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NATIONAL AGENCY FOR FOOD DRUG ADMINISTRATION AND CONTROL (NAFDAC)
NATIONAL PHARMACOVIGILANCE CENTRE (NPC)

INDUSTRY E-REPORTING MANUAL

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LIST OF ACRONYMS

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ADR	**Adverse Drug Reaction**
AE	**Adverse Events**
AR	**Adverse Reaction**
ATMP	**Advance Therapy Medicinal products**
CCDS	**Company Core Data Sheet**
CCSI	**Company Core Safety Information**
CIOMS	**Council for International Organizations of Medicinal Sciences**
GVP	**Good Pharmacovigilance Practices**
IBD	**International Birth Date**
ICH	**International Conference on Harmonization**
ICSR	**Individual Case Safety Report**
ISO	**International Standards Organization**
CRH	**Certificate of Registration Holder**
LLT	**Lower-Level Term**
MedDRA	**Medicinal Dictionary for Regulatory Activities**
MAH	**Marketing Authorization Holder**
NAFDAC	**National Agency for Food and Drug Administration and Control**
NPC	**National Pharmacovigilance Centre**
PASS	**Post Authorization Safety Studies**
PBRER	**Periodic Benefit Risk Evaluation Report**
PL	**Package Leaflet**
PSMF	**Pharmacovigilance Systems Master File**
PSUR	**Periodic Safety Update Reports**
PV	**Pharmacovigilance**
QPPV	**Qualified Person Responsible for Pharmacovigilance**

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RMP	**Risk Management Plan**
SmPC	**Summary of Product Characteristics**
SMQ	**Standardized MedDRA Query**
SOC	**System Organ Class**
SSS	**Smart Safety Surveillance**
UMC	**Uppsala Monitoring Centre**
WHO	**World Health Organization**
WHODrug	**WHO Drug Dictionary**

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1. Background

Safety is a fundamental principle in the provision of Drugs and Medicinal products for health care and a critical component of quality control. Adverse reactions to medicines have been known to result in hospitalization, permanent disabilities, and deaths. In addition to the impact of adverse drug reactions on human health, adverse drug reactions (ADRs) also have a significant impact on healthcare costs.

The Thalidomide tragedy which occurred in the late 1950's and the early 1960's, raised concerns regarding the safety of medicines and the potential dangers to public health associated with unexpected adverse reactions to medicines. Disasters associated with the use of other medicinal products occurred in many countries after the thalidomide tragedy. In response, the developed countries established reporting schemes to capture adverse reactions to medicines. The World Health Organization (WHO) following the World Health Assembly Resolution (WHA 20.51 of 1967) established an international drug monitoring scheme with 10 member countries in 1968 with a focus on the collection, collation, processing/analysis, and dissemination of relevant information.

By December 2019, the number of participating countries had risen to 136, with 30 associate member countries in the early stages of establishing their pharmacovigilance systems. There are thirty-one (31) African member countries. Nigeria became the 74th member of the WHO Program for International Drug Monitoring in September 2004.

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 goal of Pharmacovigilance is to improve the safe and rational use of medicines, thereby improving patient care and public health.

The National Agency for Food and Drug Administration and Control (NAFDAC) ACT Cap N1, LFN 2004 empowers the Agency to control and regulate the manufacture, importation, distribution, advertisement, sale and use of its regulated products. This mandate requires

the Agency to ensure the quality, safety and efficacy of all regulated products. Based on the fact that no drug is harmless, its administration for the treatment, prevention or diagnosis of any disease may be associated with an adverse reaction.

This new tool (called ***Industry e- Reporting***) has been completed and has begun to be piloted by some countries, Mexico being the first to use it in production mode.

Industry e-Reporting will allow the Pharmaceutical Industry to carry out notification, installation and operation of Pharmacovigilance, through **Reporting of Adverse Drug Reactions that occur nationwide** with the products under its representation, 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 PDF.
- Immediate sending of the report to the NPC.
- Follow-ups are done by uploading the XML file of the initial and previous report and editing them on the same platform.
- Ability to download electronic acknowledgment (acklog) in XML format.

NOTE:

Using the MedDRA and WHODrug Global dictionaries for medical coding in reporting ADR makes it much easier to record and analyze patient data in a consistent and accessible way. Therefore, NAFDAC has made it compulsory for MAHs to use both MedDRA and WHODrug to ensure proper terminologies

are used in reporting as our database terminologies are coded based on these dictionaries.

2. Goals

- Present the procedure for loading XML files into production for those members of the Pharmaceutical Industry that have already completed the implementation of E2B in their databases.
- Provide information and explain the procedure that the Pharmaceutical Industry 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 notification.

3. Content development

3.1. Initial indications

- It is suggested that the equipment used to load the cases has an energy storage device to prevent data loss.
- Maintain a stable high-speed internet connection for the proper functioning of Industry e- Reporting.
- Use in order of preference, Chrome, Firefox and Microsoft Edge browsers. Keep them updated for optimal operation.
- Safeguard the integrity and confidentiality of access accounts and passwords.
- 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 Unit (PV-Unit) and its Qualified Person Responsible for Pharmacovigilance (QPPV) updated in the NPC (NAFDAC), since communication will be by email exclusively with the Responsible Person for Pharmacovigilance

- The request must be made via email: pharmacovigilance@nafdac.gov.ng
- Three user accounts will be granted by the NPC (by the Director and, or the Head of Pharmacovigilance Division).
- It is essential that the email indicated for the user account is corporate or institutional.

Information that the request must contain:

Application	Description
MedDRA license validity status	You must indicate if you have a valid MedDRA license. It is an essential requirement that the Pharmaceutical Industry that uses Industry e- Reporting have the corresponding valid MedDRA license. It is also applicable for the XML upload module.
WHODrug license validity	You must indicate if you have a valid WHODrug license. It is an essential requirement that the Pharmaceutical Industry

status	that uses Industry e-Reporting have the corresponding valid WHODrug license. It is also applicable for the XML upload module.
Long name	It is proposed that it be the company name (max. 254 characters). Example: *MedSolutions Laboratories* 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). Example: *MEDSOLUTIONSLABS* It will be part of the letters of the *Worldwide unique case identification* (WWUID). Example: NG-MerckHealthcareKGaA-0000001, must match the WWUID of the XML files (for those laboratories that have databases that generate this ID). For companies that have E2B databases, the following are the fields that contain the requested information: • **E2B (R2)** : <companynumb> • **E2B (R3)** : 2.16.840.1.113883.3.989.2.1.3.2 (Point C.1.8.1 *Worldwide Unique Case Identification Number* of the ICH guide)

	The short name will also be seen in the *Safety Report Unique Identifier* (SRUID). Example: NG-MerckHealthcareKGaA-0000001 Companies that do not have E2B databases can propose the sender identifier and define it together with NPC. 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. For companies with databases that can or could generate XML, it must be identical to the one in your 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: E2B (R2): <messagesenderidentifier> (In the guide it is point M.1.5 Message Sender Identifier) E2B (R3): 2.16.840.1.113883.3.989.2.1.3.11 (In the guide it is point N.2.r.2 Message Sender Identifier) Sometimes it is the same as the short name, but not necessarily.

	For companies that do not have E2B databases, they can propose the sender identifier and define it together with NPC 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: • E2B (R2): See field < sender organization > (Corresponds to A.3.1.2 Sender organization in the ICH guide) • E2B (R3): (Corresponds to C.3.2 Sender's Organization in the ICH guide). 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. Email (user).
User 2 (additional)	Name (s), and surnames of the person responsible for the account. Email (user).
User 3 (additional)	Name (s), and surnames of the person responsible for the account. Email (user).

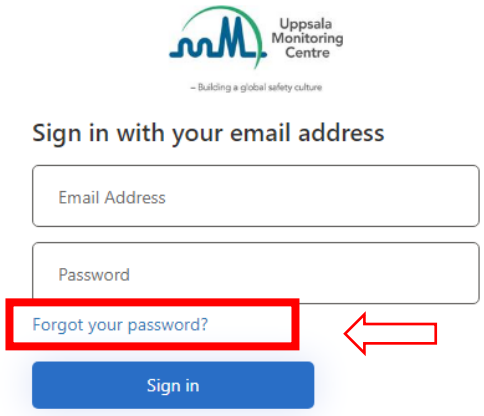
3.3. First time login and password generation

Once the National PV Centre (NAFDAC) has granted you access to the platform, you must follow the following steps to generate your password:

1. To log in and generate your password, you must go to the following link (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 NAFDAC website):

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

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



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

IMPORTANT

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.

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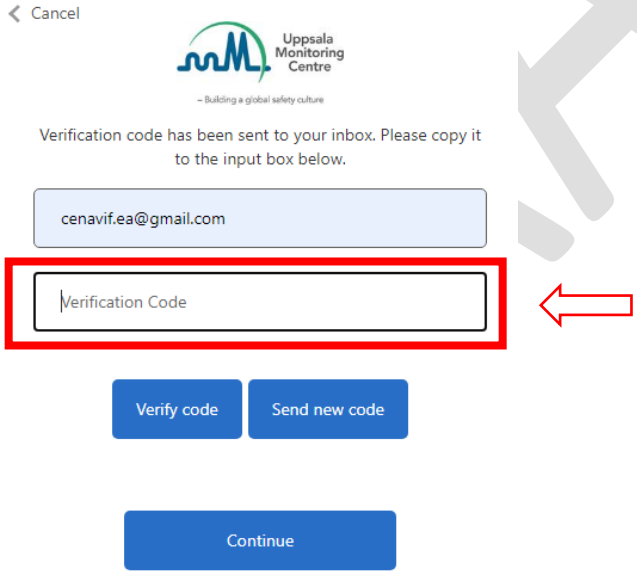
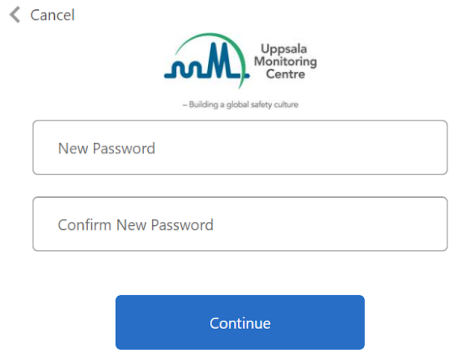
- Do not close the e- Reporting Industry window.
- A 6-digit code will be sent to your email that you must enter in the **Verification field Code**. Press the **"Verify code" button**.



