EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

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Clinical Trials Transformation

Member States Guidance: New Safety Module on the Annual Safety Report

Clinical Trial Information System (CTIS) user guidance on the New Safety Module

This guidance is applicable to the New Safety Module on Annual Safety Report (ASR), which is now part of the Member State CTIS training environment and it is foreseen to be integrated in the CTIS Member State Workspace on 28 September 2026:

- For instructions on how to access the Member State CTIS training environment: see section 6.2.3. of the Sponsor Handbook
- Instructions on how to report blocking issues and suggestions are provided in chapter 3.
- The list of known issues and workarounds on the New Safety Module can be found in Annex I: List of known issues and workarounds

To work on the Member State CTIS training environment, Member States will need to gain also Sponsor roles as they would need to submit clinical trials (see instructions in Sponsor Handbook) and ASRs (see instructions in the Sponsor Guidance: New Safety Module on the Annual Safety Report), to allow Member States to train on their assessment as per current guidance.

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1. Introduction

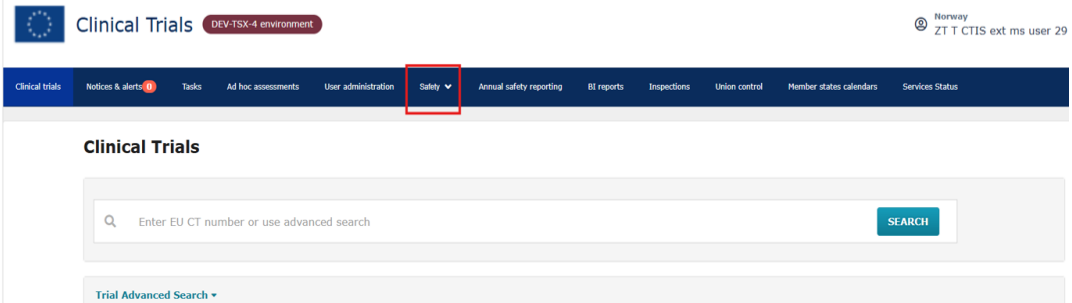
In line with Article 43 of the Clinical Trials Regulation (EU) No 536/2014, hereinafter 'CTR', sponsors shall submit annually a report on the safety of each Investigational Medicinal Product (IMP) used in a clinical trial (CT), other than placebo. The ASR (formerly known as the Development Safety Update Report, DSUR) is an annual report submitted by the sponsor to the relevant authorities that evaluates the evolving safety profile and benefit-risk balance of an IMP , including measures taken or proposed to mitigate potential risks and protect clinical trial participants. The obligation of submitting an ASR starts with the first European Union/European Economic Area (EU/EEA) authorisation of a trial and it ends with the end of the last trial conducted in EU/EEA by the sponsor with the concerned IMP. With the information provided via the ASR, the Member State (MS) can assess each IMP's safety profile and enquire further information from the sponsors. More information in section 7 of the CTR Q&A.

The Commission Implementing Regulation (EU) 2022/20 lays down the detailed rules and timelines for the coordinated assessment of ASRs submitted under Article 43 of the CTR. The New Safety Module on ASR supports the implementation of these requirements by enabling the harmonised submission, coordinated assessment, and management of ASRs in accordance with the procedures established in the Implementing Regulation.

With regards to timelines, the coordinated assessment is completed within 42 days where no Request for Information (RFI) is issued. Where additional information is required, the safety assessing Member State may issue an RFI to the sponsor: this extends the assessment timeline to a maximum of 84 days, allowing time for the sponsor to respond and for the additional information to be assessed before the Final Assessment Report (FAR) is issued.

The present document provides CT authorities with the operational guidance they need to assess ASRs submitted by sponsors through the New Safety Module on ASR. It is foreseen that this module will be integrated in the Clinical Trial Information System (CTIS) on 28 September 2026. **During the two months before this date, the New Safety Module on ASR is implemented in the CTIS training environment: sponsors and authority users can train themselves through using the Sponsor CTIS training environment and Member State CTIS training environment**. To request access to the CTIS training environment, refer to section 6.2.3. of the Sponsor Handbook (applicable also to Authority users). Once access is granted, MS user roles need to be requested: see section 2.2. on user roles.

A new 'Safety' tab is introduced in the Member State CTIS training environment, next to the existing 'Annual Safety Report' tab. As of 28 September 2026, the new 'Safety' tab will be introduced in the CTIS Member State Workspace and the 'Annual Safety Report' tab will remain available for two months, to allow MSs to finalize the ongoing ASRs submitted through the old ASR submission functionality. After this period, the 'Annual Safety Report' tab will be removed: see section 2.1. on transition period.



Note: currently there is no MS Application Programming Interface (API) foreseen on the New Safety Module on ASR that would extract CTIS data for external systems. It is included in the CTIS modernisation roadmap, but no delivery date can be indicated at this stage.

The Sponsor Guidance: New Safety Module on the Annual Safety Report provides instructions to sponsors on submission of ASRs and of responses to RFI to CTIS.

→ on this topic: watch also the CTIS bitesize talk: Annual safety report (ASR) new safety module

2. ASR Assessment

2.1. Transition period arrangements

The New Safety Module on ASR will fully replace the ASR submission functionality of CTIS. A **transition period of two months** is foreseen between the old ASR submission functionality and the New Safety Module on ASR where both will be used in parallel.

As of go-live date (foreseen to be 28 September 2026), all new ASRs will be submitted by Sponsors through the New Safety Module on ASR and creation of new ASRs in the old ASR submission functionality will be disabled. Also, the Safety Assessing Member State (saMS) selection history will be reset in the new safety module.

During the transition period of two months, the assessment of ASRs which are ongoing under the **old ASR submission functionality** can be finalised through accessing the old functionality.

Once the transition period is over (foreseen to be at the end of November 2026):

- **All ASRs for which the assessment is finalised under the old ASR submission functionality will be archived**, together with the relevant Final Assessment Reports, FARs (but not the Draft Assessment Reports, DARs) and the so-called 'saMS tracker'. The archive will be made available to European Medicines Agency (EMA) and Member States, together with a report that will facilitate their search. Sponsor will not have access to those ASRs and FARs.
- **ASRs for which the assessment will still be ongoing under the old ASR submission functionality will not be transferred into the New Safety Module and will not be archived**. Their assessment will need to be completed outside the new ASR workflow, under arrangements managed by the relevant saMS/Reporting Member State (RMS) (e.g., communication with sponsors, archiving of FARs, etc.).

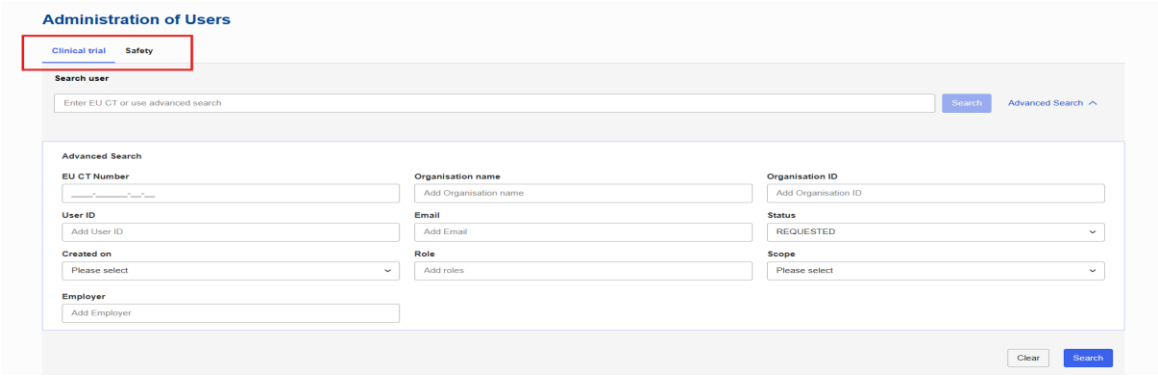
Member States are encouraged to complete the ASRs assessment during the two month transition period. Any ASRs for which the assessment will remain incomplete at the end of the two-month transition period will no longer be accessible via CTIS. Before the end of the transition period, saMS/RMS users will therefore need to:

- Download any ASR submission
- Download any RFI and RFI replies

The assessment of these ASRs and RFI replies will need to be managed outside CTIS by the already assigned saMS (or, where applicable, via the ad hoc assessment functionality), including their archival.

2.2. User Roles and Role Matrix

A new **subtab** called '**Safety'** is added in the '**User Administration**' functionality of the Member State CTIS training environment, to allow the **assignment in the training environment of MS roles within the New Safety Module on ASR**. The **'Clinical Trial' tab** allows the management of already **existing Clinical Trial related roles**. The same sub-tab appears in 'My roles' under the user profile section of every MS user. The 'Safety' subtab will be introduced in the CTIS Member State Workspace as of go live of the New Safety Module, foreseen for 28 September 2026, in addition to the 'Safety' tab that will appear on the homepage.



CTIS MS users which have an **MS Admin role in the** EAM portal test environment **will be able to manage user access to the New Safety Module on ASR of other MS users through the 'Safety' sub-tab** of the Member State CTIS training environment; however, they **do not have any viewing or business permission** to the New Safety Module. EMA Admin and European Commission (EC) Admin roles, once assigned in EAM portal test environment, have viewing permissions to the New Safety Module on ASR and no other business permissions: see the below Role Matrix.

To request **MS Admin, ASR Decision Maker Submitter**, **EMA Admin or EC Admin role**s for the Member State CTIS training environment:

1. Request access to the Member State CTIS training environment by applying the steps described in section 6.2.3. of the Sponsor Handbook (applicable to Authorities too)
2. Request the 'CTIS Training Environment Access' role in the EAM portal test environment

To prepare for when the New Safety Module goes live, **MS Admin, EMA Admin and EC Admin roles can already be requested in EAM portal**, see step by step guide Management of roles and permissions to learn how to request a role in EAM. The possibility of requesting the **ASR Decision Maker Submitter** role will in EAM portal **will be opened by the end of August 2026**. Further communication will provide the specific date.

The **ASR Decision Maker Submitter role has only business permissions (cannot assign roles),** its only available scope for this role is **'all trials'** (cannot be assigned only to a specific trial) and it is the only role that has access to **SharePoint**-based feature embedded in the saMS and ASR assessments functionalities.

The **Authority Safety Admin** role is a dedicated safety administrator role that **can be assigned by the MS Admin** through the CTIS User Management Safety subtab and it is used to manage Safety role assignments. Like the MS Admin role, the Authority Safety Admin role does not provide access to Safety Module business activities, and it can assign the following roles to users from safety sub-tab within the limits of its own authorised scope ('All' or 'Specific' trials):

- **ASR Assessor** (can only receive a 'Specific' trial scope)
- **MS Viewer** full rights (can receive an 'All' or a 'Specific' trial scope)
- **MS Inspector** (can receive an 'All' or a 'Specific' trial scope)

Access to ASR saMS and ASR assessment for a user with an ASR submitter role is determined by comparing the clinical trials included in the ASR with the clinical trials

covered by the user's ASR Submitter role scope. CTIS evaluates whether the user's assigned scope covers none or some or all the trials referenced in the ASR and grants access accordingly:

- MS Users with one of the aforementioned roles (independent of scope) are granted access all ASRs displayed in the ASR list view.
- MS Users with one of the aforementioned roles with scope 'All trials' or 'Specific trials' covering at least one CT included in the ASR are granted full access to the relevant ASR. Full access comprises the assessment screens (i.e. Draft AR, Comments, Considerations & RFI, Final AR, Summary & Conclusions) and the ASR detailed view screens (i.e. ASR Submission, FAR, RFI, Summary & Conclusion)

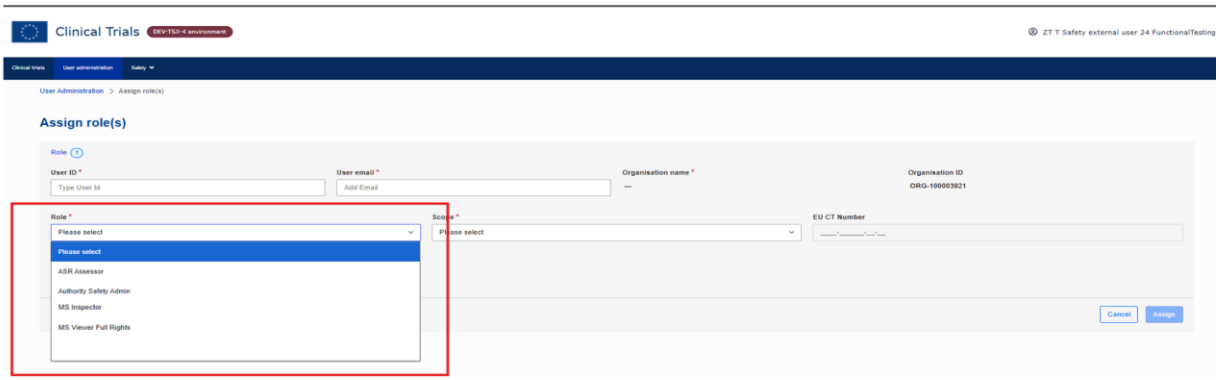
Note: some business permissions depend on business rules implemented in the system and on whether the user is or not from the Assessing Member State Concerned (MSC): as mentioned in the table, some permissions can only be executed by users belonging to the Assessing MS.

The MS roles that can assign roles within the CTIS Member State Workspace New Safety Module on ASR and roles that have access and can perform actions within the module are displayed below, together with modality of their assignment.

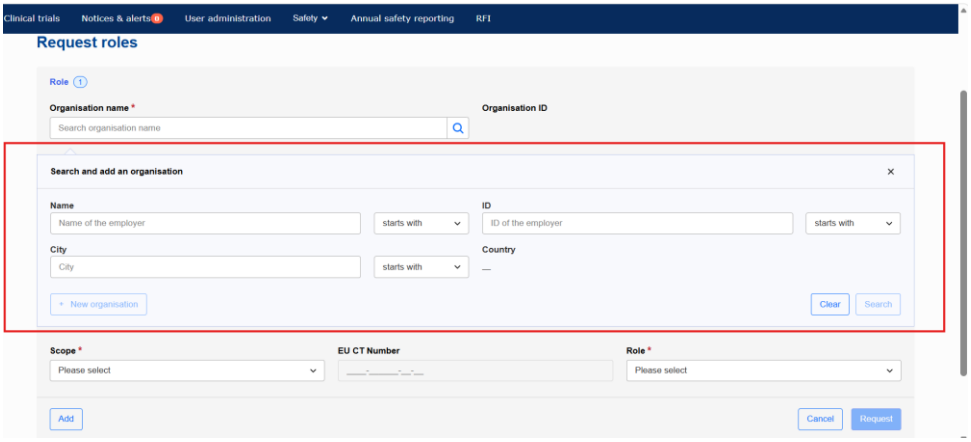
Roles Type	MS Workspace roles	Modality of assignment
Administrator Roles	EMA Admin	In the Member State CTIS training environment: EAM portal test environment In the CTIS Member State Workspace: EAM portal
	EC Admin	
	MS Admin	
	Authority Safety Admin	CTIS User Management Safety subtab (by MS Admin)
Business Roles & Scope	ASR Decision Maker Submitter (All trials)	In the Member State CTIS training environment: EAM portal test environment In the CTIS Member State Workspace: EAM portal*
	ASR Assessor (Specific trials)	CTIS User Management 'Safety' subtab
	MS Viewer full rights (All trials/Specific trials)	CTIS User Management 'Safety' subtab
	MS Inspector (All trials/Specific trials)	CTIS User Management 'Safety' subtab

*The possibility to request the ASR Decision Maker Submitter role in EAM will be opened by the end of August 2026: refer to further communication for the specific date

Admin roles can assign roles within the CTIS User Management safety subtab:



Note that, when requesting a role in 'My roles' section, the magnifying glass expands the search functionality within the page directly, and no longer in a separate window.

