VIGIMED COMPANY USER MANUAL

CLINICAL RESEARCH

COORDINATION OF CLINICAL RESEARCH IN MEDICINES AND BIOLOGICAL PRODUCTS (COPEC)

SECOND DIRECTORATE (DIRE2)

VIGIMED COMPANY USER MANUAL - CLINICAL RESEARCH

This manual aims to guide the appropriate use of this system for reporting Suspected Unexpected Serious Adverse Reactions *(SUVIDA).*
SUSAR) of medicines and biological products in the context of clinical trials for registration purposes, under RDC 945/2024.

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CLI

Second Directorate – DIRE2

Organization - Anvisa

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SUMMARY

1. INTRODUCTION

The VigiMed Empresa User Manual is intended for all sponsors and ORPCs that are conducting clinical trials in Brazil and aim to introduce VigiMed Companies and guide the appropriate use of this system for reporting reactions adverse reactions of drugs and biological products, in compliance with the Board Resolution Collegiate – RDC nº 945/2024 and its updates and other recognized guides internationally.

VigiMed is the Brazilian name given to the *Vigiflow system,* used by the World Health Organization. Health (WHO) for receiving adverse event reports and provided by *Uppsala Monitoring Centre* (UMC) - WHO-linked centre that operates the Programme International Drug Monitoring System.

The VigiMed system was adopted by Brazil in December 2018 initially to receipt of notifications of adverse events related to medicines and vaccines already registered in Brazil. At the time, the Citizen and Professional Module was made available Liberal Health *(eReporting)* and in March 2019 the VISAS and Services Module was implemented Health *(VigiFlow)* which has been gradually replacing Notivisa. Finally, the Health Module Enterprise *(eReporting Industry)* was made available in October 2020.

As of February 2021, VigiMed has also been adopted for receiving of reports of serious adverse events (SAEs) occurring during the conduct of trials clinical, as established in RDC No. 09/2015, in force at the time, in gradual replacement to NotivisaEC.

Some advantages of using VigiMed Empresas are: structure compatible with the internationally harmonized standard in the ICH E2B Guide and adopted by Anvisa; use of dictionaries for standardization of terms, such as MedDRA *(Medical Dictionary for Regulatory Activities* - Medical Dictionary for Regulatory Activities) and WHODRUG (Medical Dictionary for Regulatory Activities) WHO drugs), even for those that will not be imported in the ICH E2B XML format; inclusion of additional information in the attachment; and stability of the connection to the service when logging in and at no cost to users.

Data sent post-marketing by VigiMed Empresas feeds the database of VigiBase. This makes it possible to monitor the safety of medicines registered and under research in Brazil with the help of analytical data management tools for detecting signals qualitatively and quantitatively, against national and global data, as information is shared more quickly with the WHO, aiming at strengthening global pharmacovigilance. Sharing data with WHO, Vigibase currently only uses information received by GFARM, that is, from notifications of events occurring with already registered medicines.

VigiMed Empresas provides two interfaces that can be used at the discretion of the sponsor [Sponsors, Researcher-Sponsor and Representative Organization of Clinical Research (ORPC)]: one for manual entry of notifications and another for import of XML files, both following the ICH E2B Guide standard. Through them, Drug Registration Holders may notify Anvisa of cases of events serious adverse events (expected and unexpected) involving their products (medicines and vaccines), as provided for in the Resolution of the Collegiate Board - RDC No. 406/2020 and its updates; and Sponsors of clinical trials conducted in Brazil may report SUSARs - Suspected Serious Unexpected Adverse Reaction occurring in Brazilian territory, in accordance with the provisions of RDC No. 945/2024.

The ICH E2B(R3) Guide aims to promote the harmonization of data elements for notification when creating a standard for the electronic transmission of information between databases on a global scale. This is necessary due to the large number of potential participants for the exchange of safety information relating to the use of medicines. The success of this transmission depends on consistent interpretation and uniform common data elements and transmission procedures standardized. Therefore, the company must follow the guidelines of the ICH E2B Guide to perform a quality notification on VigiMed.

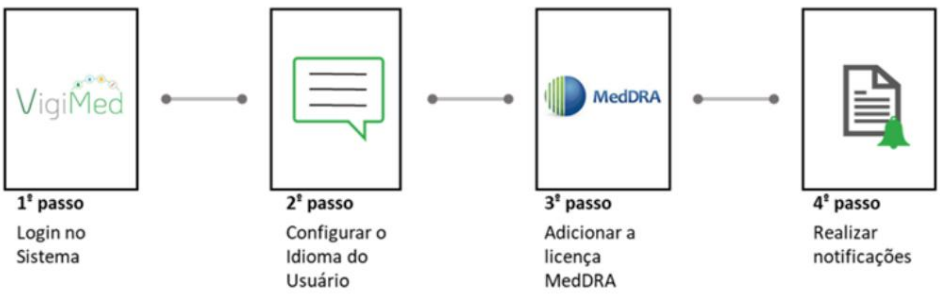
Important!

The ICH E2B (R3) Guide is the *Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs) - E2B(R3) Data Elements and Message Specification,* available that ICH page: https://www.ich.org/page/efficacy-guidelines

This Manual details how to carry out each of these notifications - initial, follow-up, of change or cancellation - either by manual entry or by importing an ICH XML file E2B.

Throughout this document, the term sponsor will also be used to refer to Investigator-Sponsor, Clinical Research Representative Organization (CRPO), companies third parties specialized in adverse event submission or regulatory consultancy (they will also be considered as representative of clinical research and may receive delegation to report SUSARs). Therefore, this document is intended for all sponsors who are conducting clinical trials in Brazil and aims to introduce VigiMed Companies in order to guide the proper use of the two interfaces.

2. SETTINGS



2.1. SENDING NOTIFICATIONS BY VIGIMED COMPANIES

The sponsor can use either the Manual Entry or the Import interface. ICH E2B XML to report SUSARs with drugs and biological products that occurred in clinical trials.

In the case of experimental drugs and biological products for submission purposes regulatory, it is mandatory for the sponsor to notify SUSARs, according to art. 64 of the RDC No. 945/2024. Aggregated data from all other adverse events that are not categorized SUSARs should be systematically evaluated by the sponsor or Committee Independent Security Monitoring, where applicable, and the results of this evaluation must be submitted to Anvisa in the Safety Update Report of Development of Experimental Drugs, as provided in RDC No. 945/2024, or whenever requested.

As determined by art. 70 of RDC No. 945/2024, the researcher must inform the sponsor about serious adverse events within 24 (twenty-four) hours from the date knowledge of the event. The sponsor must ensure that all information relevant information about SUSARs that are fatal or life-threatening are documented and notified to Anvisa within a maximum of 7 (seven) calendar days from the date of notification of the case by the sponsor, according to art. 71 of this same resolution. And all the others SUSARs, which are not fatal or life-threatening, must be reported to Anvisa within 15 (fifteen) calendar days from the date the sponsor becomes aware of the case, according to art. 72 of the aforementioned regulation.

It should also be noted that additional information on monitoring of mentioned events must be included in the form within 8 (eight) calendar days from from the date of notification in accordance with the sole paragraph of art. 71. However, at any notifications may be updated by the sponsor at this time.

2.2. REQUIREMENTS FOR USE OF VIGIMED COMPANIES

To use VigiMed, companies need to have:

- Registration granted to VigiMed Empresas by Anvisa
- Computer connected to a stable internet connection
- Use of Google Chrome browser, preferably, or another such as Mozilla, Firefox
- Acceptance of the “System Terms of Use”
- MedDRA License (strongly recommended)

• WHODrug License (recommended)

MedDRA LICENSE

MedDRA terminology is used to code adverse reactions/events (os) and other medical terms such as cause of death, indication, name of tests, medical history and diagnosis.

For guidance, license application and renewal, please see the dedicated page from MedDRA: https://www.meddra.org/subscription/process. The rates are defined according to the size of the company. Public companies can request their free licenses. Small businesses, with revenues below US$1 million, can apply for an annual license for $139. Other license fees are set according to the company's turnover.

The license, in addition to enabling MedDRA in VigiMed Empresas, also gives access to MedDRA training and other services at: https://www.meddra.org/.

To use MedDRA in VigiMed, the company needs to activate the license in the system – vide item 2.7.

Proper coding with MedDRA should follow the 'Points to Consider' documents. Consider' and 'MedDRA Terminology Best Practices', available at Portuguese and with versions updated every six months on the page https://www.meddra.org/how-to-use/support-documentation/ portuguese.

WHODrug LICENSE

Using the WHODrug dictionary for drug coding and principles assets in notifications is recommended by Anvisa.

For guidance, license application and renewal, please see the dedicated page do WHODrug e UMC: https://who-umc.org/whodrug/whodrug-subscription/. As subscription fees depend on additional products, number of locations

geographic and the number of users required for the organization. Companies public companies can apply for their free licenses.

The license, in addition to enabling WHODrug on VigiMed Empresas, also gives access training and other services from WHODrug. See the portfolio at: https://who-umc.org/whodrug/.

To use WHODrug in VigiMed, the company needs to activate the license in the system – vide item 2.7.

Proper coding with WHODrug should follow the guidelines of document 'How to use WHODrug C3 format for coding medicines', and, in the case of importing ICH E2B(R3) XML files, of the document 'Instructions for creating ICH E2B XML files (R2 and R3)', both available on the Pharmacovigilance Management (GFARM) page under 'Materials support for the use of VigiMed Empresas': https://www.gov.br/anvisa/pt-br/issues/inspection-and-monitoring/notifications/vigimed/vigimed-companies

2.3. REQUEST AND UPDATE OF REGISTRATION FOR VIGIMED COMPANIES

Registration in VigiMed Empresas will be carried out by Anvisa for each company. Each sponsor must make the initial request or any registration update on VigiMed Company, intended for the Clinical Research account, through the form available on the page of Adverse Event Notifications of Clinical Research and send it, later, to the e-mail vigimed.pesquisa@anvisa.gov.br.

Once access to VigiMed Empresas is granted to the sponsor or any data from system user is updated, the company will be notified via email sent to the contact(s) provided by the company.

To properly fill out the form, pay attention to some information:

1. Company data

1.1 Business name: name as reported in the Anvisa registration

1.2 Sender identifier:

- The sender identifier will be used to identify the company in VigiMed.
- Must have a maximum of 60 characters.
- Corresponds to the identifier of the notification issuer and will be preceded by the term 'Clinical Trial'.
    - For example: Clinical Trial - MEDSOLUTION
- Use your trade name, if possible.
- For companies with E2B-compatible systems, the value must be equal to configured for the ICH E2B (R3) guide field: N.2.r.2 Message Sender Identifier.
- For companies that only perform manual entry, it is recommended to use the same name given in the company's short name. Changes may be suggested by Anvisa.
- Once the Sender ID is set, it cannot be changed. later in the production phase, except as provided for in the ICH E2B Guide.

1.3 Organization identifier:

- The organization identifier will be the company name in VigiMed and will be used to identify the company.
- Must have a maximum of 100 characters.
- Companies with E2B compatible systems, the value must be the same as configured for ICH E2B (R3) guide field: C.3.2 Sender's Organisation.
- For companies that only perform manual entry, it must be the same value as sender identifier.
- Once the Organization Identifier is defined, it cannot be changed. later in the production phase, except as provided for in the ICH E2B Guide.

1.4 Company name abbreviation:

- Must have a maximum of 60 characters.
- the abbreviation of the company name will be used in the Notification Identification, following the structure: BR-CompanyName-NotificationNumber, referring to the field of guia do ICH E2B (R3): C.1.1 Sender's (case) Safety Report Unique Identifier.

- Propose a short name that, if possible, identifies the sponsor.
    - o For example: MEDSOLUTION.
- The chosen name will be part of the Worldwide *Unique* Identification *Case Identification Number* – WWUID).
    - o For example: BR-MEDSOLUTION C TRIALS3-123456.

    It should be noted that the abbreviated name is only the one in blue.
- Once this short name is defined, it cannot be changed later in the production phase, except as provided for in the ICH E2B Guide.

1.5 CNPJ: numbers only

1.6 DRM State (UF): acronym; only 2 characters

1.7 State (UF) of the Pharmacovigilance Unit: acronym; only 2 characters

2. User data for registration on VigiMed:

- Up to three users can be informed per company.
- The same email address can be provided to register a user who will work in more than one company or in accounts intended for Pharmacovigilance or Clinical Studies.
- Corporate emails can be used, but they will be under the responsibility of the CPF provided.

3. Adoption of VigiMed Companies

- Information on whether or not to adopt the interface for Importing ICH XML files E2B, in R2 and R3 format.
- The form for manual entry of adverse event notification data of medicines will always be available to all companies, regardless of whether or not they import an ICH E2B XML file.
- To start importing XML, the company must validate some files in a test environment, as per the document 'Instructions for creating ICH E2B XML files (R2 and R3)', published on the VigiMed Empresas page.

The estimated start date for testing and production for XML import ICH E2B is for planning purposes. There will be no penalty in case of non-compliance with the deadline, and it is even possible to update the respective date.

4. MedDRA and WHODrug Licenses:

- Implementation of MedDRA terminology is strongly recommended and the company You can use a local or global license.
- If the company does not have a MedDRA license, it is necessary to regularize its situation. and send a new form to update the information, as soon as you have possession of the license number.
- Implementation of the WHODrug Dictionary in C3 format is recommended.
- The company that does not yet have the WHODrug license in C3 format must inform that have not yet acquired it. However, as soon as you have it, you must send a new form to update the information.

5. Final comments:

- List the changed fields, to facilitate updating the registration.
- Describe the reason for submitting a new form, including any other clarifications, such as change of ownership of the company or other changes that impact the registration with VigiMed Empresas, if applicable.

2.4. SYSTEM ACCESS AND ACCOUNT ACTIVATION

After receiving the email from Anvisa informing you about granting access to VigiMed Companies, each user must:

1. Click on the link: https://industryereporting.who-umc.org/
2. Click on “Forgot your password?”
3. Enter your email in the “Email Address” field.
4. Click on 'Send verification code' and do not close the window
5. Open your email to redeem the 6-digit code

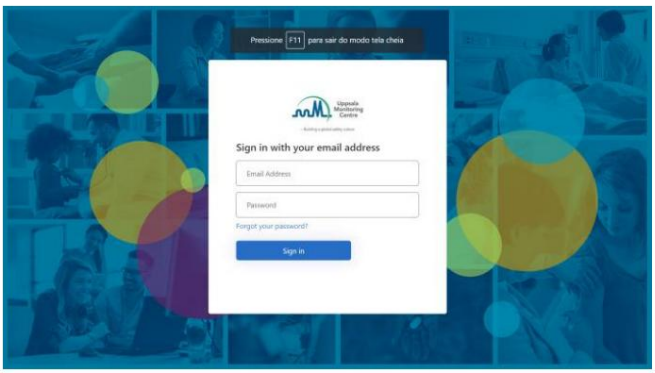
Note: If it is not in your inbox, check your spam folder. If you cannot find the email, contact us at vigimed.pesquisa@anvisa.gov.br.

