4. Introduction

VigiFlow is an ICSR management system developed and hosted by Uppsala Monitoring Centre (UMC). It is compatible with the ICH-E2B standard for electronic transmission of ICSRs.

4.1 System requirements

No client installation is needed to use VigiFlow since the system is web based and accessible over the Internet via an encrypted (https) connection. The only requirement is a web browser, preferably Mozilla Firefox (version 1.0 or later) or e.g. Internet Explorer (version 5.0 or later) and a connection to the Internet. It is recommended to have an Internet connection of at least 1 Mbit/s, otherwise the system may be slow to use. There are some additional requirements on the local computer to use the print report function and to export search and statistics results as PDF or Excel files. To view PDF files, Adobe Acrobat Reader is recommended and can be downloaded for free from Adobe (www.adobe.com).To view and analyse the Excel outputs, Microsoft Office Excel 2003 (or later) is needed.

4.2 Limited access version of VigiFlow

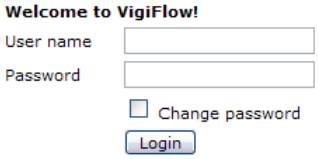
The VigiFlow limited access version has been set up to facilitate for candidates and members of the WHO Programme of International Drug Monitoring to send reports to UMC even if they are not interested in the full report management capabilities of VigiFlow. The following functionality is not included in the limited version of VigiFlow:

The top menu of the complete version (top) and the limited version (bottom) is shown here:

4.3 Log in

Log in is done with a personal user name and password from the secure web-page:

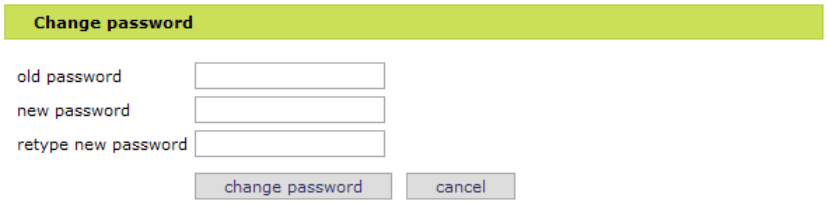
https://adr.who-umc.org



4.3.1 Change password

At log in, it is possible for the user to change the personal password. To change the password, check the box *change password* and enter your user name and the original password, then click the button *login* or press *enter*.

On the page ócChange passwordô the original password should be entered again together with the new password you wish to use.

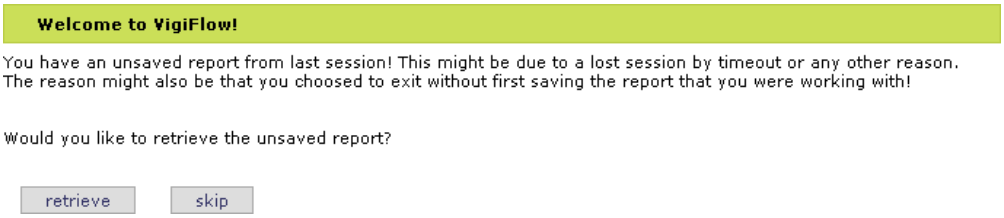


The new password should be between 8 and 20 characters long and contain both non-numeric (e.g. a, b, c, #,!) and numeric (e.g. 1, 2, 3) characters to be accepted. Passwords are not case-sensitive (e.g. a, A are considered the same).

If you click on *cancel*, normal log in will continue and you should use the original password to log in next time. If you have entered a correct new password and click on *change password*, a confirmation will be given that your password has been changed.

4.3.2 Retrieve unsaved report

If a report was open when you last logged out or if your Internet connection failed while entering a report, the next time you log in, you will be asked if you want to retrieve the unsaved report.



If you click on *retrieve*, the unsaved version of the report will open. The backup of the report is made when you change between different pages in VigiFlow so any changes on the last page open will not be included. If you do not want to retrieve the report, you can click on *skip* and the **list of reports** page will open.

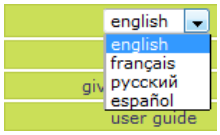
4.3.3 Language

Default language in VigiFlow is English and other available languages are Spanish, French and Russian. It is recommended to change the language directly after log in. It is possible to do at any time, but the user will be returned to the first page shown at log in after the change. The language is changed from the drop-down menu in the top left hand menu in the interface.

4.4 Enter a new report

From the top menu, choose **report handling → new report**; you will then be given the choice between entering a **standard case** or a **parent-child case** (the latter used primarily when a foetus has suffered the reaction after the mother has taken the drug).

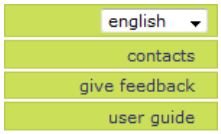
The left hand menu while entering a new report is shown to the left and demonstrates the work flow. To move to the next page as shown in the menu, either click in the menu or click on **next** at the bottom of the page. The first page shown is the **report info** page. Enter known data in the fields given here and on the following pages.

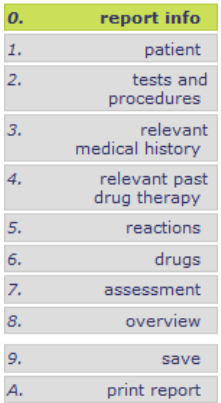


The page **overview** shows the entered data and if there are any errors on the report or missing information in mandatory fields.

Do not forget to **save** the report regularly. While saving, it is also possible to add or edit the **report comments** and to generate a **report Id** (unless the report already has an Id).

When a report has been opened for editing, it will be seen as *checked out* for all other users on the **list reports** page. To make the report available for everyone again, choose **report handling→list reports** in the top menu. Find the report in the list and click on the *check in* icon next to the report.





Until all mandatory fields in the report are filled in, it is considered incomplete and cannot be committed to the Search and Statistics database. Note that some mandatory fields can appear or disappear at certain conditions, e.g. **patient initials** are mandatory on spontaneous reports but not on literature reports or if the sender is a pharmaceutical company.

