entities to an Excel spread sheet

To create an Excel spread sheet containing all AMP entities owned by your HQ organisation ID, you can perform an advanced query and export the results in Excel.

Open the 'Queries' section in the tree-view area and select 'Owned Authorised Products' or 'Owned Development Products' as required:



In the 'Conditions' you can select further filters or your query, as required.

Once you select the fields and conditions of your query, click on 'Run to Excel':

4.12. Displaying/printing and saving information from XEVMPD

The information available in the XEVMPD can be displayed, saved, and printed in various formats. **Depending on the section, in which you are working in and on the item(s) selected**, individual entities and/or results of queries can be saved as an Excel spread sheet, XML file, RTF file or a ZIP file (in 'Create and Send Product Reports' section only).

See section *3.11. Export functions and available formats* of this document for related information.

This button allows you to save the result of your queries as a spread sheet in an Excel format.

This button allows you to generate an XML version of the XEVPRM message selected in EVWEB.

This button allows you to generate an RTF file (a typical cross-platform document format) version of the message selected in EVWEB.

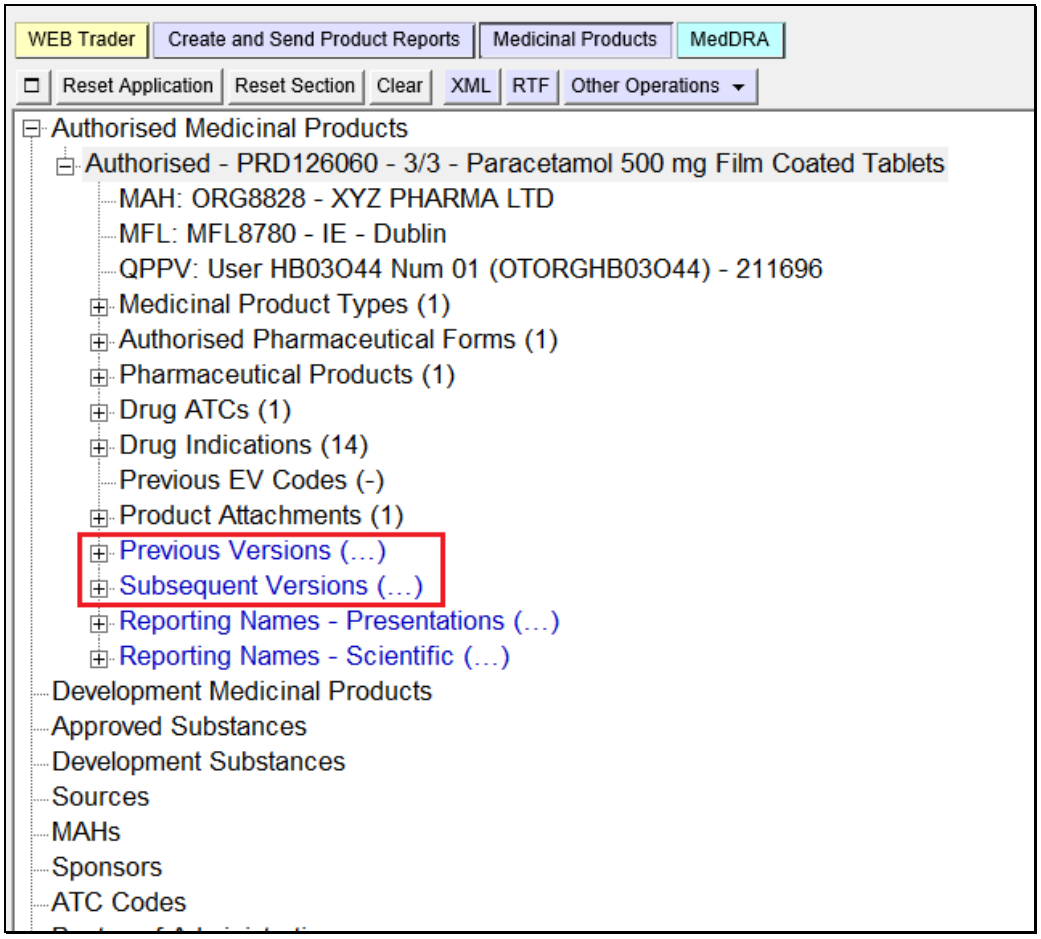
This button in the 'Create and Send Product Reports' section allows you to generate a ZIP file also containing the attachment (if present) and save it on your computer.

See section *4.8. Save, Reload and Send an XEVPRM* for information.

4.13. Retrieving previous version(s) of medicinal product entity

In EVWEB, users can view each individual version available for the EV Code of their AMP/DMP entity in the sections 'Previous Versions'/'Subsequent Versions' within the AMP/DMP entity.

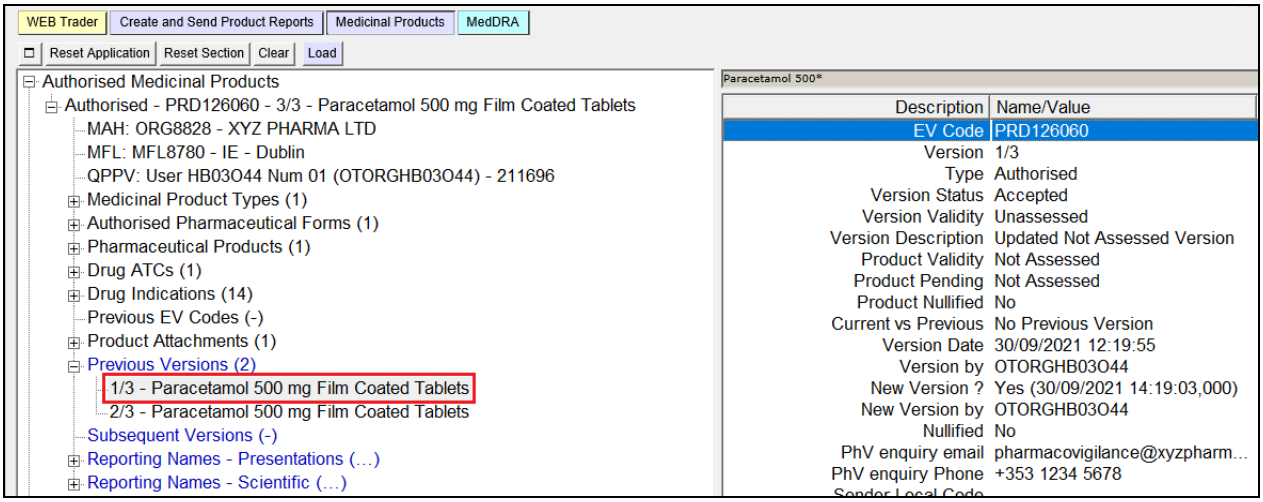
To achieve this, load the product in the tree-view area, then click on 'Previous Versions' or 'Subsequent Versions' as required:



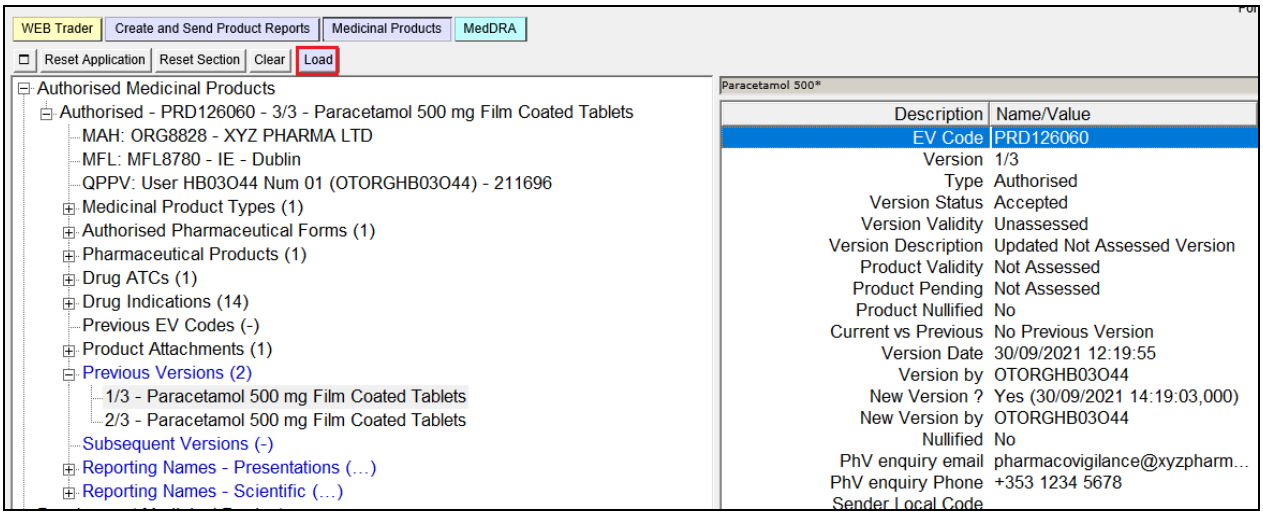
To view the versions in each section, click on the '+' sign:

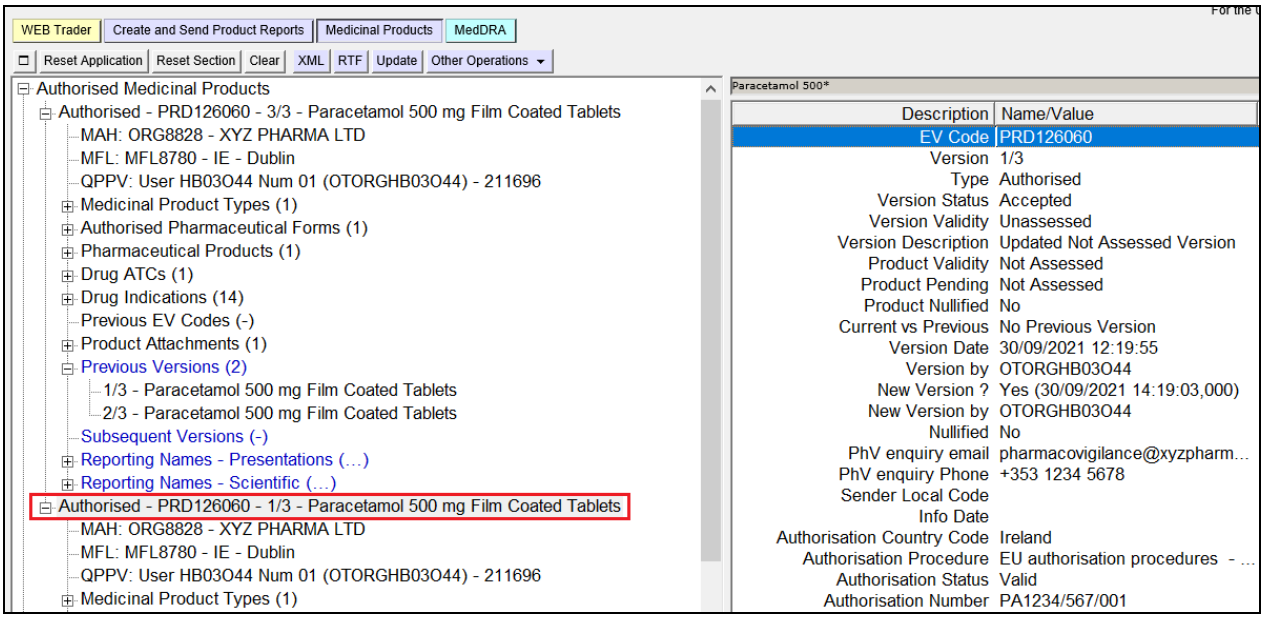
The individual versions of your product entry will be displayed:

To view the required version, click on the version you wish to view so it becomes available in the active area:



Click on 'Load' in the main menu and the version will be displayed in the tree-view area and in the active area of EVWEB:



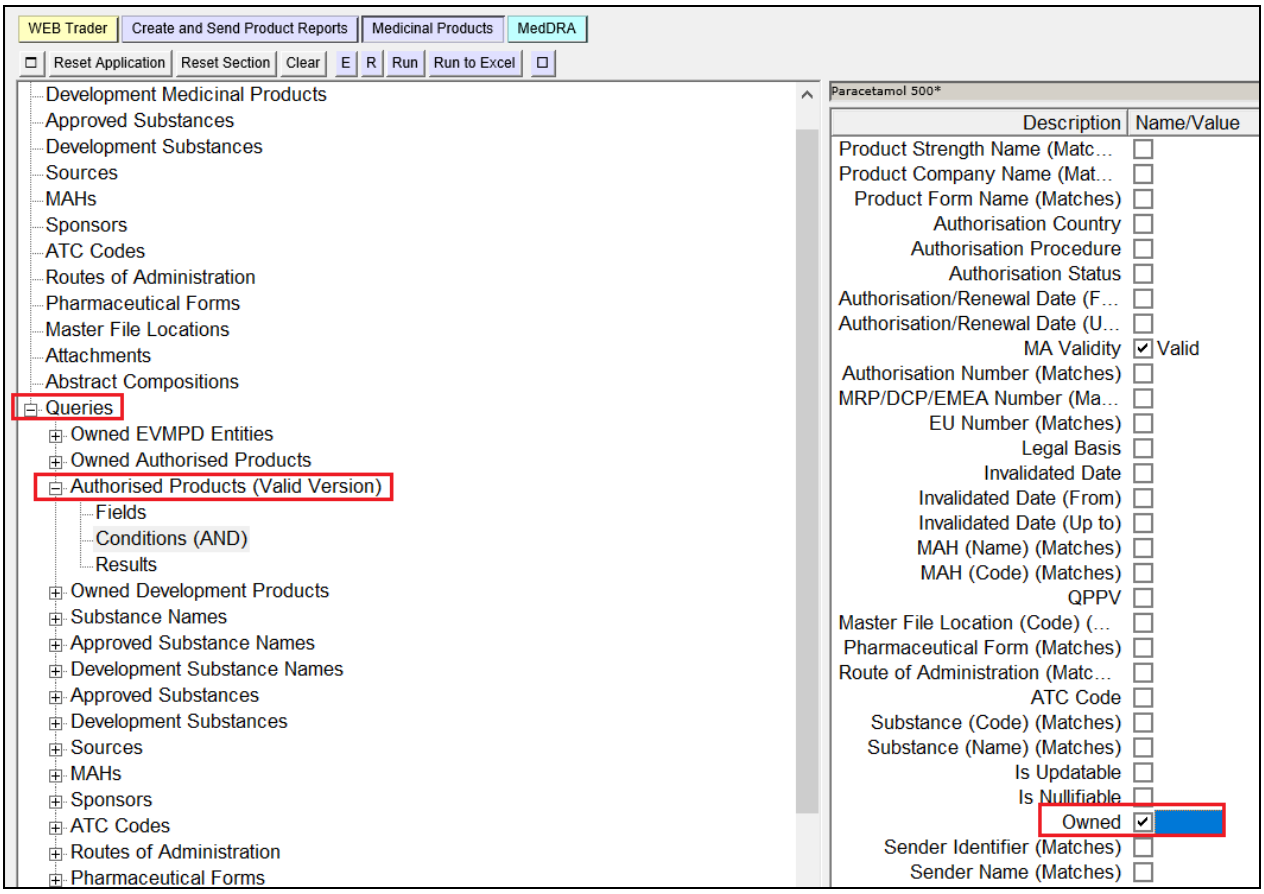


4.14. Retrieving 'Valid' versions of medicinal product entities

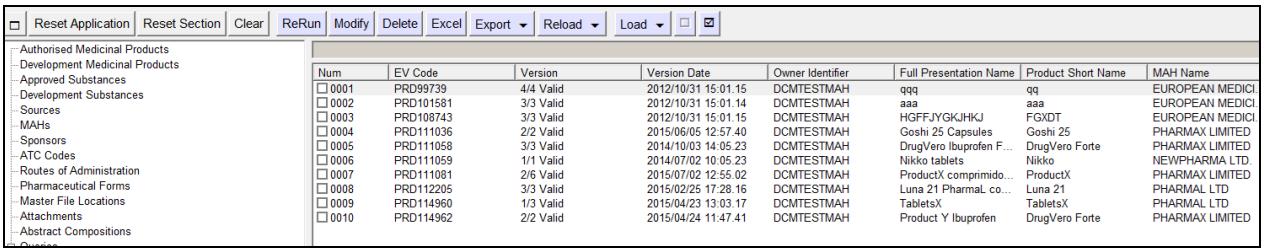
In EVWEB, you can perform an advanced query to retrieve only valid versions of your **AMP entities**.

Go to 'Advanced Queries' and select 'Authorised Products (Valid version)'.

