Manual no. 4 – Clinical Investigations

In compliance with Section 15, paragraph 1 of Act No 268/2014 Coll., on Medical Devices and Amendments to Act No 634/2004 Coll., on Administrative Fees, as amended (hereinafter referred to as the "Act on Medical Devices"), clinical investigations may be conducted only if authorised by the Institute. An application for authorisation of a clinical investigation shall be filed by the sponsor of the clinical investigation electronically, via the Registry of Medical Devices ("RZPRO"). In addition to the particulars set forth by the Code of Administrative Procedure, the application shall, moreover, contain the clinical investigation dossier as referred to under Section 21, paragraph 1(a), except for items 1, 2, and 6.

The Clinical Investigations Module is available only to those persons who are registered in the Registry of Medical Devices and, concurrently, have notified their activity of a "Clinical Investigation Sponsor" (user role Notifier), in compliance with Section 26, paragraph 5 of the Act on Medical Devices. Furthermore, the module is available to the Agency (authorised representative of the clinical investigation sponsor) to which the Notifier granted Power of Attorney via the Registry of Medical Devices – instructions for "Granting Power of Attorney to the Agency" refer.

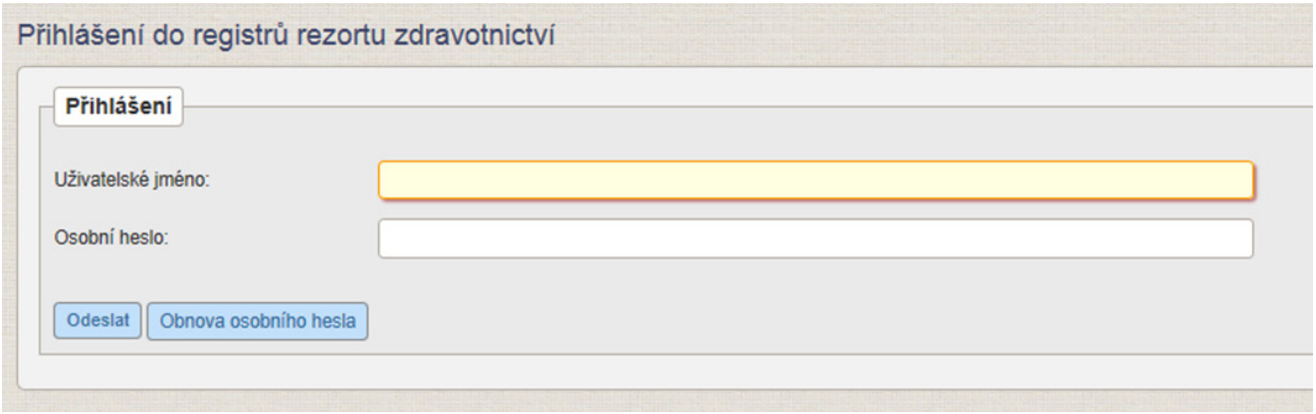
In case any act in respect of a clinical investigation is to be performed, you shall proceed as outlined below:

1. Login to the Registry of Medical Devices

1) In your internet browser (the system is supported by the following browsers: Internet Explorer, versions 8-10, and Firefox, versions 4-17), open www.rzpro.cz.

2) In the middle section of the page, you will see a hyperlink called "Access to RZPRO for experts and notifiers". Mouse-click the heading.

3) The following page, asking you to log into your user account, will be displayed. Enter your user name (usually composed of the first six letters of your surname and the first letter of your name) and password, i.e. the data you have received in the e-mail for access to the Registry of Medical Devices.



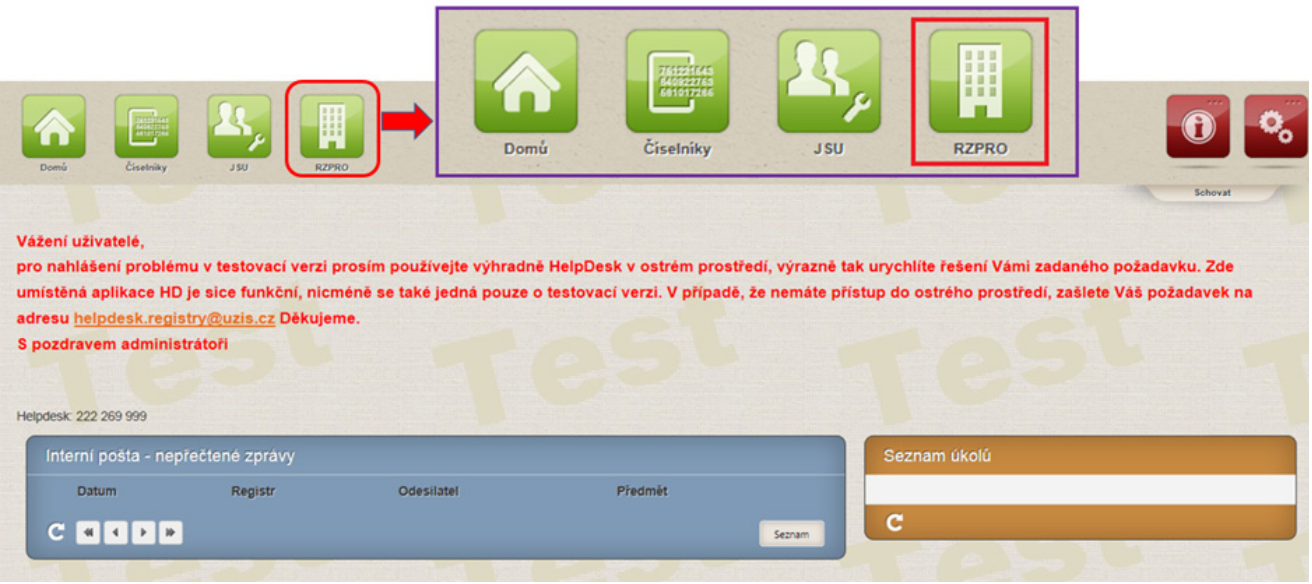
4) Once you complete the required data, click on the *"Odeslat"* (Submit) button. At that moment, check your mobile phone (or e-mail) where a one-time code will be sent. The one-time code is of limited validity. Should it expire, it would be necessary to click on the "*Zpět na odeslání jednorázového kódu*" (Back to one-time code sending) button.

5) The following screen will be displayed:

In the green field, the word "SMS" may be replaced by the word "e-mail", depending on what login option you have set up.

6) Shortly, a one-time code will be delivered to your phone number/e-mail. Type the code in the *"Jednorázový kód"* (One-time code) field and click the *"Odeslat"* (Submit) button.

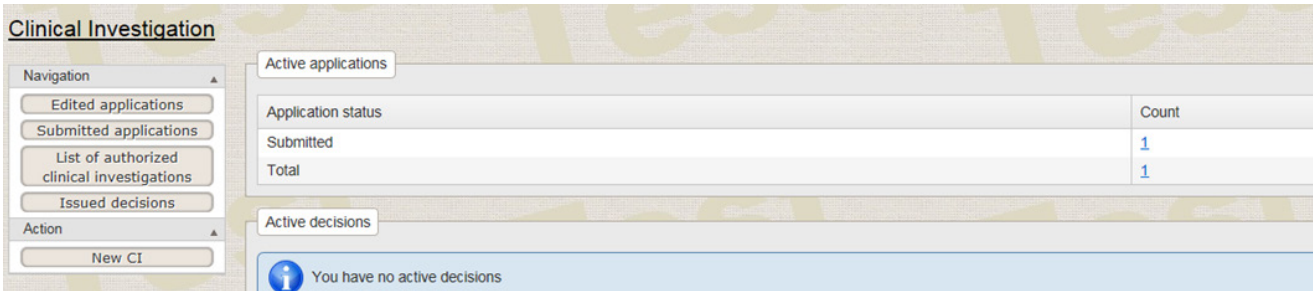
7) A page with an upper bar will be displayed. On this page, click on the green frame reading "RZPRO".



8) The screen displayed below will come up. Click on the green frame reading "Klinické zkoušky" (Clinical investigations) (the frame is displayed only after the notified activity of a "clinical investigation sponsor" has been confirmed for the person or upon receipt of a power of attorney via the JSU module in the RZPRO from a person having a confirmed notification of the "Clinical investigation sponsor" activity.

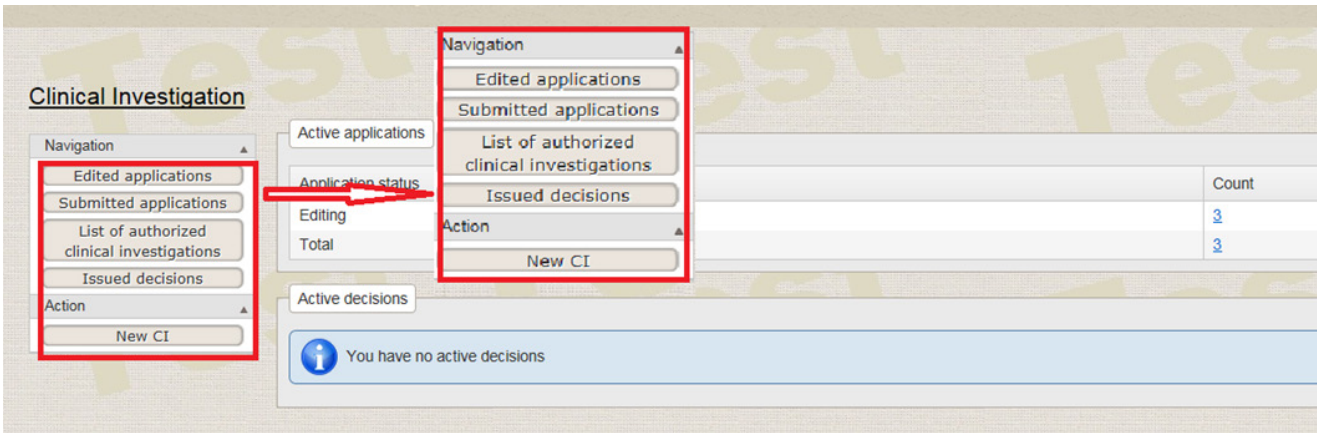
2. Clinical Investigation Module

Once you enter the Clinical Investigation Module (hereinafter referred to as the "CI" module) as per the instructions outlined above, the main window with the options menu and a dashboard will be displayed, providing a recap of the active processing status of applications, notifications, and delivered decisions. When the module is accessed for the first time and there is no application in the system, the dashboard is not displayed.