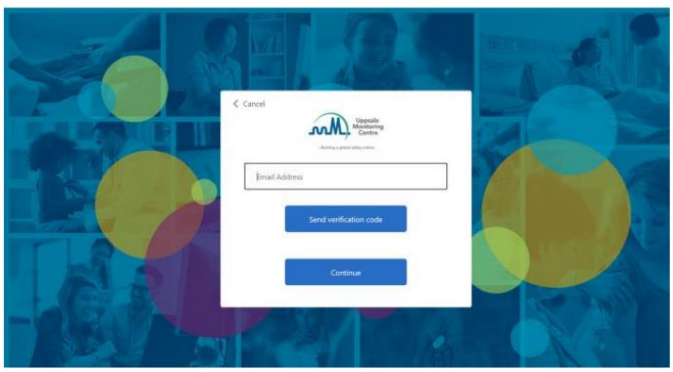
6. Enter the code received in the related field and click on “Verify code”.

7. If the code is correct, the message “The code has been verified. You can now continue” will appear. Then, click “Continue”
8. On the next page, enter your password and confirm it, following the security guidelines (password with 8 to 16 characters, combining upper and lower case letters, numbers and symbols).

9. Click on “Continue” and, if the process is successful, the page to log in to VigiMed will open. Companies with your registered email and password.

Note: to recover your password, the same procedures must be followed.



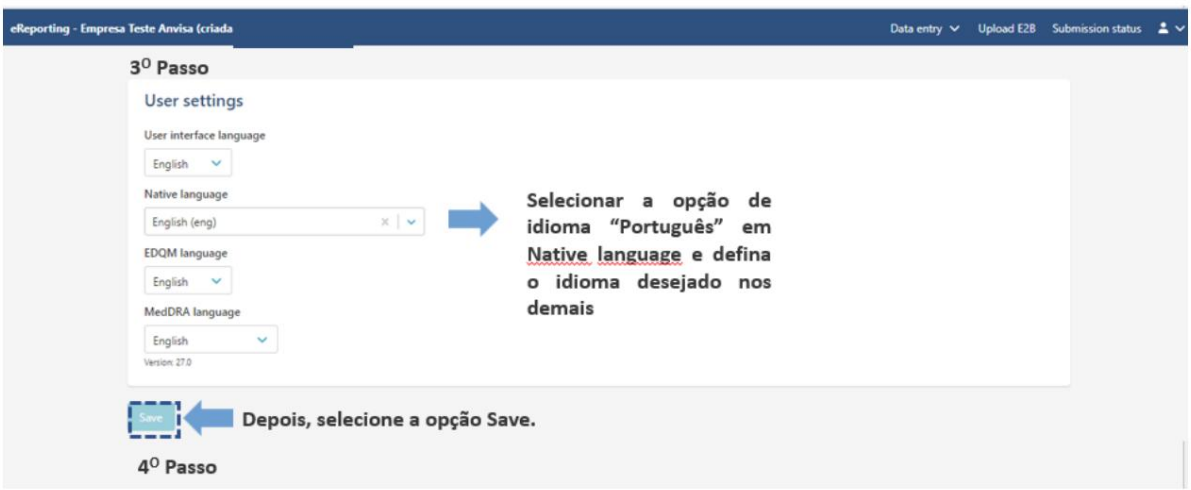


2.5. USER AND LANGUAGE SETTINGS

After completing the registration, when logging into the system for the first time via the VigiMed link Company: https://industryereporting.who-umc.org/, it will be necessary to activate the account by accepting the terms and conditions of use of the system. Then, a page will open where you must choose the language to be used in the interface. Select the language “Portuguese” and click “Save” to continue.

For later language configuration, simply click on the arrow next to the user icon (Step 1), then select the “User settings” option (Step 2).

The configuration page will open to select the interface language, the native language and the language of the dictionaries (Step 3). After selecting the language, click on “Save” (Step 4) to proceed.



2.6 VIGIMED COMPANY HOME SCREEN

The VigiMed Empresas (e-Reporting) home page has a top menu and a bottom menu. main menu for navigating the system. The top menu has the following options available:

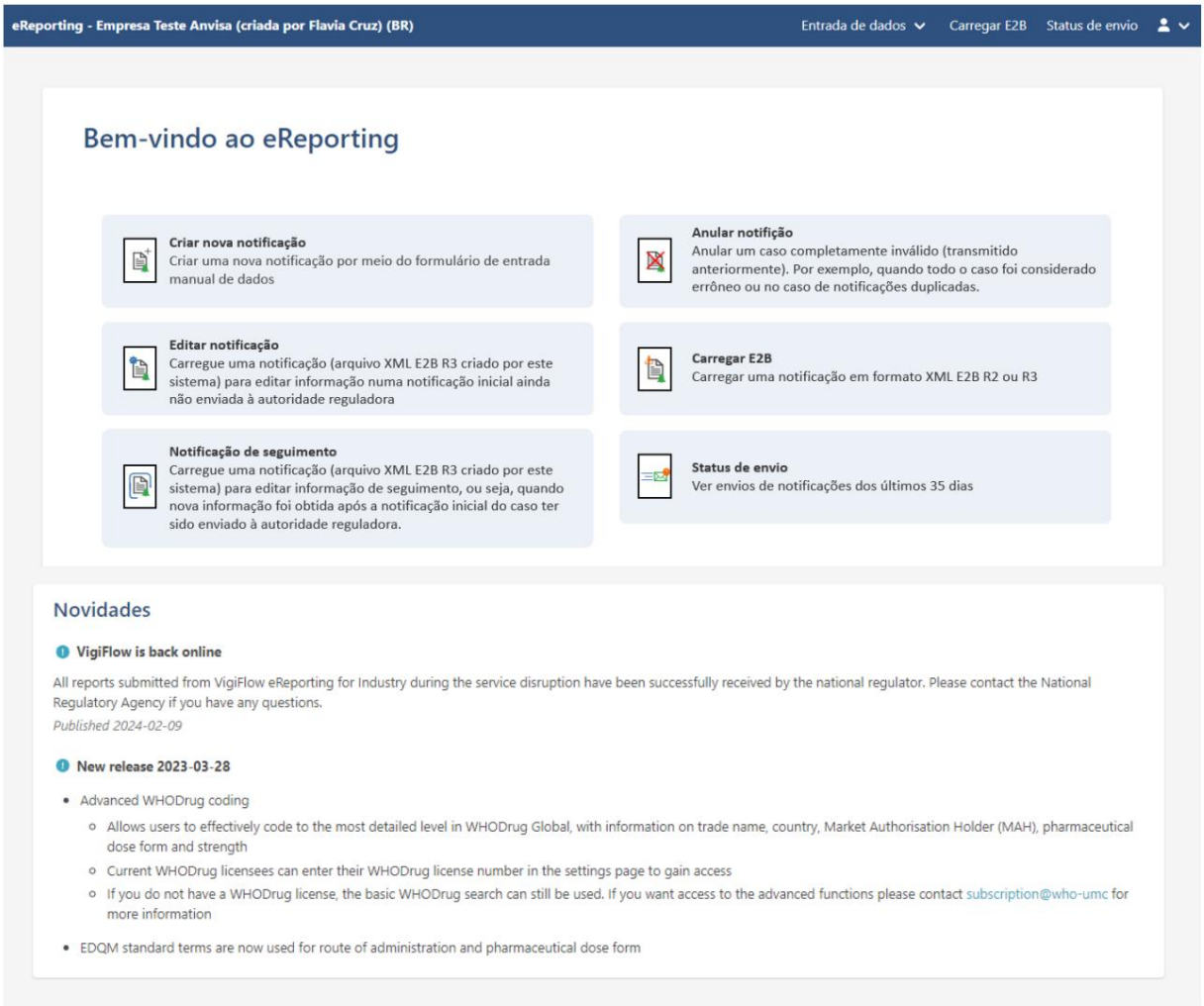
- Data entry: Manual notification entry to create and edit notification, follow-up notification and cancel notification - see items 3 to 6.
- Upload E2B: import of ICH E2B XML file - see item 7.
- Submission status: view notification submissions from last 35 days - see item 8.
- : options to check user name and email, start, configure the user and language (see item 2.4), manage licenses (see item 2.7), have access to privacy policies, terms and conditions of use, and exit.

On the home page, there is also the menu displayed on the main screen, with the action options and descriptions of each one. Below are some reports on the latest news about the System.

The main menu contains the six actions related to notifications, as follows:

- Create notification: create a new notification via the input form data manual - see item 3.
- Edit notification: Upload a notification (E2B R3 XML file created by this system) to edit information in an initial notification not yet sent to the regulatory authority - see item 4.
- Tracking Notification: Upload a notification (E2B R3 XML file created by this system) to edit tracking information, i.e. when new information was obtained after the initial notification of the case was sent to the authority regulatory - see item 5.

- Cancel notification: cancel a completely invalid case (transmitted previously). For example, when the whole case was considered erroneous or in the case of duplicate notifications - see item 6.
- Load E2B: load a notification in E2B R2 or R3 XML format - see item 7.
- Sending status: view notifications sent over the last 35 days - see item 8.



Attention!

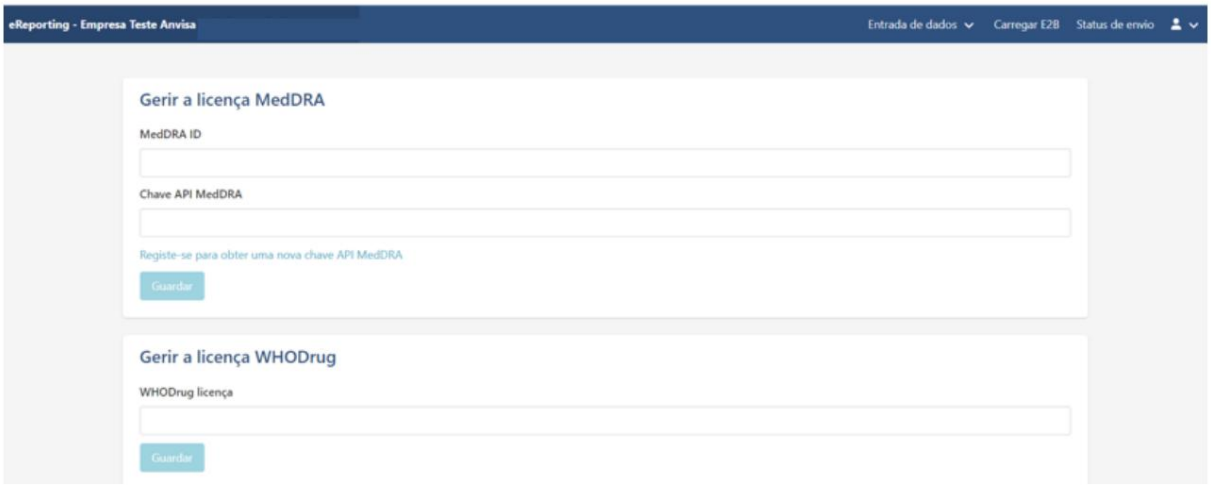
If the user (same email) is registered with more than one company or in accounts intended for Pharmacovigilance or Clinical Studies, must be selected which company or account you want to notify before starting any action.

2.7 ACTIVATION OF MEDDRA AND WHODRUG LICENSE

MedDRA terminology is used in the coding of adverse reactions/events (os) and other medical terms such as cause of death, indication, name of tests, medical history and diagnosis. For more information about the dictionary, see item 2.1.

The use of the WHODrug dictionary for the coding of drugs and active ingredients in notifications are recommended by Anvisa.

First, to use MedDRA and WHODrug, it is necessary to enable each license, by clicking on the arrow in the upper right corner and the “Manage licenses” option. Then, fill in the requested fields with the company's MedDRA or WHODrug License information and click in 'Save'.



In case of MedDRA license, to get your 'MedDRA API Key', click on the link “Register to obtain a new MedDRA API key” (https://mid.meddra.org/account/register). It will be necessary to have on hand the 'Username' and 'Password' provided by MedDRA MSSO after subscription process. More information at: https://www.meddra.org/subscription/process.

If there is any problem with your MedDRA license credentials, contact the support team.

MedDRA MSSO support: https://www.meddra.org/contact.

In the case of the WHODrug license, simply include the WHODrug license number. If there is any problem with WHODrug license credentials, contact UMC support team at e-mail: support@who-umc.org.

If the procedure presents any error on the VigiMed Empresas *(Industry e-)* page, *Reporting),* close the browser and, before opening Vigimed Empresas, perform any of the following: procedures:

- To clean the browser: abra the link to the step-by-step: support.google.com/chrome/answer/95589?co=GENIE.Platform%3DDesktop&hl=pt-BR
- Disable translator: https://support.google.com/chrome/answer/173424?hl=pt-BR&co=GENIE.Platform%3DDesktop
- Use an incognito tab: press the Ctrl + Shift + n keys at the same time. Here's how: https://support.google.com/chrome/answer/95464?co=GENIE.Platform%3DDesktop&hl=pt
- Temporarily disable your computer's antivirus during the installation procedure.

account activation

- Use other browsers (Firefox, Mozilla, Edge, etc.)

3. MANUAL DATA ENTRY INTO ICH E2B STANDARD

3.1. CREATING AN INITIAL NOTIFICATION

There are two options for creating a notification. The first option is by selecting the “Create” button. new notification” in the main menu (Step 1). The 2nd option is to click on “Data Entry”, in the top menu, and select the option “Create new notification” (Step 2).

A new page will open for you to fill in the notification fields. On the left side on the left there is a menu with all the sessions that make up the notification, containing the data elements as defined and described in the ICH E2B (R3) Guide.

In the left menu, you can navigate through the form and identify some of the data entered, such as medications and adverse reactions/events. The following will be highlighted: some care when filling out each section.

Important!

During filling, feeding errors or the absence of any mandatory data will be marked in red and need to be adjusted before saving or sending the notification.

Attention!

It is worth noting that some fields or data sets are repeatable. When If you need to enter more information, simply click the '+' button.

To express decimal units, DO NOT use a comma (,) as a separator and YES use a period (.) in patient data, such as weight and height.

3.1.1.ADMINISTRATIVE

This session consists of two groups of data: Notification Information and Notifier initial. Its purpose is to collect some data necessary for the proper processing and management of notifications, which will allow for proper identification of the notification and the notifier.

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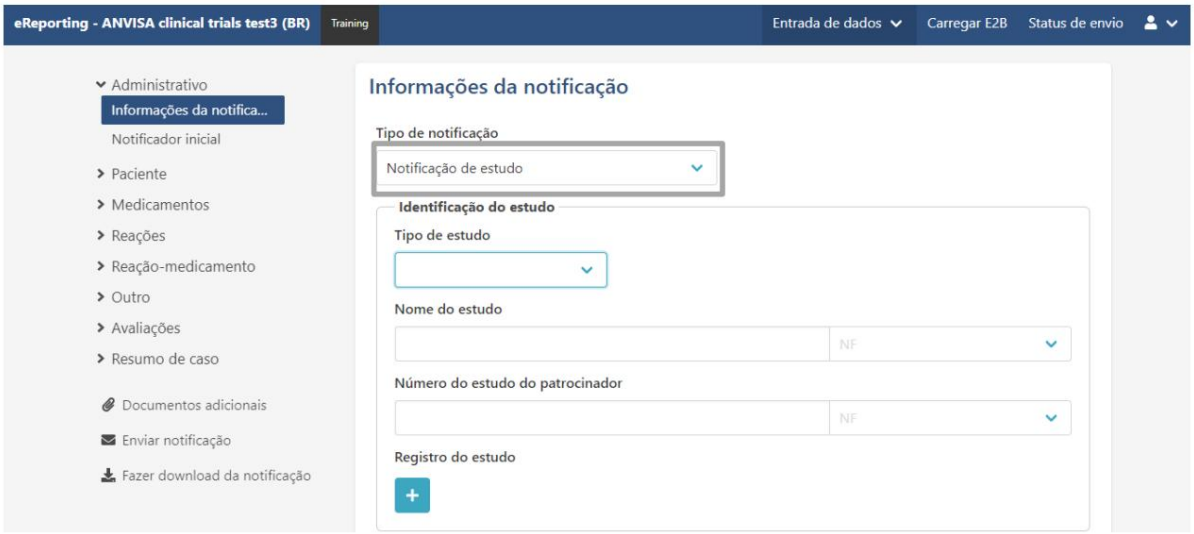
3.1.1.1. NOTIFICATION INFORMATION

In the Notification Type field, choose “Study Notification”.



