# INDUSTRY E-REPORTING MANUAL FOR REGISTRATION HOLDERS.

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**Drug Regulatory Authority of Pakistan**
**Islamabad-Pakistan**

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# HISTORY

This is the first edition of this document.

# APPLICATION

This document is for the guidance and support of registration holders of therapeutic goods for the creation of accounts and subsequent reporting of data through the industry e-reporting system to the NPC, DRAP.

# PURPOSE

Registration holders are one of the main stakeholders of the pharmacovigilance system of Pakistan. As per Pharmacovigilance Rules, 2022, there are legal responsibilities on the part of the registration holder to collect, assess and report the reports of AEs, ADRs and AEFI. Previously, the NPC-DRAP had the following channels through which these reports could be submitted; hard format (CIOMS) submission through mailing address; E2B XML submission through email npc@dra.gov.pk; and monthly/quarterly nil reports submission through official mailing address. However, the NPC-DRAP in collaboration with UMC has now launched the Industry e-reporting system for Registration Holders having two modules namely: manual data entry replacing the old hard format (CIOMS); and E2B upload module that has replaced E2B email submission. The purpose of this manual is to provide step-by-step guidelines to registration holders to get acquainted with the industry e-reporting system and subsequent operationalization.

# LIST OF ACRONYMS

| | |
|---|---|
| **ADR** | Adverse Drug Reaction |
| **AE** | Adverse Events |
| **AEFI** | Adverse Event Following Immunization |
| **CCDS** | Company Core Data Sheet |
| **CCSI** | Company Core Safety Information |
| **CIOMS** | Council for International Organizations of Medicinal Sciences |
| **DRAP** | Drug Regulatory Authority of Pakistan |
| **GVP** | Good Pharmacovigilance Practices |
| **IBD** | International Birth Date |
| **ICH** | International Council for Harmonization |
| **ICSR** | Individual Case Safety Report |
| **ISO** | International Standards Organization |
| **CRH** | Certificate of Registration Holder |
| **LLT** | Lower Level Term |
| **LSO** | Local Safety Officer |
| **MedDRA** | Medicinal Dictionary for Regulatory Activities |
| **MAH** | Marketing Authorization Holder (Registration holders) |
| **NPC** | National Pharmacovigilance Centre |
| **PASS** | Post Authorization Safety Studies |
| **PBRER** | Periodic Benefit Risk Evaluation Report |
| **PIDM** | Programme for International Drug Monitoring. |
| **PL** | Package Leaflet |
| **PSMF** | Pharmacovigilance Systems Master File |
| **PSUR** | Periodic Safety Update Reports |
| **PV** | Pharmacovigilance |
| **QPPV** | Qualified Person Responsible for Pharmacovigilance |
| **RMP** | Risk Management Plan |
| **SmPC** | Summary of Product Characteristics |
| **SMQ** | Standardized MedDRA Query |
| **SOC** | System Organ Class |
| **SSS** | Smart Safety Surveillance |
| **SRUID** | Safety Report Unique Identifier |
| **UMC** | Uppsala Monitoring Centre |
| **WHO** | World Health Organization |
| **WHODrug** | WHODrug Dictionary |
| **WWUID** | Worldwide unique case identification |

# 1 BACKGROUND

The World Health Organization defined Pharmacovigilance as '*the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other medicine-related problem*'. The ultimate goal of Pharmacovigilance is to improve the safe and rational use of medicines, thereby improving patient care and public health.

The history of pharmacovigilance dates back to the Thalidomide tragedy which occurred in the late 1950s and the early 1960s, that has raised concerns regarding the safety of medicines and the potential dangers to public health associated with unexpected adverse reactions to medicines. Cases of unexpected ADR of Phocomelia (limb deformities) were reported with thalidomide which was used in the morning sickness in pregnant women at that time across the world. In the aftermath of the thalidomide tragedy, countries across the world responded with the introduction of spontaneous reporting systems such as Form-3500 by the United States Food and Drug Administration (US-FDA) and the yellow card scheme by the United Kingdom (UK). Subsequently, the World Health Organization (WHO) following the World Health Assembly Resolution (WHA 20.51 of 1967) established the Programme for International Drug Monitoring (PIDM) with 10-member countries in 1968 with a focus on the collection, collation, processing/analysis, and dissemination of relevant information. Thereafter, in 1978, the operational activities of PIDM were outsourced to the Uppsala Monitoring Centre (UMC). Now, the WHO is the administrative head and UMC is the operational centre of the PIDM.

In Pakistan, the activities of pharmacovigilance were started in 1994 when it became an associate member of PIDM. After the promulgation of the DRAP Act in 2012, the Division of Pharmacy Services was empowered to supervise the pharmacovigilance activities in Pakistan. The National Pharmacovigilance Centre (NPC) was established under the Division of Pharmacy Services in 2017 which started its intra-country and inter-country coordination for strengthening the pharmacovigilance system in the country. With the endeavours of the NPC-DRAP, Pakistan became the 134$^{th}$ full member of PIDM in 2018. As of now, there are 157 full members of PIDM along with 23 associate members. Subsequently, the DRAP notified Pharmacovigilance Rules, 2022, which define the legal responsibilities of each stakeholder in Pakistan including registration holders. The NPC also has developed dedicated guidelines for pharmacovigilance stakeholders such as patients, healthcare professionals, registration holders, and public health programs etc. The

NPC also has dedicated tools to collect reports from different stakeholders. Following are the systems used by the DRAP through which registration holders can submit reports of ADRs/AEs to the NPC-DRAP: through hard format (CIOMS) form on mailing address; through E2B Xml format on email npc@dra.gov.pk; and monthly/quarterly Nil reports submission in hard format on the mailing address.

The DRAP in collaboration with the Uppsala Monitoring Centre has now launched the industry e-reporting which has already been piloted by some countries, Mexico being the first to use it in production mode. Now registration holders will have to submit reports of ADRs/ICSRs through a manual data entry module or E2B upload module through this new tool of industry e-reporting.

Industry e-Reporting will allow the registration holders to carry out notification (reporting), installation and operation of Pharmacovigilance, through the reporting of ADRs that occur nationwide with the medicine registered in their name, thus providing quality information in the reports.

The peculiarities of the Industry e- Reporting (for the manual upload module) are:

- Structure compatible with ICH-E2B (R3);
- Priority use of structured fields over free text fields;
- Availability of standardized fields such as MedDRA and WHO Drug Dictionary;
- Possibility of attaching additional relevant information in the form of a PDF file;
- Immediate sending of the report to the NPC, DRAP;
- Follow-ups are done by uploading the XML files of the initial and previous reports and editing them on the same platform; and
- Ability to download electronic acknowledgement (acklog) files in XML format.

**NOTE:**
Using the MedDRA and WHODrug Global dictionaries for medical coding in reporting ADRs/AEs makes it much easier to record and analyze patient data in a consistent and accessible way. Therefore, DRAP advises the registration holder to use both MedDRA and WHODrug while reporting to ensure proper terminologies are used in reporting as our database terminologies are coded based on these dictionaries. In future, the DRAP will make the use of MedDRA and WHO-Drug mandatory for reporting ADRs/AEs by all registration holders.

# 2 GOAL

- To explain the process of application submission by the registration holder for acquiring this facilities.

- To guide registration holders about the creation of first-time logins and the generation of passwords.
- Present the procedure for uploading XML files through the industry e-reporting system for those registration holders who have already completed the implementation of E2B in their databases.
- Provide information and explain the procedure that the registration holders must follow to fill in the information in the manual upload module, and in this way provide the greatest amount of information possible in the requested fields and thus promote high-quality reporting.

# 3 CONTENT DEVELOPMENT

## 3.1 Initial indication

- It is suggested that the equipment which is used to load the cases has a proper electricity backup to prevent data loss.
- Maintain a stable high-speed internet connection for the proper functioning of Industry e-reporting.
- Use these browsers in order of preference, Chrome, Firefox and Microsoft Edge. Keep these browsers updated for optimal operation.
- Safeguard the integrity and confidentiality of access accounts and passwords by not sharing the details with others.
- Comply with the provisions established in the document "**Terms and Conditions of Use**" **(Annex A**).
- Close the session when information is not being entered into the platform.
- Instability and interruptions in the internet connection and power outages, may be reasons for losing the information of a report if it has not been previously sent.

## 3.2 Application for user accounts

- For the granting of accounts, it is essential to have the Pharmacovigilance System in place and its Qualified Person Responsible for Pharmacovigilance (QPPV) or Local Safety

Officer (LSO) details are updated in the NPC-DRAP database since communication will be by email exclusively with the Responsible Person for Pharmacovigilance.

- **The request for using this new tool must be made via email to pv@dra.gov.pk. The registration holders must fill the following form and submit it to National Pharmacovigilance Centre-DRAP through aforementioned email:**

| | | |
|---|---|---|
| **Country:** | **Pakistan** | |
| **Country ISO Code:** | **PK** | |
| **Pharmaceutical company** | 1 | |
| **Short name** (*populates WWUID*) : | | (max 60 characters) |
| **Long name (legal name):** | | (max 100 characters) |
| **Sender organisation (in E2B XML)** | | (max 100 characters) |
| **Sender identifier (in E2B XML)** | | (max 60 characters) |
| **Receiver identifier (in E2B XML):** | DRAP | (max 60 characters) |
| **User 1** Given name: | | |
| Family name: | | |
| Email: | | |
| Mobile No | | |
| **User 2** Given name: | | |
| Family name: | | |
| Email: | | |
| Mobile No | | |

- Two user accounts will be granted by the NPC-DRAP (by the Director, Pharmacy Services Division / Head of NPC-DRAP).
- It is essential that the email indicated for the user account is corporate or institutional.

Information to be provided in the proforma are briefly explained. that the request must contain:

| Application | Description |
|---|---|
| **MedDRA license validity status.** | You must indicate if you have a valid MedDRA license.<br><br>In the future, it will be an essential requirement that the registration holder that uses Industry e-Reporting have the corresponding current MedDRA license. |

| | |
|---|---|
| | It is also applicable for the XML upload module. |
| **WHO-Drug license validity status** | You must indicate if you have a valid WHO-Drug license.<br>In the future, it will be an essential requirement that the registration holder that uses Industry e-Reporting have the corresponding valid WHO-Drug license.<br>It is also applicable for the XML upload module. |
| **Long name** | It is proposed that it be the company name (max. 254 characters).<br>Example: *MedSolutions Laboratories*<br>The long name is the one that will be seen in the upper left quadrant of the interface, so the company knows that has entered the correct session. |
| **Short name** | Abbreviated name (max. 20 characters).<br>**Example: *MerckHealthcare***<br>It will be part of the letters of the *Worldwide unique case identification* (WWUID).<br>Example: **PK-MerckHealthcareKGaA-0000001**, must match the WWUID of the XML files (for those laboratories that have databases that generate this ID).<br>For companies that have E2B databases, the following are the fields that contain the requested information:<br>• **E2B (R2):** <companynumb><br>• **E2B (R3):** 2.16.840.1.113883.3.989.2.1.3.2<br>(Refer to ICH guide: Point C.1.8.1 *Worldwide Unique Case Identification Number*)<br>The short name will also be seen in the *Safety Report Unique Identifier* (SRUID).<br>Example: **PK-MerckHealthcareKGaA-0000001**<br>Companies that do not have E2B databases can propose the sender identifier and define it together with NPC-DRAP.<br>It is important to mention that once this short name is defined, it cannot be modified later in the production phase. |
| **Sender Identifier** | Corresponds to the issuer identifier (max. 60 characters). The *sender identifier* is the code that allows electronic transmission between databases.<br>For companies with databases that can or could generate XML files, it must be identical to the one in their database, otherwise the reports will not be received correctly. |

| | |
|---|---|
| | For companies that have E2B databases, the following are the fields that contain the requested information:<br>• **E2B (R2):** <messagesenderidentifier><br>(In the guide it is point M.1.5 Message Sender Identifier)<br>• **E2B (R3):** 2.16.840.1.113883.3.989.2.1.3.11<br>(In the guide it is point N.2.r.2 Message Sender Identifier)<br>Sometimes it is the same as the short name, but not necessarily.<br>For companies that do not have E2B databases, they can propose the sender identifier and define it together with NPC-DRAP.<br>It is important to mention that once this ID is defined, it cannot be modified later in the production phase. |
| **Sender organization** | For companies that have E2B databases, the following are the fields that contain the requested information:<br>• **E2B (R2):** See field < sender organization > (Corresponds to A.3.1.2 Sender organization in the ICH guide).<br>• **E2B (R3):** (Corresponds to C.3.2 Sender's Organization in the ICH guide).<br>For companies that do NOT have an E2B database, it is proposed to be the same as the Sender identifier. |
| **User 1 (main)** | Name (s), and surnames of the person responsible for the account.<br>Email (user). |
| **User 2 (additional)** | Name (s), and surnames of the person responsible for the account.<br>Email (user). |

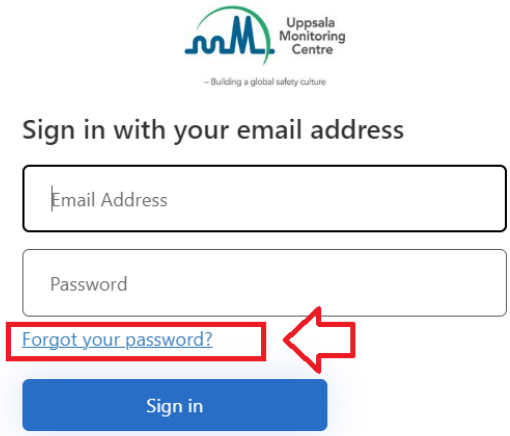
## 3.3 First-time login and password generation

Once the NPC-DRAP has granted you access to the platform, you must follow the following steps to generate your password:

- To log in and generate your password, you must go to the following link (it is recommended not to save the link in the favourites section of your browser and access from the one found in this Manual or on the DRAP website):

| |
|---|
| https://industryereporting.who-umc.org/ |

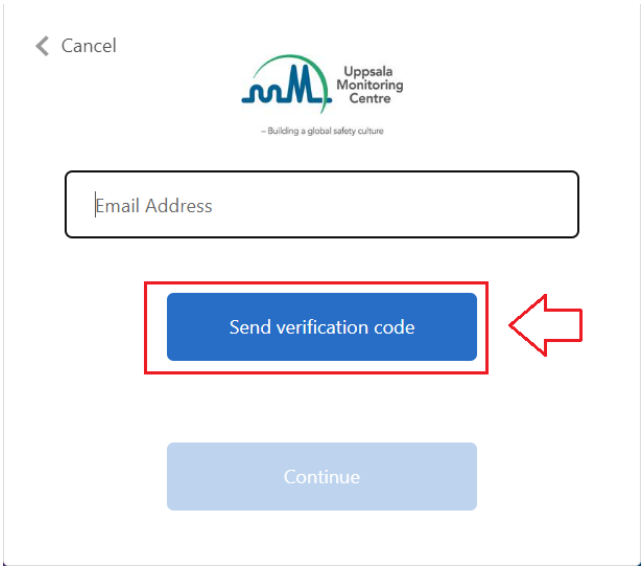
- Click on the link **(Forgot your password?)**, and follow the instructions to create a new password.



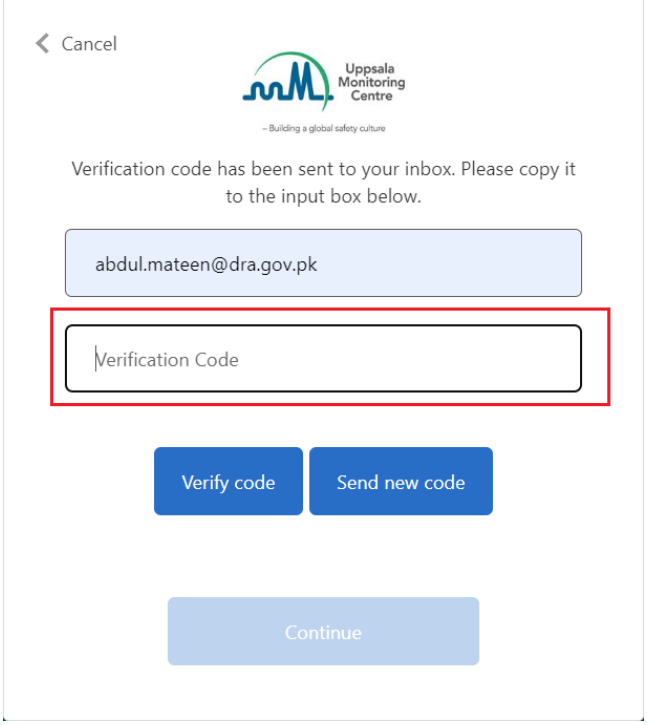

**IMPORTANT**
Do not enable automatic translation of the browser you are using, as there may be inaccurate translations of some fields when you change the interface language.