2.1. CI Module Main Menu

2.1.1. Options Menu Window



Navigation:

- **Edited (unfiled) applications** – a list of all unfiled applications of the respective person will come up together with the option to search and display the detail of the application. If you click on the application detail, the option allowing to submit the application will come up.
- **Submitted applications** – a list of all submitted applications of the respective person will come up, together with the option to search and display the detail of the application, and to run options allowing to manage the application as per the Code of Administrative Procedure (application withdrawals, appeals, etc.).
- **List of authorised CIs** – a list of all authorised clinical investigations of the respective person will come up together with the option to search and display the detail of the CI.
- **Issued decisions** – a list of all decisions issued by administrative authorities regarding filed applications of the respective person will come up together with the search option. The list of decisions is common for several modules.

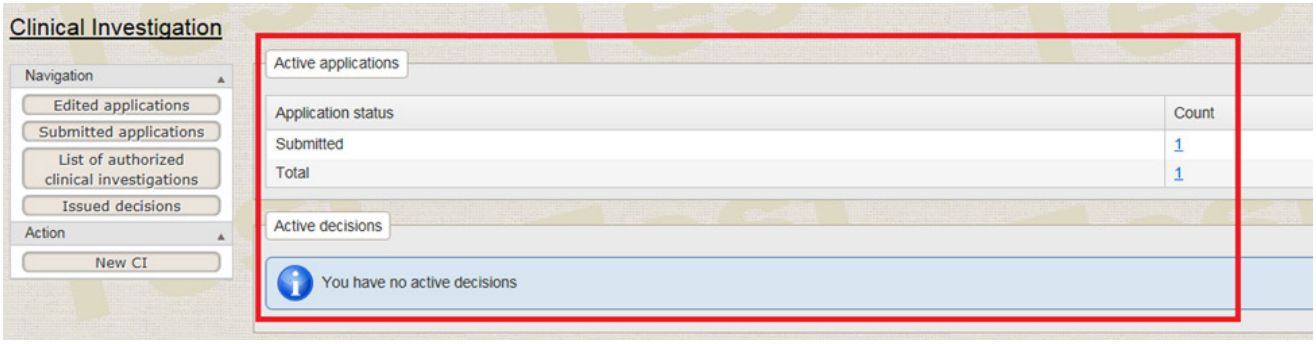
Actions:

- **New CI** – generates a form for completion of an application for a new CI authorisation and its submission.

2.1.2. Main Window Dashboard

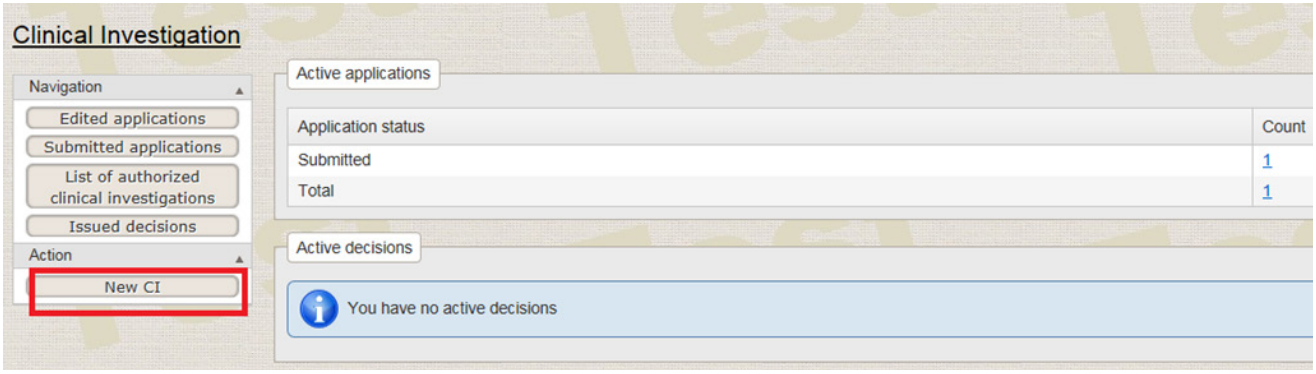
The dashboard is split into the following sections:

- **Active applications** – displays the list of active pending applications for clinical investigations in individual stages of the administrative procedure. If you click on the field showing the number of applications (column "count"), a filtered list of the person´s applications will be displayed.
- **Active decisions** – displays an overview of the issued decisions that have not yet become final by action type and status. If you click on the field showing the number of actions (column "count"), a filtered list of entities for detailed display will come up.

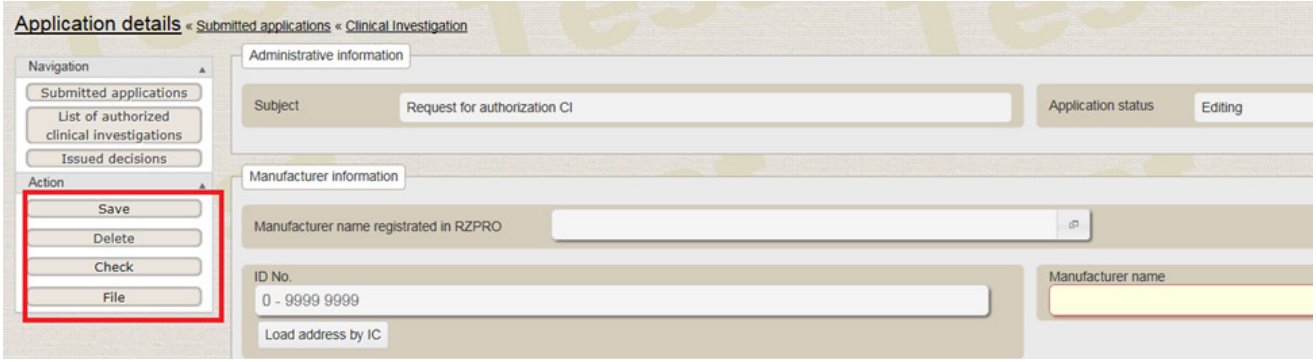


2.2. New application for Clinical Investigation Authorisation

To submit a new application for CI authorisation, click on the "New CI" button in the main window of the "Clinical Investigation" module.



The form for the submission of a new application for clinical investigation authorisation will be displayed.

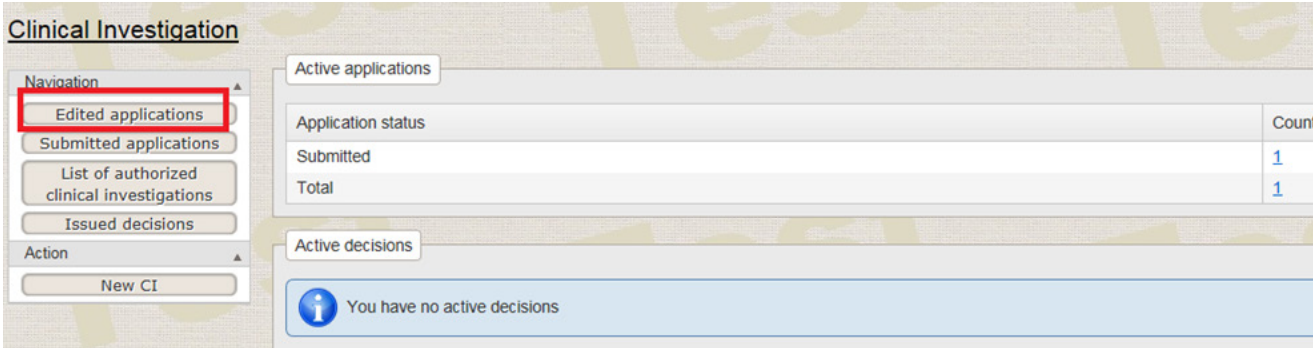


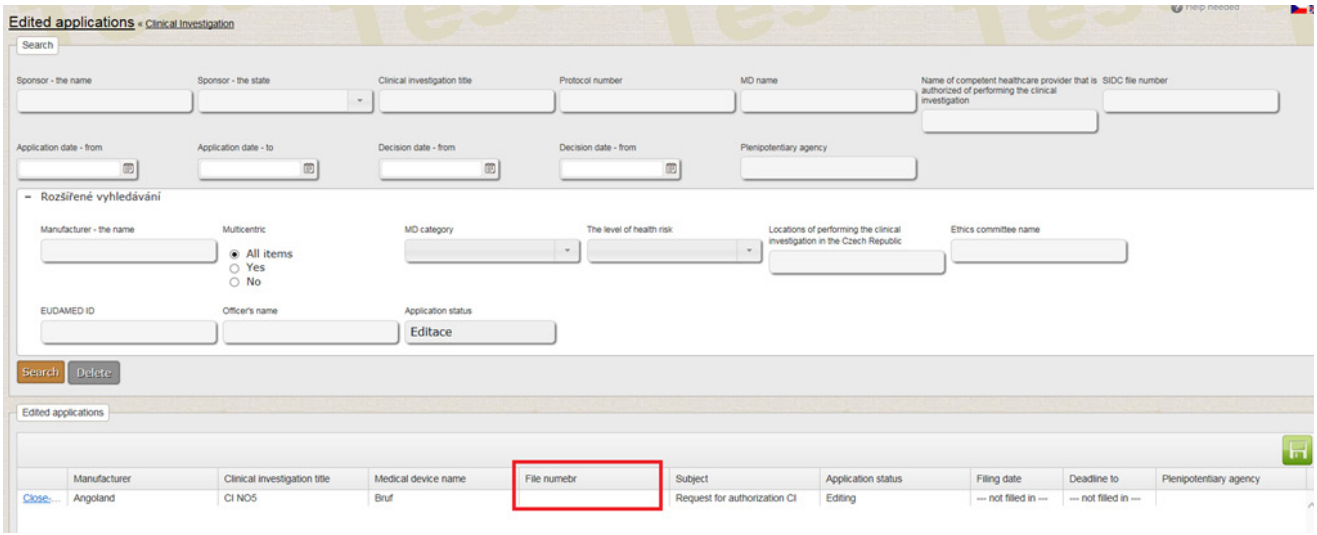
If you open the form for the submission of a new CI, the Registry of Medical Devices will enable you to perform the following with the application:

- **Save** – saves the content of the completed form and the saving is confirmed by a message in the information bar below the navigation icons. It is possible to save also partially filled-in forms and to get back to them later for completion.
- **Delete** – irreversibly deletes the currently opened application form. It is possible to delete forms in the "Edited" status only.
- **Check** – saves the content of the form and checks it for completeness of mandatory fields to be filled in and for attachments to be inserted. The result of the check is displayed in an information message.
- **File** – this option will submit the application to the Institute for processing. Prior to submission, the form completion will be checked and in case errors are identified, the submission will not be made and the user will be asked to eliminate the errors. The status of the application will change to „Submitted".

