Pharmacovigilance Guide for reporting AEs, SRAMs, ADRs, AEFIs, or any safety issues related to the use of medicines and vaccines.

March-2025

Change control: update to current institutional stationery

Av. Marina Nacional No. 60, 4th Floor, Colonia Tacuba, Miguel Hidalgo Territorial Demarcation, Mexico City, CP 11410

Tel: (55) 50 80 52 00 www.gob.mx/cofepris

Table of Contents

1. Introduction

The need for information technology systems applied to pharmacovigilance systems has been a recurring theme across all regulatory authorities. The most successful health information systems worldwide have enabled evidence-based decision-making. Pharmacovigilance, as a public health tool, requires systems for the identification, validation, analysis, and reporting of adverse drug reactions (ADRs), suspected adverse drug reactions (SDRs), adverse events (AEs), events presumed to be associated with vaccination or immunization (ESAVIs), and other safety issues related to the use of medicines and vaccines, enabling compliance with one of the crucial activities of pharmacovigilance: reporting.

2. Objectives

2.1 General objective

Describe the use of the reporting tools available to the National Pharmacovigilance Center (CNFV) for reporting SRAMs, ADRs, AEs, ESAVIs, or any other safety issues related to the use of medicines and vaccines.

2.2 Specific objectives

- Establish the tool that each member of Pharmacovigilance will use.
- Provide instructions for the correct operation of VigiFlow, the correct completion of the e-Reporting electronic form, as well as the procedure for the electronic transfer of XML-E2B.

3. Generalities

Based on the operation of Pharmacovigilance in Mexico through which its members (Figure 1) carry out the notification of SRAM, ADR, AE, ESAVI, or any other safety problem related to the use of medicines and vaccines, as well as the specifications in the transfer of information defined by the Uppsala Monitoring Center (UMC) under the international standard, as well as in the operation of the VigiFlow tool and its hosted services, the National Pharmacovigilance Center has established the means of notification that will be applied by the members of Pharmacovigilance in accordance with what is determined in NOM-220-SSA1-2016, and which are defined in Table 1.

Figure 1. Members of Pharmacovigilance

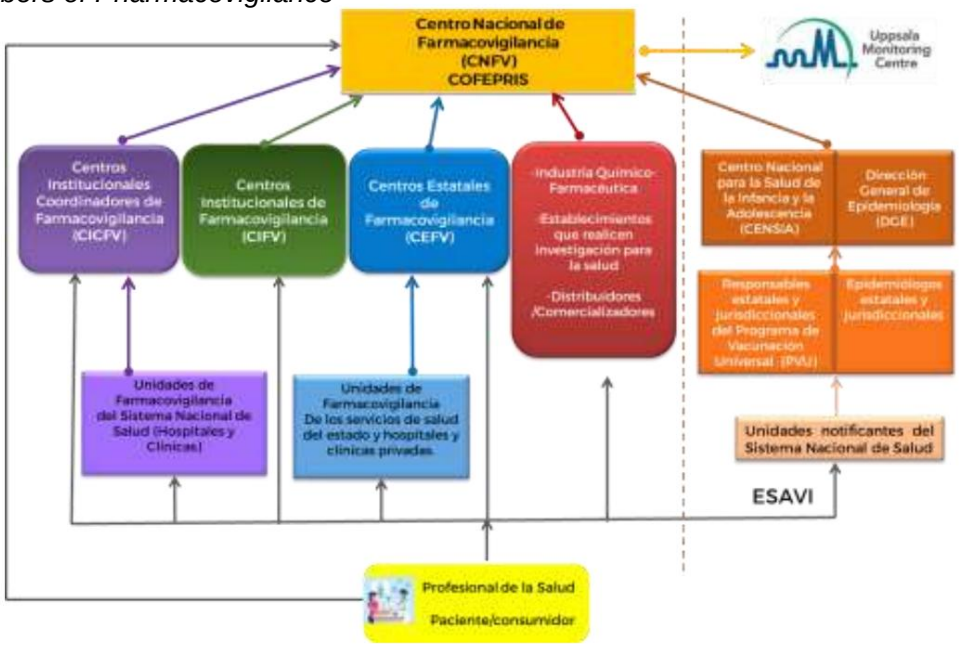


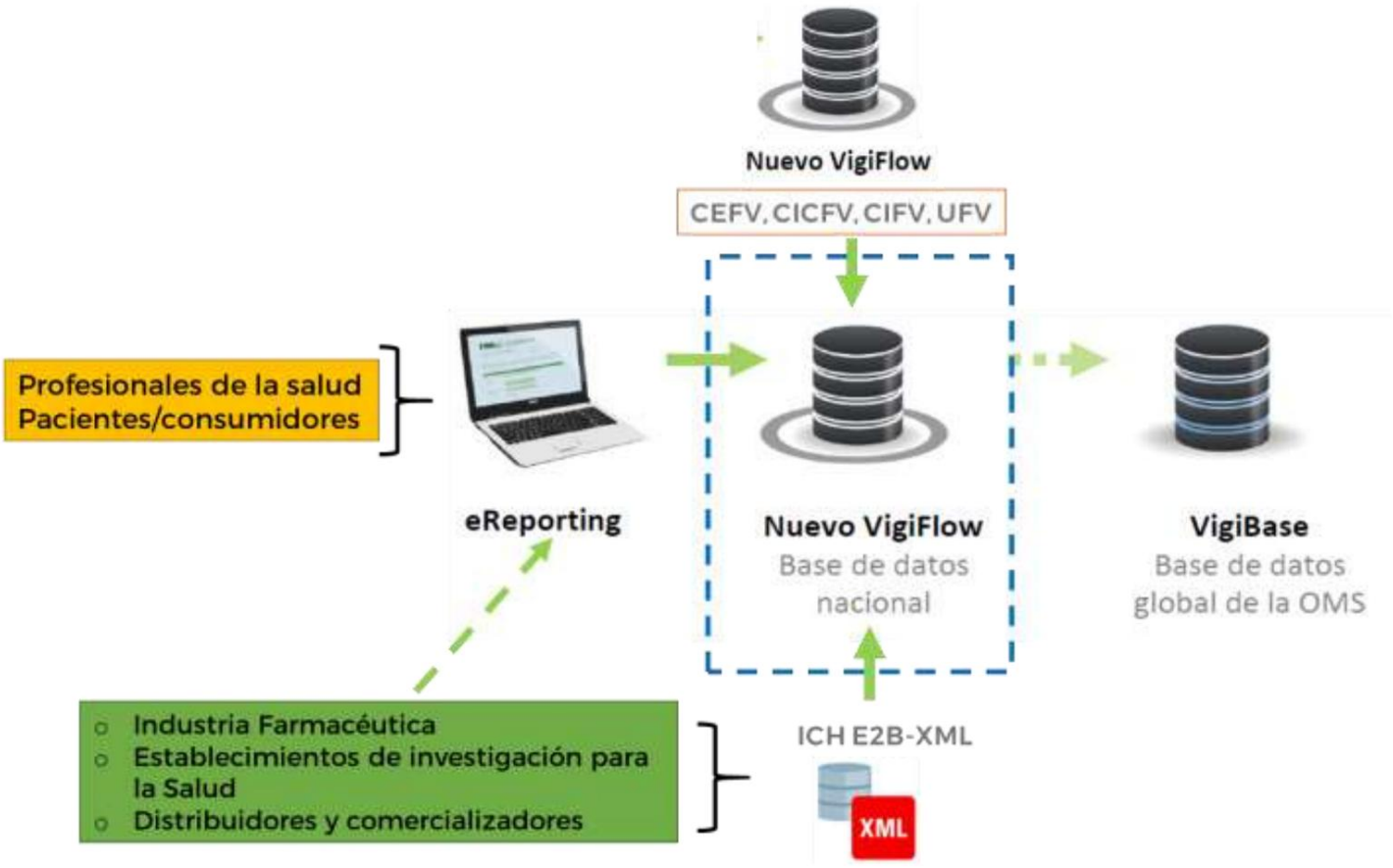
Table 1. Notification media in Pharmacovigilance.

Member	Tool to use
National Pharmacovigilance Center (CNFV)	VigiFlow
State Pharmacovigilance Centers (CEFV)	
Institutional Pharmacovigilance Coordinating Centers (CICFV)	
Institutional Pharmacovigilance Centers (CIFV)	
Pharmacovigilance Units (UFV) dependent on CEFV and CICFV	
Registration holders or their legal representatives, institutions or establishments that carry out health research, distributors/marketers that **They** have the capacity to carry out the electronic transmission of reports in XML-E2B format.	**Sending files** **XML-E2B.**

Registration holders or their legal representatives, institutions or establishments that conduct health research, distributors/marketers that **DO NOT** currently have the capacity to carry out the electronic transmission of reports in XML-E2B format.	~~e-Reporting~~
Health professionals and patients/consumers	~~e-Reporting~~ Email Phone Comprehensive Center of Services

VigiFlow at the central level is powered by different sources as shown in Figure 2:

Figure 2. VigiFlow power supplies



4. VigiFlow

4.1 Generalities

VigiFlow is an online notification management system for SRAM, ADR, AE, ESAVI or any safety problem related to the use of medicines and vaccines. It operates as the database of the National Pharmacovigilance Center, allowing the reception, processing and analysis of notifications, thus facilitating the transfer of information to the WHO/WBU global database thanks to the system's compatibility with the international standard ICH-E2B (R2 and R3). VigiFlow also allows the import of XML files with the E2B standard, in order to exchange reports with specific notifiers such as the pharmaceutical industry *(See section*

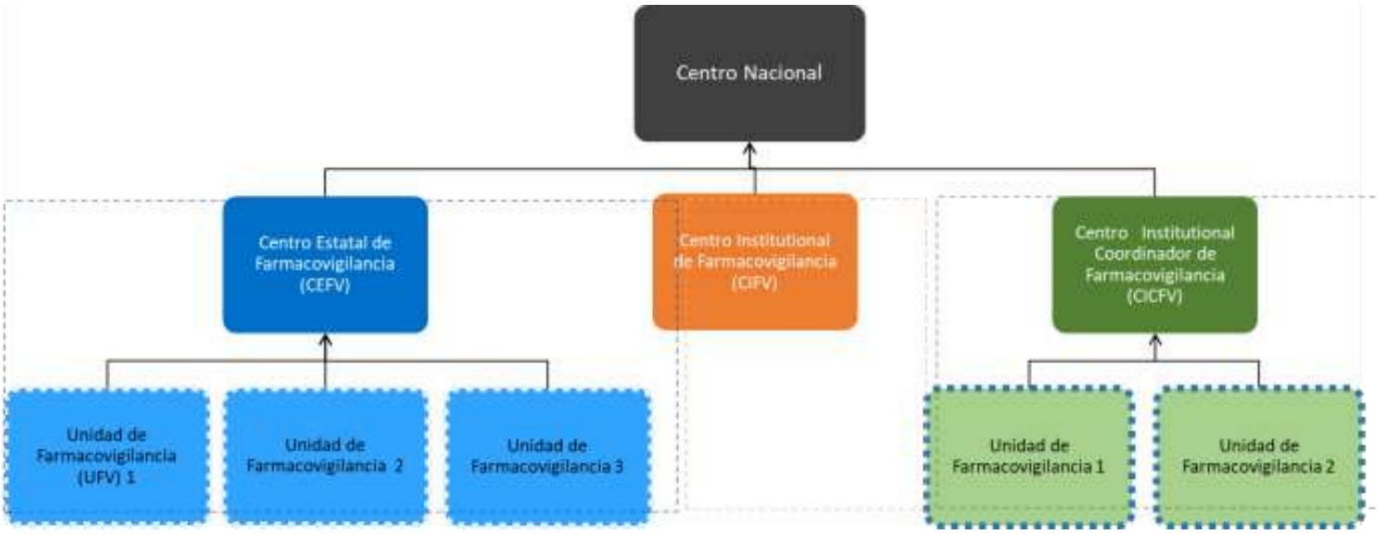
Electronic *transmission* XML-E2B).

The new version of VigiFlow allows for a hierarchical structure in its operation, enabling multiple regional Pharmacovigilance centers, as shown in Figure 3. This allows, among other things, direct reporting (in real time) to the CNFV database through three operating levels. The three levels defined for VigiFlow's operation are as follows:

Figure 3. Hierarchical structure in notification through VigiFlow.

Each organization within the hierarchical structure has access only to information from reports entered manually by that organization and organizations below that level.

Figure 4. Information flow through VigiFlow.



In addition to manually entering information into VigiFlow, there is also an electronic reporting format hosted on the COFEPRIS website. This electronic format was developed specifically to increase the participation of healthcare professionals and patients/consumers *(see e-Reporting section).*

The new VigiFlow uses structured and standardized catalogs to enter information on adverse reactions, medications, therapeutic indications, and other information (MedDRA, ICD-10, WHO drug catalog, etc.).
Note: The WHO-ART (WHO Adverse Reaction Terminology) catalogue has been deprecated for the new version of VigiFlow.

The technological resources necessary for the correct functioning of VigiFlow and e-Reporting are:

- A computer with a stable Internet connection
- Internet browsers.

4.2 Request for user accounts

It is important to note that the management of VigiFlow accounts will be handled by the Executive Directorate of Systems and Processes (DESP) of COFEPRIS.

The second level of operation (CEFV, CICFV, CIFV, CENSIA and DGE) may request accounts additional information for your organization must be sent to the following email address:

vigiflowcuentas@cofepris.gob.mx

Email requests must contain the following information:

Organization Name in VigiFlow (CEFV, CICFV, CIFV…)	**Name of the account manager requested**	**Email* (VigiFlow User)**	**Coding of notifications**	**Justification of the request for the account initial/additional**
Examples				
CEFV/CDMX	Gabriela Vazquez Morales	vazquezg@saludcdmx.gob.mx	CEFV/CDMX/ 00000/2020	The average number of notifications we receive per year in the CNFV is too much to be entered manually to be through a single account
CICFV/IMSS	Rubén Flores Market	floresmruben@imss.gob.mx	CICFV/IMSS	
CIFV/HJM *Juarez Hospital of Mexico*	Alicia López Lopez	pharmacovigilancehjmlopez@ hjm.com	CIFV/HJM/00 000/2020	

*It is required that the **email** account be an **institutional one.** If you don't have one or are having trouble with it, you can choose another account.

Third-level Pharmacovigilance Units (UFV) (units that report to the CEFV and CICFV, or those responsible for the PVU/ Epidemiology at the jurisdictional or local level, as defined) that have the technological resources to use VigiFlow must request user accounts from the CEFV, CICFV, CENSIA or DGE, as appropriate. The CEFV, CICFV, CENSIA or DGE must request user accounts for their third level from the CNFV, providing the following information:

Name of the Organization in VigiFlow of the second level	Name of the Institution of the third level	Name abbreviated proposed for the third organization level in VigiFlow	Name of the account manager requested	Mail electronic* (User of VigiFlow)	Coding of notifications of the unit of the third level	Justification of account initial/additional
Example						
CICFV/IMSS	Hospital General of Zone No. 30	UFV/IMSS/H GZ30	Franc Roldán Gomez	gomezroldanf@imss.gob.mx	UFV/IMSS/…	Based on the internal criteria of the number of annual notifications you must send a UFV to our charge to request an account VigiFlow, this UFV account meets this criterion.

Once the DESP receives the email and after approval from the CNFV, it will respond confirmation with specific instructions for accessing VigiFlow for the first time.

Second-level members may request the modification or deletion of accounts at their own or third-level levels, when appropriate, by submitting the same request by email. However, the user whose account needs to be modified or deleted must be indicated and justified.

4.3 Login

4.3.1 First-time login, application and password change

- To access VigiFlow, we recommend using Google Chrome, Mozilla Firefox, or Internet Explorer, in that order of preference.