The minimum information you have to enter on a spontaneous report for it to be considered ócompleteô by VigiFlow is the following six mandatory fields:

- **report title**
- **patient initials**
- **patient age (either date of birth, age at time of onset or age group)**

- **onset date of reaction (year only)**
- **a reaction term**
- **a drug name**

Two more fields are mandatory (three on parent-child cases); these are automatically filled by VigiFlow, but can be edited:

- **Date first received at national centre** (called date receipt most recent info for NC without RC and for CY users) is pre-filled with ñtodayôs dateò
- One of the primary source fields **family name**, **institution**, **postal code**, **country of reporter**, **reporter qualification**, **literature reference** or **study name;** of these **country of reporter** is pre-filled with country of user
- On parent-child cases one of the parent characteristics fields: **parent date of birth**, **parent age**, **parent initials** or **parent sex**; of these, parent sex is pre-filled as ñfemaleò. For overviews of the VigiFlow interface.

4.5 Send and commit reports within VigiFlow

To **send** a report to another centre either click on **send report** in the top menu of the open report, Regional Centres can also click on the *send* icon in the list of reports. First you will be taken to the **Result from verification** page, where information about missing information in mandatory fields may be given together with the **report Id** and **report title**. You can send incomplete reports to other centres. If you send a report without a report Id, one will be generated for the report. When a report has been sent to another centre it will not be available for editing at the centre it was sent from, unless it is sent back. Tip: use the **report comments** field to communicate with the recipient about the report. Only National Centres can **commit** reports. A committed report will be included in Search and Statistics, therefore only complete reports can be committed. To commit a report, click on **send report → commit report** in the top menu of the open report, or click on the *commit* icon in the list of reports. The **Result of verification** page will first appear, and on this page the choice to **send the report to** the **Uppsala Monitoring Centre when committed** will also be given for
National Centre users.

4.6 Edit a committed report

If a committed report needs to be updated, select **search and statistics → list reports** in the top menu and find the report in the list of committed reports by searching for the report. When the report is found, click on the *follow-up/amend* link to open the report for editing (only

National Centres can do this). When the updated report is committed again, you will be asked to answer if the update is a **follow-up** or an **amendment**.

5. Enter a new report

This chapter contains instructions on how to create a new Individual Case Safety Report (ICSR) and make an assessment of the case.

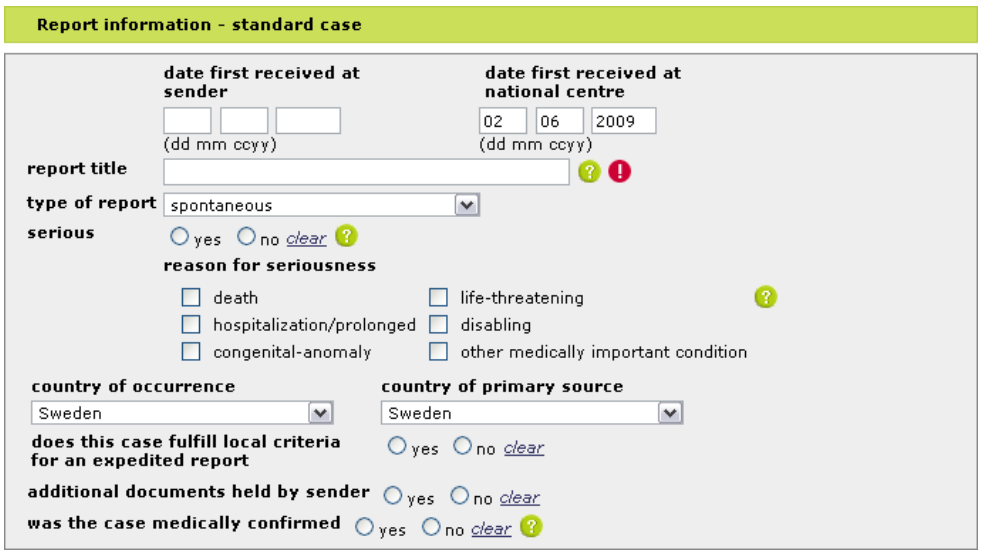
Follow the left hand menu, from **report info** to **overview**, to enter a report. Any time during the process you can **save** the report. A saved report will be found in the **list of reports** next time you log in. If you forget to save, or your Internet connection fails in the middle of entering a report, next time you log in you will be asked if you want to **retrieve** your unsaved report.

Standard case

Select **new report** → **standard case** in the top menu. The first page that opens is the **report info**.

5.1 Report info page

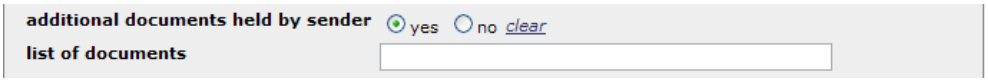
5.1.1 Report information section



1. If you are a:
   a. *Regional Centre;* the **date received at regional centre** is given automatically, but can be changed if needed. Note that this field is named **date first received at sender** for the National Centre. The National Centre can use this field on reports received from Regional Centres and on reports from other senders.
   b. *National Centre* with Regional Centres; the **date first received at national centre** is given automatically, but can be changed if needed.

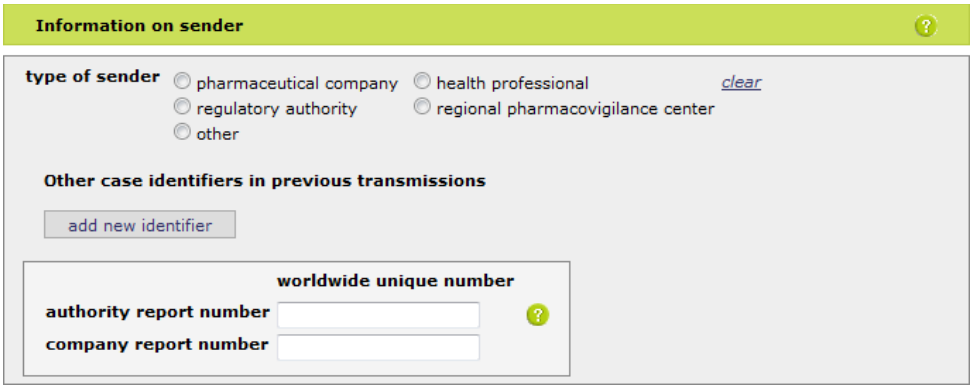
c. *National Centre* without any Regional Centres; the **date receipt most recent info** is given automatically, but can be changed if needed. Note that this field will change name to **date first received** when the report is committed.