2.2.1. Application Prior to Submission to the State Institute for Drug Control

An application which has not been submitted to the State Institute for Drug Control (hereainfter referred to as the "Institute") yet, is in the status of being edited and does not have an Institute reference number (sukls) allocated. The list of unfiled applications is available from the navigation field in the *"Clinical Investigations"* module main window.

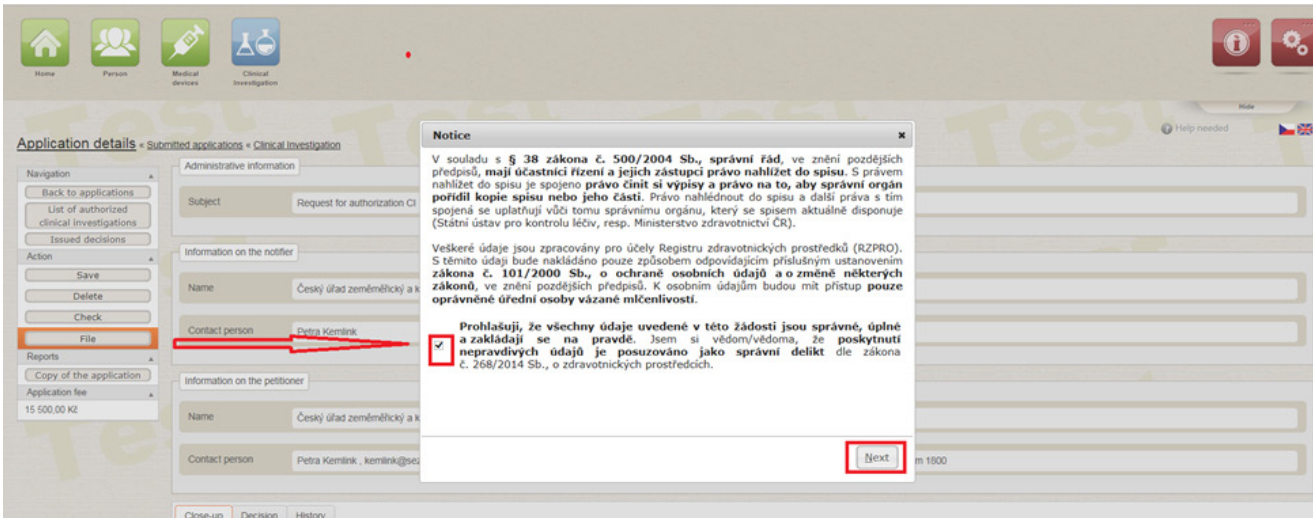


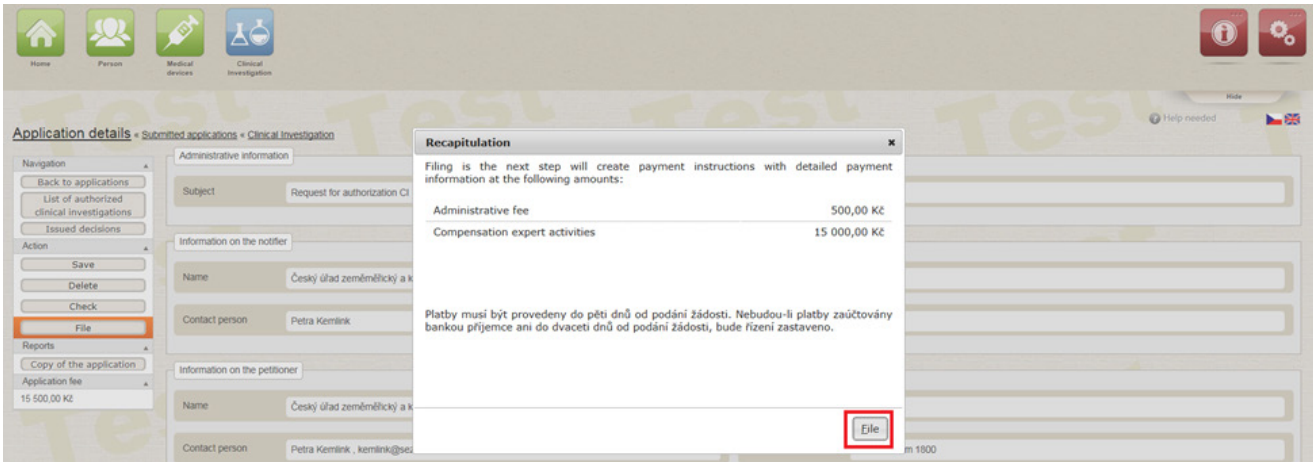


2.2.2. Submission of a New Clinical Investigation

For a detailed description of the application form for CI authorisation please, refer to the Registry of Medical Devices User Manual, chapter *"New Application for Clinical Investigation Authorisation"*, which can be found in the Registry of Medical Devices under the red ***"I"*** icon in the right upper corner under the *"Documents"* tab. The fields in the form may dynamically change to reflect the values entered in switches. Detailed instructions for form completion (for all alternatives) are available also in the Registry of Medical Devices User Manual.

If you have completed all of the mandatory fields (highlighted in yellow) and uploaded all of the mandatory attachments, the application may be filed with the Institute by pressing the ***"File"*** button. When you press the ***"File"*** button, and your submission is confirmed (see figures below), the application is already on the side of the Institute and **it may no longer be edited**. Following submission, the application may be edited only upon the delivery of the **Call for completion of the application** issued by the Institute.

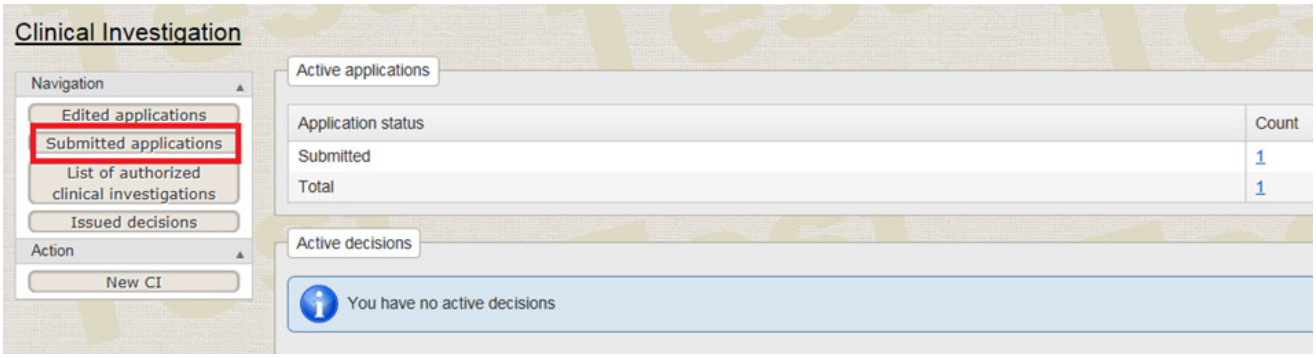




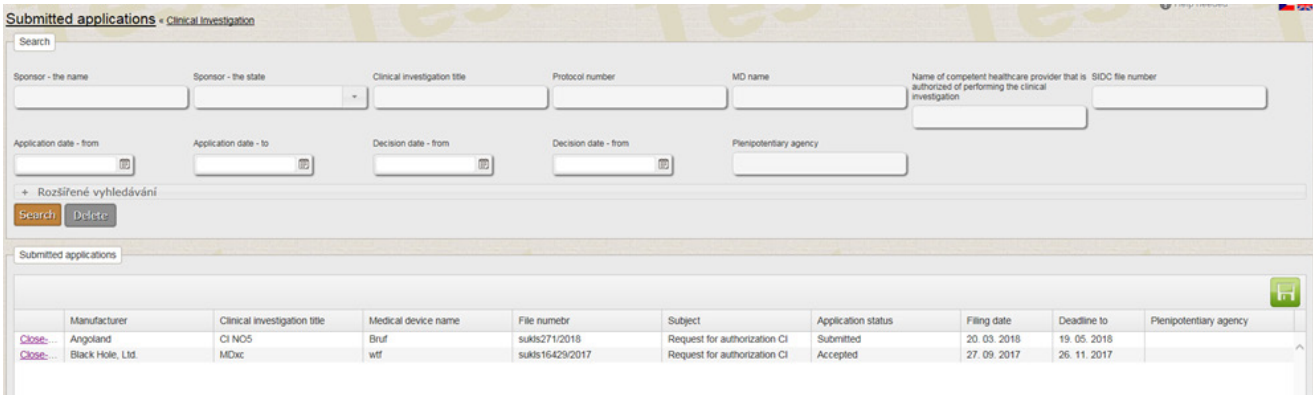
2.3. Filed Applications for Clinical Investigations

2.3.1. Searching for and Filtering of Filed Applications

In the main window of the CI module, click on the "Submitted applications" option.



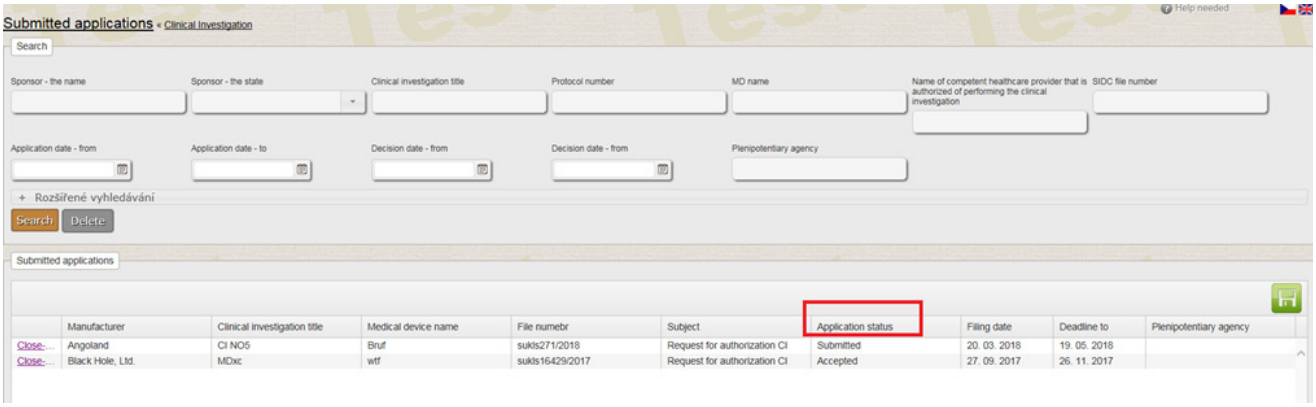
A list of all applications you have submitted will be displayed.