In the 'Conditions (AND)', select 'Owned' and run the query (using 'Run' or 'Run to Excel'):



A list of AMPs which have a product validity set to 'Valid' will become available either in the active area or in an Excel file, depending on how you run the query:

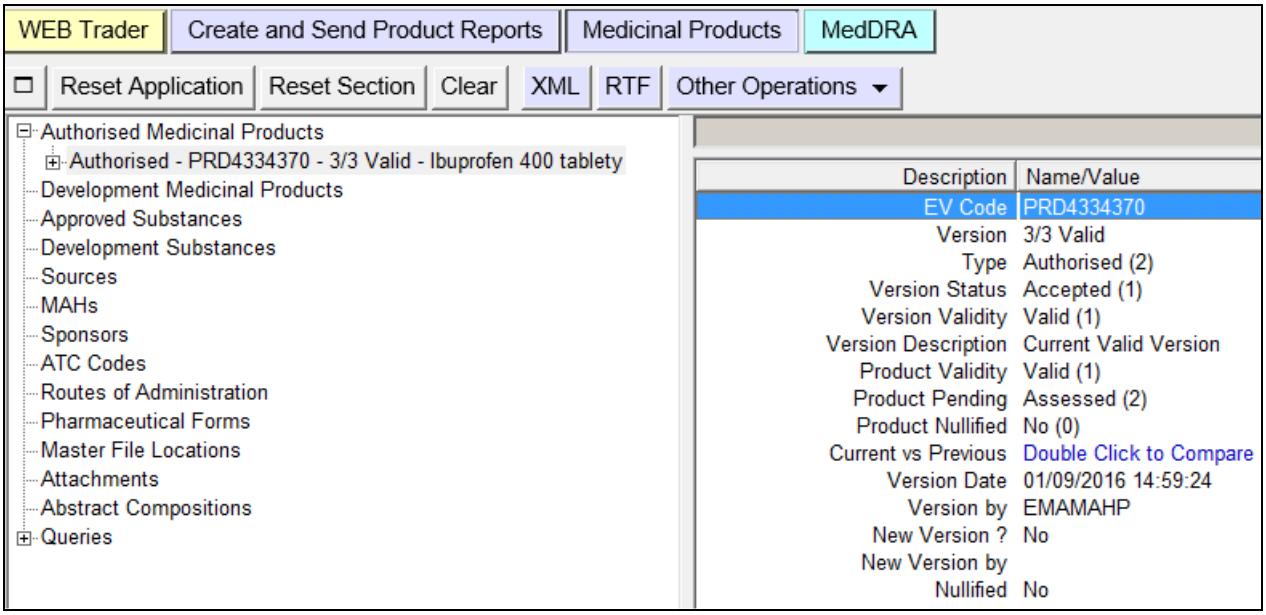


- To identify AMPs, which were not updated (i.e. operation type 'Update' was not applied for that AMP) by the MAH following a validation by the Agency:
  - In EVWEB, go to 'Advanced Queries' and select 'Owned Authorised Products';
  - In the 'Conditions (AND)', select the field 'Product Validity' and set the value to 'Valid'. Also, select the field 'Product Pending' and set the value to 'Assessed';
  - Then run the query (using 'Run' or 'Run to Excel').
- To identify AMPs, which were updated (i.e., operation type 'Update' was applied for that AMP) by the MAH following a validation by the Agency:
  - In EVWEB, go to 'Advanced Queries' and select 'Owned Authorised Products';

- In the 'Conditions (AND)', select the field 'Product Validity' and set the value to 'Valid'. Also, select the field 'Product Pending' and set the value to 'Pending Update';
- Then run the query (using 'Run' or 'Run to Excel').

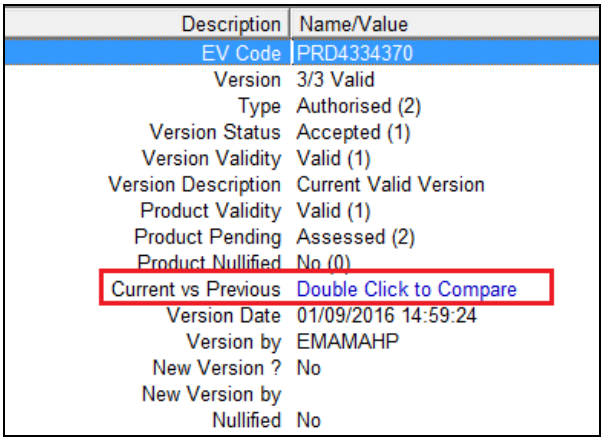
4.15. Comparing individual versions of a medicinal product entity

To compare individual versions of the medicinal product entity, retrieve the AMP entity so that it is available in the active area of EVWEB:

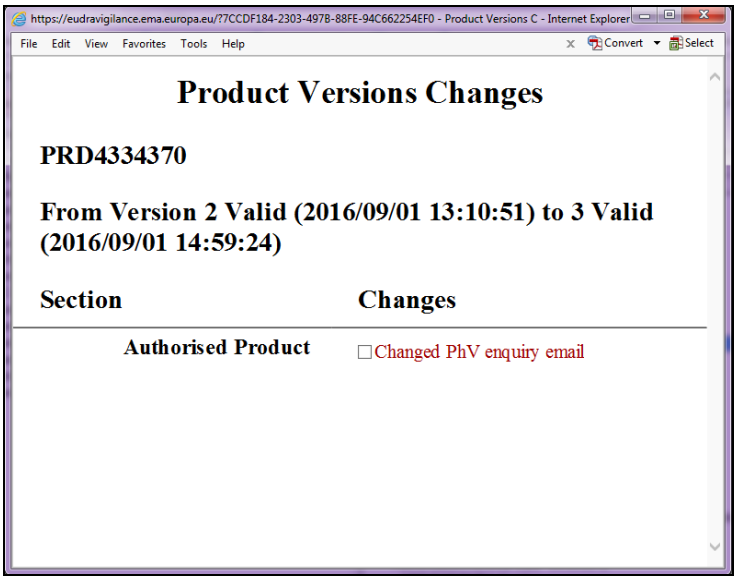


In this specific product entity, there are 3 versions.

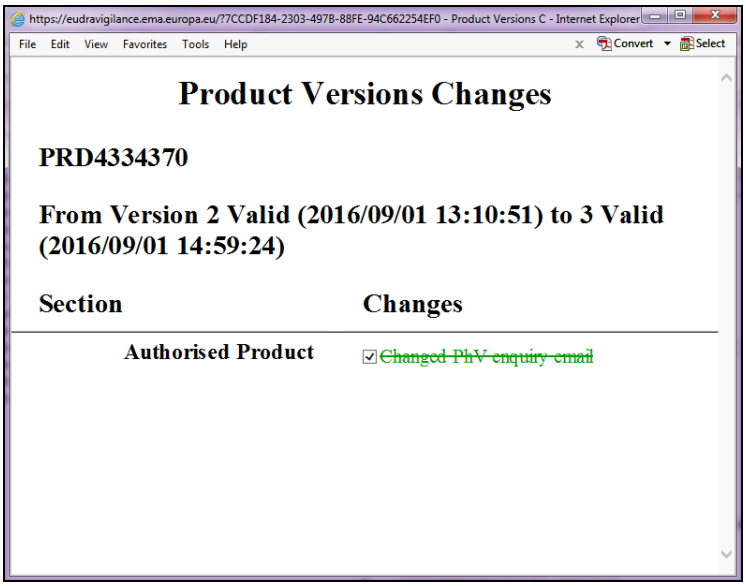
Double-click on the ***'Double Click to Compare'*** text in the 'Current vs Previous' field:



A new window will open, providing a short description of the changes made between the current (i.e. the latest) and the previous versions:



In this specific example, a change was made in the 'PhV enquiry email' field. The square box next to the field(s) is there to help the end user keep on track of the reviewed changes in case that multiple changes were made within one AMP entity. By ticking off the box(es), the user can see which changes were reviewed and which are yet to be done.



Selecting/not selecting the relevant boxes has no impact on the changes made in the AMP or indeed the EVWEB.

5. 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- marketing to post- marketing phases, for data entry, retrieval, evaluation and presentation.

This section describes the principal aspects of MedDRA, its structure and how to access and use MedDRA in EVWEB. This section also explains the process necessary to perform both simple and advanced 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 and the specific EudraVigilance license policy for Small and Medium Size Enterprises (SMEs) published at the EudraVigilance Website.

5.1. Introduction

MedDRA has been developed as a clinically validated international medical terminology for regulatory authorities and the pharmaceutical industry for use in data entry, retrieval, evaluation and presentation during all phases of the regulatory processes, from pre- to post- marketing phases. These processes include:

- 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.

Nevertheless, 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 included in the terminology whereas the failure and its health effects would be)
- Drug product terms
- Device failure terms
- Clinical trial study designs terms.

5.2. MedDRA Structure

MedDRA is organized in a hierarchical structure. MedDRA terms are grouped at different levels thus 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):

System Organ Class (SOC)

High Level Group Term (HLGT)

High Level Term (HLT)

Preferred Term (PT)

Lowest Level Term (LLT)

System Organ Class (SOC)

The System Organ Class (SOC) is the highest level of the hierarchy and provides the broadest concepts for data retrieval.

There are SOCs, and they represent 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 High Level Group Term (HLGT) is subordinate only to System Organ Classes (SOCs) and superordinate for one or more High Level Terms.

High Level Term (HLT)

A High Level Term (HLT) is subordinate to High Level Group Terms and is 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 Preferred Term (PT) is 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)

A 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

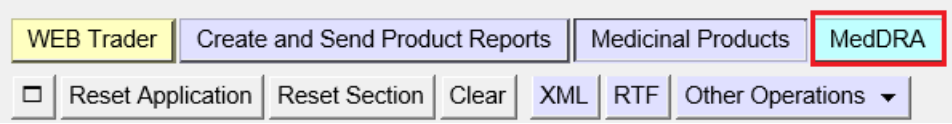
Quasi-synonyms – terms with meanings generally regarded as different, but which in practice are treated as equivalent

Special Search Categories (SPEC CAT(s))

Special Search Categories *(SPEC CAT(s))* allow linkage of terms that are neither equivalent nor hierarchically related, but share clinical concepts that cross SOC hierarchies. This is accomplished by grouping terms at the PT level that are all relevant to the same, singular issue. This is usually a disease or syndrome.