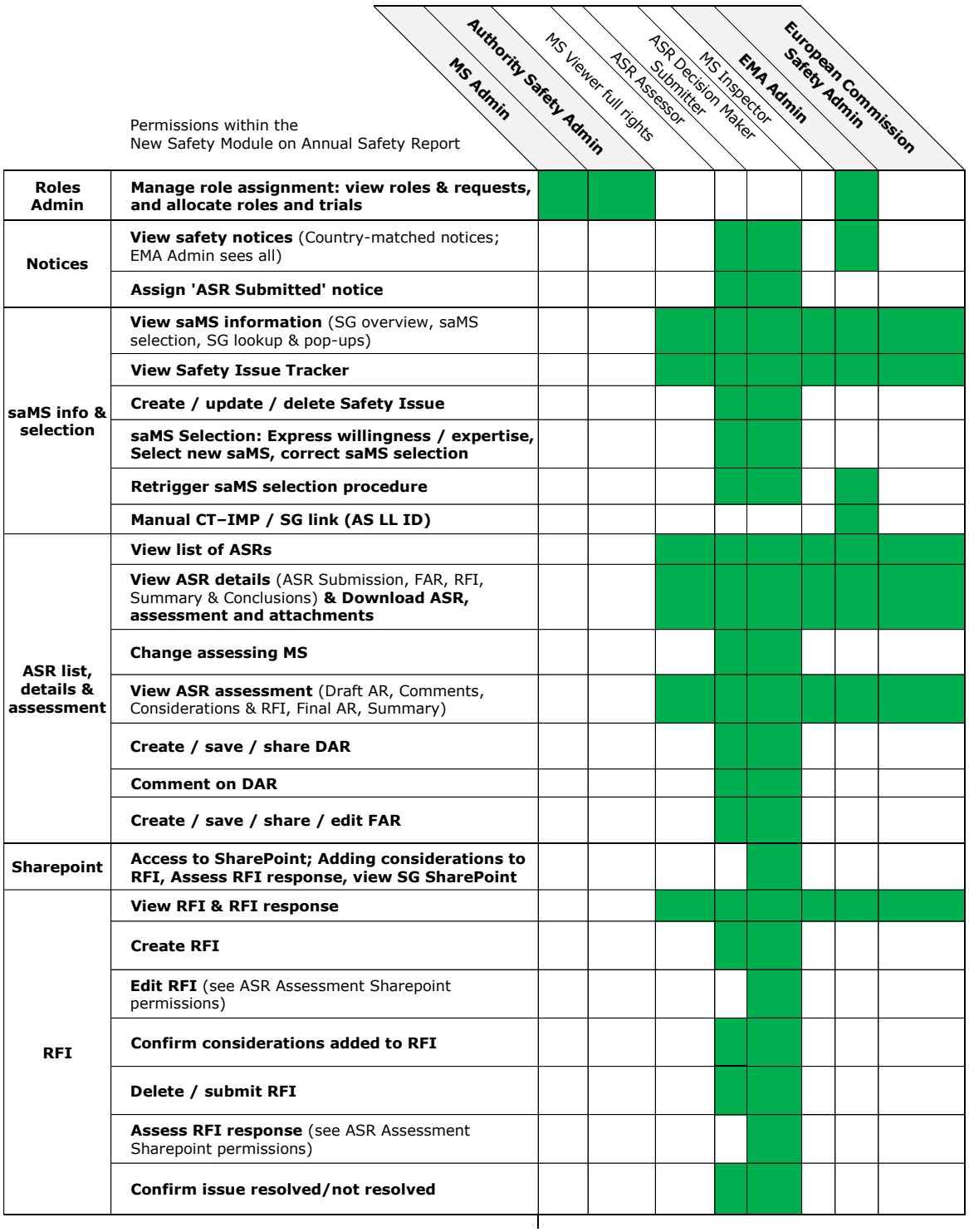


In total, there are 4 business roles for a MS within the New Safety Module on ASR: ASR Decision Maker Submitter, ASR Assessor, MS Viewer full rights, MS Inspector.

The permissions granted by ASR Decision Maker Submitter and ASR Assessor are the same, except for the access to the SharePoint-based feature embedded in the saMS and ASR assessments functionalities, granted only to the ASR Decision Maker Submitter role.

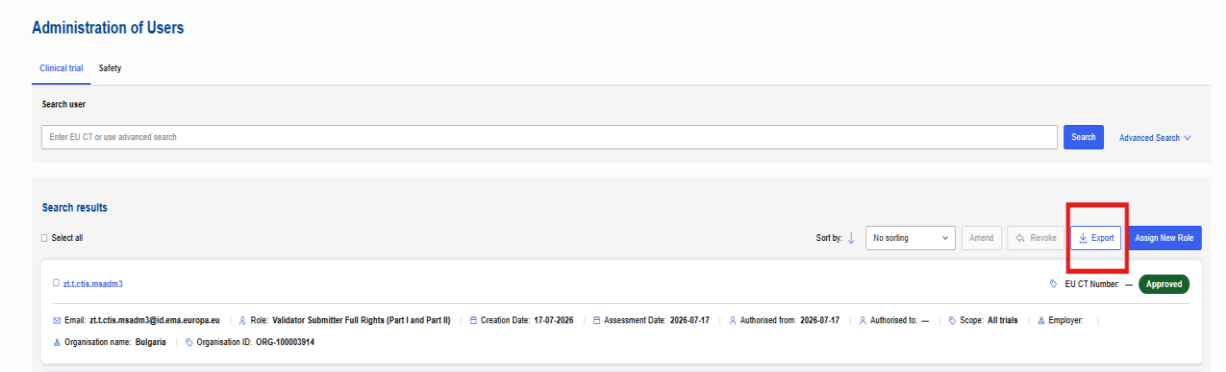
The MS Viewer full rights and the MS Inspector are only granted with view access to all the information available in the new safety module. Note that equivalent roles in the CT trial sub-tab do not have these view safety permissions and therefore, they need to be complemented with these safety ones to have granted access to both CT and safety information.

The table below ('Role Matrix') gives an overview of the permissions linked to the MS workspace on the New Safety Module on ASR for the mentioned roles. For an explanation of the specific permissions, refer to the relevant sections in this guidance.



2.2.1. Exporting the list of roles Clinical Trial and Safety roles per MS user

In User administration screen, from the clinical trial or safety sub-tabs outlined in section **Error! Reference source not found.**, administrators can search and filter results using the existing criteria (e.g. User ID, Email, Status, Scope, Employer, etc.), and results retrieved can be exported through a new 'Export' button next to the 'Assign' role one.



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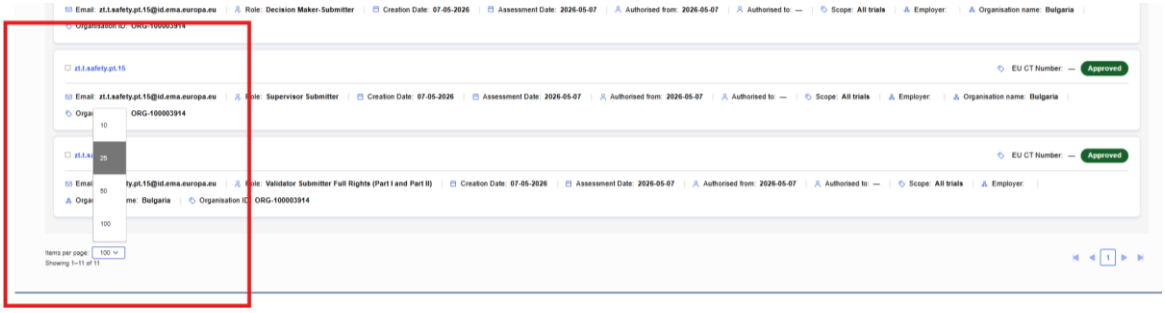
The export functionality is available to all administrators, and the 'Export' button is always visible to administrator, however it appears disabled (greyed out) and it is only enabled when the current search returns at least one result. The export works per page and for this reason pagination is enhanced so that administrator can choose the page size, to display 10, 25, 50 or 100 results per page.



The selected page size defines how many records are exported, going from 10 if the selected page size is 10 to up the maximum number of 100 if the selected page size is 100: if an administrator manages more than 100 users, more than one Excel file needs to be downloaded and then combined.

When an administrator clicks 'Export', an XLS file is generated and downloaded: the exported file contains the records of a user per row with user ID on the first column and the rest of the fields in the remaining columns.

Id	Username	Email	Employer	Organisation Name	Organisation Id	Role
239	zt.t.ctis.msadm3	zt.t.ctis.msadm3@id.ema.europa.eu		Bulgaria	ORG-100003914	VALIDATOR_SUBMITTER_FULL_RIGHTS_PART_I_AND_PART_I
244	zt.t.ctis.msadm3	zt.t.ctis.msadm3@id.ema.europa.eu		Bulgaria	ORG-100003914	INSPECTOR_SUBMITTER
47	zt.t.ctis.msadm3	zt.t.ctis.msadm3@id.ema.europa.eu		Bulgaria	ORG-100003914	MS_ADMIN
289	zt.t.perf.user88	zt.t.perf.user88@id.ema.europa.eu		Bulgaria	ORG-100003914	ASSESOR_PART_I_PREPARER_FULL_RIGHTS
155	zt.t.safety.pt.15	zt.t.safety.pt.15@id.ema.europa.eu		Bulgaria	ORG-100003914	ASSESOR_PART_I_SUBMITTER_FULL_RIGHTS
280	zt.t.ctis.msadm3	zt.t.ctis.msadm3@id.ema.europa.eu		Bulgaria	ORG-100003914	VIEWER_PART_I_FULL_RIGHTS
284	zt.t.perf.user88	zt.t.perf.user88@id.ema.europa.eu		Bulgaria	ORG-100003914	ASSESOR_PART_I_SUBMITTER_FULL_RIGHTS
156	zt.t.safety.pt.15	zt.t.safety.pt.15@id.ema.europa.eu		Bulgaria	ORG-100003914	ASSESOR_PART_II_SUBMITTER
157	zt.t.safety.pt.15	zt.t.safety.pt.15@id.ema.europa.eu		Bulgaria	ORG-100003914	DECISION_MAKER_SUBMITTER
158	zt.t.safety.pt.15	zt.t.safety.pt.15@id.ema.europa.eu		Bulgaria	ORG-100003914	SUPERVISOR_SUBMITTER

2.3. ASR submission modalities under the new safety module in CTIS

To work on the Member State CTIS training environment, Member States will need to gain also Sponsor roles as they would need to submit clinical trials (see instructions in Sponsor Handbook) and ASRs (see instructions in the Sponsor Guidance: New Safety Module on the Annual Safety Report), to allow Member States to train on their assessment as per current guidance.

Under the New Safety Module on ASR, sponsors can submit an ASR to CTIS in one of the following two ways:

- **Clinical Trial-centric**: the ASR covers a single clinical trial. In this case, **the assessing MS is by default the RMS** of the trial concerned. CT-centric ASRs are identified by the EU CT Number displayed on the ASR. Note: the RMS users who will perform ASR assessment activities will need to require roles as per section 2.2. .
- **Substance Group-centric**: the ASR covers all clinical trials associated with a Substance Group (SG). In this case, **the assessing MS is the saMS appointed for that SG** (see section 2.4.), unless another MS is appointed as assessing MS for that specific trial (see section 2.8.4.). SG-centric ASRs are identified by the SG name displayed on the ASR. A SG-centric ASR may cover trials from more than one sponsor. Only authorised, temporarily halted and suspended trials can be part of a SG: if a trial is 'under evaluation', its authorisation is revoked or it is ended, it cannot be linked to a SG. **Note**: the assessing MS users who will perform ASR assessment activities will need to require roles as per section 2.2. .

The choice between a CT-centric and a SG-centric submission lies with the sponsor. The CT-centric option would probably be used mainly by academic sponsors, while SG-centric submissions are expected to be used more frequently overall.

2.4. Substance Group - centric ASRs: saMS selection procedure

The saMS is the MS responsible for leading the safety assessment of a SG and coordinating the assessment of the corresponding ASRs. **A SG is a grouping of related active substances** (e.g. the SG 'Diclofenac' includes the active substance labels Diclofenac Acid, Diclofenac, Diclofenac Sodium and Diclofenac Potassium). A **SG is created automatically** when the first trial associated with a specific active substance is authorised in CTIS:

1. Once **the first MS authorises a trial with a new substance**, the SG is assigned a unique identifier, the RMS of the clinical trial associated to the SG is automatically designated as the **temporary saMS:** the SG is initially classified as Mononational.
2. **When a second MS authorises a trial linked to the same SG**, the SG is automatically reclassified as Multinational: **CTIS automatically initiates the saMS selection procedure,** allowing MSC to determine the appropriate saMS for the SG. Refer to section 2.8. to see how the saMS selection procedure occurs.