You can search using a filter by filling one or more of the filter fields and clicking on the "Search" button; the applications will be filtered as appropriate.

2.3.1.1. Submitted Application Status

In the list of submitted applications, under the "Application status" column, it is possible to find the current status of individual submitted applications within the administrative procedure.

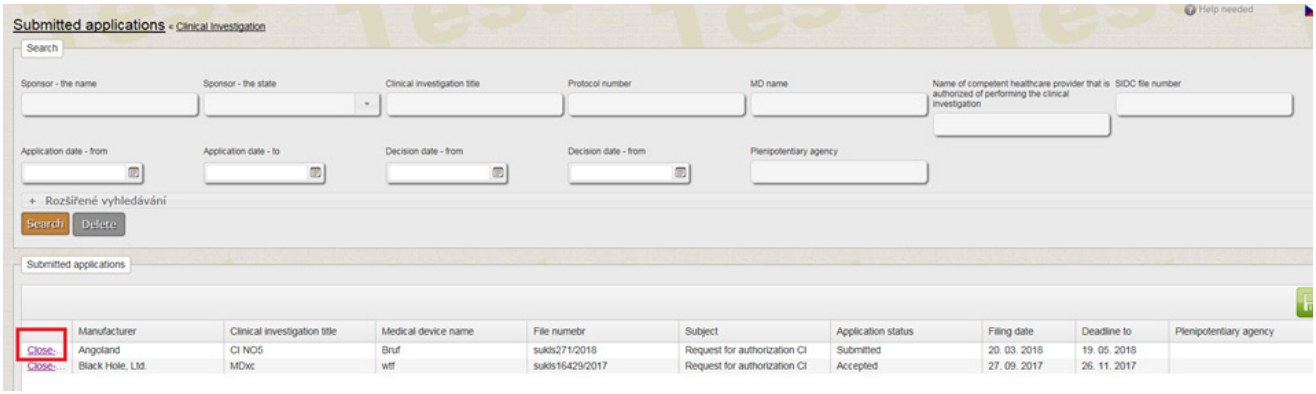


Overview of application statuses:

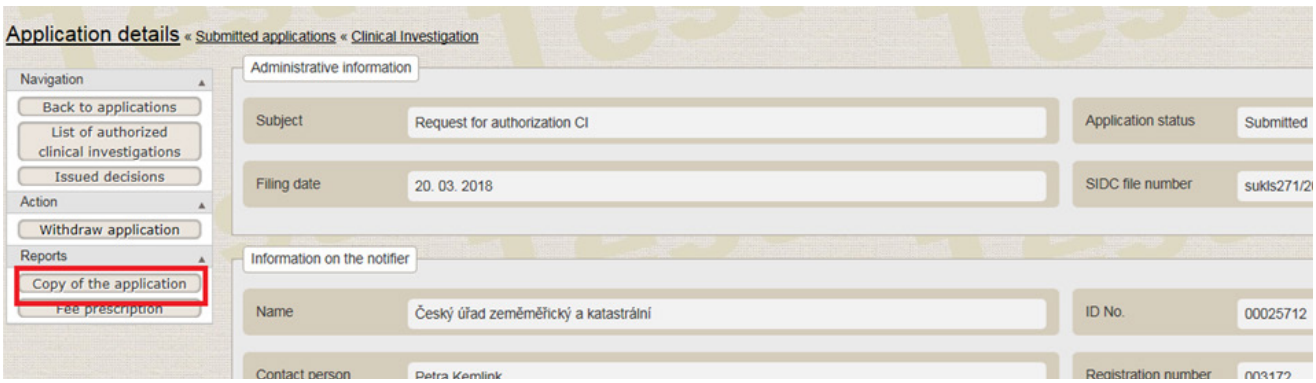
- **EDITED** – an Institute reference number has been assigned – the application contained shortcomings, upon which you were asked by the Institute to amend the application. You have opened the application detail and the edited application may be completed/amended.
- **SUBMITTED** – the application or its amendment required by the Institute has been submitted with the Institute.
- **UNDER PROCESS** – the application/required amendment is being assessed by an officer of the Institute.
- **PROCESSED** – the application/required amendment has been assessed and the outcome forwarded for signature.
- **ACCEPTED** – the application meets all of the particulars set forth by law and the Institute has issued a decision on CI authorisation.
- **CALL FOR COMPLETION** – you have received a call to amend the application; it is necessary to respond to the call **within the timeline set forth by the resolution**, which forms part of the call for completion.
- **TERMINATED** – the Institute has issued a resolution on termination of the administrative procedure regarding your application.
- **REJECTED** – the Institute has issued a decision on rejection of the submitted application.
- **APPLICATION WITHDRAWN** – you have withdrawn your application. On the basis thereof, the Institute will issue a resolution on termination of the administrative procedure. Once the resolution is issued, the status of the application will change to "Terminated".

2.3.1.2. Submitted Application Detail

To display the detail of any submitted application which has been created, saved, and submitted, click on the **"Close-up"** button in the list of filed applications.



The completed application in the pdf format will be generated by clicking on the "**Copy of the application"** button.



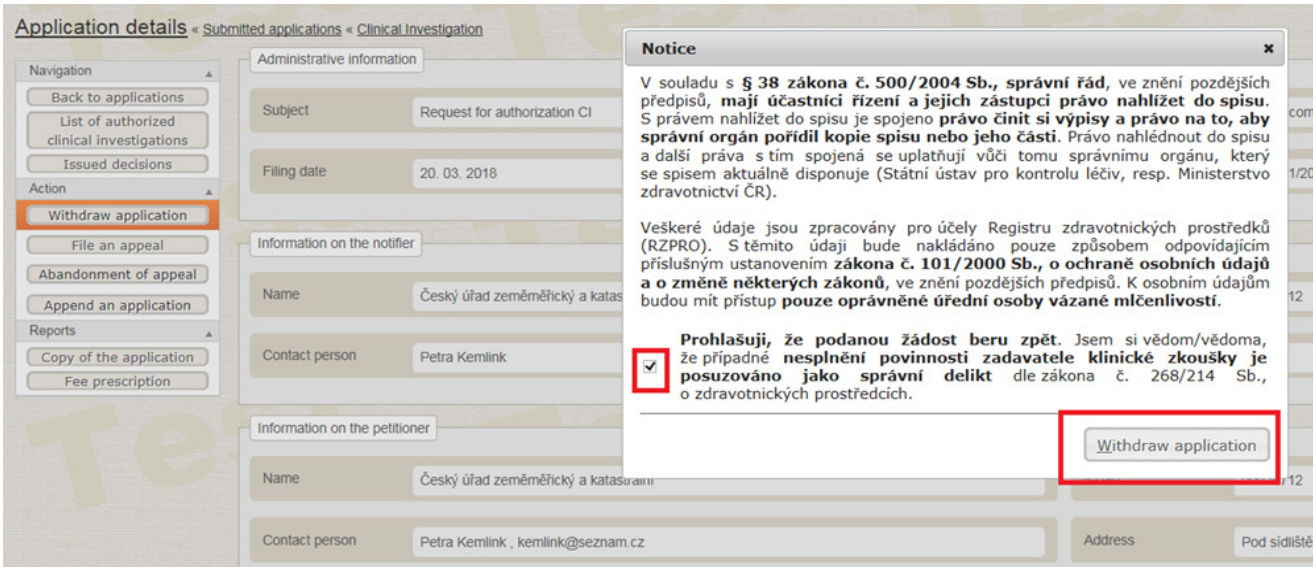
2.4. Acts to Be Taken with Regard to the Institute´s Response to a Filed Application

With regard to the Institute´s response, it is possible to carry out the following actions in the **detail of a submitted application** (see above):

- **Withdraw an application** – upon application withdrawal, the Institute will stop the administrative procedure and will no longer work with the submitted application.
- **File an appeal** – the submitter of the application files an appeal from the decision issued by the Institute. The filed appeal shall comply with the Code of Administrative Procedure.
- **Abandonment of Appeal** – the submitter waives their right to appeal, which means the decision comes into force on the given date; in case of clinical investigation authorisation, the CI may be commenced on the day following the date the decision comes into force.
- **Append an application** – allows to amend/edit the application with regard to the "call for completion" issued by the Institute.

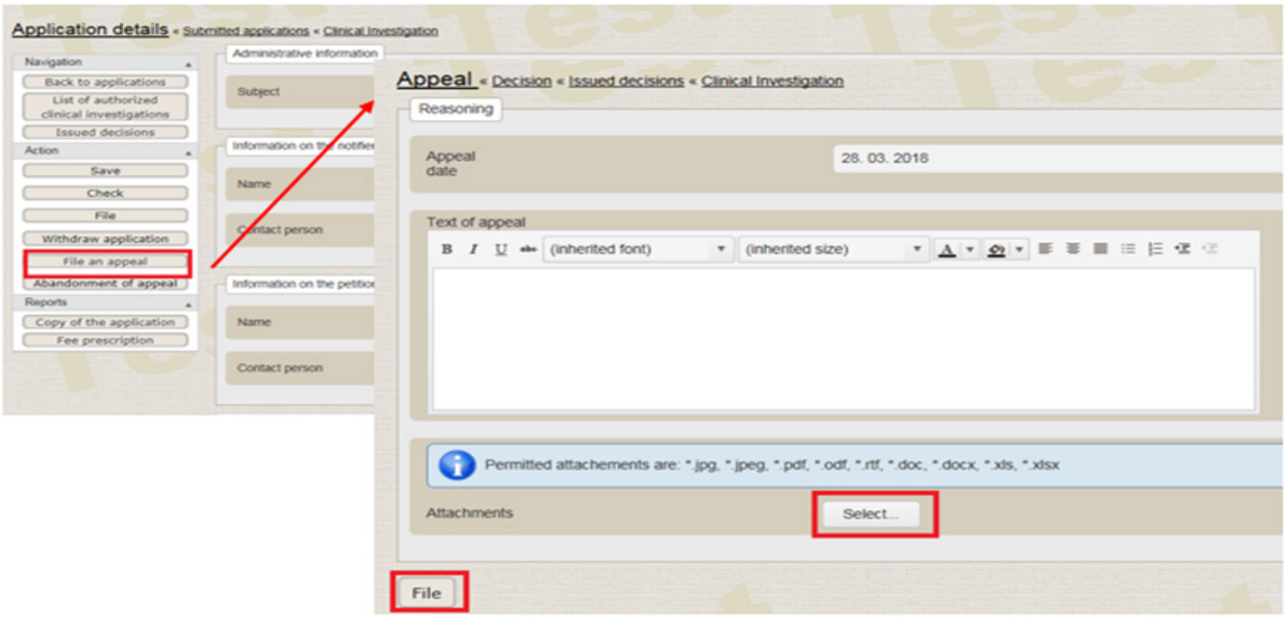
2.4.1. Withdrawal of a Filed Application

A filed application may be withdrawn by pressing the **"Withdraw application"** button. An advice will be generated. In this Advice, please tick the Declaration of taking note of withdrawal of the submitted application. Thereafter, click on the **"Withdraw application"** button (see Fig. below). A withdrawn application may no longer be edited and the Institute, having regard to the withdrawal, will issue a resolution on terminating the administrative procedure.