- Go to the link: https://vigiflow.who-umc.org/

- Enter the username in the corresponding field, that is, the email address with which the CNFV registered it in VigiFlow *(See user account request).*

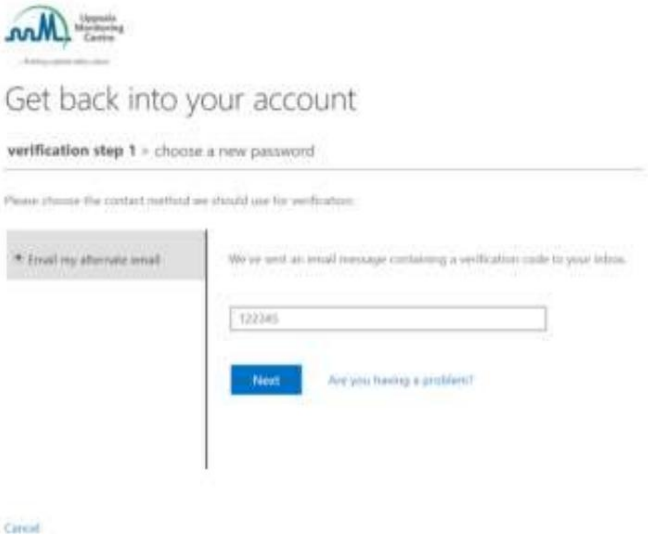
-

- Press the button: Can't access your account ?

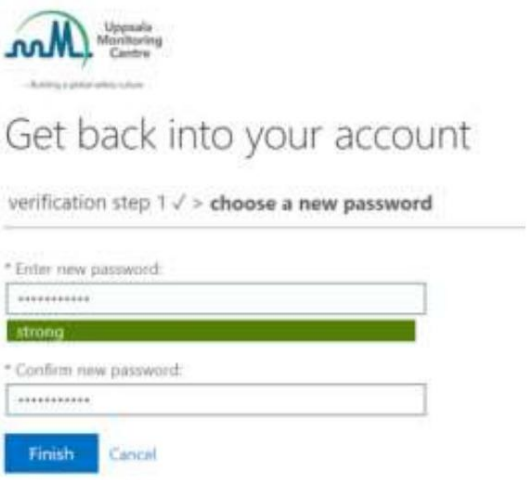
- In the **“USER** ID” field , verify the username entered.
- Enter the alphanumeric characters that appear in the box (consider upper and lower case).

- Press the “NEXT” button.
- Click the blue "EMAIL" box. It's important not to close this window. A 6-digit code will be sent to your email. Log in to your email and check the number sent to you.

- Copy the code sent to the open VigiFlow page, specifically in the box “Enter your verification code”
- Press the “NEXT” button.



- A page will appear where you must enter your new password, which must contain at least 8 characters (letters, numbers, uppercase, lowercase, symbols), and it is important that it does not resemble your username.
- Enter that same password in the box below to confirm your new password.
  password.
- Press the “FINISH” button.



- If the process was successful, a page will appear with a green **“ÿ”** and you will also be given will send a confirmation email.
- With the above process completed, you can log in from the main link of VigiFlow by entering your same username and new password.

NOTE: If you do not remember your password, it can be recovered using the same procedure described.

4.3.2 Logging in to VigiFlow

- Go to the link: https://vigiflow.who-umc.org/
- Enter your username and password in the corresponding fields.
- You can choose the *"Keep me signed in"* option so the system remembers your username and password so you don't have to enter them manually the next time you log in.
- Press the *"Sign in"* button .

IMPORTANT: You should not use your browser's automatic translator, as this may cause problems with field translations when you change the language to Spanish in VigiFlow. Therefore, if you have the automatic translator enabled, you should disable it.

Upon first login, you will be prompted to read and accept VigiFlow's terms and conditions of use.

- Click **“Accept.”** You can later read the terms and conditions of use from the VigiFlow home screen, which you can find in the bottom center under “Terms of Use.”

- The home screen you'll see is in English. You can change the language in the upper right corner of the screen where your username is located. Click the **"Language"** option and choose ***Spanish.***

If you need to log out of the system, click on the **“Log out”** option.

4.4 Main screen information

Note: The screenshots shown in this and subsequent sections are of the original character. illustrative. Some features shown may not apply to the second and third levels of VigiFlow.

The VigiFlow main screen is shown below:

The VigiFlow main screen contains a top menu with the following options:

1. **New report:** Enter a new report.

2. **Report import (XML-E2B):** function only operable by the first level (CNFV).
If you press the **"Report Import (XML-E2B)"** button , the following screen will open:

With this function, the CNFV can import XML files from the Pharmaceutical Industry *(See section XML–E2B Electronic Transmission).*

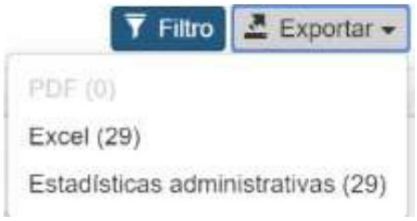
3. **Account Management:** Function only available to the Administrator user who carries out account management, i.e. the CNFV and the DESP.

Pressing the **"Account Management"** button will display the entire hierarchy of the structure arranged in VigiFlow.

4. **VigiLyze:** Feature only available for the first level (CNFV).

5. **Filter:** Displays a section of filters that will be applied to the specific notification search (see point 4.6.1 "Searching for notifications by filter") to the reports in your list, as shown below:

6. **PDF/Excel:** export all reports included in the list in Excel format through two modalities: Excel and Administrative Statistics.



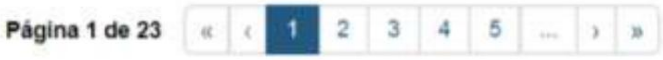
Below the main menu you will find the list of entered reports.

The display of entered reports has the following characteristics:

- The first level will display reports entered manually and all those entered through the second and third levels of VigiFlow. The list will also include reports entered through e-Reporting *(see e-Reporting section)* and reports imported through XML-E2B electronic transfer *(see XML-E2B Electronic Transmission).*
- Each member of the second level will be able to view the reports they manually entered into VigiFlow and, if applicable, the reports entered by the third-level UFVs under their charge, as well as those delegated to them by the first and second levels.
- Each member of the third level will only be able to view the reports they manually entered into VigiFlow, as well as those delegated to them by the first and second levels.

The lower section of the main screen as shown in the following table, contains a series of options that allow you to refer to different sites of interest:

Option	Function
Uppsala Monitoring logo Center	Links to the official UMC website
Contact	Links it to your email server to send an email to the UMC contact center
Privacy Policy	It links you to the Privacy Policy section of VigiFlow on the UMC website
Cookies	It links you to a section of the UMC website for a better understanding of the use of *Cookies*

Option	Function
Terms of use	It displays a window with the terms of use of VigiFlow
Help	It links to the VigiFlow website
MedDRA version: 22.1	Shows you the version of the MedDRA dictionary that VigiFlow currently includes
Page scroll bar	 >: next page >> last page <: previous page <<: first page

4.5 Entering a new report.

4.5.1 Preliminary Considerations.

Before manually entering a notification into VigiFlow you should consider the following: as a criterion for a good registration of a notification.

4.5.1.1 Duplicity detection.

VigiFlow, as a tool that draws on information from multiple sources, is not immune to receiving duplicate cases, that is, notifications containing the same information but with different coding. Therefore, before submitting a notification, you should ensure that it has not been previously submitted by your own organization or by a third-level Pharmacovigilance Unit.

For this, you must use specific search filters (see section 4.4 “Search Information”). main screen”) in order to detect duplication, such as:

- Initials
- Sex
- Date of birth
- Suspicious medication
- Reaction/event (MedDRA)

If you find that the notification has already been entered previously, you should check and identify whether the notification you were about to enter has additional relevant information that could modify the report already in VigiFlow (follow-up). If so, open the report corresponding to the first notification and enter the additional information.

4.5.1.2 Save a report.

As a good practice, it is important **to save** the report from the beginning of entering information in order to not lose the information entered due to mishaps such as internet disconnection, power failure, or any situation that prevents you from continuing to fill out the report.

By clicking the save button 

, will show you the following message:

If the **"Save"** button is gray instead of blue, it means that you have not added information that modifies the report.

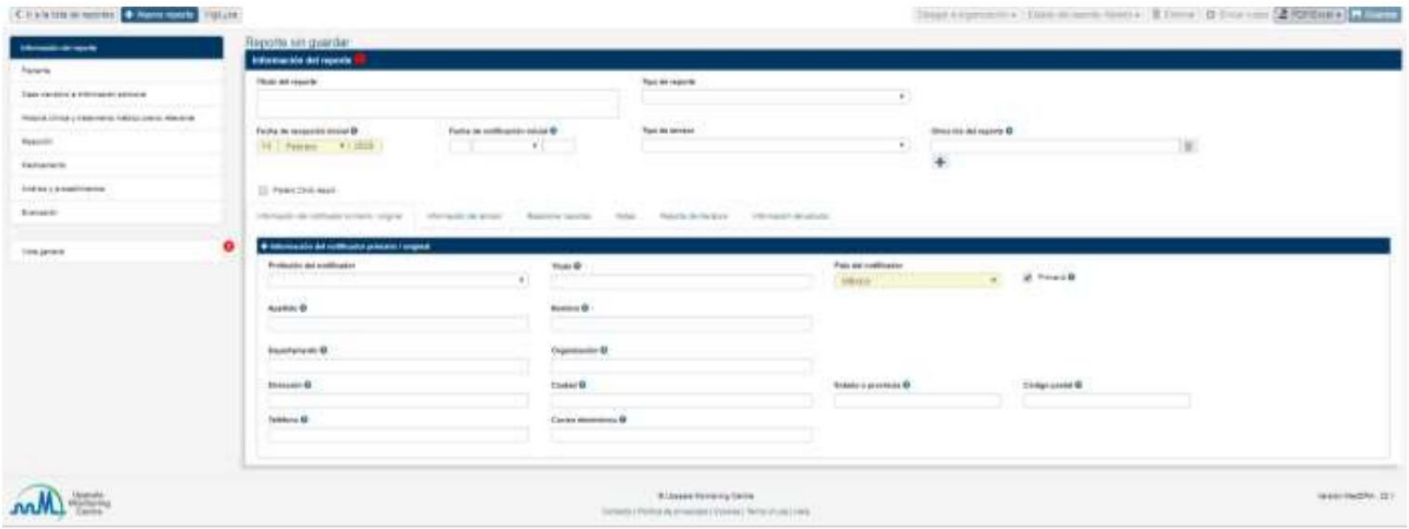
While it is possible to SAVE a report that does not include one or more required fields, without these fields, it will not be possible to submit the report to the WHO global database. Therefore, it will be the primary responsibility of the notifier (who manually enters the report into VigiFlow) or, if the report is delegated to the previous level, to collect the missing information to improve the quality of the information.

If you need to exit a report capture (by pressing "Go to report list") and you have not saved it at any time, the system will display a message like the following:

Choose the desired option.

In order to manually enter a notification/report into VigiFlow, you must click on the **"New report"** option on the main screen.

When entering a new report, the following window will appear:



The following buttons are displayed at the top right.

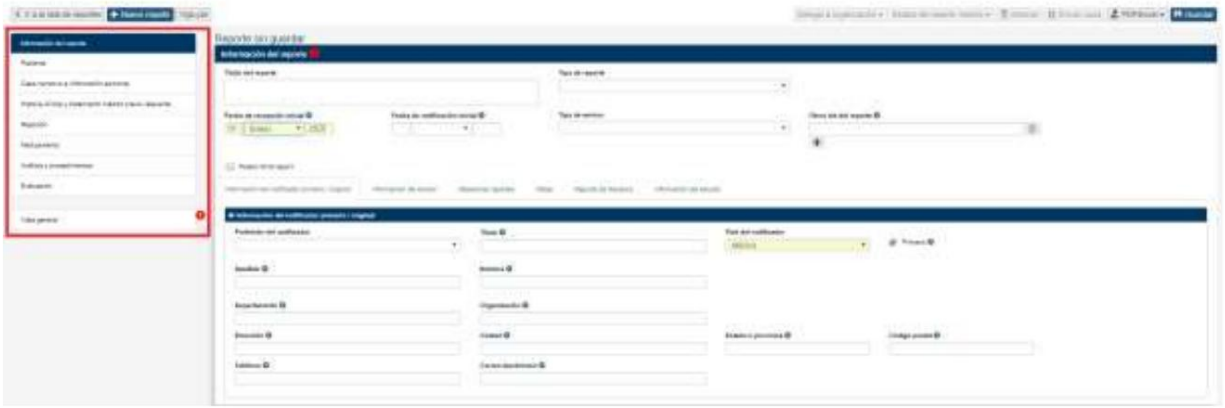
- **Go to report list:** returns to the VigiFlow home page where the list is displayed. of reports.
- **New report:** Enter a new report.
- **VigiLyze:** button enabled only for the CNFV that allows you to open the WHO global adverse reactions database.

- **Delegate to organization:** see section 4.6.4 "Delegation".
- **Report Status: Open:** You can assign a status to the report to organize your workflow. The default setting is "Open." For more details on this button, see section 4.9 "First, Second, and Third Level Functions in VigiFlow Operation."

- **Delete:** see section 4.6.5 "Deleting a report".
- **Send copy:** Send a copy of the report to the WHO global database to allow analysis in VigiLize. This option is only available for the CNFV.
- **PDF/Excel:** A menu appears with the option to download the PDF version of the report.

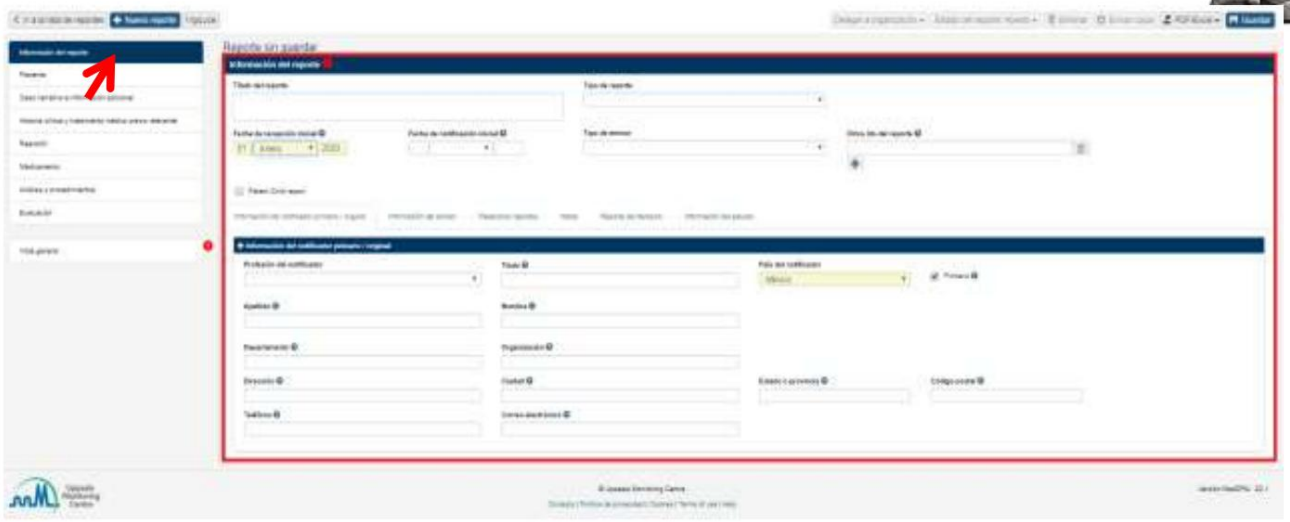
• **Save:** Saves the information entered up to that point. See 4.5.1.2 Saving a Report for details.

Continuing with the entry of a new report, a menu will be displayed on the left side with all the sections that make up a report:



In an enlarged way, the following menu is observed:

On the right side you will find the fields that include the specific section that is find marked in blue.



You can enter notification information either by clicking on each section in the left menu, or by choosing the **"Overview"** option , which displays all the sections and fields included in the report.