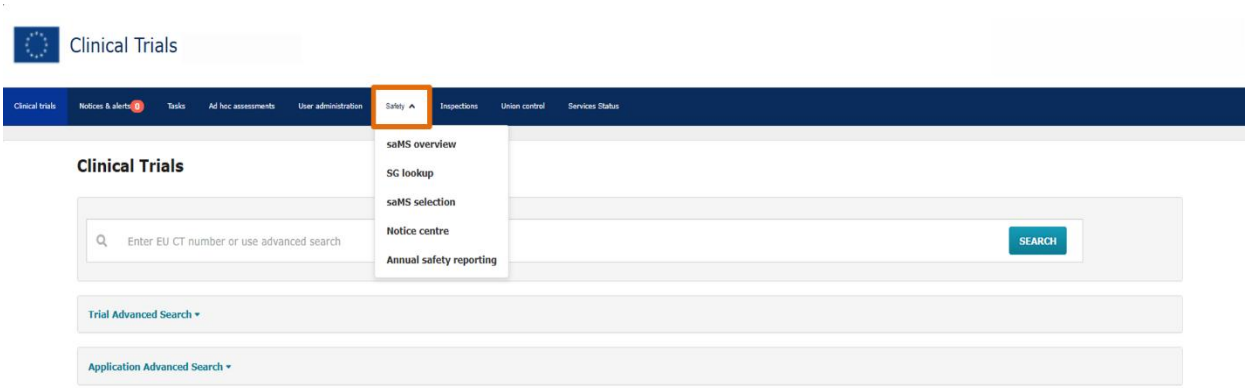
Note that even if a SG is assigned to a specific saMS, it is still possible to assign to the assessment of an ASR to a different MS, on ad hoc basis, if agreed among the MSs: refer to section 2.8.4. for further details.

2.5. The New Safety Module 'Safety' tab

Through hovering on the 'Safety' tab of the New Safety Module on the ASR, five options are displayed:

- **saMS Overview** provides an overview of SGs, associated clinical trials, participating MS, and current saMS assignments. The page also provides access to the Safety Issues Tracker, the SG working folder (in SharePoint), and to the overview of CTs associated with a SG. Refer to section 2.6.

- **SG Lookup**: enables users to search for SGs using information available from CTIS or eXtended EudraVigilance Medicinal Product Dictionary (XEVMPD), such as the EU CT Number, IMP information, or active substance. Refer to section 2.7.
- **saMS Selection:** supports activities related to the appointment, reassignment, and correction of saMS for a multinational SG. This tab also provides access to historical saMS selection procedures. By default, this page displays multinational SGs with ongoing saMS selection procedures, although additional records can be displayed by modifying the search criteria. Refer to section 2.8.
- **Notice Centre**: provides system-generated notifications related to SGs, ASRs and saMS activities, enabling users to monitor relevant changes and events within the CTIS Safety Module. Refer to section 2.9.
- **Annual Safety Reporting**: provides access to ASRs, including information on the saMS. Users can access submitted reports and perform activities related to the assessment process through this page. Refer to section 2.10.



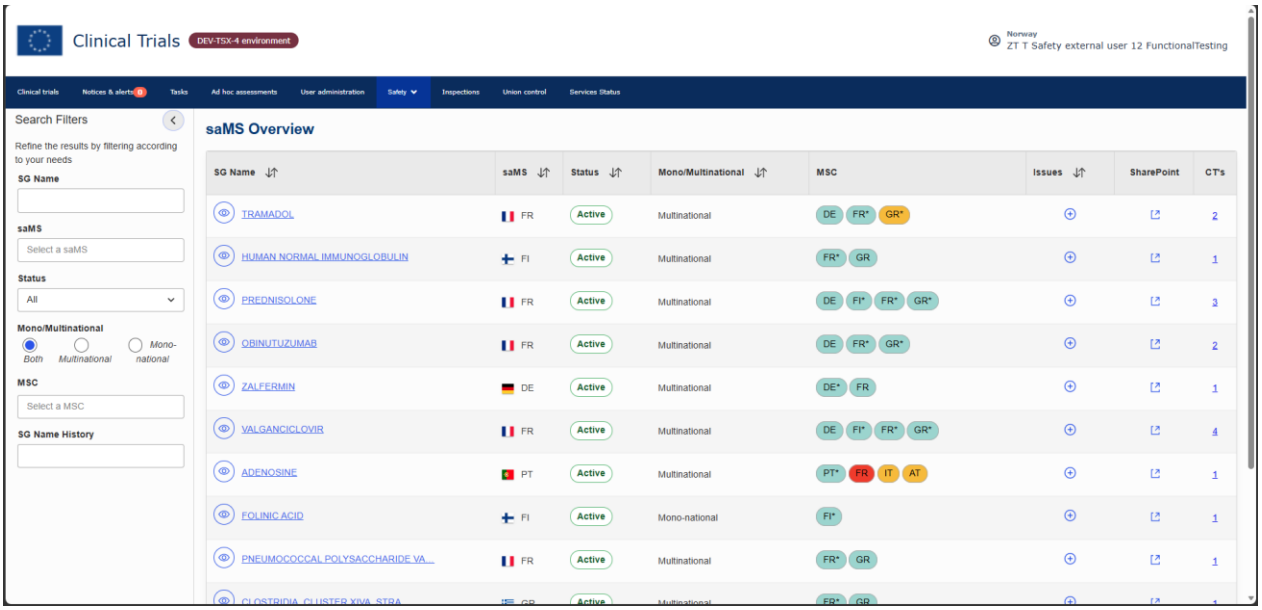
All tabs within the CTIS Safety Module include **search and filtering capabilities** to help users identify and retrieve relevant information. The search criteria and column sorting are reflected in the results page URL, which can be bookmarked or shared to recreate the specific page. The Search Filters panel is available on the left-hand side of the screen and can be expanded or collapsed as needed.

2.6. saMS Overview tab

The **saMS Overview tab** serves as the main dashboard for viewing and monitoring **SGs**. On the left, the Search Filters panel allows users to filter or search for specific SGs of interest. For each SG, users can see:

- the **saMS** assigned to the SG, that is selected as per section 2.4. (for mononational SG) and 2.8. (for multinational SG)
- The **SG status**, which is generally 'Active' and changes to 'Inactive – Pending' once all clinical trials associated with a SG have ended. Three months after the last trial ends, the status is automatically set as 'Inactive'; when a (new) trial is associated to the SG, the status is reverted to 'Active'. Note that a SG remains available in the Safety Module even after becoming 'Inactive': a SG is only removed if the corresponding substance information is deleted from XEVMPD, in cases where two SGs are merged or a substance is nullified
- If it is **mononational**/**multinational**, see section 2.4.

- The '**MSC'**, indicating the MS who have authorised trials under this SG; the combined status of the trials for each MS is indicated by colour coding: green (Authorised), orange (Halted or Under Evaluation), and red (Suspended or Not Authorised). MS that are RMS of any associated CT are marked with an asterisk (*)
- The 'Issues', which is the **Safety Issues Tracker**, displaying the last modification date of submitted safety issues or a (+) to add a Safety Issue when there is none. The date or (+) icon can be clicked to open the Safety Issue tracker pop-up, where users can add, read, amend or delete the safety issues (see below)
- The **SharePoint** working folder provides the link to the dedicated folder for the SG. In this folder, safety assessors can store collaborative documents and EudraVigilance Clinical Trial Module (EV- CTM) assessments in accordance with their Best Practice guidance
- the **number of trials associated with the SG**: through clicking on the number, the CTs Overview of that SG opens, see section 2.6.1.)

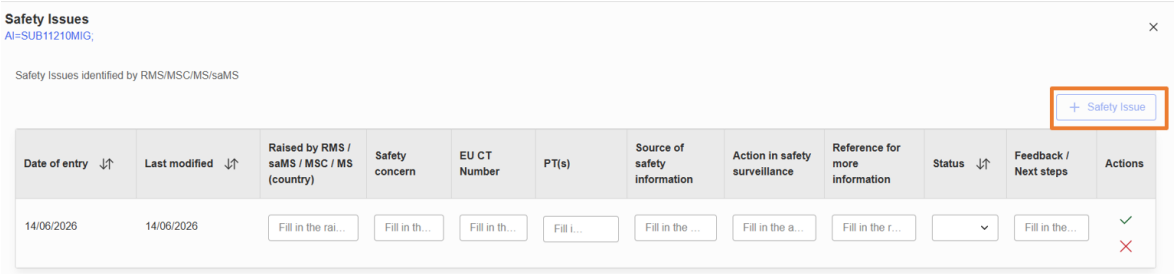


Through clicking on the '+' icon of the **Safety issue tracker**, an MS can record, for each safety issue:

- **Raised by RMS / saMS / MSC / MS (country**): Member State responsible for raising the safety issue
- **Safety concern**: description of the identified safety issue
- **EU CT Number**: identifier of the trial associated with the safety issue, where applicable
- **Preferred Term (PTs)**: Relevant Preferred Term(s) (MedDRA) associated with the safety concern
- **Source of safety information**: source from which the safety information originated
- **Action in safety surveillance**: description of actions taken or planned as part of safety surveillance activities
- **Reference for more information**: reference to supporting documentation or additional information

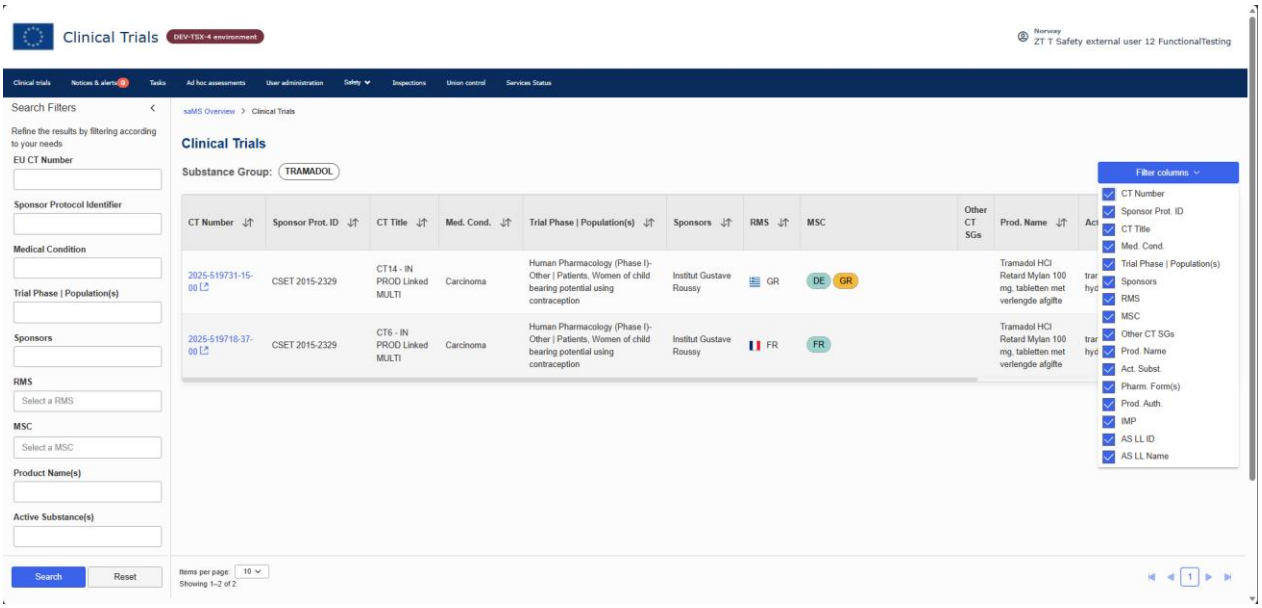
- **Status**: current status of the safety issue (Ongoing, On Hold, or Closed)
- **Feedback / Next steps**: additional comments, follow-up actions, or planned next steps
- **Actions**: to save changes or delete a safety issue that was created in error

Existing entries can be **updated** to reflect new information or changes in status, additional references, or further safety surveillance activities. Note: **deleting** a safety issue cannot be undone.



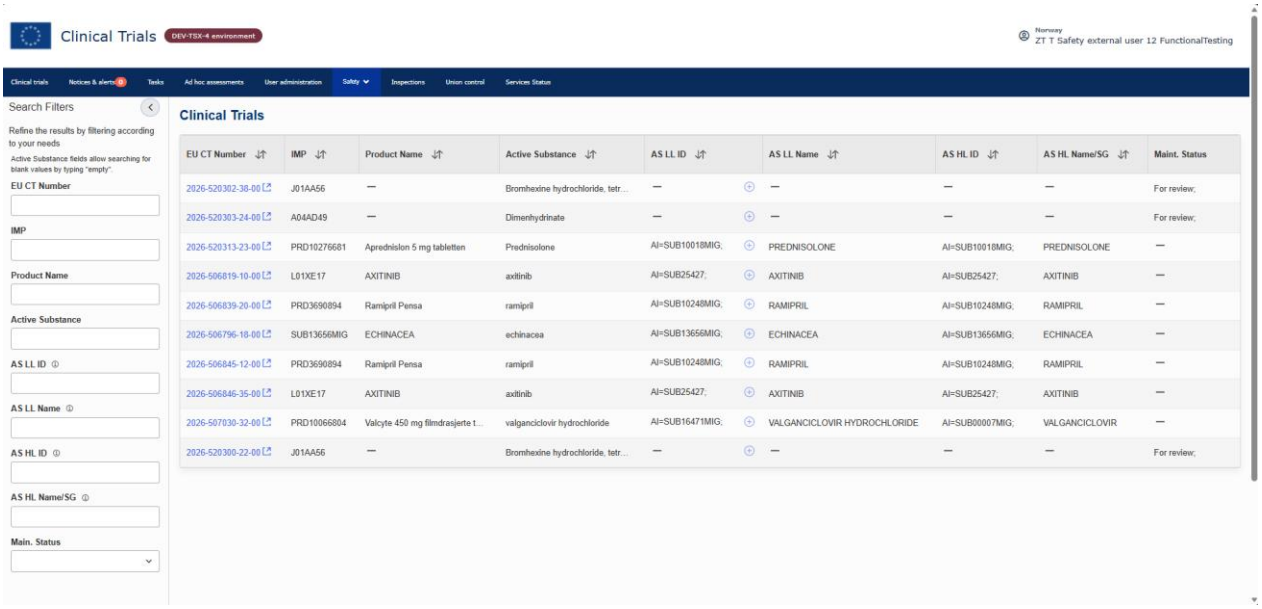
2.6.1. Clinical Trials Overview per SG page

Users can find a **listing of all active CTs per SG** in a separate view, which can only be accessed via the hyperlink in the 'CTs' column on the **saMS overview** (section 2.6.) or **SG Lookup** (section 2.7.) pages. The page and applies filters can be saved by users via the URL.
Each row captures a single CT, showing the trial specific information: the EU CT Number, Protocol ID, clinical trial title, medical condition, trial phase, study population, primary sponsor, RMS, and MSC. In addition, users find aggregated IMP information for this trial: the product name, active substance (as listed in CTIS), pharmaceutical form, authorisation status, IMP identifiers, Other test IMP Substance Groups covered in the same trial, and the calculated Active Substance AS LL ID (Active Substance Low Level identifier), AS LL Name (Active Substance Low Level name), AS HL Name/SG (Active Substance High Level name or associated Substance Group). The screen has a search filter, column sorting and column filter where users may exclude unwanted columns from the view.