5.3. MedDRA in EVWEB

You can access the MedDRA section of EVWEB by clicking on the 'MedDRA' button on the main menu.

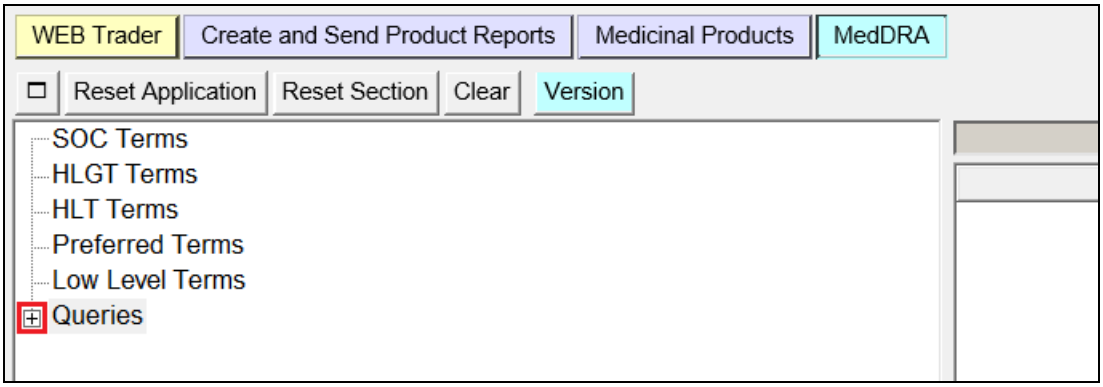


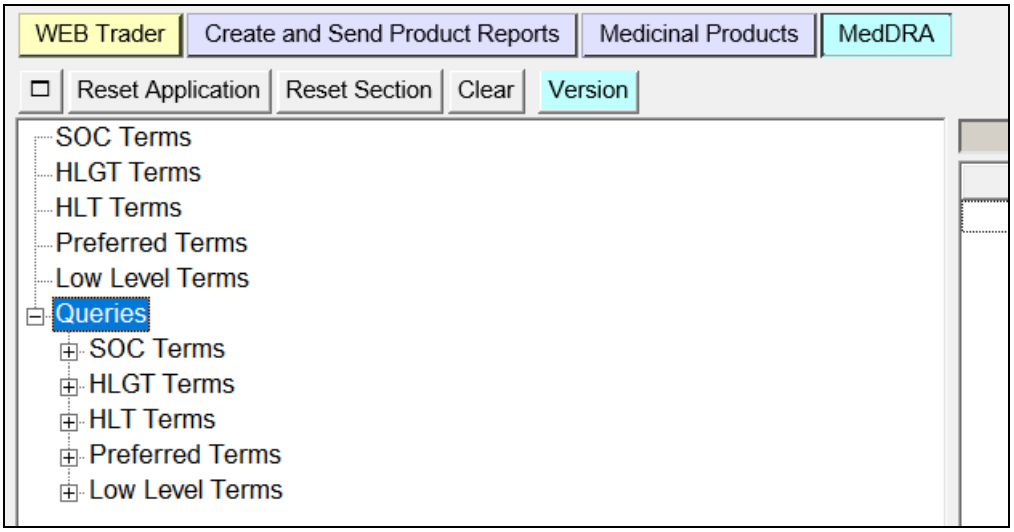
The MedDRA section allows you to perform searches among SOC Terms, HLGT Terms, HLT Terms, Preferred Terms and Low-Level Terms.

As in other sections of EVWEB, searches can be performed in two different ways:

- Simple query
- Advanced query.

To perform an advanced query, expand the 'Queries' section in the tree-view area:





Each query term has its own sub-menu, allowing to choose between 'Fields' and 'Conditions' to perform a query.

Fields for SOC Terms:

SOC Code

SOC Name

SOC Abbreviation

Conditions for SOC Terms:

SOC Code

SOC Name

HLGT Code

HLGT Name

HLT Code

HLT Name

PT Code

PT Name

LLT Code

LLT Name

Fields for HLGT Terms:

HLGT Code

HLGT Name

Conditions for HLGT Terms:

SOC Code

SOC Name

HLGT Code

HLGT Name

HLT Code

HLT Name

PT Code

PT Name

LLT Code

LLT Name

Fields for HLT Terms:

HLT Code

HLT Name

Conditions for HLT Terms:

SOC Code

SOC Name

HLGT Code

HLGT Name

HLT Code

HLT Name

PT Code

PT Name

LLT Code

LLT Name

Fields for Preferred Terms:

PT Code

PT Name

Conditions for Preferred Terms:

SOC Code

SOC Name

HLGT Code

HLGT Name

HLT Code

HLT Name

PT Code

PT Name

LLT Code

LLT Name

Fields for Low Level Terms:

LLT Code

LLT Name

LLT is current?

Conditions for Low Level Terms:

SOC Code

SOC Name

HLGT Code

HLGT Name

HLT Code

HLT Name

PT Code

PT Name

LLT Code

LLT Name

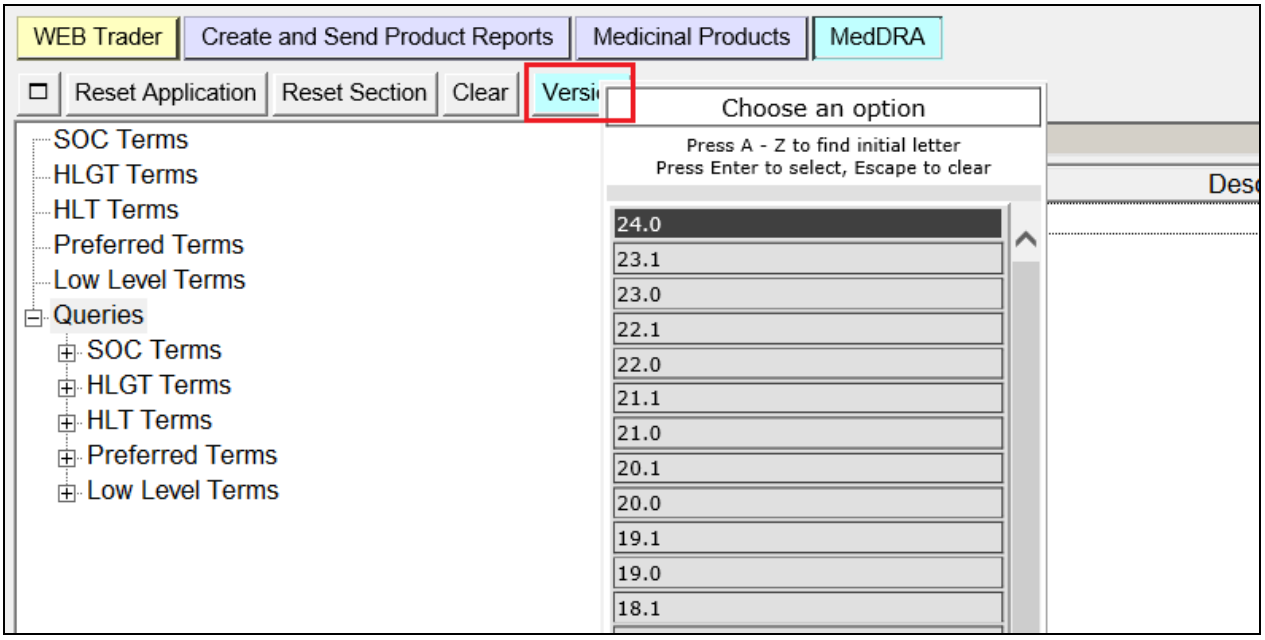
In all cases, query search allows you to select one or more 'Fields' and one or more 'Conditions' to restrict the results of the search.

MedDRA version

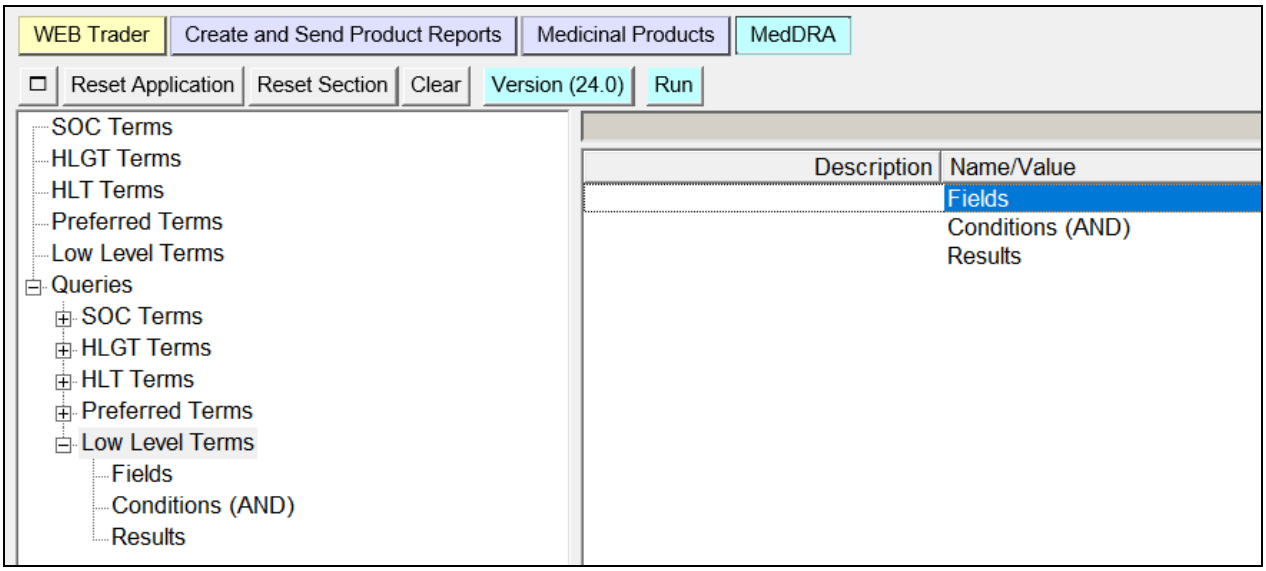
EVWEB allows you to select a specific version of MedDRA to perform your simple and advanced queries.