- 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 NAFDAC website):

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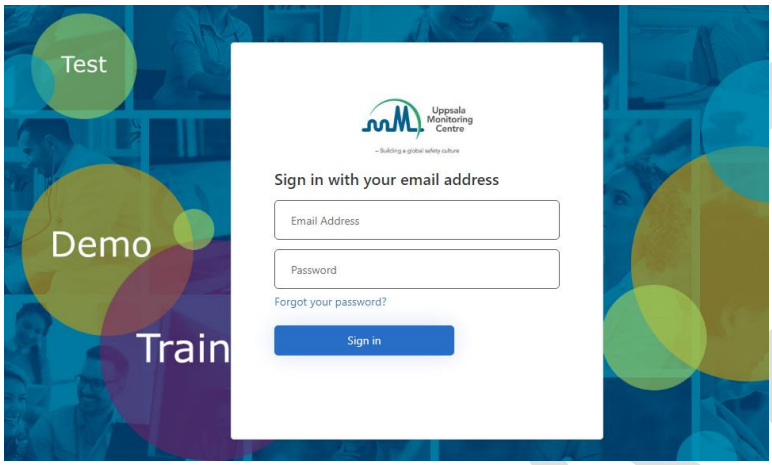
https://industryereporting.who-umc.org/

- ✓ 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:

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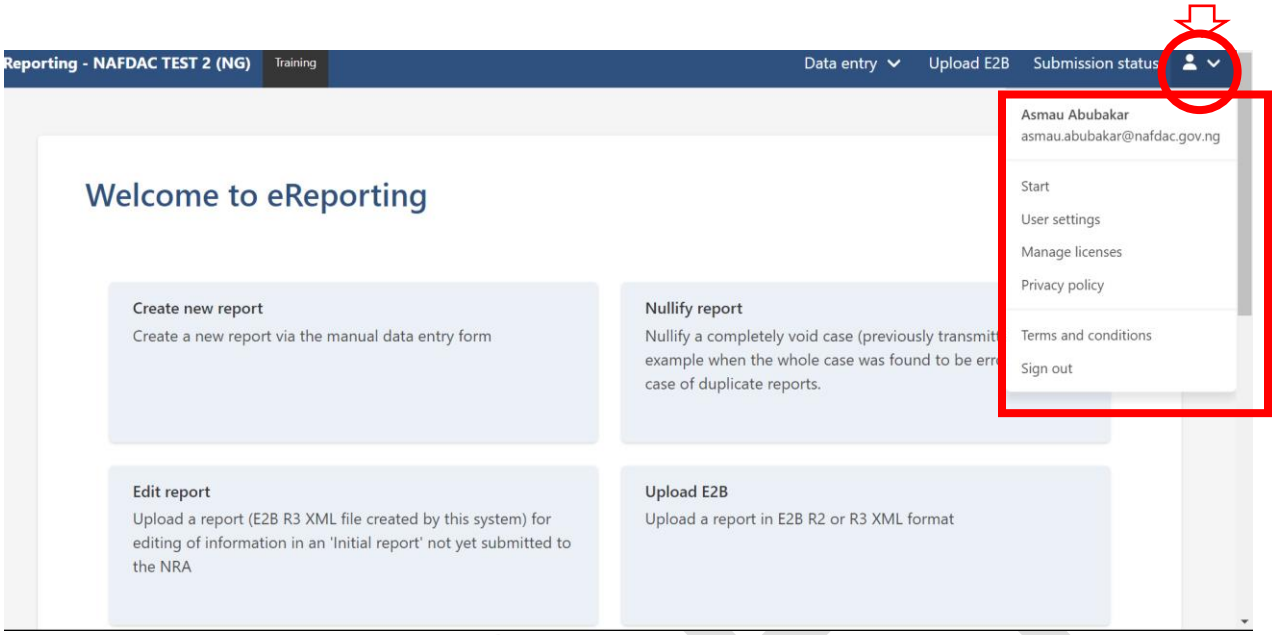


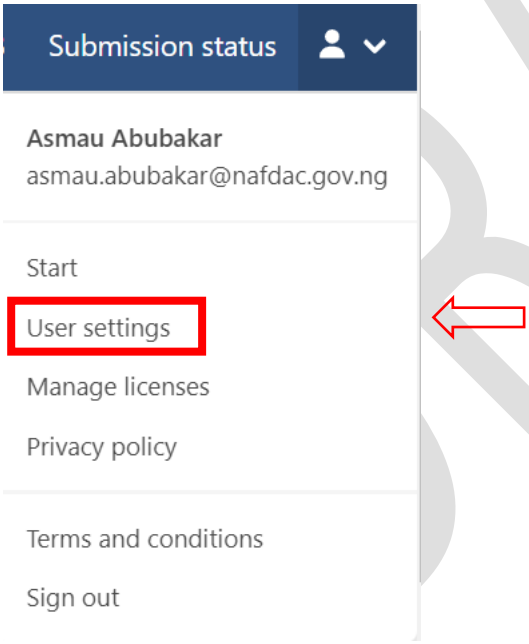
In the upper right part of the screen, there is a main menu where you can view: the user settings, privacy policies, and logout.

Each function available on the menu is detailed below:

Function	Description
Start	Move you to the main screen. When entering a report, please make sure you have submitted and downloaded it first before going back to the home screen, otherwise the information entered will be lost.
User Settings	Interface language settings.
Manage Licenses	MedDRA and WHODrug license administration.

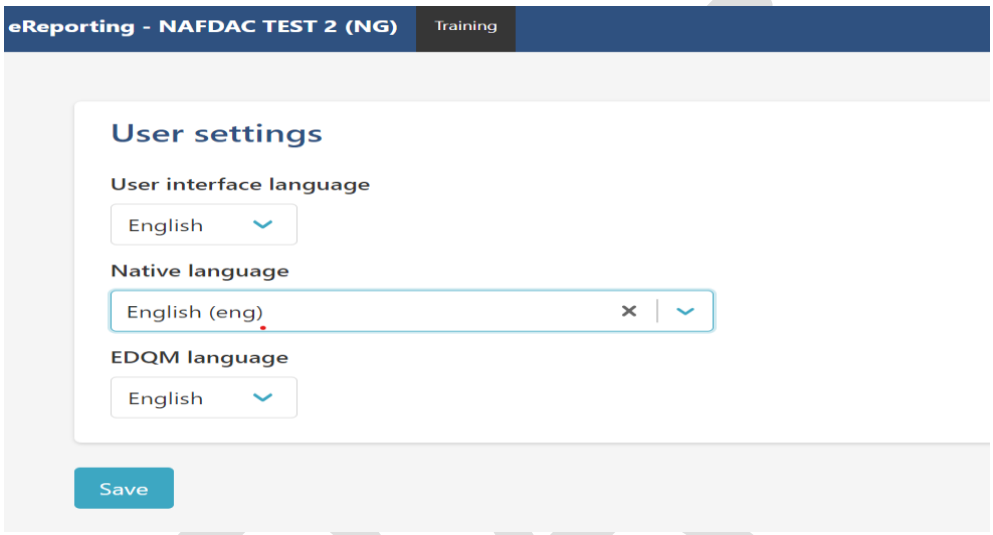
Privacy Policy	It redirects you to the UMC web page where the privacy policy is described.
Terms and Conditions	Legal clauses that establish the way in which the system can be used.
Sign off	If you are entering a report, please first make sure you have submitted and downloaded it before logging out, 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 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.

- **Data entry (for manual filling):** directed to the manual entry of the report information into the system.

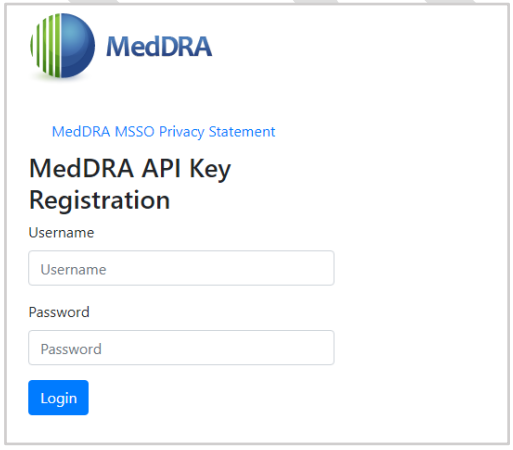
- *Create New Report:* This module contains instructions on how to create a new Individual Security Case and how to manage it in the system.
- *Edit Report:* This option allows you to load a previously entered report.
- *Follow-up Report:* This option allows you to upload a previously entered report, for follow-up purposes.
- *Nullify Report:* This option allows you to cancel a report previously created by this system.

- **E2B upload:** Module for notification through files in XML format

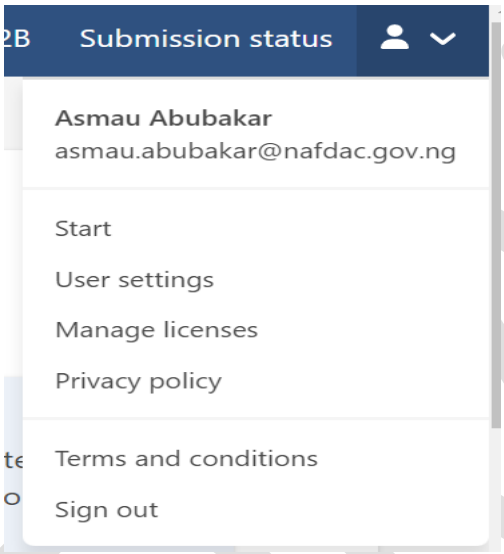
3.5. MedDRA license activation and management

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 e- Reporting Industry): https://mid.meddra.org/account/register



2) Provide “username” and “password” of your MedDRA license. Click on “Login”
3) If the process was 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 e - Industry Reporting
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”

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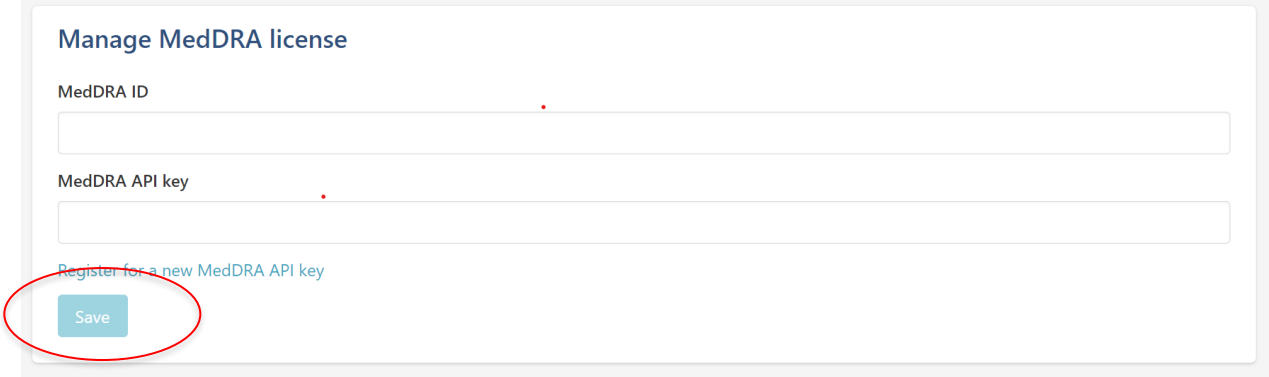

8) If the process was successful, the information will be saved and the following message will be displayed indicating that your license has been validated to use MedDRA within e- Reporting Industry
9) Return to the main screen.
   When entering/editing a report, in the sections where MedDRA is available, 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 e - Reporting Industry allows a general search for the desired term, so the information presented in the result is concrete, 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/For issues related to MedDRA licensing subscription models, contact MSSO directly through the following channels:

- Web form: https://www.meddra.org/subscription/process
- email: mssohelp@meddra.org

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Important

The incorporation and use of the MedDRA dictionary is compulsory for both loading modules.

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 MAH 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. WHODrug 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.

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, NAFDAC makes the use of this terminology compulsory 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 WHODrug 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 was 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/

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.

Important

The incorporation and use of the WHODrug dictionary is compulsory for both loading modules.

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

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

Disclaimer: Each MAH is responsible for performing/verifying the renewal of their organization's WHODrug license with UMC, in order to be able to use terminologies in the industry e-reporting in a legal manner.

For issues related to WHODrug license subscription models, please contact UMC directly through the following channels:

- Web form: *https://who-umc.org/whodrug/whodrug-subscription/product-enquiry/*
- email: *support@who-umc.org*

Disclaimer: NAFDAC does not receive any benefit for the acquisition of these licenses, nor does it have any interference in the licensing process.