2.7. Substance Group (SG) Lookup tab

The SG Lookup supports safety monitoring and SG management by providing a consolidated view of all associated clinical trials, test IMPs and corresponding Active Substance (low-level) and Active Substance (high-level) or SG information. This screen and the filters (left side) provide users with the opportunity to quickly find the correct SG using either the EU trial number or IMP information as reference. The information displayed is taken from XEVMPD.



2.8. saMS Selection tab

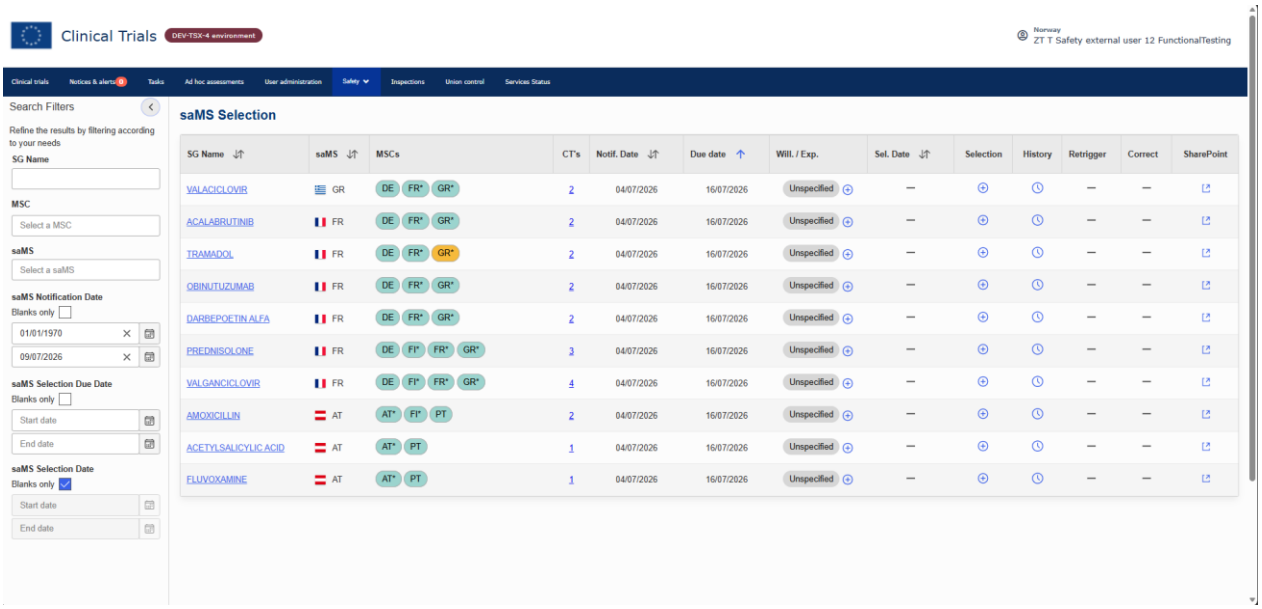
A saMS selection procedure is applicable to multinational SGs and it may be initiated:

- **Automatically**: CTIS Safety Module automatically initiates a saMS selection procedure when a SG changes from Mononational to Multinational status when there are 2 or more MSC for the SG. This is generally following the second authorisation of a multinational trial (with a different RMS) or the authorisation of a mononational trial in a second country for the same substance: see section 2.4. . A Substantial Modification (SM) to a CT or changes to the Substance Groups may also result in saMS Selection.
- **Manually** by an authorised user, through the option 'retrigger saMS selection' on the saMS Selection page, see section 2.8.3. , in line with the CT safety assessor Best Practices document.

The saMS Selection page contains information on all SGs (mononational and multinational both with ongoing and concluded saMS selections) and supports the saMS appointment, correction, and reappointment to a SG. By default, only **SGs with ongoing saMS selection are displayed**: to see all SGs, users can unselect the filters in the left-side panel.

The page displays information on the current (temporary, selecting) saMS, the MSC(s), the CTs associated with the SG (see section 2.6.1.), the Notification date and the Due date for the saMS selection, and the SharePoint link of the SG. The other columns (Express Willingness/Expertise, 'Select date', 'Selection', 'History', 'Retrigger' and 'Correct') are populated during the saMS selection process.

The search panel on the left can be used to filter a specific SG that requires saMS selection based on the available search criteria and the results in the table can be sorted by selected search criteria to facilitate identification of substances requiring action.



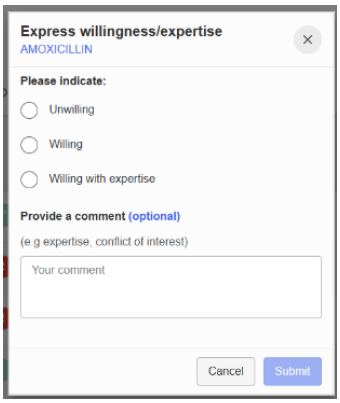
The **saMS selection procedure** includes the following **steps**: the initiation of a saMS selection procedure and the expression of willingness and the expression of willingness with expertise by participating MSs (see section 2.8.1.), the appointment of a final saMS (see section 2.8.2.) and, where necessary, the retriggering or correction of a saMS assignment (see section 2.8.3.).

2.8.1. Initiation and expression of willingness/expertise by participating MSs

Once a **saMS selection procedure is triggered**, the saMS Notification date and a **12-day saMS Selection due date** are set. **All MSs can express their willingness** to act as the saMS, and indicate expertise associated with the SG.

Once the Notice Center displays the notice 'saMS Selection Procedure initiated', the following steps can be performed by any MS **user with ASR Safety Assessor/ASR Decision Maker Submitter** role:

1. On the saMS Selection page, locate the relevant SG and click the ⊕ icon in the **Express Willingness/Expertise** column.
2. Select your willingness (Unwilling, Willing, or Willing with expertise) to be the saMS for the SG in the pop-up window. Additional comments may be provided where appropriate and in accordance with MSs best practices. Note that **the CT information available for the relevant SG can be viewed** via the hyperlink in the 'CTs' column (see section 2.6.1.)



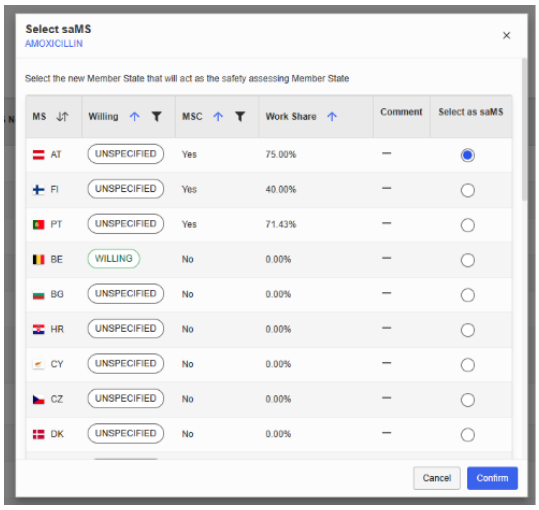
3. Click on 'Submit' to save the response. Note that **once submitted, the willingness status cannot be reverted to an unspecified state**.

The selected option is then updated in the saMS Selection page.

2.8.2. Assignment of final saMS by the temporary saMS

To complete a saMS selection procedure, **the temporary saMS** (automatically nominated when the SG was mononational, see section 2.4.), who has an **ASR Safety Assessor/ASR Decision Maker Submitter** proceeds as follows:

1. Clicks on ⊕ in the **saMS Selection** column to open the selection window. This displays information for all MSs, including willingness status, whether the MS is a MSC, workshare information and any comments.
2. Reviews the information available in the saMS Selection tab to support the selection or reassignment of the saMS in order to identify the appropriate MS.
3. **Selects and confirms the appointment of the definitive saMS**. CTIS then displays a confirmation message and the appointment is finalised.



Once the final saMS has been appointed, the 'Selection Date' column displays the date when the saMS selection was executed and saMS selection notification and due dates are cleared. In addition, **CTIS generates a notification** to all participating MS, where the following is displayed: the selected saMS, the MS that completed the selection procedure, and a copy of the saMS selection information recorded in CTIS.

Once appointed, the new saMS takes over the responsibility of safety assessment for the SG.

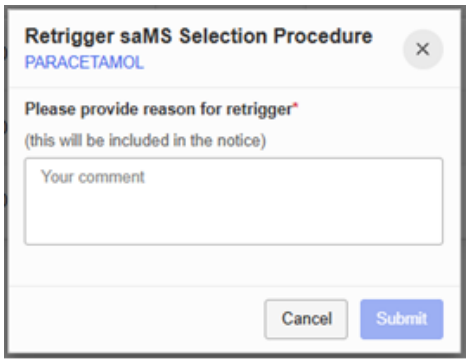
As described in section 2.8.3. , the saMS selection process can also be **re-initiated** to appoint a new saMS **or corrected** in case an incorrect MS was selected. Historical information related to previous selections can also be viewed through the '**History'** column, see section 2.8.5. .

2.8.3. Retriggering or correction of a saMS assignment

The selected saMS can **retrigger** a saMS selection procedure, if applicable in accordance with the MS relevant best practice guidance. **Note**: only the currently assigned saMS has the appropriate rights to proceed with retriggering a saMS assignment.

If a MS user identifies a SG for which a new saMS selection may be required and the user is not the assigned saMS, the MS should contact the assigned saMS. To retrigger a saMS selection procedure, the **currently assigned saMS**:

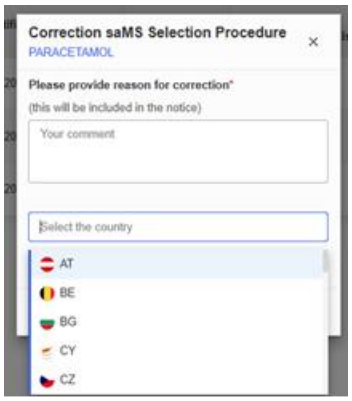
1. Selects the 'Retrigger saMS Selection' icon in the 'Retrigger' saMS Selection column of the saMS Selection page. The default filters may need to be adjusted or removed to list the relevant SG
2. Provides a comment explaining the reason for the retrigger. Both the Member State initiating the procedure and their comment are included in the notice that is generated when the new saMS selection procedure starts



The **Correction saMS Selection** functionality allows users to correct an existing saMS assignment when an incorrect assignment has been made. For example, in case of correction of a recently completed saMS selection procedure where an incorrect MS was selected by mistake; or resulting from a system issue, where the assigned saMS does not reflect the intended outcome of a previous selection procedure; a correction of a saMS assignment could be needed following changes to a SG, such as a split or merge, where the resulting assignment is not appropriate; or in case of reassignment of a mononational SG by mutual agreement between MSs to facilitate safety monitoring activities and make use of available expertise. Note that the correction functionality should only be used to rectify an incorrect saMS assignment where the appropriate saMS can be clearly identified. Where possible, users are encouraged to liaise with the relevant Member States before applying a correction. Contrarily to the 'retrigger' functionality, the saMS correction doesn't need to be done necessarily by the selected saMS. **Note that the saMS correction cannot take place when a saMS selection procedure is ongoing**.

To proceed, a user with **ASR Safety Assessor/ASR Decision Maker Submitter** needs to:

1. Open the corresponding icon available in the 'Correct' saMS Selection column of the saMS Selection page. The default filters may need to be adjusted or removed to list the relevant SG.
2. Provide a justification in the **Reason for Correction** field. This field is mandatory and should contain a clear explanation of the reason for the correction. The information recorded during the original saMS selection procedure can be found in the Notices (Notice Centre) for reference.



Once the correction has been completed, CTIS records the updated saMS assignment and maintains the history of the correction for traceability purposes.

2.8.4. Change of the Assessing MS for a specific ASR

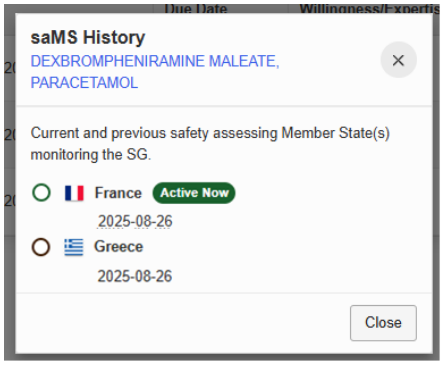
Once an ASR is submitted, the assessing MS is the one assigned to the SG (for SG centric ASR) or the RMS (for CT-centric ASR), However, it is possible for those users belonging to the safety assessing MS/RMS to change the assessing member state of a specific ASR, provided that such a reassignment has been agreed upon outside the system. **This functionality is only available until the DAR is shared and it only takes effect for that specific ASR**. From the 'Annual Safety reporting' section (see section 2.10.), the current safety assessing MS/RMS proceeds as follows:

1. Navigate to the Annual Safety Reporting tab and locate the ASR for which the reassignment is required
2. Click the 'Change Assessing MS' icon
3. Select the new assessing MS country and click on 'Submit'

When the change is completed, both the previous and the new assessing MS receive the 'Assessing MS changed' notice in the 'Notice Centre' tab. **Note that the reassignment does not change the saMS assigned to the Substance Group in the saMS module** (see section 2.8.), as long as it is not triggered (see section 2.8.3.).

2.8.5. saMS History

The saMS History window displays the history of saMS assignments for the selected SG, showing when an MS acted as the saMS. When a SG is merged with or split from another SG, the relevant saMS history is carried over to the resulting SG, as applicable. The saMS History window can be opened from the saMS History column of the **saMS Selection page**.



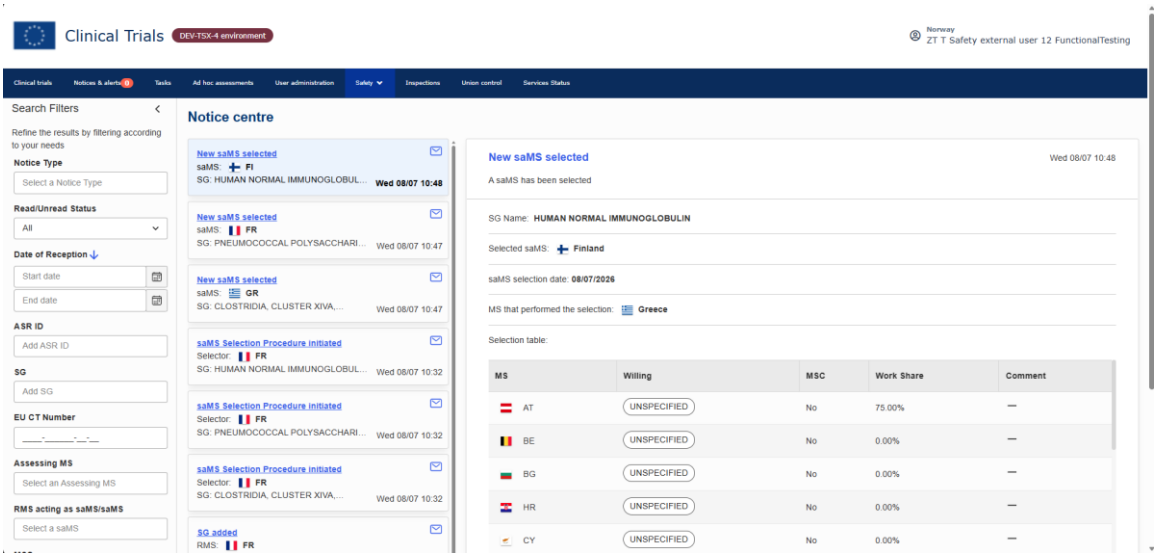
Note that historical information is available only from the go-live date of the New Safety Module on ASR. Assignments preceding the date of go-live are not recorded but archived in SharePoint: see section 2.1. on transition period.