2. Fill in a **report title** of choice. *(This is a Mandatory field.)*
3. Select the appropriate **type of report**.
4. Enter if the reaction was **serious** or not. If you select óyesô, it is mandatory to also select one or more **reason for seriousness** to explain why the report is serious.
5. The **country of occurrence** (where the adverse drug reaction occurred) and the **country of primary source** are given automatically as country of user, but can be changed if needed.
6. If óyesô is selected for **additional documents held by sender**, the free text field **list of documents** will appear.



5.1.2 Information on sender

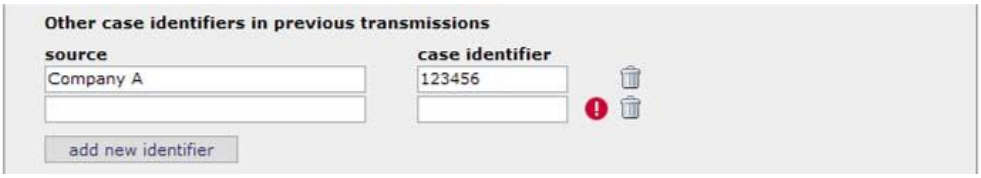
Select **type of sender**. In this section the **sender** is the organization that sent the report to the National Centre. Note that the sender is the same as the primary source if the primary source sent the case directly to the National Centre.



If **type of sender** is óregional pharmacovigilance centreô, the fields **sender**, **person responsible** and **regional centre report Id** will also be available:

Fill in the name of the **sender** if not given automatically. The **person responsible** is given automatically as the name of the user, but can be changed if needed. The **regional centre report Id** can be filled in by a Regional Centre (only necessary if different from the VigiFlow Report Id) and cannot be edited by the National Centre.

To provide **other case identifiers in previous transmissions**, click the *add new identifier* button. The fieldôs **source** and **case identifier** will appear. See figure below. *(It is Mandatory to enter both a* source *and a* case identifier *for each added new identifier.)*



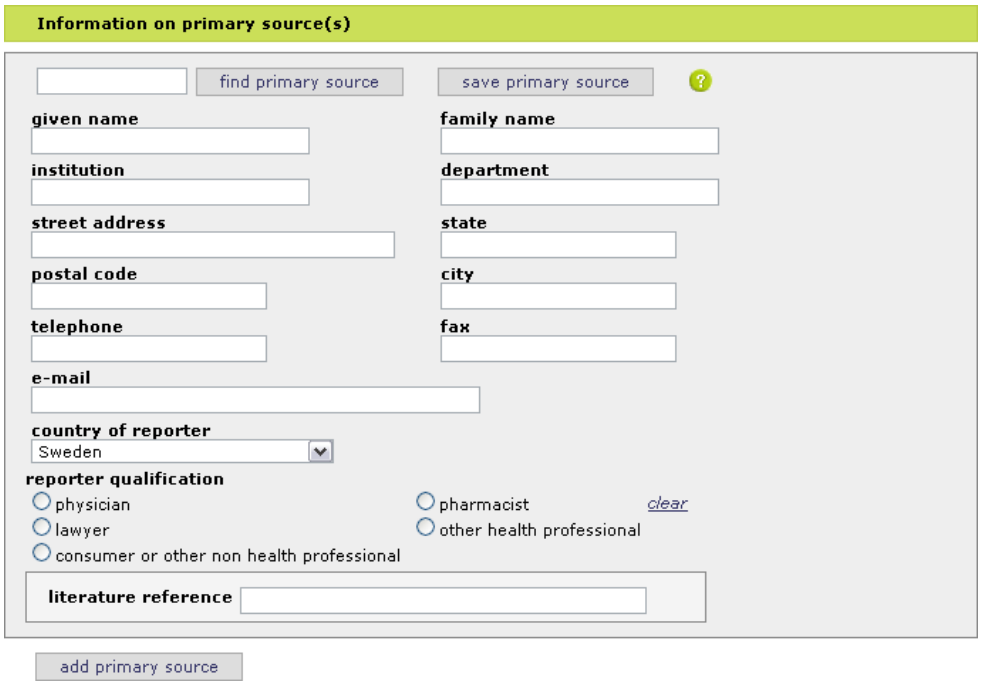
A **worldwide unique number** will be generated automatically (when a **report Id** is generated) unless one is entered. See the help text (the icon by the field) for further instructions.

5.1.3 Information on primary source(s)

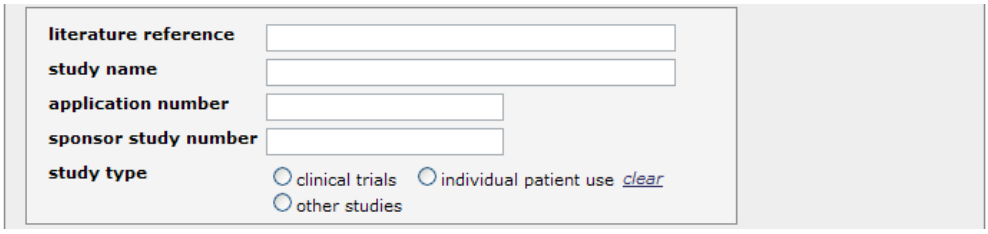
The primary source is the person that first reported the facts; it can be the consumer (patient) or the doctor of the consumer for instance. Different countries allow reports from different primary sources. In this section the primary sourceôs contact information should be entered. A field for **literature reference** is also available here; this should only be used if the literature article is the primary source.