-In the "**Email Address**" field, you will need to enter your username (email).

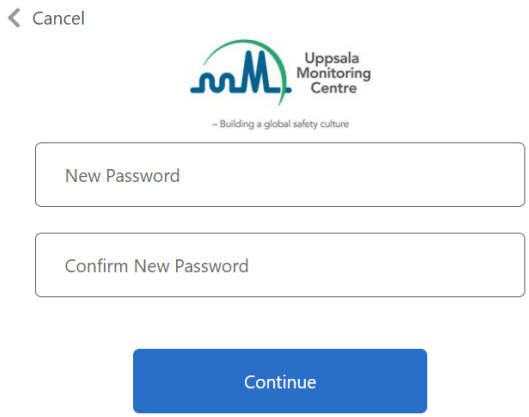
-Press the **send button verification Code**.



- Do not close the Industry e-Reporting window.
- A 6-digit code will be sent to your email that you must enter in the **Verification Code Field**. Press the "**Verify code**" **button**.




- If the code is correct, it will show you the message "*The code has been verified. You can now continue*".
- - Press the **"Continue**" button.



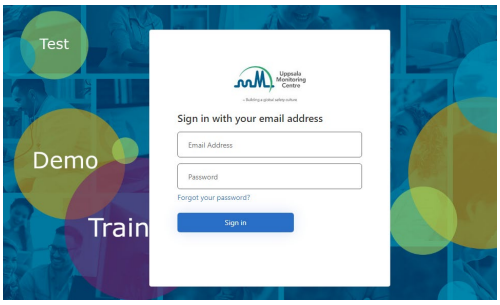
- A screen will be displayed where you will need to enter your new password. Your password must contain a MINIMUM of 8 characters (letters, numbers, uppercase, lowercase, symbols), and it is important that it does not resemble your username.
- Type that same password in the box below to confirm it.
- Press the **"Continue**" button.
- If the process is successful, the system will redirect you to the home screen to enter your username and password.
- **NOTE**: if you do not remember your password, the recovery must be carried out with the same procedure described above.

## 3.4 Login

- To log in, you must go to the following link (copy and paste it into your browser, it is recommended not to save the link in the favorites section of your browser and access from the one found in this Manual or on the DRAP website):

| https://industryereporting.who-umc.org/ |
|---|

- Enter your username and password in the corresponding fields.
- Press the "**Sign in**" button.



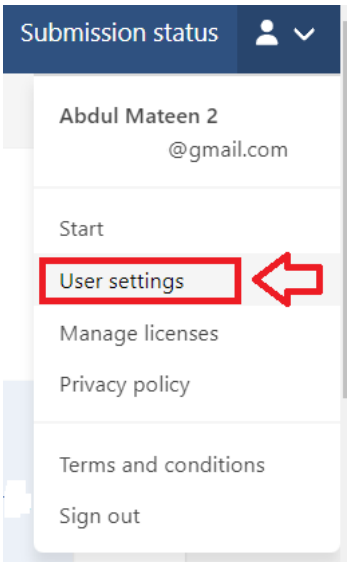

### 3.4.1 Starting Screen

- Once you have logged in, you will find the main screen:

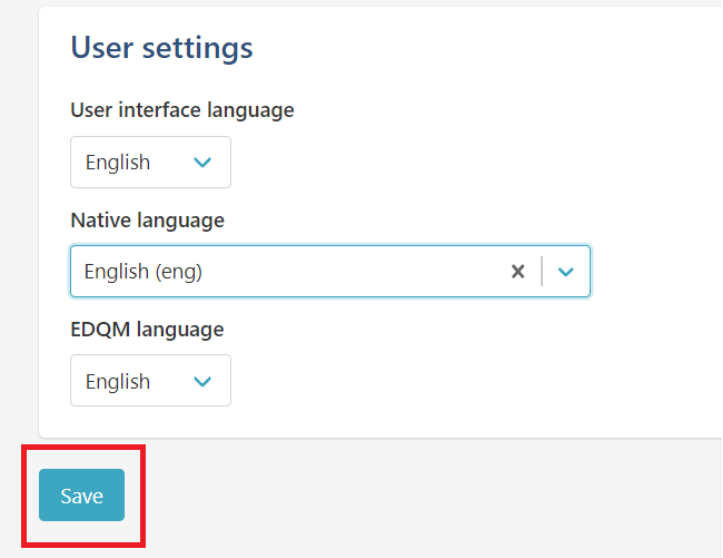

- In the upper right part of the screen, there is a main menu where you can view: the user settings, privacy policies, and logout.
- Each function available in the menu is detailed below:

| Function | Detail |
|---|---|
| **Start** | Moves you to the main screen. If you are entering a report, please make sure you have submitted and downloaded it first before going to the home screen, otherwise the information entered will be lost. |
| **User Settings** | Interface language settings. |
| **MedDRA License** | MedDRA & WHO-Drug license administration. |
| **Privacy Policy** | It redirects you to the UMC web page where the privacy policy is described. |
| **Terms and Conditions** | Legal clauses that establish the way in which the system can be used. |
| **Sign off** | If you are entering a report, please first make sure you have submitted and downloaded it before logging out, otherwise the information entered will be lost. |

- To change the interface language, locate the user settings option in the upper right menu.




- You can choose English as the user interface language.
- Choose "**English"** as your native language, which will allow you to automatically fill in the fields where it is requested to choose the language of a term placed in a specific field.
- To save the changes press "**Save".**




- Return to the main screen with the **"Start"** option from the upper right menu.

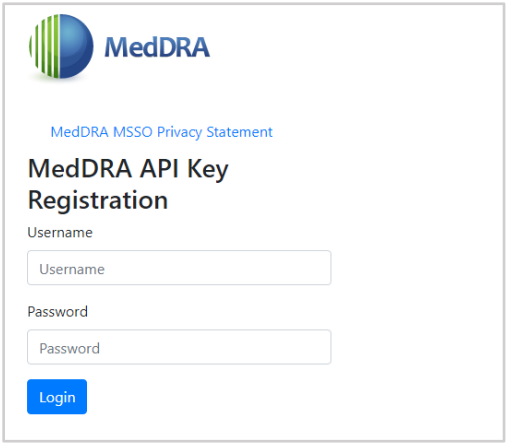
### 3.4.2 Main menu


There are two mechanisms for entering a new report, ***manual entry*** or ***E2B upload***.

1. **DATA ENTRY (FOR MANUAL FILLING):** Directed to the manual entry of the report information into the system.
    - ***Create a new report****:* This module contains instructions on how to create a new individual case safety report and how to manage it in the system.
    - ***Edit report****:* This option allows you to load a previously entered report.
    - ***Follow-up report****:* This option allows you to upload a previously entered report, for follow-up purposes.
    - ***Nullify report****:* This option allows you to cancel a report previously created by this system.
2. **E2B UPLOAD:** Module for reporting or uploading files through XML format.

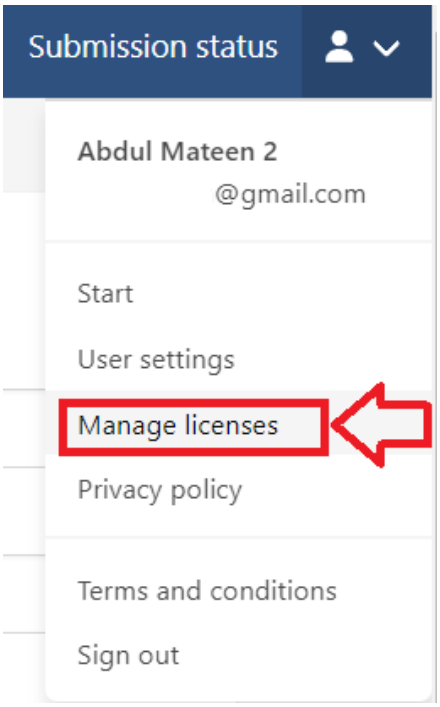
## 3.5 MedDRA license activation and management

Use of MedDRA within the manual upload module requires license activation within the tool. You must obtain an API key (interface of application programming) to validate that the company license is in order. To do this, you must do the following:




1) Enter the following email address (external site to Industry e-Reporting): https://mid.meddra.org/account/register
2) Provide the "**username**" and "**password**" of your MedDRA license. Click on "**Login**"

3) If the process is successful, the page will provide you with the API key for the entered MedDRA user. If it was not successful, check your username and password and try again or contact your MedDRA provider.
4) Copy the API key.
5) Log in to the Industry e-Reporting system.
6) Locate the option "**MedDRA License**" in the upper right menu.




7) In the first field, place your MedDRA user and in the second the API key generated in the steps previously described. Click on "**Save**".
8) If the process is successful, the information will be saved and the following message will be displayed indicating that your license has been validated to use MedDRA within the Industry e-Reporting system.
9) Return to the main screen.
   When entering/editing a report, in the sections where MedDRA is available, you will be able to search for the corresponding MedDRA term.

It should be noted that the MedDRA viewer contained in the corresponding fields in Industry e - Reporting allows a general search for the desired term, so the information presented in the result is concrete, and specific and does not intend to replace the functions and characteristics offered by

the MedDRA web browser. Therefore, if you require an extended consultation, please use the MedDRA web browser at the following link: https://tools.meddra.org/wbb/

**IMPORTANT:**

**The incorporation and use of the MedDRA dictionary is compulsory for both loading modules if the registration holder intends to code the drugs/reaction etc. and use terminologies**

Once you have activated the MedDRA license, you do not need to repeat the process each time you log in.

In case of expiration of the MedDRA license, Industry e-reporting will block the encoding in the MedDRA fields. The user must review the details in the upper right menu in the "MedDRA License" option and if necessary, it must be validated again as indicated in the previous steps.

**DISCLAIMER:** Each registration holder is responsible for performing/verifying the renewal of their organization's MedDRA license with MSSO, in order to be able to use terminologies in the Industry e-reporting in a legal manner.

## 3.6 WHO-Drug license activation and management

Coding medicines systematically provides identifiers to ensure traceability within the process of adverse reaction reporting, data analysis and risk communication associated with medicines and vaccines.

The WHODrug Global is a globally recognized terminology developed and maintained by the UMC and is part of the WHO and regulatory agencies' international strategy for the standardization of medicinal product identifiers. It is also a terminology that in its C3 format allows compliance with the ICH E2B R3 (formerly M5) standards of the ICH in terms of standardization in the coding of medicines and vaccines.

**Therefore, DRAP advises using this terminology in its C3 format for the coding of drugs and vaccines according to the instructions specified below and in Annexes E and F of these instructions.**

The use of WHODrug advanced coding (C3 format) within the manual upload module and the configuration of XML files with WHO-Drug requires a valid license. To validate your license, you must do the following:

1) Locate in the top right menu the option "**Manage Licenses**" and then "Manage WHODrug license".

2) Enter your WHODrug license number in the corresponding field. Click on "**Save**".

3) If the process is successful, the information will be saved and the message "Your WHODrug license is valid" will be displayed, indicating that your license has been validated to use WHODrug within Industry e-reporting.

4) Return to the main screen. When entering/modifying a report, in the sections where WHODrug is available, you will be able to search for the corresponding WHODrug term. It should be noted that the WHODrug viewer contained in the corresponding fields in Industry e-Reporting allows a general search for the desired term, so the information presented in the result is concrete, specific and is not intended to replace the functions and features offered by the WHODrug web browser (WHODrug Insight). Therefore, if you need to perform an extended query, please use WHODrug Insight at the following link: https://who-umc.org/whodrug/whodrug-global/applications/whodrug-insight/

5) In fields where there is a possibility to code with WHODrug (indicated by the legend (WHODrug), you should code as specifically as possible according to the available information and using the WHODrug C3 format. Consult the documents: How to use WHODrug C3 format for drug coding and Technical Guide for the use of WHODrug Global in XML files uploaded in VigiFlow Industry e-reporting for E2B (R3) compliance (the latter for users with E2B databases and producing XML files), and annexes to this document and also available in the WHODrug User Area (WHODrug licensed users' area) of the UMC, accessible through the following link: https://who-umc.org/whodrug/whodrug-global/applications/whodrug-user-area/

These best practices and the use of the C3 format apply to all fields that can receive information with WHODrug and are available to validly licensed users.

## 3.7 Specific indications for the entry of reports through Industry e-Reporting.

In order to define the process that has to be followed in relation to reports that were submitted in previous systems to the e-Reporting Industry (submission by email or hard format), regardless of whether you use the XML upload module or the manual upload module, you must follow the following important instructions:

- The submission of individual case safety reports through Industry e-Reporting will be solely and exclusively for new cases and their respective follow-ups and will not apply to older cases submitted through any channel.
- If you notified an initial case and follow-ups through the previous mechanism via email, you must follow up and close it in the same way, that is, via email.

- This new tool will not apply to the submission of monthly/quarterly nil reporting; therefore, the registration holders should follow the existing system of reporting.

# 3.8 MODULE I: MANUAL DATA ENTRY.

## 3.8.1 Generalities

### 3.8.1.1 "NF" Codes: Null Flavor (Missing Information)

Null Flavor (NF) codes are a collection of codes that specify why a valid value is not present. These codes can be found at the end of certain fields, for example, Primary Reporter Country, Patient Initials, Therapeutic Indication, etc.

- Unknown.
- Asked but unknown.
- Not Asked.
- Masked/concealed.

It should be noted that these codes may only have justification of use for not providing the field information if the system necessarily requires filling in that field to send the report to the NPC.

If in a field that contains an NF code, the information is not available and it is not mandatory for the report to be sent, you can leave it blank and leave the preset NF marker.

The system will indicate in red those minimum fields necessary to send the report.

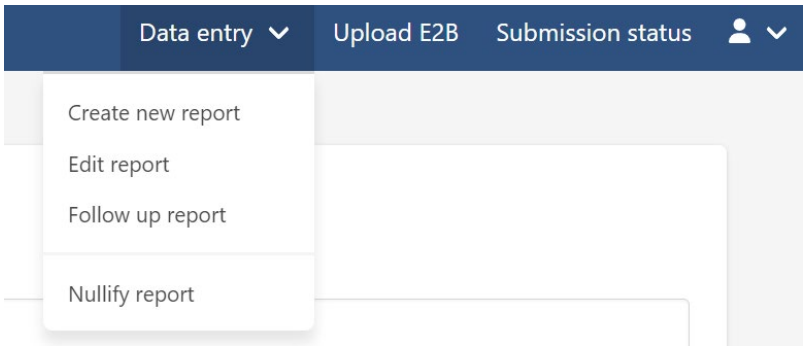
### 3.8.1.2 Common icons in the different sections:

| | |
|---|---|
|  | Allows you to add a corresponding section or field where the button is located. For example: Medication, Therapeutic indication, Dose, Reactions, Causality evaluation, etc. |
|  | Allows you to delete a field or an entire corresponding section where the button is located. Bear in mind that if you delete a section or field and it is essential for sending the report, you must fill in the requested information again. |
|   | Allow you to go to the next section. In the manual data entry module, it is not mandatory to completely fill out a section to move on to the next. At the end, the minimum fields necessary for the sending will be marked in red, and you will have to return to the corresponding section to provide the missing information or correct it. |

### 3.8.1.3 Management of the Report in the System

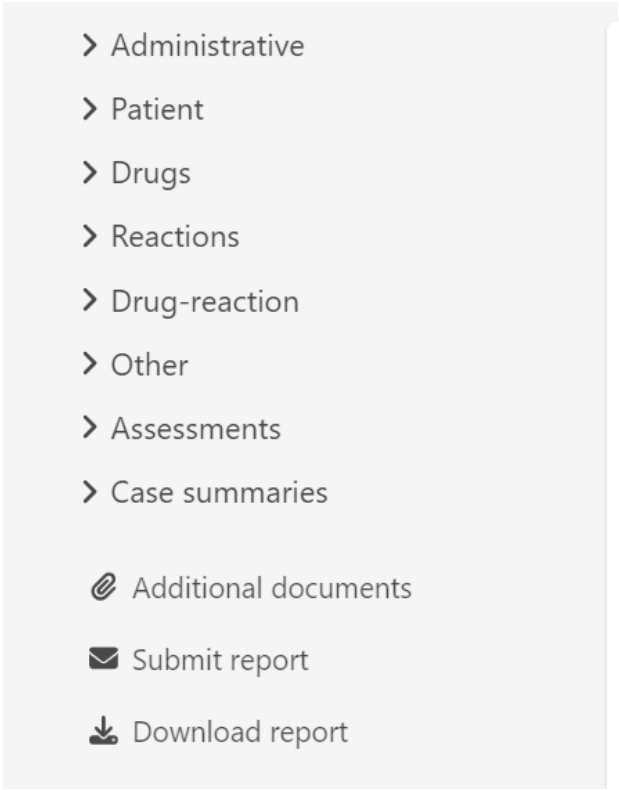
This module contains instructions on how to create a new Individual Case Safety Report and how to manage it in the system.