4.5.2 Mandatory fields to complete a report

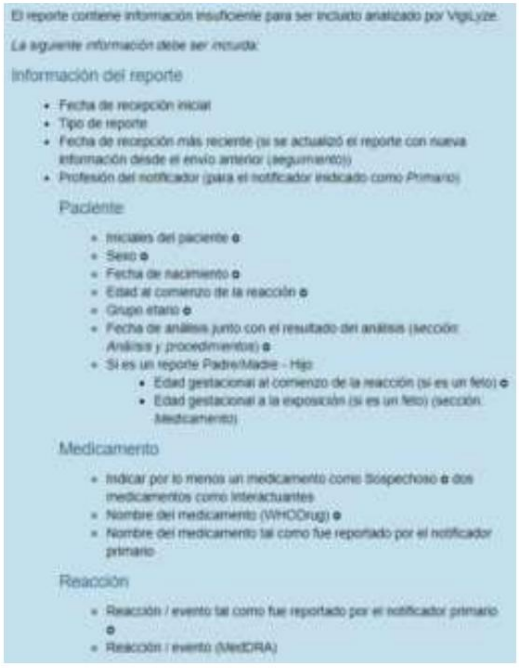
It is important to mention that VigiFlow requests mandatory fields in order to establish a report as valid, which are based on international requirements in
Pharmacovigilance and are the following:

Section	Required field
Report information	Initial receipt date, Report type, Most recent receipt date (modify this last date only when the report information is updated, i.e., during a follow-up), Occupation of the primary notifier (known in Mexico as *Informant* according to NOM-220-SSA1-2016).

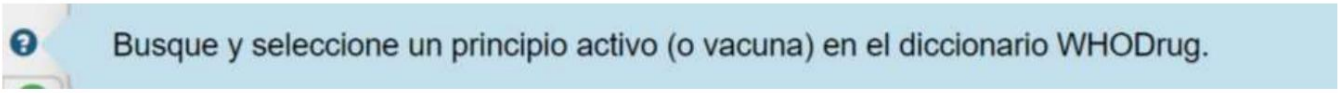
Patient	• Patient's initials or • Sex or • Date of birth or • Age at onset of reaction or • Age group or • Date of analysis together with the analysis result (section: Analysis and procedures) or • If it is a Father/Mother – Child report o Gestational age at onset of reaction (if a fetus) or o Gestational age at exposure (if a fetus) (section: Medicine)
Medicine	• At least one Suspected drug or two drugs Interactants • Name of the medicine (Distinctive or generic name) or • Name of the medication as reported by the notifier primary (in open field)
Reaction	• Reaction/event (MedDRA) or • Reaction/event as reported by the primary reporter (in free field)

When information is entered into any VigiFlow field, it changes color. YELLOW, differentiated from the empty white fields, as shown below:

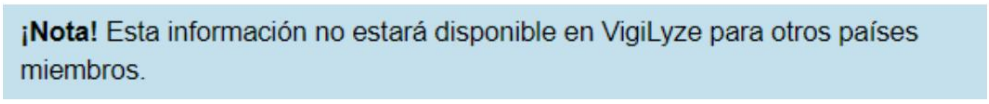
Required fields will be displayed in each report section using icons. You can explore them in each , section, or use the *Overview* option , which will display the full list of required fields throughout the report.



You will also find icons marked as such that when pressed, they will show you help boxes for filling out a specific field, for example: if you click on the icon corresponding to "name of the medication" located in the "medication" section, it will show you the following message:



You should also consider that there are fields with **private information** that the system will notify you will not be shared with other countries when the report is shared to the global database, as shown below:



4.5.3 Report information

This section is divided into two subsections. The first refers to identification of the report and contains the following fields:

You must include detailed information as shown in the following table:

Name of the field	Required information
Report title	This field will necessarily **be left blank,** it will only be filled in when the CNFV considers it necessary, for which the CNFV will communicate to VigiFlow users what title or information they should enter in this field.
Report type of	You will find the options: • *Spontaneous:* This is a report that comes to you from the informant without requesting it and is given in routine clinical practice. • *Study Report:* Choose this option for clinical study reports. If you choose this option, you must complete the "Study Information" section. Other: This option will specify literature reports, stimulated reporting notifications, and active surveillance or "active reporting." • *Not available to sender (unknown).*
Initial receipt date of	This refers to the date on which the report was first received by the entity that will capture the information in VigiFlow, whether at the first, second, or third level.
Date notification initial of	Refers to the date the case was first recorded by the initial notifier. In the case of stimulated notifications, such as through pharmacovigilance studies looking for ADRs, AEFIs, or SAMs, the initial notification date will be the date on which the ADR was found in the clinical record.
Most recent receipt date	This date will only apply when entering follow-up information and refers to the date on which follow-up information was received at the Pharmacovigilance Center (first, second, or third level).
Issuer type Refers to	the UFV, CEFV, CICFV, CIFV and even the CEFV that is entering

Name of the field	Required information
	manually the notification in VigiFlow. A catalog is displayed with the following options: • Pharmaceutical laboratory • Health professional • **Regional Pharmacovigilance Center** (if a report is submitted by the CEFV, CIFV, CICFV or their third-level UFV, they must choose this option) • Patient/consumer • **Regulatory authority** (this option is only applicable for reports submitted by the CNFV) • Other (e.g. distributor, study sponsor, contract research organization, or non-commercial organization)
Other Ids of the report	You must enter the coding assigned to your organization, based on what is specified for CEFV, CICFV, CIFV and UFV. Examples: • CEFV/AGS/00001/2020 • CICFV/IMSS/00001/2020 • CIFV/HGAEPY/00001/2020 • UFV/JAL/ANKER/00001/2020 Additionally, if a follow-up is entered, you must add a new “Id” by clicking on the “plus” sign (+). A new empty field will appear where you must enter the coding assigned to your organization, followed by a slash (/), the letter “S” and the tracking number corresponding to the notification. Examples: In the case of a first follow-up, i.e. when updated information on a report was received for the first time: • CEFV/AGS/00001/2020/S1 • CICFV/IMSS/00001/2020/S1 • CIFV/HGAEPY/00001/2020/S1 • UFV/JAL/ANKER/00001/2020/S1 Example: A UFV enters a new report and subsequently its first follow-up. 

Name of the field	Required information
	In this field, you can enter as many IDs as the issuer requires to facilitate a report search that may not be possible through the preset filters in VigiFlow. Examples include: internal case identification number, patient medical record number, file number, protocol code in the case of clinical studies, among others. In general, you can add as many IDs as you consider necessary, taking advantage of their usefulness to identify and find a specific notification or group of notifications. It is the responsibility of the CEFV and CICFV to review, verify, and validate the information contained in the reports submitted by their UFV (third level). Once the report is validated, the coding corresponding to the corresponding CEFV or CICFV will be added. Example: A level 2 Pharmacovigilance Center (CEFV) receives a notification from its corresponding UFV and, after reviewing and validating it, adds its corresponding coding. 
Security Report ID	Once the report is saved for the first time, the system creates this ID, which is composed of the following 3 elements: **<country code>-<organization name>-<consecutive number>** This security report ID can be viewed in two sections in the report information section: 
Report Number	If the report was entered manually in VigiFlow, the report ID

Name of the field	Required information
unique global identification	The security and Globally Unique Identification Numbers will be the same. They will only differ when the CNFV imports XML-E2B files, where the Globally Unique Identification Number will be represented by the name and country of the organization (pharmaceutical industry) that submitted the XML file.
(Parent Child report) Parental report	When you have a report where the patient is a fetus or newborn suspected of having been exposed to one or more medications and has experienced one or more adverse reactions, you must select this option. When you do so, specific information fields for this type of report will be enabled in the "Patient" section and must be filled out. Also, in the "Medication" section, two specific fields will be displayed: the "Administration Route" used by the father or mother and the gestational age at the time of exposure. This section is essential for reporting medication or vaccine exposure before and during pregnancy, as well as the corresponding follow-up established by NOM-220-SSA1-2016. There are cases where the father can influence the adverse reaction experienced by the fetus. For example: A drug that causes mutations in the genetic material of sperm, which can lead to alterations in the embryo; elimination of a drug through seminal fluid.

The second subsection consists of six information tabs, which we'll call "components." Each component should include detailed information where applicable, as shown below:

ÿ **“Primary Notifier Information” Component**

For our regulations, this section should be interpreted as information about the "reporter," who may be a patient/consumer or healthcare professional. This section should capture the information corresponding to the person who reported the case to the sender.

It must include detailed information as shown in the following table:

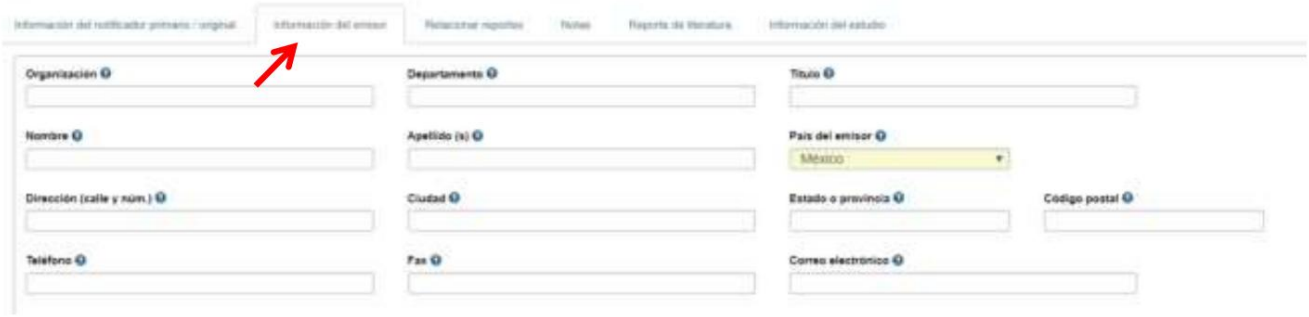
Field	Information required from the informant
Profession of the notifier	Choose from the options: “doctor,” “pharmacist,” “other healthcare professional,” “consumer,” or “other professional.”
Qualification	If you choose "physician" in the notifier's profession field, you can add the doctor's specialty in this field, or if you choose "other health professional," you can specify this professional's specific profile, as well as if you choose "other professional."
Notifier Country Mexico will automatically appear. Do not modify.	
Primary	You can add more than one notifier if the report has been sent through physical means such as paper before reaching you, but only one should be marked as "primary" in this box.
Last name	Informant's paternal and maternal surnames
Name	Name(s) of the informant
Department	If you are a physician, pharmacist, or healthcare professional working in a healthcare institution, please provide the specific department or area within the institution from which the case was reported.
Organization	If you are a doctor, pharmacist, or healthcare professional working in a healthcare institution, please provide the name of the institution.
Address	Street, exterior and interior number, neighborhood
City	Municipality or territorial demarcation
State or province	Federative Entity
Zip code	CP
Phone	Telephone with area code
Email Email	

Except for the field “notifier's profession” all other information entered in This section will not be shared with the WHO global database.

It should be noted that if the primary/original reporter is a patient/consumer, it will be difficult to collect all the information requested in the table above. There are also fields that are not applicable to this reporter (department and organization), so the fields applicable to the patient/consumer must be selected.

ÿ **“Issuer Information” Component**

For the purposes of our regulations, this section should be interpreted as the information of the "notifier" of the case (the person who submits information related to a SRAM, ADR, AE, ESAVI, or any safety issue related to the use of medicines and vaccines to the CNFV). Therefore, the information corresponding to the person who is manually entering the report in VigiFlow must be entered here. The issuers may be the UFVs that report to the CEFVs or the CICFVs. They may also be the CEFVs themselves, CICFVs, CIFVs, or even the CNFV.



The fields requested in this section are similar to those for the primary/original notifier, but it should be noted that, for the issuer, it is possible to have information for all required fields. For the following fields, it is suggested to include the following information:

- Organization: name of the hospital, clinic where the third-level UFV is located, or name of the department, institute, second-level hospital, or name of the regional or national regulatory authority (when a CEFV or COFEPRIS are the issuers).
- Department: UFV, CEFV, CICFV, CIFV, CENSIA, DGE or CNFV.
- Title: Specify the specialty (if applicable) of the health professional who acts as transmitter.

Examples of identifying the primary/original reporter and issuer in a report.

a) A patient informs the person in charge of the UFV at the General Hospital in Zone X about a SRAM they experienced. In this case, the patient is the primary/original reporter (informant) and the UFV (third level) that enters the report into VigiFlow is the "sender."

b) A healthcare professional sends a paper report to the CEFV/CICFV/CIFV, and the latter captures it in VigiFlow. The healthcare professional will be the primary/original reporter, and the CEFV/CICFV/CIFV will be the sender.

c) The CNFV receives a notification from a patient via telephone. The patient is the primary/original notifier, and the CNFV will be the sender.

In certain circumstances, both the primary/original notifier and the issuer are the same person.

Example: a UFV that carries out intentional SRAM search with its patients
institution, hospital, clinic, etc.

ÿ **"Relate reports" component**

In this section, you can link reports that you believe may be related for some reason. To do so, enter the title(s) of the related reports (you can also enter the Security Report ID or Globally Unique Identification Number) in the ***"Related Report"*** field and describe why you believe the reports are related in the ***"Reason"*** field .

This section can be used to address problems related to the use of medications and vaccines, such as accidental overdoses in a medical unit, use of a medication after its expiration date, medication errors, suspected counterfeit medication, occupational exposure, among others. Within NOM-220-SSA1-2016, this section may address the reporting of two or more similar serious cases in the same location, with the same medication and from the same batch. These cases must be reported immediately, no later than 48 hours after becoming aware of the cases.

ÿ **"Notes" component**

This is a free-text field where you can add internal comments about the report, for example, specifying the report type: **stimulated, active.** This information will not be shared with the global database or exported to Excel or PDF.

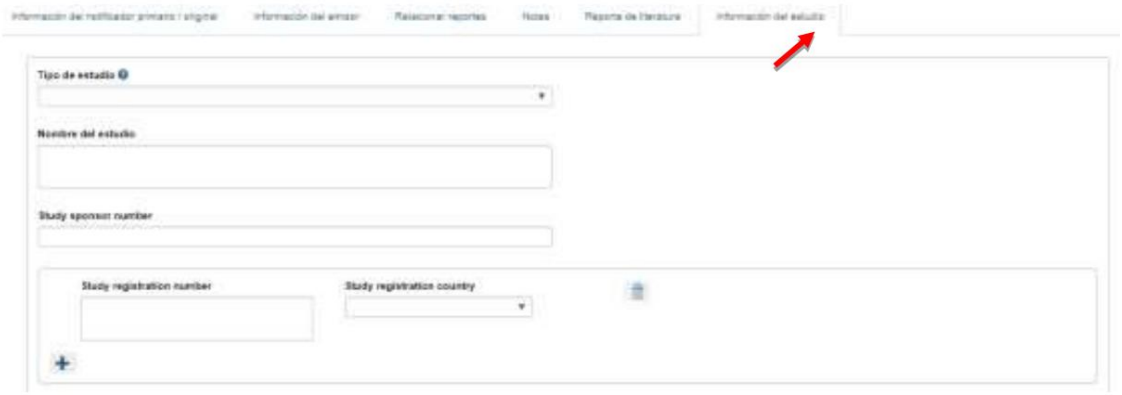
ÿ **"Literature Report" Component**

If you have a literature report and specified it in the *Report Type* field by selecting "Other," you must include the bibliographic reference(s) from which you obtained the report in this section. Citations should be in Vancouver Style.

You can add another reference by clicking on the icon .

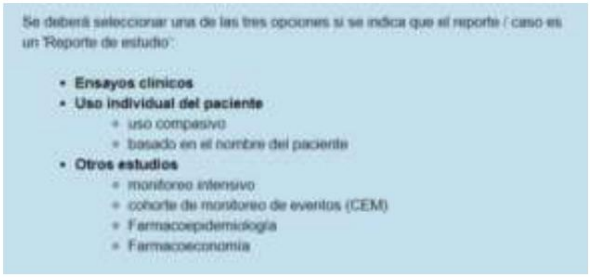
ÿ **"Study Information" Component**

If the report is a Clinical Study case and you specified it in the *report type* field
As a "clinical study report", you must include additional information about the study in the study information section.