Click on the button 'Version' that will be displayed in the dynamic button set on the main menu.

A drop-down menu will be displayed allowing you to select a MedDRA version as required:



Once a version is selected, you can start performing simple and advanced queries for that specific MedDRA version.



If you do not specify any version, the simple and advanced queries are performed with the current MedDRA version.

5.4. How to perform a Simple query

You can start a simple query from any MedDRA level listed in the tree-view area:

SOC (System Organ Class Terms)

HLGT (High Level Group Terms)

HLT (High Level Terms)

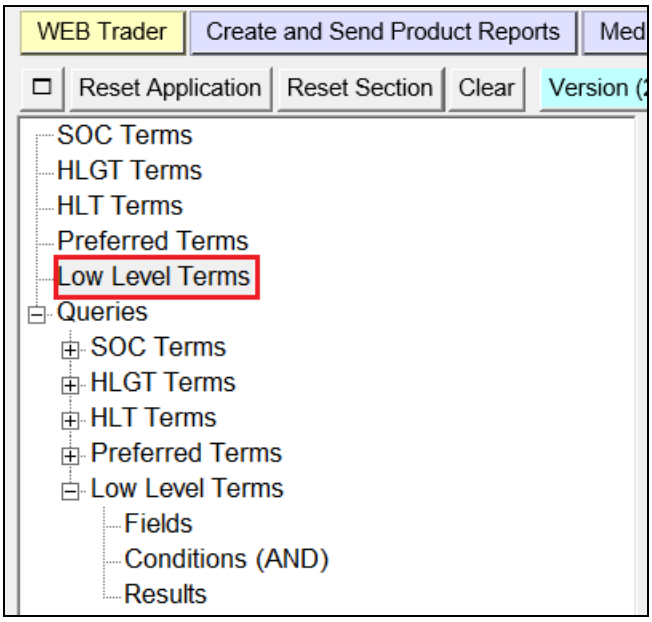
PT (Preferred Terms)

LLT (Low Level Terms)

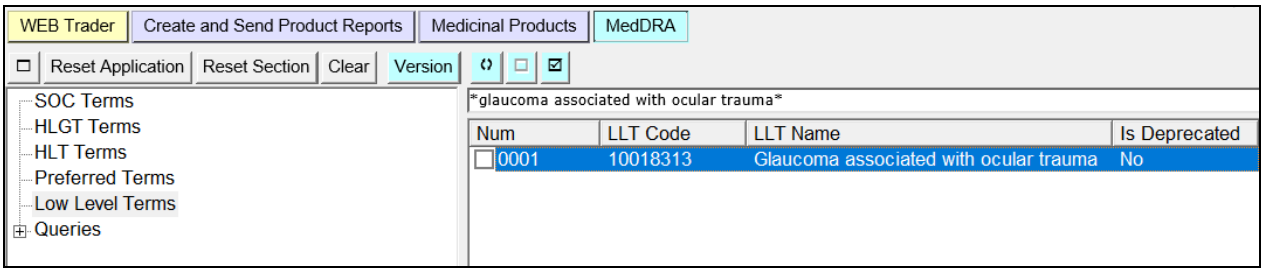
'SOC Terms' is the default selection presented by the system.

As an example, we will perform a simple query starting from the Low Level Term 'Glaucoma associated with ocular trauma'.

Select 'Low Level Terms' in the tree-view area:

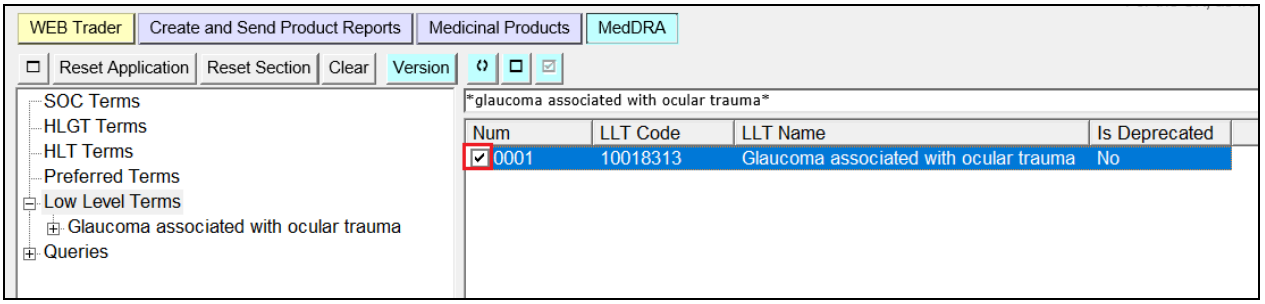


Type: "**glaucoma associated with ocular trauma**" in the simple query field on the top of the active area and press 'Enter' on your keyboard to perform the query. The results are displayed in the active area:

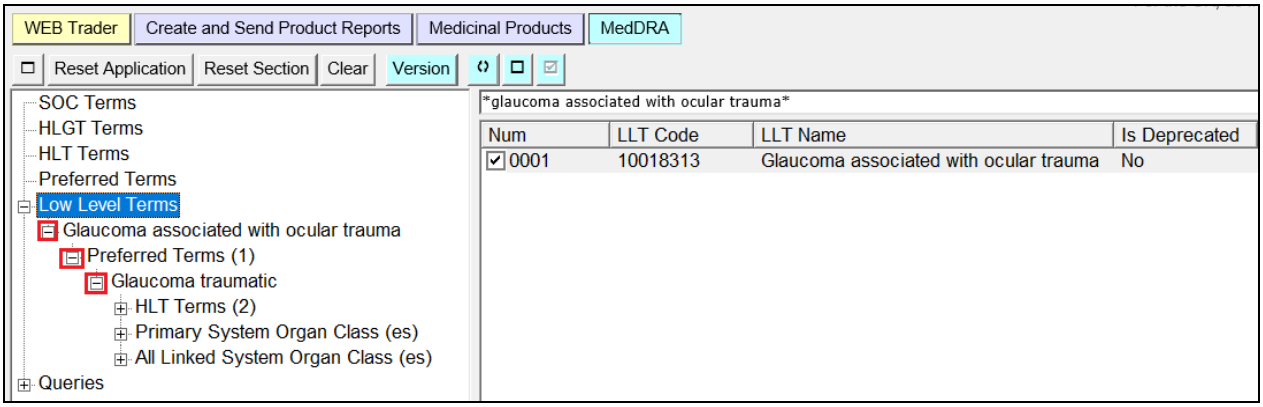


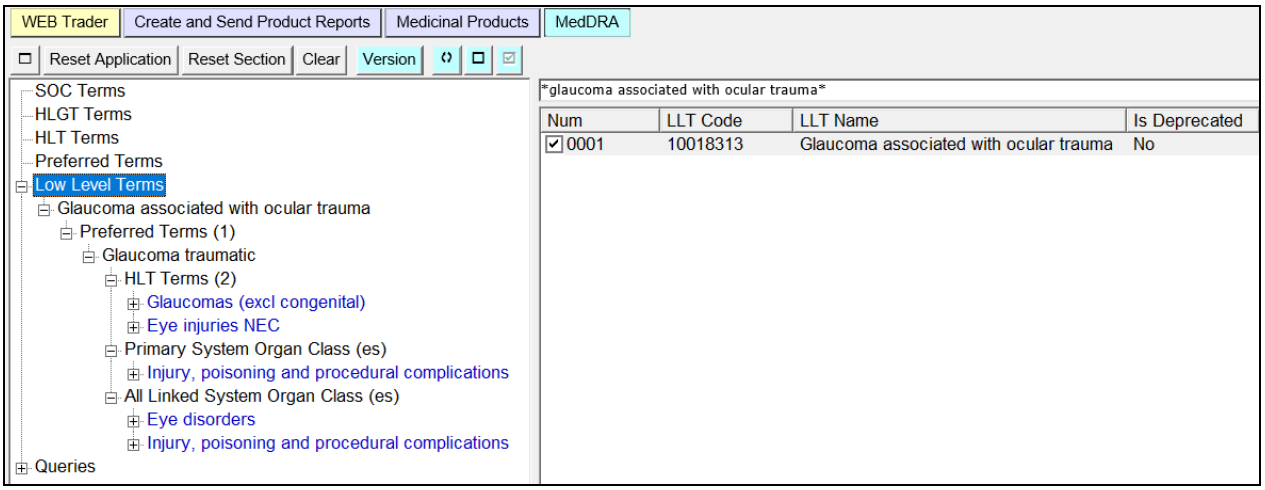
The columns' heading in the active area will provide the following information: 'Num' (number of items found), 'LLT Code' and 'LLT Name'.