To enter the data through the manual data entry module, identify the "***Data entry option in the upper right menu***"



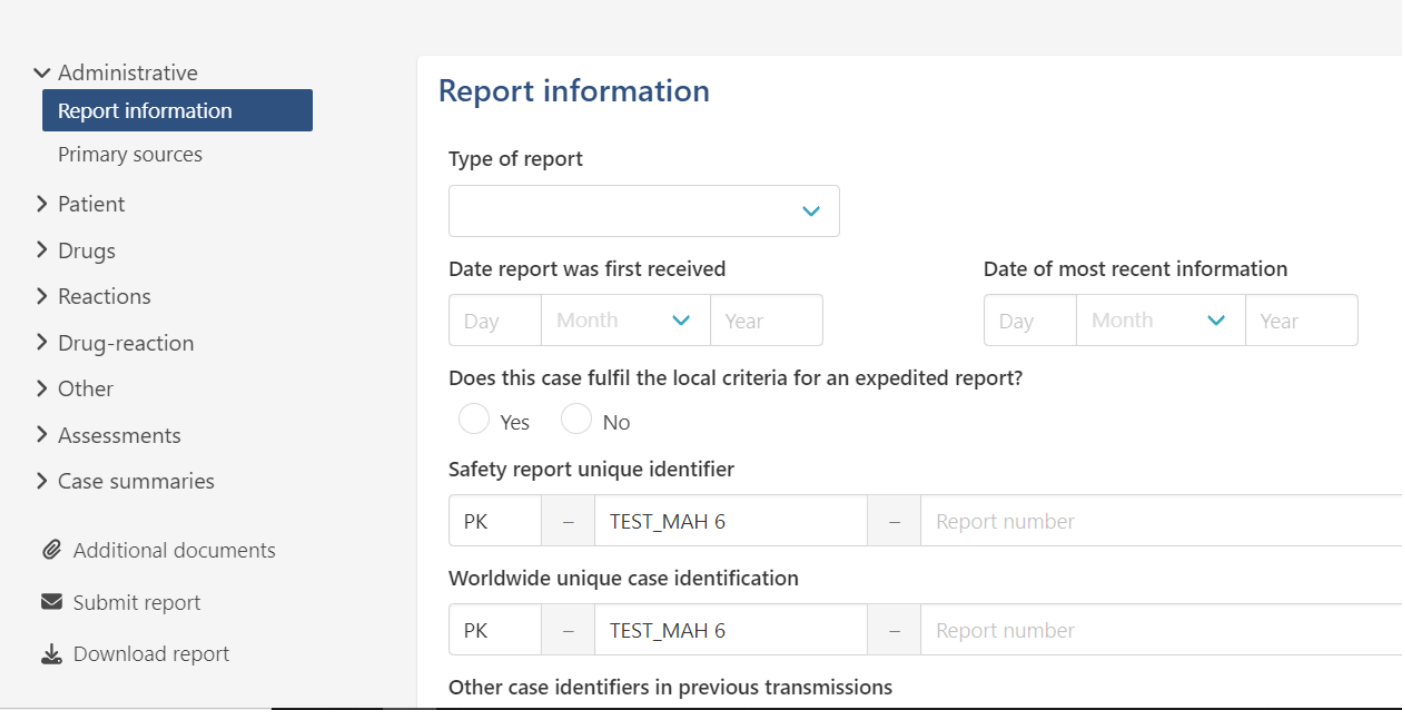

## 3.8.2 Create a new report

It consists of eight (8) sections as can be seen below:



### 3.8.2.1 Administrative

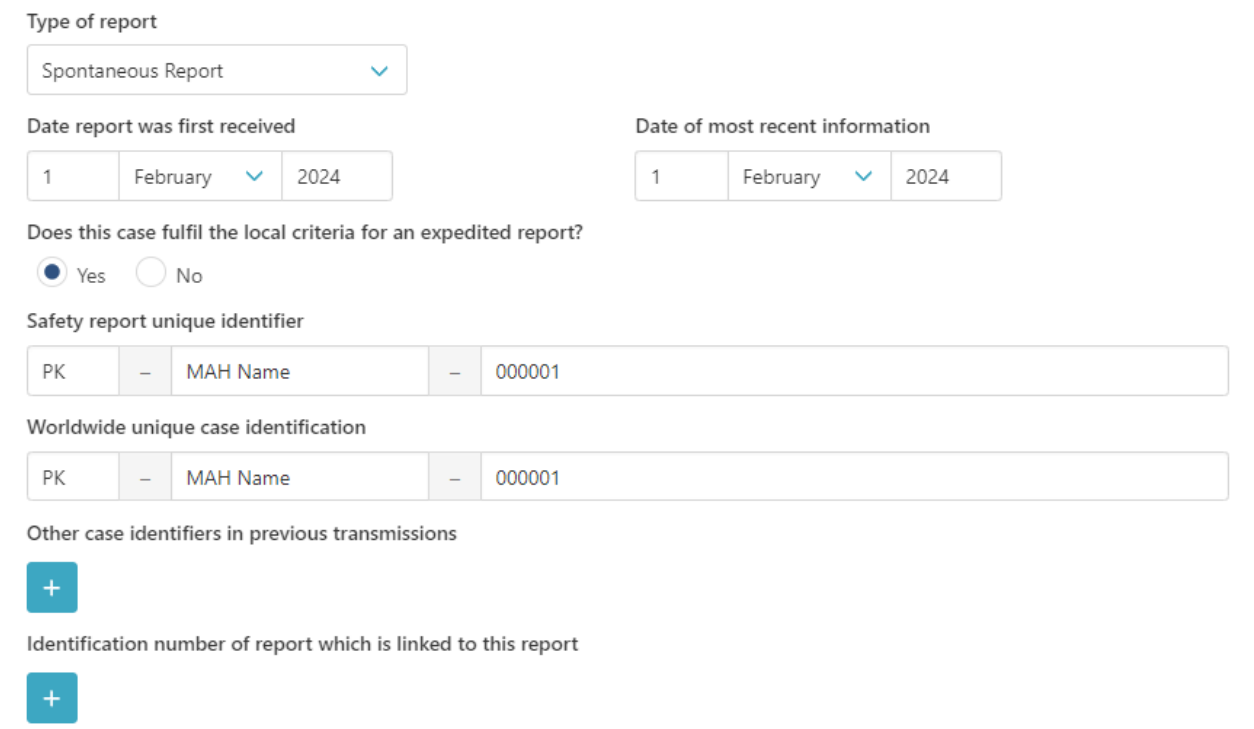
#### 3.8.2.1.1 Report Information




##### 3.8.2.1.1.1 Spontaneous reports

The **type of report** is a field in which you must choose whether it is a *spontaneous report* or a *study report*

***When the spontaneous reports*** option is selected, additional fields will be displayed such as:




These fields are briefly explained here.

- **Date on which the report was received for the first time:** Date of knowledge for the first time at the National Pharmacovigilance Centre (NPC). Select the date in the fields available for this purpose (Day / Month / Year). **This is a Required Field**.
- **Date of most recent information:** Corresponds to the date when the NPC received the last information that gave rise to the respective monitoring of a case. Select the date in the fields available for this purpose (Day / Month / Year). **This is a Required Field.**

  The date of submission to the authority corresponds to the day the case is entered and sent and this is automatically provided to the National Pharmacovigilance Center (NPC) when the case is sent.
- **Does this case fulfil the local criteria for an expedited report**? **This is a Required Field.**
  - Indicate "**YES**": for serious reports that result in death or that meet any of the seriousness criteria: life-threatening, caused or prolonged hospitalization

disability/incapacity, congenital anomaly/birth defect, or some other medical condition important.

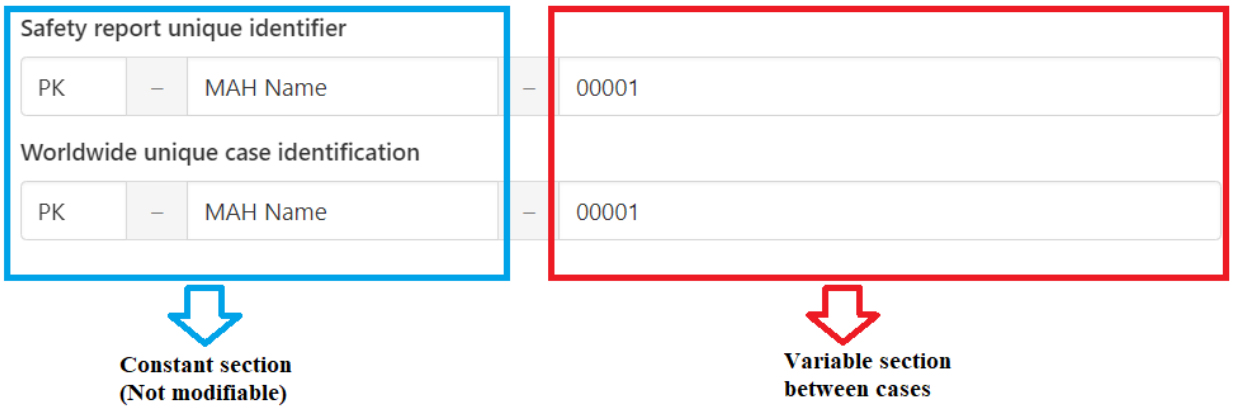
- Indicate **"NO":** for reports classified as non-serious.

| PK | – | MAH Name | – | 000001 |
|---|---|---|---|---|

Worldwide unique case identification

| PK | – | MAH Name | – | 000001 |
|---|---|---|---|---|

- **Worldwide Unique Case Identification (WWUID):** This is the first identifier assigned to the report, if the company does not have a database that generates a code, this will be the first code assigned to the report. If the company has an E2B database, the WWUID will be the same as the code generated by the database. The WWUID is composed first of all by the initials of the country, i.e., **PK**, followed by the short name of the company (which must be established by the NPC and cannot be modified later), and finally, the number that identifies the report.
- **Safety Report Unique Identifier (SRUID):** This is another identifier that can be assigned to a case following the same format as the WWUID in case it is needed.

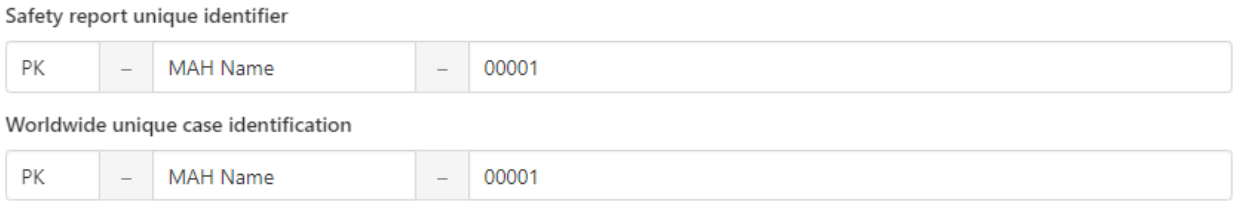



The constant section of both identifiers, once they have been defined with NPC, cannot be modified later. If you need to use another internal laboratory ID or specific notification codes requested by NPC, add it in the " *Other case identifiers in previous" field. transmissions".*

When you enter a report into the system, the constant section of both identifiers is already predefined, so it is not necessary to modify these IDs.

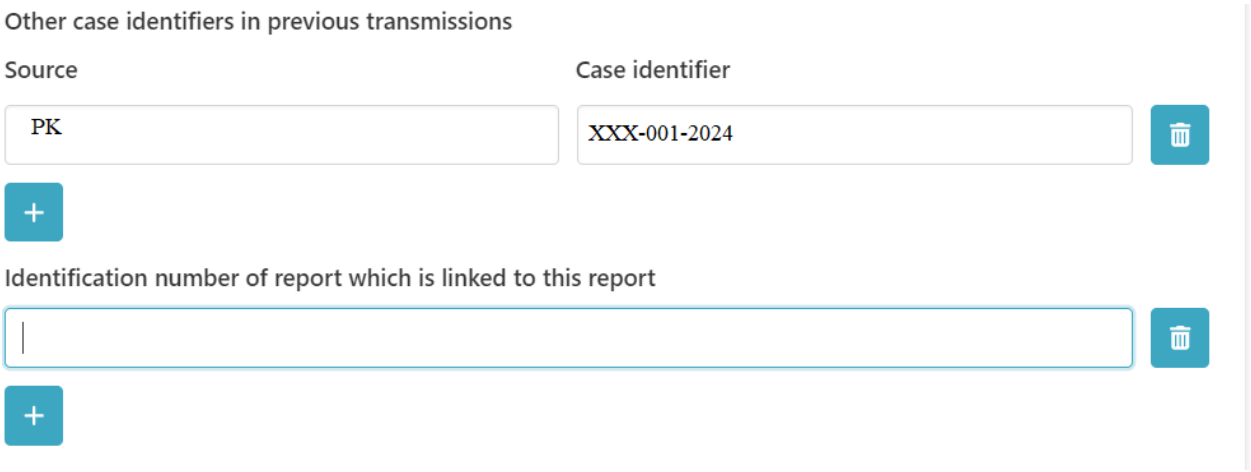
The variable section of the WWUID and SRUID must consist of a consecutive number of at least 5 digits, which must be unique for each case. Therefore, the first report that you enter in the manual upload module must be 00001.

**EXAMPLE**

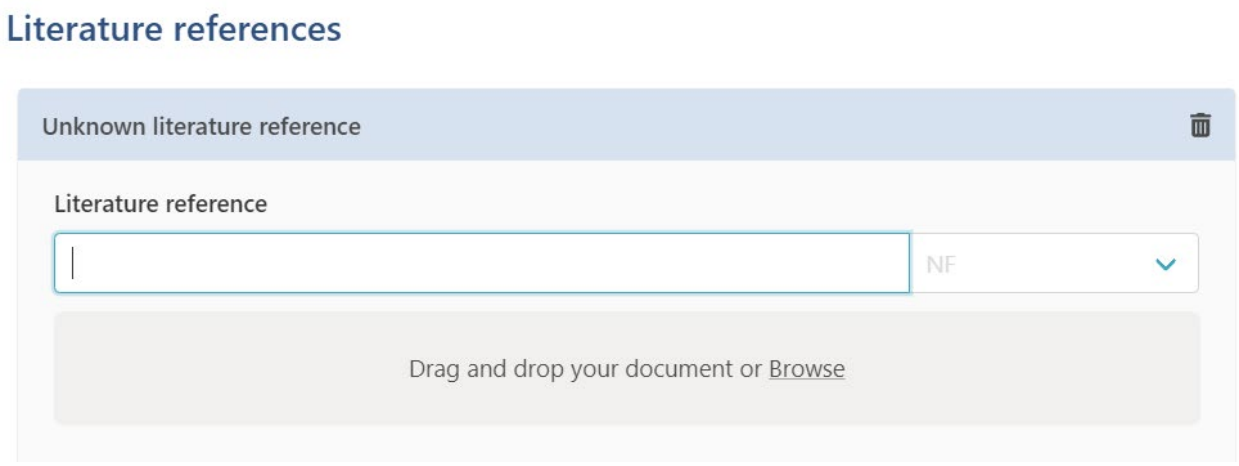



The **Unique Identifier of the Safety report** and the **Global Unique Identification Number** are unique for each report, therefore, in follow-ups, the system will not allow you to modify them.