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

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

- The notification of individual case reports to e- Reporting Industry will be solely and exclusively for new cases and their respective follow-ups.
- If you are notified of an initial case and follow-ups through the previous mechanism via email, you must follow up and close it through the same way, that is, via email.

3.7.1. Manual entry module

3.7.1.1. Generalities

3.7.1.1.1. "NF" Codes: NullFlavor (Missing Information)

NullFlavor (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 Notifier Country, Patient Initials, Therapeutic Indication, etc.

- A stranger
- 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.

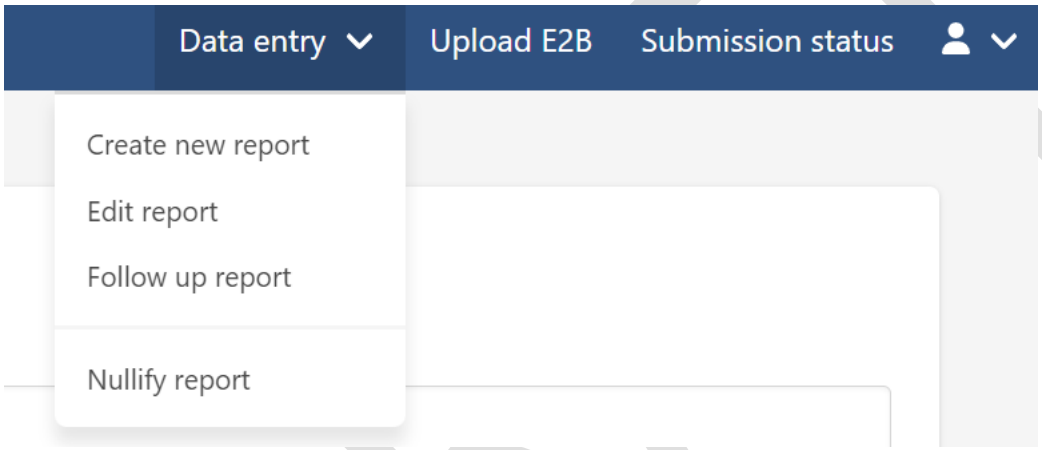
3.7.1.1.2. Common icons in the different sections:

Icon	Function
	Allow you to add a corresponding section or field where the button is located. For example: Medication, Therapeutic indication, Dose, Reactions, Causality evaluation, etc.
	Allow 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.

3.7.1.2. Management of the Report on 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 manual upload module, identify the ***Data entry option in the upper right menu***



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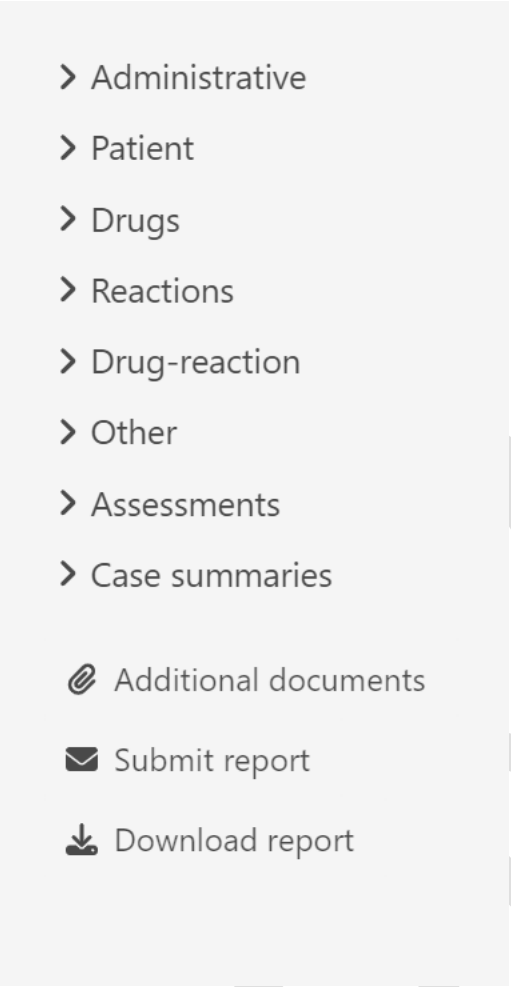
3.7.1.2.1. Create a new report

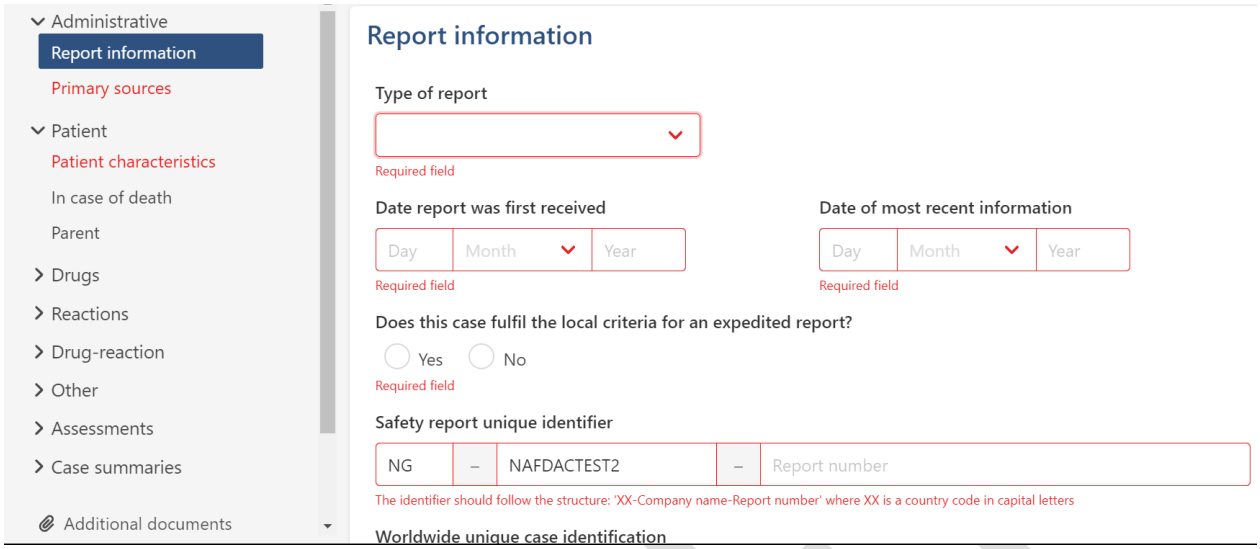
It consists of eight (8) sections as can be seen below:



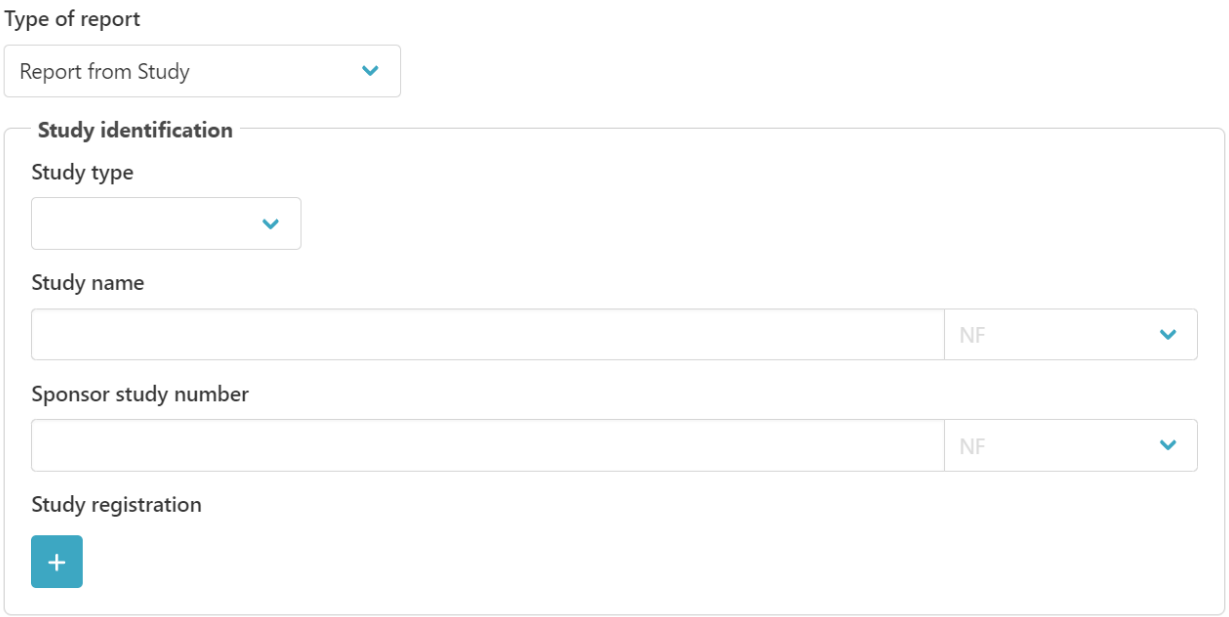
- ✓ **Administrative**
  - ➢ **Report Information**

Effective Date:
Review Date:

Doc. Ref. No. PV-GDL-019-00



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

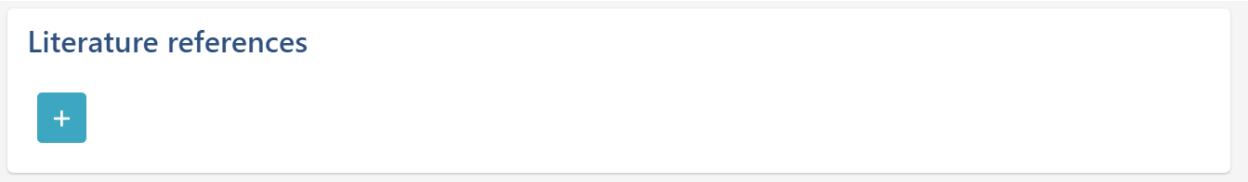


When study report option is selected, additional fields will be displayed such as:

- Type of study
    - Clinical Trial: for intervention studies
    - 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 letter of the Regulatory Authority.
Sponsor study number: study identification code as it appears in the authorization letter of the Regulatory Authority.

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

- **Date 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 notification 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 meet the local criteria to be a report requiring priority attention?** This is a ***Required Field*****.**
  - Indicate **"YES":** for serious notifications 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 notifications classified as non-serious.

Effective Date:
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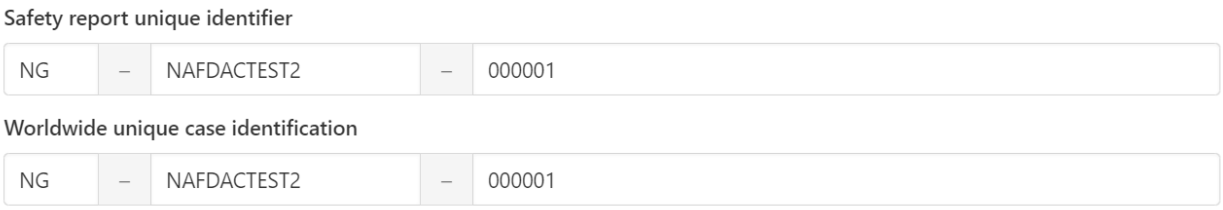
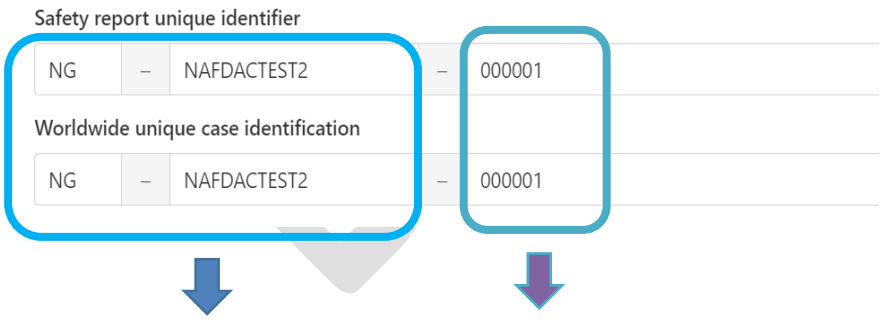


- **World Unique Identification Number (WWUID):** this is the first identifier assigned to the report, if the company does not have a database that generates a code, this will be the first code assigned to the report. If the company has an E2B database, the WWUID will be the same as the code generated by the database. The WWUID is composed first of all by the initials of the country, i.e., NG, 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.