2.9. Notice centre tab

The **Notice Centre** provides a central location for viewing system **generated notices of the CTIS Safety Module**, enabling users to monitor changes affecting SGs (i.e. 'SG added', 'SG renamed', 'SG deleted', 'New CT added to SG', 'All CTs ended for SG'), saMS assignments (i.e. 'saMS Selection Procedure initiated', 'New saMS selected', 'Assessing MS changed'), and ASR activities (i.e. 'ASR submitted', 'DAR issued', 'RFI response submitted', 'FAR issued'). Newly received notices are automatically marked as 'Unread', while notices that have been opened are identified by an open envelope icon, and unread notices are identified by a closed envelope icon.

Notices and relevant **email notifications are role-based** and emails are received by any user with full access to the ASR: for SG-centric ASRs, this means having one or more ASR Submitter role(s) with combined scope covering **all** CTs included in the ASR; a user has an ASR submitter role for only part of the CTs included in an ASR, the user will not receive the email.

Users can use the available **search filters** to locate specific notices and sort the results as appropriate. By default, notices are sorted by **Date of Reception** with the most recently received notice displayed at the top. **Notices remain available in the Notice Centre for 90 days from the date of receipt, after which they are automatically deleted**. Note that it is not possible to export the list of notices displayed in the Notice Centre (e.g. to an Excel file).

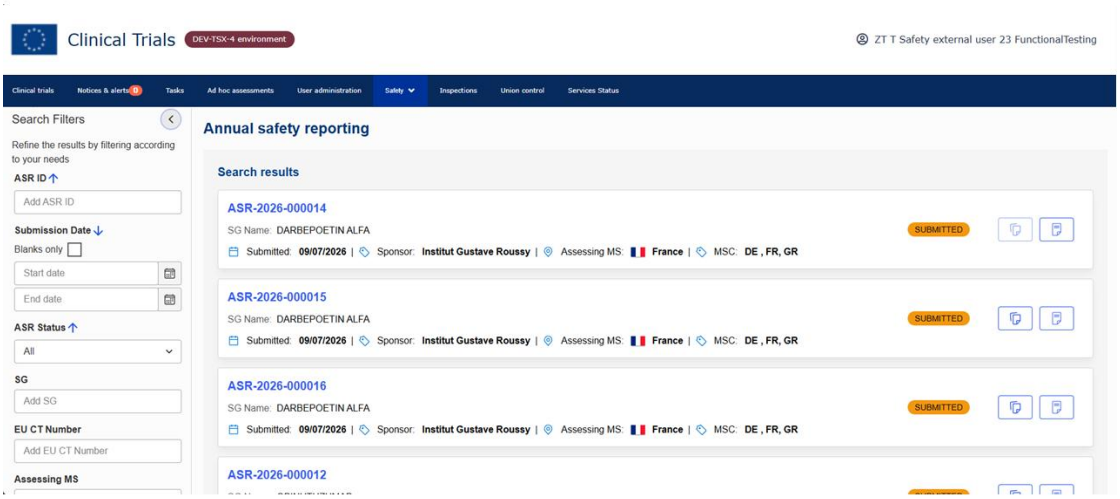


2.10. Annual safety reporting tab: How to assess an ASR

The **Annual Safety Reporting** tab provides access to submitted and finalised ASRs, including information on the assessing MS / RMS, and allows MS users to perform activities related to the ASR assessment process. Users can use the available **search filters** to locate specific ASRs and sort the results as appropriate, by, for example, ASR ID (the unique identification number of each ASR) or ASR Status (submitted or finalised, depending on the assessment status).

Each ASR listed in the ASR section is identified by its ASR ID and contains details such as the EU CT Number (for a CT-centric ASR) or the SG name (for a SG-centric ASR), the submission date, the sponsor, the assessing Member State and the MSC(s) for the trials in scope. By clicking on an ASR ID, users can access a detailed view of the ASR, including submission details, and, if present, any RFIs associated with the ASR, the FAR, and the summary and conclusions.

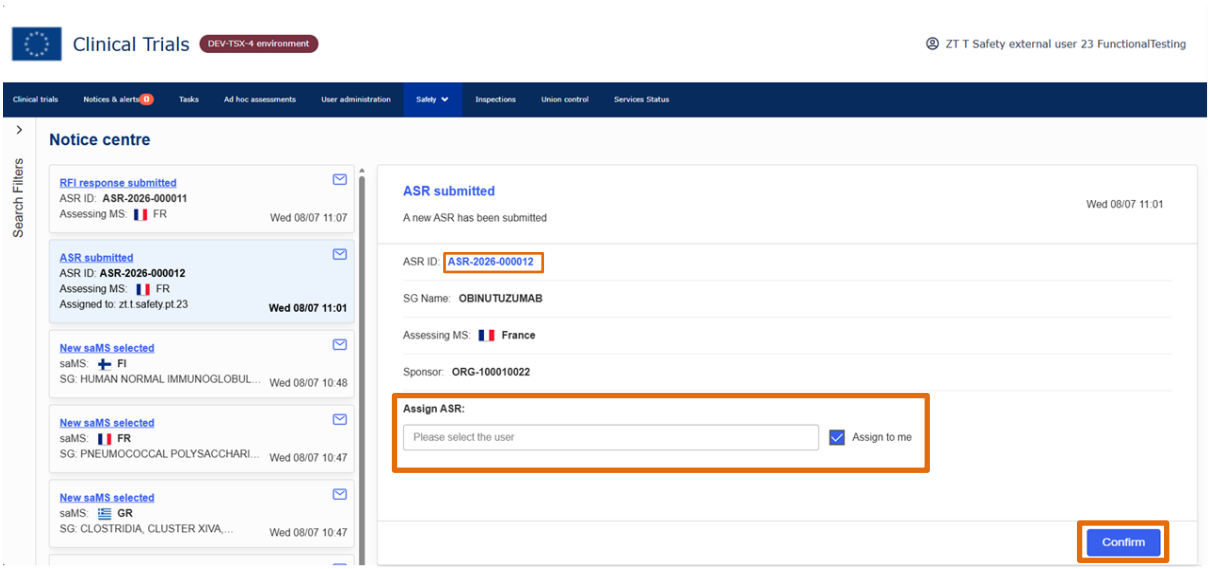
On the right, users can click on the icons to access the 'Assessment' screen (see section 2.10.3.)and to Change the Assessing MS (see section 2.8.4.).



2.10.1. Assigning the assessment of an ASR

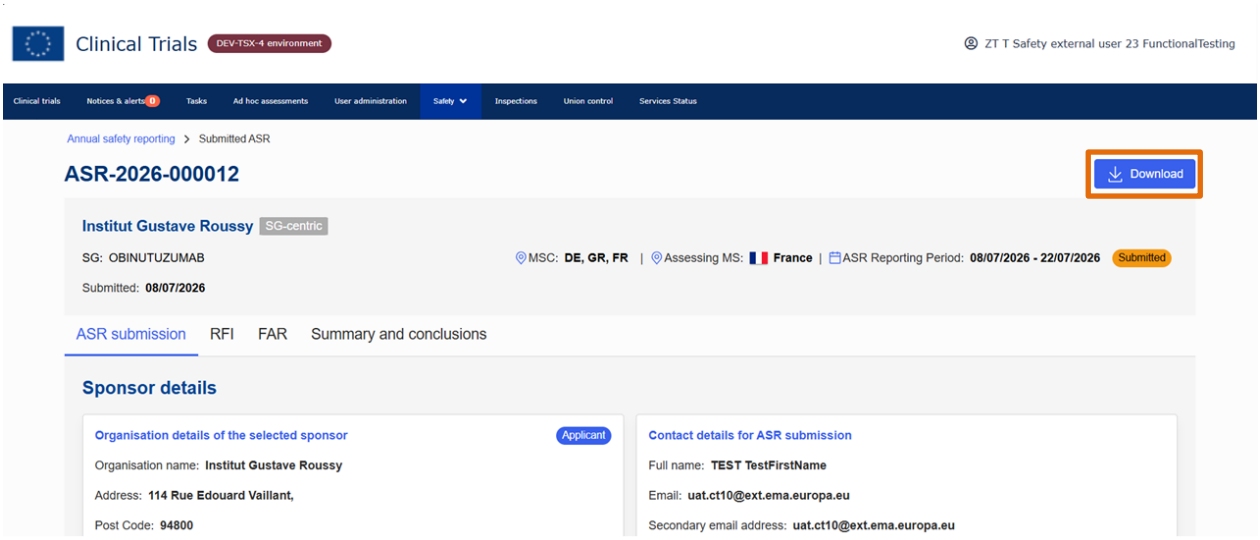
Once an ASR is submitted by the sponsor, an 'ASR submitted' notice is generated in the Notice Centre (see section 2.9.). The following steps are applicable to a user that belongs to the safety assessing MS /RMS and has an **ASR Decision Maker Submitter** role or the **ASR Assessor** role:

1. Click on the notice and check the ASR (the 'ASR Assessment' screen can be opened by clicking on the ASR ID)
2. Assign the ASR to yourself through clicking on 'Assign to me' or assign it to a user within your organisation through using the searchable user list and select the appropriate user. The list displays each user's ID from the same MS as the logged-in MS user who has either the **ASR Decision Maker Submitter** role or the **ASR Assessor** role
3. Click on 'Confirm'



2.10.2. Downloading an ASR

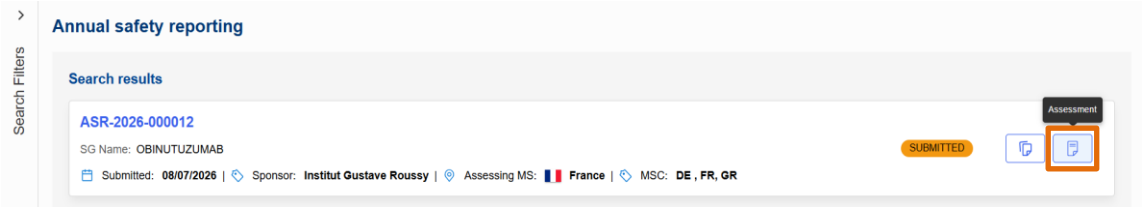
Once an ASR is submitted, **MS users can download the ASR and related documents** (e.g. IB or any attached document to the ASR) from each document placeholder. It is also possible to navigate to the **Annual Safety Reporting** tab, click on the relevant ASR ID, and then select the ''Download' button in the upper-right corner of the page. This will generate a .zip file containing the HTML page displaying the submitted ASR and any related document submitted by the sponsor (e.g. ASR document, SmPC, Investigator Brochure, etc). **Note**: the full ASR package download (i.e. ASR, supporting documentation, RFIs, responses and assessment information) from the 'Download' button will only be enhanced after go-live of the New Safety Module.



2.10.3. Assessment of an ASR

The following steps are applicable to the safety assessment MS/RMS user with **ASR Safety Assessor/ASR Decision Maker Submitter role** that was assigned to the relevant ASR (as per section 2.10.1. , or, if the ASR was reassigned, in line with section 2.8.4.):

1. Navigate to the Annual Safety Reporting tab and for the relevant ASR and click on the 'Assessment' icon in the right-hand side, or ASR ID in the notice generated in the Notice Centre tab.



2. The ASR assessment screen opens, and it displays, at the top, a **progress bar with the different steps** of the assessment process. All steps can be performed by the safety assessing MS (for SG centric ASR) or the RMS (for CT-centric ASR), while some steps (view the shared DAR, provide comments, provide considerations in the RFI working document) can also be performed by other Authority users (MSCs and non-MSCs). Refer to the Role Matrix in section 2.2. to know the appropriate roles for each step.

    1. **Draft AR:** the assessing MS/RMS assesses the ASR, creates the ASR-DAR , save it and share it (see sections 2.10.3.1. and 2.10.3.2.).

    2. **Comments:** the assessing MS/RMS and the rest of the MSCs review the ASR and the ASR–DAR and provide additional comments (see section 2.10.3.3.): note that this section is open already to MSCs as of receipt of the ASR, even before the ASR-DAR is shared.

    3. **Considerations and RFI:** if needed, the assessing MS/RMS or MSCs can create an RFI (and contribute with considerations, if they have the **ASR Decision Maker Submitter role**); once finalised, the assessing MS/RMS submits RFI; the assessing MS and the rest of the MSCs assess the RFI response, once received by the sponsor (see section 2.10.3.4.)

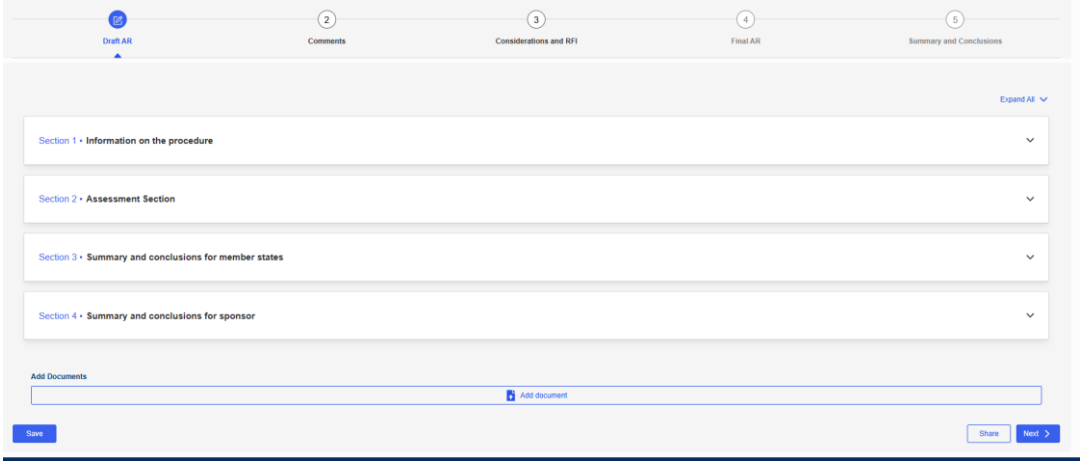
4. **Final AR:** the assessing MS finalises the assessment and shares the FAR (see section 2.10.3.5.)
5. **Summary and Conclusions** (see section 2.10.3.6.)