- **Other case identifiers in previous transmissions** (Other case identifiers in previous transmissions): If you have an internal encoding in your organization or other requested indicators, you can add them by clicking the "+" icon.
    - This field can include IQF codes, IDs generated in systems prior to Industry e-Reporting, as well as codes established for notifications of additional activities of Risk Management Plans (RMP).
- **Identification number of reports that are linked to this report** (Identification number of reports which are linked to INITIAL report): When you have cases that are related in some way to the one you are reporting (for example, a serious event that happened in a family), put the WWUID of the related cases. It does not apply to cases that are follow-up.

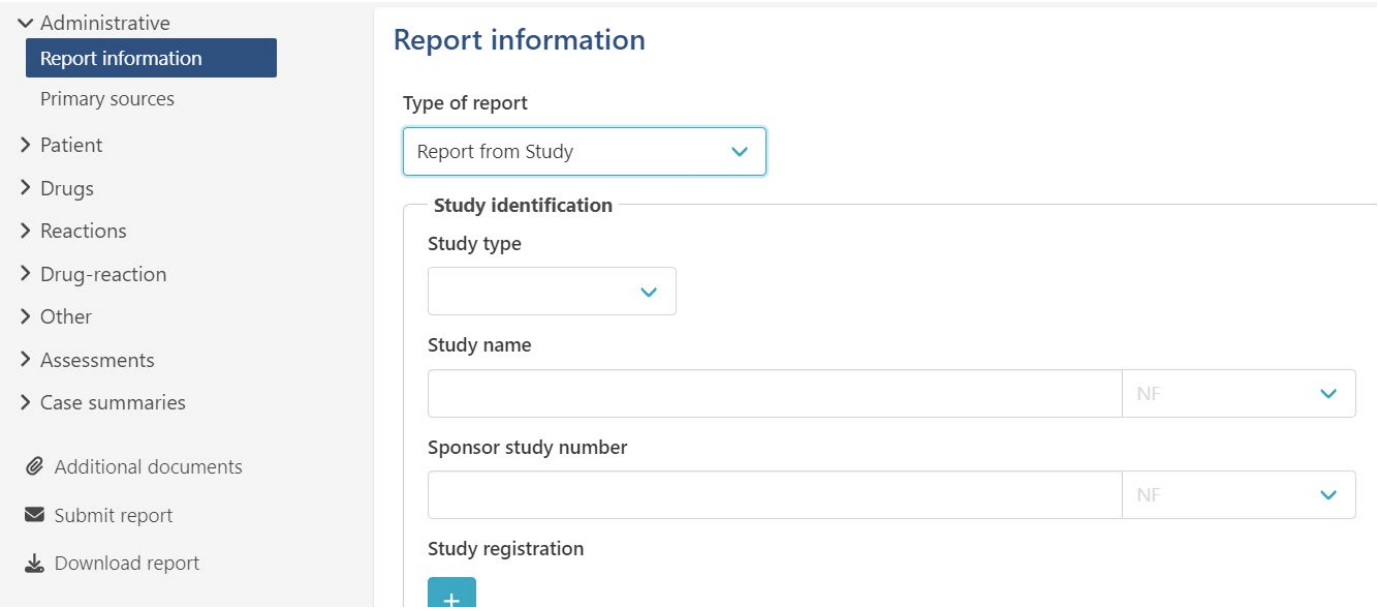


- **Literature references:** This field will only be used if a literature case is reported (see Type of report) and you must place the bibliographic reference from which you obtained the case. Optionally, it is possible to add files of the case literature references (in the original language), as long as the copyright of the document is not violated to share it. To upload a file, drag and drop it onto the grey section or open it from your file explorer with the "Browse" option. Add literature references in PDF format to avoid format incompatibilities.




### 3.8.2.1.1.2 Study reports

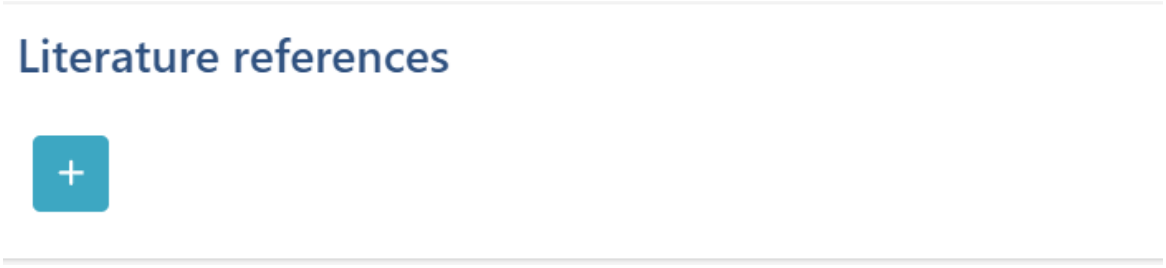
The **type of report** is a field in which you must choose whether it is a *spontaneous report* or a *study report.*



*When the study report* option is selected, additional fields will be displayed such as:

- Type of study
  - Individual Patient Use: For compassionate use programs.
  - Other studies:
    - Observational studies.
    - Records.
    - Post-market use programs.
    - Patient support programs.
    - Disease management programs.
    - Surveys aimed at patients or health professionals.
    - Pharmacovigilance studies.
    - Compassionate Use Programs.
- **Name of the study:** Enter the name of the study as it appears in the authorization (registration) letter of the Regulatory Authority (DRAP).
- **Sponsor study number:** Study identification code as it appears in the authorization (registration) letter of the Regulatory Authority (DRAP).

  For Literature notifications, the option of a spontaneous report or study report must be chosen based on the origin of the case. In these cases, it is necessary to add the literature reference from which the case was obtained, placing it in the Bibliographical References field. This is a required field if the report is from the literature.




If the origin of the literature report is not clear, you should choose the **other option**.

**NOTE:** The option not **available to the sender** should not be used.

- **Study registration**: Click "+" and add the study registration number and the country of the registration fields.

- For the other fields such as date report was first received, date of most recent information, WWUID, SRUID, other case identifiers in previous transmissions etc. please refer explanation provided in the above section of spontaneous reporting.

**IMPORTANT.**

**Cases of suspected unexpected adverse drug reactions (SUSARs) and serious adverse events (SAEs) occurring during clinical trials should be reported to the Chairman or Secretary Clinical Study Committee, Clinical Trial section of the DRAP through email (CT_AE.reporting@dra.gov.pk). For further details visit the guidelines to conduct clinical research in Pakistan and Bio-Study, Rules, 2017.**

#### 3.8.2.1.2 Primary Source:

Information referring to the primary/original reporter.

- **Primary source for regulatory purposes –** Necessarily enables this option. The main source of information is the person who provides the facts about the case. In the case of multiple sources, the "Primary Source for Regulatory Purposes" is the person who first reported the facts to the reporter. The report must only have one primary source for regulatory purposes.
- **Qualification:** Corresponds to the profile of the primary reporter. (Obligatory field). You will have to choose between:
    - Physician
    - Pharmacist
    - Other healthcare professionals
    - Lawyer
    - Consumer or other non-healthcare professionals. Choose this option if the primary reporter is the patient/consumer or a relative of the latter.
- **Country:** By default, choose **"Pakistan".** However, on some occasions, the country of the reporter may be different if, for example, a patient/consumer purchases a medication in Pakistan and the event/reaction occurs in another country.

The following fields about the reporter are not necessary, but you can include the information if you have it or you can do without them for reasons of confidentiality or refusal of the reporter.

- Title
- Given Name
- Middle name, (if applicable)
- Family Name
- Organization
- Department
- Street
- City
- State or province
- Postcode
- Telephone

You can add other primary sources with the *"**Add Primary Source**" option,* however, the report should only have one primary source enabled for regulatory purposes.

### 3.8.2.2 Patient

#### 3.8.2.2.1 Patient characteristics

- **Name or initials**: Provide initials of the paternal and maternal surnames and name(s) in that order, or in the case of post-authorization safety studies, the patient's identification code.
- **Sex**
- **Date of Birth**
- **Age at onset of reaction/event**
- **Age group**

(It is sufficient to fill out only one of the age fields: Enter the most accurate information allowed under the relevant confidentiality requirements)

- **Gestation period when the reaction/event was observed in the fetus)**: Enter the value and choose the unit of time from the catalogue. It should only be filled out if the patient is pregnant, otherwise, leave it blank.
- **Date of last menstrual period**: If you do not have the complete date, you can enter only one (year) or two fields (month and year).
- **Weight** (kilogram)
- **Height** (centimeter)

The following fields are not relevant to the quality of the report, however, if you have the information, you can provide it or simply leave the fields blank:

- Medical file number of the general practitioner.
- Specialist record number.
- Hospital record number: Corresponds to the clinical file number.

#### 3.8.2.2.2 In case of death

If the outcome of the reaction/event is death, provide the following information:

- **Date of death:** If you do not have the full date, you can enter only one (year) or two fields (month and year).
- **Cause of death as reported by the primary source:** If you have the information, enter the MedDRA term (Level LLT) of the cause of death.
- **Was the autopsy performed**? If you have information to affirm or deny, please provide it. If you choose YES, you could provide information from the following field.
- **Cause of death determined at autopsy**: If you have the information, enter the MedDRA term (Level LLT) of the cause of death.

#### 3.8.2.2.3 Parent

(Parent-child/fetus report). When the neonate or fetus, exposed to one or more medications through the parents, presents an event/reaction other than early spontaneous abortion/fetal death, information should be provided for both the neonate/fetus and the father and mother in the same report.

- **Is this a parent-child/fetus case**?)

  **If you select YES**, additional fields will be displayed for the parent who was the source of exposure to the suspected medication. If you have the information, please provide as much information as possible. The further fields displayed after checking “yes” are the name or initial of the parent, sex of the parent, date of birth

of parent, age of parent, date of last menstrual period, weight of parent, and height of parent.

- If you don't know the answer to the question, leave it blank.
- **Relevant past drug history of the parent:** Provide information on the history of medications relevant to the assessment used by the parent who was the source of exposure to the suspected medication. To add information, click the plus sign to add details about the medicines.
- **Medical history of parent:** Provide information about the relevant medical history and concurrent conditions of the parents.

### 3.8.2.3 Drugs

**IMPORTANT:** In fields marked with the (WHODrug) legend, employ the WHODrug C3 format to code drugs with the utmost specificity based on the available information. For detailed guidance on using the WHODrug C3 format, refer to the document "How to Use the WHODrug C3 Format for Drug Coding".

**Characterization of the role of the Drug:**

Choose between the following options:

- Suspect.
- Concomitant.
- Interacting: If you choose this option you must have at least two interacting drugs.
- Drug not administrated.

**Medicinal product name as reported by the primary source.**

You must place the trade (brand) name if you have such information and in parentheses the generic name. If you report other medications as poly-pharmaceuticals, you should NOT make a report for each active ingredient that makes up the medication.

**Medicinal product (WHODrug)**

**Country where the drug was obtained:**

**Action taken with the drug:**

Choose between:

- Drug withdrawn
- Dose reduced
- Dose increased.
- Dose not changed
- Unknown
- Not applicable

**Authorization/Registration number:**

Registration number of the medicine, which must be of the suspected medicine issued to the Registration holder or his Legal Representative.

**Country of authorization/registration:**

Select the country where the drug was authorized or registered.

**Name of the registration holders:**

Company name of the holder of the medicine registration or its legal representative.

**Cumulative dose to first reaction**: Select the quantity of dose and subsequent unit from the drop-down list.

**Gestation period at the time of exposure:** Select gestation period from the drop-down list (month, week, day, trimester)

**Additional drug information (free text field)** In this free text field you can add information that you have not been able to add through the fields that make up the Drug section, for example, the expiration date of the drug.

**Additional information on the drug (selection field):** Select the option that best suits the case from the drop-down list, only if applicable, otherwise leave it blank.

**INDICATIONS AS REPORTED BY THE PRIMARY SOURCE**

**Indication as reported by the primary source:** Enter the therapeutic indication for which the drug is being given as reported by the primary source.

**Indication (MedDRA):** Place the MedDRA term (Level LLT) of the therapeutic indication for which the drug is being given.

**Dosages**

**Batch/Lot Number**

**Dose:** Enter the value and select the unit of measure from the dropdown list. In the case of medicines that contain more than one active ingredient, it may be expressed as a unit of dosage measure.

**Dosing Interval:** Enter the value and select the time unit from the dropdown list.

**Dosage text:** If you have the treatment time, put it here.

**Pharmaceutical dosage form:** Select from the dropdown list pharmaceutical dosage form as applicable.

**Pharmaceutical dose form text:** Indicate in the free text field the pharmaceutical form corresponding to the case.

**Start of administration:** If you do not have the complete date, you can enter only one (year) or two fields (month and year).

**End of administration:** If you do not have the complete date, you can enter only one (year) or two fields (month and year). If you continue with the treatment, leave it blank.

**Duration:** Place the value and select the unit of time from the dropdown list.

**Route of administration:** Use the drop-down list to choose the route of administration that corresponds to the case.

**Route of Administration in text** – Use this free text field only if you do not find the specific route of administration in the drop-down list or the "*other" option should be chosen.*

To be able to add more suspected or concomitant medications, choose the option "*Add medication"*

If you have more than one dosing regimen for the same drug (e.g. different dosages, batches, dates of administration, etc.), you can add the "+" icon instead of adding another drug.

If you intend to add another suspected, concomitant or interacting drug you can click the "**Add drug**" option and enter the data as per the same pattern mentioned above.

### 3.8.2.4 Reactions

**Reaction/event as reported by primary source:** Place the MedDRA term (Level LLT) of the reported reaction/event in parentheses.

Verify that the English field, English (Eng) is maintained.

In this section, you MUST NOT RECORD the medications administered to the patient for the treatment of reactions/events.

**Language of the reported reaction/event:** Verify that the field English (Eng) is maintained.

**Translation of reaction/event as reported by the primary source:** Leave the field empty.

**Reaction/event (MedDRA):** Select the corresponding reaction from the MedDRA dictionary.

**Term highlighted by the reporter**

**Is this a serious reaction?** Select the option that corresponds to the case. If you select the ***"Yes"*** option, you must necessarily select one of the following severity criteria:

- Life-threatening
- Results in death
- Caused or prolonged hospitalization
- Disabling/incapacitating
- Congenital anomaly/birth defect
- Other medically important condition

**Outcome at the time of the last observation:** Select from the drop-down list the option that corresponds to the outcome of the adverse reaction at the time of the report:

- Recovered / Resolved
- Recovering / Resolving
- Not recovered / Not resolved / ongoing
- Recovered / Resolved with sequelae
- Fatal
- Unknown

**Medical confirmation by a healthcare professional:** It is generally affirmative when the primary reporter (primary source) is a physician or other healthcare professional, however, when a medically qualified consumer/patient, friend, relative, or caregiver of the patient can provide medical documentation (for example, data laboratory tests) that support the occurrence of an event/reaction and indicate that an identifiable healthcare professional suspects a causal

relationship between a medicinal product and the reported adverse reaction, may be considered medically confirmed.

**Start of reaction/event:** If you do not have the complete date, you can enter only one (year) or two fields (month and year).

**End of reaction/event:** If you do not have the full date, you can enter only one (year) or two fields (month and year). If the event/reaction continues, leave it blank.

**Duration:** If the primary source provides the information or if the start and end dates of the event/reaction allow it, establish the duration of the event.

**Country where the reaction/event occurred:** Choose "Pakistan". There may be exceptions, for example, the patient acquired the drug in Pakistan, travelled to another country and presented an ADR.

**To add** more reactions/events choose the option *"**Add reaction**"*

### 3.8.2.5 Drug-Reaction

#### 3.8.2.5.1 Rechallenge

**Was a rechallenge performed?** If you have information that indicates a re-administration, select **"Yes".** If the information does not indicate it, leave it blank. If you choose yes, you must fill in the field that will be enabled:

**Outcome of rechallenge**: Choose between:

- The reaction recurred: It corresponds to a positive rechallenge.
- The reaction did not recur: It corresponds to a negative rechallenge.
- Outcome unknown
- Not applicable

Since Industry e-reporting requests re-exposure/rechallenge information for both concomitant and suspected medications and the National Center is only interested in rechallenge for suspected medications, leave the re-exposure fields for concomitant medications empty.