• Type of study: you must choose between "Clinical Trials", "Individual Patient Use" or "Others".

ÿ Select **Clinical Trials** for Interventional Clinical Studies (Phase I to IV)
ÿ Choose **Individual Patient Use** for *Compassionate Use* cases .
ÿ Select **Other Studies** for cases from intensive monitoring, event monitoring cohorts, pharmacoepidemiology studies, and pharmacoeconomics studies. Pharmacovigilance studies can be classified under this heading (including those included in Risk Management Plans).



- Study name: You should preferably include the name of the study as established in the authorization issued by the Health Authorization Commission. If this name is not available, include the title as reported.

- **Study sponsor number:** study sponsor number.
- **Study registration number:** Study registration number or protocol number, if available, preferably as established in the authorization issued by the Health Authorization Commission.
- **Study registration country:** Study registration country.

4.5.4 Patient

This section is critical for patient identification. You must remember which fields are required in this section to obtain a valid report.

4.5.4.1 Basic fields

You must include detailed information as shown in the following table:

Field	Information required from the informant
Initials*	You must start in capital letters by placing the first letter of the paternal surname, followed by the first letter of the maternal surname and finally place the first letter of the name(s). Example: Raúl Alberto Aceves González, should be coded as follows: manner • First letter of the paternal surname = A • First letter of the maternal surname = G • First letter of name(s) = RA Remaining as follows: **AGRA** If the report is from a clinical study, the initials will be replaced by the identification code assigned to the study subject. If you do not have this information, leave the field blank.
Sex	Choose the option as appropriate between *male, female* or *unknown.*
Date of last menstruation	This box will only be enabled if you selected *female* in the gender field. If relevant and have the information, enter the date in the format *dd/ select month/ yyyy.* You can enter at least the year.
Weight (kg)	Enter the information in kilograms and, if necessary, use a period as a decimal separator.
Height (cm)	Enter information in centimeters.
Date of birth	Enter your date of birth in the format *dd/ select month/ yyyy.* You can enter at least the year.
Age at onset of reaction	If you don't know the date of birth, you can add the age at the time the reaction occurred in the corresponding field.
Age group	It is not necessary to indicate the age group to which the patient belongs, only if both the date of birth and the age at the beginning of the treatment are unknown. reaction you can enter the patient/consumer's age group. Choose from: fetus, neonate, infant, child, adolescent, adult, or senior.

* This information will not be shared with the WHO global database.

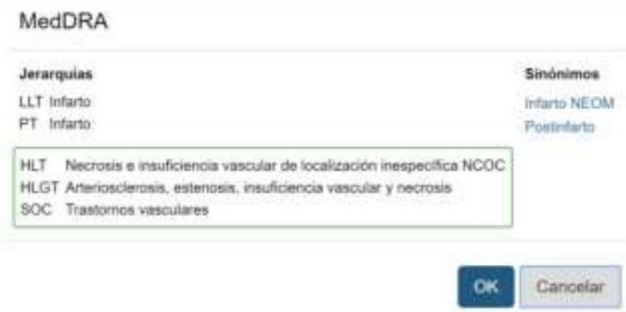
4.5.4.2 Additional fields

There are additional fields where you can add information about a research project. severe case and cause of death.

In this section you must include detailed information as shown in the following table:

Field	Information required from the informant
Specialist identification number*	If an identification number is provided, this field can be used to identify the specialist who treated the patient.
General practitioner identification number*	If an identification number is available, this field can be used to identify the general practitioner who treated the patient.
Hospital record number*	If you have a medical record number, you can provide the information in this field.
Number identification of the investigation*	If an investigation was conducted on the case and you have an investigation number, enter the identifier in this field.
Date of death	Enter the information if available in the format *dd/ select month/ yyyy.* You can enter at least the year.
Was an autopsy performed?	If you know the information, indicate whether an autopsy was performed by selecting the corresponding box (YES, NO, UNKNOWN). If you have selected an option and need to remove it, you can clear the boxes by clicking "Clear fields."

Field	Information required from the informant
	Selecting “YES” will display the option “Cause of death determined by autopsy.”  You can enter the autopsy-determined cause of death via the MedDRA dictionary catalog (search and select the MedDRA preferred term (LLT) that most closely matches the autopsy-determined cause of death) or via free text in the “Autopsy-determined cause of death” field (include the autopsy-determined cause of death with words or short phrases). If you choose to do it through the MedDRA catalog you can do so by typing the desired term in the field, and the options that are closest to your search will be displayed, or you can choose it directly by browsing the complete MedDRA hierarchy with the icon . When you have chosen it, as shown in the next image:  Clicking the icon will display the higher-level hierarchies of the chosen term, as well as other lower-level terms. This way, you can easily check whether there is another term that better matches the one reported by the initial reporter and is related to the same medical concept as the preferred term (PT).

Field	Information required from the informant
	
Cause of death	If you do not have autopsy information and the report contains information about the cause of death, you can add it. as: • Cause of death (MedDRA): Search and select the lowest MedDRA term (LLT) or preferred term (PT) that most closely matches the reported cause of death by typing the desired term in the field or you can choose it directly by browsing the full hierarchy from MedDRA with the icon . • Cause of death as reported by the primary/original reporter: In this free text field, record the cause of death using words or short phrases.

* The information contained in these fields will not be shared with the WHO global database.

If you selected the “Parent-Child Report” checkbox in the *Report Information* section , you must fill out the fields in the “Patient” section with the information corresponding to the newborn or infant (not entirely applicable to a fetus). The same information will apply to the “Medical History” section.

In this section additional fields will be displayed to add information about the parents, which is summarized below:

- Parent/guardian information: Identification data (initials, sex, weight, height, etc.): fill out according to the patient fields.
- Previous parental medical history: Enter relevant medical history, for example, illnesses, conditions such as pregnancy, surgeries, psychological trauma, risk factors, among others, using the MedDRA catalog or free text. Enter the start and end dates of the illnesses, as well as comments from the treating physician. If you want to add another relevant condition to the medical history, you must press the icon. .

- Parental prior treatment: In this section, relevant medications previously administered to the parents will be entered. Previous experience with similar medications may also be included. The distinctive name, generic name, and therapeutic group are recorded in free text. It is also possible to enter the reason for prescribing the medication (in the MedDRA catalog), any ADRs the parents have experienced with the medication (enter "No adverse reaction" if the parents have not suffered any reaction), and the start and end dates of treatment (it is possible to enter at least the year). If you want to add another medication in this section, you must press the icon.

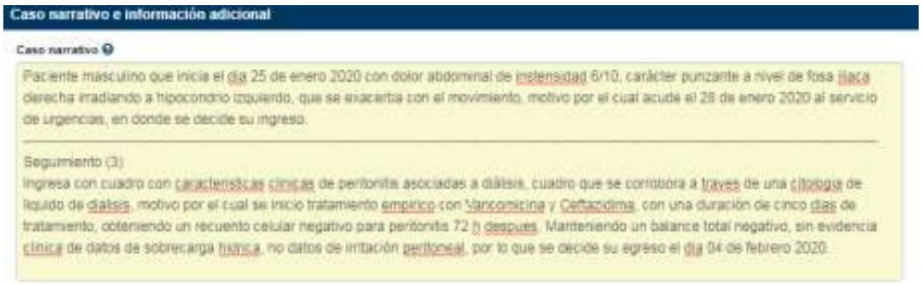
4.5.5 Narrative case and additional informat

In this section you will find two free text fields as shown in the following image:

Narrative Case: You must include the narrative of the case with the words and phrases used by the informant (as notified by him), maintaining the original narrative.

In case of updating a report (See point 4.7 Entering additional information of a report (FOLLOW-UP)) a dividing line must be added at the end of the previous text of the “Narrative case” field and below this place the legend “Follow-up (Follow-up number)” and then write the additional information.

Example:



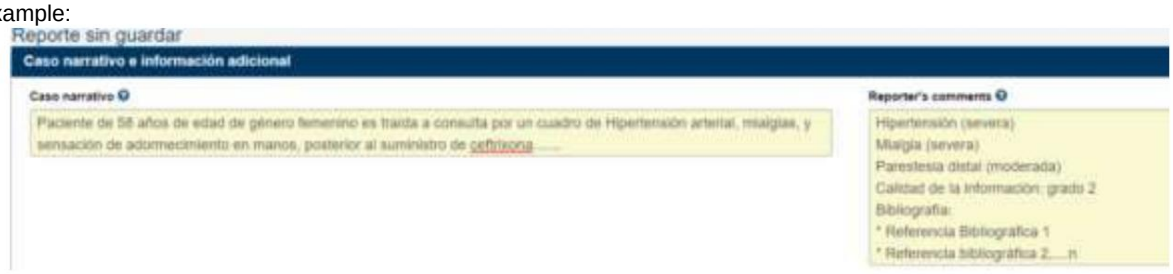
Notifier's comments: Since Mexico's Pharmacovigilance regulations require classification by severity and quality of information, which is not required by other countries, VigiFlow does not have specific fields for these two classifications. Therefore,

UFVs, CEFVs, CIFVs and CICFVs are requested to use this free field to enter the following information:

- Severity of the manifestations (based on the provisions of section 8.1.6 of NOM-220-SSA1-2016): mild, moderate, and severe. Only for manifestations classified as NOT SERIOUS.

- Degree of information (based on the provisions of section 8.1.4 of NOM-220-SSA1-2016) of the case: grade 0 to 3.
- Bibliographic References: The Naranjo algorithm has been established for UFV, CEFV, CICFV, and CIFV as a methodology for assessing causality; therefore, the bibliographic references used to support the causal classification must be provided. Citations must be written in Vancouver style.

Example:



It should be noted that the information contained in these fields can be exported to Excel format for analysis.

4.5.6 Medical history and relevant previous medical treatm

In this section, you should enter relevant information (that helps with causal assessment) about the patient's medical history and relevant conditions (diseases, conditions such as pregnancy, surgeries, psychological trauma, risk factors, among others) and previous medical treatment (relevant medications previously administered to the patient and that have been discontinued prior to the occurrence of the SRAMs; previous experience with similar medications may also be included).

It must include detailed information as shown in the following table:

Section	Field	Required information
History Clinic	**History clinic relevant (MedRA)**	You can add a relevant condition via the MedDRA dictionary catalog (search and select the MedDRA lower case term (LLT) or preferred term (PT) that most closely matches the condition you are searching for). You can do this by typing the desired term in the field, which will display the options that best match your search, or you can select it directly. Navigating the full MedDRA hierarchy with the icon . When you find it, select it as shown in the following image:  Clicking the icon will display the higher-level hierarchies of the selected term, as well as other lower-level terms. This way, you can easily check if there is another term that better matches the one you reported and is related to the same PT medical concept. 
	Medical record relevant	You can also add other information on relevant conditions via free text to this field when it cannot be structured in MedDRA. It is the responsibility of the second level of VigiFlow operations (or the first level, when applicable) to review this free text information and convert it into a standardized MedDRA term.

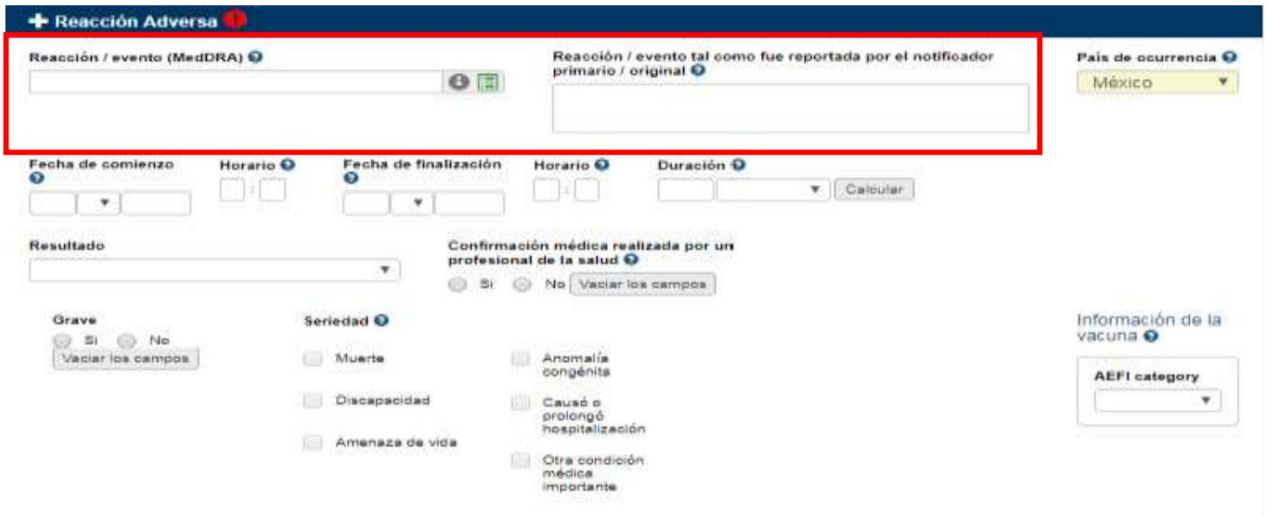
Section	Field	Required information
	Date of start	Date the relevant condition began. You can enter at least the year.
	End of date	Date the reported relevant condition ended. You can enter at least one year. If the medical condition persists, leave this date blank.
	Continued?	Select if the medical condition persists (continued). If you have enabled any option and need to remove it, you can clear the boxes by clicking "Clear fields."
	Comments from the doctor	You may add information regarding the treating physician's comments on the relevant condition.
Treatment previous medical	**Treatment previous medical**	This refers to the treatment the patient took at some point prior to the adverse reaction and has since discontinued. If the treatment is continued, it will be a concomitant medication and must be recorded in the "Medication" section. In this free text field you must enter the distinctive name and generic name in parentheses. Example: Doloron (ketorolac)
	Indication (MedRA)	Enter the reason for prescribing the previous medical treatment using the MedDRA dictionary. Search and select the lowest-ranking term (LLT) or preferred term (PT) that most closely matches the reported term.
	Reaction (MedRA)	If the patient experienced any adverse reactions to this previous medical treatment, you can record them in this field using the MedDRA catalog. Search and select the lowest-ranking term (LLT) or preferred term (PT) that most closely matches the desired adverse reaction term. If the patient did not experience any reactions to this medication, you should enter *"No adverse reaction."*
	Date of start	Start date of previous medical treatment. You can enter at least one year.
	End of date	End date of previous medical treatment. You can enter at least one year. If treatment is ongoing, leave this field blank.

If you want to add another relevant condition or another medication as a pretreatment in this section, you must press the icon. It is possible to delete additional relevant conditions or medications by pressing the icon.

4.5.7 Reaction

In this section you should record the SRAM, RAM, EA, ESAVI or any other problem of safety related to the use of medicines and vaccines.

The Adverse Reaction section looks like this:



The system allows you to enter information about a reaction using the following form:

a) Using the MedDRA dictionary.

b) Using the free field (Reaction/event as reported by the primary/original reporter). This field can be used when a suitable MedDRA term is not found,

It is requested to leave both options, both what was originally reported and the corresponding MedDRA term, in this way and if necessary, the relationship between the term as reported by the primary/ original reporter and the term entered by the issuer can be analyzed.

Please note that reactions entered in free text cannot be searched using the search filters on the VigiFlow home screen.

