EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

FAQs

Assess an annual safety report

CTIS Training Programme – Module 20

Version 1.1 – September 2021

What you will find

- Answers to general questions regarding the Annual Safety Report (ASR).
- Answers to questions regarding the assessment of an ASR.
- Answers to questions regarding the process of creating a Request for information related to an ASR.
- Answers to questions regarding the ASR roles and permissions.

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FAQs

In this document, we list common questions regarding *Module 20: Assess an Annual Safety Report*. They are categorised into general questions regarding the Annual Safety Report (ASR), the assessment of an ASR, the process of creating a Request for Information (RFI) related to an ASR, and the roles and permissions related to ASR. The specific learning objectives of this module are:

1. Remember what an Annual Safety Report (ASR) is and when a sponsor can submit one.
2. Understand the phases of the assessment of an ASR.
3. Understand how to search, view, and download an ASR.
4. Understand how to assess an ASR.
5. Understand how to request additional information to the sponsor.
6. Understand the roles and permissions involved in the ASR process.

We encourage you to read these questions and answers carefully. If you have any questions that 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 questions

1.1. What is an annual safety report?

The Annual Safety Report (ASR) is a document provided by the sponsors to the authorities regarding the monitoring and evaluation of the evolving safety profile of the Investigational Medicinal Product (IMP) and the mitigation of potential risks. According to Article 43 of the Clinical Trial Regulation[1], sponsors shall submit annually a report on the safety of each IMP used in a trial. This obligation starts with the first authorisation of a trial and finalises with the end of the last trial conducted with the IMP. With the information provided via the ASR, the National Competent Authorities (NCAs) can both assess each IMP's safety profile and enquire further information from the sponsors.

1.2. Who are the actors involved in the ASR process?

The two main actors involved in the ASR processes are the sponsor organisations and the Member States. The actions that each of them is expected to perform are the following:

- The sponsor users submit the ASR so that the Member States Concerned (MSCs) can assess it. Sponsors also respond to the Requests for Information (RFIs) created by the safety assessing Member State (saMS) in the context of the assessment of the ASR.

- The Member States Concerned users assess the ASR submitted by the sponsors, a process lead by the safety assessing Member State (saMS). The saMS is responsible for preparing and sharing the draft ASR-Assessment Report (ASR-AR), creating and consolidating considerations, creating RFIs (if applicable) and assessing the response, and providing a finalised assessment of the ASRs. MSCs can also create considerations and assess the ASR RFI responses from the sponsors, if applicable.

1.3. What is a safety assessing Member State?

The safety assessing Member State (saMS) is the Member State (MS) that is both leading the safety assessments and responsible for the assessment of a specific ASR. In case there is a single MSC involved in the ASR, that MSC will be automatically appointed to be the saMS.

[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 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

1.4. Can an ASR be related to more than one trial?

Yes, when sponsors are completing the ASR submission form, they will obtain a list of all the authorised trials for which they have an ASR user role. From that list, users can select all the trials related to the ASR.

1.5. Can an ASR be related to more than one MSC?

Yes. If a sponsor selects one or more trials that involve more than one MSC for an ASR submission, all the MSCs of the selected trials will automatically be associated with that ASR.

1.6. Can an ASR be related to more than one IMP?

Yes. When sponsors are completing the ASR submission form, users can select multiple trials which can involve multiple IMPs *(please refer to question 1.4 for more information)*. After the selection of the trials involved in the ASR, sponsor users can choose the IMPs per trial.

1.7. How many IMPs can be selected per trial?

For all the trials included in an ASR, at least one IMP per trial should be selected in the ASR submission form.

1.8. What is the ASR ID code?

The ASR ID is the unique identification number of the ASR that can be used, for example, to search for it using the basic search functionality in the 'Annual safety reporting' tab. The ASR ID is a composition of unique details separated by a hyphen. For example, the code ASR-2021-00001 is structured the following way:

Acronym	Current year	Sequential number of ASRs created
ASR	2021	00001

1.9. Can users download an ASR in bulk?

Yes. On an ASR page, users can click on the 'Download' button located on the right-hand side of the page to download a ZIP folder containing relevant information about ASR. This action will download the following items:

- The ASR submission documents.
- The ASR assessment documents.
- The request documents for each RFI.
- The response documents for each RFI.
- A text file listing the zip file contents.
- A CSV file for each RFI.

1.10. Can users download specific ASR documents?

Yes. In both 'ASR Submission' and 'Assessment' sub-tabs of an ASR page, users can first locate the specific section and document they are looking for; and then click on the blue download icon next to each document. This action allows users to download the document in the file type and with the title in which it was initially uploaded in the ASR submission form.