If a literature article is used for supporting information, it can instead be entered in the *references* or the *sender's comments* fields on the assessment page. It is possible to enter more than one primary source by clicking on the *add primary source* button. It is possible to sort added primary sources; only the top primary source is included on PDF printouts. *(For each primary source it is mandatory to add information on one* family name, institution, postal code, country of reporter, reporter qualification, literature reference *or* study name.*)*

It is possible to **save primary sources** so that the entered information can be reused on other reports with the same primary source. To be able to save as primary source, the minimum information needed is either **given name**, **family name** and **institution** or **literature reference**, or **study name**. Click on the *save primary source* button when the information has been entered. To reuse a saved primary source click the *find primary source* button and add the relevant source. Note that saved primary sources are personal and not available to other users.



If the **type of report** is a ŏreport from studyô there will also be fields about the study to fill in under the primary source section:

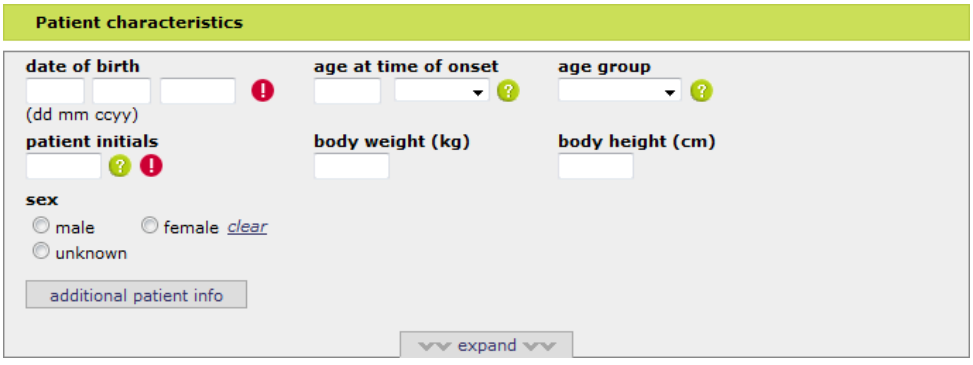


When the **report info** page is filled in with the information you have, click the *next* button or on **patient** in the left hand menu to continue to the **patient** page.

5.2 Patient page

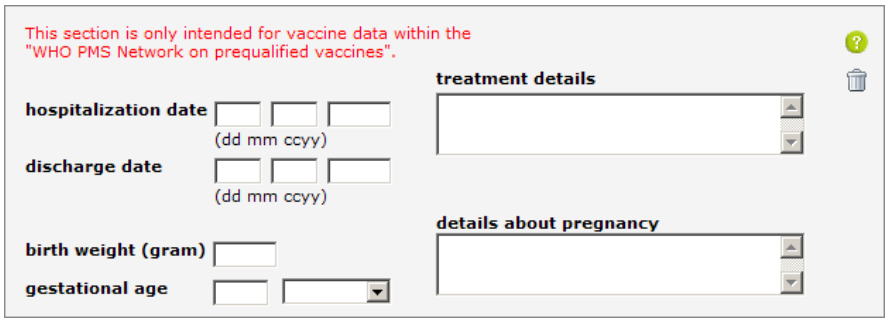
5.2.1 Patient characteristics

The **patient** page contains fields about patient characteristics and death related information.



1. The patient age can be entered as either **date of birth**, **age at time of onset** or **age group**. *(This is a mandatory field. You have to enter either patient birth* year, age at time of onset *or* age group.*)*

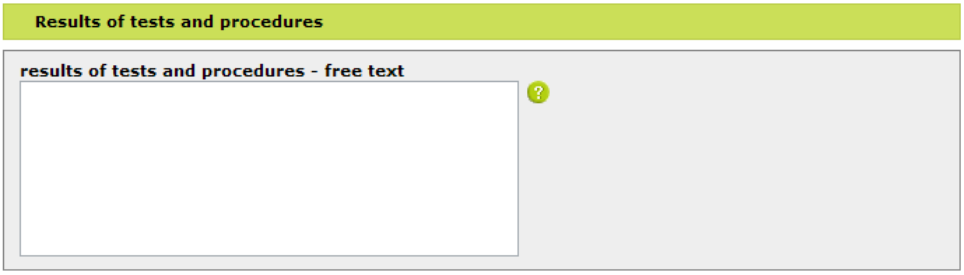
   The **age at time of onset** will be calculated automatically if **date of birth** and **onset date of reaction** (on the **reactions** page) are completely filled in. **Age group** will be calculated automatically, when **age at time of onset** is filled in. Otherwise it can be entered manually. If no information about patient age is known, it is possible to enter **age group** ‗unknown'.
2. Enter the **patient initials**. *(This is a mandatory field.*)* **Tip**: instead of entering the initials it is possible to write ‗privacy' or ‗unknown'.
   - Note*: These fields are not mandatory if* type of report *is 'literature' or if* sender *is 'pharmaceutical company'.*
3. If the patient is **female**, the **date of last menstruation** can also be entered.
4. The additional patient info button should only be used by participants in the WHO Post Marketing Surveillance Network on Pre-Qualified vaccines. When the button is clicked, additional fields for vaccine report data are added. Data entered in these fields will not be exported to the external E2B file or to VigiBase/VigiSearch; it; it will only be visible in the internal E2B file and the PDF print. The fields are not E2B compatible and should be removed by clicking on the trash icon in the section if they are not used.