#### 3.8.2.5.2 Time interval from administration and start of reaction:

The interval between drug administration and the onset of the reaction/event.

- **Time from the first dose and the start of the reaction**: Enter the value and select the unit of time from the drop-down list.
- **Time from the last dose and the start of the reaction**: Enter the value and select the unit of time from the dropdown list.

### 3.8.2.6 Others

#### 3.8.2.6.1.1 Test results

**Test Name:** Enter the name of the test performed as reported here.

**Test Name (MedDRA):** Enter the appropriate MedDRA term for the test performed.

**Test date:** If you do not have the complete date, you can enter only one field (year) or two fields (month and year).

**Test result:** Enter the value and choose the unit of measure from the drop-down list. You can use the symbols =, >, <, ≥, or ≤ which you will find in the drop-down list located to the left of the free text.

**Test Result Code:** This element allows a descriptive element to indicate the result of the analysis that you can select from a drop-down list:

- Positive
- Negative
- Borderline
- Inconclusive

**Test result (in text):** if you were not able to put the test result in the structured field because you did not find the unit of measure in the drop-down list, put the result in this free text field expressing the unit of measure. If you used the *Test Result field,* leave it blank.

**Normal low Value:** In this field, you must enter the "*lower value*" in the normal range for the test, which is usually published by the laboratory that provided the result.

**Normal high Value:** In this field, you must enter the "*highest value*" in the normal range for the test, which is usually published by the laboratory that provided the result.

**Comments:** If you have additional information about the test performed that is not included in the structured fields, please place it in this free text field.

**To add more laboratory tests, choose the option "*Add test result*" (Add laboratory results).**

### 3.8.2.6.1.2 Drug History

**Name of the drug as reported:** You must enter the brand name if you have it and the generic name in parentheses.

**Medicinal product (WHODrug):** Search the available database and check and check for the available brand name. If not available enter the generic name in WHODrug

**Indication (MedDRA):** Enter the MedDRA term (Level LLT) of the therapeutic indication for which the drug is being given.

**Reaction (MedDRA):** Fill in the corresponding MedDRA term (Level LLT).

**Start date:** If you do not have the complete date, you can enter only one field (year) or two fields (month and year).

**End date:** If you do not have the complete date, you can enter only one field (year) or two fields (month and year).

To add more drugs from the previous medical treatment, choose the option ***"Add drug history"***

### 3.8.2.6.1.3 Medical History

**Any relevant medical history reported?** Select **Yes** or **No** as appropriate, if you check the **Yes option**, the following fields will be displayed:

**a) Patient Medical History**

**Relevant medical history and concurrent conditions (not including reaction/event) in free text:** corresponds to relevant information (that helps causal evaluation) of the clinical history and concomitant conditions (diseases, conditions such as pregnancy, surgeries, psychological trauma, factors of risk, among others) of the patient. If you do not have information about the patient's medical history, leave it blank.

**b) Structured information on relevant medical history:**

**Medical history (disease/surgical procedure/etc.)** Enter the MedDRA term(s) (Level LLT) of the relevant conditions in question. If you do not have information about the patient's medical history, leave it blank.

**Medical Doctor's comments:** Correspond to information provided by the doctor about the case. If you do not have information, leave it blank.

**Start date:** If you do not have the complete date, you can enter only one field (year) or two fields (month and year).

**Continuing?** Indicate yes or no as appropriate in relation to whether or not the condition in question still persists/is ongoing at the time of this report.

**End date:** If you do not have the complete date, you can enter only one field (year) or two fields (month and year).

**Family History:** If checked, then details about the family history should be provided in the case narrative field mentioned above.

**c) To add any other relevant clinical history, you can click on the "+" icon.**

### 3.8.2.7 Assessment

**Method of assessment:** Place in the free text field the name of the methodology used.

**Source of assessment:** Corresponds to the identity that performs the evaluation. In the first instance, the evaluation of the **UFV** must be placed, but you can also add the evaluation of the primary reporter (informant) if you have it.

**Result of assessment:** Place in the free text field the evaluation result for each reaction/event according to the methodology that was used. In order to place the result, it is necessary that at least one suspected drug or two interacting drugs have been entered into the report.

To add more causality assessments, choose the option *"**Add causality assessment**"*. If you have an assessment, for example, from the reporting physician, you can add it; place the Primary reporter in *"Assessment Source"*.

### 3.8.2.8 Case summaries

**a) Narrative case summary and other information**

**Case narrative:** You must place the narrative of the case with the words and phrases used by the primary source (as notified by it), maintaining the original narrative. Quote the clinical manifestations. Indicate the certain and/or presumptive clinical diagnosis that

motivated the medication and subsequently the signs and symptoms of the adverse reaction. If a hitherto unknown therapeutic effect is detected, it can be indicated in this space. In the case of congenital malformations, specify the moment of pregnancy when the impact occurred.

In this field, you must also enter the medications to treat the reaction/adverse event.

If you report another safety problem related to the use of medicines and vaccines, you must describe what the problem is (overdose, suspected counterfeiting, misuse, abuse, medication error, off-label use, occupational exposure, among others).

When you enter trace information in this field (*View Edit Report*), place it below the initial or previous trace information, separating it as follows:

Follow-up 1, 2, 3, 4, etc., Information received on the day...

**---------- ----------(with a dotted line)**

If the case is considered closed or will require follow-up, you must also specify it in this field.

Since this field has a limit of 20 thousand characters, there is a possibility that for some very long narrative cases, this field is insufficient. You can use the *native language case summary and reporter comments field* to continue with the case text.

**Reporter comments**. In this field, you can add additional comments provided by the primary source if you have them.

**Company diagnosis:** You can add company diagnosis from the MedDRA term.

**Company's comments:** Additional comments that the notifying Pharmacovigilance unit can provide or

**Case summary and reporter's comments in native language**: Do not use, or leave blank, unless the narrative case is longer than 20,000 characters and the *Narrative Case field* is insufficient.

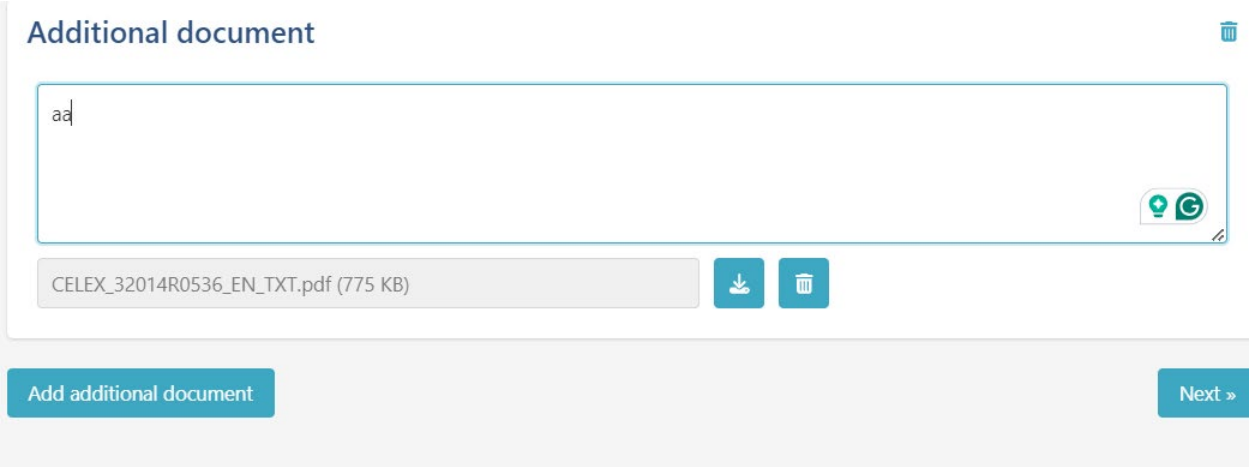
### 3.8.2.9 Additional documents

This section will allow you to upload documents relevant to the causality assessment of the case. Some examples can be (but are not limited to these):

- Test results
- Death certificate
- Vaccination certificate

Place the name of the document in the free text field and upload the file in PDF format, either by dragging and dropping it into the grey section or by opening it from your file explorer with the “Browse” option.

If you need to attach more documents, you can do so with the ***"Add additional document"*** *option.*

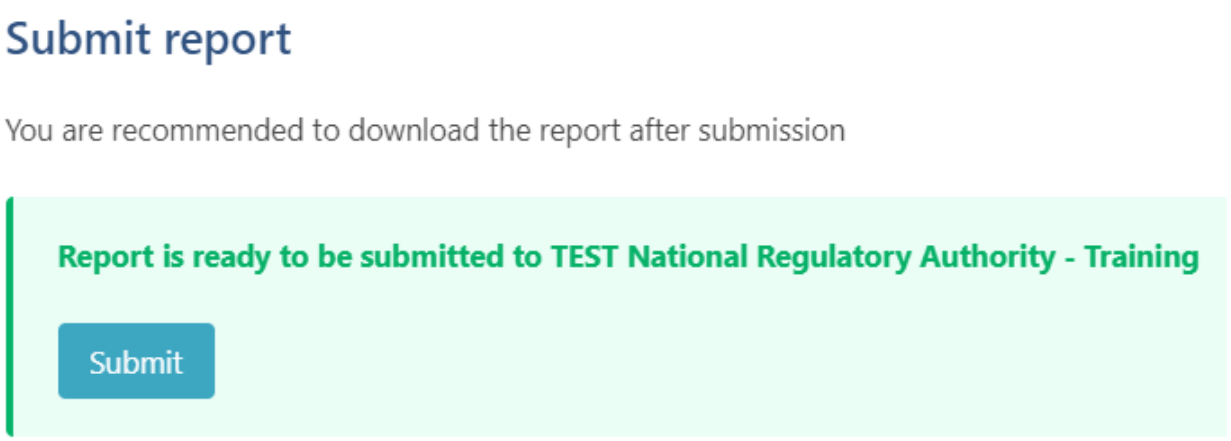



**IMPORTANT**
It is necessary that the documents you need to attach are in PDF format and do not exceed 2 MB to be able to load them without problems.

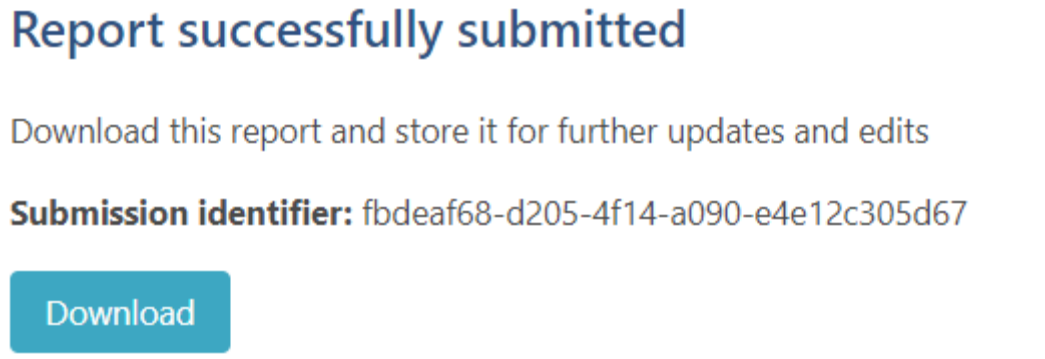
### 3.8.2.10 Submit Report

In order to send the report, it is necessary that you have captured the minimum information required by the system. If you have not done so, this section will list the missing or wrong information, which you will need to include or review. The missing information in the different sections that make up the report will also be presented in red.

**IMPORTANT**
If the notification does not meet at least the 4 fundamental criteria (information quality grade 0) it should not be sent. You must do a search for missing information to be able to report the case.




When you have the information for your report ready, click *"Submit"*




### 3.8.2.11 Download Report

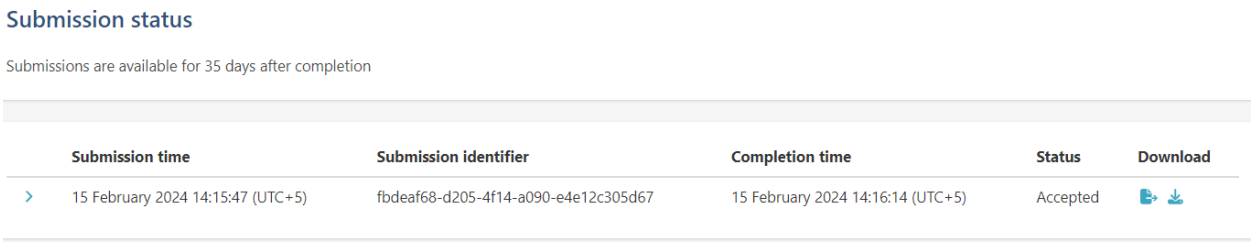
It is absolutely necessary to ***immediately download*** the report once you have submitted it, as this will be the only way to get this case's XML file and track it. The information generated during the capture of the report will be downloaded in an XML file.

**IMPORTANT**
If you do not download the report file in this part of the process, it will NOT be possible to download it later.

Clicking ***Download*** will download the XML file. It is important that you keep this file on your backup, as you will need to use it if you need to follow up on the case. See "***Edit Report***". By default, the system will name the file with the Worldwide unique case identification.

Additionally, Industry e-Reporting provides confirmation receipts known as acknowledgement logs (acklog) of the captured reports, which will only be available for 35 days after the notification is sent. You can find and download them in the *"**Submission status**"* section on the upper right menu. If your Pharmacovigilance database allows you to run these electronic confirmation receipts, they will work as such for your database.

It is very important to differentiate the XML file from the report that is downloaded after sending and this is essential for subsequent follow-ups, to the acknowledgements of receipt (acklog). The latter are not designed for tracking loading.

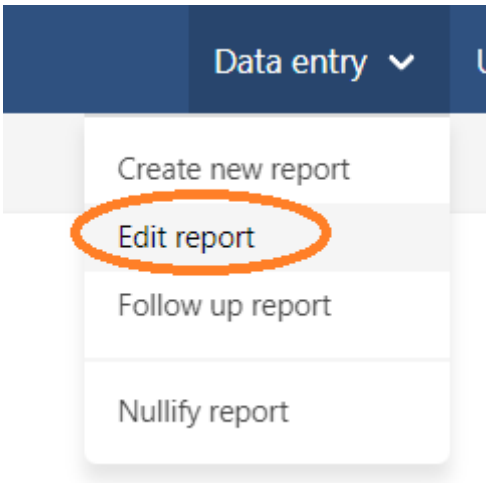



You can open the acklog in Chrome or another browser, and identify the end time and send time of your report. You will notice that for the value "creation Time value" is established in UTC time (coordinated universal time) so, for purposes of compliance with notification times, you must consider the difference in hours in relation to Pakistan time.

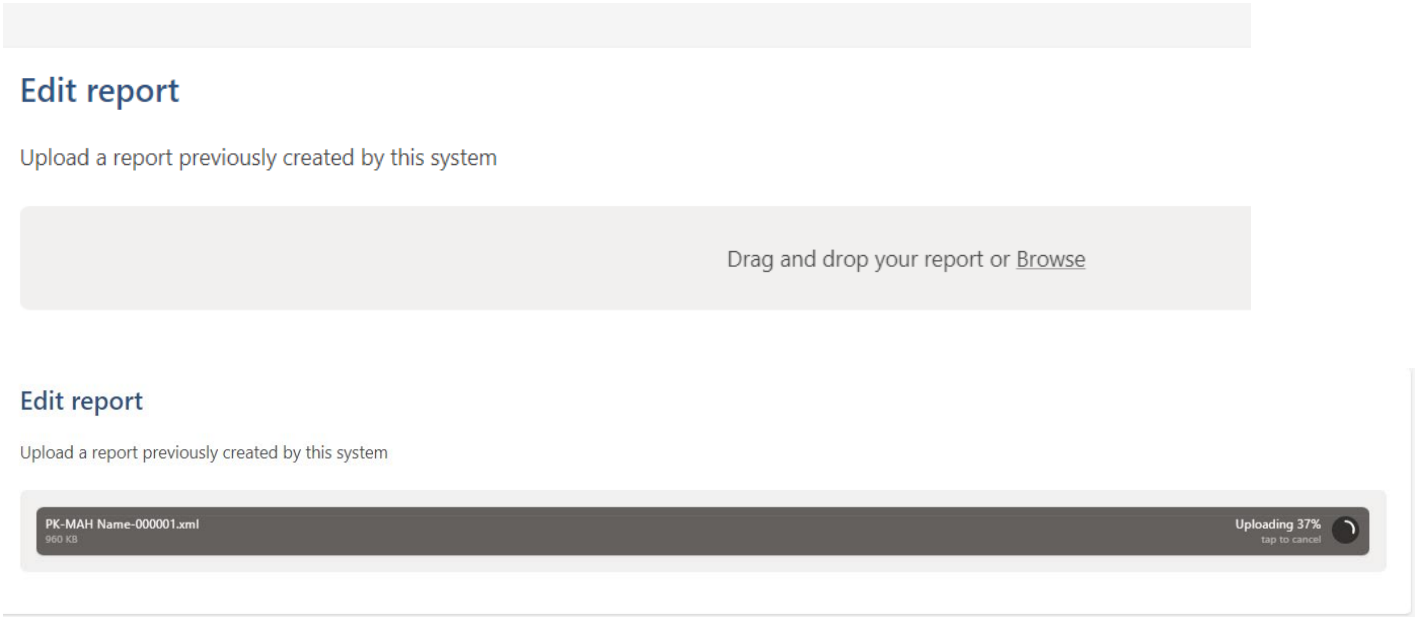

## 3.8.3 Edit Report

This option allows you to upload a report (E2B XML file) created in this system, to edit information from an initial report not yet sent to the regulatory authority.