The following sections describe each step in detail.

2.10.3.1. Draft AR: The safety assessing MS / RMS drafts the DAR

In this stage, **the safety assessing MS/RMS performs the assessment of the ASR and populates the DAR structured fields,** uploading also any supporting document(s), if needed. Where applicable, the ASR-DAR fields are already prefilled with data extracted from the ASR submitted by the sponsor: these fields are displayed greyed-out and cannot be edited. While filling in the fields, the **'Save'** button can be used, which is available throughout the process.

The **ASR-DAR contains four sections** of structured data and a section at the bottom where **supporting documents** can be added (Word or PDF files formats of only up to max 50 Mb size).



Section 1 - Information on the procedure

Most fields are populated automatically from the ASR submission. The **assessing MS indicates whether it acts as the RMS**: for a CT-centric ASR, the assessing MS is by default the RMS of the trial; for a SG-centric ASR, the assessing MS is the saMS selected for the SG concerned.

Section 2 – Assessment section

In this section, the assessing MS selects the **type of assessment** that is being conducted for the ASR:

- In-depth assessment: a full assessment covering all sections of the ASR
- Reduced assessment: a simplified assessment; the reason for performing a reduced assessment of the ASR need to be selected from a drop-down list

The choice between an in-depth and a reduced assessment should be made in accordance with the applicable best practice guidance for safety assessors.

In addition, **structured assessment questions** must be completed. Optional descriptive fields include the therapeutic indication, the class, the mode of action and further details of the IMP. The main structured questions, several of which are mandatory, are answered by selecting Yes/No:

- Is the assessment compliant with the ASR format? If 'No' is selected, additional information must be provided
- Have new safety issues been identified? If 'Yes' is selected, the safety issues concerned must be indicated
- Were actions taken in the reporting period for safety reasons? (mandatory).
- Are there updates on safety issues raised in previous ASRs? If 'Yes' is selected, further details must be completed
- Relevant information – comments (optional free-text field).
- Does the new information in the ASR change the benefit-risk profile of the IMP in the sponsor's opinion? (mandatory)
- Does the new information in the ASR change the benefit-risk profile of the IMP in the Member State's opinion? (mandatory). Regardless of the answer, comments must be provided to support the MS position
- Is a Request for Further Information (RFI) needed? (Yes/No)

Section 3 – Summary and conclusions for Member States

This section includes, among others, the following **Yes/No questions**, several of which open additional fields when answered affirmatively: whether there are any safety issues to be aware of; whether any action is required; and whether any action by the sponsor is required to follow up, or actions are to be taken by the Member States.

Section 4 – Summary and conclusions for the sponsor

The key question is whether the ASR is agreed without further action required by the sponsor (Yes/No). If 'No' is selected, the action(s) requested from the sponsor must be indicated.

When completing the ASR-DAR sections mentioned previously, note that:

- Free-text fields display a character counter on the right-hand side, indicating the maximum number of characters allowed.
- The DAR can be saved at any time and completed progressively; a confirmation message is displayed on the right-hand side of the screen when the draft has been successfully saved.
- If the saMS attempts to share the DAR while mandatory information is missing, the system performs a technical validation: a message indicates that information is missing and the incomplete sections are highlighted in red. The DAR cannot be shared until they are completed.
- When uploading a supporting document, the saMS enters the title, date and version of the document. For each uploaded document, icons on the right-hand side allow the user to download the document, edit its metadata (title and version) or remove it, for example if it was uploaded in error.

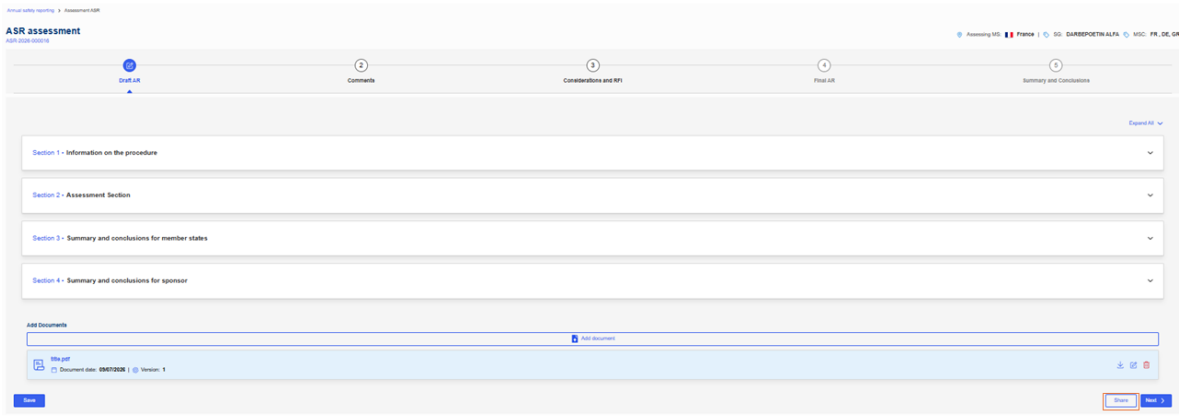
Add documents

In this section, any supporting documents can be added by the assessing MS/RMS. Note that Word or PDF files formats of only up to max 50 Mb size are acceptable.

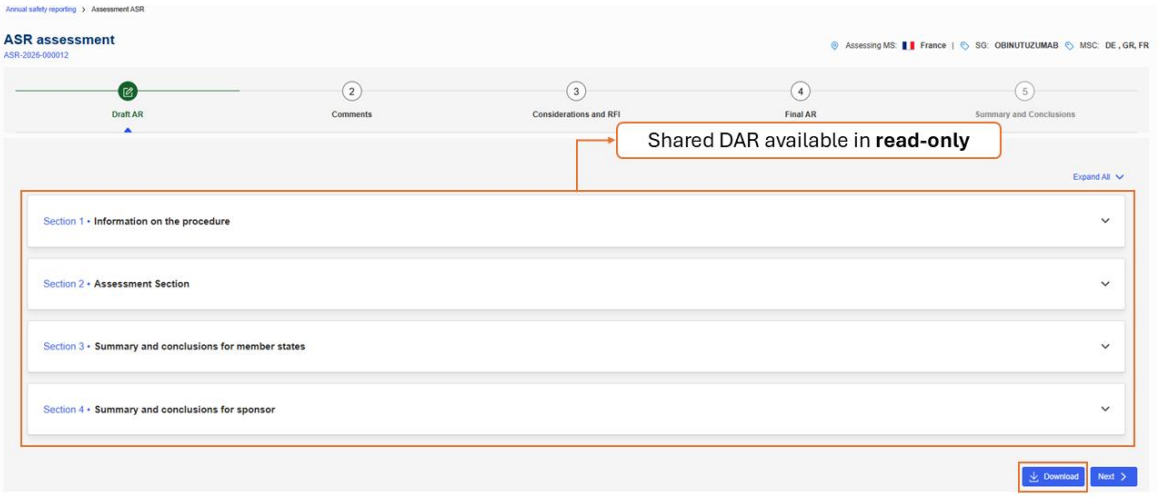
2.10.3.2. Draft AR: The safety assessing MS / RMS shares the DAR and MSCs view it

Once all mandatory ASR-DAR fields are filled in as per previous sections:

1. The assessing MS shares the DAR with the rest of the MSCs by clicking on the 'Share' button on the bottom left. **Note: once shared, the ASR-DAR becomes read-only for all users, including the assessing MS.**



2. The MSCs receive a 'DAR issued' notice in the 'Notice Centre': they can now view the structured data fields filled in by the assessing MS/RMS (in 'Read-only' mode) and any document uploaded; they can also download the DAR by clicking on the 'download' button:



Note: The ASR-DAR cannot be viewed by other MSCs until it is shared (the area would be blank with the phrase 'No data available at this time').

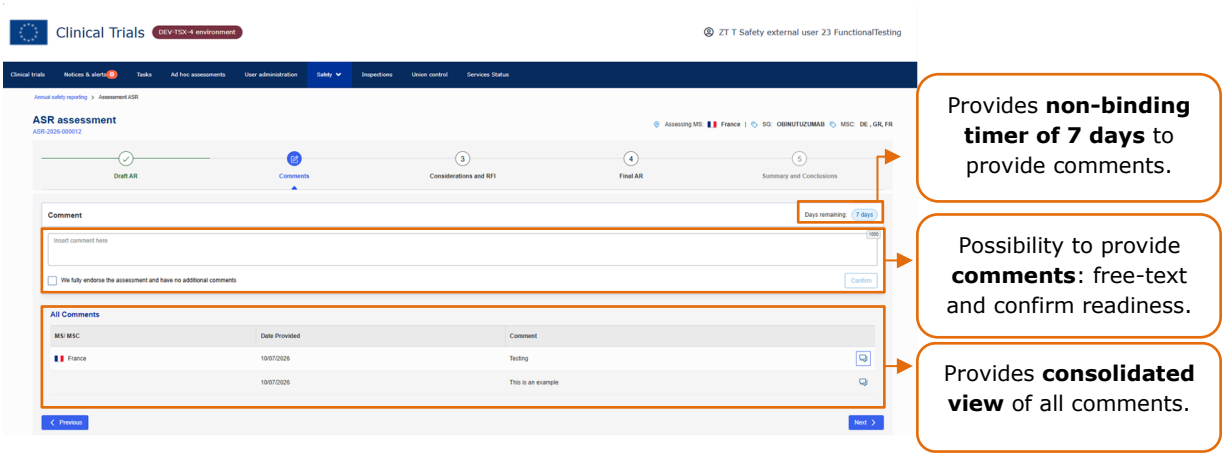
2.10.3.3. Comments: MSC(s) Review Draft ASR–AR and provide additional considerations

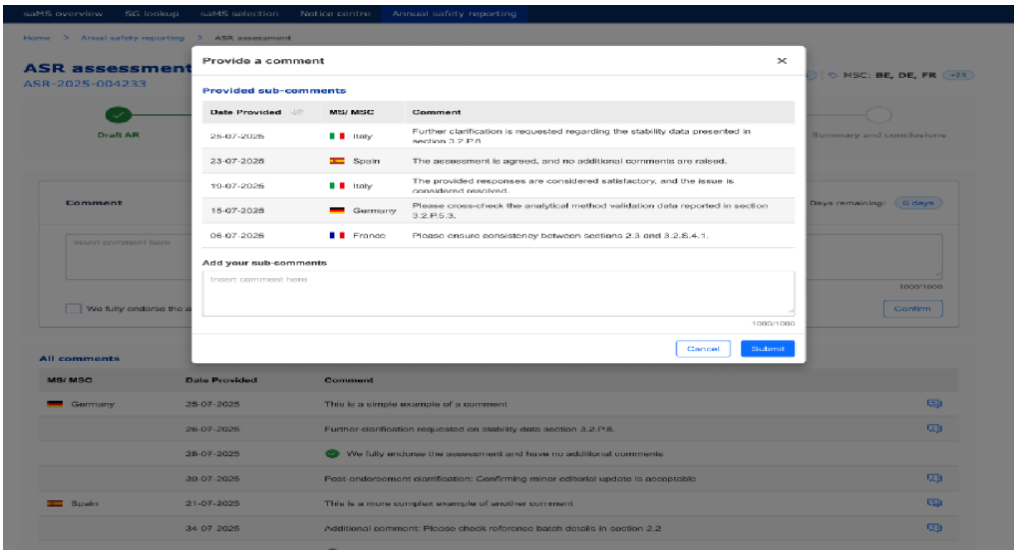
The Comments section is open as soon as the ASR is submitted, so MSCs can start providing comments. From the ASR-DAR submission, the MSCs users have a non-binding timeline of 7 days to provide comments. The following steps are applicable to Assessing MS/RMS and MSCs users with the role **ASR Safety Assessor/ASR Decision Maker Submitter**:

1. Read the ASR-DAR (displayed as per section 2.10.3.2.)
2. Depending on whether you have comments on the ASR-DAR:

- *If you would like to comment on the ASR DAR:* provide your comments in the 'Comments' section and click on 'Confirm'. The comment now appears in the 'All comments' table at the bottom.
- *If you agree with the ASR-DAR and you have no comment:* tick on the option 'I fully endorse the assessment and have no additional comments'. The confirmation appears in the 'All comments' table at the bottom.

3. If applicable, reply to comments raised by other MSCs/assessing MS/RMS through the field 'Add your sub-comments'
4. The assessing MS/RMS monitors whether all MSCs have completed their review and the assessment can proceed to the next step: see section 2.10.3.4. . Note that comments are not integrated in the ASR RFI or DAR. In addition, note that users can add comments also afterwards, even if all MSCs have endorsed the assessment of the ASR: the possibility to comment on the ASR-DAR remains open until the ASR-FAR is shared.





