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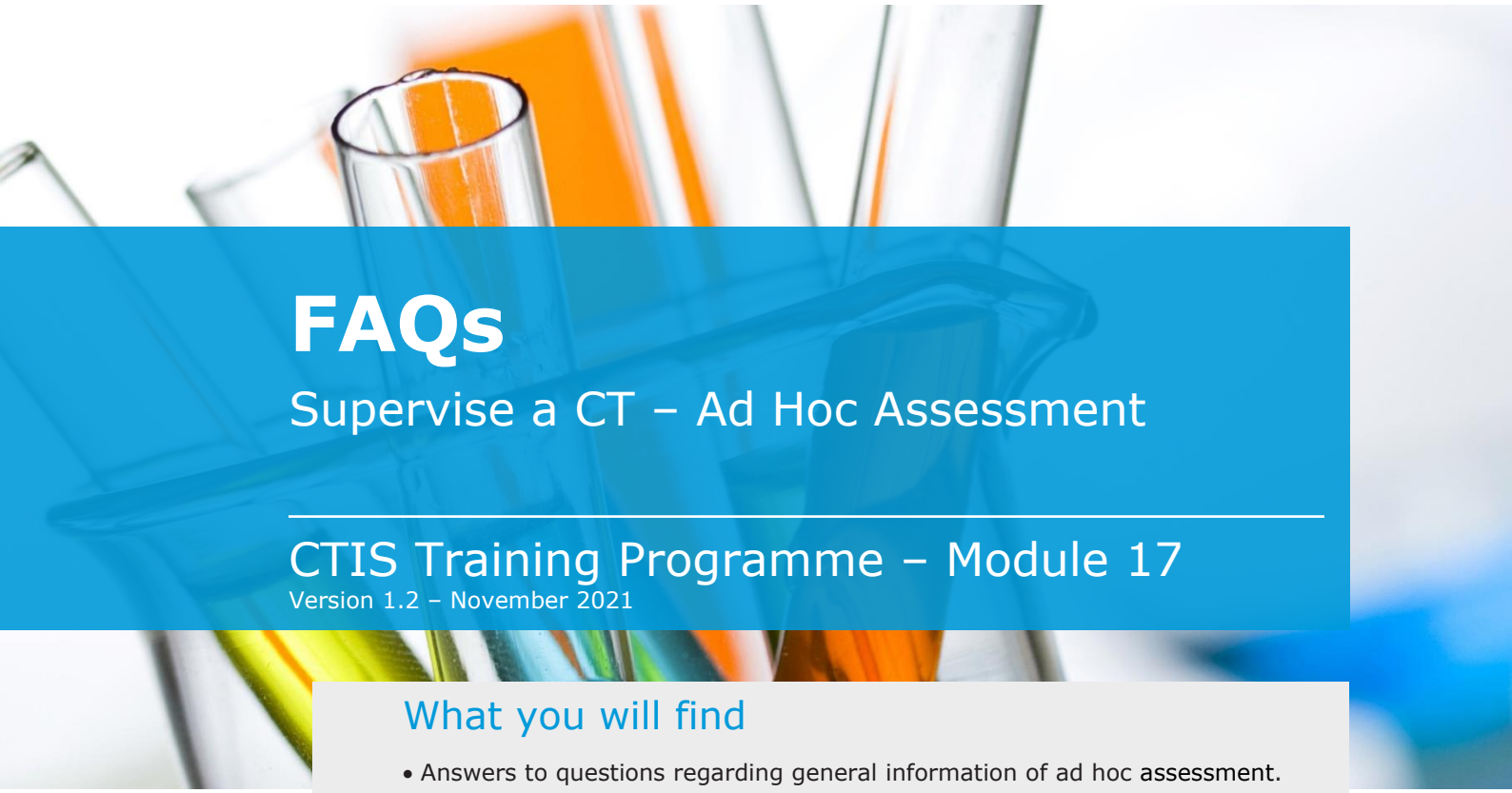

FAQs

Supervise a CT – Ad Hoc Assessment

CTIS Training Programme – Module 17

Version 1.2 – November 2021

What you will find

- Answers to questions regarding general information of ad hoc assessment.
- Answers to questions regarding the creation of an ad hoc assessment.
- Answers to questions regarding the requests for information and consultation with other the MSs.
- Answer to questions regarding the update and completion of an ad hoc assessment.
- Answers to questions regarding how to search, view and download an ad hoc assessment.
- Answers to questions regarding the roles and permissions.