Choose the " ***Edit report*** " option from the top menu.




Upload the XML file generated in the initial submission, which you should have saved on your computer, either by dragging and dropping it into the grey section or by opening it from your file explorer with the "**Browse**" *option.*



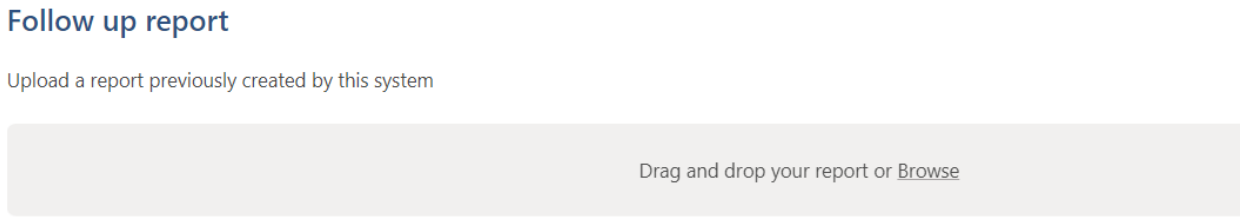

Wait for the report to load. The report will open immediately with all the sections that make it up, enabled for editing.

### 3.8.4 Follow-up report

This option allows you to upload a report (E2B XML file) created in this system to enter follow-up information, that is when new information has been obtained after the initial case report has already been sent to the regulatory authority (DRAP).

**Remember**: A follow-up report is one in which important information is added or completed for the causality evaluation of the case. For example, if you have (it is not limited to):

- Reaction start and end dates
- Medication administration dates
- Addition of concomitant medications
- Addition of comorbidities
- Addition of laboratory results




Upload the XML file generated in the initial submission or previous follow-up, which you should have saved on your computer, either by dragging and dropping it into the grey section or by opening it from your file explorer with the "**Browse**" *option.*


Wait for the report to load. The report will open immediately with all the sections that make it up, enabled for editing.

Add the new information or respective modifications of the tracking in the corresponding fields, among them, it is essential to update the *most recent information Date* that corresponds to the date when you received the tracking in your Pharmacovigilance unit. It is important that in the follow-up, in addition to adding the new information in the specific fields, you also update the case narrative with the new information. To separate the information from the initial or previous follow-

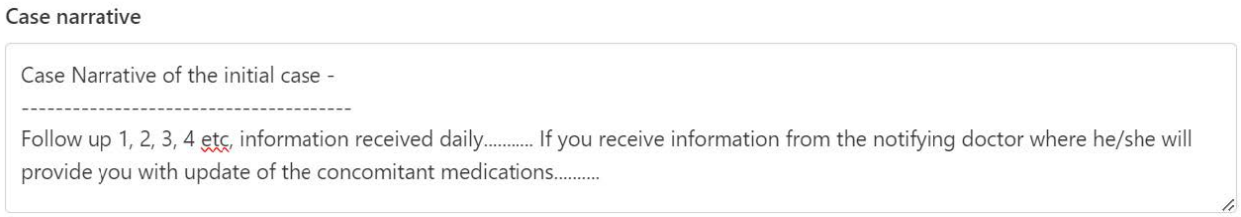
ups, use a line and place the new information below, adding the text: Follow-up 1, Follow-up 2, as appropriate.

**IMPORTANT**
For tracking purposes, the file corresponding to the acknowledgement (acklog) available in the Send Status window should NOT be used for this purpose.

## 3.8.5 Narrative Case

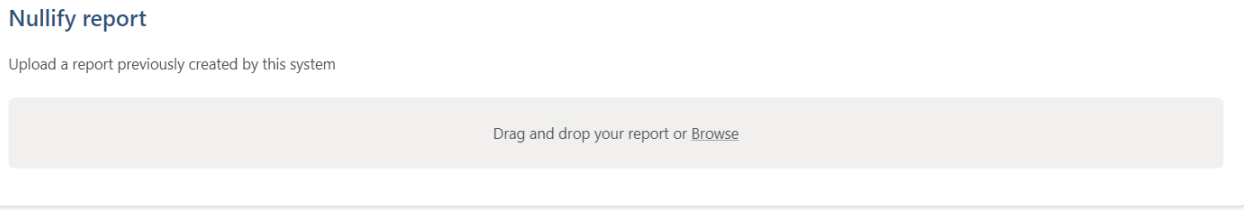
Once you have finished capturing the tracking information, you must submit the report and download the corresponding XML file. Remember that if you don't download the file, you won't be able to track it later.

Remember that the acklog file should not be used in this activity as the file is not designed for tracking.



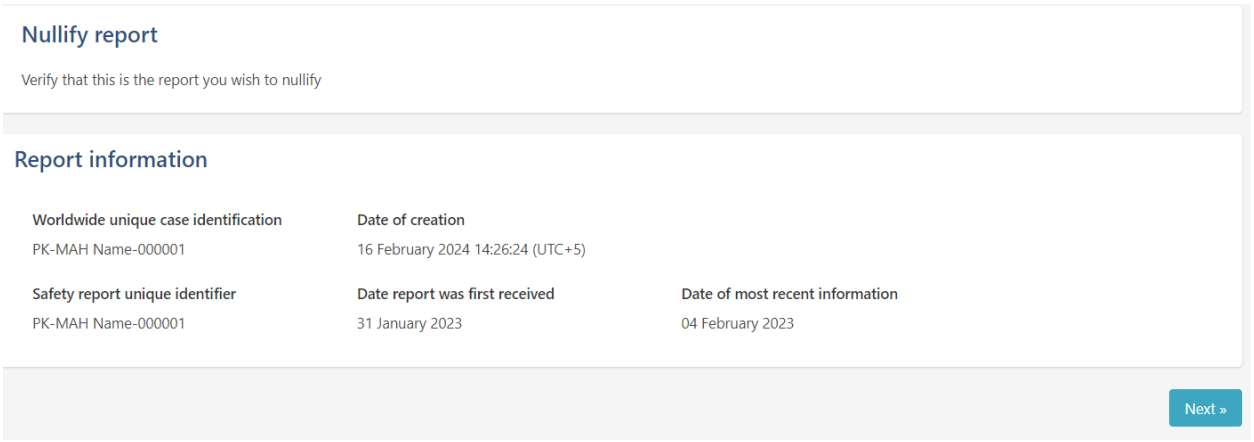

## 3.8.6 Nullify Report

This option allows you to permanently override a (previously transmitted) case. For example, when the entire report was wrong or in case of duplicate reports.

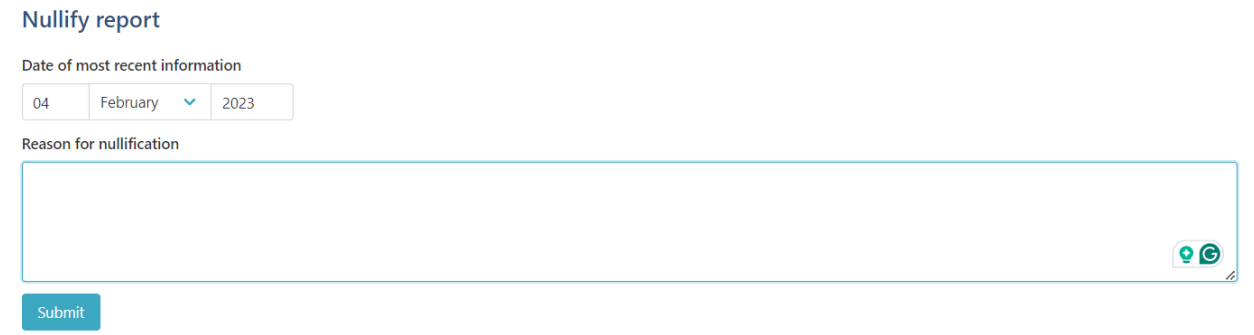



Load the generated XML file you want to override, which you should have saved on your computer, either by dragging and dropping it into the grey section or by opening it from your file explorer with the “Browse” *option.*

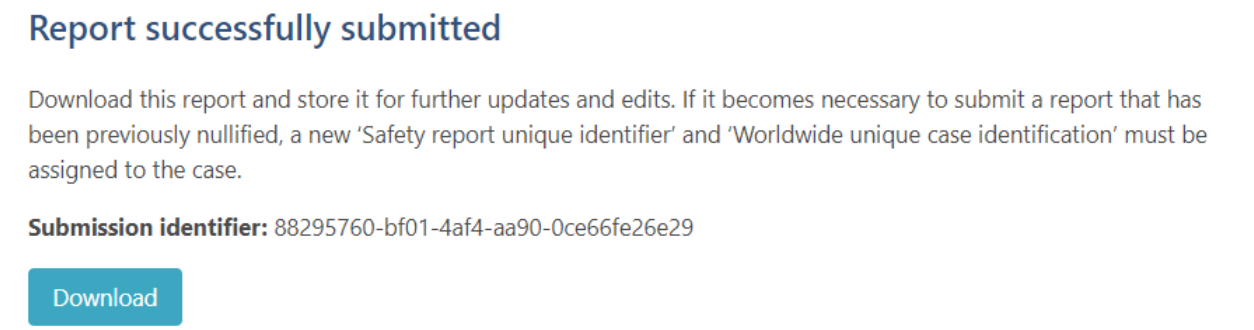

Verify the information of the report you want to cancel




In case everything is correct in the report that you want to cancel, press the *Next button*




A reason for deletion must be entered. Then press the *Send button*

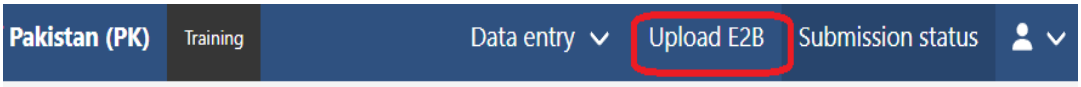


Download the deleted report XML file and save it to your computer for future updates.

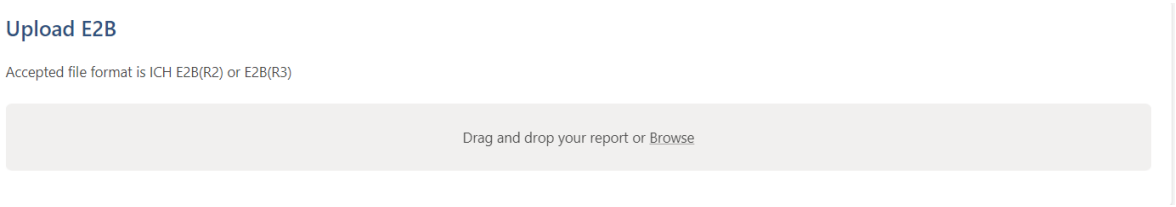
## 3.9 MODULE II: E2B UPLOAD MODULE

This module is exclusive for use by those registration holders who already have a database that can transmit E2Bxml files as per ICH guidelines.

1. In the upper right menu, choose the option *"Load E2B"*



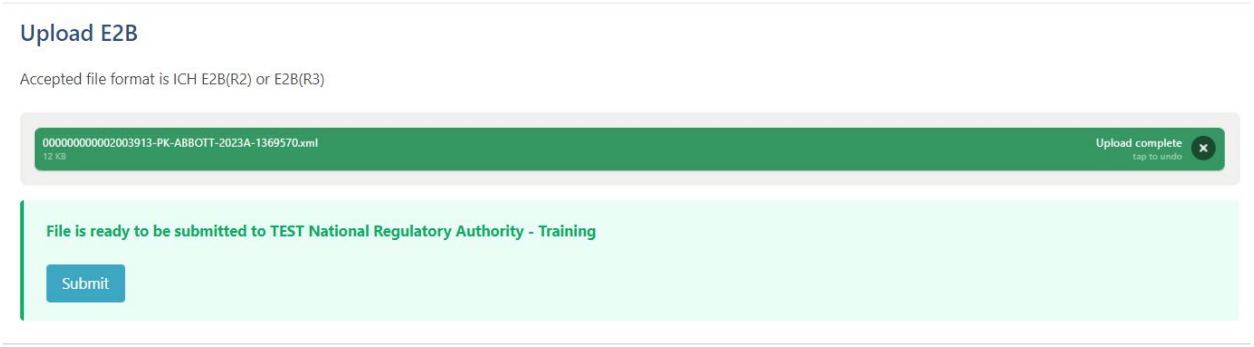

2. Once inside, you will find the following screen:




3. Files should be uploaded individually. Drag the XML file to the grey box or click "Browse" to open your file explorer.

Once you drag or select the XML-E2B file it will start to load as shown below:

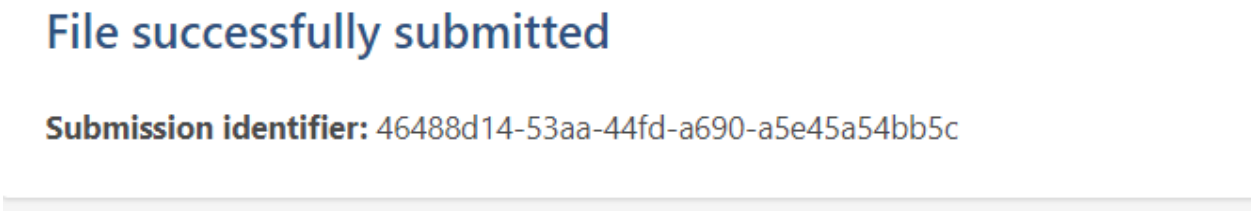

If the file meets the ICH R2 or R3 format specifications, it will be uploaded successfully as shown below:




4. Click on "*Send*"

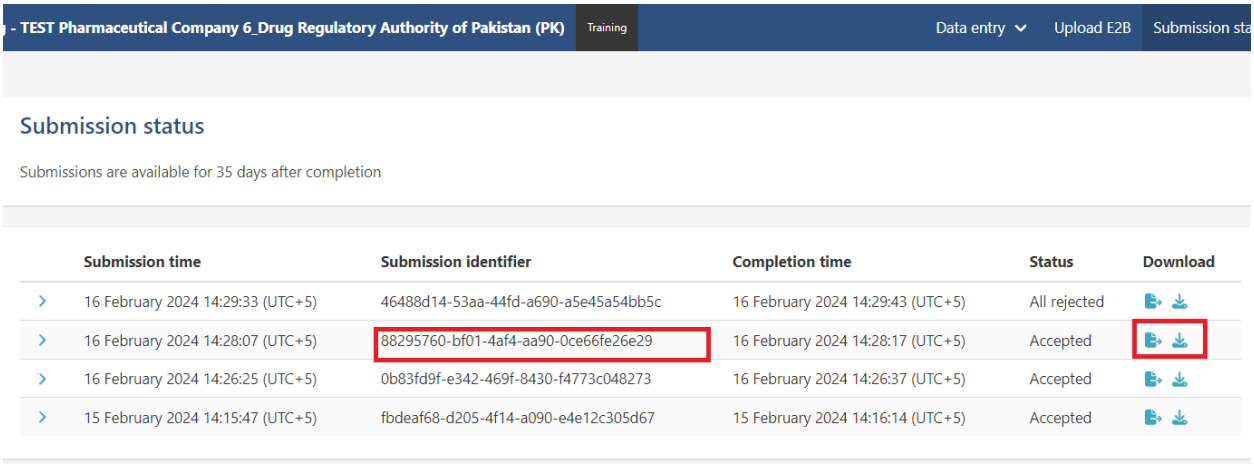
**IMPORTANT**

It is essential that you download the acklog as soon as possible once the XML has been loaded since the system will only be able to save the history of the previous 35 days. Once this limit is passed, you will no longer be able to download the acklog. It is the issuer's responsibility to have a backup of the generated 'acklogs', since the NPC will not be able to generate 'acklogs' again once they are removed from the history.