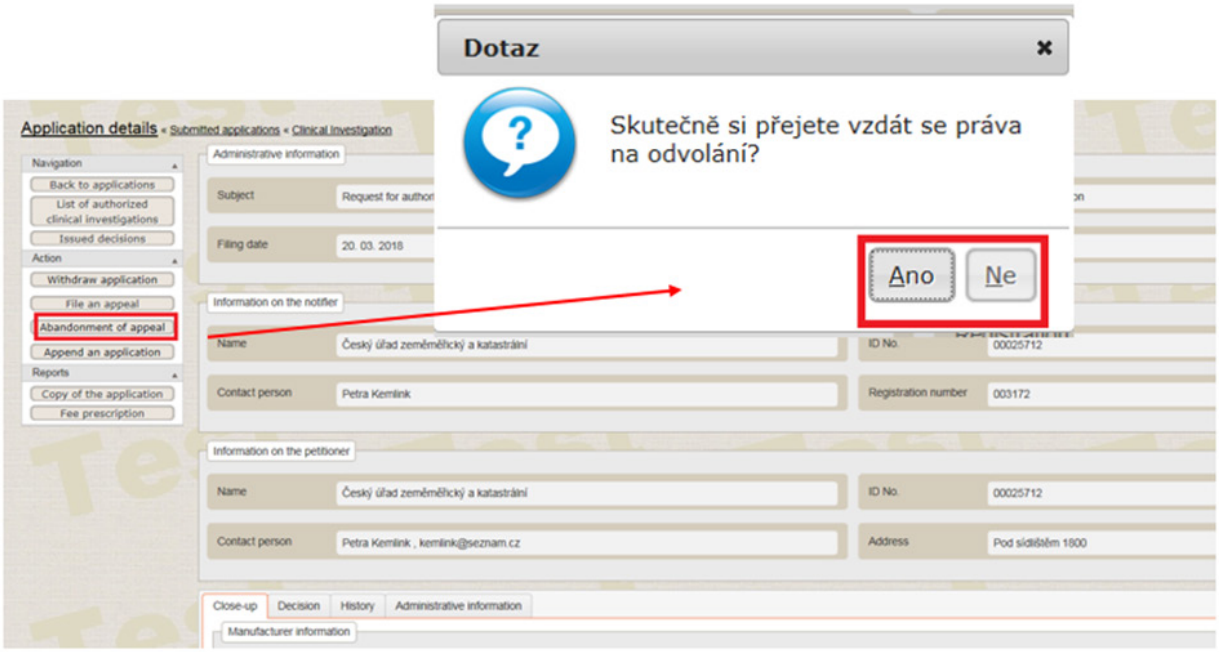
2.4.2. Appeal from Institute's Decision

It is possible to file an appeal from a decision by clicking on the **"File appeal"** button. A form for the entry of the text specifying the reasons for appeal will come up together with the **mandatory** upload of a document containing the submitter´s appeal in the form of an attachment (click on the **"Select"** button). An appeal is filed by clicking on the **"File"** button.



2.4.3. Abandonment of Right to Appeal

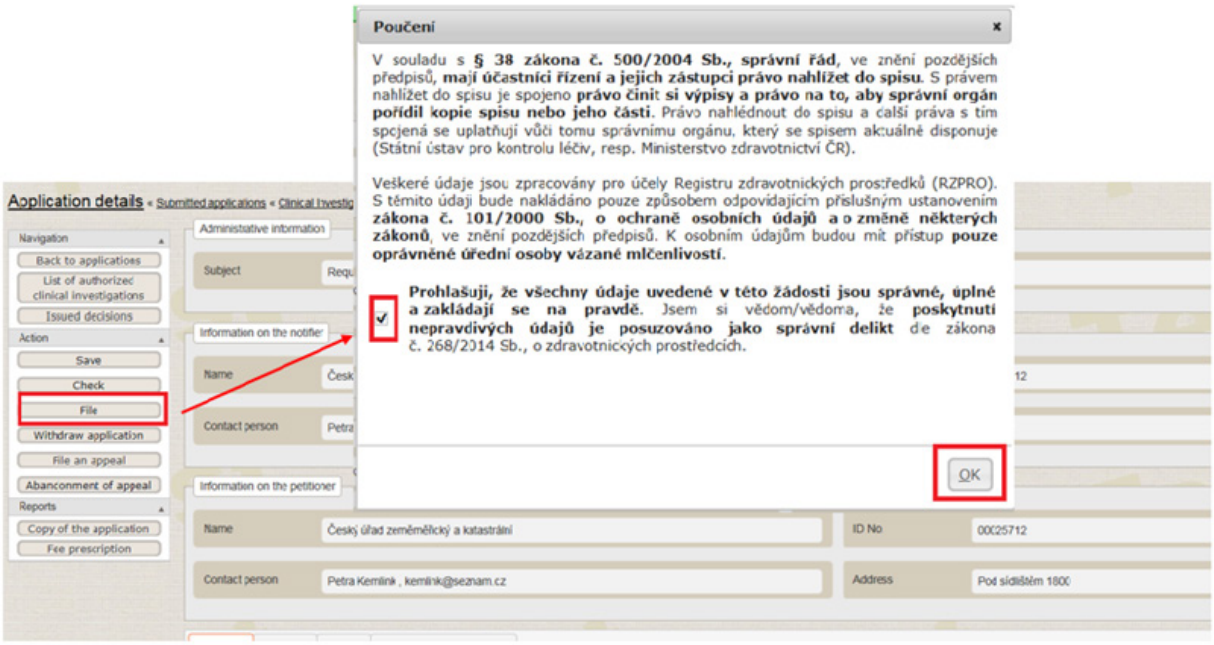
In case the applicant needs the decision issued by the administrative authority to come into force earlier than upon the timeline specified for appeals from the decision in question, it is possible to waive the right to appeal from the decision. The right to appeal may be waived by clicking on the **"Abandonment of appeal"** button and subsequently confirmed by clicking on the **"Ano"**(Yes) button.



2.4.4. Amendment of a Submitted Application

To amend an application on the basis of requirements specified in the call for completion, click on the **"Append an application"** button. A form identical to the one for submission of a new CI will come up, with fields from the previous submission of the concerned CI completed. These may be amended or new attachments may be uploaded.

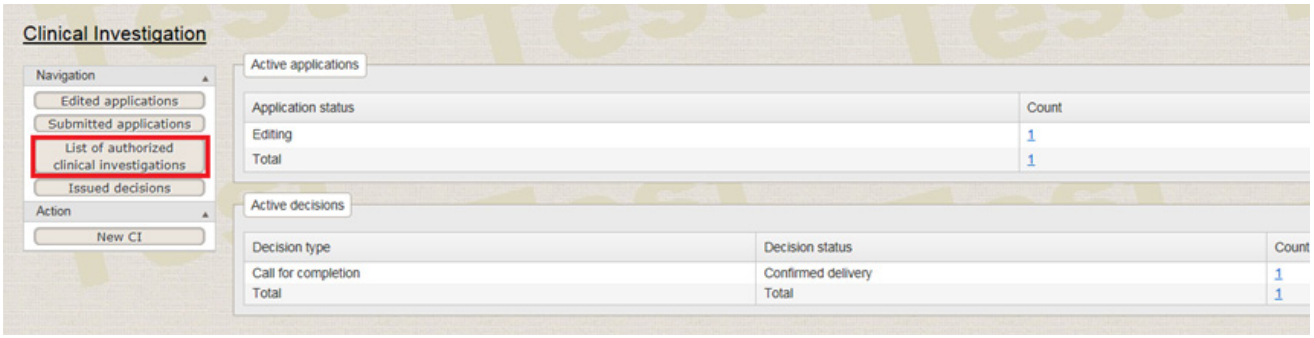
The application may be amended item-by-item. To save your changes gradually, always click on the **"Save"** button. Once you complete all of the particulars required by the call for completion, click on the **"File"** button to file the amended application with the Institute. To verify whether the application has been filed, check whether the application status has changed from **"Edited"** to **"Filed"**.