5. The patient characteristics section can be expanded to show more fields.

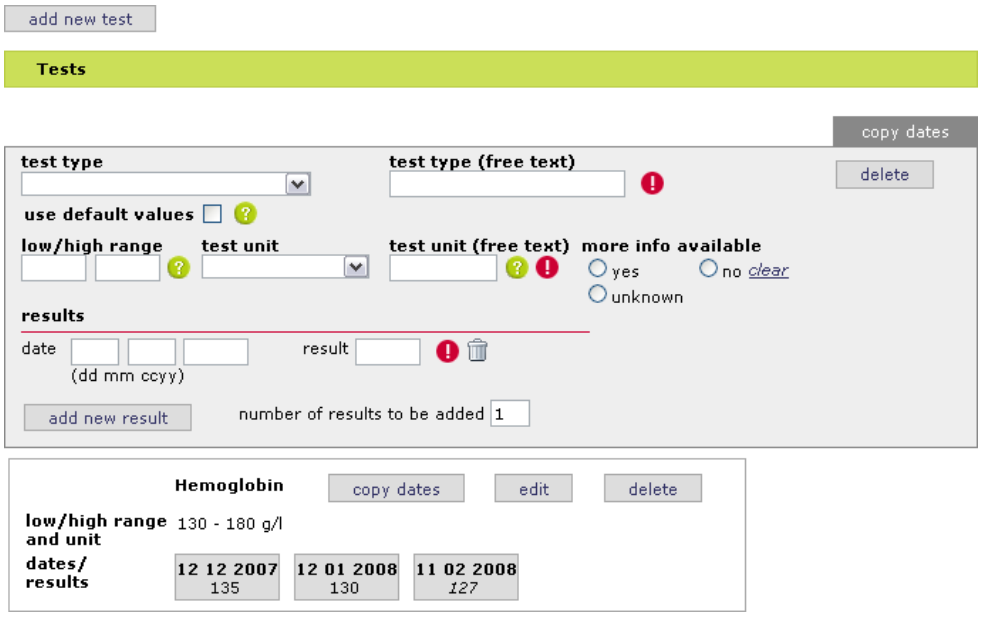
5.3 Tests and procedures page

Data about tests can be added as free text, structured information in tests or both.



5.3.1 Tests

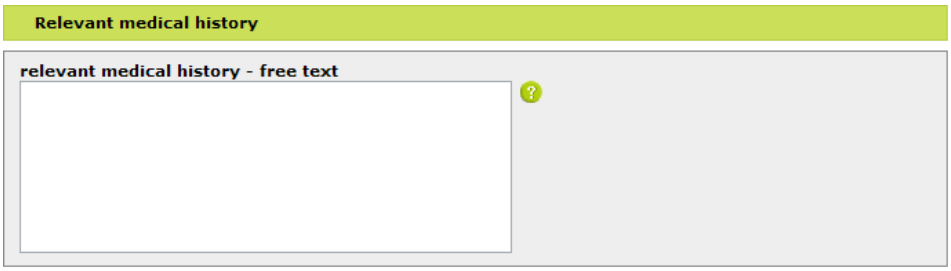
To add structured information about a test, click on the *add new test* button. Each added test can contain test results from many dates. To add a new test with the same test dates as another test, click on *copy dates* in that test. It is also possible to *edit* or *delete* added tests. Test results that are outside the specified range are shown in *italic* text.



5.4 Relevant Medical History Page

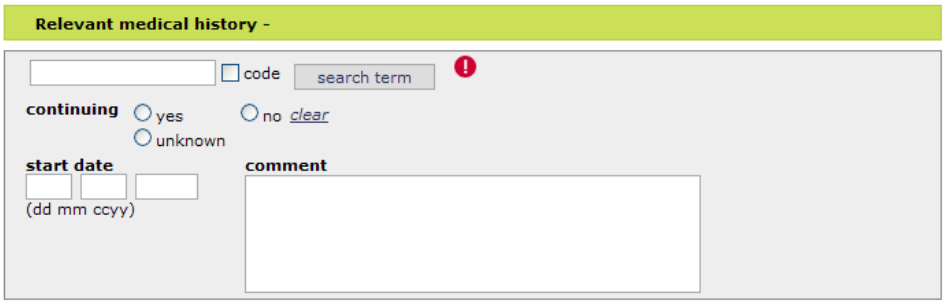
5.4.1 Relevant medical history – free text

The **free text** field for relevant medical history is a common field for all relevant medical histories.



5.4.2 Relevant medical history – structured

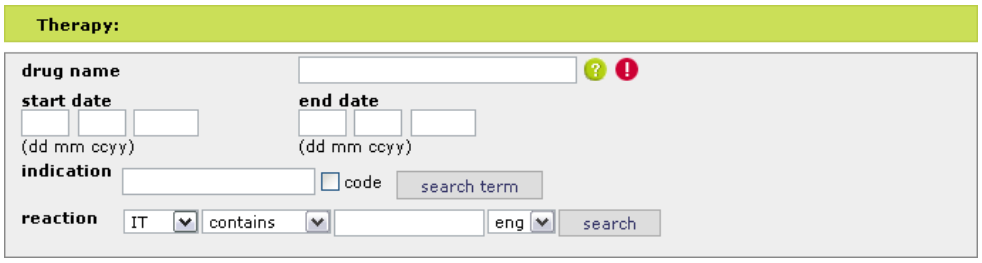
Click on the *add relevant medical history* button for each medical history you want to add structured information about. Each added medical history will appear in a list. From this list it is possible to sort, edit and delete the added medical histories. Any errors or warnings on a particular medical history will be shown as a warning icon in the list.



5.5 Relevant past drug therapy

A relevant past drug therapy is added by clicking on the button *add past drug therapy*. Several past drug therapies can be added and they will all appear in a list. In this list it is possible to sort, edit and delete all added relevant past drug therapies. Any errors or warnings on a particular past drug therapy will be shown as a warning icon in the list.

5.5.1 Therapy



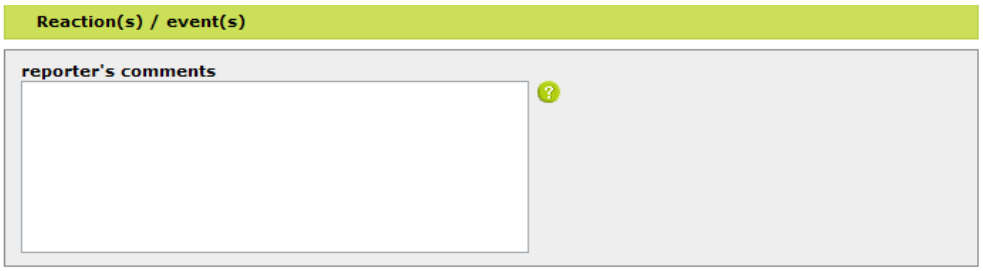
The **drug name** is added as free text. *(The* drug name *is a mandatory field for each added relevant past drug therapy.*

5.6 Reaction page

The reaction page is divided into a free text section for all reactions and a repeatable section for structured information on each reaction.