Note the Submission identifier.

5. In the upper right menu click on "*Submission Status"* to download the acklog.




Identify the report you uploaded via *submission identifier.* Click on the icon to download the corresponding acklog.

6. Upload the acklog to your system to verify the successful import.

It is important to log out when not using the platform. To do this, go to the top menu on the icon , and select " *Log out* "

**IMPORTANT (WHAT TO DO IN CASE OF PARTIAL UPLOAD OR FAILED REPORTS)**

In some cases, if the information provided by company through proforma and the data in E2B xml files is not the same, then the system will reject the E2B xml files and the upload status will be "failed". Likewise, if E2B xml file contain more than ICSRs and some of these ICSRs do not have the matching information, then these be will be rejected and other files having accurate information will be uploaded and the status will be "partial upload"

Therefore, whenever, the registration holders face this sort of problem they need to download the files and look for the errors in the relent fields that need correction. The field should be identified, discussed with NPC-DRAP and accordingly corrected for smooth upload of E2Bxml files.

# ANNEX A: TERMS AND CONDITIONS FOR THE USE OF INDUSTRY E-REPORTING SYSTEM.

**Description**

***Industry E-Reporting*** is a platform developed by the Uppsala Monitoring Center (UMC) specifically for the registration holder to report to the NPC-DRAP, Individual Case Safety Reports (ICSRs) or reports of Adverse Drug Reactions (ADR), Adverse Events (AE), Adverse Event Following Immunization (AEFI), and any safety problem related to the use of medicines and vaccines through a standardized platform designed for the best collection of information. E-Reporting for the Industry is linked to VigiFlow, which is the tool used to manage Adverse Drug reaction reports throughout the country. Being a member of the World Health Organization Programme for International Drug Monitoring (WHO-PIDM), the National Pharmacovigilance Centre (NPC), DRAP operates the VigiFlow database at the National level for the management of reports of ADRs.

**Declarations:**

DRAP declares that:

I. In line with the provisions of extant applicable regulations, the National Pharmacovigilance Centre is in-charge of issuing the policies and guidelines for the operation of Pharmacovigilance in the national territory, among which are:

> To establish and disseminate requirements and guidelines for Pharmacovigilance activities- for the reporting of AEs, ADRs, AEFIs and any other safety problems related to the use of medicines and vaccines; including electronic tools for reporting, their operation and considerations for their use as well as guidelines for implementation.

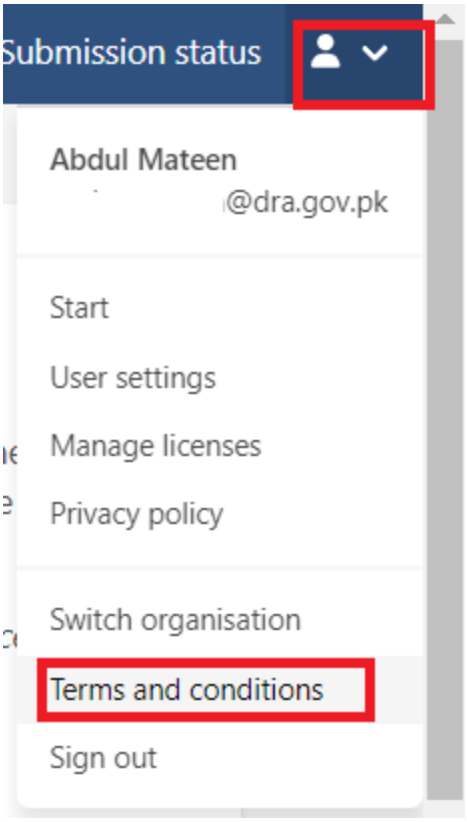
**The User declares that:**

I. As a user of e-Reporting for the Industry, you certify that you belong to a pharmaceutical company or a representative of a registration holder in Pakistan.

II. You are aware of the content and obligations that arise from this letter of terms and conditions of use of e- Reporting for the Industry, and therefore you are obliged in terms of this, to comply with the following rules of access and use.

III. You agree that NPC and the Uppsala Monitoring Center (UMC) will withdraw your access if you violate any of the following rules for access and use of Industry e- Reporting.

For more information, visit the section *Terms and Conditions* located in the main menu



# ANNEX B: GLOSSARY OF TERMS

- **Active surveillance:** Is a process that involves, enhanced or targeted monitoring for certain events or therapeutic goods and seeks to ascertain completely the number of adverse events or adverse drug reactions through a continuous pre-planned process.
- **Adverse Reaction (ADR):** Means response to drug or therapeutic goods which is noxious and unintended and occurs at doses normally used for the prophylaxis, diagnosis or therapy of disease or for the restoration, correction or modification of physiological function. A response in this context means that a causal relationship between a therapeutic good and an adverse event is at least a reasonable possibility. An adverse reaction, in contrast to an adverse event, is characterized by the fact that a causal relationship between a therapeutic good and an occurrence is suspected.
- **Adverse Event (AE):** Means any untoward medical occurrence in a patient or clinical investigation subject, on the administration of a drug or therapeutic good and which does not necessarily have a causal relationship with this treatment.
- **Adverse Event Following Immunization (AEFI):** Means any untoward medical occurrence which follows immunization and which does not necessarily have a causal relationship with the usage of the vaccine.
- **Causality Assessment**: Means the evaluation of the likelihood that medicine or therapeutic good was the causative agent of an observed adverse reaction.
- **CRH**: "**Registration holder**": The company or legal entity in whose name the registration for a therapeutic good has been granted and is responsible for all aspects of the therapeutic goods and compliance with the conditions of registration
- **DRAP:** The Drug Regulatory Authority of Pakistan established under the DRAP Act, 2012 for effective coordination and enforcement of the Drugs Act, 1976 (XXXI of 1976) and to bring harmony in inter-provincial trade and commerce of therapeutic goods and to regulate, manufacture, import, export, storage, distribution and sale of therapeutic goods.
- **Drug:** Substance defined as Drug as defined under Schedule 1 of the DRAP Act, 2012.

- **E2B**: standardized electronic transmission of individual case safety reports (ICSRs) as per ICH E2B guidelines.
- **Healthcare Professionals:** means any member of the medical, dental, pharmacy, nursing professions, any allied health professional or any other person who in the course of his professional activities may prescribe, recommend, purchase, supply, sell or administer a therapeutic good including medical technologies as registered or enlisted by the Authority.
- **International Council on Harmonization (ICH):** The International Council for Harmonisation of Technical Requirements for Pharmaceuticals for Human Use (ICH) is unique in bringing together the regulatory authorities and pharmaceutical industry to discuss scientific and technical aspects of pharmaceuticals and develop ICH guidelines.
- **Individual Case Safety Report (ICSR):** A report describing a suspected adverse drug reaction related to the administration of one or more medicinal products or therapeutic goods to an individual patient.
- **Marketing Authorization Holder (MAH):** "***Registration Holder***" The holder (an individual, institute, manufacturer, company, importer, distributor, development partner/donor agency, etc.) of a marketing authorization to market a medicinal product. For the purpose of this policy document, the MAHs will have full responsibility and liability for their product on the market and full responsibility for ensuring that appropriate action can be taken when necessary.
- **Medication Errors:** Means any preventable event that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of the healthcare professional, patient or consumer.
- **National Pharmacovigilance System (NPS):** The nationwide therapeutic goods safety system, coordinated by the DRAP to improve benefits and reduce harm related to the use of medicines and therapeutic goods through the efficient mobilization of various stakeholders and resources at all levels and in all sectors.
- **National Pharmacovigilance Centre (NPC):** The National centre working under the Division of Pharmacy Services, DRAP and established under Rule 3 of Pharmacovigilance Rules, 2022.

- **National Pharmacovigilance System File (NPVSF):** Describes the key elements of pharmacovigilance activities of multinational registration holders in Pakistan including details of an LSO.
- **Passive Pharmacovigilance:** A process where healthcare professionals or patients send spontaneous reports describing an adverse drug reaction or event after one or more therapeutic goods are administered to the registration holders or regulatory authority.
- **Periodic Benefit-Risk Evaluation Report** (PBRER)/PUSR: Document which presents a comprehensive, concise, and critical analysis of new or emerging information on the risks of the drugs or therapeutic goods, and on its benefit in approved indications, to enable an appraisal of the product's overall benefit-risk profile. This document is submitted to the regulatory authority after the registration of the drug as per the periodicity and timeline defined in the rules.
- **Pharmacovigilance**: Means the science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other therapeutic good-related problems.
- **Pharmacovigilance System:** Means a system used by the registration holder to fulfil the tasks and responsibilities listed in pharmacovigilance rules and is designed to monitor the safety of therapeutic goods and detect any change to their risk-benefit balance.
- **Pharmacovigilance System Master File (PSMF):** The PSMF describe the pharmacovigilance system of the registration holder and supports/documents its compliance with the requirements as laid down in pharmacovigilance rules and guidelines, and also contributes to the appropriate planning and conduct of audits by the registration holder, the fulfilment of supervisory responsibilities of the QPPV, and inspections or other verification of compliance by NPC and DRAP.
- **Qualified Person for Pharmacovigilance (QPPV)/Local Safety Officer (LSO):** A qualified person for pharmacovigilance (QPPV) is a person having such experience and qualification as defined by DRAP, who shall be responsible for pharmacovigilance system and shall reside and operate in the country, and shall also be responsible for establishment and maintenance of the pharmacovigilance system. In the case of a multinational

registration holder, the nomination of a local safety officer (LSO) will be accepted, who shall reside and operate in the country. However, in the case of a local registration holder, there should be a dedicated QPPV who should reside and operate in Pakistan.

- **Reporter:** Any person who report a suspected adverse drug reaction to the relevant regulatory or competent authority (NPC-DRAP.).
- **Registration Holder:** Means manufacturer or importer possessing registration or enlistment of therapeutic goods, as the case may be as per Pharmacovigilance Rules, 2022.
- **Serious Adverse Event or Reaction**: means an untoward medical occurrence that at any dose results in patient death, is life-threatening, requires inpatient hospitalization or results in prolongation of existing hospitalization, results in persistent or significant disability or incapacity, is a congenital anomaly or birth defect or is judged to be a medically important event or reaction.
- **Signal:** means reported information on a possible causal relationship between an adverse event and a drug or a therapeutic good, the relationship being unknown or incompletely documented previously. Usually, more than a single report is required to generate a signal, depending upon the seriousness of the event and the quality of the information. The publication of a signal usually implies the need for some kind of review or action.
- **Spontaneous Reporting**: A system whereby case reports of adverse drug events are voluntarily submitted from health professionals and registration holders to the National regulatory authority; or unsolicited communication by a healthcare professional or consumer to a company, regulatory authority or other organization such as World Health Organization, and poison control centre that describes one or more adverse drug reactions in a patient who was given one or more therapeutic goods and that does not derive from a study or any organized data collection scheme.
- **Therapeutic Goods:** Includes drugs or alternative medicine or medical devices or biologicals or other related products as may be notified by DRAP. Further explanation of each class of therapeutic goods is given in Schedule II of the DRAP Act, 2012.

# ANNEX C: CAUSALITY ASSESSMENT

**WHO-UMC system for standardised case causality assessment**

| *Causality term* | *Assessment criteria** |
|---|---|
| **Certain** | • Event or laboratory test abnormality, with plausible time relationship to drug intake<br>• Cannot be explained by disease or other drugs<br>• Response to withdrawal plausible (pharmacologically, pathologically)<br>• Event definitive pharmacologically or phenomenologically (i.e. an objective and specific medical disorder or a recognised pharmacological phenomenon)<br>• Rechallenge satisfactory, if necessary |
| **Probable / Likely** | • Event or laboratory test abnormality, with reasonable time relationship to drug intake<br>• Unlikely to be attributed to disease or other drugs<br>• Response to withdrawal clinically reasonable<br>• Rechallenge not required |
| **Possible** | • Event or laboratory test abnormality, with reasonable time relationship to drug intake<br>• Could also be explained by disease or other drugs<br>• Information on drug withdrawal may be lacking or unclear |
| **Unlikely** | • Event or laboratory test abnormality, with a time to drug intake that makes a relationship improbable (but not impossible)<br>• Disease or other drugs provide plausible explanations |
| **Conditional / Unclassified** | • Event or laboratory test abnormality<br>• More data for proper assessment needed, or<br>• Additional data under examination |
| **Unassessable / Unclassifiable** | • Report suggesting an adverse reaction<br>• Cannot be judged because information is insufficient or contradictory<br>• Data cannot be supplemented or verified |

* All points should be reasonably complied with

# ANNEX D: FREQUENTLY ASKED QUESTIONS

**Can I report a case that occurred outside of Pakistan on the e-reporting for industry?**

No, the tool is aimed at reporting Adverse Drug Reactions that occur in the country i.e. Domestic cases.

**What reports are subject to reporting? Spontaneous reports / Literature /Post Authorization Safety Studies, Risk management plans.**

Reports from post- authorization safety studies, spontaneous reports and literature reports.

**What are the minimum criteria for reporting?**

For a report to be considered valid, it is necessary to have at least the following information: an identifiable reporter, an identifiable patient, one or more suspected drugs/medications/vaccine, and one or more adverse reactions. For more information consult the ICH guidelines.

**Can I submit a case that does not meet the 4 minimum criteria?**

**No**, additionally the system will indicate the minimum mandatory fields (according to the ICH-E2B standard) to be able to send a case to NPC-DRAP.

**How many users will be provided per Pharmaceutical company (registration holder), should the password be unique per user or is it necessary to create a password for each user?**

At the moment, two (02) users will be granted to each registration holder, either for the manual upload module or for the XML upload module. Each user must generate their own password.

**What should be done in the event of a Pharmacovigilance (PV) contract company that is a representative of more than one registration holder/MAH/CRH?**

In this case, the contract pharmacovigilance company must notify DRAP of the information of each of the companies they represent, taking into account the company name and identifiers. It must be noted that this is different from when an MAH/CRH/registration holder buys the license of some products of another MAH/CRH/registration holder, for example:

**Case 1**

PV Company **A** represents the Pharmacovigilance activities of MAH B products.

In this case, the identifiers required in the system (company name, short name, sender identifier and sender Organization) must be those corresponding to the owner of the products, that is, MAH B and would be registered in the system as follows:

**Short name MAH B (Short name Company A)**, this means that the report corresponds to a product from MAH B, made by PV company A, who oversees carrying out Pharmacovigilance for MAH B.

**Case 2**

MAH A **bought the License** of some products of MAH B.

In this case, the owner of the product is MAH A, and the identifiers required in the system (company name, short name, sender identifier and sender Organization) must be those corresponding to the owner of the products, that is, MAH A, and would be registered in the system as follows:

**MAH A (Short name of MAH A):** this means that it corresponds to a report of a product from MAH A.

**Case 3**

MAH B sold the license of some of its products to MAH A, but MAH B still owns other products and carries out their pharmacovigilance.