The European Medicines Agency developed this training material to enhance public access to information on the Clinical Trial Information System (CTIS). This material describes a preliminary version of CTIS and may therefore not entirely describe the system as it is at the time of use of this material. The Agency does not warrant or accept any liability in relation to the use (in part or in whole) or the interpretation of the information contained in this training material by third parties.

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FAQs

In this document, we list common questions regarding *Module 17: Supervise a CT – Ad hoc assessment*. They are categorised into: questions regarding general information of ad hoc assessment; questions regarding the creation of an ad hoc assessment; questions regarding the requests for information and consultation with other MSs; questions regarding the update and completion of an ad hoc assessment; questions regarding the search, view, and download of an ad hoc assessment; questions regarding the roles and permissions. The specific learning objectives of this module are:

1. Remember what an ad hoc assessment is and when an MS can create one.
2. Understand how to create, cancel, save, and share an ad hoc assessment.
3. Understand how to raise an RFI, consult with other MSs, update and complete an ad hoc assessment.
4. Understand how to search, view, and download an ad hoc assessment.
5. Understand which user roles are involved in the ad hoc assessment process.

We encourage you to read these questions and answers carefully. If you have any questions which are not covered in this document, please contact us at CT.Training@ema.europa.eu so that we can update this document accordingly. This document will be progressively enriched with the input of the experts involved in the validation of the training material, the Master Trainers disseminating the materials, and the end-users.

1. General information

1.1. What is an ad hoc assessment?

Process that allows Member States to launch an assessment regarding a submitted notification, an investigational medicinal product, or any other information relevant to the supervision of a trial. During this process, the Member State can request additional information from the sponsor and consult with the other Member States.

1.2. When can an ad hoc assessment be created?

An ad hoc assessment can be created by a Member State after a Clinical Trial Application (CTA) has been authorised and at least one of the following situations has occurred and need to be considered:

- An event has occurred during the trial.
- An event not directly related to the trial has occurred (e.g. a new IMP safety data).

1.3. Which actors are involved in an ad hoc assessment?

The Member States of the European Union, who will be represented by National Competent Authorities (NCAs) and Ethics Committee in CTIS, and the Sponsors in case requests for information (RFIs) are raised.

- **Member States:** They are able to create, update and complete an ad hoc assessment. They can also search, view, or download an ad hoc assessment that has been already completed. The assessing Member State is the MS that starts the ad hoc assessment and the discussion with the other MS, and that can raise an RFI to the sponsor.
- **Sponsors:** They participate in the process in case the MSs raise a request for information.

1.4. What are the reasons for creating an ad hoc assessment?

The ad hoc assessment process enables the Member State to assess information based on different reasons, depending on if it is related to a notification, an investigational medicinal product, or any other information relevant to the supervision of the trial.

The notifications that can trigger an ad hoc assessment are:

- **Temporary halt:** Article 2 (28) of the Clinical Trials Regulation[1] (CT Regulation)

[1] European Commission, *Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC*, EU Official Journal L158. 16

defines the temporary halt of a clinical trial as an interruption not provided in the protocol of the conduct of a clinical trial by the sponsor with the intention of the sponsor to resume it. It can be related to subject safety and/or benefit-risk balance or not.

- **Serious breach:** Notification to inform of a breach likely to affect to a significant degree the safety and rights of a subject or the reliability and robustness of the data generated in the CT. These notifications must be made no later than 7 days from the date on which the sponsor became aware of the breach (Article 52 of the CT Regulation[2]).

- **Unexpected event:** Notification of an incident that might influence the benefit-risk assessment of the medical product or that would lead to changes in the administration of a medical product or the overall conduct of a CT (e.g. a significant hazard to the patient population). These notifications must be made no later than 15 days from the date the sponsor became aware of the event (Article 53 of the CT Regulation[3]).

- **Urgent safety measure:** Notification of an unexpected event that is likely to affect the benefit-risk balance of a CT significantly, and the appropriate urgent safety measures to protect the subjects that have been taken by the sponsor and/or the investigator. The sponsor shall notify the Member State Concerned (MSC) accordingly and within 7 days from the date on which the measures were taken (Article 54 of the CT Regulation[4]).