- **Security 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.



Constant section (Not modifiable)

Variable section between cases

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

Safety report unique identifier

NG	–	NAFDACTEST2	–	000001

Worldwide unique case identification

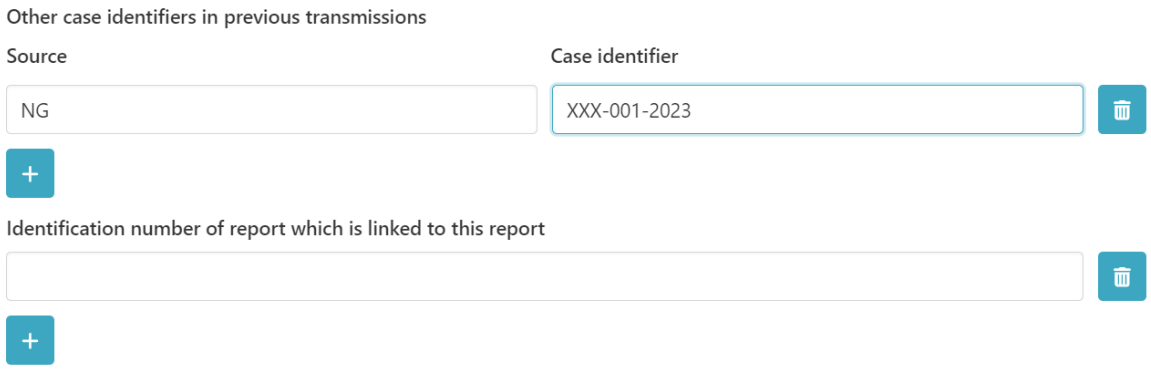
NG	–	NAFDACTEST2	–	000001

The **Unique Identifier of the security 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.

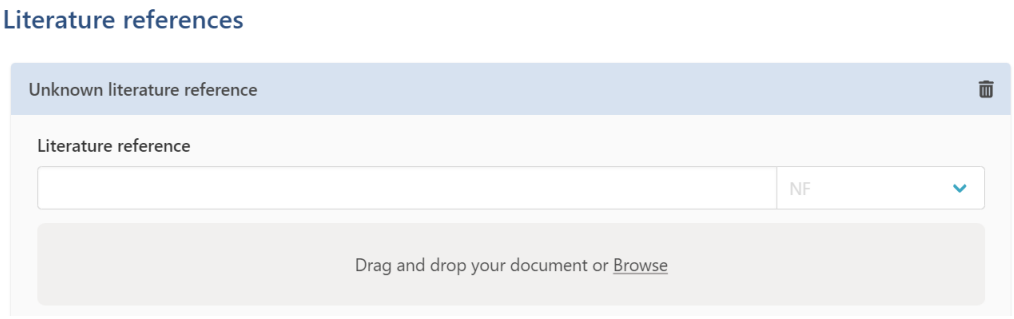
- **Other case identifiers in previous transmissions** (Other case identifiers in previous transmissions): If you have an internal encoding in your organization or other requested indicators, you can add them by clicking the "+" icon.

  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 report which are linked to INITIAL report): When you have cases that are related in some way to the one you are reporting (for example, SAE that happened in a family), put the WWUID of the related cases. It does not apply to cases that are follow-up.



- Bibliographic References (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 gray section or open it from your file explorer with the “Browse” option. Add literature references in PDF format to avoid format incompatibility.



➢ **Primary Source:** Information referring to the primary/original notifier.

○ **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 submitter. The report must only have one primary source for regulatory purposes.

-Qualification: corresponds to the profile of the primary notifier. *Obligatory field.* You will have to choose between:

✓ Healthcare Professionals (Doctor, Pharmacist, Nurse, Medical Laboratory Technologist, etc.)

✓ 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 Nigeria. However, on some occasions the country of the reporter may be different if, for example, a patient/consumer purchases a medication in Nigeria and the event/reaction occurs in another country.

The following fields about the notifier 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 notifier.

- Qualification

- Name
- Middle name, (if applicable)
- Surnames
- Organization
- Department/Area
- Address
- City
- State
- Postal Code
- Phone

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.

✓ **Patient**

➢ **Patient characteristics**

- Name or initials: Provide initials of the paternal and maternal surnames and name(s) in that order, or in the case of Clinical Studies, the patient's identification code.
- Sex
- Birthdate
- 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 time when the reaction/event was observed in the fetus): Enter the value and choose the unit of time from the catalog. 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
- Height

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 registration number
✓ Hospital file number: Corresponds to the clinical file number
✓ Research number: For patient identification in clinical studies.

- **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.

- **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.

- If you don't know the answer to the question, leave it blank.
- Mother's relevant medication history: 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.
- Parents' medical history: Provide information about the relevant medical history and co-occurring conditions of the parents.

✓ **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:

- Suspicious
- Concomitant
- Interacting If you choose this option, you must have at least two interacting drugs.
- Unadministered medication

Name of the medication as reported by the primary source: You must place the trade 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.

Hereafter the WHODRUG catalog will be included for this section.

Country where the drug was obtained:

Action taken with the drug: Choose between:

- Withdrawn drug
- reduced dose
- increased dose
- Unmodified dose
- Unknown
- Not applicable

Authorization/application number: NAFDAC registration number of the suspected medicine. In the case of a Clinical Study report of a drug that does not have a NAFDAC number, you can enter the authorization number of the clinical study protocol granted by the Authority.

Country of Authorization/Application: Select the country where the drug was authorized

Name of the holder/applicant: Company name of the holder of the sanitary registry or legal representative. For Clinical Studies, it must be placed in the name of the sponsor.

Cumulative dose at first reaction:

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

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

- **Indications as reported by the primary source**

Indication as reported by the primary notifier: 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 or in EC the indication for which the clinical study is being conducted. Hereinafter the MedDRA dictionary will be included for this section.

Dose

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.

Dose 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 form: 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 with the "+" icon instead of adding another drug.

✓ **Reactions**

- **Reaction/Event as Reported by Primary Source:** Place the MedDRA term (Level LLT) of the reported reaction/event in parentheses.

From now on, the MedDRA dictionary will be included for this section and when this happens, the literal term will be placed in this free text field, that is, originally as reported by the primary notifier, and which will be useful above all for those cases where there is no exact match to a MedDRA term.

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 reaction / reported 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 notifier

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

- Life threatening
- Death cause
- Caused or prolonged hospitalization
- disability / incapacity)
- Congenital abnormality/birth defect
- Other medically important conditions

Result 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 / In progress
- Recovered / Resolved with sequel
- Fatal
- A stranger

Medical confirmation by a healthcare professional: It is generally affirmative when the primary notifier (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 Nigeria. There may be exceptions, for example, the patient acquired the drug in Nigeria, traveled to another country and presented an ADR.

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

✓ **Reaction to Medication**

➢ **Re-exposure**

Was the patient re-exposed to the drug? 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:

- **(Re-exposure** result): choose between:
  - ✓ The reaction was repeated: it corresponds to a positive rechallenge.
  - ✓ The reaction was not repeated: it corresponds to a negative rechallenge.
  - ✓ unknown result
  - ✓ Not applicable

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

➢ **Time interval from administration to onset of reaction:** interval between drug administration and the onset of the reaction/event.

- **Time from first dose and start of 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.

✓ **Others**

➢ **Test results**

Test Name: Enter the appropriate MedDRA term for the test in question.

Herein, the MedDRA dictionary will be included for this section.

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

Test result: in the free text field, 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.

Study Result Code: This element allows a descriptive element to indicate the result of the analysis:

- Positive
- Negative
- Limit
- Unfinished

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 use the *Test Result field,* leave it blank.

Low Normal 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).

- **Medication history**

Name of the medicine as it was reported: You must place the brand name if you have it and the generic name in parentheses.

Hereinafter the WHO drug catalog (WHODrug) will be included for this section.

Indication: Enter the MedDRA term (Level LLT) of the therapeutic indication for which the drug is being given. Hereinafter the MedDRA dictionary will be included for this section.

Reaction: Fill in the corresponding MedDRA term. Herein the MedDRA dictionary will be included for this section

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

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

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

- **Clinical history**

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

Relevant clinical 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.

Structured information about 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.

Herein, the MedDRA dictionary will be included for this section.

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 (year) or two fields (month and year).

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

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

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

- **Evaluations**

Evaluation method: place in the free text field the name of the methodology used.

Evaluation source: 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 notifier (informant) if you have it, or of the sponsor/investigator for CE.

Evaluation result: 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 in 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 Primary Notifier in *"Assessment Source".*

✓ **Narrative Case**

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 problem it 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...

Effective Date: Doc. Ref. No. PV-GDL-019-00
Review Date:

----------(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.

Notifier Comments: In this field you can add additional comments provided by the primary source if you have them.

Company comments: additional comments that the notifying Pharmacovigilance unit can provide or, in the case of clinical studies, the comments of the study sponsor.

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

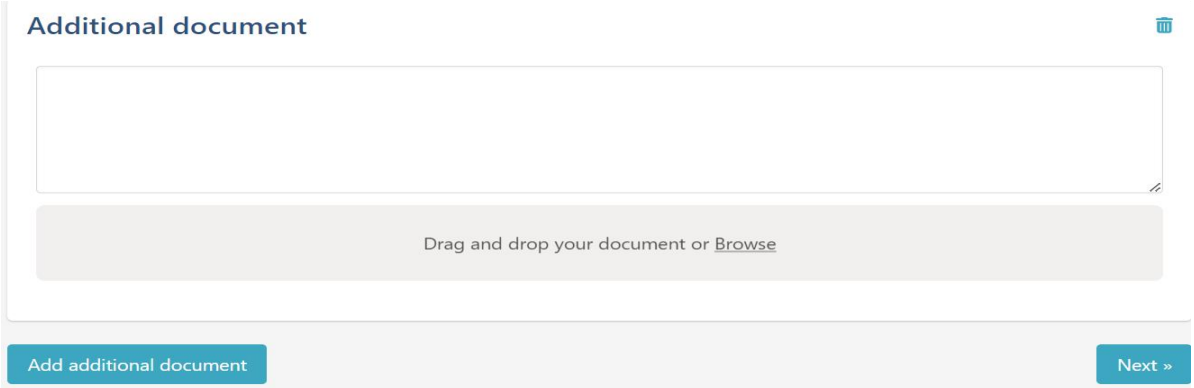
✓ **Additional documents**

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 gray 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

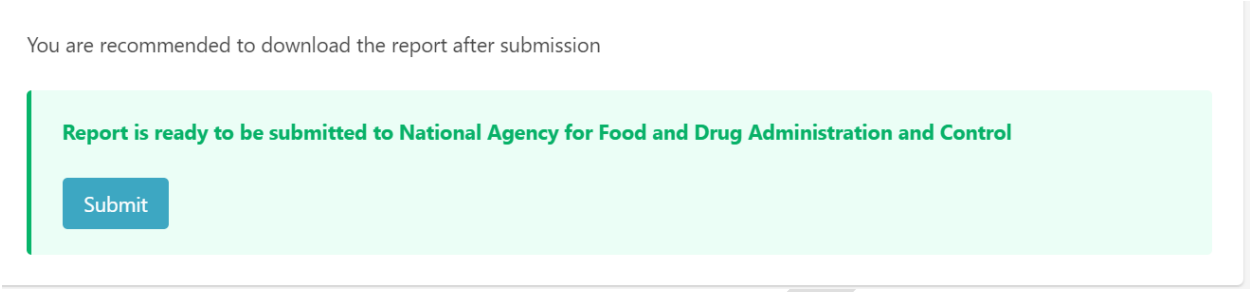
It is necessary that the documents you need to attach are in PDF format and do not exceed 2 MB to be able to load them without problems.