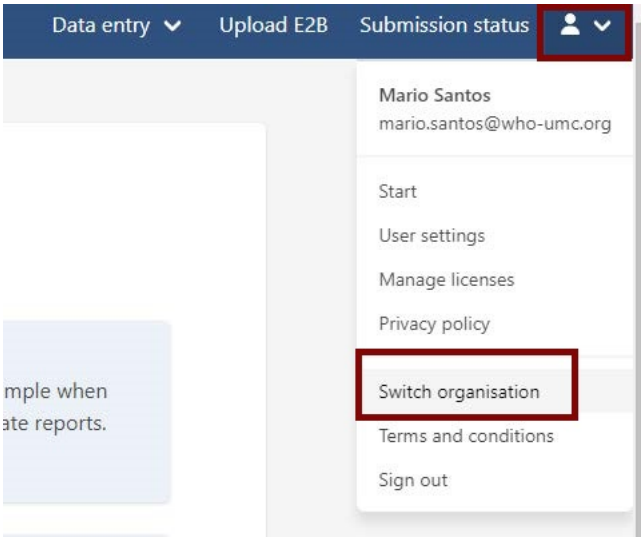
In this case, the owner of the product is MAH B, and the identifiers required in the system (company name, short name, sender identifier and sender Organization) must be those corresponding to the owner of the products, that is, MAH B, and would be registered in the system as follows:

Short name of MAH B: this means that it corresponds to a report of a product from Laboratory B.

**Can we supply the same email for different business reasons?**

This situation will only be valid in the event that your company represents more than one MAH/CRH/Registration holder (in pharmacovigilance activities). In this way, with the email

indicated when entering the tool, you will be able to choose which company the report you are making belongs to.




**What should be done in the event of a follow-up of reports submitted prior to the implementation of this module?**

If a report was initially reported via email or through an existing procedure, you will need to submit follow-ups until it is closed via email/existing procedure.

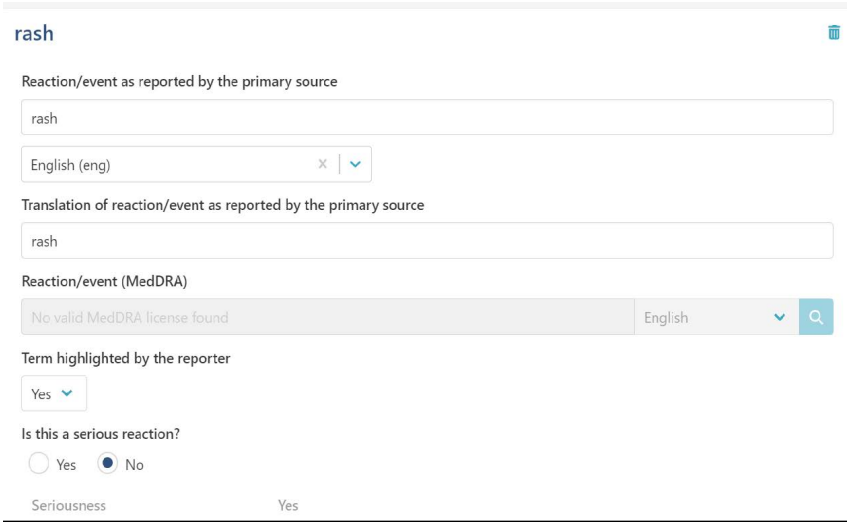
**Is it possible for two users to report simultaneously (if there is more than 01 user)?**

**Yes**. The two accounts that are granted per MAH are independent and the cases can be entered into the manual data entry module or uploaded into the XML upload module simultaneously. However, an account cannot be used simultaneously by more than two people.

**Is the adverse event reported literally/colloquially and also in MedDRA?**

Yes, in the reaction/event as reported by the primary source field, the term is placed literally, as indicated by the primary source. The MedDRA term (Level LLT) is used in the Reaction/Event structured field.

The assessor should always code the reaction term provided by the primary source to the corresponding MedDRA term.




To Code the Reaction *Rash*. Click on the drop down and choose the LLT for Rash.

**Is it necessary for each MAH to have a MedDRA license?**

Yes, it is essential that those registration holders **who intend** to code have a current MedDRA license. As of now not mandatory for all; but, it will be made mandatory in the future.

**Is there an option on the platform to save the case and finish it later?**

No. If you leave a case entry incomplete and you log out without submitting and downloading it, you will not be able to retrieve the information later and will need to enter it again.

You are required to enter the case in its entirety, submit and download the file, and acknowledge receipt (acklog) before logging out.

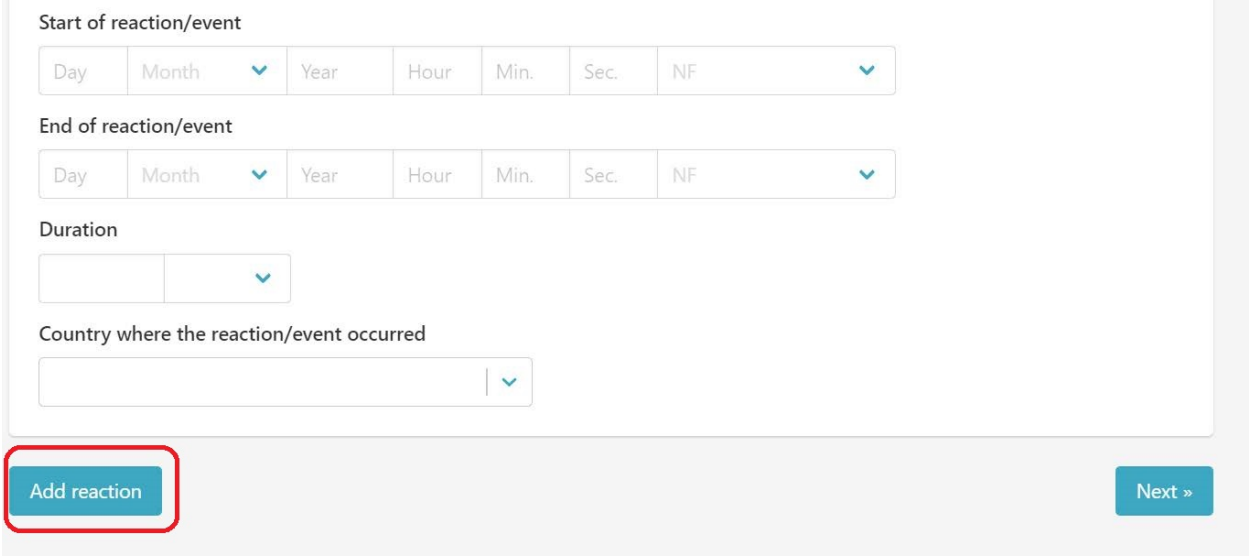
**Will there be a time limit for uploading a case? How long can the session be kept active?**

No, there is no time limit as long as you are constantly entering information in short periods. But if the page remains open without activity for long periods, after a while the session will be closed for security.

It is requested to keep the session active only if you are entering the information, otherwise you must close it.

**Should a report be made for each suspected drug?**

No. An individual case report may contain one or more suspected drugs, as well as one or more AEs, ADRs, AEFI.




**Where do you get the WWUID (Worldwide unique case identification)?**

The constant part is made up of the Country ISO code **(PK)** and the Short Name of the company. The variable part consists of a consecutive number of at least 5 digits which must be unique for each case.

**What is the difference between the Safety Report Unique Identifier and the Worldwide Unique Case identification?**

The WWUID is the first identifier assigned to the report. The unique identifier of the safety report and the identification number that can be assigned to a case following the same format as the WWUID in case it is needed. For the moment, for the manual data entry module, it will be requested that the WWUID and the Safety Report ID are the same for a report.

**Is it possible to go back between sections to edit information in case of having made a mistake in the entry?**

It is possible. Navigating between sections is not limited to providing all the required information in one section to move on to the next.

**Is it possible to save the information to continue with the report or should it be done in the same session?**

The entry of a report must be done in one session. The system does not save the report until you submit it.

**In the case of reports from literature, is it a requirement to attach the reference publication?**

It is not a required field, but it is suggested to attach it if you have it.

**In the case narrative section in all three sections, how many characters can be entered?**

The capacity of the Narrative Case field is 20 thousand characters (considering spaces). If your report has a case narrative that exceeds this limit, place the rest of the text in the Case Summary and Reporter Comments field in English language.

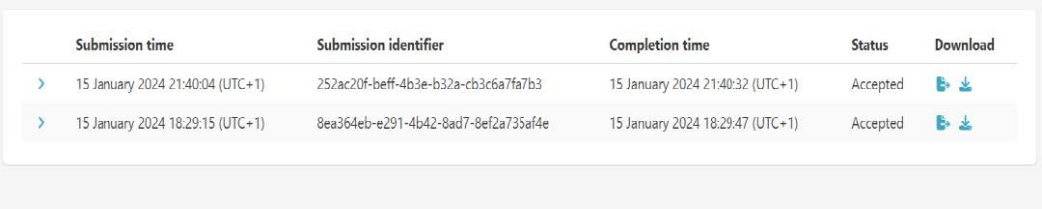
**Should the causality of each of the reported PTs be included, regardless of whether it is a suspect or concomitant?**

The causality assessment must be carried out for each AE/ADR/AEFI, and it is only applicable for the suspected drug(s)/vaccine(s)

**How can you review previously uploaded cases and within the time before they are deleted?**

Previously uploaded cases, speaking of all the information entered in them, are not available in Industry E-Reporting platform. What will be available will be the acklog (from the last 35 days) in the *Submission Status tab* of the upper right menu.

The Industry e- reporting platform does not work as a database of cases; the Pharmacovigilance Division/section of MAH must have a backup of the reported cases.



| | Submission time | Submission identifier | Completion time | Status | Download |
|---|---|---|---|---|---|
| › | 15 January 2024 21:40:04 (UTC+1) | 252ac20f-beff-4b3e-b32a-cb3c6a7fa7b3 | 15 January 2024 21:40:32 (UTC+1) | Accepted | |
| › | 15 January 2024 18:29:15 (UTC+1) | 8ea364eb-e291-4b42-8ad7-8ef2a735af4e | 15 January 2024 18:29:47 (UTC+1) | Accepted | |

Click on the Acklog and download it for future use. It is advisable to download it immediately.

**If there is no missing or erroneous data in red before submitting the case and the case still cannot be submitted, what should be done?**

You should review the report again in detail, section by section. As long as you provide the minimum information required and do not have missing or erroneous/wrong data in red, the report can be sent without a problem.

**By what mechanism do you recommend evaluating/assessment of the causality of the reports?**

NPC-DRAP recommends the implementation of the World Health Organization (WHO) - Uppsala Monitoring Centre (UMC) Standardized Causality Assessment Criteria.

**Should all reports carry the causality assessment?**

Yes, it is necessary that all reports include their due evaluation of causality. It should be remembered that the assessment is carried out for each pair of "drug-reaction"; therefore, causality assessment for all the reactions caused by suspected medication will be carried out.

**If I'm going to report a follow-up, do I need to enter the entire case again**?

No, it does not require entering the entire case again. After submitting the initial case in the manual data entry module, you should immediately download the XML file and save it to your computer directory (storage) (it is recommended to establish procedures to manage and back up these files). When you need to follow up, you must choose the *Edit option report* (edit report) from the top menu of *Data Entry*; here you need to open the initial case file and once this is done the system will load all the information you initially entered. You must make the modifications and additions of information that the follow-up requires, also adding in the Narrative Case field, the additional follow-up narrative.

Remember that the Acklog file should not be used in this activity as the file is not designed for tracking.

**In the case of manual reporting to E2B transmission, can the Acklog generated in the manual upload be used for monitoring in E2B transmission? or is it only loaded in XML of the sent tracking.**

The 'acklog' is simply a digital confirmation that your data was received. However, if you initially entered case through the data entry module, you can also upload them through the upload E2B module. *To ensure seamless integration with VigiFlow, ensure that the WWUID, short name, and Sender ID are consistent throughout the process. Accurate company data is essential for recognizing follow-up reports.*

**If I didn't download the report, is it no longer possible to download it?**

It can be downloaded on the Submission Status Tab (for 35 days). It is advised to download and save it immediately after the report is sent.

**If other problems appear that are not mentioned in this guide, how and where should they be reported?**

It can be reported to the NPC-DRAP using this email pv@dra.gov.pk

**Is there a contingency plan if the platform doesn't work? How would cases be reported?**

It can be reported through the paper format on the mailing address of the NPC and/or sent to the NPC-DRAP email (npc@dra.gov.pk) as was the practice before this new tool. The report should be sent through the industry e-reporting platform as soon as it is back online.

**In the event of an error in the platform and/or unavailability of the system, is there any other option for reporting cases?**

Industry e-Reporting is continuously monitored and updated by the UMC to ensure its correct operation. When the UMC performs updates, it takes no more than a few hours to complete so access may be intermittent for some users. In this case, you must wait at least 3 hours and try the access again. In the event that you cannot access Industry e-Reporting for more than 24 hours and that it is due to a cause unrelated to the UMC (you can document it with a screenshot if your internal procedure requests it), please report the error to pv@dra.gov.pk and constantly monitor until service is restored.

If you have a problem accessing the platform, please try the following:

- Access from the link found in this manual and not through the one saved in your computer's cache or history.
- Delete the cookies of the browser used.
- Access the platform through another browser.
- Make sure that the correct username and password are entered.
- If you have forgotten your password, you must generate another one so that you can access the module.

**What happens if in the Submission Status section, the end time is empty and the submission status of my notification/report is displayed as pending and I don't have the acklog issued and available for download?**

When this type of situation is detected, it is not necessary to notify (report) it. The module is continuously monitored, so the data related to the time of transmission and submission identifier may be considered as evidence of sending.

Once the successful transmission is confirmed, the same module will automatically issue the acklog and it will be available for download, only for 35 days. In the event that an acklog is pending download, it will be the user's responsibility to monitor its status in order to download it immediately to complete the documentation corresponding to the case.

When downloading the XML, it is necessary to confirm that the following data is contained, since it confirms the successful transmission of the information:

<acknowledgement typeCode ="AA"> AA --Application Acknowledgment Accept (message successfully processed, no further action)

In case of receiving an acklog with any of the following encodings, it will be necessary to load the information:

AE--Application Acknowledgment Error (error detected, error response has additional detail, some ICSR message(s) need further action)

AR --Application Acknowledgment Reject (parsing error, no data extracted, resend the entire transaction).

**How will the pharmaceutical industry (registration holder) perform a quality control or review of the information entered?**

This is at the discretion of each member of the pharmaceutical industry in accordance with their internal procedures. One option is to do a review using the report generated in XML and document the review.

**What should we do if our XML case is rejected?**

Specifically speaking of the XML upload module, when you upload the acklog to your system and the rejection is identified, your internal procedure should set the necessary fixes to re-upload it. Anyhow, you need to download the acklog file and need to check for the relevant fields based on which the file was rejected and accordingly work for its correction.

**If there is a security problem that does not generate an adverse event, should it be reported**?

No, other safety problems related to the use of medicines and vaccines are only reportable if they are accompanied by clinical manifestations (not necessarily related to the safety problem).

**Where will the drugs used to treat the adverse event (for the management of) be entered in the manual data entry module? In the narrative?**

In the free text field Narrative case.

**When initially working with the manual data entry module and then migrating to XML, does the short name have to be provided from now on?**

Yes, the long name, the short name, and the sender identifier must be provided. These data must be the same as those initially provided for the manual data entry module and used to generate XML-E2B. This will prevent future problems with receiving cases in the XML upload module.

**Can the causality assessment method be medical judgment?**

Priority use of standardized assessment methodologies is requested.

**Should reports of SUSARs and SAEs occurring during clinical trials be also reported through this platform?**

Cases of suspected unexpected adverse drug reactions (SUSARs) and serious adverse events (SAEs) occurring during clinical trials should be reported to the Chairman or Secretary Clinical

Study Committee, Clinical Trial section of the DRAP through email (CT_AE.reporting@dra.gov.pk ). For further details visit the guidelines to conduct clinical research in Pakistan and Bio-Study, Rules, 2017.

**If you cannot find the specific drug you wish to report through the WHODrug dictionary, what should you do?**

Please follow the steps described in the document "*How to use the WHODrug C3 format for drug coding*" and send an email to DRAP with the same information sent to the UMC.

**Will the MedDRA version that handles e- Reporting be the most recent?**

Yes, the most recent version will be used and will be updated as MedDRA MSSO releases new versions.

**For any questions regarding license subscriptions, please contact.**

- For MedDRA dictionary: mssohelp@meddra.org
- For WHODrug dictionary: support@who-umc.org

ANNEX E: How to use the WHODrug C3 format for drug coding Version 2.0 (As Attachment).

ANNEX F: Technical guidance for use of WHODrug Global E2B(R3) 2.0 (As Attachment).

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