To see further details of the result of your query, select the result in the active area and the result of our search will be displayed under 'Low Level Terms' in the tree-view:

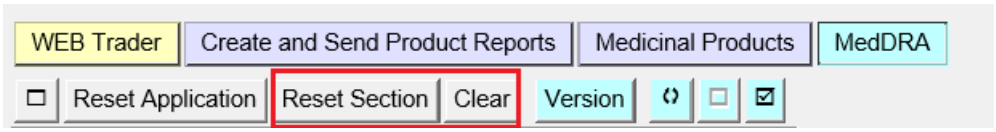


Click on '+' at the left side of 'Glaucoma associated …' in the tree-view area to move from 'Low Level Term' up to 'Preferred Terms'. Follow the same principle to view the SOC, HLT and SPEC CAT(s):





To delete the queries performed in the MedDRA section, you can either deselect all items in your active area and use the 'Clear' functionality in the main menu, or click on the 'Reset Section' button:



5.5. How to perform an Advanced Query

You can perform advanced queries through the query function, located in the tree-view area. An advanced query performs a more customized and structured search than the generic one.

Click on '+' next to 'Queries' in the tree-view area. The MedDRA hierarchical terminology levels will be displayed:

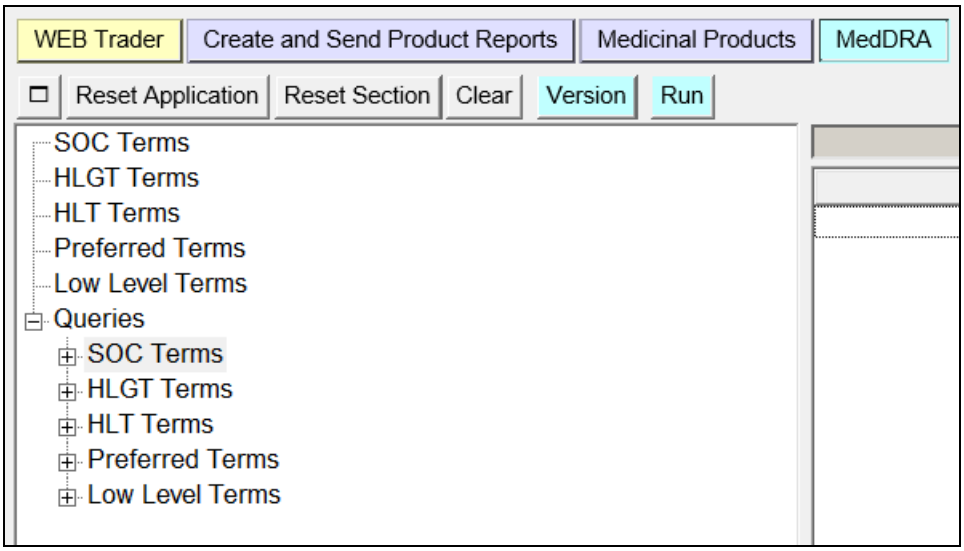
SOC (System Organ Class Terms)

HLGT (High Level Group Terms)

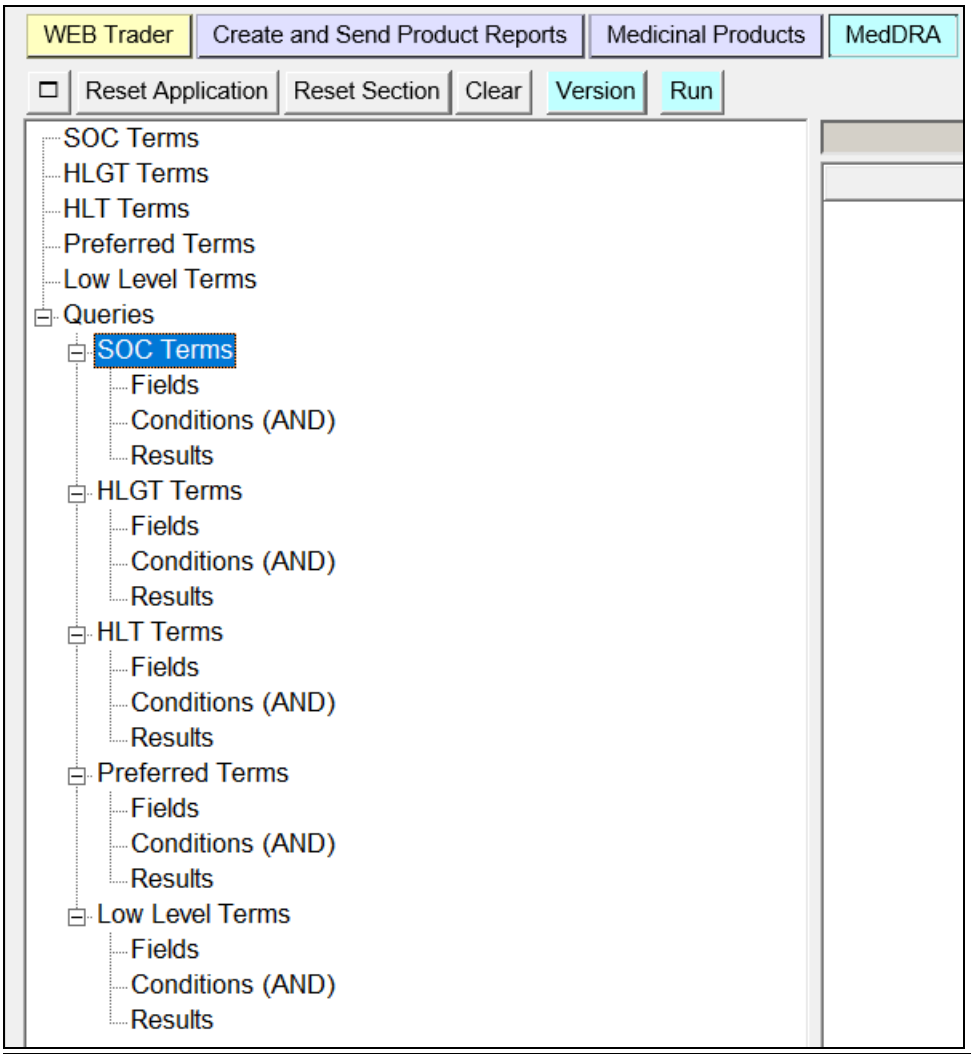
HLT (High Level Terms)

PT (Preferred Terms)

LLT (Low Level Terms)



You can now expand each item by clicking on '+' at the left side of each single item.



At each level, 'Fields', 'Conditions' and 'Results' will be displayed.

'Fields' and 'Conditions' are the two variables that you will have to choose in order to carry out an advanced query. The 'Results' sub-section will display the results of your query. For more details about how to perform an advanced query see section *3.6.2. Advanced Query*.

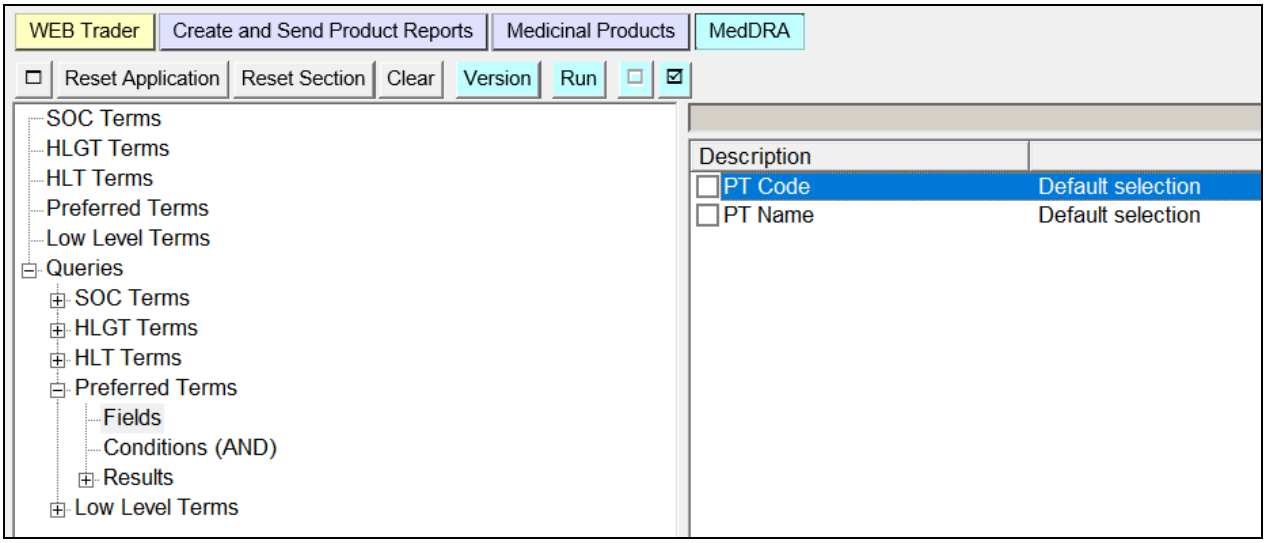
The following example describes how to perform an advanced query. We will search all Preferred Terms (with their relevant codes) linked to the High Level Terms containing the word 'glaucoma'.