✓ Send Report

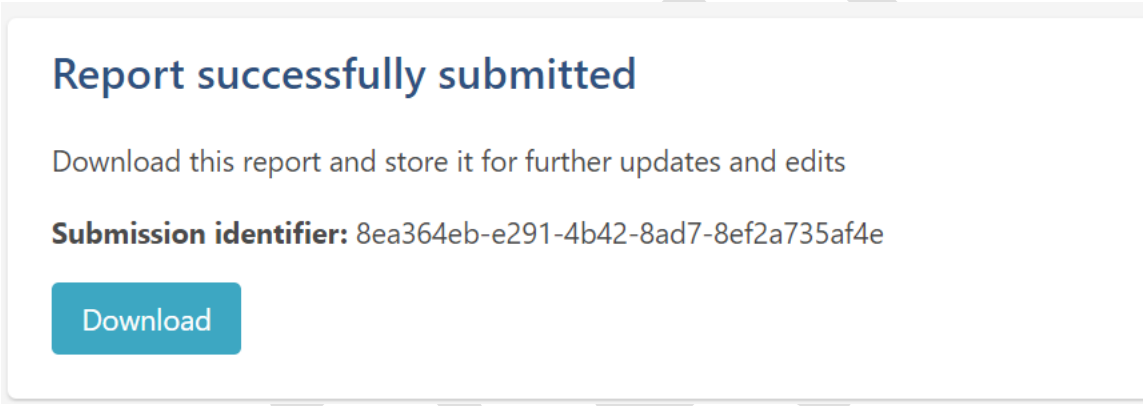
To send the report, it is necessary that you have captured the minimum information required by the system. If you have not done so, this section will list the missing or erroneous information which you will need to include or review. The missing information in the different sections that make up the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



- **Download Report**

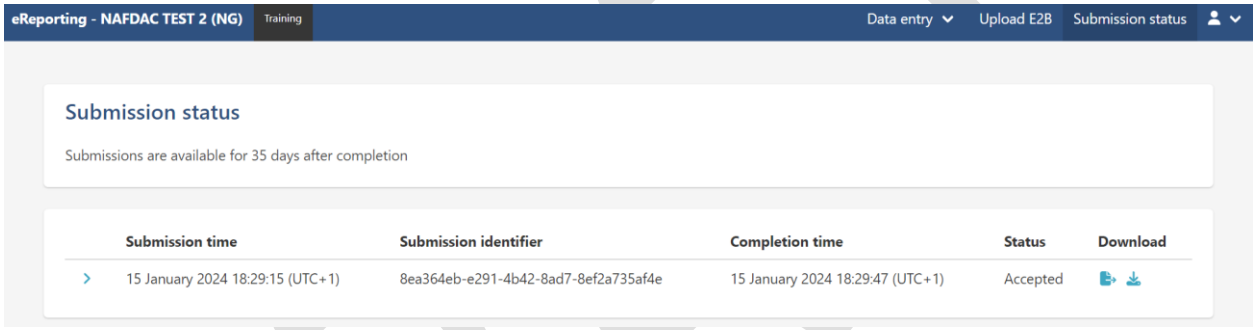
It is necessary to ***immediately download*** the report once you have submitted it, as this will be the only way to get this case's XML file and track it. The information generated during the capture of the report will be downloaded in an XML file

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

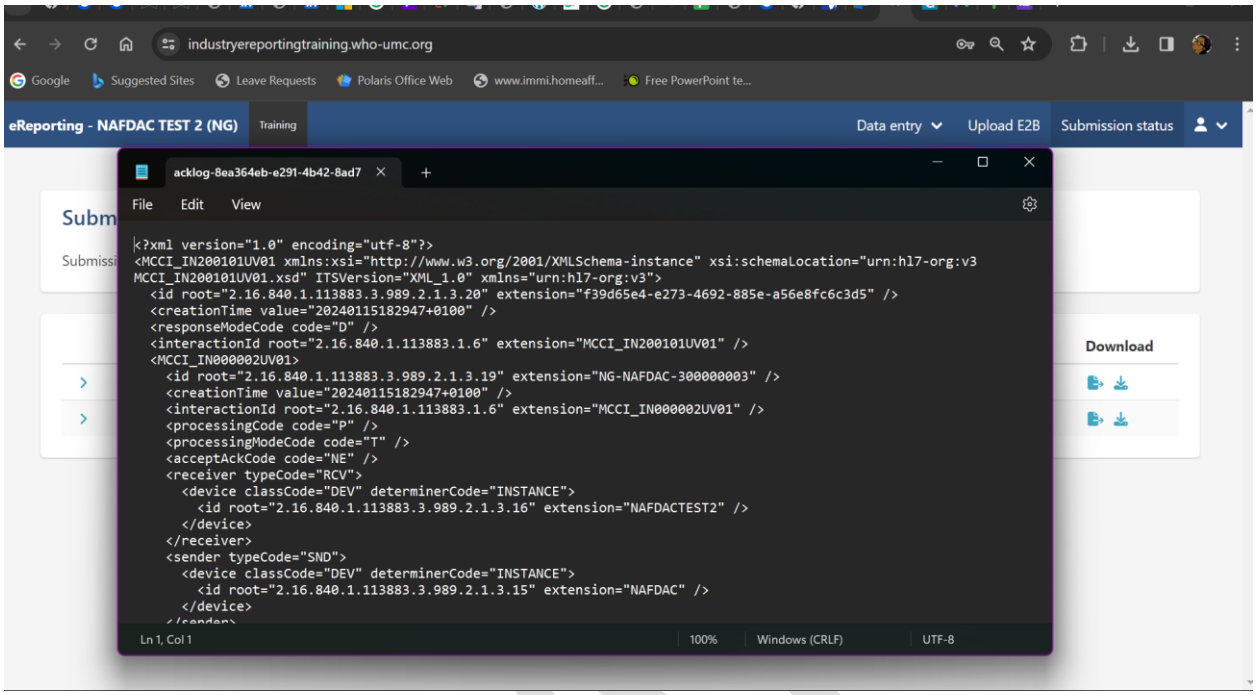
Clicking *Download* will download the XML file. It is important that you keep this file on your backup, as you will need to use it if you need to follow up on the case. See "Edit *Report*". By default, the system will name the file with the Globally Unique Identification Number.

Additionally, Industry e-Reporting provides confirmation receipts known as the acknowledgement log (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.



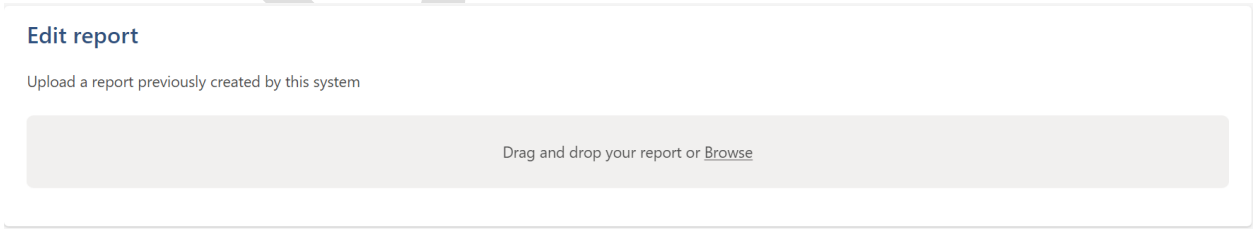
You can open the acklog in Chrome or another browser and identify the end time and send time of your report. You will notice that for the value "creation Time value" is established in UTC time (coordinated universal time) so, for purposes of compliance with notification times, you must consider the difference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



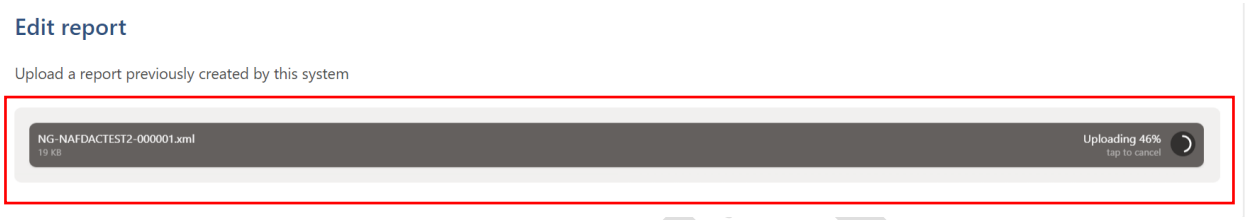
3.7.1.2.2. Edit Report

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. ***To save a report without submitting to the regulatory authority, the user can click on download report on the interface.***

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 gray 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.

3.7.1.2.3. 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.

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

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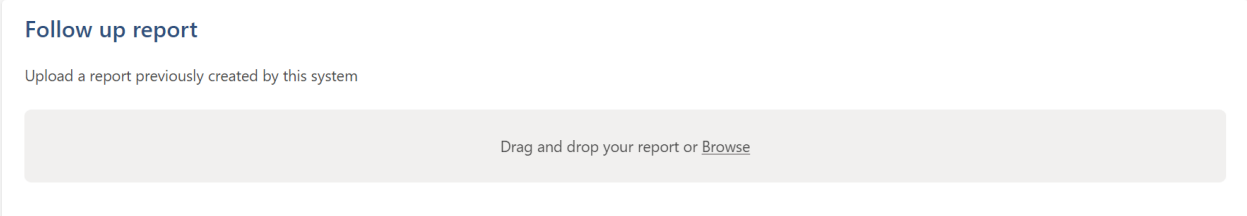

Upload the XML file generated in the initial submission or previous follow-up, which you should have saved on your computer, either by dragging and dropping it into the gray section or by opening it from your file explorer with the "Browse" *option.*

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.