All fields contained in the “Notification Information” group must be completed. mandatory, except “Other identification of notification in previous transmissions” and “Notification identification number that is related to this notification”.

All fields contain important and essential information for an analysis. complete. We can exemplify with the fields “Study Name” and Study Number of the sponsor” (protocol code), which do not prevent the continuation of filling out of the notification, but they are of utmost importance to identify the clinical trial in which SUSAR occurred. Therefore, all fields must be filled in.

In the “Study Name” field, describe, in addition to the title of the clinical trial, the record of the petition in which the clinical trial protocol was requested (Specific Trial Dossier Clinical):

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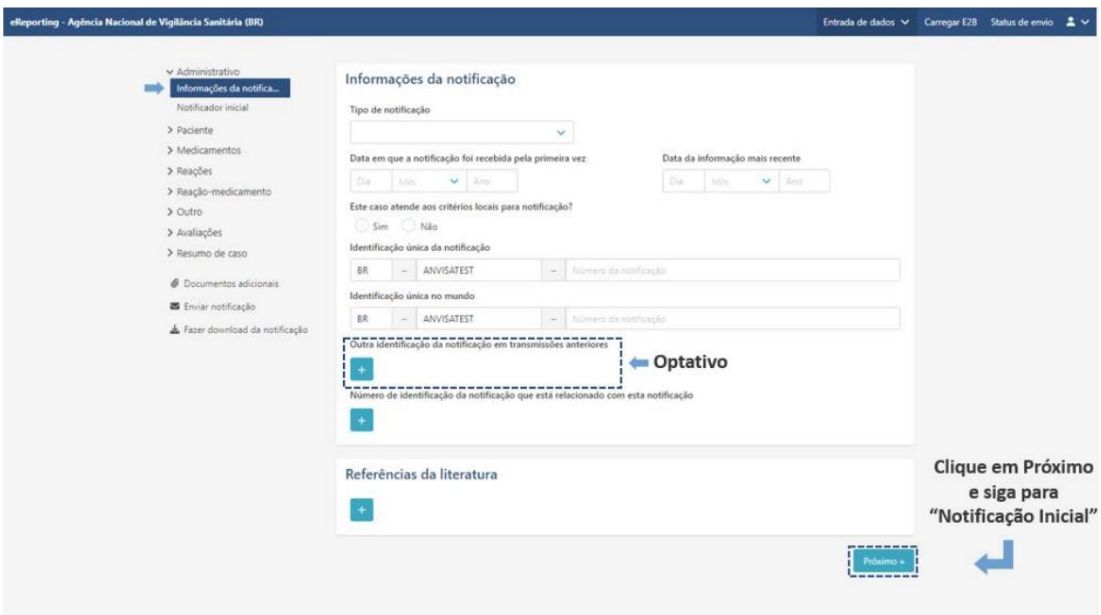
o Example: "Phase 2/3, randomized, double-blind, placebo-controlled study for to evaluate the efficacy and safety of XXXX in participants with XXXXXX" – Exp. No. XXXXXXX/XX-X

> Attention! The Unique Notification Identification and the Worldwide Unique Identification must follow the structure defined in the ICH E2B Guide:
>
> XX-ShortName-NotificationNumber
>
> XX is the country code in capital letters and, in this case, it must be BR;
>
> Short Name must be the same as that provided in the registration;
>
> Company notification number

The first two data will be filled in automatically by the system and should not be changed. The notification number must be managed for the company. The subsequent submission of another form with the same Unique Notification ID and Unique Identification in World will be understood by the system as a follow-up notification (for Follow-up Notifications, see item 3.5).

If necessary, indicate an additional notification number, simply click on the icon corresponding to the field "Other notification identification in previous transmissions" and enter the data.



3.1.1.2. INITIAL NOTIFIER

The Initial Notifier information must be completed with the investigator's details.

main office of the center where the SUSAR that is being reported occurred. To assist in contacting

If there is a need to supplement or investigate the case, please provide: **Name,**

Last name, State (UF in acronym) and Telephone.

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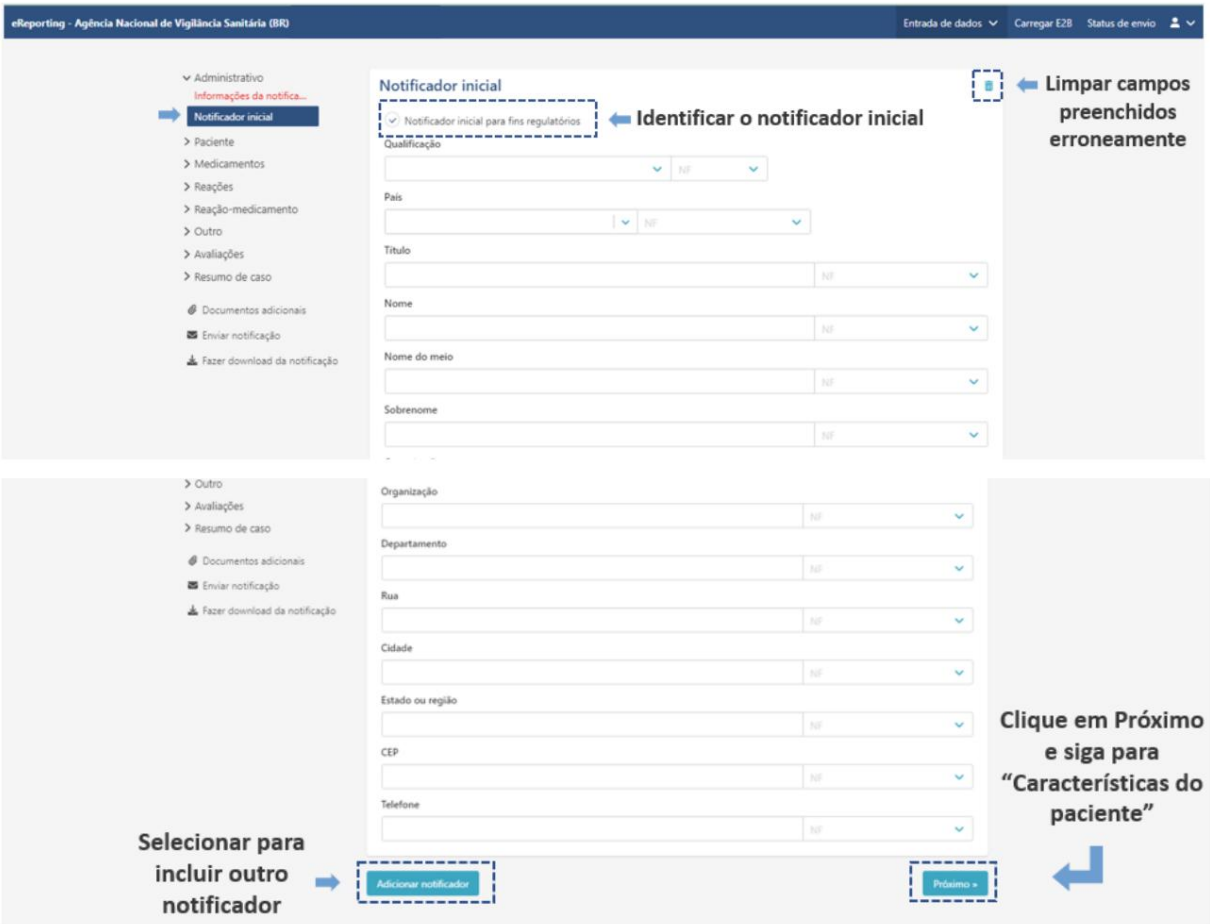
> Whenever possible, provide all information: First Name, Last Name, State and Telephone Number. For the State, include the abbreviation of the UF.



In the “Organization” field, enter the name of the Institution where the center is located.

search (hospital, clinic, health service), if applicable. In the “Department” field,

describe the name of the Research Center.

If more than one notifier is informed, select “Initial notifier for purposes of

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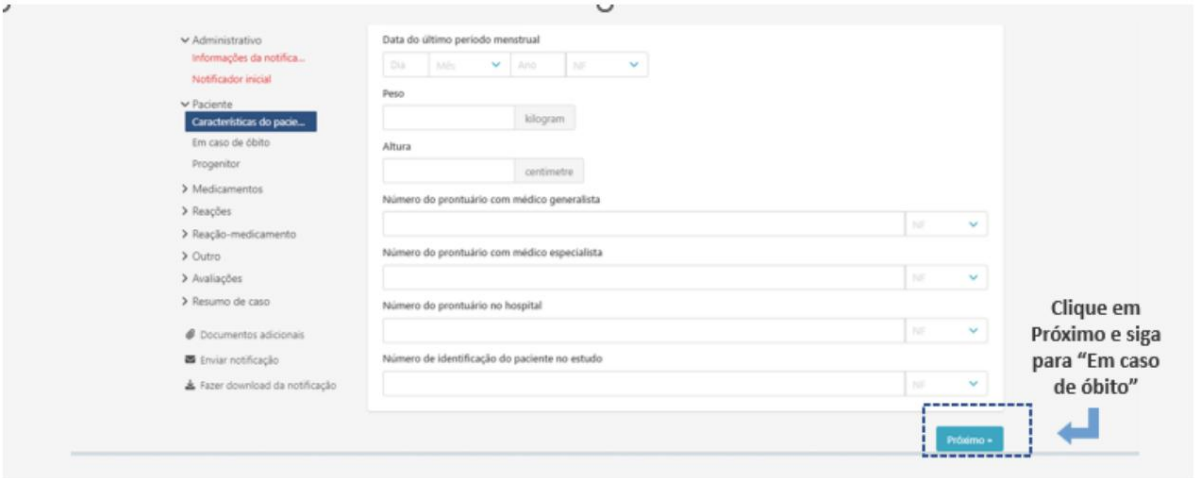
regulatory” in which the primary source is identified and where the case occurred.

3.1.2.PATIENT

This session consists of three groups of data: 'Patient characteristics'; 'In case of 'death' and 'Parent'. Intended for filling in information regarding the clinical trial participant and, as the case may be, about death, or information relating to the parent who was exposed to the drug in which the adverse event was observed in the child (embryo, fetus, newborn or child – *Parent-child notification).*

3.1.2.1. PATIENT CHARACTERISTICS

For data protection purposes, please provide the initials of the clinical trial participant's name. You can also use the predefined values: Unknown; Asked, but Unknown; Not asked; Masked. Only one of the information regarding age needs to be informed if possible.



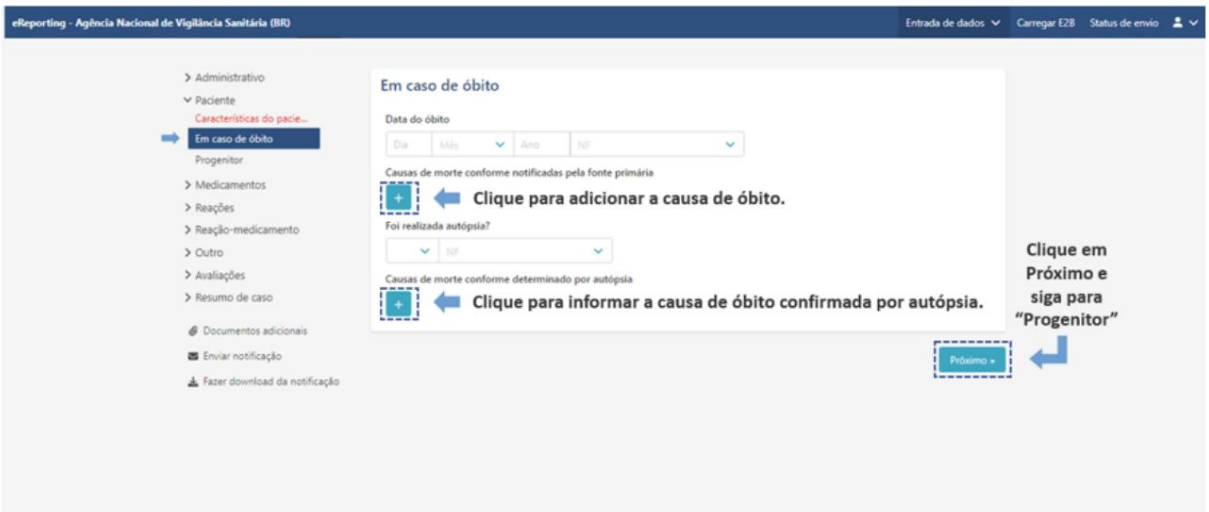
To express decimal units in patient data, such as weight and height, DO NOT use a comma (,) as a separator and DO use a period (.).

The 'Patient Study Identification Number' field must be completed.

3.1.2.2. IN CASE OF DEATH

This data group includes fields intended for filling in information.

referring to the participant whose reaction resulted in death.



In the field “Cause of death as reported by the initial reporter” describe the cause of death in the opinion of the investigator.

Important!

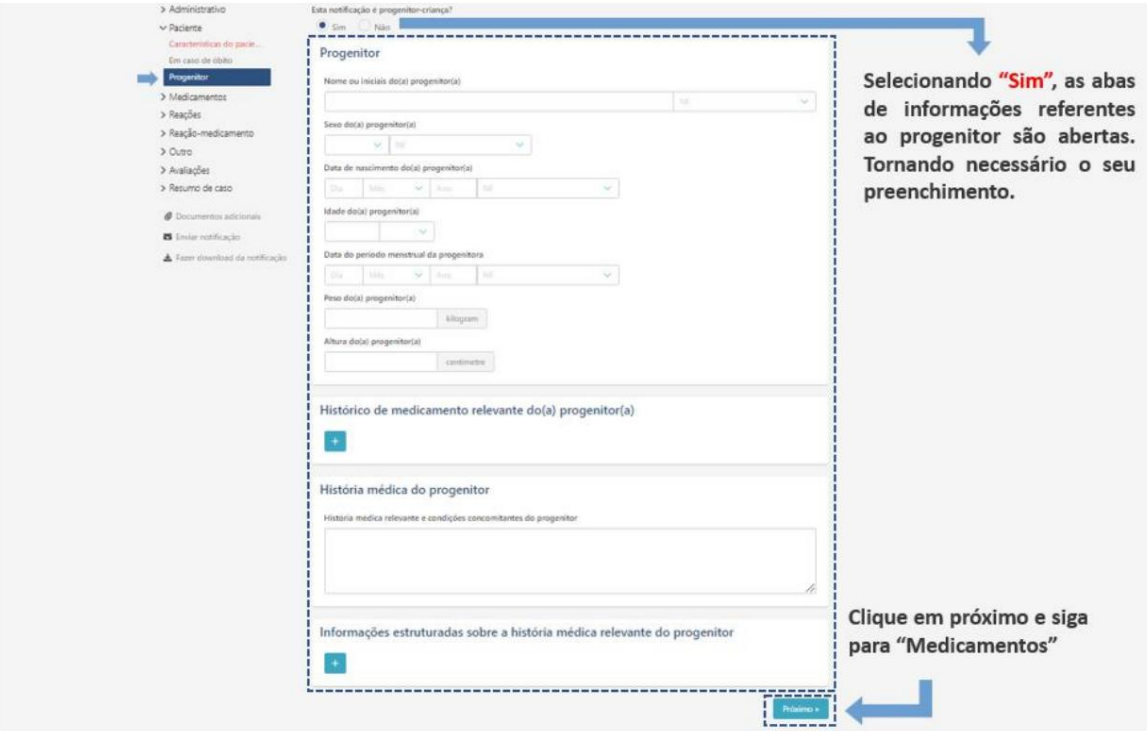
To report the reported cause of death and the cause of death determined by autopsy, if applicable, using MedDRA; the company license needs to be enabled (see item 2.7). For instructions on how to code, see item 3.1.4.1.