You must include detailed information as shown in the following table:

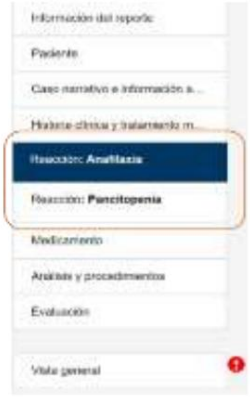
Field	Information required from the informant
Reaction / event (MedDRA)	You can add a relevant condition via the MedDRA dictionary (search and select the MedDRA lower case term (LLT) or preferred term (PT) that most closely matches the reported condition). You can do this by typing the desired term in the field where it is

	It will display the options that best match your search, or you can choose it directly by displaying the full MedDRA structure. with the icon . When you have chosen it, as shown in the next image:  Clicking the icon will display the higher-level hierarchies of the chosen term, as well as other lower-level terms. This way, you can easily check if there is another term that better matches the one you reported and is related to the same PT medical concept. 
Reaction/event as reported by the primary/original reporter	Enter the term(s) used by the original/primary reporter in the language in which the report was received to describe the reaction.
Country of origin : For	SRAM, RAM, AE, ESAVI, or any other safety issue related to the use of medications and vaccines. Mexico will automatically appear; if not, you can select it from the catalog.
Start Date: Date of onset of the SRAM, ADR, AE, AEFI, or any other safety issue related to the use of medications and vaccines. It is suggested to provide the full date, but in an expedited report, you can include at least the year.	
Schedule	If available, enter the time (hours and minutes) in 24-hour format when the reported reaction began. Consider: 12:00 to noon 00:00 to midnight
Date of	End date of the adverse reaction. It is suggested to have

ending	the full date, but in an expedited report, you can enter at least the year. If the reaction continues, you should leave this field blank. If a date is entered in this field, it must be consistent with the information entered in the "result" field, since only the Recovered/Resolved and Recovered/Resolved with Sequelae options would apply.
Schedule	If available, enter the time (hours and minutes) in 24-hour format when the reported reaction ended. Note: 12:00 to noon 00:00 to midnight
Duration	The duration can only be calculated if the occurrence and end dates are complete (day/month/year).
Result	Choose the adverse reaction outcome from: Recovered/resolved, Recovering/resolving, Recovered/unresolved, Not Recovered/resolved with sequelae, Fatal, or Unknown. If you choose the “fatal” option, it must be consistent with the severity/seriousness criterion.
Confirmation medically performed by a health professional	Enable “YES” when the report comes from a healthcare professional who confirmed the event. Since UFV, CEFV, CICFV, CIFV, and others have healthcare professionals as reporters, almost all reports will be marked with the “YES” option. The exception will be when the original reporter is a patient or consumer. If there is If you have enabled any option and need to remove it, you can clear the boxes by pressing the “Clear fields” option.
Serious	Select the "YES" checkbox when the reaction meets the established severity criteria. If you have enabled any options and need to remove them, you can clear the boxes by clicking "Clear fields." The severity classification must be applied to each reaction, so there may be severe reactions in some cases and non-serious ones in others.
Seriousness Criteria These	criteria will only be enabled if the severity checkbox is selected. Choosing between death, disability, life-threatening, congenital anomaly, caused or prolonged hospitalization or other important medical condition (which in NOM-220-SSA1-2016 specifies how “they are considered medically important”)

	Seriedad ☐ Muerte ☐ Anomalía congénita ☐ Discapacidad ☐ Causó o prolongó hospitalización ☐ Amenaza de vida ☐ Otra condición médica importante

If you need to add another reaction you must press the icon . When adding more than one reaction, you'll be able to view them in the left menu, as shown below:

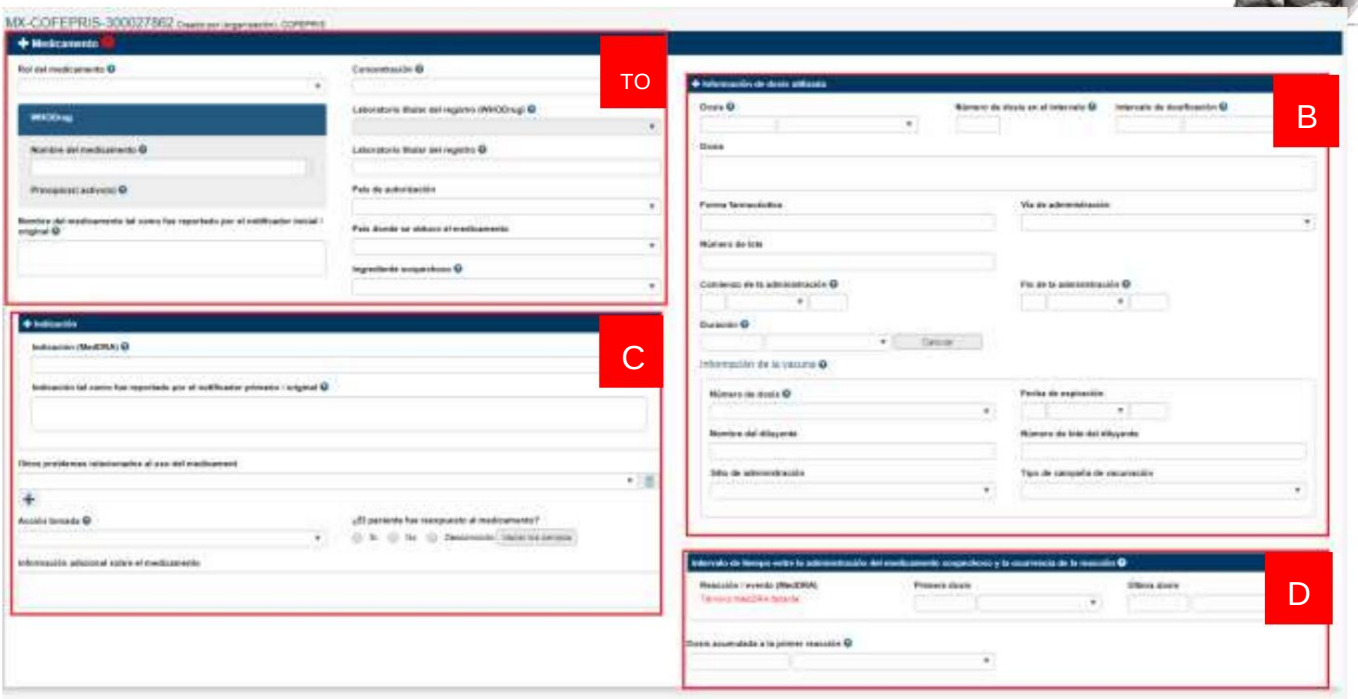


If you need to delete a reaction you added, press the icon .

4.5.8 Medication

This section can be divided into 4 fundamental quadrants:

A. Information on the suspected medication(s), concomitant and interacting medications.
B. Information on the dose used.
C. Information on the therapeutic indication.
D. Time interval between the administration of the suspected medication and the occurrence of the reaction.



You must include detailed information as shown in the following table:

A. Information on the suspected, concomitant and interacting	
Role of the medication	You must choose between “suspected”, “concomitant”, “interacting” or “unadministered” medication. You should consider which is the suspected medication and the others will correspond to concomitant medications (except in some exceptions where entering more than one suspected medication is justified). If the SRAM, AE, ADR, ESAVI is due to the interaction between two or more medications, you should leave these medications as interacting, since the system will ask you for at least two medications for an interaction. Since VigiFlow is prepared to receive other problems related to the use of medicines and vaccines where there is a possibility of not having administered the medicine (e.g. probable counterfeiting), it is possible to select the “unadministered medicine” option from the catalogue. Rol del medicamento Sospechoso Concomitante Interactuante Medicamento no administrado

A. Information on the suspected, concomitant and interacting	
WHODrug Name of the medication	VigiFlow maintains a catalog of medications that is regularly updated by regulatory authorities using this platform. You can search by the distinctive name (trademark), if available, or by the generic name. Please note that this field is sensitive to accents ('). Some active ingredient names are in English. Therefore, you should prefer to search for terms in Spanish. If you cannot find the term in Spanish, select the English language. When entering the name of a medication, you must consider the information available about the name and enter it according to the following order of priority: 1. **Distinctive name:** Enter the name of the medicine according to the distinctive name and verify that the active ingredient(s) correspond exactly to the medicine. This is because the trade name of a medicine in Mexico may be the same in another country, but the active ingredients could be different. Example: The distinctive name being sought is NOLOTIL (Magnesium Metamizole/Dextropropoxyphene)  In this case, option “b” will be chosen. 2. **Generic name:** Enter the medication with the generic name and verify that the active ingredient(s) correspond exactly to those indicated on the medication. 3. If you do not have the full name of the drug, search the catalog for the name of the **active ingredient** without the compound's salt. Example: Only the generic name "diclofenac" is available; typing "diclofenac" in the catalog will display the following options: "diclofenac sodium", "diclofenac potassium", "diclofenac diethylamine", "diclofenac", among others. The "diclofenac" option should be selected.

A. Information on the suspected, concomitant and interacting

In this case, option b will be chosen.

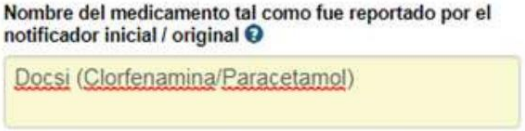
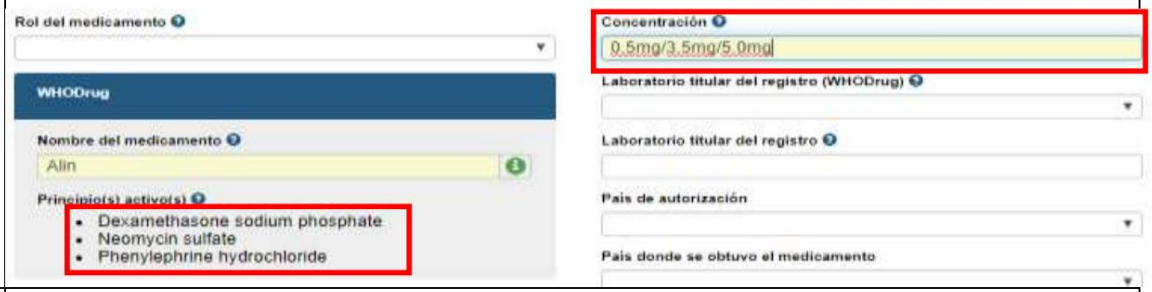
If you cannot find the desired medication(s) or drug(s) in the catalog, you must enter it in the **"Drug name as reported by the initial/original notifier" field.** You should consider that structured fields, i.e., those found in catalogs such as MedDRA or WHODRUG, among others, allow for better information analysis and are searchable from the main VigiFlow screen.

In the case of clinical studies, especially comparative studies, the drug combination being studied may not be listed in the catalog, and it is not known which one might be the suspect. Therefore, you will need to add another drug, click the button, and enter the specifications for the second drug.

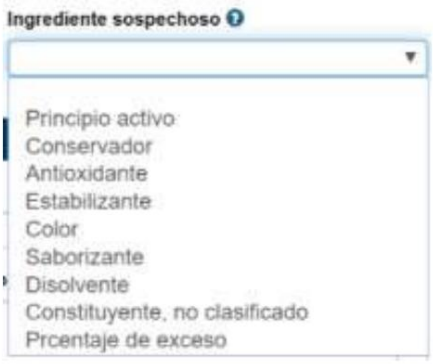
It should be noted that the WhoDrug catalog includes the option to use “placebo” as a drug name when required.

Example.

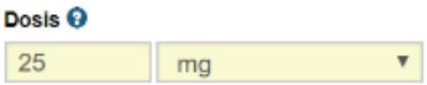
When comparing the study drug to placebo, the placebo is entered as another drug. As shown in the following example:

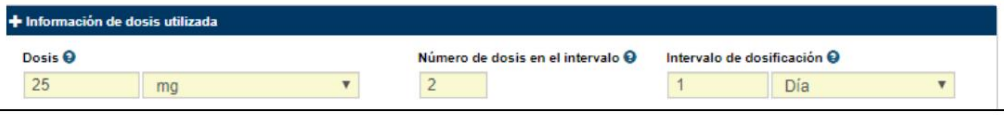
A. Information on the suspected, concomitant and interacting	
Name of the medication or as such was reported by the original initial notifier /	In this field, you must enter the name of the medication or drug as reported by the informant (if applicable). It is suggested to include the distinctive name, if available, and the active ingredient(s) in parentheses, in the order indicated on the label. You can also use this field when, after a search in the WHODRUG catalog, the desired medication or drug was not found. Please note that the information entered in this free text field will not be recognized for the filtering process from the main VigiFlow screen. 
Concentration n	You must enter the concentration stated on the medication label. Example: 50 mg. For combination medications (which contain more than one active ingredient), you must add the concentration of all active ingredients in the order they appear in the WHODRUG catalog. Example: ALIN information is available (Dexamethasone 0.5, phenylephrine 5.0mg, neomycin 3.5mg) 
Laboratory holder of the record (WHODrug)	When you select a drug (distinctive name) in the WHODRUG catalog, the system may present a list of predefined pharmaceutical laboratories in this field. You can select the correct one based on the drug's label. If you cannot find the laboratory name described in this predefined list, you should leave this field blank and enter the correct name of the pharmaceutical company in the "registration laboratory" field.

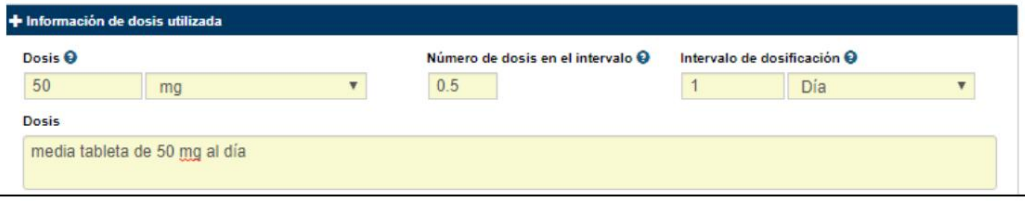
A. Information on the suspected, concomitant and interacting	
	
Laboratory holder of the record	If you cannot select the laboratory that holds the health registration for the reported medicine from the aforementioned catalog, enter it in this field. 
Country of authorization	You must enter the country of authorization of the medicine.  In exceptional situations, the CNFV will determine and communicate to issuers how to use this field.
Country where it is obtained he medicine	You must enter the country of authorization for the medication, which, under national regulations, must automatically be Mexico, with some exceptions (e.g., when importing medications due to an epidemiological emergency or if the medication was imported from another country for *compassionate use).* In exceptional situations, the CNFV will determine and inform issuers how to use this field. 
Suspicious ingredient	This field displays a list of the components of a medication. If you are certain that a component other than the active ingredient is responsible for SRAM, EA, or ESAVI, you can select it from this catalog. Otherwise, you should leave the "Active Ingredient" option.