The other aspects of the CT that can trigger an ad hoc assessment are:

- **SUSAR related:** A suspected unexpected serious adverse reaction is an untoward and unintended response to a study drug, that is fatal or life-threatening.

- **Investigational Medical Products (IMP) class and mode action**: It can trigger an ad hoc assessment if a safety issue is affecting medicinal products with a similar mode of action. The mode action is capture in the uploaded documents, e.g. Protocol.

- **Other:** Relevant information to the supervision of a trial.

1.5. Is it mandatory to create a corrective measure before starting an ad hoc assessment?

No. An ad hoc assessment can be performed independently from a corrective measure.

However, a corrective can stem from an ad hoc assessment (also other events such as Inspections, notifications, etc). An ad hoc assessment conclusion can deem that a corrective measure is necessary. Then a corrective measure can be created after the ad hoc assessment conclusion is submitted

of April 2014. Available at: https://ec.europa.eu/health/sites/default/files/files/eudralex/vol-1/reg_2014_536/reg_2014_536_en.pdf

[2] European Commission, *Regulation (EU) No 536/2014 of the European Parliament and of the Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC*, EU Official Journal L158. 16 of April 2014. Available at: https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-1/reg_2014_536/reg_2014_536_en.pdf

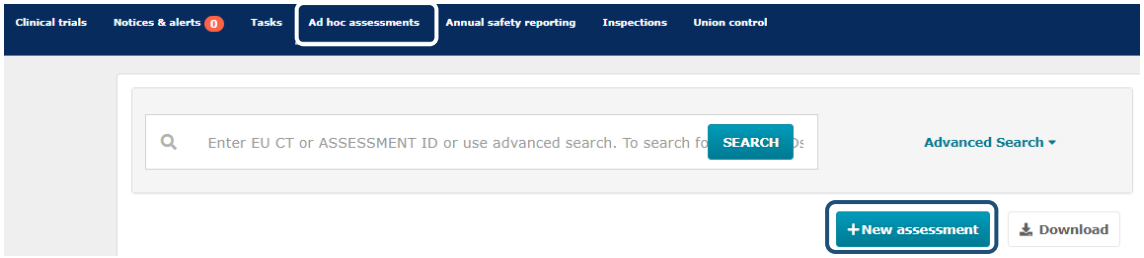
[3] Idem

[4] Idem

2. Creation of an ad hoc assessment

2.1. How can users create an ad hoc assessment in CTIS?

An ad hoc assessment can be created through the 'Ad hoc assessment' tab available on the top panel of CTIS. Once the Member State clicks on the 'New assessment' button, it is possible to start populating each of the sections of the ad hoc assessment form.



2.2. What are the sections of an ad hoc assessment?

There are five sections within the ad hoc assessment form:

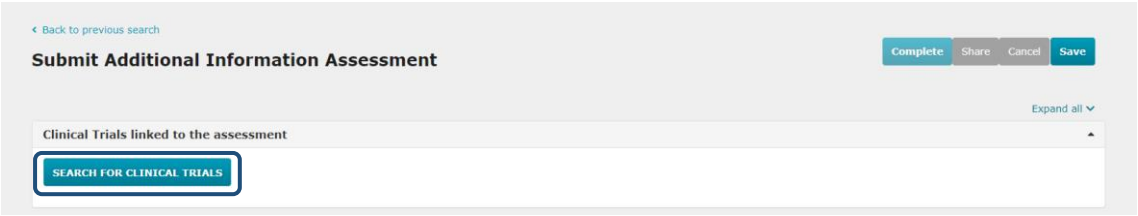
- **Clinical Trials linked to the assessment:** Section to search for clinical trials and link them to the additional information assessment process.
- **Assessment details:** Section to indicate the information required for the conduct of an ad hoc assessment. The section is divided into three parts: Assessment title, Linking, and Affected countries.
- **Request for information (RFI):** Section to submit a request for information to the sponsor.
- **Discussion:** Section to share comments or relevant information with other Member States.
- **Assessment outcome:** Section to include the outcome and overall recommendations regarding the ad hoc assessment.