2.5. Authorised CI Administration

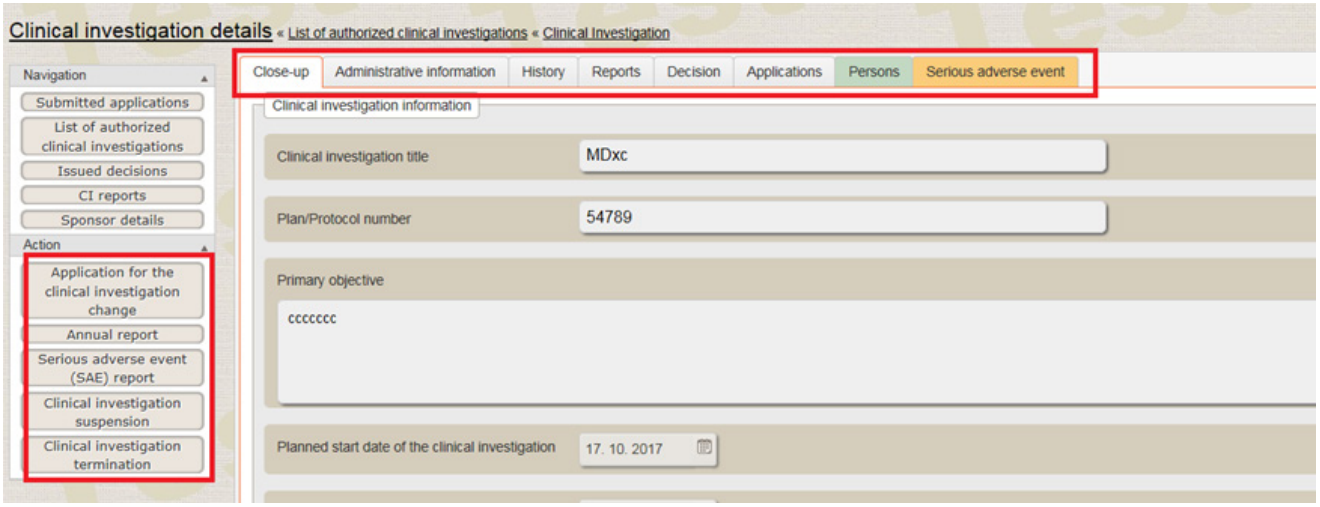
2.5.1. List of Authorised CIs

In case you desire to display the list of approved applications for clinical investigations, use the **"List of authorised clinical investigations"** option.



A list with the possibility to apply filters will be displayed, just as described under section *"2.3.1. Searching for and Filtering of Filed Applications"*. The description of the individual fields of the search filter is available from the Registry of Medical Devices User Manual.

For more details on the clinical investigation, the possibility to submit reports on CI commencement, submission of the annual report, etc., and the conduct of other acts (application for CI modification, application for continuation of a CI suspended by the sponsor or by the Institute), click on the **"Close-up"** of the respective CI **in the list of authorised CIs**. The CI detail will come up with individual tabs containing detailed information on the CI and a panel of buttons for the submission of individual reports and applications which may be submitted in respect of the authorised CI.



2.6. Acts Conducted in Respect of Authorised CIs

Acts conducted in respect of authorised CIs (reports, applications for CI modification) may be carried out in the Registry of Medical Devices only if you click on the **"Close-up"** of the respective CI in the **"List of authorised clinical investigations"** option!

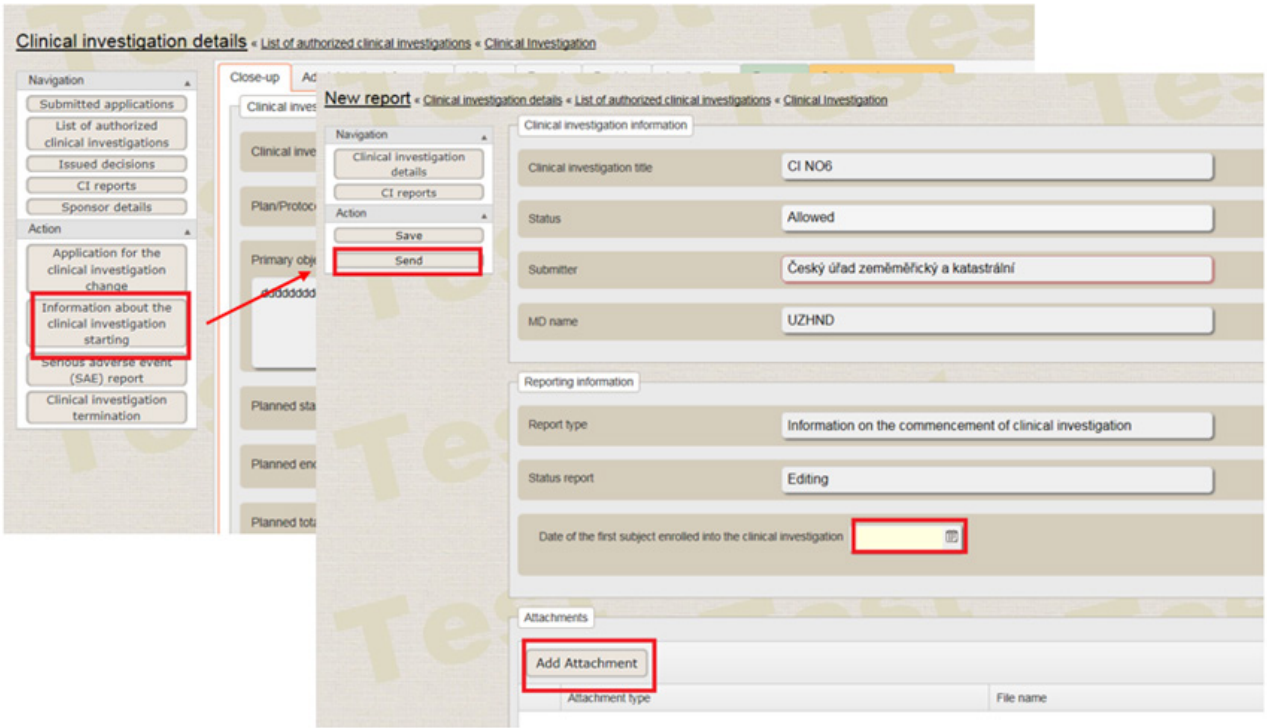
When you click on the button for individual reports, it is possible to go back by clicking on the **"Close-up"** button.

The following acts may be carried out under the Detail of an authorised CI:

- **Application for CI change (modification)** – may be filed also prior to the start of the CI
- **Information on Clinical investigation starting (commencement)** – following the submission of the report on the CI starting (commencement), this act is no longer available and the original report cannot be edited.
- **Annual report** – the button for its submission will be displayed only after the submission of the Information on CI commencement.
- **Serious adverse event (SAE) report** – this serves for the purposes of reporting a SAE; the list of SAEs reported via the Registry of Medical Devices is available from the "Serious adverse event (SAE) report" tab.
- **Clinical investigation suspension** – the button for notifying suspension of a CI will be displayed only after the information on CI starting (commencement) has been submitted.
- **Clinical investigation termination** – after the report on the termination of the clinical investigation is submitted, the only options available are SAE reporting and submission of the final report.
- **Final report** – the button for the submission of the final report will be displayed only after the report on clinical investigation termination has been submitted.

2.6.1. Commencement of a Clinical Investigation

The sponsor is obliged to forthwith report the commencement of the clinical investigation in compliance with Section 19, paragraph 2(i) of the Act on Medical Devices. To report the commencement of the CI, click on the **"Information about the clinical investigation starting"** (CI commencement) button in the Detail of the authorised CI. It is necessary to enter the date of CI commencement in the displayed form and it is possible to insert attachments (optional). If you click on the **"Send"** button, the report for the Institute will be displayed. The report on CI commencement may only be submitted once. The submitted report may no longer be edited.

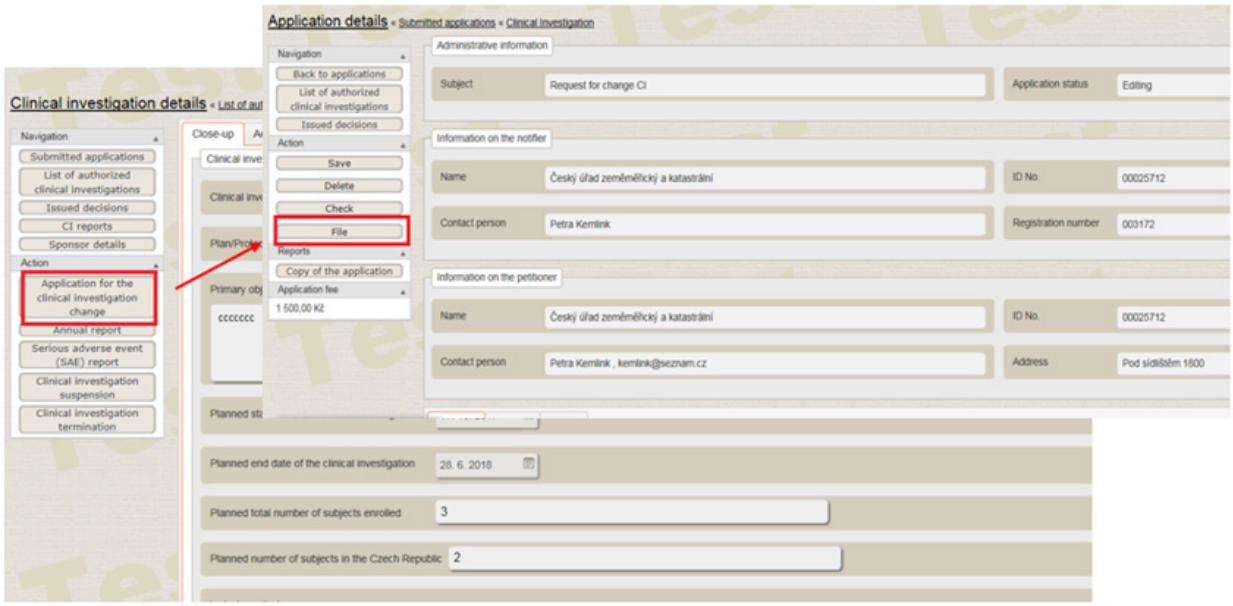


2.6.2. Application for the change (modification) of a Clinical Investigation

If the sponsor wishes to make amendments to the conditions of the clinical investigation, they shall be obliged to apply for the Institute's approval of such changes in compliance with Section 15, paragraph 4 of the Act on Medical Devices.

In the CI detail, click on the **"Application for the clinical investigation change"**. A new **"Application for CI change"** will be automatically created and saved with the "Edited" status and fields from the latest effective version of the CI registration will be populated in the application. The application requires editing – completion of the field **"Justification for application of the clinical investigation change"** and insertion of the necessary attachments (the mandatory attachments being the "A proposal of changes in clinical investigation documentation" and a „written approval of the ethics committee with changes of clinical investigation documentation"). Thereafter, save the application using the **"Save"** button. If the application is complete, it is possible to submit it for the Institute´s approval of the modification of the clinical investigation (through the **"Send"** button). Following submission, the status of the application will be changed to "Submitted" and it may be displayed in the list of applications. The subsequent options available are the same as those outlined under section 2. 2. 2. *"Submission of a New Clinical Investigation"*.