A. Information on the suspected, concomitant and interacting	
	

To add another medication you must press the icon . If you want to delete the section you must press the icon

B. Information on the dose used	
Dose	This structured field, along with the "Number of doses in interval" and "Dosing interval," should be interpreted as the medication's dosage. In the dose field, you must enter the number and dosage units from the catalog. Example: If you are given 25 mg once a day, Dose = 25 mg.  This structured field will only be used for medicinal products with a single active ingredient. For medicinal products with two or more active ingredients, it will be left blank and the "Dose (free text)" field will be used to specify the corresponding doses of each active ingredient.
Number of doses in interval	This is the number of times the medication is taken. Using the previous example, 25 mg twice a day: Dose in interval = 2
Dosing of interval	It consists of the interval between the administration of the dose. Example: 25 mg twice a day, you should enter 25 mg in “Dose”, 2 as “number of doses in the interval” and 1 day in “dosing interval”. Using this example, the data would be entered as shown in the following image:

B. Information on the dose used	
	
Examples. Reported dosage = half a 50 mg tablet daily. • Dose = 50 mg • Number of doses in the interval = 0.5 • Dosing interval = 1 day Reported dosage = two 5 mg tablets three times a day (every 8 hours) • Dose = 5 mg • Number of doses in the interval = (2) • Dosing interval = 8 Hours. Reported dosage = 5 g as a single dose. • Dose = 5 g • Number of doses in the interval = 1 • Dosing interval = 1 total	
Dose (free text) This free	text field allows you to enter the dose as reported by the informant. The second level is responsible for reviewing and/or transforming this free text into the structured fields mentioned above. When a drug contains more than one active ingredient, this information will not be included in the structured dosage field; it will simply be written there. If the dosage indicates the duration of treatment, the dosage interval will be entered in the structured field, and the duration of treatment will be entered in the "free text" field. Example: Reported dosage: 1 tablet 50 mg daily for 7 days.  When prescriptions are indicated for doses less than 1 unit, for example, “half a tablet”, the full dose of the tablet will be entered in

B. Information on the dose used	
	the “Dose” field and the “Number of doses in interval” field will be set to 0.5. Example: 
Shape Pharmaceutical	This field is in free text format; however, the following pharmaceutical forms established in the Pharmacopoeia of the United Mexican States should be considered: • Aerosol, Capsule, Eye drops, Cream, Elixir, Emulsion, Foam, Medicinal gas, Gel, Gum, Pills, Granules, Implant, Jelly, Syrup, Laminate, Liniment, Lotion, Wafer, Ovule, Patch, Paste, Pill, Powder, Solution, Suppository, Suspension, Tablet or caplet, Ointment.
Batch number	You must add the lot number of the reported medication. You must remember that NOM-220-SSA1-2016 establishes that for biological/biotechnological medications and vaccines, in addition to meeting the minimum level of information, you must include the lot number and name of the medication. manufacturing laboratory.
Beginning of the administration	Enter the medication start date in the format *dd/ select month/ yyyy.* If you don't have the full date, you can enter at least the year.
End of the administration	Enter the medication completion date in the format *dd/ select month/ yyyy.* If you don't have the full date, you can enter at least a year. If treatment continues, you should leave this field blank and in the “Action Taken” section you should complete the action taken regarding the medication. When a treatment pause or dose change is indicated, the dates covering the first period before the pause will be entered. A new dose will be added by clicking on , and information regarding the second period/second dose will be entered. the icon
Duration	The system can automatically calculate the treatment duration only if you provide the complete dates. However, if you do not have the information on the administration dates or for situations with administration durations shorter than one day, for example,

B. Information on the dose used	
	example, hours, you can enter this duration manually.
	
Vaccine information This section allows you to provide additional information about vaccination in the event of a ESAVI	
Number of doses You	must choose from the catalog which dose corresponds to the vaccination. For example: 2nd dose of DPT (Diphtheria, Tetanus, Pertussis) 3rd dose of OPV (Oral Polio Vaccine)
Date of expiration	Enter the expiration date of the reported vaccine (in the format *dd/ select month/ yyyy).* This field applies not only to vaccines but also to any medication, even if the field is labeled "for vaccines." The expiration date indicated on the medication's primary packaging must be specified.
Diluent of the name	Free text field to enter the name of the diluent used in the vaccination.
Diluent lot number	Free text field to enter the lot number of the diluent used in the vaccination.
Place of administration	Choose your vaccine administration site from the catalog below: • Left arm (Brazo izquierda) • Right arm (Brazo derecho) • Arm (unspecified) • Left thigh • Right thigh • Thigh (unspecified) • Oral (Oral) • Other. If you choose this option, you must specify the exact administration site in the “Additional information about the drug” free-text field.

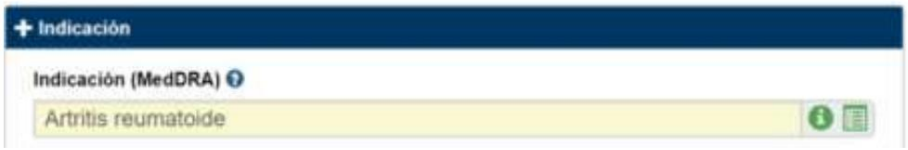
B. Information on the dose used	
Type of vaccination campaign	Choose the vaccination session where the vaccine was administered from the catalog among the following options: • Mass campaign: for national weeks of health or epidemiological emergency. • Routine session: for intramural sessions in routine vaccination • School based • Travel clinic • Work clinic • Other. If you choose this option, you must specify the type of vaccination campaign in the “Additional information about the medicine” free text field.

Example:

To add another dosage referring to the same medication or active ingredient you must press the icon + of this subsection. If you wish to delete the subsection, you must press the icon 🗑

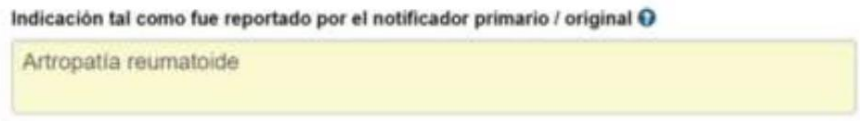
In the Indication section, detailed in the following table, refer to information on the **therapeutic indication.**

C. Indication	
Indication (MedDRA)	Search and select the lowest-level MedDRA term (LLT) or, failing that, the preferred term (PT) that most closely matches the therapeutic indication as reported by the original/primary reporter. You can do this by typing the desired term in the field that will display the options that best match your search, or you can select it directly by displaying the full MedDRA structure with the

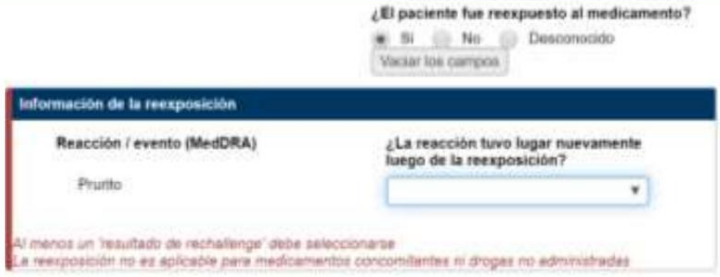
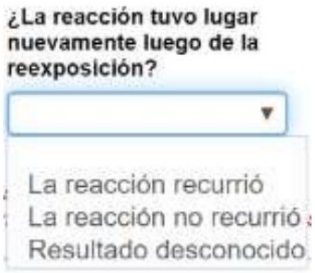
<table>
<tr><th colspan="2">C. Indication</th></tr>
<tr><td></td><td>icon . When you have chosen it, as shown in the following image:
 

Clicking the icon will display the higher-level hierarchies of the chosen term, as well as other lower-level terms. This way, you can easily check if there is another term that better matches the one you've reported and is related to the same PT medical concept.

If you do not have information on the indication for which the medication was prescribed, you should search the catalog for the option "use of a drug for an unknown indication."</td></tr>
<tr><td>Indication such as was reported by the primary/ original reporter</td><td>You must place the indication as it was notified by the original / primary notifier.

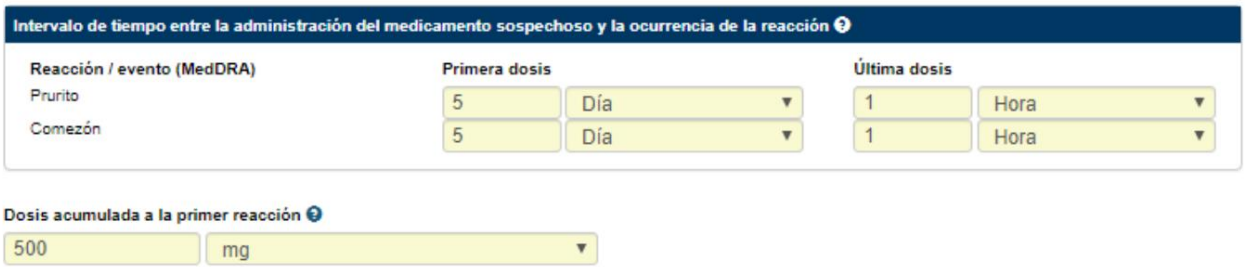
You can also use this field when you can't find a suitable term in MedDRA. It's the second level's responsibility to review and convert this free-text term into the MedDRA structured catalog in your and third-level notifications.
 
</td></tr>
<tr><td>Other problems related to the use medicine</td><td>This field includes a catalog that allows for the entry of other safety issues related to the use of medications and vaccines that are not ADRs. These other issues can be entered in MedDRA terminology within the "Reaction" field, as well as signs/symptoms caused by these issues that are not causally related to the medication. If the safety issue did not cause any signs/symptoms, "No adverse reaction" should be entered in the "Reaction" field.</td></tr>
</table>

C. Indication	
	Falsificación Sobredosis Medicamento usado por el padre Medicamento usado después de la fecha de caducidad Lote probado y encontrado dentro de las especificaciones Lote probado y encontrado fuera de las especificaciones Error de medicación Mal uso Abuso Exposición ocupacional Uso fuera de indicación Any other problem that you cannot find in the catalog can be classified as a medication error and described in the “Additional Medication Information” field. If the case requires it, you can add more than one problem related to the use of the medication and vaccine by pressing the icon. You must press the icon. If you want to delete it .
Action taken Action taken	regarding the medication as a result of the adverse reaction. For example, if the medication was recalled, you should select *Recalled Medication from the catalog.* Acción tomada Medicamento retirado Dosis reducida Dosis aumentada Dosis no modificada Desconocido No aplicable The “not applicable” option can be used in the following situations: • the patient died • Vaccines (only one dose is administered) • Treatment was terminated prior to the reaction(s) • when the medication was not administered
Did the patient go to the re-exposure medication?	This section provides information on the results of a readministration of the SUSPECTED medication (readministration does not apply to concomitant medications or medications that were not administered). If you select "Yes," additional fields will open regarding the readministration and its consequences.

C. Indication	
	 Once these additional fields are enabled, you must choose from the catalog "Did the reaction occur again after re-exposure?", the consequence of re-administration was:  It is important to note that a *"restatement"* is only applicable when the following criteria are met. 1. The medication was withdrawn due to an ADR. Not to be confused with the time required for the next dose. 2. The patient fully recovered from the ADR, with or without treatment after withdrawal of the suspect medication. 3. Once recovered, the medication was administered again. This section is intended to determine a recurrence of ADRs to a drug to strengthen the causality analysis.
Information additional on the medicine	In this free text field, you can add information that has not been entered through the fields that make up the *Medication section.* In addition, in this field you must indicate: • Study drug code in the case of a Clinical Study. • Health registration of the medicine if it has the information And you will need to add the legends where applicable: • *"The drug was not found in the whoDrug catalog";* when the drug was not found in said catalog. • *"the distinctive name does not match the combination of*

C. Indication	
	"active ingredients"; when the names of the combination of active ingredients are not listed exactly as indicated on the label, regardless of the order. For example: occasions where when searching for the distinctive name in the catalog, an active ingredient is missing or has an extra one.

D. Time interval between the administration of the suspected drug and the occurrence of the reaction This section is very useful for covering situations where the interval between drug administration and the occurrence of the reaction is very short, for example, as may occur in anaphylaxis or arrhythmia.	
Reaction/Event (MedDRA) Will show you	the reaction(s) added to your report.
First dose In this	field you must enter the interval between the administration of the first dose of the suspected medication and the start of each reaction.
Last dose	In this field you must enter the interval between the last dose administered of the suspected medication and the onset of each reaction.
Cumulative dose at first reaction	It refers to the total dose administered to the patient from the first dose until the first sign/symptom. Example: if a patient has consumed 100 mg daily for 5 days and subsequently presented the reaction, the cumulative dose at the first reaction is 500 mg, presenting itching and pruritus one hour after the last administration, as shown in the following image.



4.5.9 Analysis and procedures

This section should address the clinical examinations and procedures **relevant** to the case, which may have been performed to diagnose or confirm the reported SRAM, AE, ADR, or AEFI, including those performed to investigate a cause unrelated to the medication.

ONLY abnormal results should be reported.

Field	Requested information
Name of the analysis	Add the name of the analysis via the desired MedDRA term or select it directly from the browser by clicking the Enter the .
Date of analysis	date of the reported analysis icon in the format *dd/ select month/ yyyy.* If you don't have the full date, you can enter at least the year.
Analysis results	Enter the quantity in the free text field and select the unit of measurement from the catalog. If you can't find the correct unit of measurement in the catalog, you must enter the result in the "Results" free text field.
Minimum standard value	You must enter the reference values provided by the laboratory.
Maximum standard value	
Type of analysis	When you can't find the analysis name in the MedDRA terminology, you can place it in this free text field, although it is requested to prioritize the search in the MedDRA field.
Results	Use this field as an optional addition to the “Analysis Result” when the desired unit of measurement is not found. You can describe the analysis result as free text.
Notifier's Comments	You may add any additional comments regarding the tests and results performed on the patient.

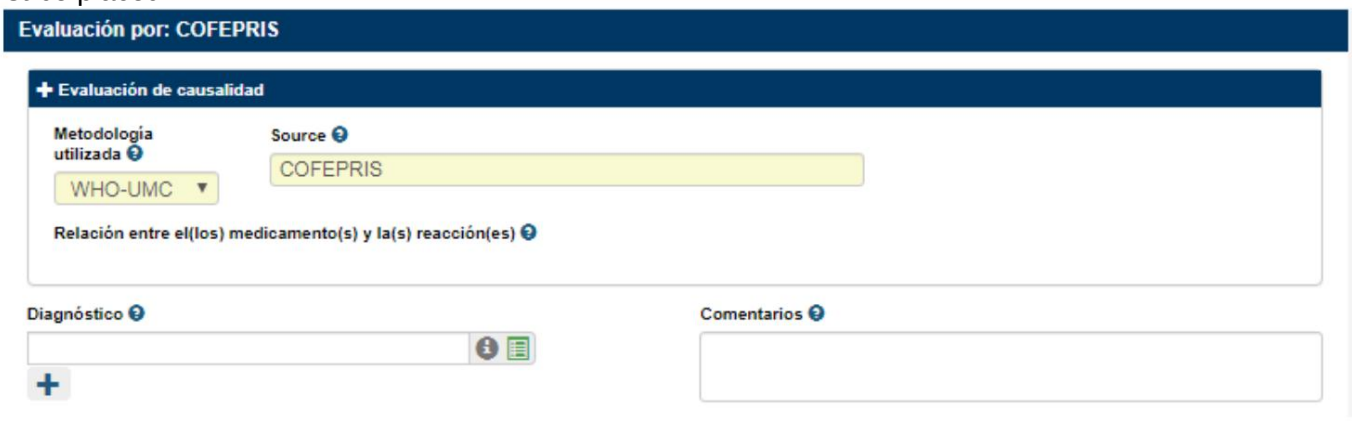
For example:

Blood tests for suspected drug-induced anemia.

To add another Analysis and procedure, you must press the icon you must press the icon . If you want to delete it .

4.5.10 Evaluatio

In this section, the result of the causality assessment carried out by the third and/or second level must be placed.

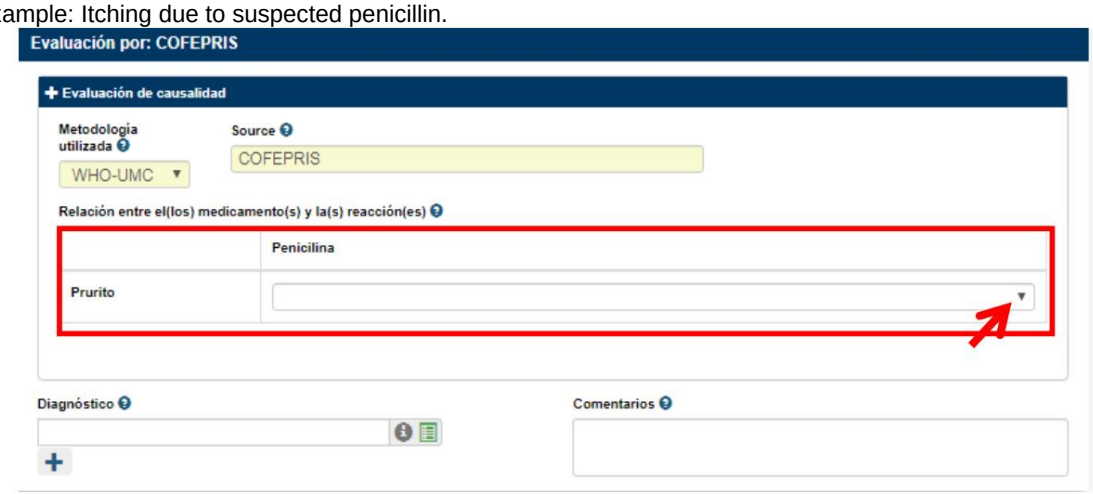


Methodology used: the system allows you to choose between the following methodologies:

- Naranjo algorithm
- WHO Probabilistic Categories (WHO-UMC Causality)
- WHO categories for AEFI (WHO-AEFI)
- French method

To enter the causality result, you must have entered a suspected or interacting drug in the corresponding drug section and at least one SRAM in the structured MedDRA catalog. The suspected drug/adverse reaction(s) combination will be automatically entered in this section.