5.6.1 Reaction(s)/event(s) – free text field

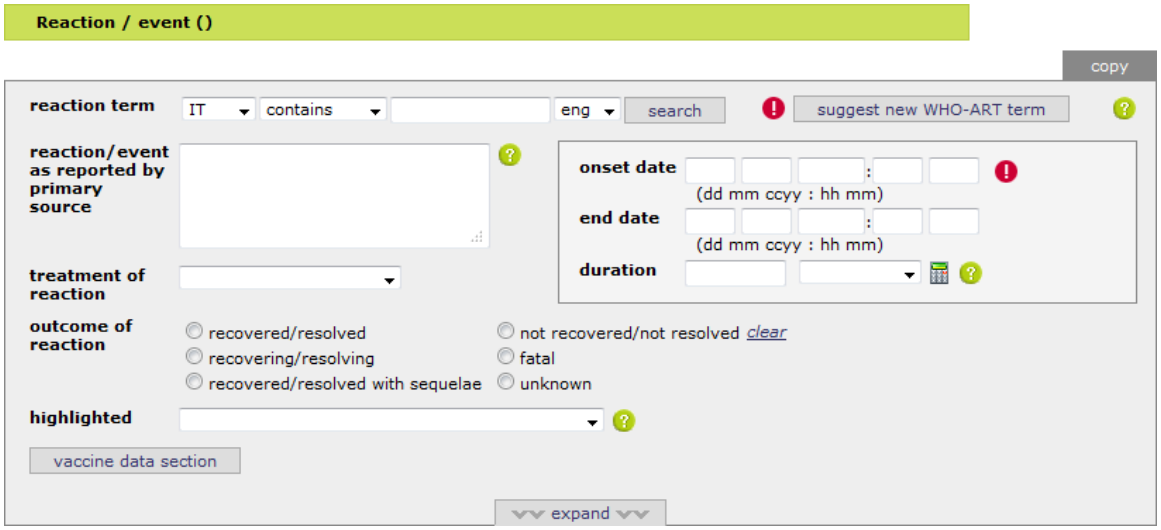
The free text field **reporter's comments** are a common field for all added reactions/events. This field should be used for comments from the primary source that are relevant for all reactions.



5.6.2 Reaction / event

Click on *add new reaction* for each reaction or event for the case. It is mandatory to have at least one reaction added to each report. Each added reaction/event will be shown in a list. In this list it is possible to sort, edit and delete added reactions/events. The delete icon in this list will delete the reaction and all information added with the reaction, compare with the delete icon by an added reaction term. Any errors or warnings on a particular reaction will be shown as a warning icon in the list. The reaction that is shown in **bold** text is
open for editing below the list.

The primary reaction should be moved to the top of this list. To add a new reaction with the same information as an already added reaction, click on *copy* in the upper right corner when the relevant reaction is displayed. All information entered about the reaction (except for relatedness) will then be copied into a new entry.



A **reaction term** is a *Mandatory field* for each reaction on the report. Use the search functions to find and select a reaction term An added term can be removed by clicking the trash icon next to the term, note that all other information added (like dates and outcome) will not be affected.

The field **reaction/event as reported by primary source** is a free text field to add the original wording about the specific reaction Enter **onset date**. *(*Year *is a Mandatory field except if the* type of report *is 'literature' or the* sender *is 'pharmaceutical company'.)* It is also possible to enter the exact time of the reaction by using the fields for hours and minutes. If complete **onset date** and **end date** are entered, but no hours and minutes, the **duration** will be calculated automatically; click on the calculator icon to fill the field. If **onset date** and **end date** are incomplete or identical, a known **duration** can be entered manually (e.g. 1 day, continuing, 20 minutes).

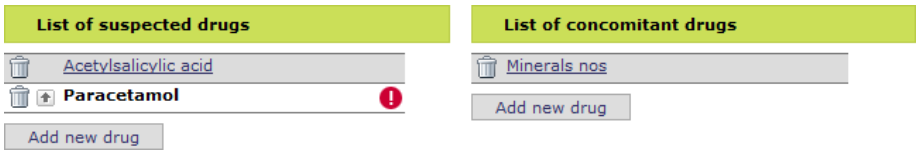
Other fields are **treatment of reaction**, **outcome of reaction** and **highlighted**.

5.7 Drugs page

Both **suspected** and **concomitant** drugs can be added to the report. It is mandatory to add at least one **suspected drug** (or two **interacting** drugs) on each report.

All added drugs are listed at the top of the page. In this list it is possible to sort, edit or delete all added drugs. The delete icon in this list will delete the drug and all information added with the drug, compare with the delete icon by an added drug name, see point