2.3. How can Member States select the clinical trial for the assessment?

When populating the 'Clinical Trials linked to the assessment' section, the assessing Member State can select one or more clinical trials from the same sponsor on which the ad hoc assessment is to be made.

For this purpose, the user can select the 'Search for clinical trials' button and complete some

fields to start the search (e.g. Product name, EU CT number, Sponsor, etc.). From the results obtained, the Member State has to indicate the specific trial and the associated Investigational Medical Products (IMP).

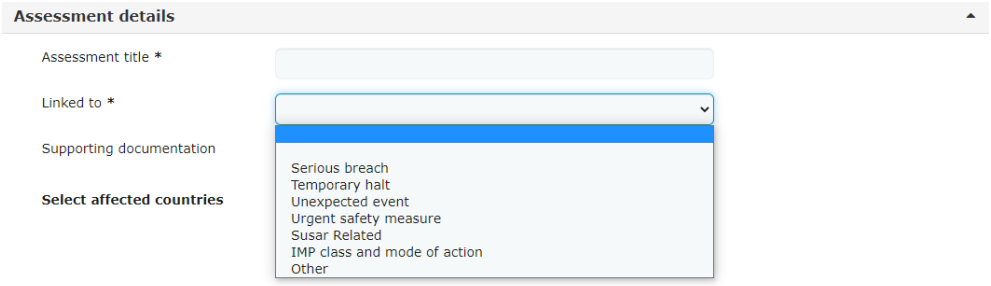


2.4. Can an ad hoc assessment be linked to more than one clinical trial?

The additional information assessment can be linked to one or more clinical trials, but always with the same sponsor.

2.5. How can Member States link the assessment to a notification or other aspects of the CT?

Within the 'Assessment details' section, Member States can link the assessment to a notification or other events that may have occurred. This can be done, through a drop-down list that displays the following options: temporary halt, serious breach, unexpected event, urgent safety measure, SUSAR related, IMP class and mode action or other.



If the Member State selects temporary halt, serious breach, unexpected event, or urgent safety measure, the associated notification submitted for the selected trial in the ad hoc assessment form can be indicated by ticking the corresponding box and click on the 'Link to assessment' button. In case Member States want to view the details of a notifications, they can go to the 'Notification' sub-tab and access the notification from there.

2.6. Can an ad hoc assessment be linked to more than one notification?

Member States can select one or more notifications of the same type to be used in the ad hoc assessment form.

2.7. How can users save an ad hoc assessment?

Member States can save the ad hoc assessment form at any point in time. However, in order to enable the 'Request for information' and 'Discussion' sections, the users need to save the form after populating the sections: 'Clinical Trials linked to the assessment' and 'Assessment details'. To do that, users can select the 'Save' button located at the upper-right corner of the ad hoc assessment form.

2.8. How can users cancel an ad hoc assessment?

Once the form is saved, CTIS enables the 'Cancel' functionality. Users can select the 'Cancel' button located at the upper-right corner of the ad hoc assessment form in order to cancel it.

Member States are able to cancel the ad hoc assessment only if the assessment has not been shared or completed.

2.9. How can users share an ad hoc assessment?

Once the form is saved, CTIS enables the 'Share' functionality. Users can select the 'Share' button located at the upper-right corner of the ad hoc assessment form in order to share it with the other Member States.

The MSC and affecting MSs will receive an alert and all MSs will receive an notice through the 'Notice & alerts' tab informing that an ad hoc assessment has been initiated.

After the ad hoc assessment is shared, the Member State is not allowed to cancel the assessment.

2.10. Does the assessment outcome change the status of the clinical trial?

No, the assessment outcome is informative and does not trigger any change in the status of the clinical trial. If a change in the clinical trial status is needed, the assessing Member State can only recommend an action, for example, a corrective measure.

3. Request for information and consultation with other MSs

3.1. What is an RFI created as part of an ad hoc assessment?

An ad hoc assessment RFI is a request submitted by the assessing Member State to the sponsor in the context of an ad hoc assessment in order to receive additional information.