Example: Itching due to suspected penicillin.



You must select the Orange algorithm for medications and the AEFI categories for vaccines, in accordance with the guidelines provided by the CNFV for UFV, CEFV, CICFV, and CIFV.

When the UFV carries out the causality classification, the second level (CICFV, CEFV) and the CNFV will not be able to modify this first evaluation, but they will be able to add a causal evaluation. Different evaluations can be added, for example, additional if it is necessary to reclassify it by clicking on the icon + . in the case of clinical studies, there are evaluation methods that are different from those found in the list, but the source from which the evaluation was taken must be indicated in the "comments" field.

Therefore, each organization can view its own causal assessment and that of the previous levels, but can only edit its own. Only the CNFV can delete causality assessments from levels 2 and 3.

Field	Requested information
Methodology used	Select the methodology to be used. UFVs, CEFVs, CICFVs, and CIFVs **MUST** use the **Naranjo algorithm.** The CNFV will validate the causal classification of level 2 and, if deemed necessary, will provide an additional causal assessment other than that proposed by level 3. In the case of clinical studies, another causality assessment may be used as long as they are validated algorithms.

Field	Requested information
Fountain	VigiFlow automatically displays the name of the organization to which the user belongs. In cases where the causality assessment was reported by a primary reporter who does not belong to any UFV, the name of the source of said assessment may be changed, and the assessment carried out must also be added as specified above.
Relationship between the medication(s) and the reaction(s)	You must choose from the catalog the causal classification that will be applied for the evaluation between the suspected drug(s) and the SRAM, ESAVI. The causality assessment will not apply to other safety issues related to the use of medicines and vaccines (overdose, misuse, abuse, off-label use, among others).
Diagnosis	If you have clinical experience and the case contains sufficient information, you can combine the reported signs and symptoms into a diagnosis that you should add in MedDRA terminology.
Comments	In this field, you can add information that supports the causal evaluation, for example, the score count obtained from the Naranjo algorithm, as well as the bibliography used for said evaluation.

4.5.11 Overview

This section allows you to view all the information you've entered in the report. Its usefulness lies in the fact that it allows you to more easily view the entire content instead of navigating section by section. It also allows you to identify the minimum required fields required to share the report with the global database.

You must remember to SAVE the report at any time by pressing the icon at the top right.

To exit the report, press the “Go to report list” button.

If you did not save the report during the information entry process, clicking the link "Go to the report list" and you will see the following warning:

If you dismiss the changes, any information you captured in the report will not be saved.

4.6 Report management.

For the proper functioning and utilization of the platform, agreements have been proposed on procedures for managing the handling and flow of information. This is intended to facilitate and coordinate VigiFlow management with all organizations that feed the database.

4.6.1 Searching for notifications by filte

The main VigiFlow screen displays a section with the following search filters:

- **Initial receipt date (from)/ Initial receipt date (to):** search by date range (from…to) according to the date the notification was entered into VigiFlow.

- **Report title:** search based on the “report title” field.
- **Report status:** search according to the report status: open, under evaluation, closed.
- **Issuer type:** search according to the type of issuer: pharmaceutical laboratory, healthcare professional, regional Pharmacovigilance center, patient/consumer, regulatory authority, other.

- **Report type:** Search according to the type of report: spontaneous, study report, other, not available to the sender (unknown).
- **Notification method:** search according to the source of entry into VigiFlow: Manual data entry, e-Reporting, mobile application (under construction), amount - validated, amount - not validated, unknown.
- **Notifier's profession:** Search according to the type of primary notifier (informant): physician, pharmacist, other health professional, lawyer, consumer, or other professional.

- **Report ID:** Search based on information entered in the “Other Report IDs” fields (see section 4.5.3 “Report Information”).
- **Initials:** Search according to the information entered in the “Initials” field (see section 4.5.4 “Patient”).
- **Sex:** Search according to the patient’s sex:

male, female,
a stranger.

- **Date of birth:** search according to the patient's date of birth, either by the following combinations: dd/m/yyyy, --/m/yyyy or --/--/aaaa. You must enter at least the year, otherwise the search will not be performed.

- **Reaction/event (MedDRA):** Search by reaction/event using MedDRA terminology. The result of a general *SOC* search will include reports with the lowest-ranking terms *(LLT)* belonging to that *SOC.*

- **Serious:** search according to the classification marked in the “Reaction” section. “adverse” by severity of events: yes or no.
- **Severity criteria:** search according to the criteria selected in the “Adverse Reaction” section: life-threatening, congenital anomaly, caused or prolonged hospitalization, disability, death, other important medical condition.
- **Reaction outcome:** Search according to the reaction outcome selected in the “Adverse Reaction” section: recovered/resolved, recovering/resolving, not recovered/unresolved, recovered/resolved with sequelae, fatal, unknown.

- **Assigned to:** Search based on the name of the person with an account registered in the VigiFlow database to whom a report was assigned.
It is also possible to filter “unassigned” reports.

- **Delegated to (organization):** Search for notifications delegated to a specific organization (CNFV, CEFV, CICFV, CIFV, or UFV). It's worth noting that when a report is created, the system automatically delegates it to the organization that created it.

- **Created by:** Search for notifications created by a specific organization (CNFV, CEFV, CICFV, CIFV, or UFV). You can select the "Include suborganizations" box to include notifications from the third-level organizations under your control in the search.

- **Drug name (patent-WHODrug):** search according to the distinctive name of the drug (or vaccine) recorded in the “Drug name” field of the “Drug” section and which was registered through the WHODrugs dictionary.

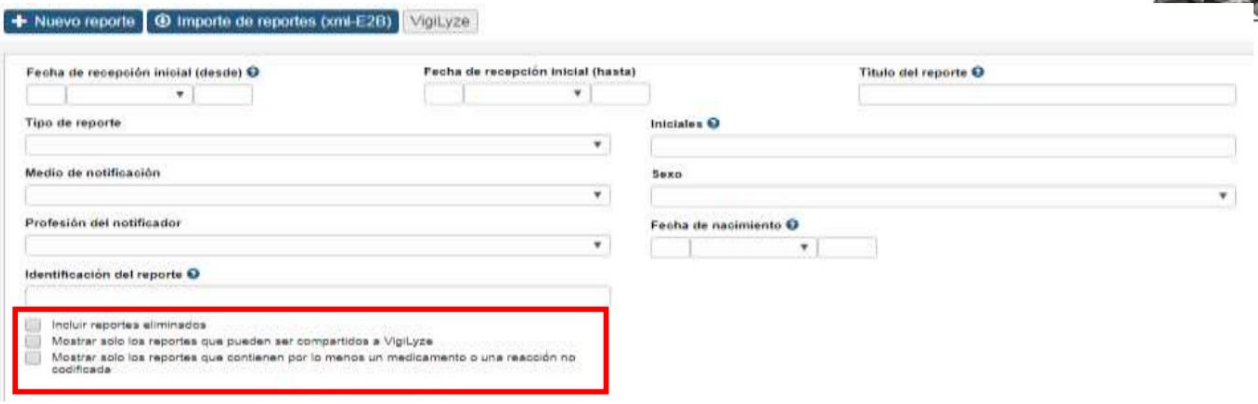
- **Active ingredient(s) (WHODrug):** Search according to the active ingredients of the entered drugs. You can include as many active ingredients as required; the search will include those notifications that contain exactly the combination of all the active ingredients entered. • **ATC code:** Search according to the ATC
code corresponding to the reported drugs. You can search with the full ATC code or with the first characters. In this case, the search will contain notifications with all drugs belonging to this classification.

  Example: Search using the ATC code "N02"; the results will show all notifications for medications with this classification that "act on the nervous system with analgesic properties."

- **Other problems related to the use of the medication:** search according to the option selected in the “other problems related to the use of the medication” field in the “Medication” section: Counterfeit, overdose, medication used by the parent, medication used after the expiration date, lot tested and found within specifications, lot tested and found out of specifications, medication error, misuse, abuse, occupational exposure, off-label use.

- **Batch number/diluent lot number:** search according to the information entered in the “batch number” and/or “diluent number” fields in the “Medicine” section.

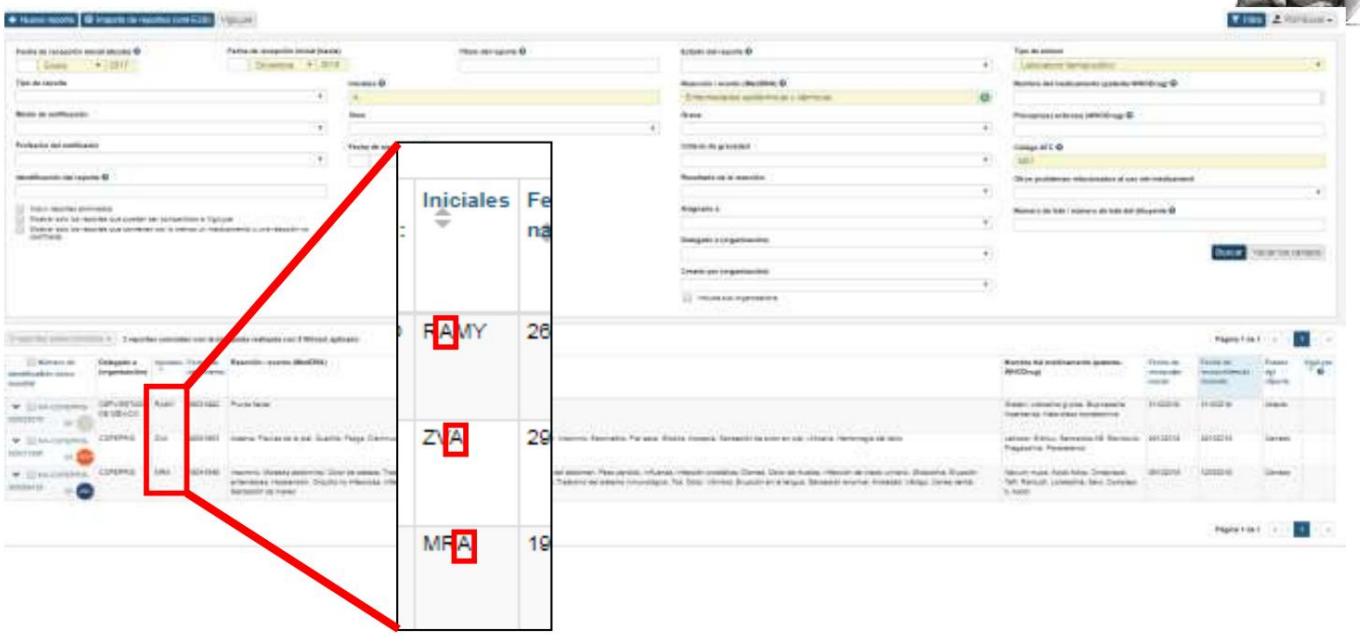
In addition to the filters already mentioned above, on the main screen of VigiFlow
You can find boxes with specific features for filtering notifications:



- **Include deleted reports:** Includes reports that have been deleted by any of the following: all three levels. See *4.6.5. Deleting a report.*
- **Show only reports that can be shared with VigiLyze:** Reports that have all the minimum required fields to be sent to the global database will be included.
- **Show only reports that contain at least one medication or uncoded reaction:** Reports that have at least one medication recorded in the corresponding free text field or at least one adverse reaction recorded in the corresponding free text field will be displayed.

Please note that when entering text into search fields, VigiFlow will filter out all notifications that contain part or all of the text entered in the fields corresponding to the filters used.

Example: A search is required for the total number of spontaneous notifications received from January 2017 to December 2019, reported through a pharmaceutical laboratory in which serious epidermal and dermal diseases occurred caused by anti-inflammatory drugs prescribed for muscle pain (ATC code: M01), which caused or prolonged the hospitalization of patients whose first name initial contains A.



As you can see, the search criteria returned three notifications that met the search criteria entered. Additionally, as mentioned, the search engine included notifications containing the letter "A" as part of the patient's initials.

4.6.2 Searching for notifications from an organiza

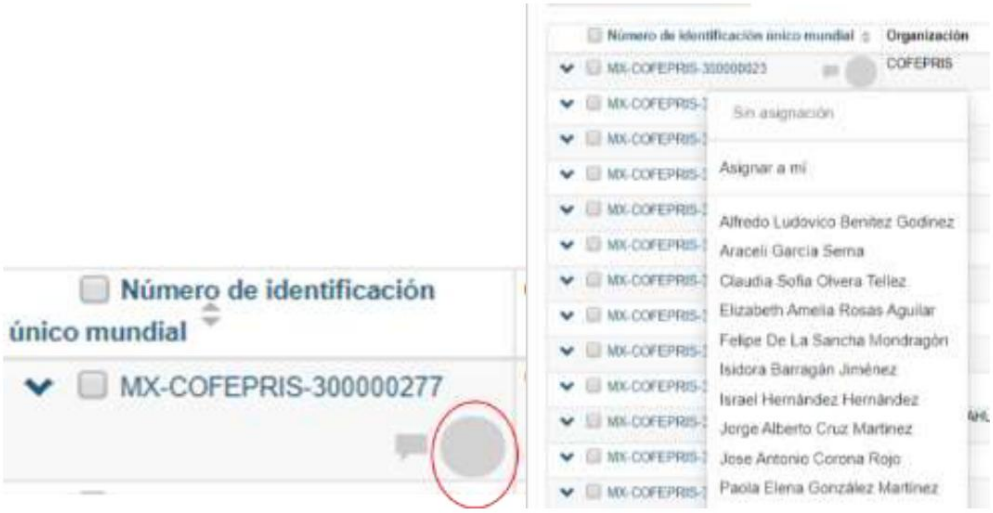
If you need to search for notifications from a specific organization in your database, you can carry it out in different ways, but the following two are suggested:

1. Through the "Created by (organization)" filter. When you open the catalog in this field, the users from your own organization and, if applicable, the third-level users you manage will be displayed. In some situations, an organization may have notifications delegated to your organization, for example, when a healthcare professional from your institution submits a notification via e-Reporting and the CNFV delegates this report to the UFV or the second-level user. In this situation, you can also use the "Delegated to (organization)" filter to search for notifications from a specific organization.
2. Using the "Report ID" free-text field, you can search for a report or series of reports based on the coding assigned to it, i.e., the one established for CEFV, CIFV, CICFV, and UFV. If you don't have the complete coding, you can search for part of it.

4.6.3 Notification Assignment

VigiFlow allows you to assign a report to a specific user (when your organization has more than one user) within your own organization or to yourself, in order to distribute the workload in capturing, reviewing and validating information.

To assign the report, you must locate the report in question in the report list on the main VigiFlow screen. To the right of the *report's Globally Unique Identification Number,* you will find a gray circle. Clicking on it will display a menu with the members of your organization, as shown below:



When assigned, the gray circle will change color and include the initials of the user to whom the report was assigned:

The process of assigning and reassigning reports will depend on the internal organization.
of each CEFV, CIFV, CICFV and UFV.
To find reports assigned to a specific user, use the "Assigned To" filter. Opening the catalog with this filter will display all users in your organization.