3.1.2.3. PROGENITOR

This information group aims to collect information regarding the father or mother whose exposure to the drug resulted in an adverse reaction/event in the child (embryo, fetus, newborn or child) (Parent-*child notification).*

To fill in these fields, you must select the YES option.

This section should be completed only when the answer to “Is this a parent-child notification?” is YES and only when the mother or father has not had any adverse reactions/ events. Otherwise, this section should not be used.



To express decimal units in parental data: weight and height, DO NOT use a comma (,) as a separator and DO use a period (.).

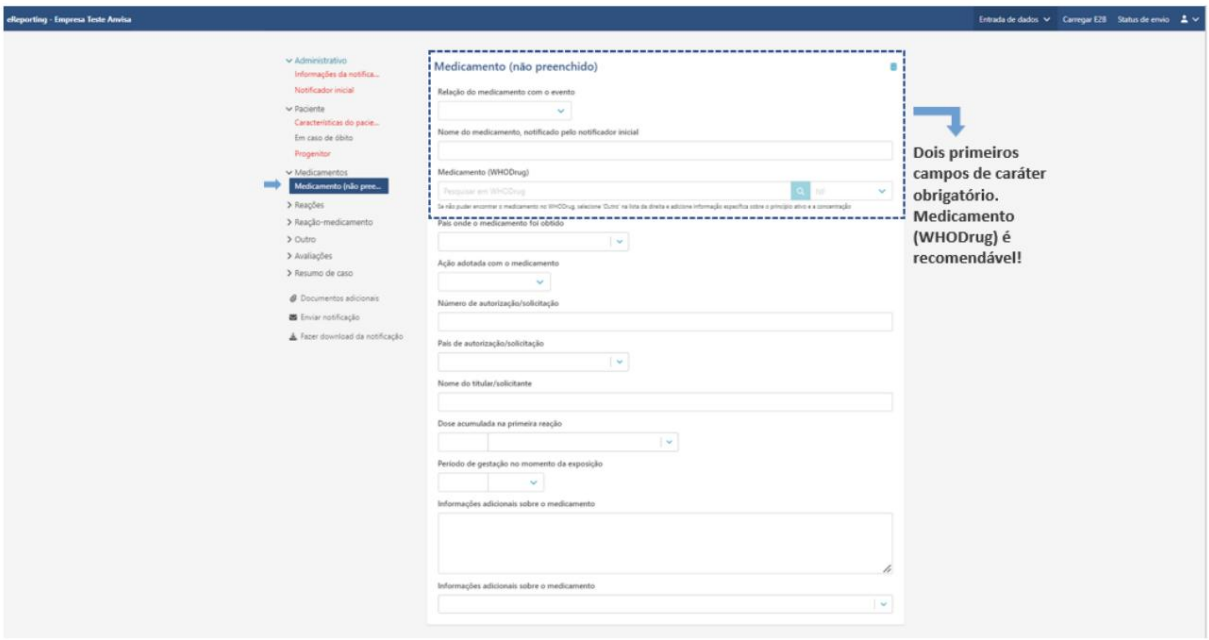
3.1.3.MEDICINE

This section includes general information about the medication, indication and dosage. It is if from a set of repeatable data, that is, different ones can be added medicines or different dosages for the same medicine.

If the same medicine has more than one dosage, dose or batch, simply click on the icon "+" to duplicate fields, instead of adding a new medication.

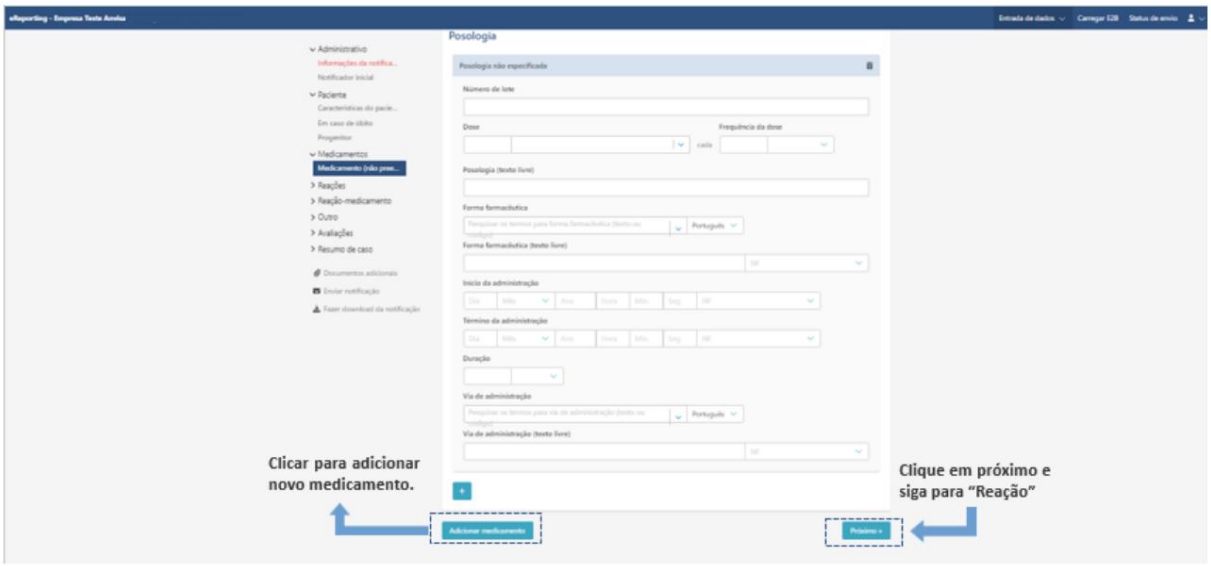
Important!

To report the drug or active ingredient in WHODrug, the license from company must have been previously activated (see item 2.7).



Important!

To report the indication using MedDRA, the company's license must be activated (see item 2.7). For instructions on how to code, see item 3.1.4.1.



It is important that as much data as possible is provided, aiming to obtain quality in notification.

In the "Additional information about the drug" field, inform whether the sponsor knows the allocation of the clinical trial participant, adding information about, for example, the breaking of blinding, if applicable.

3.1.3.1. CODING IN THE WHODRUG DICTIONARY

To include WHODrug drug information in manual input, you must:

- insert the commercial name in the 'Medicine (WHODrug)' field, as per the registration product, or the name of the active ingredient;
- click on the magnifying glass to search;
- in the window(s) that open, select the most appropriate correlation to the name of the medication or vaccine informed by the notifier, considering:
  - or if B3 license: the pair "commercial name (Patent Name) and active ingredient (AI – Active ingredient or AI(v) Active Ingredient variant)" suitable or only generic name (active ingredient),
  - or if C3 license: select the most specific level informed by the notifier, consider: the active ingredient(s), commercial name of the medicine, Drug Registration Holder (DRM), pharmaceutical form and dose.

In manual entry, the B3 license is enabled for all companies. Using the dictionary WHODrug in C3 format remains recommended, until the amendment of RDC 406/2020 makes it mandatory. Using the C3 format it is possible to select the largest amount of information about notification medications or vaccines with just a few clicks.

Attention!

To use WHODrug in C3 format in VigiMed, the company needs to activate the license in the system – see item 2.7. Proper coding with WHODrug must follow the guidelines in the document 'How to use the WHODrug C3 format for drug coding', available on the VigiMed Company page.

The WHODrug dictionary is constantly updated with drug information and vaccines registered in Brazil, by Anvisa and UMC. However, if the name is not found commercial for the drug to code, only the name of the active ingredient must be provided in WHODrug and include the commercial name of the medication in the free text field (Name of Medication, notified by the initial notifier) or in the Narrative.

In this case, if the company already has the WHODrug license in C3 format, it is also possible request the inclusion of the medicine through Change Request, a tool available on the page from WHODrug, in the user area. Requests can be made individually or to a batch of medicines and vaccines simultaneously. The link to the package insert must be provided medicine at Anvisa as reference information for validation of the terms to be entered in WHODrug. The same procedure can be adopted if it is found some inconsistency in the company's drug data in WHODrug. The updates in the manual entry of VigiMed Companies will be made available less than 36 hours after the request.

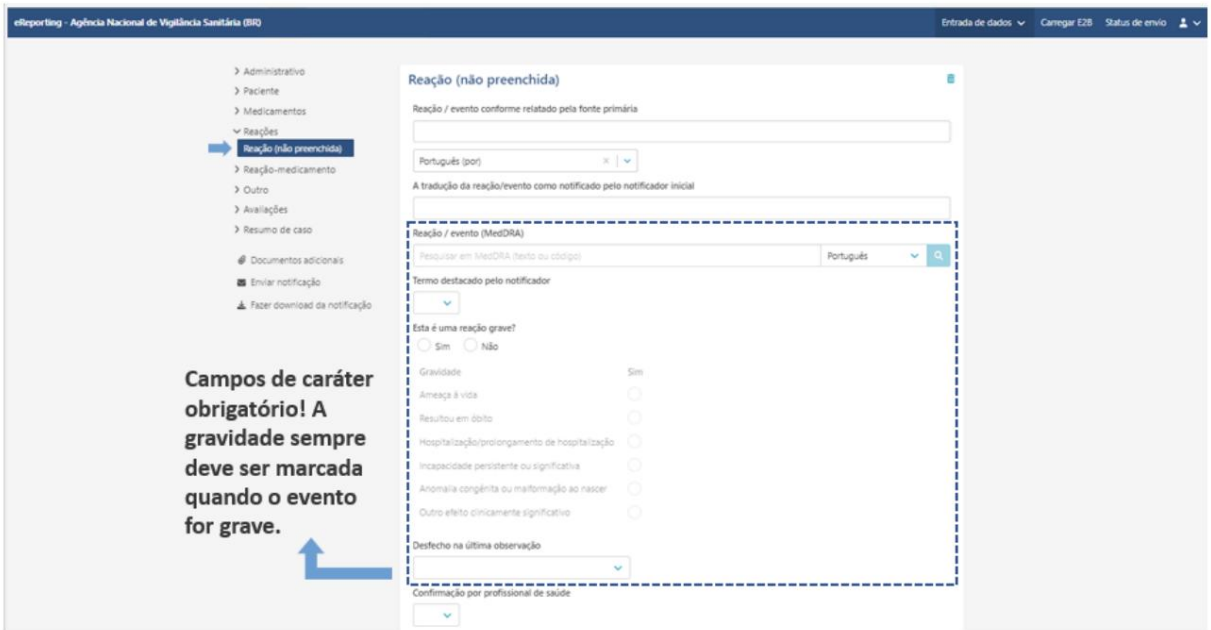
Important!

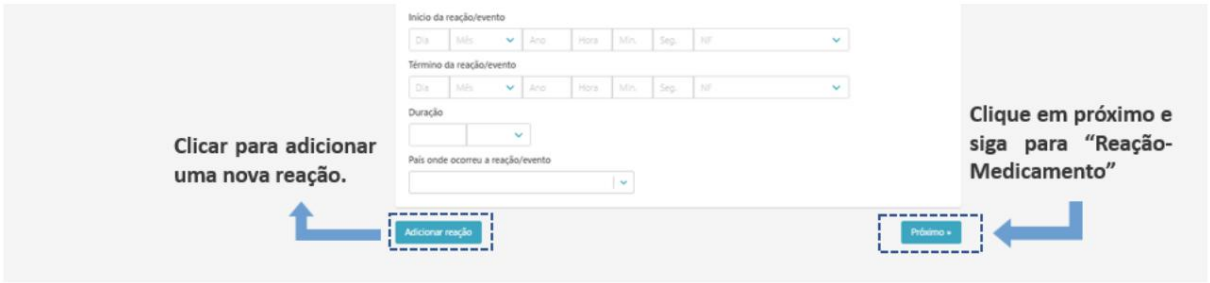
When selecting terms, pay attention to the description of the active ingredient that can be arranged in the form of salt or base. When choosing a term for the trade name, pay attention to the active ingredient that is related to it. Choose the name of the medicine with the spelling following the registration with Anvisa; what can it be checked in the DOU or in the Electronic Bulletin from Anvisa.

3.1.4.REACTIONS

This session consists of fields intended for collecting information related to SUSARs observed in the clinical trial participant. In addition to information about the adverse event, in the field “The translation of the reaction/event as reported by the initial reporter” must be other data are provided, such as the start date of the event, the severity, the date of the knowledge of the event by the sponsor, among other information.

The terms that correspond to the name of the reported reaction/event must be selected. by the notifier. In addition to the data on the adverse event, other information must be reported data, such as the date the reaction began, its severity, among other information.