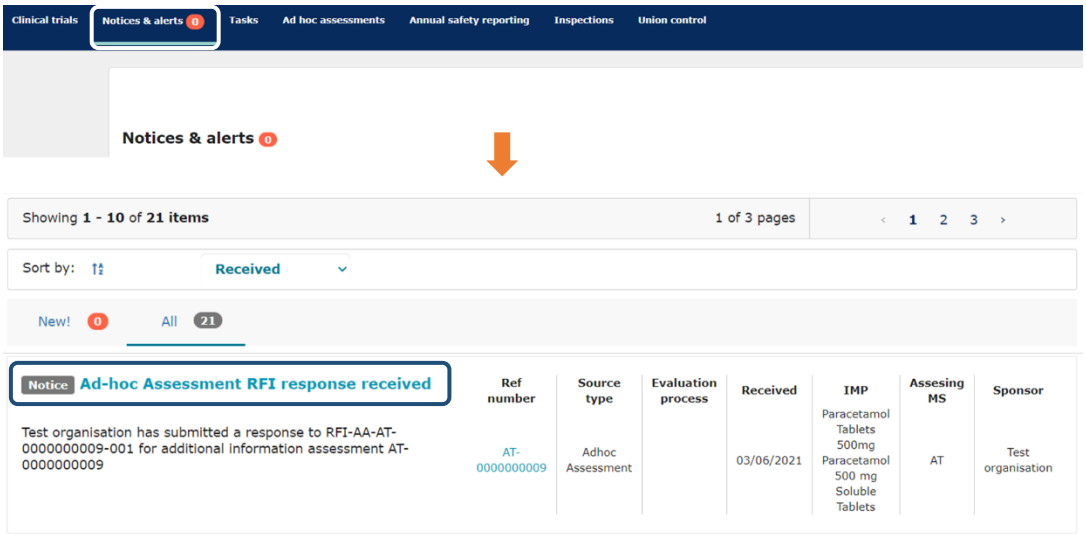
The assessing Member State is able to request information from the sponsor in case additional details are needed. For this purpose, users can expand the 'Request for

information (RFI)' section and complete the form: question details, due date, and additional document, if necessary.

Information on how a non MSC can create an RFI will be included in the training materials after the process has been validated.

3.2. How are Member States notified that the sponsor has replied the RFI?

Once the sponsor has responded to the request for information, the Member States receive a notice in the 'Notices & alerts' tab. The Member States will assess the answer and decide if a new request is needed.



3.3. What is a discussion raised as part of an ad hoc assessment?

The discussion forum is a communication tool available in CTIS for the Member States to consult or report on issues related to the trial. The assessing Member States can initiate the discussion with other Member States. For this purpose, the user needs to fill in the fields of the 'Discussion' section (reason for the discussion, requested date, and additional documents if necessary) and click on the 'Share' button to distribute it with the Member States.

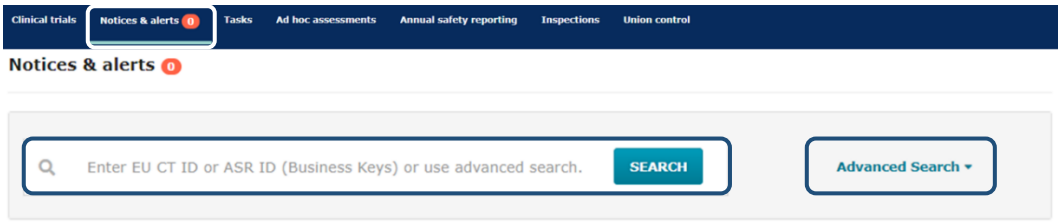
3.4. Which Member States have access to the discussion?

This information is visible to all Member States. Any MS, not only the MSC for the selected trials, can take part in the discussion initiated as part of an ad hoc assessment.

3.5. Where can Member States view and respond to the discussion?

Member States can search and respond to this discussion by accessing the 'Notices & alert' tab available on the top panel of CTIS and clicking on the generated alert.

The user may search by EU CT number, assessment ID or use the advanced search filters to apply multiple parameters (e.g. source type, reception date, etc.) in order to find the relevant alert.



Member States can include written comments as well as attach documents to respond to the discussion. Once the Member States have responded to the discussion, all Member State receives an alert in the 'Notices & alerts' tab.

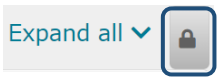
3.6. Can the sponsor view the Member States' discussion on the ad hoc assessment?