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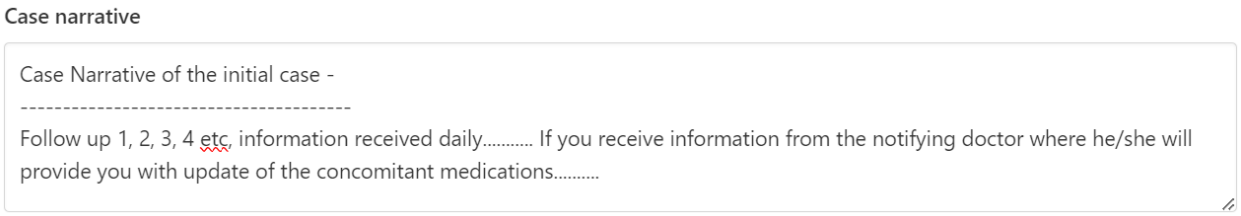
Narrative Case

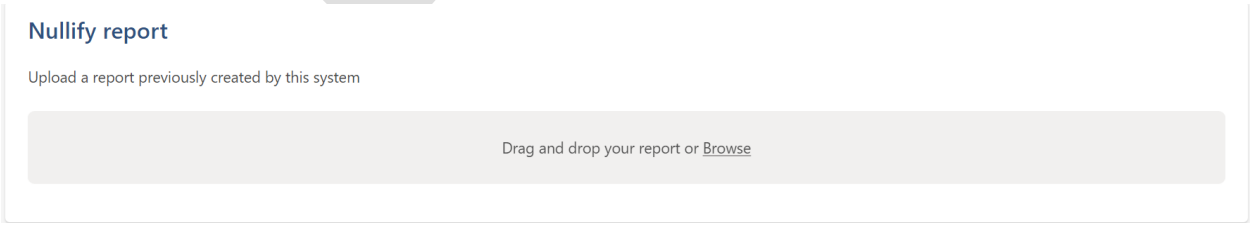


Once you have finished capturing the tracking information, you must submit the report and download the corresponding XML file. Remember that if you don't download the file, you won't be able to track it later.

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

3.7.1.2.4. 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.



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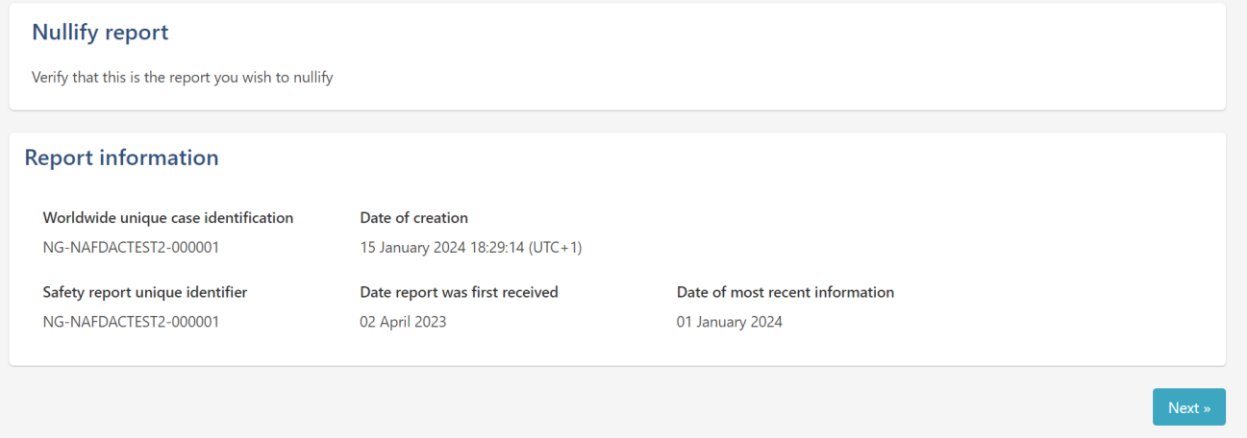
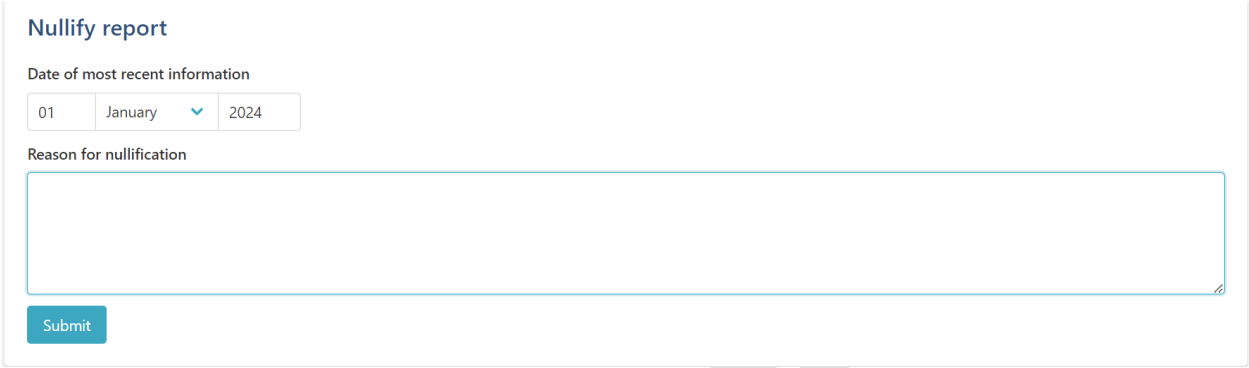
Load the generated XML file you want to override, which you should have saved on your computer, either by dragging and dropping it into the gray section or by opening it from your file explorer with the “Browse” *option.*

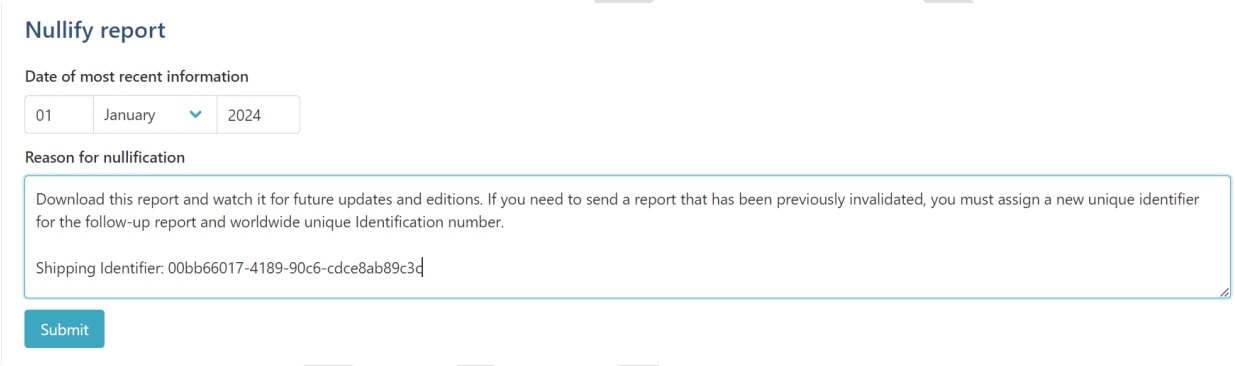
Verify the information of the report you want to cancel



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*

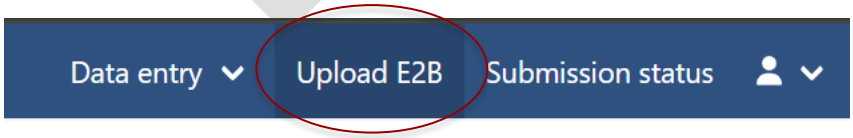


Download the deleted report XML file and save it to your computer for future updates.

3.7.2. Upload E2B module

This module is exclusive for use by the industry that already has the approval of the NPC to carry out the notification in this way.

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



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

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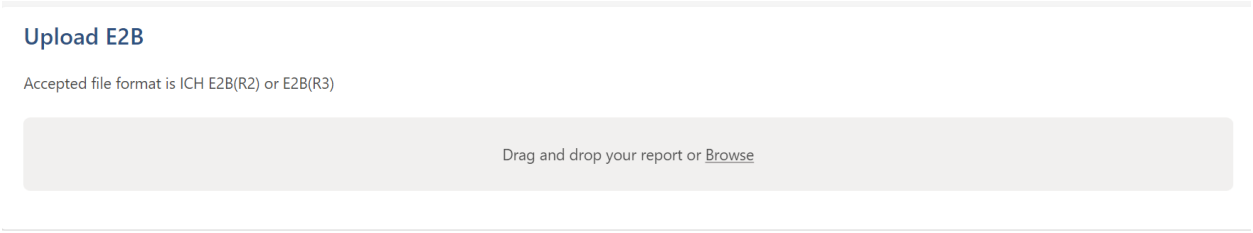
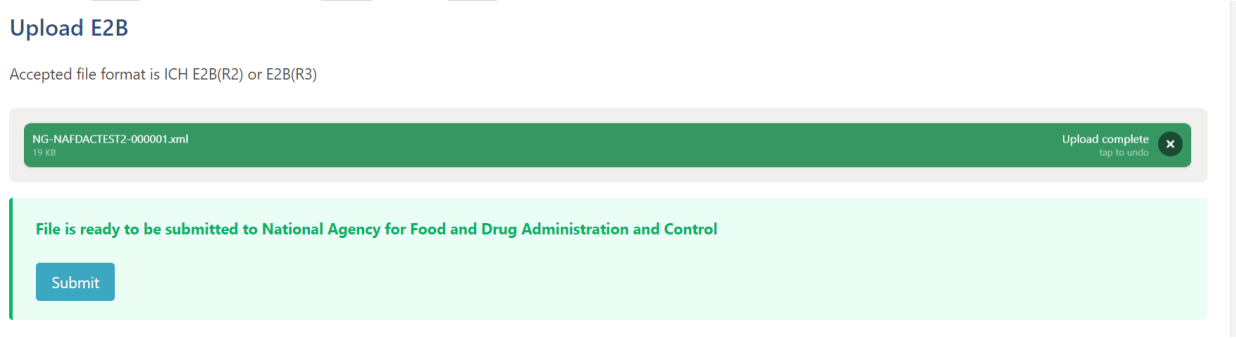


3. Files should be uploaded individually. Drag the XML file to the gray box or click "Browse" to open your file explorer.

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

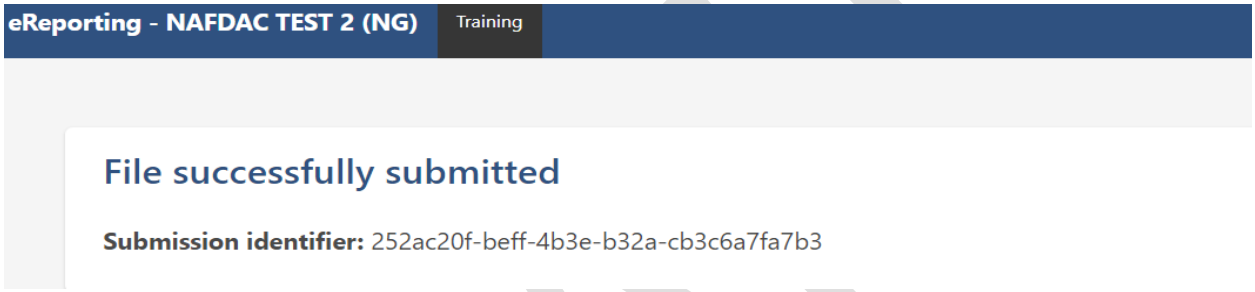
If the file meets the ICH R2 or R3 format specifications, it will be uploaded successfully as shown below:



4. Click on "*Send*"

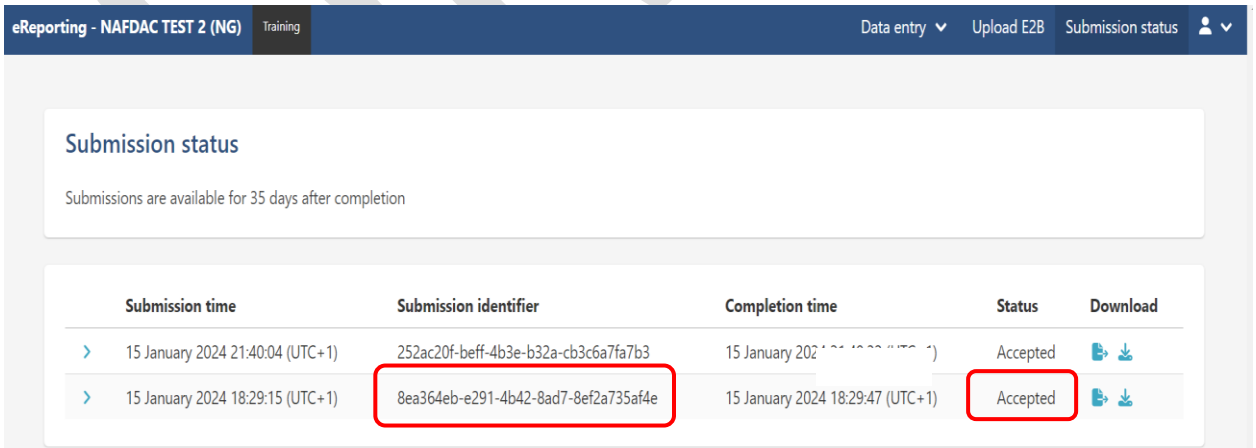
Important

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 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* "

4. Annex A: Terms and conditions for the use of the e- Reporting Industry

Description

Industry E- Reporting is a platform developed by the Uppsala Monitoring Center (UMC) specifically for the pharmaceutical industry to notify the Regulatory Authority of Individual Case Safety Reports 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 nationwide. The National Pharmacovigilance Centre (NPC), NAFDAC operates VigiFlow at the national level as a country belonging to

the International Drug Monitoring Program of the World Health Organization (WHO) for the management of reports of adverse drug reactions.