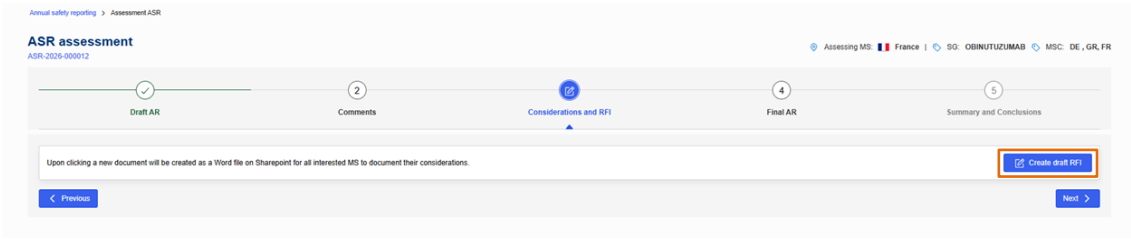
2.10.3.4. Considerations and RFI: Consolidate considerations, Submit RFI and Assess RFI responses (if applicable)

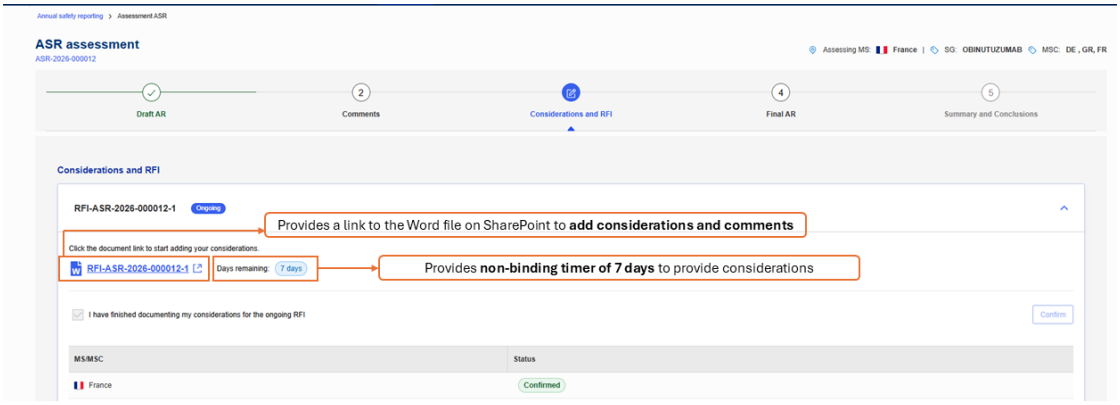
If needed, **Assessing MS, MSCs and non-MSCs can create the draft RFI** (and contribute with considerations, if they have the **ASR Decision Maker Submitter role**) but only the assessing MS/RMS can submit or delete the RFI. The following steps are applicable to Assessing MS/RMS and

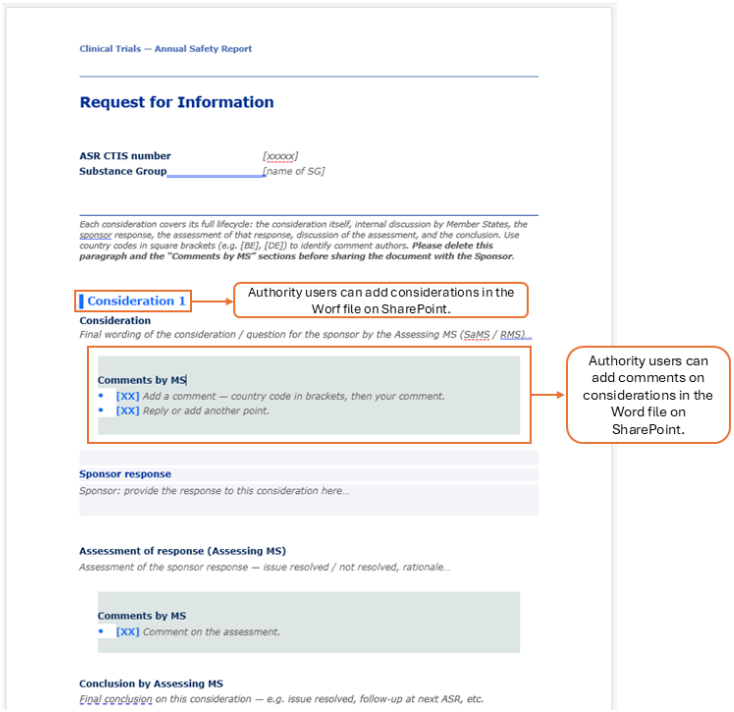
MSCs users with the **ASR Safety Assessor/ASR Decision Maker Submitter role** and that are responsible for the relevant ASR:

1. Create the draft RFI by clicking on the 'Create draft RFI' button. Note that once the first MS user has clicked this button, it is no longer visible for other users as the system will navigate to another screen displaying a draft RFI document generated by the system in Word format in a new browser. This document has an **RFI ID** (unique identification number), its status is 'ongoing' and is stored in a dedicated **SharePoint folder**: to access it, a user needs to have the **ASR Decision Maker Submitter role.**

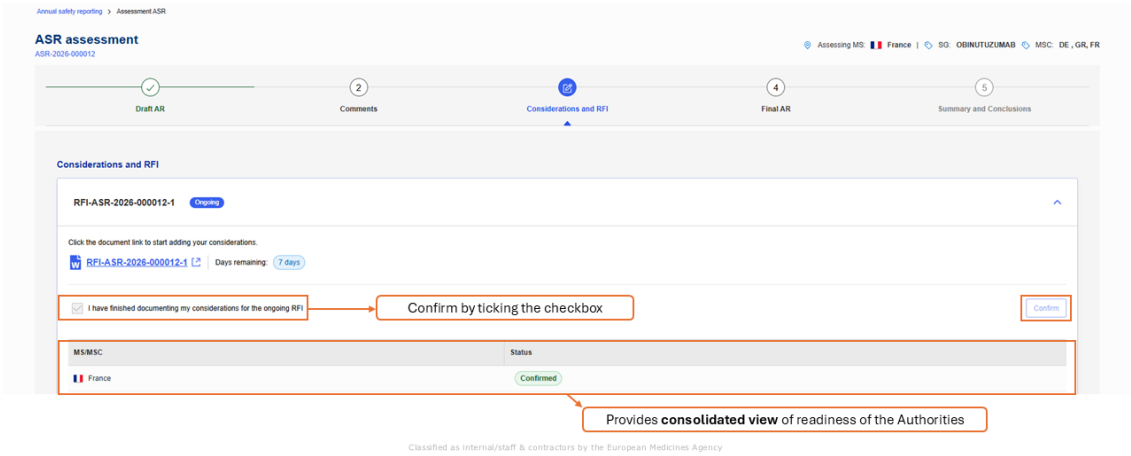
2. Within 7 days from the date the RFI document is generated, **assessing MS/RMS and MSCs users who have an ASR Decision Maker Submitter role can add considerations to the 'ongoing' RFI** and comment on each other's considerations in the SharePoint document, via the 'Considerations and RFI screen'. Note that this 7-day deadline is non-binding (the system does not prevent users from editing once this deadline has passed). The document can be edited by multiple MS users at the same time: this enables collaboration between MS users with the **ASR Decision Maker Submitter role**: use the **Open icon (↗) to open the RFI response in SharePoint**: the Word document opens in a new browser window, allowing users to review, comment on, and collaborate on the document directly in SharePoint. This version retains a full record of every change ever made to the document, known as 'version history' (version history can be viewed through clicking on 'File' on top, and then selecting 'Version history'). Note that the **Download icon (⬇)** allows to download the RFI response as the version of the document at a specific point in time. It does not retain any version history: **any comments or changes made during the assessment are therefore captured only in the SharePoint working version.** **Note:** only one RFI can be active at a time.







3. Once the MSCs/MSs finish adding their considerations, they go back to the 'Considerations and RFI' section, tick 'I have finished documenting my considerations on the ongoing RFI' and click on the 'Confirm' button. **Note: this confirmation is not mandatory and it can only be provided once.** Once an MS clicks on confirm, this will be displayed in the below table.



4. Once all considerations have been provided in the RFI document, the saMS '**cleans-up'** the file through accepting track changes, remove comments, MS names, notes etc.

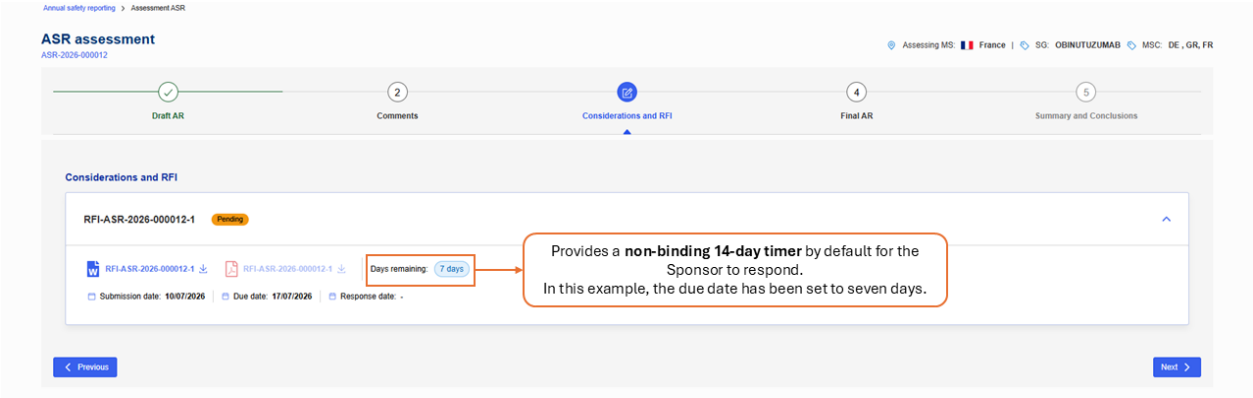
5. The **safety assessing MS/RMS** user **clicks on 'Generate document'**. A timestamped copy of the RFI document is created and can be downloaded by clicking on the download icon.

6. The safety assessing MS/RMS user performs a **final review** of the document, making sure that the RFI is understandable and can be shared with the sponsor, and, if needed, adds a due date for the sponsor's reply. If no due date is selected, the due date for the sponsor's reply is set by default to 14 days from the date of submission.

7. **The safety assessing MS/RMS user clicks on 'Submit' button. Note that the 'Delete RFI' and 'Submit' buttons are enabled only for the assessing MS.**

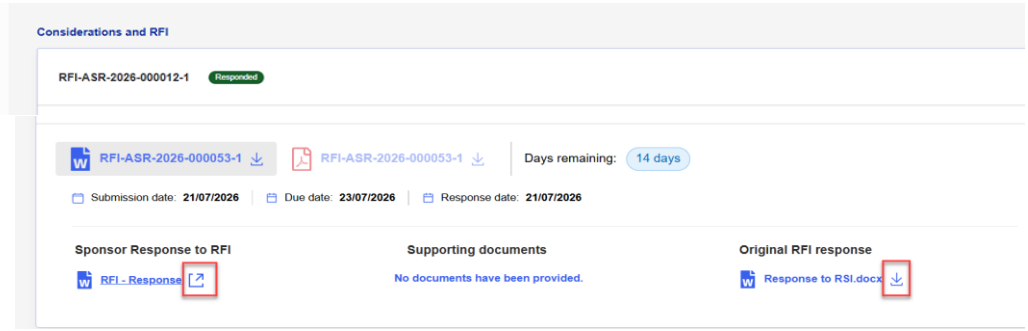
Once the saMS has submitted the RFI to the sponsor:

- the status of RFI changes to 'Pending' and the SharePoint link is no longer available from the screen. The system displays downloadable copies of the final submitted document in Word (download icon ⬇ only). These are snapshot copies and do not contain version history.
- the sponsor receives an 'Assessing MS issued RFI' notice
- the system displays a non-binding countdown of 14 days (or less, depending on the due date indicated by the assessing MS in step 6) for the submission of the sponsor's RFI responses



8. On the sponsor side, the 'Assessing MS issued RFI' notice is displayed in the sponsor Notice Centre with a timestamp and the sponsor is expected to upload the RFI response document (Word format) and any supporting document (PDF format). Once the sponsor submits the RFI response, **the assessing MS receives a notice 'RFI response submitted'** in the Notice Centre and the RFI status changes to 'Responded'. A **SharePoint version of the RFI response document submitted by the sponsor** is generated (displayed under the heading 'Sponsor response to RFI'), **allowing saMS/MSCs/MSs to jointly discuss the RFI response received from the sponsor** (see next step). Note that the initial RFI submitted to the sponsor, as well as the RFI responses (displayed under the heading 'Original RFI response') and any additional documents submitted by the sponsor (displayed under the heading 'Supporting documents') are downloadable (⬇) from this section.

9. The saMS/MSCs/MSs with the **ASR Decision Maker Submitter role** use the **Open icon (↗) to open the RFI response in SharePoint**: the Word document opens in a new browser window, allowing users to review, comment on, and collaborate on the document directly in SharePoint. This version retains a full record of every change ever made to the document, known as 'version history'. **Any comments or changes made during the assessment are therefore captured only in the SharePoint working version**



Note: to retrieve the SharePoint version of the RFI submitted to the sponsor (and not just the final downloadable version), the MS user can:

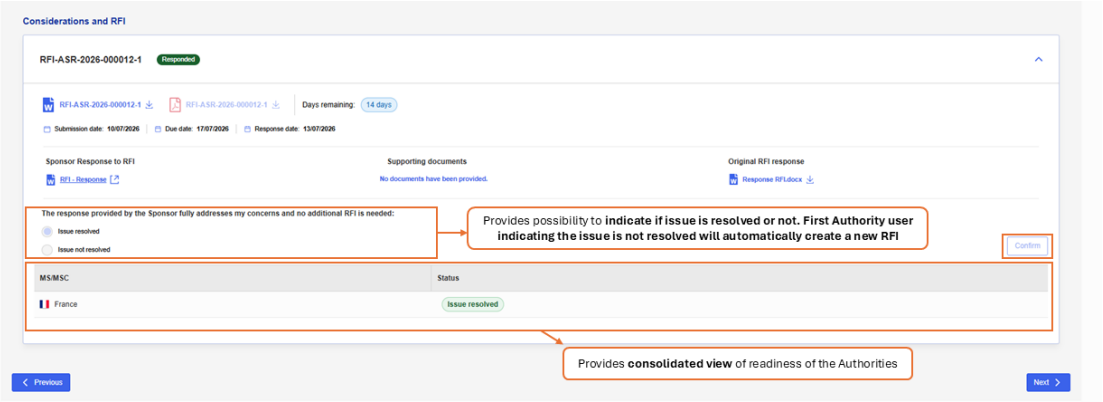
a. Click the arrow icon (↗) next to the Sponsor Response to RFI document, and, once in Word Online, click the cloud icon next to the document title at the top of the screen. A small panel will appear showing the file location as a breadcrumb path.

b. Click on one of the folder links in that breadcrumb to navigate to the underlying SharePoint folder. The user is now in the RFI response folder. Navigate up one level to the RFI folder. The original RFI file (e.g. RFI-ASR-2025-00423-1) will be listed there

c. To see its history, click on the original RFI file to open it, click File in the top menu, then Version History to review the full change history.

10. Depending on whether the sponsor response to the RFI is satisfactory, the saMS/MSCs/MSs use the relevant checkbox and clicks on 'confirm', to indicate if the response provided by the sponsor:

- Satisfies all considerations raised: go to step 11
- Does not satisfy all considerations raised: go to step 12



11. *If the **RFI response is deemed insufficient by at least one Authority user**,* then a **new draft RFI is automatically created**. The workflow is the same as the first draft RFI: refer to step 5. Note that RFIs are handled sequentially: only one RFI can be active at a time, and a new RFI can only be submitted after the sponsor has responded to the previous one.

12. *Once the response(s) to the RFI is/are deemed acceptable,* the '**Next >' button is enabled,** only for the safety assessing MS, **and is to be clicked by the safety assessing MS**.