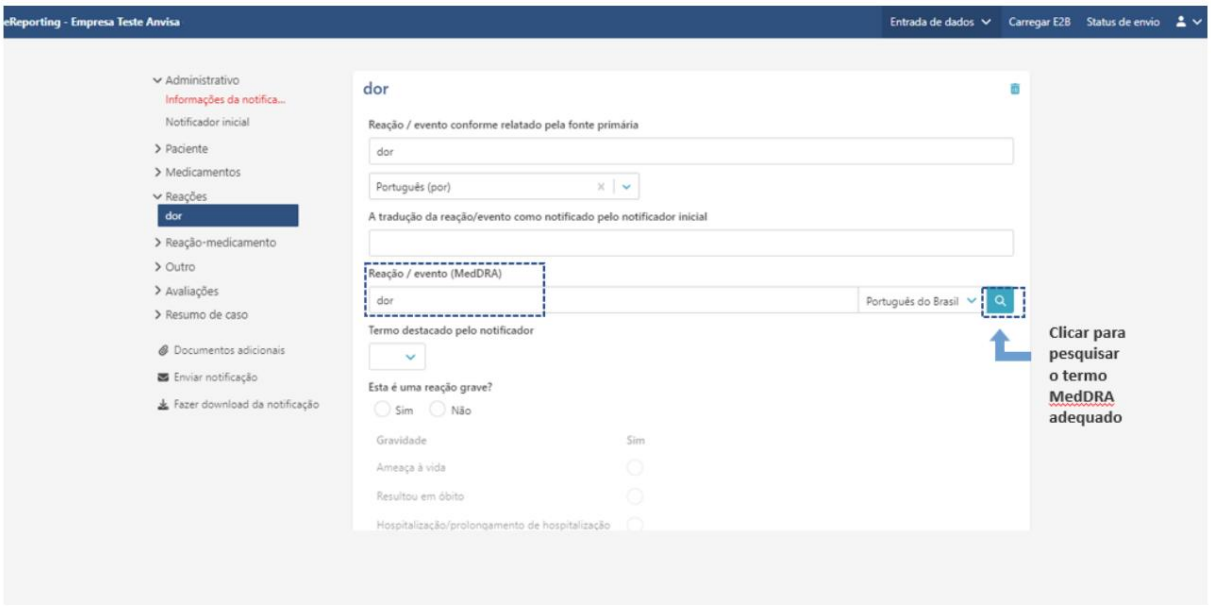


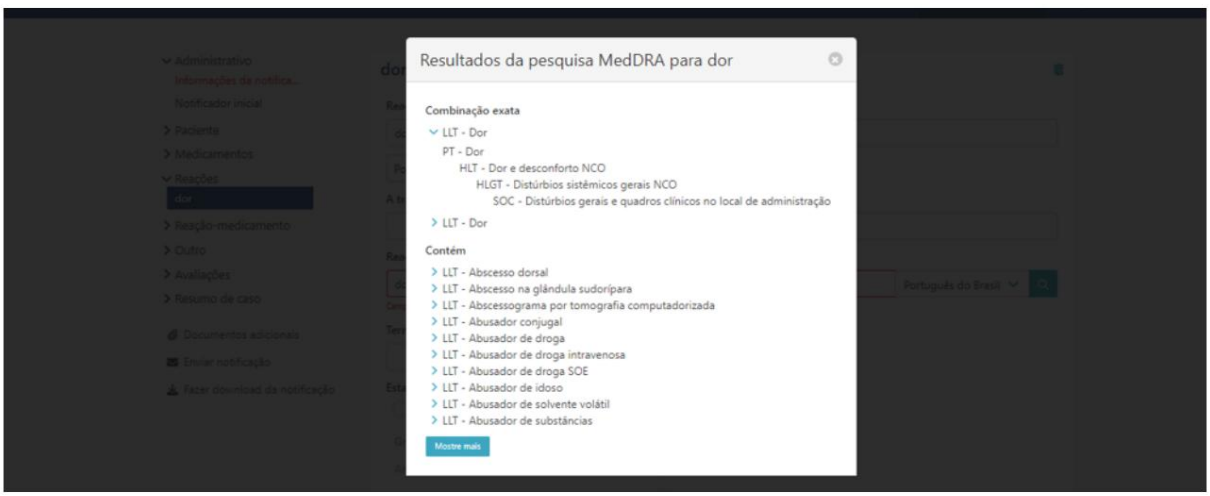
3.1.4.1. CODING IN MEDDRA TERMINOLOGY

For coding in MedDRA terminology, simply enter the desired term or code in the “Reaction/event (MedDRA)” field and the related language, click on the magnifying glass to search and choose one of the most appropriate MedDRA terms.

Proper coding with MedDRA must follow the documents 'Points to Consider' and 'MedDRA Terminology Best Practices', available in Portuguese and with versions updated biannually on the page: https://www.meddra.org/how-to-use/support-documentation/portuguese .

It is suggested to use the MedDRA Browser (https://www.meddra.org/browsers) to help search for the most appropriate terms, locate the MedDRA code, compare terms in different languages, versions, check terms according to the terminology hierarchy, etc.





3.1.5.DRUG REACTION

This session has two groups: Re-exposure and Time Lapse. It is intended for filling in information regarding re-exposure to the suspected drug(s) and

the outcome of this re-exposure, as well as the time/period between the administration of the doses of the suspected drug and the onset of the reaction. Such information helps in the assessment of causality of each drug versus adverse *reaction/ event*

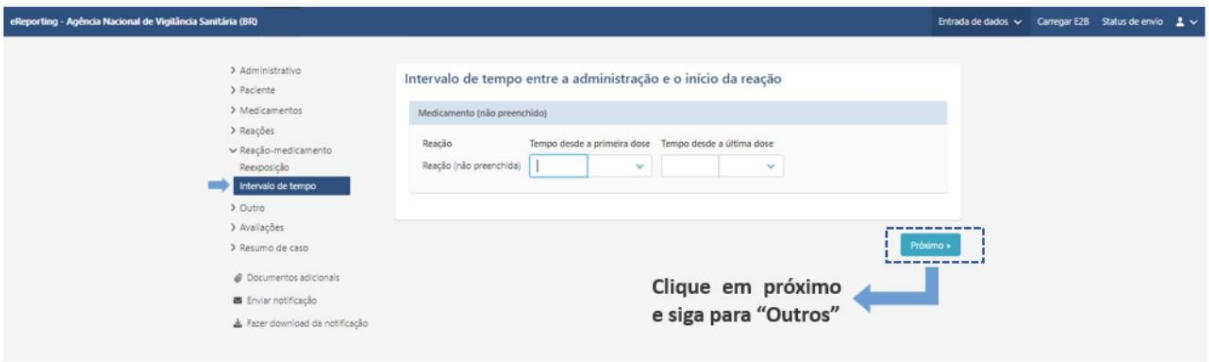
3.1.5.1. REEXPOSITION

Report whether or not the clinical trial participant was re-exposed to each medication suspect informed. If positive, it is mandatory to inform the outcome of the re-exposure and, If not, just click “Next” to move on to the “Time Range” group.

3.1.5.2. TIME INTERVAL

The Time Interval data group must be filled with information regarding the interval between administration of the medication and the occurrence of the adverse reaction/event.

It must be reported for each previously added suspected drug, whenever possible.



Observation. In the event that the medication has not been administered prior to the occurrence of SUSAR, leave the field blank.

3.1.6.OTHERS

This section is divided into three groups that contain fields intended for filling in of data relating to examinations and tests carried out, medical and medication history.

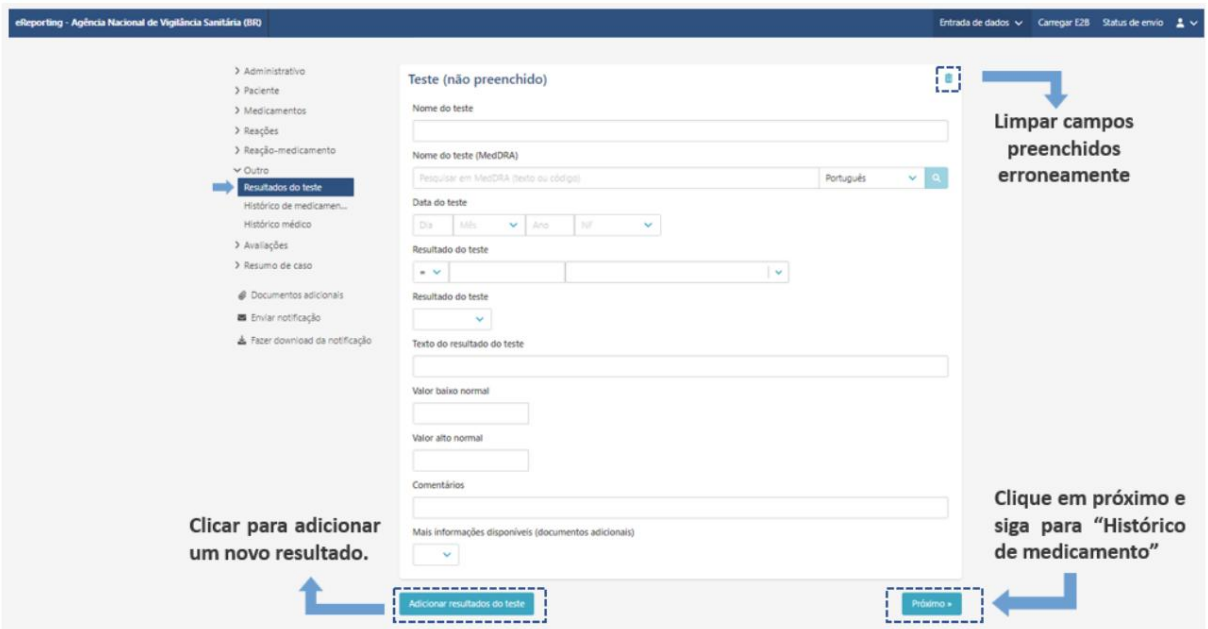
The objective is to include information that helps in understanding the case in question, which makes it possible to exclude explanatory causes for the adverse reactions/events observed during causality analysis.

2nd

3.1.6.1. TEST RESULT

This section records the tests and procedures performed to diagnose or confirm the reaction/event, including those performed to investigate (exclude) a non-existent cause related to medications. Both positive and negative results should be reported. Although structured information is preferable, there is the possibility of transmit the information as free text.

Therefore, whenever possible, the MedDRA terms that correspond to the name of the test to which the patient was subjected and inform, by typing, the values corresponding to the result of this test. Additional information or information that was not contemplated in the fields available on the form must be entered in the fields free text.



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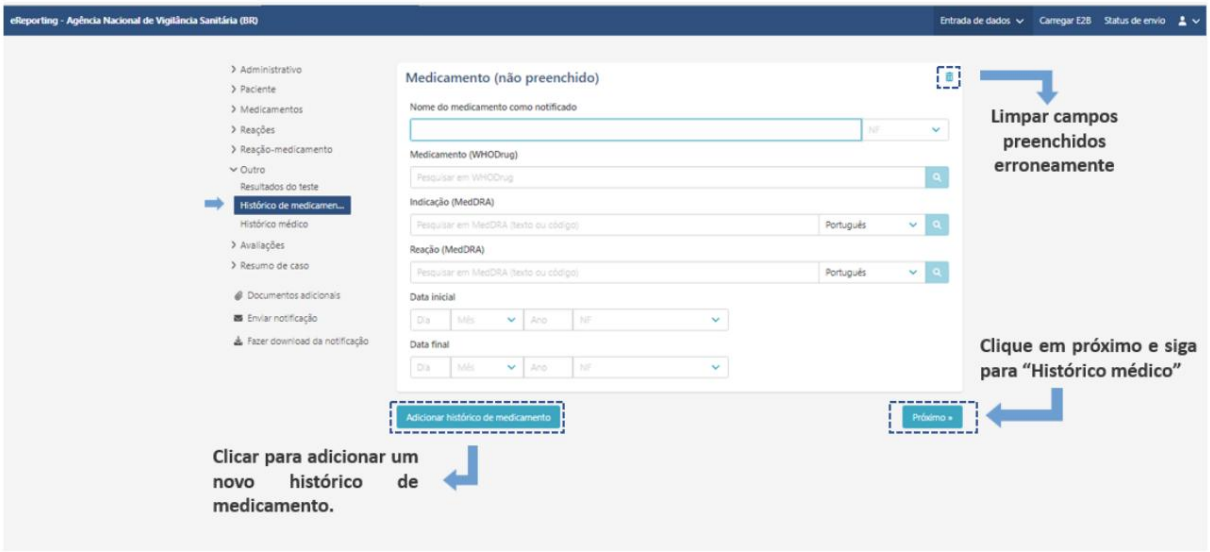
3.1.6.2. MEDICATION HISTORY

The medication history corresponds to the report of information regarding the medications that the patient used before the occurrence of the adverse reaction/event in question. Include information relevant to understanding the case.

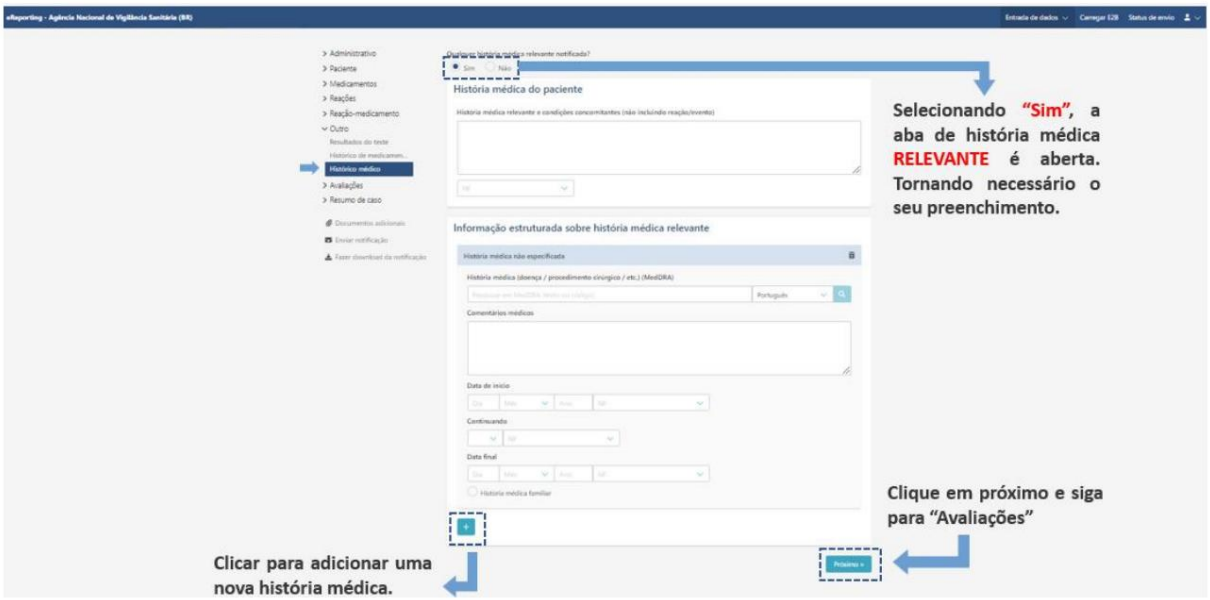
This section does not address medications taken concomitantly or that may have contributed to the current reactions/events. Medical judgment should be applied to consider discontinued medications that may be suspect based on half-life elimination and known pharmacodynamic effects.



> Medications for continuous use started before the reported reaction/event, which continue to be used, must be reported in item 3.1.3. Medication, selecting the "Concomitant" option in the "Relationship of medication with the event" field.

3.1.6.3. MEDICAL HISTORY

The patient's medical history refers to diseases acquired by the patient prior to manifestation of the reported adverse reaction/event. Includes clinical conditions of the patient that are relevant to the case, including information such as illnesses, pregnancy, procedures surgical, psychological trauma, risk factors, etc.



3.1.7. EVALUATIONS

The "Assessments" section allows you to record the causality assessment for each drug, suspected or interacting, in relation to adverse reactions/events informed, using pre-established methods. Each 'drug and reaction' pair informed must contain its causality assessment result.