Declarations:

NAFDAC declares that:

I. In line with the provisions of extant applicable regulations, the Pharmacovigilance Directorate oversees 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 notification of AEs, ADRs, AEFIs and any other safety problems related to the use of medicines and vaccines, including electronic tools for the notification, 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 Representative of Marketing Authorization holder in Nigeria.

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 e- Reporting for Industry.

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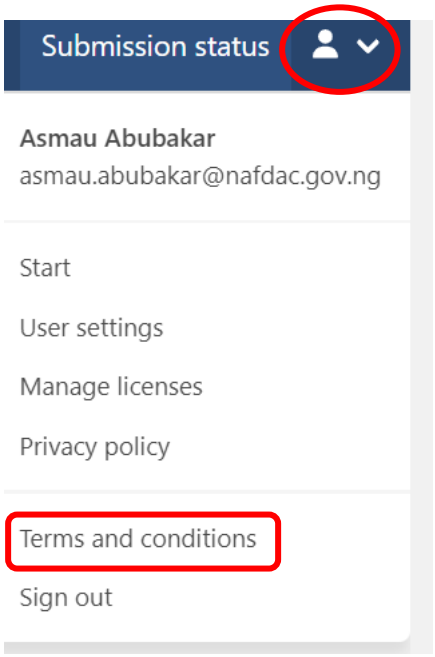
For more information, visit the section *Terms and conditions* located in the main menu



5. ANNEX B.
GLOSSARY OF TERMS

Adverse Drug Reaction (ADR)	A response to a drug which is noxious and unintended, which occurs at doses normally used in man for the prophylaxis, diagnosis, or therapy of disease, or for the modification of physiological function.

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Adverse Drug Reaction Reporting Form	A form designed and distributed by the National Pharmacovigilance Centre (NPC) for reporting ADRs
Adverse Event	Any untoward medical occurrence in a patient administered a medicinal product and which does not necessarily have a causal relationship with the treatment.
Active Pharmacovigilance	Active measures that are taken to detect adverse events. This is managed by active follow-up after treatment and the events may be detected by asking patients directly or screening patient records. The most comprehensive method is Cohort Event Monitoring (CEM).
Algorithm:	Systematized decision process, which consists of an ordered sequence of steps, in which each of these depends on the result of the preceding one. The use of algorithms to make clinical decisions tends to decrease the variability between observers.
Causality Assessment	The method used for estimating the strength of relationship between product(s) exposure and occurrence of adverse reaction(s). Causality assessment includes evaluation of temporal relationships, association with (or lack of association with) underlying disease, presence (or absence) of a more likely cause, and biologic plausibility.

CRH:	The company or legal entity, in whose name the marketing authorization for a product has been granted and is responsible for all aspects of the product and compliance with the conditions of marketing authorization.
Drug	Any substance which has a physiological effect when ingested or otherwise introduced into the body.
E2B:	Standardized submission format for the transmission of individual case safety reports.
Expedited Adverse Event Reporting	Refers to urgent reporting of selected adverse events through the Division of Acquired Immunodeficiency Syndrome (DAIDS) Adverse Experience Reporting System. All reported events must also be entered into the Adverse Event Log.
Expected Reaction	A reaction that is consistent with the applicable product information or characteristics of the drug. The reaction can be explained from the mechanism of action of the drug.
Health Product	Any product, substance or a mixture of substances used or purported to be suitable for use that is manufactured or sold for use in the diagnosis, treatment, mitigation, modification or prevention of a disease, abnormal physical or mental state, or the symptoms thereof, in

	humans or animals; or for restoring, correcting or modifying any somatic, psychic or organic function in humans or animals. A health product can include medicines, herbal products, vaccines, antisera, biological and blood products.
Health Products Regulation	All the processes involved in the pre-marketing evaluation, marketing authorization, and post-marketing review of medicines, vaccines, devices, and other health products to ensure compliance with established standards of quality, safety, and efficacy.
Healthcare Professional	A healthcare professional is a qualified person who has acquired the requisite knowledge, skills and competences to deliver proper health care in a systematic and acceptable way to any individual in need of healthcare services.
Healthcare Provider	A healthcare provider may refer to a health professional or other officially recognized people or organizations that provide healthcare services.
ICH:	International Conference on Harmonization, ICH for its acronym in English, consists of a joint project of regulatory authorities and the pharmaceutical industry from Europe, the United States and Japan, united with the aim of harmonizing technical and scientific

	requirements with the aim of to guarantee the quality, safety and efficacy of medicines.
Marketing Authorization Holder (MAH)	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	Any preventable events that may cause or lead to inappropriate medication use or patient harm while the medication is in the control of healthcare professionals, patient or consumer. Such events may be related to professional practice, healthcare products, procedures and systems including prescribing, order communication, product labeling, packaging and nomenclature, compounding, dispensing, distribution, administration, education, monitoring and use.
Medicine	Any substance or product administered to humans for the prevention, diagnosis, or treatment of any disease or its symptoms or for the modification of physiological function.

National Agency for Food and Drug Administration and Control (NAFDAC)	An agency established by the Federal Government of Nigeria through promulgation of the NAFDAC Decree 15 of 1993 (as amended) now cited as Act Cap N1 LFN 2004 to control and regulate the manufacture, importation, exportation, distribution, advertisement, sale, and use of food, drugs, cosmetics, chemicals/detergents medical devices and all drinks including packaged water.
National Pharmacovigilance System (NPS):	The nationwide medicine safety system, coordinated by the Nigerian Drug Regulatory Agency (NAFDAC) to improve benefits and reduce harm related to the use of medicines by the public through the efficient mobilization of various stakeholders and resources at all levels and in all sectors.
Passive Pharmacovigilance	There are no active measures taken to look for adverse effects other than the encouragement of health professionals and others to report safety concerns. Reporting is entirely dependent on the initiative and the motivation of the potential reporters. This is the most common form of pharmacovigilance. It is commonly referred to as spontaneous or voluntary reporting. In some countries this form of reporting is mandatory.
Periodic Safety Update Report (PSUR)	A report produced by an MAH intended to provide an update of a worldwide safety experience (with some

	focus on Nigeria) of a medicinal product to the competent authorities at defined times post authorization.
Pharmacovigilance	Science and activities relating to the detection, assessment, understanding and prevention of adverse effects or any other drug-related problems.
Reporter:	Any person who describes a suspected adverse effect to the relevant regulatory or competent authority (NPC, NAFDAC etc.).

Serious Adverse Event or Reaction	A serious adverse event or reaction is any untoward medical occurrence that at any dose results in death, requires in-patient hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity or is life-threatening. *To avoid any confusion or misunderstanding of the difference between the terms "serious" and "severe", the following clarification should be noted. The term "severe" is not synonymous with "serious". Severity is used to describe the intensity of a specific event (i.e., mild, moderate or severe). The event itself may be of relatively minor medical significance (such as severe headache). Seriousness (not severity) which is based on patient/event outcome or action criteria serves as a guide for defining regulatory reporting obligations.*
Side Effect	Any unintended effect of a health product occurring at doses normally used in man which is related to the pharmacological properties of the drug.
Signal	Reported information on a possible causal relationship between an adverse event and a drug, the relationship being unknown or incompletely documented previously.
Spontaneous Report	An unsolicited communication by MAHs, healthcare professionals, or consumers that describes one or more

adverse drug reactions in a patient who was given one or more medicinal products and that does not derive from a study or any organized data collection scheme.

Spontaneous Reporting A system whereby case reports of adverse drug events are voluntarily submitted by health professionals and MAHs to the National Pharmacovigilance Centre.

Unexpected Adverse Reaction: An adverse reaction, the nature or severity of which is not consistent with the applicable product information or characteristics of the drug.

QPPV: An individual named by a Marketing Authorization Holder (MAH) as the main person responsible for ensuring that the company (the MAH) meets its legal obligations under the Good Pharmacovigilance Practice Regulations, Section 3C for monitoring of the safety of the product marketed in Nigeria.

6. ANNEX C

CAUSALITY ASSESSMENT ALGORITHM

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WORLD HEALTH ORGANIZATION (WHO) - UPPSALA MONITORING CENTRE (UMC) CAUSALITY ASSESSMENT CRITERIA	
Causality Term	**Assessment Criteria (all points should be reasonably complied)**
Certain	● Event of laboratory test abnormality, with plausible time relationship to drug intake ● Cannot be explained by disease or other drugs ● Response to withdrawal plausible (pharmacologically. pathologically) ● Event definite pharmacologically or phenomenological (i.e. an objective and specific medical disorder or a recognized pharmacologic phenomenon) ● Rechallenge satisfactory, if necessary
Probable/likely	● Event or laboratory test abnormality, with reasonable time relationship to drug intake ● Unlikely to be attributed to disease or other drugs ● Response to withdrawal clinically reasonable ● Re challenge not required

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Possible	● Event or laboratory test abnormality, with reasonable relationship to drug intake ● Could also be explained by disease or other drugs ● 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) ● Disease or other drugs provide plausible explanation
Conditional/unclassified	● Event or laboratory test abnormality ● More data for proper assessment needed, or ● Additional data under examination
Unclassifiable/Unassessible	● Report suggesting and adverse reaction ● Cannot be judged because information is insufficient or contradictory ● Data cannot be supplemented or verified