Fields: Preferred Terms

Conditions: High Level Terms containing 'glaucoma'

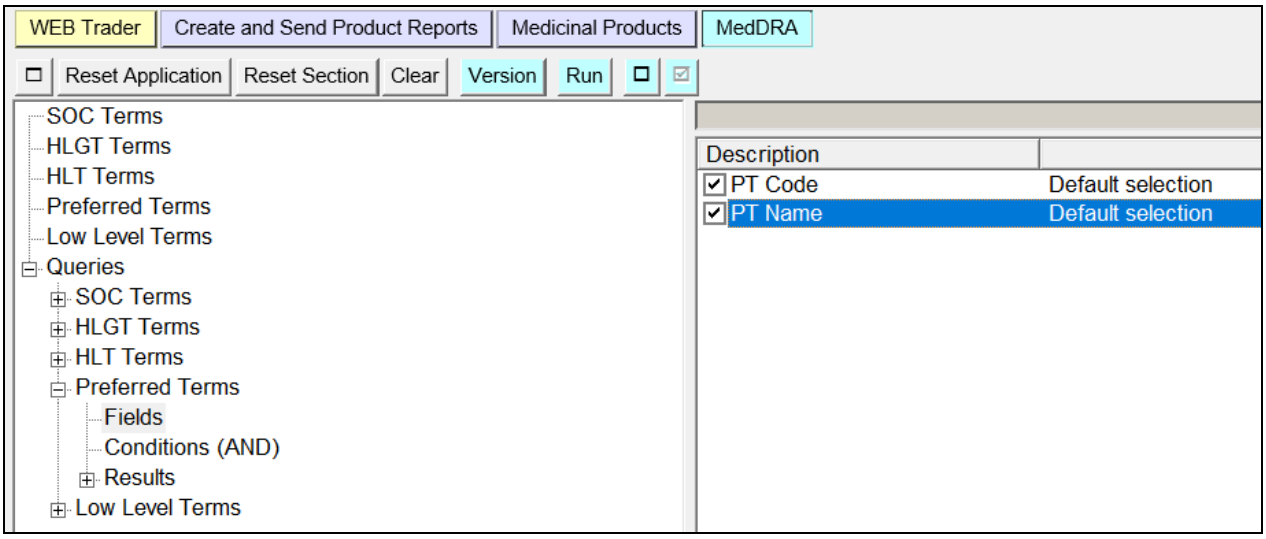
Click on '+' at the left side of the 'Queries' in the tree-view area. Then, click on '+' at the left side of 'Preferred Terms' that appears under the 'Query' item in the tree-view area.

Now click on 'Fields'. 'PT Code' and 'PT Name' are now displayed in the active area.



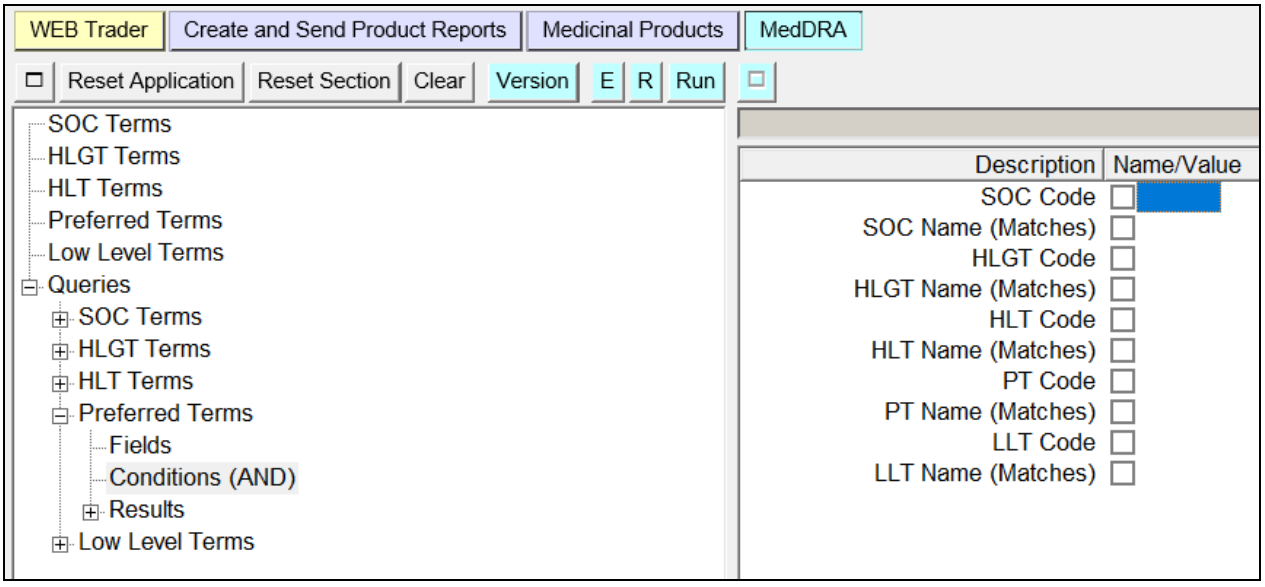
To see both the codes and the names of the 'Preferred terms', select 'PT Code' and 'PT Name' in the active area.

Both 'PT Code' and 'PT Name' items appear now as checked.



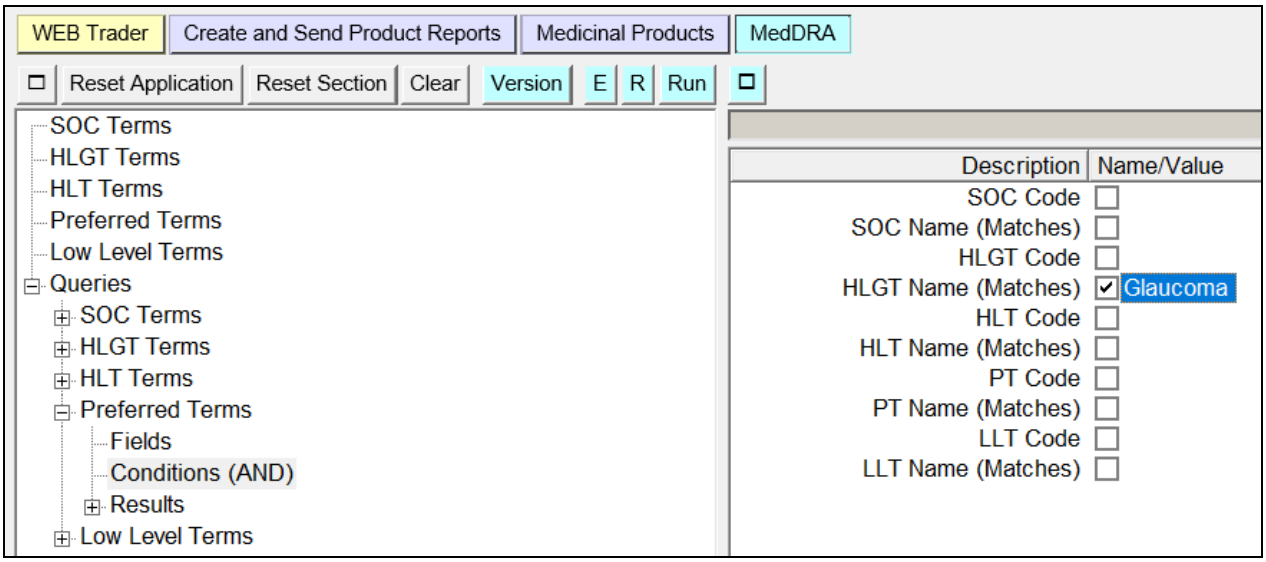
Now select 'Conditions' in the tree-view area, to define the conditions of the search.

The two columns in the active area will provide the following information: 'Description' and 'Name/Value'.