You must type in the free text fields, in:

- "Evaluation method", the name of the methodology used. The evaluation method must be the same method described in the clinical protocol
- "Source of evaluation", the name of the evaluator, that is, the person, department or organization responsible for the causality assessment. The first assessment to be recorded in the notification must refer to the one performed by the study sponsor and this must be reported in this field

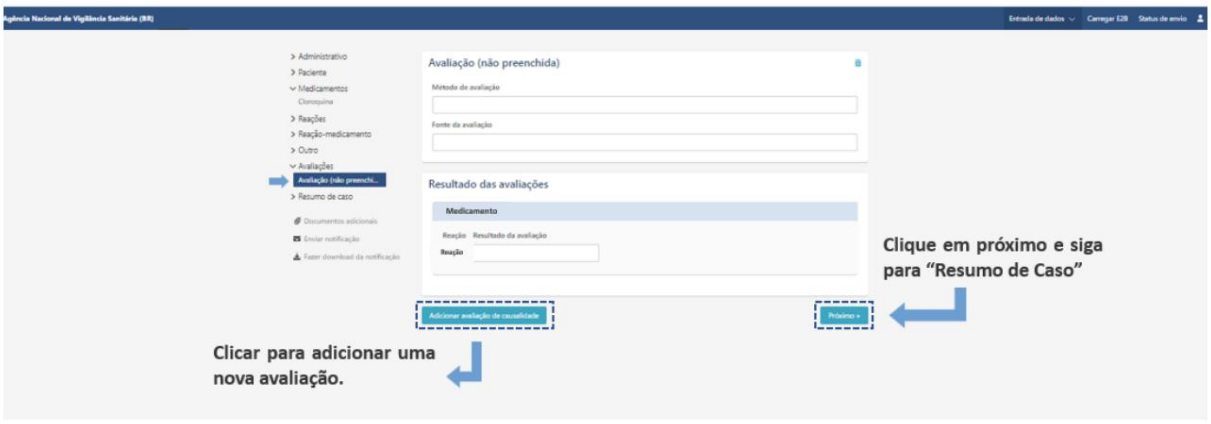
"Evaluation results"

The main methods and their respective values are:

- WHO causality, which may be the "Evaluation result":
  - the Defined
  - the Likely
  - the Possible
  - the Unlikely
  - o Conditional/Unclassified
  - o Not accessible/Not classifiable

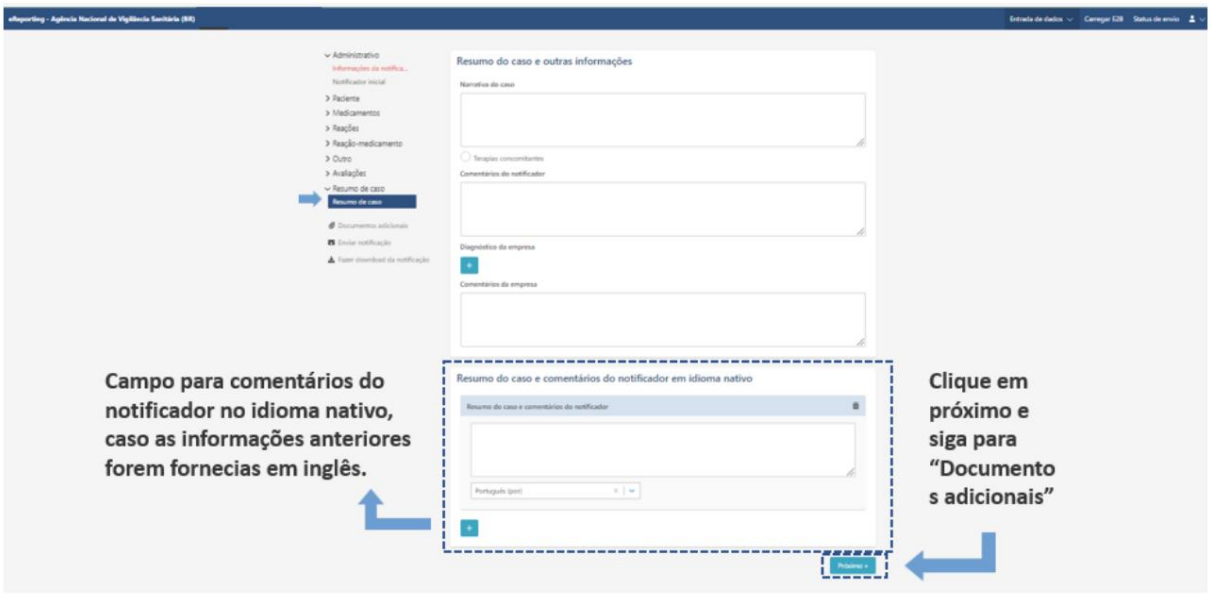
- Naranjo algorithm, which can be the “Evaluation result”:
  - the Defined
  - the Likely
  - the Possible
  - the Doubtful
- WHO AEFI (for vaccines), which may be the “Evaluation result”:
  - o A1 – Product-related reaction
  - o A2 – Reaction related to vaccine quality
  - o A3 – Immunization error
  - o A4 – Anxiety reaction associated with vaccination and/or stress triggered in response to vaccination (EDRV)
  - o B1 – Consistent temporal relationship, but no evidence in the literature for establish a causal relationship
  - o B2 – Research data are conflicting regarding causality
  - o C – Inconsistent or coincidental association/Undetermined
  - D – Unclassifiable

If you need to add more than one causality assessment for the same medication *versus* adverse *reaction/ event ,* simply click on the "Add causality" option, as indicated in the image below. The second assessment to be reported must be related to the assessment by the clinical trial investigator.



3.1.8.CASE SUMMARY

In this section there are three free text fields that must be filled with information about the case, that is, the detailed narrative about the reported case, the comments relevant information from the notifier and the company's comments (in this case, the sponsor).



Attention!

This section should not include identifiable data of the patient, healthcare professionals health and notifiers. If the notification is made in a language other than the Portuguese, Case Summary and Reporter's Comments should be added in native language (Portuguese).

According to the ICH E2D guide, the purpose of a narrative is to summarize all relevant and related clinical information, including patient characteristics, details of therapy, medical history, clinical course of the event(s), diagnosis including outcome, laboratory evidence, and any other information that supports or refutes an adverse drug reaction. The narrative should serve as a comprehensive and self-contained "medical history." The information should ideally be presented in a logical time sequence, i.e., in the chronology of events occurring to the patient, rather than the chronology in which the information was received.

3.1.9.ADDITIONAL DOCUMENTS

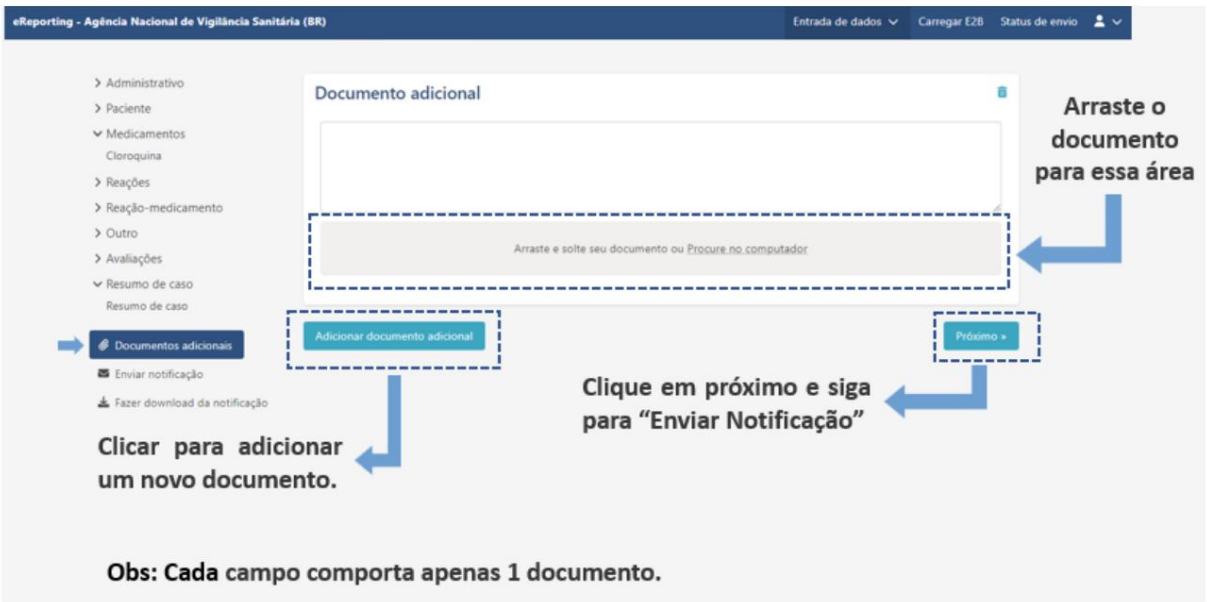
In this section, you can attach documents relevant to the case, especially if they contribute to the assessment of causality of the case, such as reports from the safety monitoring committee, medical reports, examination results, vaccination card, death certificate, among others.

It is important that the attached document contains a name that identifies it and that they are Enter the names of the documents in the free text field before attaching them. If you need to attach more documents, simply click on the "Add additional document" option, as shown in the figure below.

There are two ways to attach a document:

1. Drag and drop the file into the corresponding field (see figure below).
2. Find the file in your computer's directory and upload it. To do this, simply click on "Browse your computer", identify the file and then upload it.

The system allows you to attach files in the following formats: dcm, dicom, doc, docx, htm, html, jpeg, jpg, pdf, rtf, tif, tiff, txt, xls, xlsx. Files must not exceed 2 MB in size to be able to upload them without problems.



3.2. SENDING THE NOTIFICATION

Once you have completed filling out the notification, you must send it to Anvisa. To do so, go to the "Send notification" section. If there is a need to correct or complete any mandatory field, the "Send" button will be disabled and what needs to be revised will be highlighted in red.

If the notification is filled out correctly, simply click on "Send" and wait for the message "Notification sent successfully" to appear.

After issuing the successful sending message, the identification code of the submission and, below that, there is the "Download" button, through which you can download the manually fed notification file (see item 3.3).

It is extremely important that the file is downloaded and saved on the computer or HD so that it can be changed or updated later (follow-up notification).

It is suggested that a folder be created to save the downloaded files, as well as saving the image containing the shipping ID number, which serves as proof. of transmission.

2nd

To finalize and verify that the entire notification process was successfully completed, the notification submission status must be checked. The submission identifier that appeared after submission should be used to locate the AckLogs *(ICH ICSR Acknowledgement Message) file.* The AckLog is a confirmation message generated by the system that must be saved and verified for each submission, as per item 5 of this Manual.

Attention!

Information on the status of sending the notification, archiving the notification and the AckLog are available for 35 days on the Shipping Status page. For security, download AckLog immediately after sending the notification to the Anvisa.

After the 35-day period, it is not possible to recover any of the files. In this case, to carry out a follow-up, change or cancellation, it will be necessary

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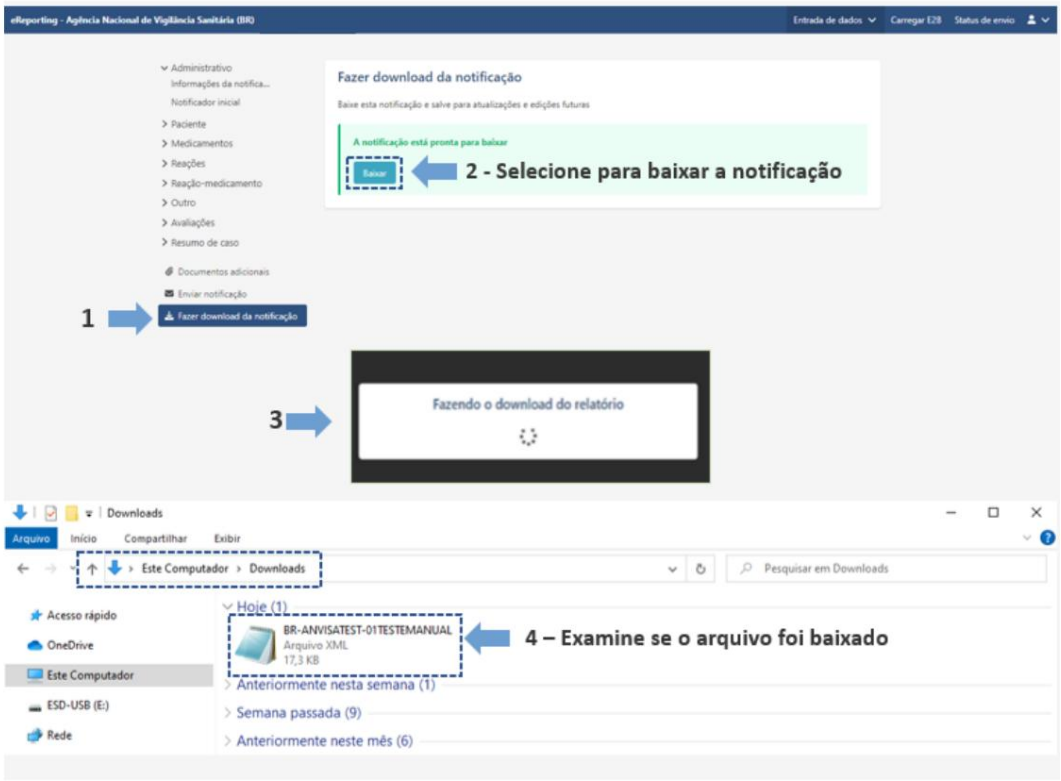
re-feed the entire notification form. This should be avoided as

implies duplication of notification in the database.

3.3. DOWNLOADING THE NOTIFICATION

To download the file, click on the “Download” option, within the “Download notification” section, as shown in the figure below. This option will only be enabled for notifications with the mandatory fields filled in and no errors identified in the file validation.



As stated in the previous section, it is extremely important that you download

of the notification before or after sending it to Anvisa. With this file in hand, it will be possible to edit

the file previously sent for a change or follow-up notification, without

need for retyping, or send a cancellation for the case.

Important!

The downloaded file will be in ICH E2B (R3) XML format and will be named after the Globally Unique Identification number of the notification in question.

If the company does not have a system to upload the E2B(R3) XML file, it can alternatively use the notification editing functionality (see

item 4.) to load the file and view the notification information in the related fields, without making changes or saving or sending such data.

3.4. Editing a Notification

Editing/updating a notification should occur whenever there is new relevant information to be added to the case or if the open case is pending evaluation.

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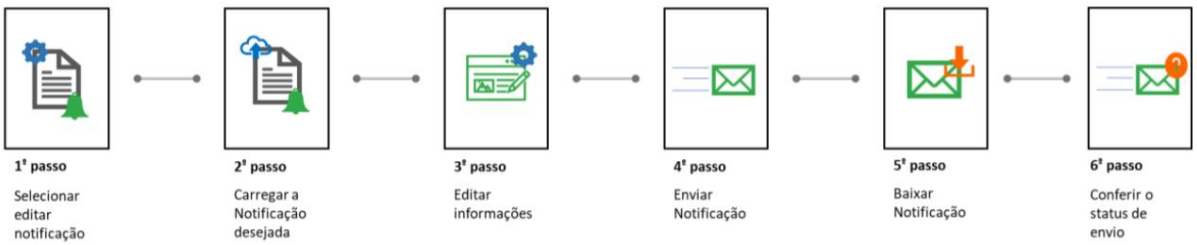

It must be done from the notification file saved in the previous submission. That is why it is so important to save the file on the computer or dedicated HD when sending the notification. It is not possible to recover the sent file that was not saved at the time of the procedure. If this happens, it will be necessary to fill in the entire form again.

The user has two options to start editing. The first option is to click on “Edit Notification” in the menu. The second option is to click on Data Entry in the top menu and then on Edit Notification.

To upload the previously sent notification file (XML), after locating the file on your computer, simply drag and drop it onto the (gray) indicator bar or click on “Browse on computer”, open the file explorer on your computer, locate the file and upload it.

Immediately after the information is fully loaded, it will feed into a new form and be available for viewing and editing.