2. Assessment

2.1. What is the first task of the assessment of an ASR?

After the sponsor submits an ASR, the appointment of the saMS process starts (in case the ASR involves multiple MSCs). Once appointed, the saMS can start the assessment tasks of the ASR such as the circulation of the Draft Annual Safety Report Assessment Report (ASR-AR).

2.2. What tasks can be performed after the appointment of the saMS?

The tasks performed during the assessment of the ASR are:

- **Circulate Draft Annual Safety Report Assessment Report (ASR-AR) and provide considerations** (performed by the saMS).
- **Review Draft ASR–AR and provide additional considerations** (performed by the saMS and the rest of MSCs).
- **Consolidate considerations** (performed by the saMS).

- **Submit RFI** (if applicable) (performed by the saMS).
- **Assess RFI response** (performed by the saMS and the rest of MSCs).
- **Finalise the assessment** (performed by the saMS).

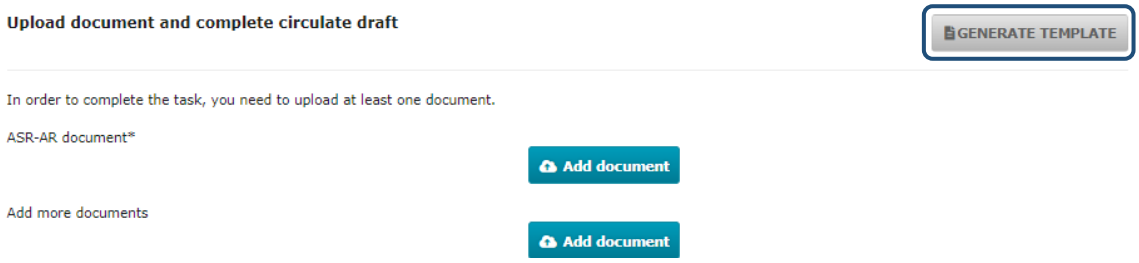
2.3. Can the saMS extend the tasks of the assessment of an ASR?

The saMS can decide to extend, only once, some of the tasks, such as the circulation of the Draft ASR-AR or the conclusion of the ASR assessment.

Moreover, raising an RFI will extend the timelines of any pending tasks of the assessment of an ASR.

2.4. Can the saMS generate a template for the Draft ASR-AR?

Yes. The saMS can generate a template for the task Circulate draft ASR-AR. This template is available in the ASR process and will include pre-populated information of the ASR.

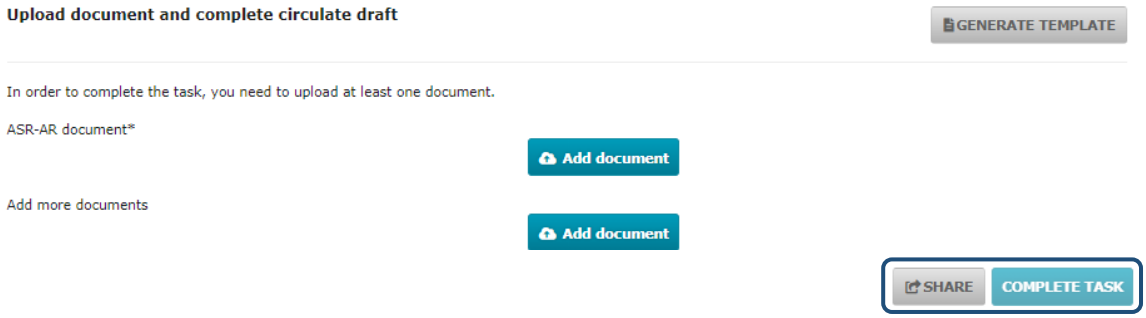


2.5. Which file type is accepted for the Draft ASR-AR?

The Draft ASR-AR must be submitted in a Word file in CTIS for its circulation. The saMS can use a pre-generated template.