No, the discussion amongst Member States will only be visible to Member States. It should be noted that sponsors have no visibility on anything related to an ad hoc assessment

4. Update and completion of an ad hoc assessment

4.1. How can users update an ad hoc assessment?

Users can update an ad hoc assessment by selecting the 'Padlock' button at the upper-right corner of the ad hoc assessment form. The assessing Member State can update any of the sections of the form at any point in time. It is important to note that in order to make these updates visible to the other Member States, the assessing Member State needs to save the form and then share it. In this way, the latest version of the form is visible to all Member States.



If the assessment has been cancelled or completed it can not be updated.

4.2. When can an ad hoc assessment be completed?

An ad hoc assessment can be completed after the users populate all the required sections of the assessment form, including the assessment outcome. To do that, users select the 'Complete' button located at the upper-right corner of the ad hoc assessment form.

Once the assessment is completed, users are not able to update it.

4.3. What happen if the ad hoc assessment outcome is 'Suspend trial'?

If as part of the ad hoc assessment outcome it is recommended to suspend the trial, a corrective measure should be created. Please note that the ad hoc assessment outcome has no impact on the clinical trial status, if a change in the trial is needed, it will be applied through the recommended corrective measure.

4.4. Is it possible to update a completed ad hoc assessment?

If the ad hoc assessment is completed, it is not possible to update any of the sections of the completed form. A new ad hoc assessment will need to be created.

4.5. Is it possible to cancel a completed ad hoc assessment?

No. It is not possible to cancel a completed ad hoc assessment. Users can cancel an ad hoc assessment if the form has not been shared or completed.

4.6. How can users close an ad hoc assessment?

Once the form is shared, CTIS enables the 'Close' functionality. The Member State can go to the main page of the 'Ad hoc assessment' tab by selecting the 'Close' button located at the upper-right corner of the ad hoc assessment form.

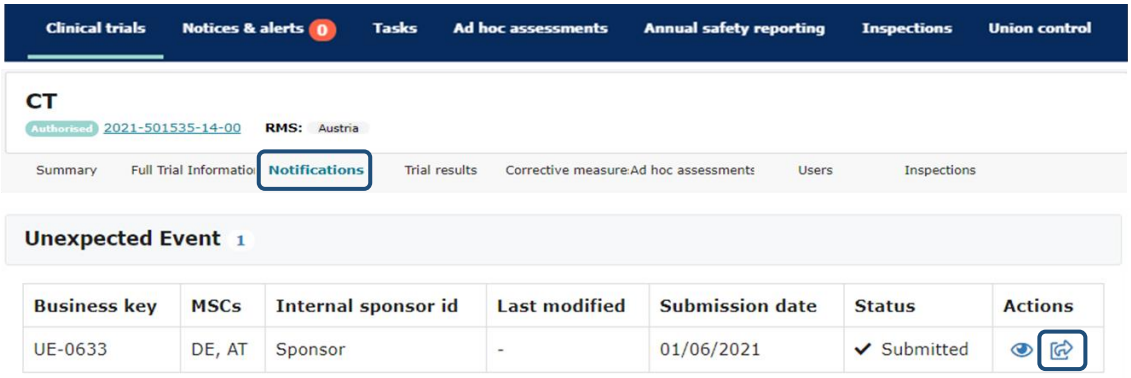
Member States are able to close the ad hoc assessment only if the assessment has been shared or completed.

4.7. How can users link the assessment outcome to the notification?

In case the ad hoc assessment has been triggered by the submission of a notification, the Member States can populate the assessment outcome in the notification in order to trigger the publication of the notification.

For this purpose, users can access the Notification sub-tab and select the assessment outcome ID that is available in the related notification. Then they can include or attach documents to support the ad hoc assessment and submit the notification assessment outcome.

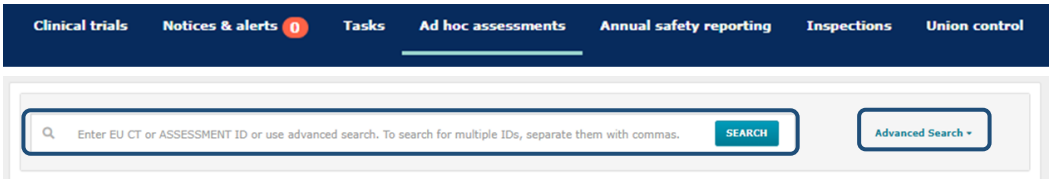
Please, note that these steps will enable the publication of the notification and the assessment outcome done by the Member State.