4.6.4 Delegation of notifications

This feature allows a report to be delegated (assigned responsibility for verifying and validating information) to an organization at any level. This is useful when there is missing information or information that needs to be corroborated by the previous level. Thus, the CNFV can delegate reports to the CEFV, CICFV, and CIFV, and these, in turn, can delegate them to the UFV, if applicable. If the information entered allows it, the CNFV can delegate notifications from e-Reporting to the CEFV, CIFV, CICFV, and CENSIA/DGE, so that they are aware of and manage these cases according to their jurisdiction. These, in turn, if applicable, can delegate them to their UFV.

Centers without a VigiFlow account that submit notifications via e-Reporting will be delegated by the CNFV to their corresponding second-level organizations. Those UFVs with a VigiFlow account that for some reason sent notifications to the CNFV via e-Reporting will be delegated to their corresponding UFV. This delegation will be accompanied by a message that can be viewed in your report list.

Example: the CNFV receives a notification entered by hospital X that does not have a VigiFlow account, in which, due to its entered information, its origin can be identified, which would correspond to a 2nd level organization.

The second- or third-level organization to which a report was delegated is free to delegate it back to the next level if it confirms that the notification is not applicable. It must include a message describing the situation.

To proceed with the delegation, you must identify the specific report(s) and enable the box located to the left of the *Global Unique Identification Number of the report.*
Then, press the "# selected reports" button at the top. Your organization and, if applicable, the VFUs dependent on your CEFV or CICFV will be displayed. Select the organization to which you want to delegate the report(s).

The CNFV will always be able to view and edit all reports that have been created or delegated to other organizations at levels 2 and 3.

See *First, second and third level functions in VigiFlow operation.*

The process of delegating reports from third-level UFVs will be solely to their respective second-level bodies (CEFV, CICFV) and not directly to the CNFV.

4.6.5 Deleting a report

This feature allows you to delete an existing report from your database. To do so, access the report from the *Reports List* and click the "Delete" button in the top right menu.

You must enter the reason for deleting the report. The deleted report will remain inactive (you will no longer be able to edit it) and will not appear in the *Report List.* VigiFlow will only allow you to access the case's PDF document, for which you must locate it using the search filters and select the *"Include deleted reports"* checkbox on the main screen.

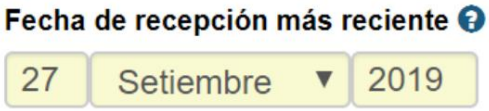
It should be noted that deleting reports is a sensitive issue and should only be carried out when truly necessary, with a limited justification being a duplicate report. This can be avoided by following the instructions in section *4.5.1.1. Duplicity Detection.* Therefore, it is suggested that each UFV, CEFV, CICFV, CIFV, and CNFV keep a record of deleted reports, specifying at least the user, date, and reason for the deletion, allowing them to monitor these cases.

4.7 Entering additional information for a report (follow-up)

NOTE: It is important to highlight the relevance of this section for the traceability of the additional information that has been added to the initial report and that we know as *Follow-ups.*

When you need to add additional information (follow-up) to a report already captured in VigiFlow, it is not necessary to capture it as a new report. You must find and open the initial report from your list of reports on the screen. In the "Report Information" section, you must locate the

"Most recent received date" field and enter the date you are entering the tracking information.



This date must be different from the *Initial Received Date.* You must then enter all additional information in the corresponding sections of the report.

You should not add any Report Title, but you should add an additional tracking coding (S1, S2… Sn) in the Other Id field.

Once you have added all the additional information, you must save the report and go to the "Report List."

You can view previous versions of the last modified report through the report history. Locate the report in the list and click the arrow to the left of the *report's Globally Unique Identification Number.* The following will appear:

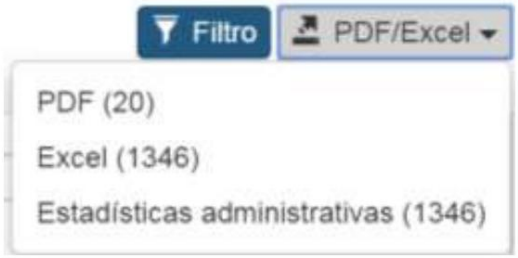
The history will show you the modified versions of the notification, the date, the user and will allow you to download the file in PDF format with the information from the previous versions of that case.

4.8 Information backup

As a particular feature of VigiFlow, the notifications entered may be exported to Microsoft Excel directly or can be downloaded in PDF format.

Each CEFV, CICFV, CICFV and UFV must define in their internal procedures the frequency with which they should generate backups of their information.

To back up all the information in your database, go to the FILTERS section on the VigiFlow home page and select the "Initial Receipt Date (From)" and "Initial Receipt Date (To)" fields. You can generate the backup from the date your first report was entered to the present or by period, but keep in mind that the system has a limit of a maximum of 1,000 reports that can be exported to Excel. These will be the only filters you should apply, so all other filters should be left blank. When you press "Search," the query will return the reports entered during the selected period.



Export the information using the "Excel" option, as this option allows you to view all the information entered in each report. The "Administrative Statistics" option shows you a summary of the exported cases using relevant indicators such as statistics by sex, age group, severity, report type, issuer type, among others.

The generated Excel file must be saved on your storage drive.

To export reports in portable document format (PDF), select the report and choose the PDF option. A compressed file containing all the exported cases will be downloaded individually.

4.9 First, second and third level functions in VigiFlow operation

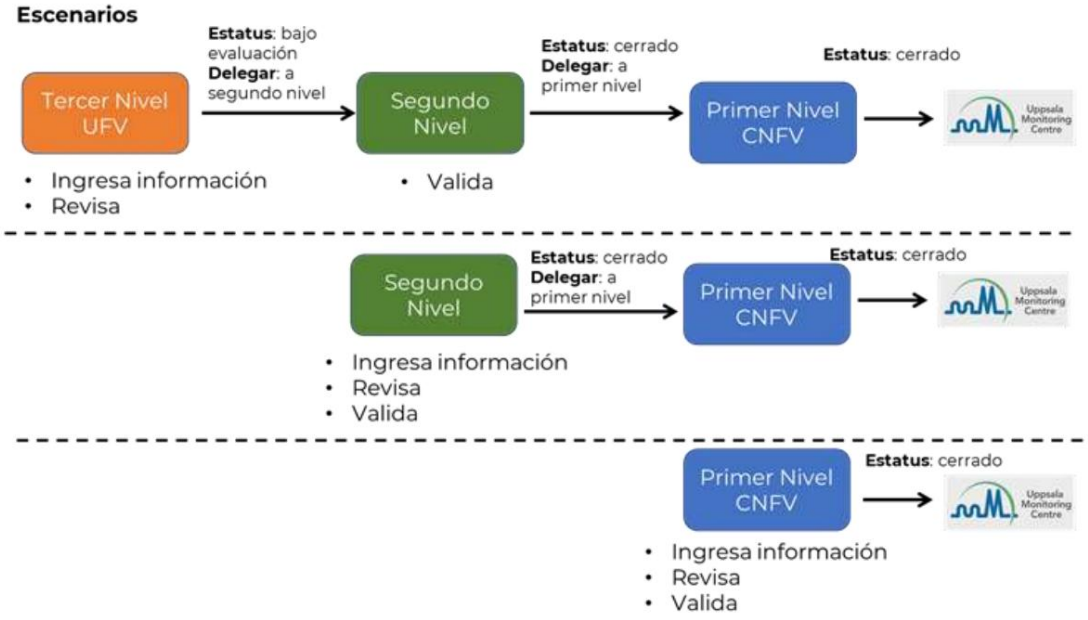
Since VigiFlow is a real-time reporting platform, where a notifier can immediately view a report upon entering and saving it, it is necessary to establish a methodology that defines responsibilities for capturing, reviewing, and validating information at each level. It's important to remember that all three levels can manually enter reports into VigiFlow, keeping in mind the following:

- A notification entered by a 3rd level organization (UFV) will be visible and editable by:
  or The same, its corresponding second level and the first level

- A notification entered by a 2nd level organization (CEFV, CICFV, CIFV, CENSIA/DGE) will be visible and editable by:
  - or The same and the first level
- A notification entered by the 1st level (CNFV) will be visible and editable by:
  - a. The same

Depending on the level that you manually enter the report in VigiFlow, the responsibilities that must be carried out at that level, as shown below:

Figure 5. Functions and report status for the 3 levels of VigiFlow operation.



The validation process is fundamental and its objective is a thorough review to corroborate the consistency, integrity, and completeness of the information in structured fields. This allows, among other things, to standardize reported terminology, enable report searches through VigiFlow's filter tool, and prepare the information for submission to the WHO global database. Information contained in free-text fields cannot be identified and filtered for generating statistics from the main VigiFlow screen.

To be able to define that a report is ready to be attended to by the immediate level higher, it is necessary to identify it in some way so that said level can view it.

- You can review the information **captured** in the section corresponding to “Income” from a report.”
- Information **review** consists of verifying that at least the minimum fields required by the system have been entered into the report, reviewing the consistency and integrity of the information.
- Information **validation** consists of transferring all the information from the free-text fields to structured fields, such as patient identification catalogs, the MedDRA dictionary (reaction/event, relevant clinical history, analysis, and procedure), and the drug dictionary (WHODRUG) in the "Medication" section. Validation also includes reviewing the pre-assessment of the causal notification (Naranjo algorithm). Level 2 is responsible, if applicable, for entering the corresponding coding in "Other Report IDs" for third-level UFV reports.

Once the report has been captured and reviewed by the **third level,** the report status must be set to **"Under evaluation"** and then delegated to the corresponding CEFV, CICFV, CENSIA/DGE.

The **second level** identifies this report, validates it according to the established procedures, and saves it with the report status **"Closed."** After this, it must be immediately delegated to the CNFV for final validation and submission to the WHO global database.

5. E-Reporting

5.1 Generalities

It is a standardized format for reporting SRAM/ADR/ESAVI via the internet, developed by the UMC to facilitate reporting by **patients/consumers and healthcare professionals.**

Notifications entered in this electronic format are transmitted directly to the CNFV database in VigiFlow.

In order to provide a means of notification for registration holders or their legal representatives, institutions or establishments that carry out health research, distributors/ marketers that **DO NOT currently have** the capacity to carry out the electronic transmission of reports in XML-E2B format to the CNFV, the temporary use of e-Reporting has been arranged for this purpose.

You can access e-Reporting through the COFEPRIS website. On the main screen, in the "LINKS OF INTEREST" section, click on "Did a medication harm you?" and then look for the link to access e-Reporting:

https://primaryreporting.who-umc.org/Reporting/Reporter?OrganizationID=MX

5.2 Entering a notification in e-Reporting

For more information, see:

1. Instructions for using e-Reporting for reporting adverse reactions (discomfort caused by medications) by healthcare professionals and patients or consumers.

2. Instructions for the use of e-Reporting for Health Registration Holders or their Legal Representatives, Institutions or Establishments where health research is conducted, and Distributors/Marketers.

Both instructions can be viewed and downloaded from the COFEPRIS website or via the following link:

https://www.gob.mx/cofepris/acciones-y-programas/como-notificar-una-sospecha-de-reaccion-adversa?state=published

6. Electronic transmission XML-E2B

6.1 Generalities

Currently, adverse reaction reports must be communicated through communities interested in pharmacovigilance throughout the life cycle of medicines, especially during ongoing post-marketing monitoring.

Electronic reporting facilitates information transfer and makes safety data readily available for further processing and analysis. These advantages enable regulatory authorities, health record holders, healthcare professionals, and patients/ consumers to make better-informed decisions about medicine use.

The lack of harmonization in the systems that generate electronic reports could lead to difficulties in reconciling adverse reaction reports worldwide. Having a harmonized standard helps maximize the compatibility of pharmacovigilance information and minimize future compatibility complexities. Therefore, regulatory authorities and the pharmaceutical industry must work together toward a harmonized standard that facilitates the transfer of electronic reports.

The standard for the transfer of electronic adverse reaction reports is established internationally by the *International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use* **(ICH),** which brings together regulatory authorities and the pharmaceutical industry to harmonize the scientific and technical aspects of drug registration. The first guideline established for electronic transfer was the ICH-E2B Guideline "Information Elements for the Transmission of Individual Case Safety Reports." The need to exchange a high volume of information worldwide efficiently and automatically has led to periodic revisions of the ICH-E2B document. Since 2001, when E2B (R2) was implemented, there have been many developments in electronic reporting requirements and good pharmacovigilance practices. Therefore, the ICH E2B (R3) Guideline was recently developed, which includes new requirements for compliance by registration holders and other pharmacovigilance stakeholders interested in reporting drug safety information.

The new VigiFlow allows the import of XML files compliant with the international ICH E2B (R2) and ICH E2B (R3) standards. To this end, the CNFV must work with industry to establish the technical requirements for implementing the standard in pharmaceutical industry systems.

6.2 Technical documents

Health record holders or their legal representatives, establishments that conduct health research, and distributors/ marketers interested in standardizing their systems for the electronic transfer of reports must comply with the following general documents on the ICH E2B guidelines (R2 and R3):

- ICH E2B (R2) Individual Case Safety Report (ICSR) specification and files related.

  or http://estri.ich.org/e2br22/index.htm

- ICH E2B (R3) Individual Case Safety Report (ICSR) Specification and Files related

  or http://estri.ich.org/e2br3/index.htm

Other technical documents, such as the CIOMS to ICH-E2B transfer format and the list of requirements for generating XML-E2B files, will be shared in due course with each health registration holder or their legal representative, establishments conducting health research, and distributors/marketers interested in standardizing their systems.

7. Definitions

- **ATC:** Anatomical, Therapeutic, Chemical classification system; system instituted by the WHO
- **Uppsala Monitoring Centre (UMC):** WHO Collaborating Centre in the Programme International Drug Monitoring System.
- **State Pharmacovigilance Center (CEFV):** the body designated by the State and Mexico City Health Secretariat to participate in the execution of Pharmacovigilance activities, in accordance with NOM-220-SSA1-2016 and applicable regulations, in coordination with the National Pharmacovigilance Center.
- **Institutional Pharmacovigilance Center (CIFV):** the Pharmacovigilance Unit of an institution of the National Health System that participates in the execution of Pharmacovigilance activities.
- **Institutional Pharmacovigilance Coordinating Center (CICFV):** Body responsible for coordinating the various Pharmacovigilance Units of an institution.
- **National Pharmacovigilance Center (CNFV):** to the area of the Evidence and Risk Management Commission, attached to the Federal Commission for Risk Protection

Health, which is responsible for issuing policies and guidelines for the operation of Pharmacovigilance in the national territory, in accordance with applicable regulations.

- **ICD-10:** International Classification of Diseases.
- **E2B:** Standardized sending format for the transmission of security reports individual cases.
- **LLT:** Lower Level Term.
- **MedDRA:** Medical Dictionary for Regulatory Activities.

- **Contract Research Organization (CRO):** A person or organization (commercial, academic, or other) contracted by the sponsor to perform one or more of the sponsor's duties and functions related to the study.
- **Drug withdrawal:** the action of suspending the drug causing the reaction along with the result of the reaction (e.g., whether the patient recovered or not).
- **Rechallenge:** the process of re-administering a medication after experiencing an SRAM, as well as the outcome of such re-administration (e.g., whether the reaction recurred or not)
- **SOC:** System Organ Class, Classification by organs and systems.
- **VigiLyze:** Tool through which VigiBase is accessed.
- **Compassionate use:** the provision, on compassionate grounds, of a medicine to a patient or group of patients who suffer from a chronic or seriously debilitating disease or who are considered life-threatening and who cannot be satisfactorily treated with an authorized medicine.

- **VigiBase:** international database of individual safety reports from member countries of the WHO International Drug Monitoring Programme.

Av. Marina Nacional No. 60, 4th Floor, Colonia Tacuba, Miguel Hidalgo Territorial Demarcation, Mexico City, CP 11410
Tel: (55) 50 80 52 00 www.gob.mx/cofepris