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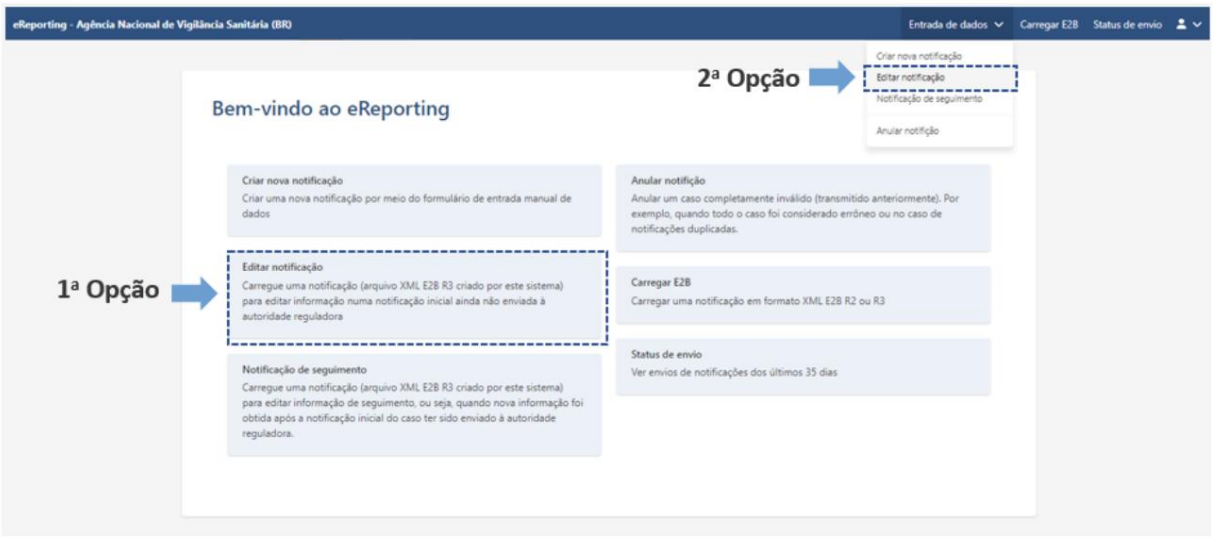
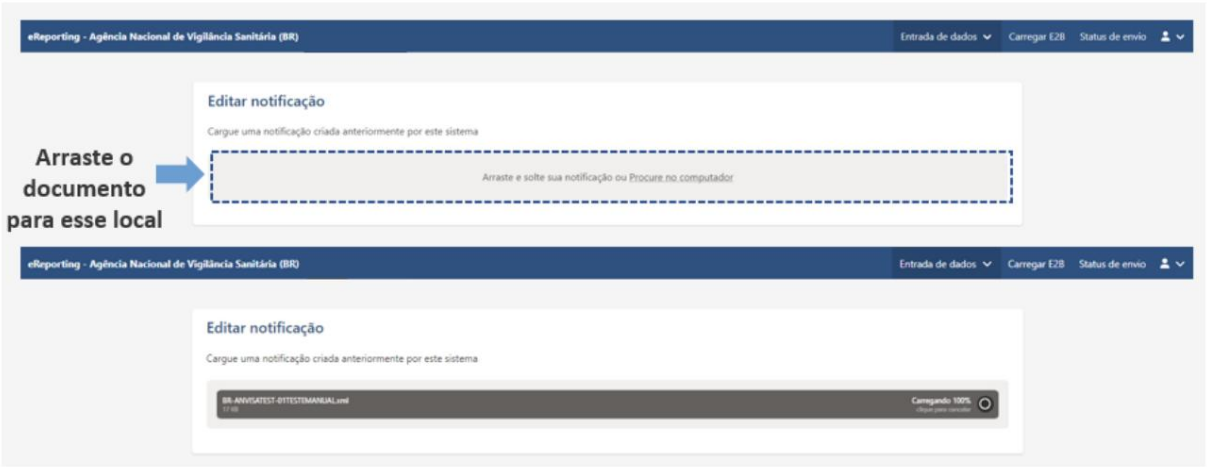




Important!

After the notification has been edited, a new one must be sent to Anvisa.

(see item 3.2) and downloaded the file again (see item 3.3) to

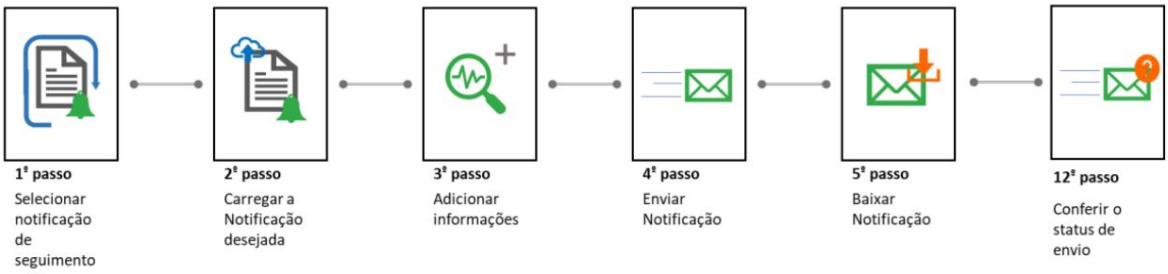
if you have the latest version of the notification file in your possession, if necessary in the future notification.

In the case of follow-up of a notification previously sent by Notivisa, it will be necessary make an initial notification in VigiMed (by manual entry or xml import) for the further updates continue to be monitored by the system.

The Notivisa notification number can be entered in the field: Other identification of the notification (in the E2B (R3) XML file) corresponds to data elements C. 1.9 Other Case

Identifiers). You can also include a note in the company's narrative or comments.
(in the E2B XML file it corresponds to data elements B. 5 Narrative case summary and
further information, para R2, e H Narrative case summary and further information, para R3.

3.5. CREATING A FOLLOW-UP NOTIFICATION



Monitoring or updating a notification must occur every time there is a new one.
relevant information to be added to the case or if the open case is pending
evaluation. It must be carried out from the notification file saved in the previous submission.

The user has two options to start creating the segment. The first is to click on
“Tracking Notification” in the menu. The 2nd option is to click on Data Entry in
top menu and then “Follow-up Notification”:

To upload the file (XML) previously sent in the notification, after locating the file
on your computer, simply drag and drop it onto the (gray) indicator bar or click on “Browse

on your computer", open file explorer on your computer, locate the file and carry it.

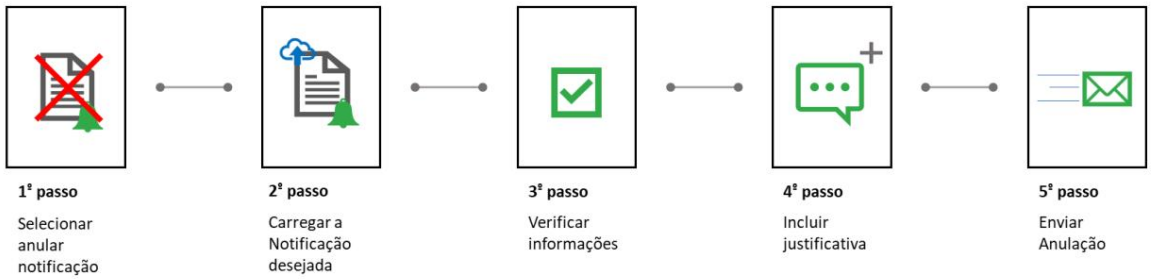
Immediately after full loading, the information will feed a new form and will be enabled for viewing and adding information.

2nd

Important!

After the end of the follow-up, a new submission must be made to Anvisa (see item 3.2) and download the file again (see item 3.3) to have in mind possession of the latest version of the case, if necessary for future follow-up.

3.6. CANCELLING A NOTIFICATION BY MANUAL ENTRY

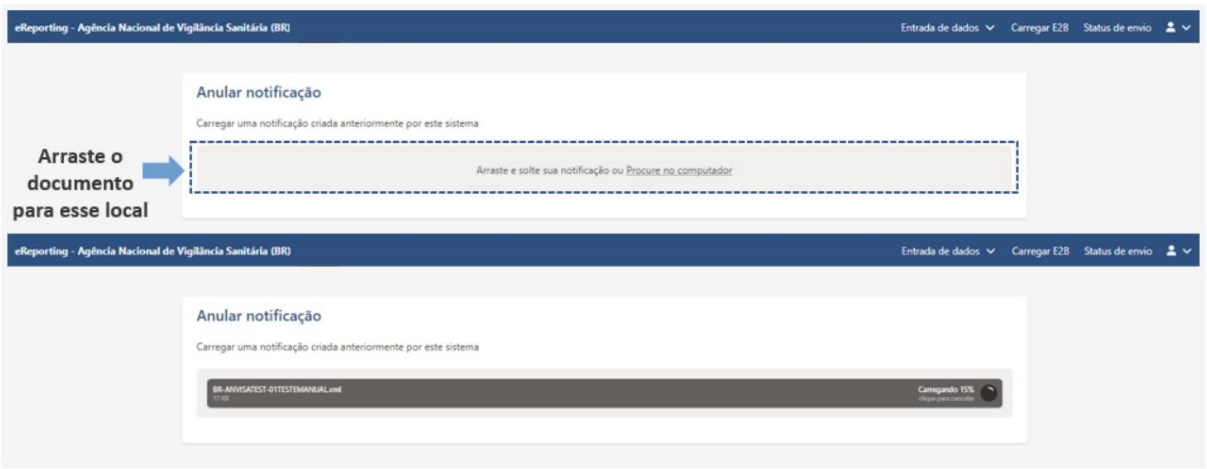


Cancellation of notifications should be performed in case the user identifies notifications invalid, that have already been transmitted or in case of duplicate notifications.

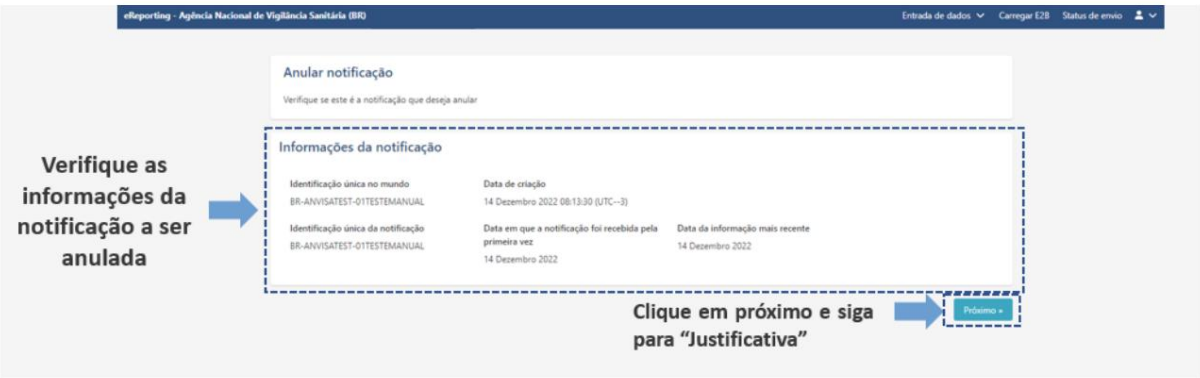
CLI

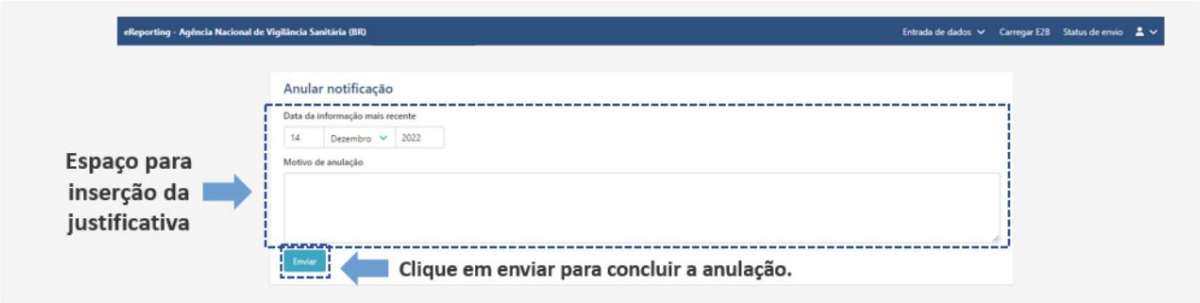
The user has two options to cancel a notification. The first is to click on “Cancel” notification” in the menu. The 2nd option is to click on Data Entry in the top menu, and then click “Cancel notification”.

Cancellation of a notification is carried out from the notification file saved when sending previous. To load the file (XML) previously sent in the notification, after locating the file on your computer, simply drag and drop it onto the (gray) indicator bar or click in “Browse my computer”, open file explorer on your computer, locate the file and upload it.



After full loading, the notification identification information will be presented for confirmation by the notifier. By clicking “next”, the notifier will be directed to the justification necessary to carry out the cancellation of the case.





Attention!

By canceling the notification, your Unique Worldwide Identification is closed in the system and no follow-up will be possible. If it is an error in some version, the notification should not be canceled; it should be performed a follow-up notification with the necessary changes using the option edit notification.

4. NOTIFICATION WITH ICH E2B XML FILE IMPORT

4.1. TESTS FOR IMPORTING ICH E2B XML FILES

The preparation of the ICH E2B XML file must follow the data package guidelines related to the ICH E2B standard and the Instructions for creating ICH E2B XML files (R2 and R3) (version 2.0), available on the VigiMed Empresas page, which includes the specifications regional for the file.

Regarding content, the same guidelines can be considered for manual notification, set out in item 3, in addition to considering the ICH Guides.

Important!

The ICH E2B (R3) Guide is the *Implementation Guide for Electronic Transmission of Individual Case Safety Reports (ICSRs) - E2B(R3) Data Elements and Message Specification,* available that ICH page: https://www.ich.org/page/efficacy-guidelines

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Before starting the import of the ICH E2B XML file, the company must perform validation of some files in the VigiMed Empresas training environment, as per Instructions for creation of ICH E2B (R2 and R3) XML files (version 2.0). While initial testing is not completed, the company must use the manual input interface, detailed in item 3 of this document. In the case of tests for system evolutions, the company can continue in production with the files from the previous version, until the tests for implementation are completed.

Important!

Companies that adopt the ICH E2B XML import will be able to use the interface manual input as an alternative tool in cases of failures in sending the XML files, if it takes time to investigate and correct the error by part of the company, or even by UMC/OMS.

4.2. IMPORTING ICH E2B XML FILE

To import an XML file, whether it is initial, follow-up, change or cancellation, open the ICH E2B XML file import interface by clicking on the "Upload E2B" option. E2B)", in the top menu of VigiMed Empresas or click on “Load E2B” in the main menu.