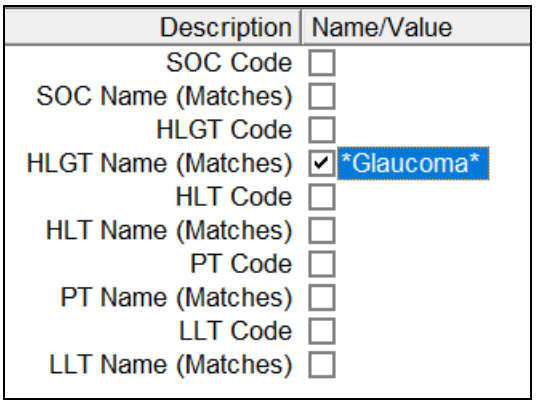


To find the Preferred Terms related to the HLT terms containing the word 'Glaucoma', we need to specify as a condition for this query 'HLT Name' contains 'Glaucoma'.

Click on the white square displayed in the active area next to 'HLT Name', Press 'Enter' on the keyboard and type '*glaucoma*' in the text field just on the right side of the selected item. Then press 'Enter' on the keyboard in order to have the information available in the active area



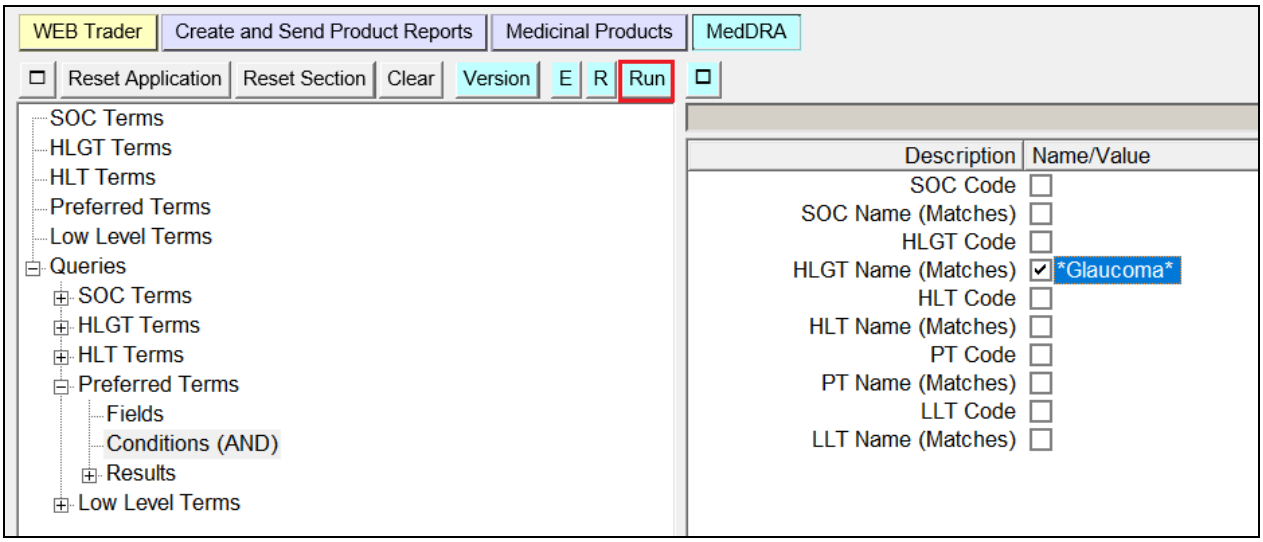
To extend the search to all High Level Terms containing the word glaucoma, you should enter an asterisk (*) at the beginning and at the end of the word that you are entering:

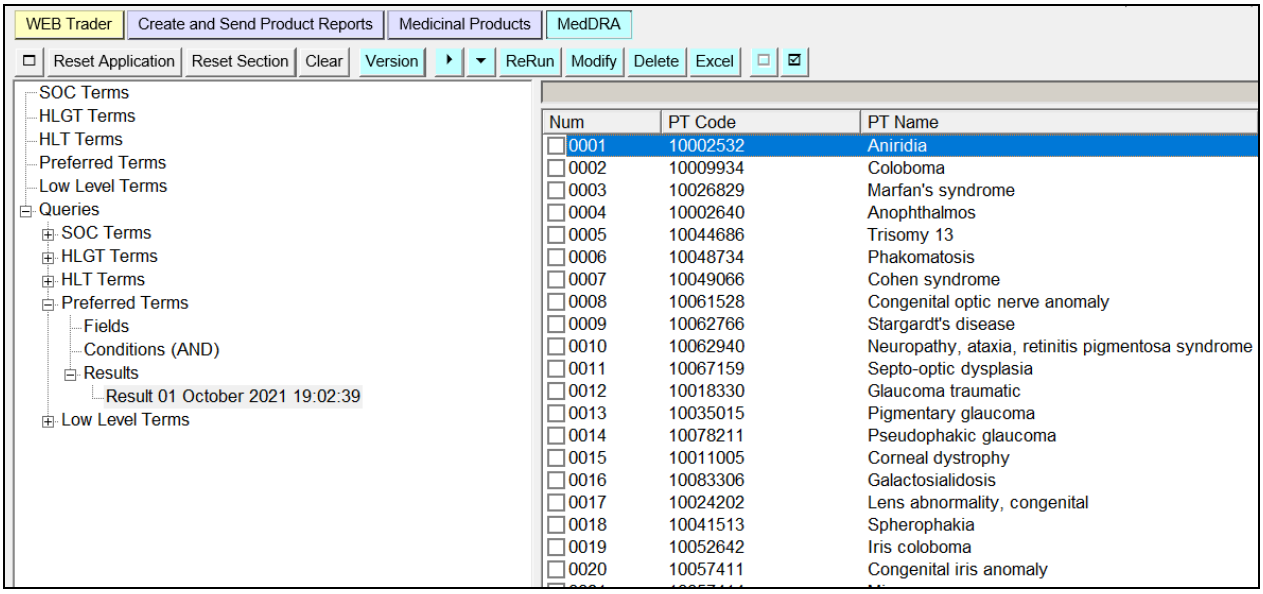


A new dynamic button ('Run') has appeared on the main menu. Click on 'Run' to perform the query.

You may have to wait a few seconds before the results of your query are displayed.

The result will appear in the active area.





The results are displayed in the form of a list of Preferred Terms that are linked to the High Level Term containing the word 'glaucoma'. The two columns in the active area will provide the information concerning 'PT Code' and 'PT Name' as we had selected these two fields in the advanced query.

The results will be recorded in the tree-view under 'Results'. You can now select and analyse one or more of the Preferred Terms displayed in the list by clicking on the little white square under the 'Num' column.

Please see *3.5.3. Checklists* for details on how to manage and navigate a checklist in EVWEB.

5.6. Current status for LLT

EVWEB provides information whether a Low Level Term is current or not in the selected version. When you browse information on LLTs, the active area displays information on the current status of LLT.

The information on the 'current status' of the LLT is based on the MedDRA version selected.

6. List of Abbreviations and Acronyms

AMP	Authorised Medicinal Product
AS	Approved Substances
ATC	Anatomic Therapeutic Chemical (details at www.whocc.no)
CAS	Chemical Abstract Service (Number)
CAP	Centrally Approved Product
CBD	Chemical Biological Description
CV	Controlled Vocabulary
DBMS	Database Management System
DCP	Decentralised Procedure
DMP	Development Medicinal Product
DS	Development Substances
EEA	European Economic Area
EDI	Electronic Data Interchange
EDQM	European Directorate for the Quality of Medicines
EMA	European Medicines Agency
ESTRI	Electronic Standards for Transmission of Regulated Information (gateway technical specification)
EU	European Union
EVDBMS	EudraVigilance Database Management System
EVHUMAN	Unique Identifier of the EMA (for XEVMPD transmissions)
EVWEB	EudraVigilance web-based reporting application (XEVMPD Data Entry Tool)
EWG	Expert Working Group (in ICH or at the EMA)
FDIS	Final Draft International Standard (in ISO)
https	Hypertext Transfer Protocol Secure
ICSR	Individual Case Safety Report
ISO	International Standardization Organization
IM	Implementation Measure
IMP	Investigational Medicinal Product
INN	International Non-Proprietary Name

MAH	Marketing Authorization Holder
MDN	Message Disposition Notification
MedDRA	Medical Dictionary for Regulatory Activities
MFL	[Pharmacovigilance] Master File Location
MRP	Mutual Recognition Procedure
MS	Member State (in the EU)
MSSO	MedDRA Services and Support Organisation
NAP	Nationally Authorised Product
NCA	National Competent Authority
PF	Pharmaceutical Form
PIL	Product Information Leaflet
PL	Package Leaflet
PPI	Printed Product Information
PSI	Printed Substance Information
QPPV	Qualified Person responsible for Pharmacovigilance Activities
SME	Small and Medium Size Enterprise
SmPC or SPC	Summary of Product Characteristics
SSI	Structured Substance Information
SSL	Secure Socket Layer
UCUM	Unified Code for Units of Measure
XCOMP	EudraVigilance External Compliance Testing Environment (aka Test or Pre-Production Environment)
XHTML	eXtensible HyperText Markup Language
XEVMPD	eXtended EudraVigilance Medicinal Product Dictionary
XEVPRM	eXtended EudraVigilance Product Report Message
WHO	World Health Organisation
XSD	XML Schema Definition
ZIP file	Zipped compressed file