5. Search, view and download an ad hoc assessment

5.1. How can users search for an ad hoc assessment?

Users can search for an ad hoc assessment in the 'Ad hoc assessment' tab. Member States can search for a specific assessment by indicating the EU CT number, assessment ID or, alternatively, using the 'Advance Search' button which includes fields such as EU CT number, Assessment type, Assessing MS, etc.



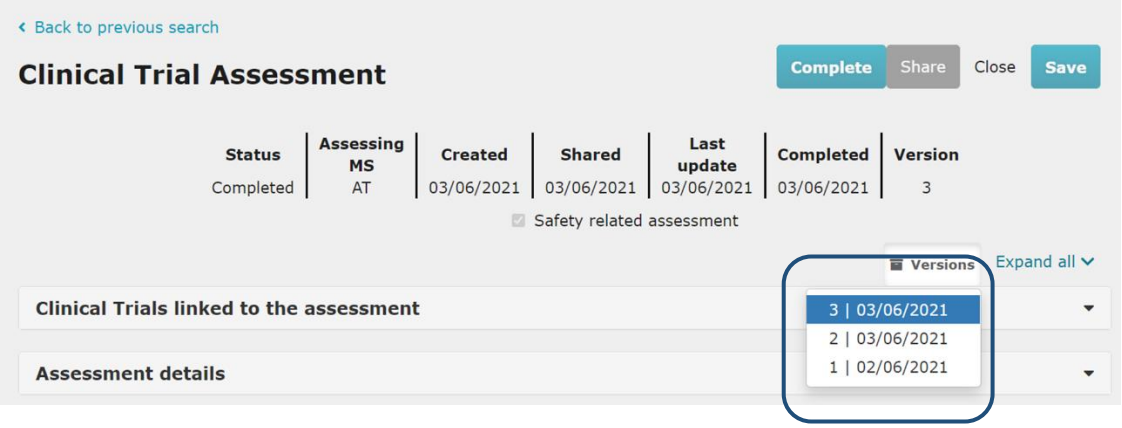
5.2. How can users view a completed ad hoc assessment?

Users are able to view a completed ad hoc assessment in read-only mode. For this purpose, they can use the search functionality in the 'Ad hoc assessment' tab.

5.3. How can users view previous versions of an ad hoc assessment?

In case an update is done to the ad hoc assessment form, a versioning mechanism is applied in the system. Users are able to view previous versions of an ad hoc assessment in read-only mode. Only the latest version of an ad hoc assessment can be subject to further update.

The different versions of the ad hoc assessment form can be accessed by clicking on the versions icon located at the upper-right corner of the ad hoc assessment form.



5.4. Are the ad hoc assessments form published?

No. None of the ad hoc assessment forms populated by the Member States nor the RFI responses from the sponsors for an ad hoc assessment are published.

However, in case the ad hoc assessment has been triggered by the submission of a notification, the Member States can populate the assessment outcome in the notification in order to trigger the publication of the notification. *Refer to question 4.7 for more information.*

5.5. How can users download an ad hoc assessment?

In the Authority domain, after having applied a search and identified the ad hoc assessment of interest, the users can download an excel file with a summary of such ad hoc assessment by clicking on the 'Download' button available on the 'Ad hoc assessment' tab. If no filters are applied, all ad hoc assessments are downloaded.

6. Roles and permissions

6.1. What roles and permissions are involved in the ad hoc assessment process?

Below you can see the distribution of roles by type of activity:

- **Share/update an ad hoc assessment and submit RFI on ad hoc assessment:** Supervisor Submitter.
- **Create/Cancel draft on ad hoc assessment and share discussion:** Supervisor Submitter; Supervisor Preparer.
- **View an ad hoc assessment**: Viewer Part I Full rights/Restricted rights; Viewer Part II; Validator (Preparer/Submitter) Full rights (Part I and Part II); Validator Preparer restricted rights (Part I exc IMPD and Part II); Assessor Part I Preparer restricted rights; Assessor Part II (Preparer and Submitter); Supervisor (Preparer/Submitter); Inspector (Preparer/Submitter); ASR Assessor; ASR Decision

Maker-Submitter.

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