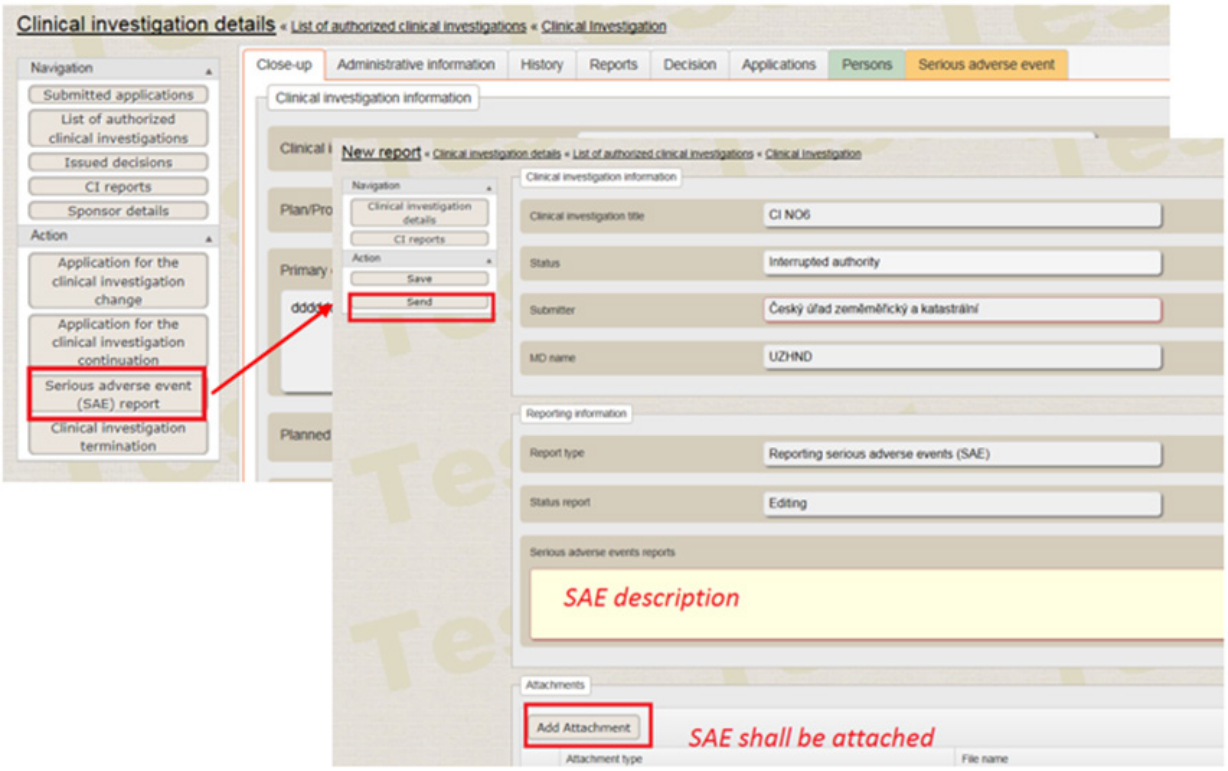
If you have created the application for clinical investigation change by mistake, it may be deleted by clicking on the **"Delete"** button, if it has not been submitted.



2.6.3. Serious Adverse Event (SAE) Reporting

In compliance with Section 19, paragraph 2(n) of the Act on Medical Devices, the sponsor is obliged to inform the Institute of arising SAEs immediately upon their occurrence.

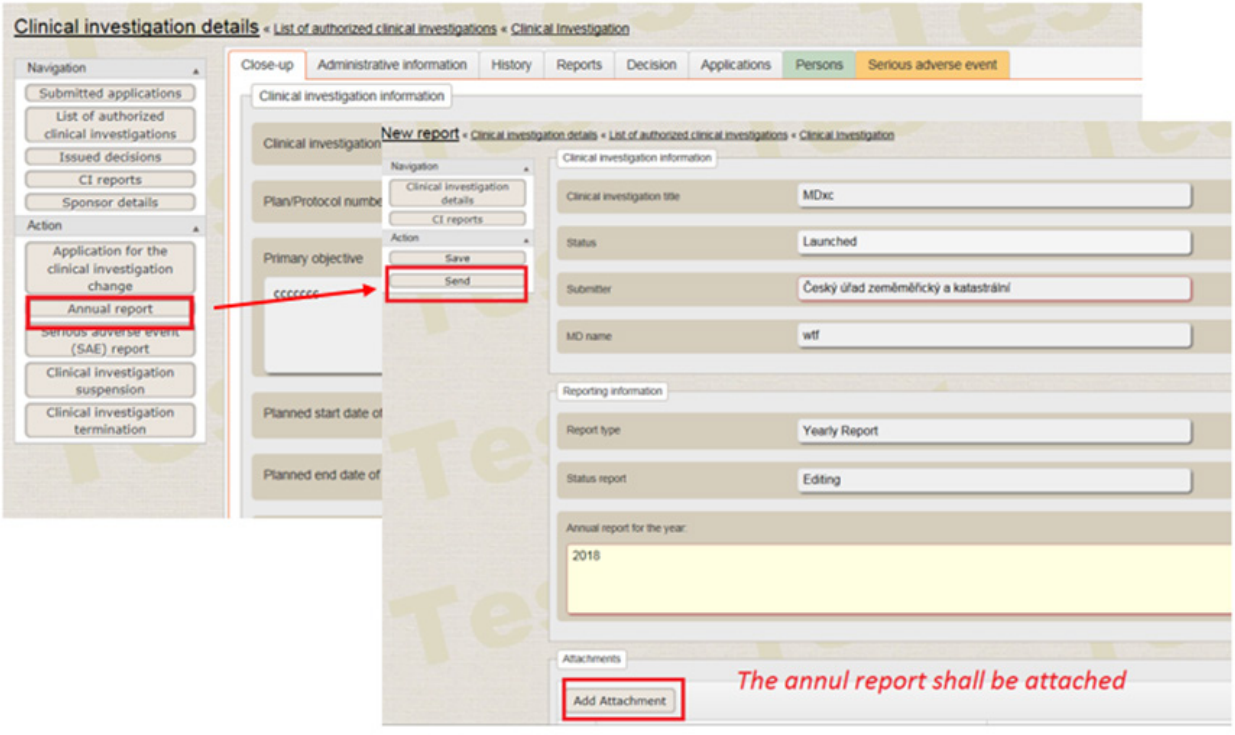
To report an arising SAE or modification thereof, click on the **"Serious adverse event (SAE) report"** option in the Detail of the authorised CI. The mandatory fields are the text description of the SAE and the SAE report form as per MEDDEV 2.7/3 uploaded as an attachment.



2.6.4. Annual Report

The annual report on the course and safety evaluation of the clinical investigation has to be submitted by the sponsor by 31 January of the following year in compliance with Section 19, paragraph 2(j) of the Act on Medical Devices.

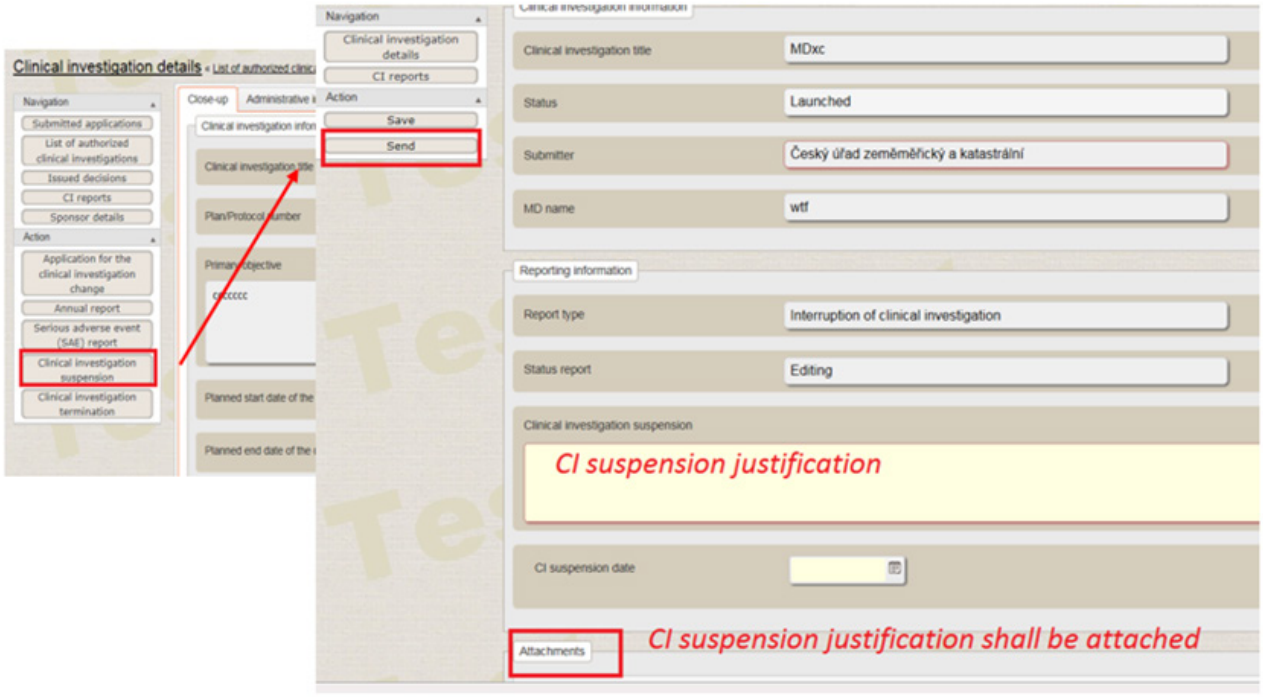
To submit the annual report, click on the **"Annual report"** button in the detail of the authorised CI. This button is available only after the Information on CI starting (commencement) has been submitted via the Registry of Medical Devices (*section 2.6.1. "Commencement of a Clinical Investigation" refers*).