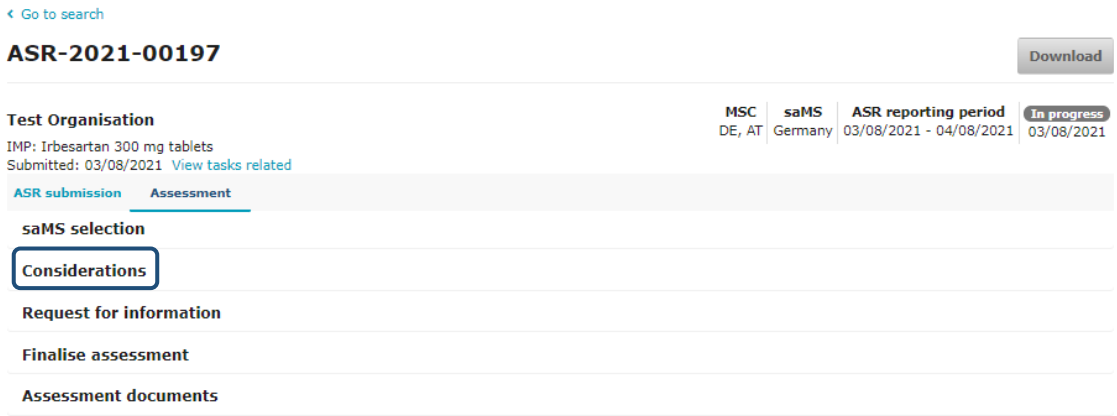
2.6. How can users complete the task 'Circulate Draft ASR-AR'?

Users must click on the 'Share' button at the bottom left corner of the page before they can select the 'Complete task' button.



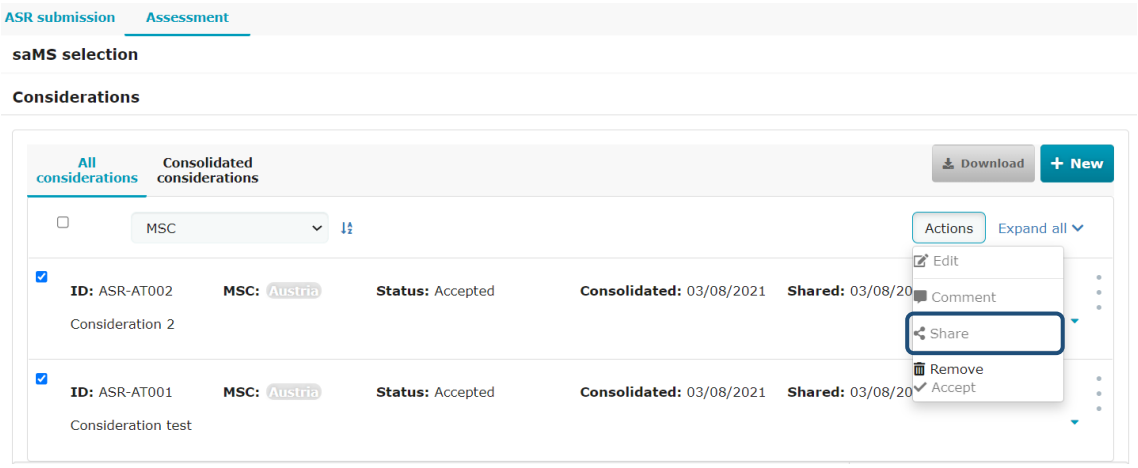
2.7. When can MSCs start documenting their considerations on the ASR documentation?

MSCs (including the saMS) can document their considerations before the saMS circulates the draft ASR-AR. This can be done from the 'Assessment' sub-tab of the ASR Page, concretely under the 'Considerations' section.



2.8. How can the saMS view the considerations provided by the other MSCs?

The saMS can see the considerations after the MSCs share them. The MSCs, including saMS, can select the consideration by clicking on the checkbox next to it and select the 'Share' button under the 'Actions' dropdown menu.



2.9. How can MSCs communicate with each other during the assessment of an ASR?

MSCs can communicate with each other by using the comments functionality when documenting considerations to the Draft ASR-AR and the ASR documentation, as well as by assessing responses to any potential RFI.

2.10. Which actions can the saMS perform when consolidating the considerations?

The saMS can use the following buttons to consolidate the considerations:

- **Accept:** Accepting the considerations as documented by another MSC.
- **Adapt:** Editing the consideration and including comments to adapt the consideration submitted by another MSC.
- **Merge:** Creating one consideration from two similar considerations.
- **Not included:** Declining a consideration.

2.11. What is the 'Finalise assessment' task?

The 'Finalise assessment' task allows the users to transfer the assessment conclusions (to Member States and sponsors) into structured data fields and provide additional information in order to share and submit the final ASR-AR.

2.12. Which questions does the Summary and Conclusion for Member States include?

The Summary and Conclusion for Member States include the following questions:

- Are there any safety issues to be aware of and/or to follow up?
- Is there any action required to follow up and/or to take?
- Requested action to sponsor to follow up?
- Corrective measure required?
- Is the ASR compliant with ASR (ICH E2F) format?

The answers to these questions will be accessible only for the Member States. If the saMS responds positively to any question, additional information must be provided.