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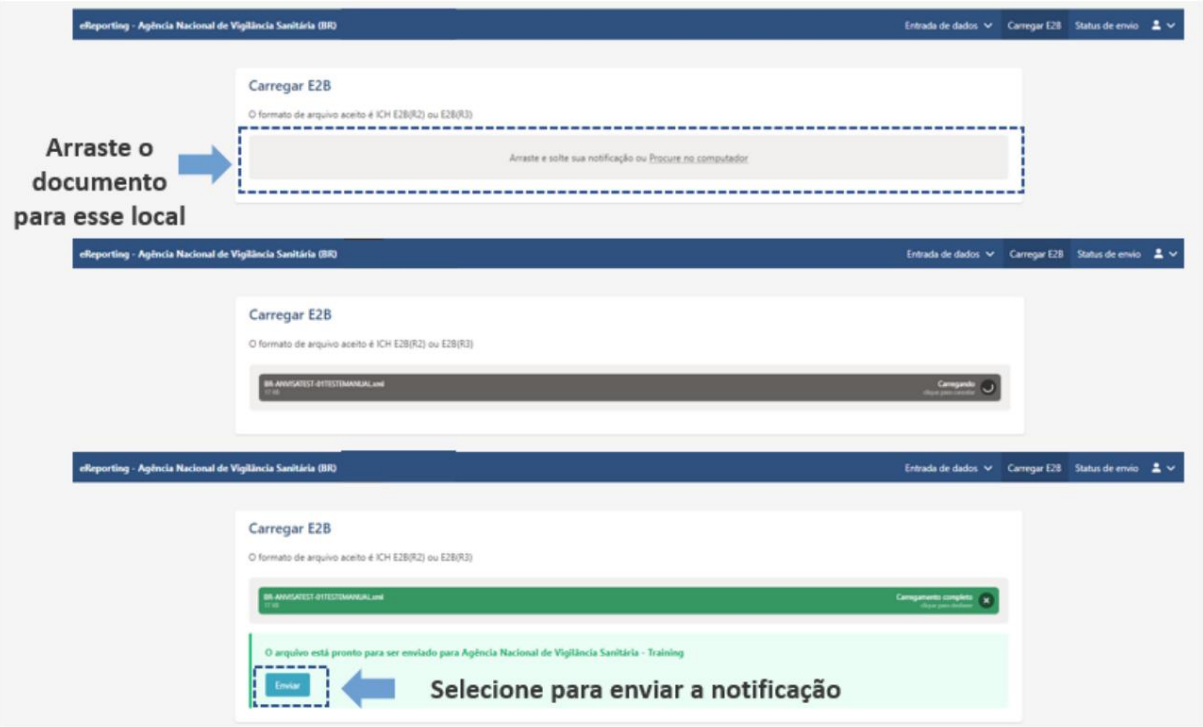
When you click on the "Upload E2B" option, a screen will appear containing a space specific for loading files, which can be done in two ways:

dragging and dropping the file into the delimited space or searching for the file through the browser and selecting it.



After dragging or selecting the ICH E2B XML file, it will start loading as figures below. If the file is accepted, it will be uploaded and enable the “Upload” option. (Submit)”. Click on “Submit” and the message “File uploaded successfully” will be displayed. displayed if the notification submission process was successful. Upon completion of the process, a submission identifier code will be displayed.

Finally, to verify that the entire notification process has been completed successfully, you must check the Notification Sending Status. The sending ID that appeared after the submission should be used to locate the AckLog file (ICH ICSR Acknowledgement Message).

The AckLog is a system generated confirmation message that will need to be saved and verified for each shipment, as per item 8 of this Manual. The shipping status information of the notification and the AckLog are available for 35 days on the Shipping Status page. Put security, download AckLog immediately after sending the notification to the Anvisa.

Attention!

This ICH E2B XML file import procedure is what should be followed for initial, follow-up, change or cancellation notification.

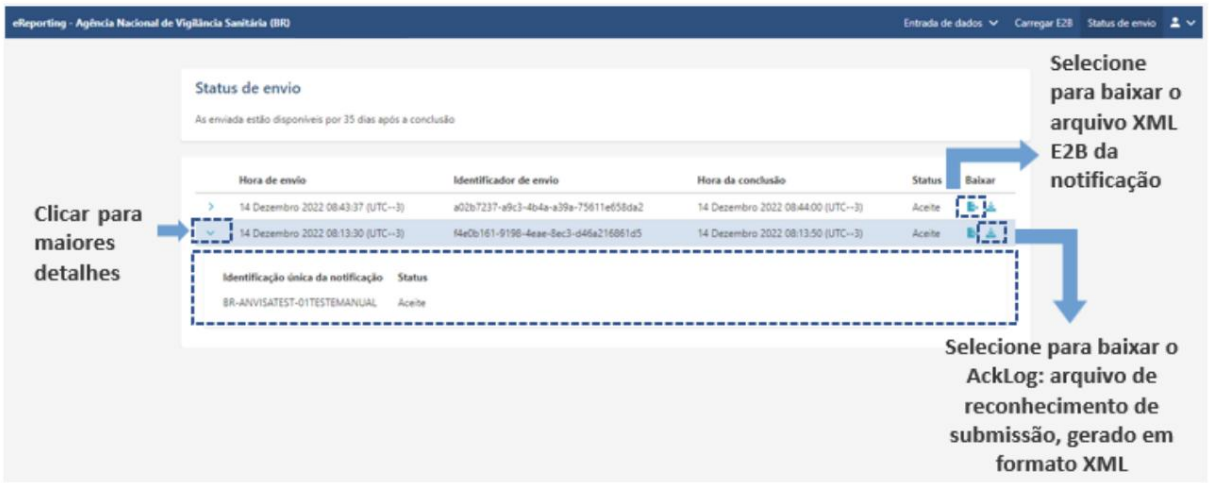
In the event of an error in any version, the notification should not be cancelled; it should be perform a change notification when importing a new ICH E2B XML file.

By canceling the notification, your Unique Worldwide Identification is closed in the system and no follow-up will be possible anymore.

5. NOTIFICATION SENDING STATUS

5.1. CHECKING THE STATUS OF SUBMITTING THE FILE TO ANVISA

To access the Shipping Status option, the user can choose to click on the menu under “Shipping Status”. shipping” or access it through the top menu, in the “Shipping status” option. Through this tab, you can view the panel with the history of notifications sent in the last 35 days, both by manual entry and by importing ICH E2B XML. The following will be displayed: following information: submission date and time, submission identifier, completion date and time of the submission, submission status, and the submission notification and AckLog files for download.



Attention!

The Submission Status confirms whether the file has been sent to Anvisa. Only files with “Completed” status have had their submission completed successfully.

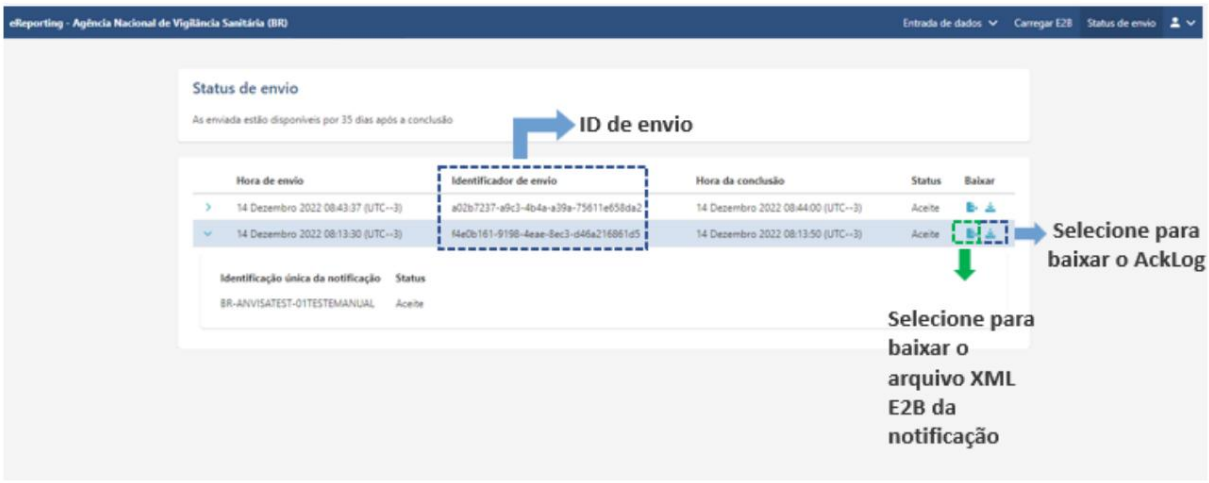
To know if the files were received without error by Anvisa, it is necessary check the notification AckLog file, especially in case of importing XML ICH E2B (see item 5.2).

5.2. CHECKING THE NOTIFICATION ACKLOG

The Submission Status only shows that the report was successfully submitted from VigiMed Enterprises. *(Industry e-Reporting)* to VigiMed *(VigiFlow),* but the latter may still reject the file.

The means to verify whether the notification was correctly received by Anvisa (for both interfaces) is with the loading of Acklog into the company's system, which imports Acklog into version R3 on their systems, or reading the Acklog for companies using manual entry or who import Acklog in version R2 into their systems.

The AckLog *(ICH ICSR Acknowledgement Message)* file is an acknowledgment message generated by the system that will need to be saved and verified for each submission.



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To download and save the Acklog, under "Submission status":

- Use the notification of interest by “Sending ID”,
- Click on the icon to download the corresponding “AckLog”.
- Click on the icon to download the “ICH E2B Notification XML file”.

After downloading AckLog, if you use a system that imports Acklog in version R3, load it into system to check whether the operation was successful or whether there are errors in the notifications that prevented its receipt in VigiMed. If you use a system that imports Acklog in version R2 or does not have a system to load the Acklog, you need to check the file manually.

The fields and values in the Acklog file that indicate the report was loaded correctly or not for VigiMed *(VigiFlow)* are as follows:

E2B R3

Received correctly

OK

AA=Accept - successfully processed!
Transmission Acknowledgement Code;
<acknowledgement typeCode="AA">

CA=Commit Accept
Acknowledgement Code for an ICSR Message;
<acknowledgement typeCode="CA">

Refused

Error

CR=Commit Reject (not loaded)

<acknowledgement typeCode="CR">

<acknowledgementDetail>

<text>Existing ICSR is nullified, followup not allowed.</text>

or

<acknowledgementDetail>

<text>Invalid MedDRA code found: 0</text>

AE=Parsial

<acknowledgement typeCode="AE">

<acknowledgementDetail>

<text>Could not persist all information</text>

AR=Reject

<acknowledgement typeCode="AR">

<acknowledgementDetail>

<text>Could not understand the import data: The 'extension' attribute is invalid - The value " is invalid according to its datatype 'urn:hl7-org:v3:st' - The actual length is less than the MinLength value., Line: 17 Position: 53. The 'extension' attribute is invalid - The value is invalid according to its datatype 'urn:hl7-org:v3:st' - The actual length is less than the MinLength value., Line: 426 Position: 51. </text>

Below is an example of E2B R3 Acklogs where the fields that need to be verified:

<?xml version="1.0" encoding="UTF-8"?>

<MCCI_IN200101UV01 **xmlns="urn:hl7- org:v3"**

ITSVersion="XML_1.0" xsi:schemaLocation="urn:hl7-org:v3 **MCCI_IN200101UV01.xsd"**

xmlns:xsi="http://www.w3.org/2001/XMLSchema-instance"> <id **extension="842e09df-**

bb47-48d3-90f9- d5d36a06c39b"

root="2.16.840.1.113883.3.989.2.1.3.20"/> <creationTime

value="20201005201537+0200"/> <responseModeCode

code="D"/> <interactionId

extension="MCCI_IN200101UV01" root="2.16.840.1.113883.1.6"/> <MCCI_IN000002UV01> <id

extension="UMC-

UMCORG-276" root="2.16.840.1.113883.3.989.2.1.3.19"/>

<creationTime **value="20201005201537+0200"/>** <interactionId
extension="MCCI_IN000002UV01" root="2.16.840.1.113883.1.6"/> <processingCode code="P"/
><processingModeCode code="T"/> <acceptAckCode code="NE"/> <receiver
typeCode="RCV"> <device
determinerCode="INSTANCE"
classCode="DEV"> <id extension="UMC" **root="2.16.840.1.113883.3.989.2.1.3.16"/**
> </device> </receiver> <sender typeCode="SND"> <device determinerCode="INSTANCE"

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classCode="DEV"> <id
extension="UMC" **root="2.16.840.1.113883.3.989.2.1.3.15"/>** </device> </
sender> <attentionLine> <keyWordText code="1" codeSystemVersion="1.0"

codeSystem="2.16.840.1.113883.3.9 89.2.1.1.24"/> <value **value="20200929133859+0000"** xsi:type="TS"/> </
attentionLine>
<acknowledgement typeCode="CA"> <targetMessage> <id **extension="SE-**
UMCTEST-000007"
root="2.16.840.1.113883.3.989.2.1.3.1"/> </
targetMessage>
<acknowledgementDetail> <text/></acknowledgementDetail> </acknowledgement> </MCCI_IN000002UV01>
<receiver
typeCode="RCV"> <device
determinerCode="INSTANCE"
classCode="DEV"> <id
extension="UMC"
root="2.16.840.1.113883.3.989.2.1.3.18"/
> </device> </receiver> <sender typeCode="SND"> <device
determinerCode="INSTANCE" classCode="DEV"> <id extension="UMC"

root="2.16.840.1.113883.3.989.2.1.3.17"/
> </device> </sender> <attentionLine> <keyWordText code="2"
codeSystemVersion="1.0" **codeSystem="2.16.840.1.113883.3.9 89.2.1.1.24"/>** <value

extension="842e09df-
bb47-48d3-90f9- d5d36a06c39b" root="2.16.840.1.113883.3.989.2.1.3.21" xsi:type="II"/> </attentionLine>

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<attentionLine>
<keyWordText code="3" codeSystemVersion="1.0" **codeSystem="2.16.840.1.113883.3.9 89.2.1.1.24"/>**

<value value="20200929133859+0000" xsi:type="TS"/>
</attentionLine>
<acknowledgement typeCode="AA">
<targetBatch>
<id extension="a60401bb-
e8f1-4d4f-925d-66ab95d48525" root="2.16.840.1.113883.3.989.2.1.3.22"/>
</targetBatch>
<acknowledgementDetail>
<text/>
</acknowledgementDetail>
</acknowledgement>
</MCCI_IN200101UV01>

File sent and received correctly:

- AA =Accept - successfully processed
- CA=Commit Accept

Attention!

After checking, if there is an error or failure, the XML file must be checked and corrected.

for new import or new form by manual entry must be

filled.

If the error persists, send the ICH E2B XML file of the error notification (generated

by the company system or saved after manual entry), the error Acklog and what

has already been carried out by the company in order to solve the problem through e-

mail vigimed.pesquisa@anvisa.gov.br.

6. FINAL CONSIDERATIONS

This is the second version of the VigiMed Companies User Manual – Clinical Research, which aims to adequately guide the process of reporting SUSARs with medicines and biological products, when applicable, through the system, when these are being evaluated in clinical trials in Brazil.

This Manual may be updated whenever new needs are identified, as well as when possible updates occur in the *eReporting Industry* by UMC/WHO.
or in the ICH E2B Guide. The latest version will be available on the VigiMed website on the Portal of Anvisa.

In case of system errors or access problems, send an email to vigimed.pesquisa@anvisa.gov.br.

For any other questions, please send your query using the Contact Us Electronic Form.

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7. CHANGE HISTORY

Data	Version	Changes	Observations
02/2021	1.0	Initial version	Preparation
02/2025	2.0	Manual review for update inclusions of VigiMed Companies system. Review of registration on VigiMed Companies: new link, simplification of the form and inclusion of two new fields: Organization Identifier (sender organisation) and collection of third party user data for registration with VigiMed Companies.	Review for update