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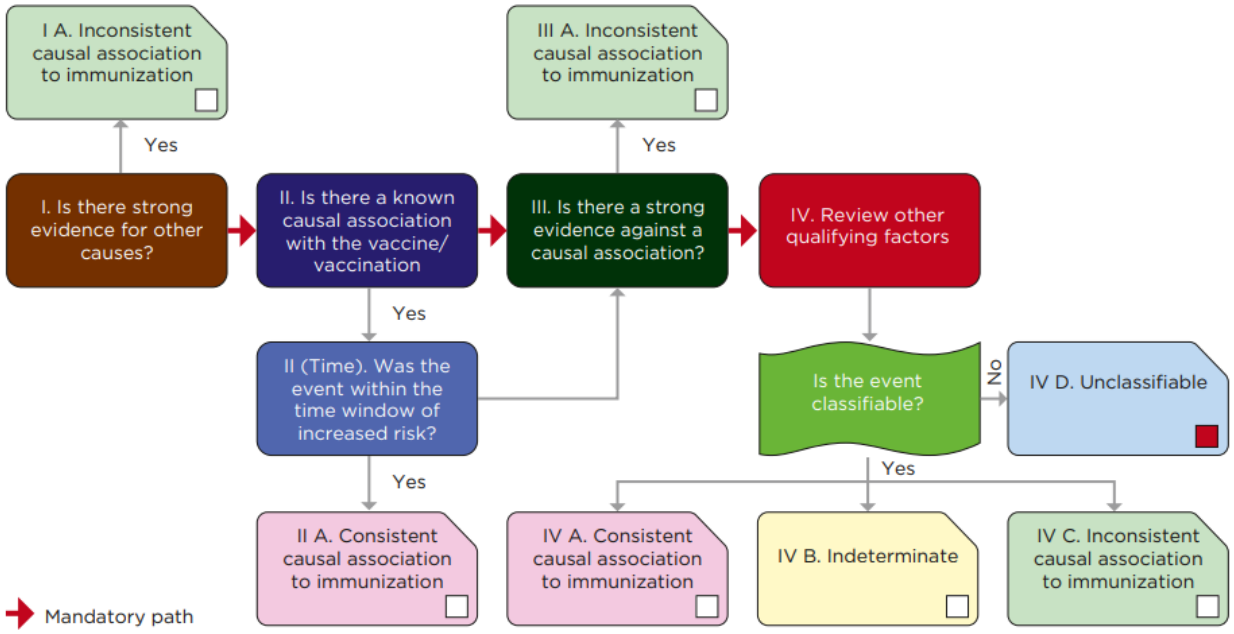


7. ANNEX D.

FREQUENTLY ASKED QUESTIONS

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

No, the tool is aimed at reporting Adverse Drug Reactions that occur in the country

What reports are subject to notification? Clinical studies / Spontaneous reports / Literature / Risk management plans, IPS

post- marketing, clinical 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: identifiable primary source, identifiable patient, medication, and adverse reaction. For more information consult the ICH guidelines.

Can I notify 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 NAFDAC.

How many users will be provided per Company, should the password be unique per user or is it necessary to create a password for each user?

At the moment, **three (3)** users will be granted for each MAH or CRH, 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 MAH/CRH?

In this case, the contract pharmacovigilance company must notify NAFDAC of the information about 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 buys the license of some products of another MAH/CRH, example:

✓ Case 1

PV Company A **representing** 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.

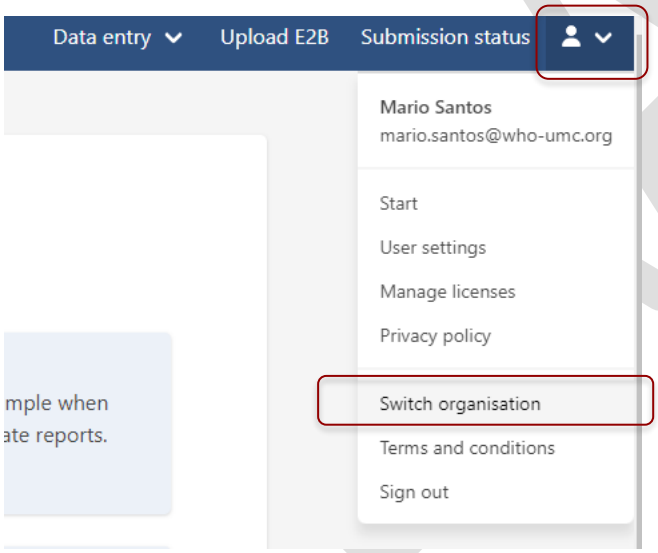
In this case, the owner of the product is MAH B, and the identifiers required in the system (company name, short name, sender identifier and sender Organization) must

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 (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, you will need to submit follow-ups until it is closed via email.

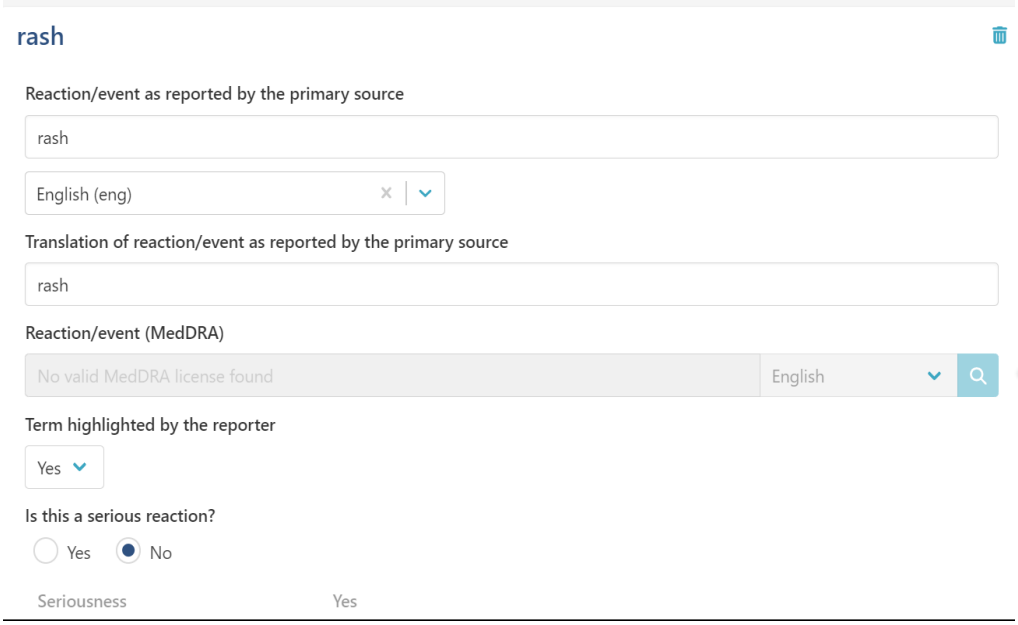
Is it possible for two users to report simultaneously (if there is more than 1 user)?

Yes. The Three accounts that are granted per MAH are independent and cases can be entered into the manual upload module or uploaded XML into the XML upload module simultaneously. But 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



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

MedDRA term.

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

Yes, it is essential that those who use this tool have a current MedDRA license.

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

No. If you leave a case entry incomplete and 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.

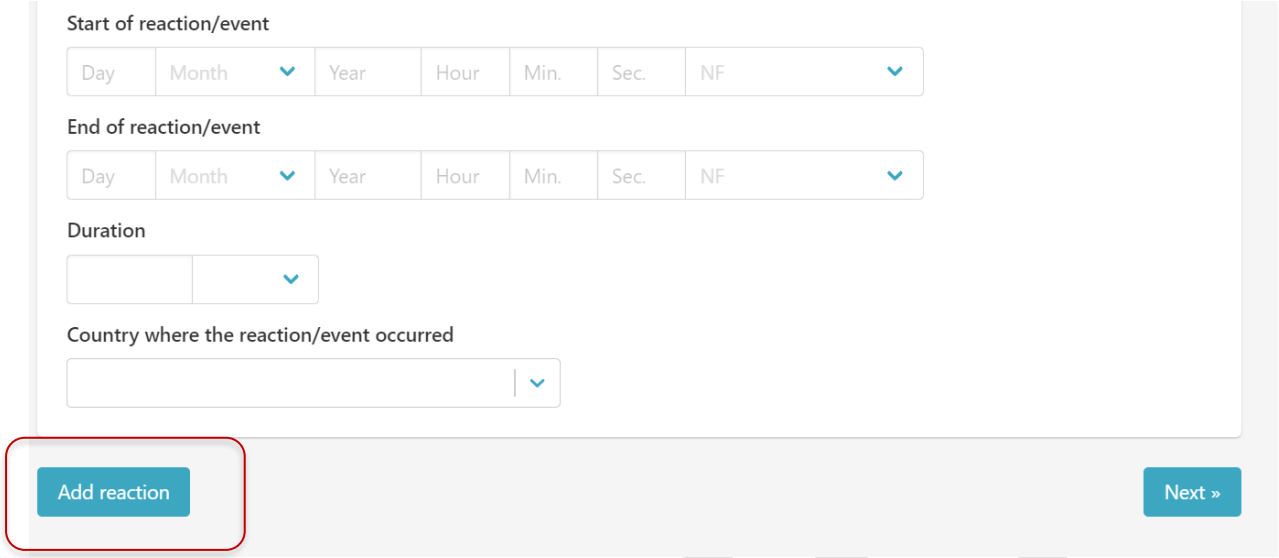
Will there be a time limit for uploading a case? How long can the session be kept active?

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 enter information, otherwise you must close it.

Should notification 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 Identification Number)?

The constant part is made up of the Country ISO code (NG) 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 Unique Security Report Identifier and the Globally Unique Identification Number?

The WWUID is the first identifier assigned to the report. The unique Identifier of the security 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 upload 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.

For clinical trials, is the clinical trial drug always the suspect drug?

You can add more than one suspect drug but the study drug and/or comparators in blinded studies should be marked as suspect at least.

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.*

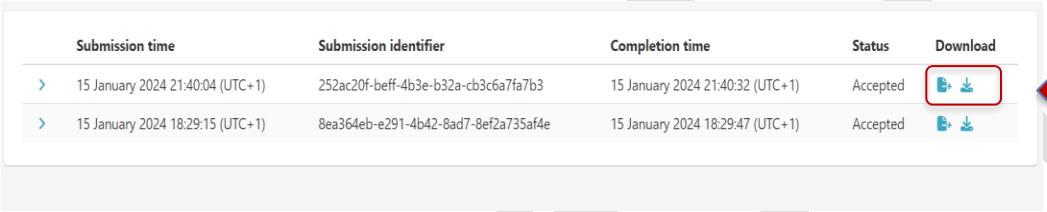
Should the causality of each of the reported PTs be included, regardless of whether it is a suspect or concomitant?

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

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

Previously loaded cases, speaking of all the information loaded 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 section* of the upper right menu.

The Industry e- reporting platform does not work as a database of cases; the MAH Pharmacovigilance Division must have 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 data in red, the report can be sent without a problem.

By what mechanism do you recommend evaluating the causality of the report?

NAFDAC recommends the implementation of the World Health Organization (WHO) - Uppsala Monitoring Centre (UMC) 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 evaluation is carried out by the pair "medication-reaction" so that as many evaluations as there are reactions 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 upload module, you should immediately download the XML file and save it to your computer directory (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 Information 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 notification 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.

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 using this email Pharmacovigilance@nafdac.gov.ng

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

It can be reported through the paper format and sent to the pharmacovigilance email (Pharmacovigilance@nafdac.gov.ng). The report should be sent through the e-reporting platform as soon as it 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 pharmacovigilnce@nafdac.gov.ng 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 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 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 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.

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 be loaded in the manual loading module? In the narrative?

In the free text field *Narrative case.*

When initially working with the manual 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 upload module and used to generate XML-E2B. This will prevent future problems with receiving cases in the XML upload module.

Can the causality evaluation method be medical judgement?

Priority use of standardized evaluation methodologies is requested.

If you cannot find the specific drug you wish to report through the WHODrug catalog, 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 NAFDAC 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.

Effective Date: Doc. Ref. No. PV-GDL-019-00
Review Date:

For any questions regarding license subscriptions, please contact:

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

8. ANNEX E

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

9. ANNEX F

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