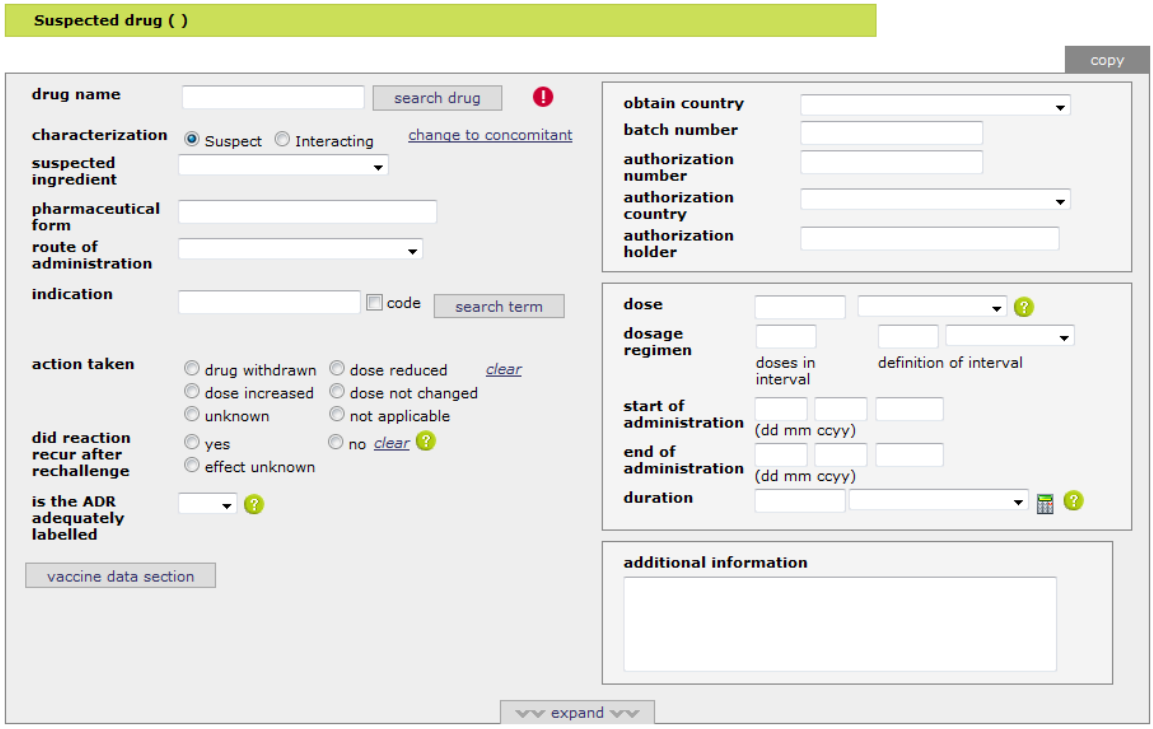
Any errors or warnings on a particular drug will be shown as a warning icon in the list. The list of **suspected drugs** also includes **interacting drugs**. The drug that is shown in **bold** text is open for editing below the lists.



To add a new drug click on the button *add new drug* under list of suspected drugs or list of concomitant drugs. It is possible to later change an added drug, from suspected drug to concomitant drug, or *vice versa* by clicking on the link *change to concomitant/suspected* next to the field **characterization**.

To add a new drug with the same information as an already added drug, click on *copy* in the upper right corner when the relevant drug is displayed. All information entered about the drug (except for the relatedness) will then be copied into a new entry.

5.7.1 Suspected drug



A **drug name** is a *Mandatory field* for each drug on the report. Clicking on *search drug* will take you to the **Search for drug** page where you can use several search criteria to find a drug name to add to the report

a) If a rechallenge was performed, fill in the field **did reaction recur after rechallenge**. To specify which reaction recurred, **Relatedness of drug(s) to reaction(s)**.

b) If no rechallenge was performed (or if you do not know), leave the field blank.

c) If complete **start** and **end of administration** dates are entered, **duration** will be calculated automatically. Click on the *calculator* icon to fill the field. If start and end dates are incomplete or identical, you can manually enter a known **duration** (e.g. 1 day, 5 months, long term, treatment continued).

5.7.2 Concomitant drug

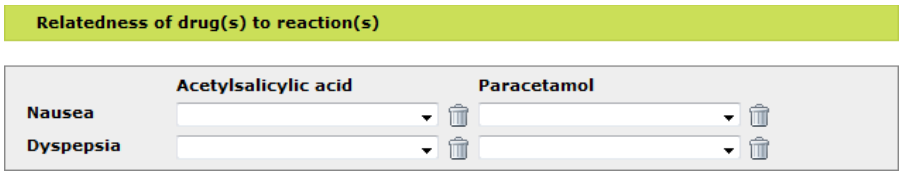
The fields for entering a concomitant drug are almost the same as for a suspected drug. The only fields that differ are **suspected ingredient** and **did reaction recur after rechallenge** which are not present for concomitant drugs.

Relatedness of drug(s) to reaction(s)

The section **Relatedness of drug(s) to reaction(s)** will appear on the **drugs** page as well as on the **reactions** page. This is where the actual causality assessment is performed.

6. The causality assessment

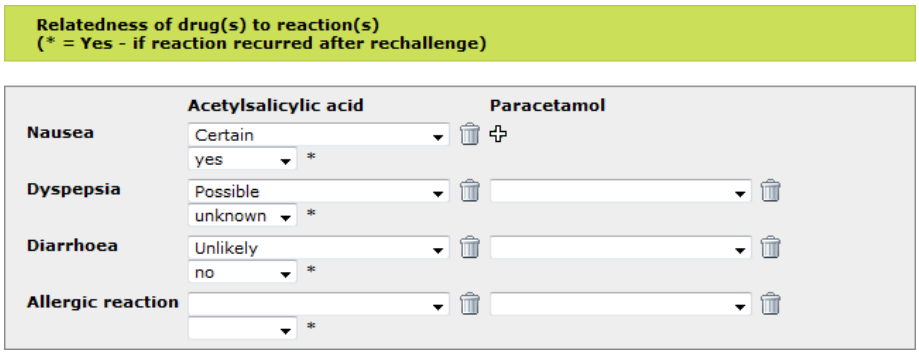
The **Relatedness of drug(s) to reaction(s)** section is where the causality assessment is entered. The section appears on both the **reactions** and **drugs** page and will reflect the reactions and drugs entered on those pages. In the made-up example below the reactions óDyspepsiaô and óNauseaô and the drugs óAcetylsalicylic acidô and óParacetamolô have been added.



In this section, there are fields for causality and rechallenge (the field for rechallenge will only appear if you have answered óyesô for **did reaction recur after rechallenge** on the **drugs** page). You have the possibility to remove and add relations between drugs and reactions. To remove a relation, click on the *trash* icon .

How likely is it that the reaction occurred due to the patient taking this drug?

This is the actual causality assessment!



6.1 VigiFlow is using the WHO causality assessment.

Note that the values for causality assessment differed slightly before the release of VigiFlow 5.0 in November 2012*; reports entered before this will keep the differing values unless the value is manually changed into one of the current values.

7. Assessment page

The actual causality assessment takes place on the **reactions** page or on the **drugs** page under the heading **Relatedness of drug to reaction.** On the **assessment** page you can add additional information about the case.