2.6.5. Suspension of a Clinical Investigation

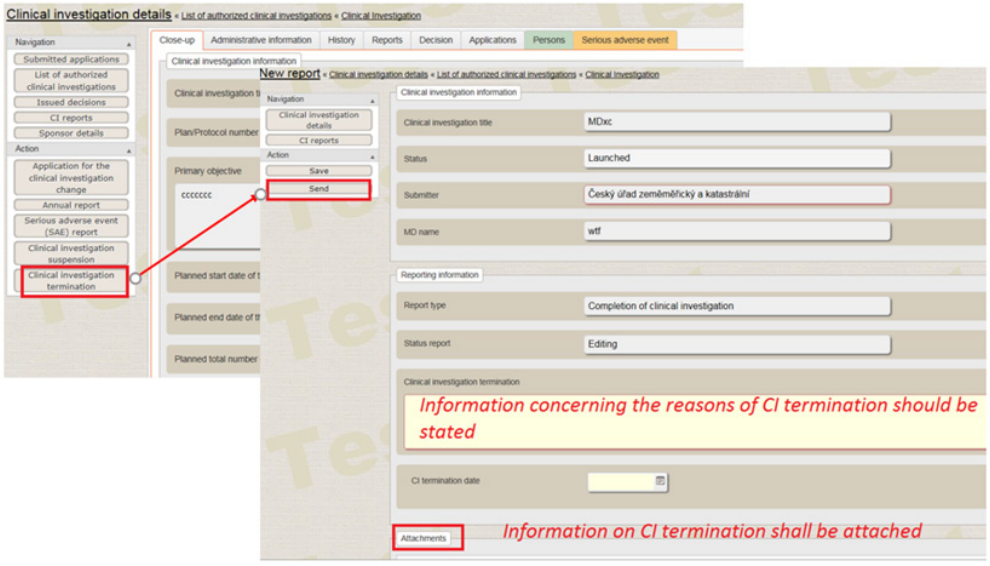
A suspension of a clinical investigation has to be reported by the sponsor within the timeline of 30 days of the suspension in compliance with Section 19, paragraph 2(k) of the Act on Medical Devices.

To report a clinical investigation suspension, click on the **"Clinical investigation suspension"** button. To resume a suspended CI, proceed as outlined under section 2.7.1 *"Continuation of a Clinical Investigation Suspended by the Sponsor or by the Institute"*.



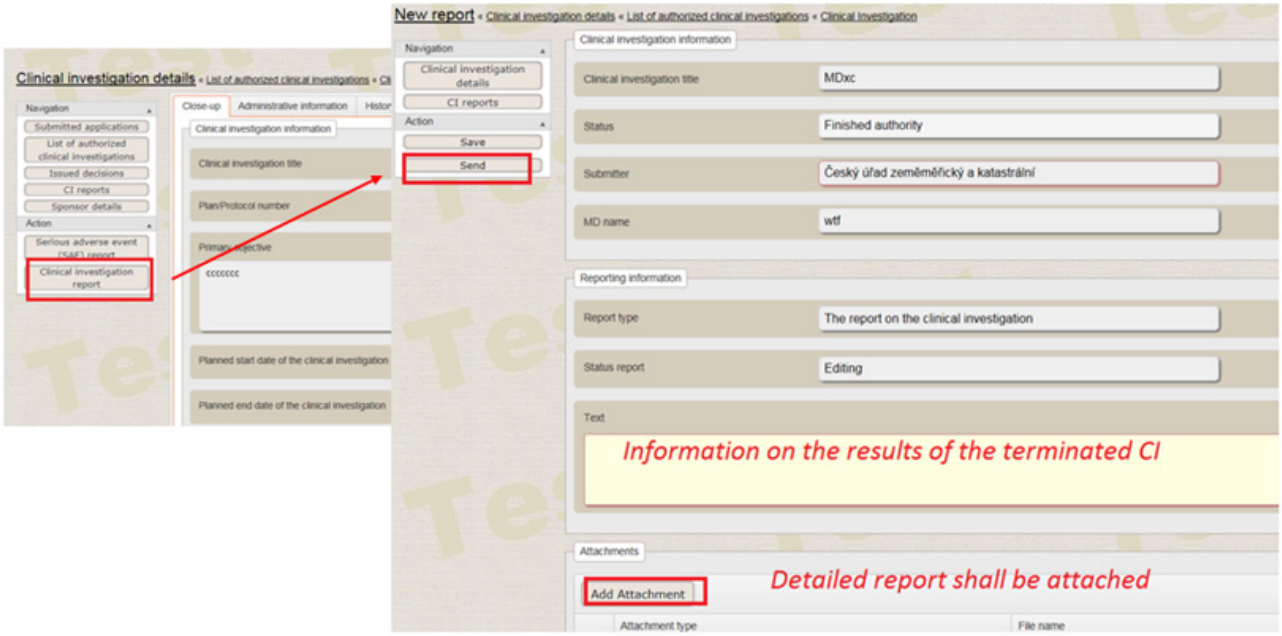
2.6.6. Termination of a Clinical Investigation

Termination of a clinical investigation has to be reported by the sponsor within the timeline of 30 days of CI termination in compliance with Section 19, paragraph 2(k) of the Act on Medical Devices. To report clinical investigation termination, click on the **"Clinical investigation termination"** button.



2.6.7. Final Report on the Clinical Investigation

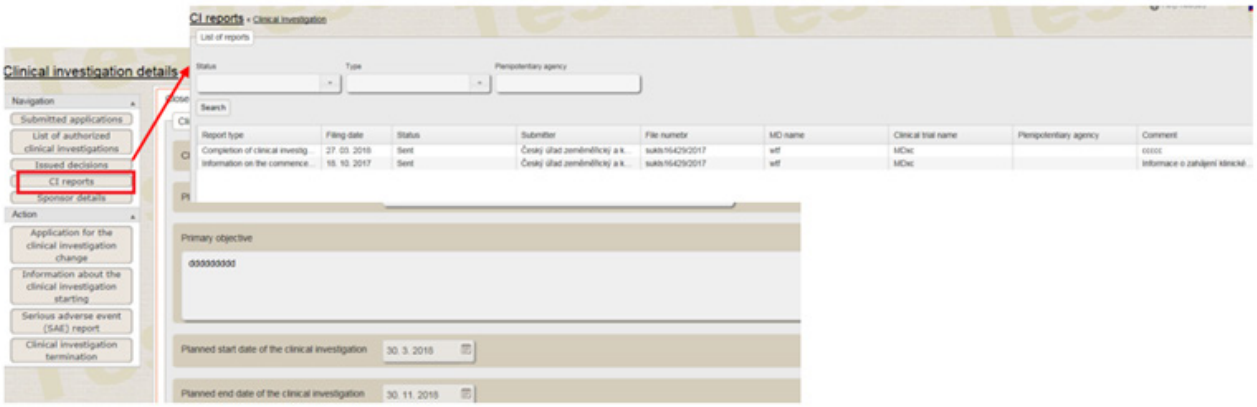
The final report on the clinical investigation has to be submitted by the sponsor to the Institute following termination of the CI in compliance with Section 19, paragraph 2(l) of the Act on Medical Devices.
To submit the final report, click on the **"Clinical investigation report"** button.



2.6.8. List of Individual Reports

If you wish to display the list of reports for individual CIs, click on the **"CI reports"** button. The list is designed to display a listing of individual reports from all authorised clinical investigations.

It is possible to search the list using filters, to sort the reports in ascending/descending order by one of the columns. The report detail may be opened by clicking on the row of the respective report.



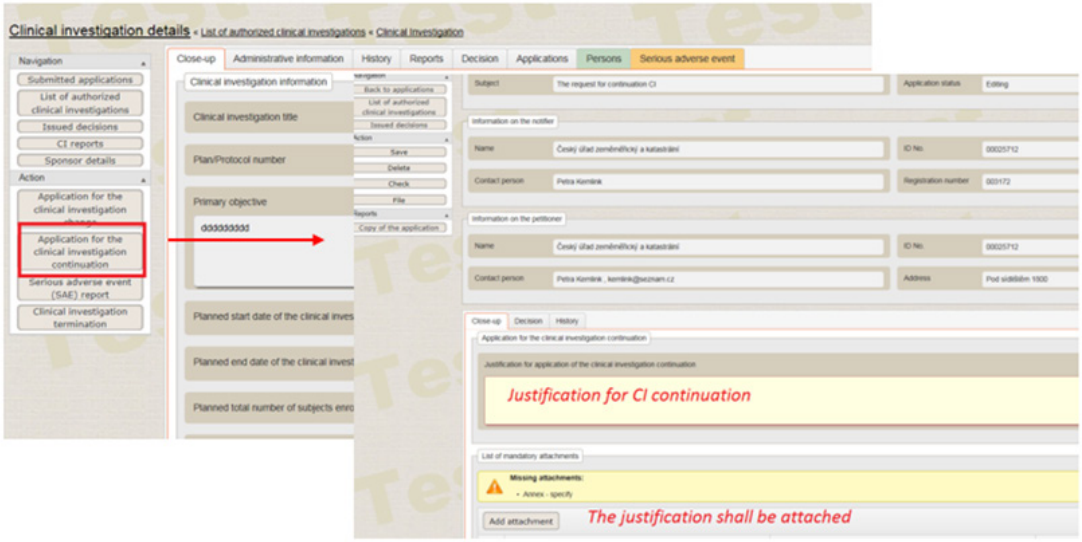
2.7. Suspension of an Authorised Clinical Investigation by the Institute

The Institute may temporarily suspend conducting of an authorised clinical investigation thereby in compliance with Section 15, paragraph 5 of the Act on Medical Devices.

You will be informed of the suspension of the clinical investigation by means of a delivered resolution issued by the Institute.

2.7.1. Continuation of a Clinical Investigation Suspended by the Sponsor or by the Institute

Once the reasons for suspension cease to exist, it is possible to file an application for CI continuation in respect of a suspended CI by means of a report and to apply for Institute´s resolution on authorisation to resume the CI.



2.8. Ex-officio Halting of an Authorised Clinical Investigation by the Institute

The Institute may halt conducting of an authorised clinical investigation thereby in compliance with Section 15, paragraph 5 of the Act on Medical Devices.

The decision on halting an authorised clinical investigation by the Institute will be displayed on the dashboard in the main window of the CI module and will be available from the **"Issued decisions"** list in the main window or in the Detail of a specific CI.

It is possible to file an appeal from the decision on halting an authorised clinical investigation by the Institute via the Registry of Medical Devices (*section 2. 4. 2. "Appeal from Institute´s Decision" refers*). If the decision on the halting of a clinical investigation comes into force, it shall be permanent and an application for CI continuation may no longer be submitted.

Should you encounter any **unclarities regarding the procedures to be followed in the Clinical Investigation Module**, please contact SÚKL at:
email: SZP_RZPRO_dotazy@sukl.cz
tel. 272 185 704

Should you encounter **technical problems** when filing your application, please contact ÚZIS:
tel: 222 269 999 – general UZIS helpline
helpdesk.registry@uzis.cz

Generals questions should be addressed to SÚKL at: 272 185 333

Medical Devices Branch
2018