2.13. Which questions does the Summary and Conclusion for sponsors include?

The Summary and Conclusion for sponsors include the following questions:

- Are there any new issues?
- Acceptable action is taken by sponsors?
- Specific action is required by sponsors?
- Due date for specific action?
- Requested action?

The answers to these questions will be accessible to the sponsors. If the saMS responds positively to any question, additional information must be provided.

2.14. How can the saMS complete the task 'Finalise assessment'?

After responding to the questions on the 'Finalise assessment' page, the saMS must upload the ASR-AR. The saMS must select the 'Share' button to complete the task.

Please, keep in mind that the saMS will not be able to finalise the assessment if:

- There are any outstanding Requests for Information awaiting a response from the sponsor.
- The due date of the 'Review ASR-AR' task has not expired (14 days for multinational trials).
- There are any considerations received which have not been consolidated.
- The final ASR-AR document has not been uploaded.

2.15. How are the rest of the MSCs informed when the ASR-AR is shared?

MSC users with ASR roles will receive a notice in the 'Notices & alerts' tab for each event related to the assessment of an ASR.

After the saMS shares the ASR-AR with the rest of the MSCs, a notice will be generated in the 'Notices & alerts' tab of the MSC indicating the occurrence of this event.

2.16. Which file types of the ASR-AR are supported in CTIS?

The saMS can upload the ASR-AR either in Word or in PDF file.

2.17. Does the ASR documentation become public?

The ASR documentation will not be publicly available. This means that the information of the ASR will not be reflected on the CTIS public website. Nevertheless, the Member States that are not MSCs will also have access to the ASR information.

3. Requests for Information related to an annual safety report

3.1. Can all the MSCs create ASR RFIs?

No. Only the saMS can create an RFI related to an ASR. However, MSCs can provide considerations before and after the saMS has circulated the Draft ASR-AR. Once the considerations are shared, the saMS can consolidate them and create an RFI, if applicable.

3.2. What happens if the sponsor does not respond to an RFI?

If a sponsor does not submit a response to an RFI by the deadline established by the saMS, the RFI will lapse.

3.3. What are the sections of an ASR RFI?

An ASR RFI is composed of four sections:

- **RFI details:** Includes the details, such as the ASR RFI ID, saMS, submission, due and response dates, and the RFI reason.
- **Considerations:** List of considerations received; by clicking on the 'Respond' button, the user can type responses to each consideration.
- **Supporting documents:** The documents section allows users to see the documentation that the saMS has added to the RFI. It will also enable the sponsor user to add documentation by clicking on the 'Add document' button.
- **RFI response submission:** Checkbox to agree with the submission statement and the 'Submit' button to submit the sponsor's response to the ASR RFI.

3.4. What is the ASR RFI ID code?

The ASR RFI ID code is a unique identification number for the RFIs received in the context of an ASR, which can be used, for example, to search for it using the basic search functionality in the RFI tab. The ASR RFI ID is a composition of unique details separated by a hyphen. For example, the code RFI-ASR-2021-00001-001-01 is structured the following way:

Acronym	Current year	Sequential number of ASR created	Sequential number of the RFI	Each consideration sequential number
RFI-ASR	2021	00001	001	01

3.5. How is the saMS informed when an RFI response is submitted?

Once the RFI is responded, a task and a notice will be generated. The saMS can view the response by selecting the generated task 'Assess RFI response'. This will automatically redirect to the page of the ASR in question, under the 'Assessment' tab and the 'Request for information' section.

The saMS can also access the RFI via the notice received in the 'Notices & alerts' tab of CTIS. By clicking on the notice, they will be automatically redirected to the RFI section of the ASR page in question.

3.6. What is the assessment of the ASR RFI responses?

The ASR RFI response from a sponsor follows an assessment process similar to the responses to other types of RFIs. An ASR RFI response is assessed by the saMS, through the 'Assess RFI response' task to submit an assessment of the ASR RFI response. The saMS is also able to reply to each written sponsor response. After the saMS has assessed the response, the MSCs can comment on the assessment of the ASR RFI response made by the saMS.

4. Roles and permissions

4.1. What user roles are involved in the ASR process?

Two roles are involved in the assessment of an ASR in each MSC (including the saMS): ASR Decision Maker-Submitter and ASR Assessor. Below we list the different permissions for both of them:

- **Consolidate considerations; Create/view/submit ASR RFI; Create/share ASR AR; Extend/release ASR task (any task):** ASR Decision Maker-Submitter.
- **Assign/release ASR tasks (assigned to me); Upload/view ASR documents; Create/share considerations; Add ASR RFI assessment comments; Download ASR assessment details; View ASR AR:** ASR Decision Maker-Submitter and ASR Assessor.

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