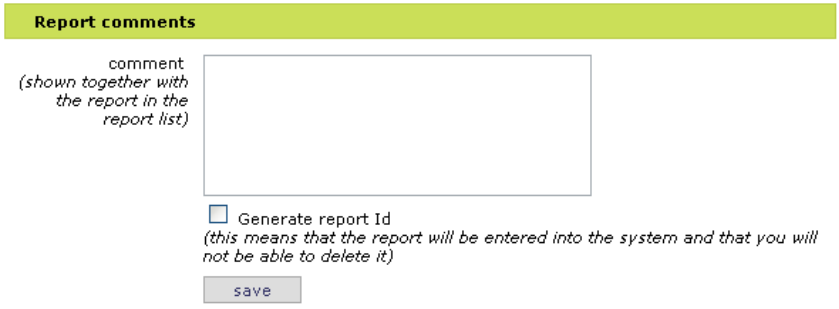
a. **Case narrative**; this is the field for the detailed description of the case as received from the primary source
b. **Sender's comments**; enter any discussion or alternative diagnoses from the note that in this section, the National Centre is considered the sender. Regional Centres can also add their comments.
c. **Sender's diagnosis**; enter the senderôs diagnosis by clicking on the *search term* link. For this field also, the National Centre is considered the sender. Regional Centres can also add their diagnosis as a suggestion to the National Centre.
d. **Imported sender's comments and diagnosis**; this field is only available on imported reports. Here the senderôs comments and senderôs diagnosis from the entity that sent the report to the National Centre will be found.

8. Save report

You can save a report at any time during the process of entering information, and resume later. The report does not have to be complete in order to be saved. If you have forgotten to save the report before exiting VigiFlow, on how it can be retrieved next time you log in.

Select **save** from the left hand menu. In the field **Report comments** you can write your comments on the case (optional). This information can later be found in a green note (the *comment* icon) next to the report title, in the **list of reports** (select **report handling → list reports** in the top menu). The report comment will also be included on *internal PDF printouts* of the report.

Note that the comment will be deleted when the report is committed and cannot be restored.



There is an option to **Generate report Id** by checking the box. An Id will be generated automatically if the report is sent to another centre or committed.

Note! It is not possible to completely delete a report after generating a report Id, but a National Centre can nullify the report.

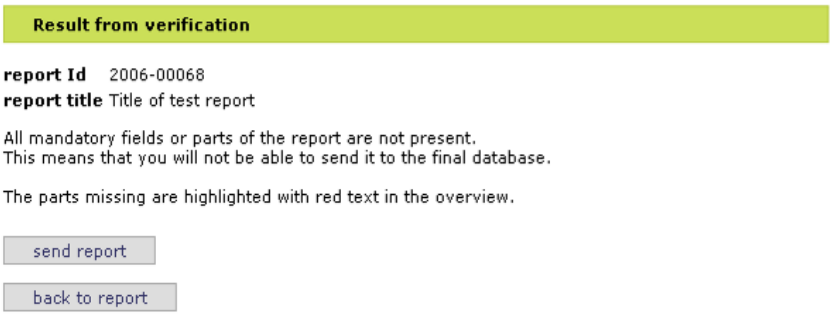
Click the *save* button. A message saying ó*The report was successfully saved*ô should be shown together with the **Report Id** if an Id has been generated. On the confirmation page there are also links to go *back* to the report, *go to report listing* and to go to the *administrative information* for the report.

9. Send report

1. A saved report can be sent to another centre even if it is not complete, and a list of available receivers is shown during the process. *Regional Centres* can send a report to the *National Centre*, or to other Regional Centres (if available). A *National Centre* can send a report to *Regional Centres* (if available) e.g. for questions or comments.
    a. To send a report, you can either:

b. Select **report handling → send report → send report** in the top menu when the report is open for editing.

c. Or, for *Regional Centres,* there is also an option to click on the *send* icon in the list of reports (found under **report handling → list reports** in the top menu).



2. The page **Result from verification** opens, stating the **Report Id** and **Report title**. You will also receive a warning if mandatory information is missing on the report. You can choose to go back and enter the missing parts or send the report as it is.

3. If you are satisfied with the report, click the *send report* button. The **Report comments** page opens. Write your comments on the case (optional). Below the **Report comments** you will find the **Send the report to another centre** list.

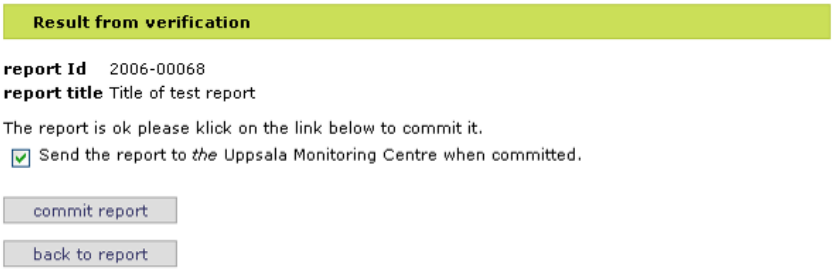
4. Click on the *send* icon for the **Centre** you want to send the report to. If the report has no **report Id** one will be generated automatically.

5. A message saying ó*The report was successfully sent*ô should be shown together with the **Report Id**. On this page there is also an option to print the report. For National Centres there is also an option to go to the administrative

10. Commit report

Only National Centres can commit reports to make them available for search and statistics. To be able to commit a report, the report has to be complete and correctly filled in.

1. To commit a report either:
   a) Click on the *commit report* icon in the list of reports (found under **report handling→list reports** in the top menu).
   b) When the report is open for editing select **report handling → send report → commit** in the top menu.



2. Information about the report is shown on the **Result from verification** page. If the report is incomplete, i.e. there is information missing in *Mandatory fields*, you have to go back and enter the missing information before you can commit the report.
3. If the report is complete, National Centres can choose to check the box ó**Send the report to the Uppsala Monitoring Centre when committed**ô.
4. Click the *commit report* button. If the report has been committed before you will be asked if the report is a follow-up or an amendment for more information. Click on *commit report* again when you have selected one of the choices.
5. A message saying ó*The report was successfully sent*ô should be shown together with the **Report Id** when the commit is completed. On this page there is also an option to print the report.

A committed report will no longer appear under **report handling → list reports**, instead it can be found under **search and statistics → list reports**.