13. Any created draft RFI can always be deleted only by a user of the safety assessing MS can delete it.

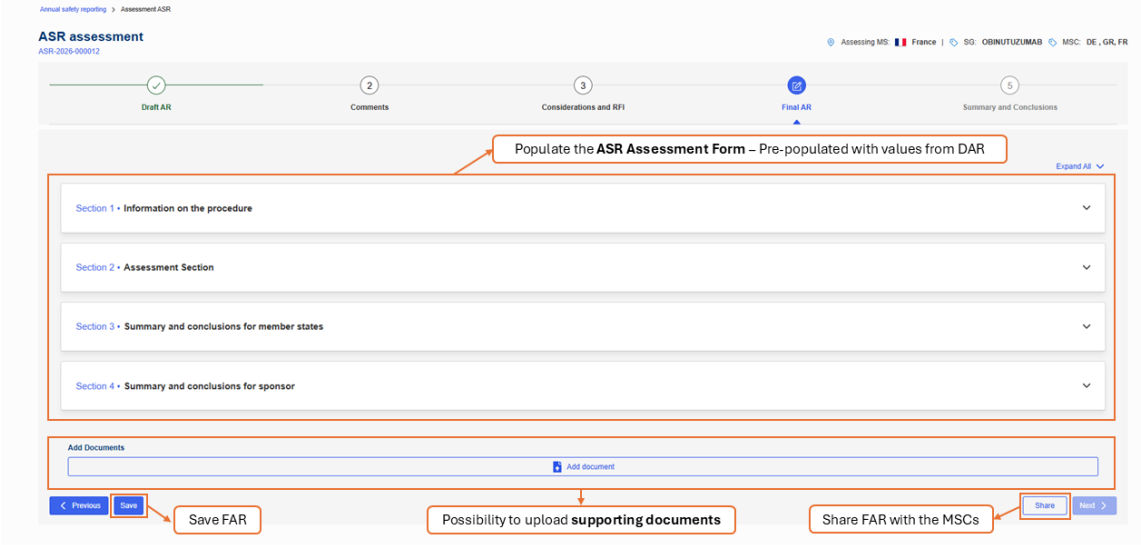
2.10.3.5. Final AR: the safety assessing MS finalises the ASR assessment

The Final AR is pre-populated with the DAR values immediately after the DAR has been shared (see section 2.10.3.2.), and integrated with the RFI response. Once the safety assessing MS clicks on 'Next' (see section 2.10.3.4.):

1. Edits the pre-populated DAR values (if needed) and completes the FAR section, also through adding any optional document, to reflect the outcome of the ASR assessment and on the RFI responses. By clicking on 'Save', the changes made are saved.
2. Clicks on 'Share' so that the **FAR becomes visible to the MSC**s. A 'FAR issued' notice is issued to the MSCs and the status of the ASR becomes 'Finalised'. Once shared, MSCs have 'Read-only' access to the FAR and the sponsor receives an ''ASR Assessment finalised' notice

Note that:

3. *If needed,* the safety assessing member state/RMS can re-open the FAR for administrative corrections via the 'Edit' button. Note: this button is only available to the safety assessing member state and **can only be used once**. The FAR can then be shared again to MSCs. The assessment status remains 'Finalised' and no new notice will be sent to MSCs. Once the FAR is re-shared, it is permanently locked and cannot be re-opened for edit.



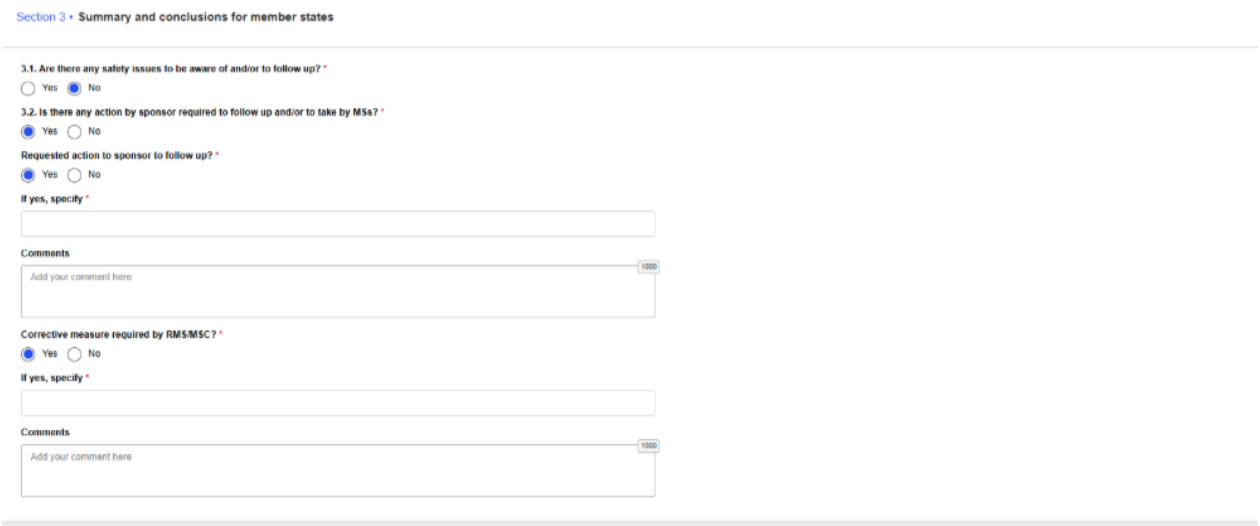
Note that the ASR, the ASR FAR and any ASR RFI and their structured data are **never published**. However, all Member States (also those that are not MSC(s) for the trials that are in scope of the ASR) have access to the submitted ASR information.

2.10.3.6. Summary and Conclusions

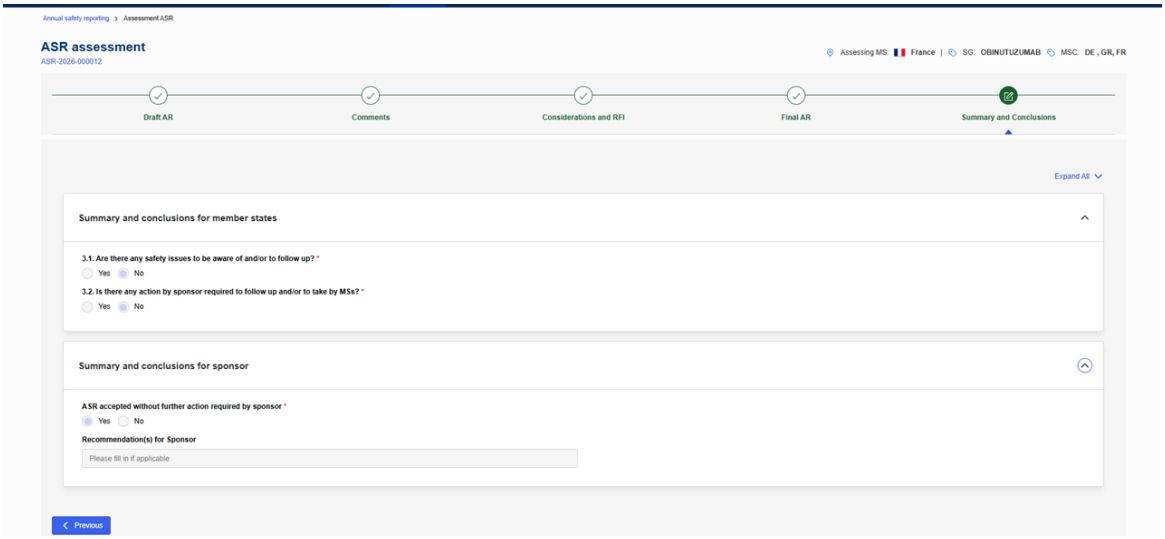
Once the ASR assessment is finalised by the assessing MS as per section 2.10.3.5. , the 'Summary & Conclusions for Member States' section becomes visible to MSCs/MSs and shows in 'Read-only' mode the information as entered by the saMS in the FAR. The safety assessing MS:

1. Replies to the questions on whether there are any safety issues and any action required to follow up. If the ASR is no longer agreed without further action, the answer to 'ASR agreed without further action required by the sponsor' can be changed to 'No', indicating the

action(s) requested from the sponsor, the corresponding deadline(s) and any recommendations. If a corrective measure is required by the assessing MS/RMS/MSC(s), the checkbox indicating that action is required by the sponsor and/or the MS(s) must be first be selected. The corresponding fields on the corrective measure can then be completed. This will be reflected in the 'FAR issued' notice sent to MSCs, which will indicate that a corrective measure is required.



2. A **'Summary & Conclusions for Sponsor'** section is made available to include any recommendations for the sponsor, if needed, in order for them to check the conclusion of the ASR assessment, including FAR and any required action(s), with due date(s) and recommendations.



3. CTIS Support

If the behaviour of CTIS training environment in relation to the New Safety Module differs from what is described in this guidance or demonstrated during the Bitesize talk, users **should first carry out the following checks:**

- For a specific issue such as missing tabs, timeouts or empty warning messages, consult the Annex I: List of known issues and workarounds to determine whether the issue has already been identified and whether a workaround is available
- For login-related issues, check whether the issue can be solved following the guidance provided for EMA Account Management

If none of the above applies, and the issue **cannot be solved internally or by using an available workaround**, **users should describe the issue to the relevant MS Master Trainer**: refer to contact details shared in the **Member State Master Trainers sub- channel in Teams**.

Member State users **should not submit Safety Module Training Environment tickets directly to EMA**. All blocking issues and relevant blocking questions must first be reported to the designated MS Master Trainer for assessment.

Once being informed by a MS user regarding an issue or question, the MS Master trainer proceeds as follows:

1. Assess whether the issue is not in line with the present Guidance and it is not present in the Annex I: List of known issues and workarounds
2. **Assess whether the issue or question is a blocker,** which is when it:
    - **prevents the completion of a training activity**
    - has no reasonable workaround
    - prevents access to essential functionality, data or services, and
    - requires resolution before the affected process can continue

To support efficient triage and resolution of issues and questions, **the Member State Master Trainer should report blocking issues/questions via EMA CTIS Service Desk** (see section 3.1.) or report non-blocking issues/questions/feedback via Slido, see section 3.2.

3.1. The MS Master trainer reports blocking issues/questions

The following instructions apply to **a MS Master trainer that needs to report blocking issues/questions** on the New Safety Module on ASR:

1. Use the Request form for questions and the Incident form for technical issues.
2. Indicate in the '**Subject'** field that the issue concerns the **'CTIS training environment – New Safety module'** and Select **'CTIS training environment'** in the '**CTIS Request type'** field.
3. Provide a detailed **description** of the issue or question, including:
    - The area (e.g. saMS selections, notice centre etc) or screen affected
    - The steps performed (e.g. created a new ASR and attempted to submit it)

- The expected result (e.g. ASR is successfully submitted)
- The actual result observed (e.g. Error message displayed and submission fails)
- The impact on the training activity (e.g. prevents completion of the training exercise)
- Any supporting screenshots including the full view from the user's perspective

The EMA will follow up on the relevant issue/question via the Service Desk.

3.2. The MS Master Trainer reports non-blocking issues and feedback

Non-blocking issues or it is an observations, minor defects and general feedback should <u>not</u> be escalated to EMA through the Service Desk.

The following instructions apply to **a MS Master trainer that needs to report non-blocking issues/questions/feedback** on the New Safety Module on ASR:

1. Access **Slido** using code #MemberStates or by scanning the QR code below:

2. Check whether the same or a similar observation/issue has already been submitted. If so, upvote the existing entry rather than submitting a duplicate.
3. If no similar issue/question/feedback appears on the Slido, proceed with submitting it

This channel will be monitored and used for observations and feedback that may be considered during the finalisation of the development of the New Safety Module on ASR.

For further information on CTIS training and support, see section 6 of the Sponsor Handbook.

Annex I: List of known issues and workarounds

The purpose of this Annex is to describe issues known to occur in the Member State CTIS training environment upon implementation of the New Safety Module on ASR. Relevant workarounds to apply are described. Each issue is numbered and connected to a number (‘[ADO-xxxxxx]’): this number is unique and is used internally by EMA to identify and track the issue from reporting to resolution.

1. Overarching issues affecting CTIS and New Safety Module

This section covers known issues that cut across both the Access and User Management screens (User Administration, My Roles and the Personal Profile) and the Safety module.

1. Issue: Due to intermittent technical issues, screens related to access and user management, as well as safety may fail to load: results may not appear, may keep loading indefinitely, or may return a generic error message. [ADO-331900].

> **Workaround:** Refresh the screen or retry after a short interval. If the problem persists, contact the EMA CTIS ServiceDesk.

2. Access and User Management

This section covers known issues related to user account management, role assignment and access control, including the User Administration and My Roles screens across the Clinical Trial and Safety tabs, and the Person Profile screen.

1. Issue: When a user is on the 'My Roles' page or the 'User Administration' tab and refreshes the browser, the system redirects to the Clinical Trials homepage, and the current page context is lost. [ADO-318624].

> **Workaround:** Navigate back to the intended page after refreshing. Avoid using browser refresh on these screens.

2. Issue: When a browser tab is duplicated and the user logs out in the duplicate, the original tab refreshes and returns to the login screen, but the duplicated tab shows the logout message without automatically refreshing. [ADO-320212].

> **Workaround:** Manually refresh or close the duplicated tab after logging out.

3. Issue: In the User Administration Safety tab, the NOA Organisation advanced-search filter does not return any data. [ADO-324867].

> **Workaround:** Use alternative search fields until the issue is fixed.

4. Issue: When assigning a role and adding a new NOA organisation location with a document attached, the submit action does not complete successfully. [ADO-325110].

> **Workaround:** Perform changes in OMS directly.

5. Issue: When adding or deactivating a location, the attachments section does not yet follow the required behaviour (PDF-only, multiple documents, per-file size limit and document actions). [ADO-326258].

> **Workaround:** Perform changes in OMS directly.

6. Issue: User with role EMA Admin or National Organization Admin experience very long loading times when opening the Clinical Trials tab in User Administration. [ADO-329880] [ADO-334497].

Workaround: There is no workaround until the issue is fixed. Contact the EMA CTIS ServiceDesk.

7. Issue: In the User Administration Clinical tab, the European Commission Admin cannot amend or revoke roles. [ADO-332121].

Workaround: There is no workaround until the issue is fixed. Contact the EMA CTIS ServiceDesk.

8. Issue: Attempting to deactivate a trial site (location) via the Personal Profile returns an error. [ADO-332294].

Workaround: There is no workaround until the issue is fixed. Contact the EMA CTIS ServiceDesk if deactivation is required.

9. Issue: In the User Administration Safety tab, requested roles do not expire as expected. [ADO-333269].

Workaround: There is no workaround until the issue is fixed.

10. Issue: When an MS Admin assigns a role via the Safety tab with a NOA organisation, it is saved without that NOA organisation. [ADO-334512].

Workaround: There is no workaround until the issue is fixed. Contact the EMA CTIS ServiceDesk for urgent assignments.

11. Issue: Searching for a NOA organisation by name returns incorrect values. [ADO-334702].

Workaround: Verify the organisation using additional identifiers until the issue is fixed.

12. Issue: In User Administration, the Clinical Trial tab is visible to Authority Safety Admin users when it should be hidden from them. [ADO-334264].

Workaround: Authority Safety Admin users should disregard the Clinical Trial tab until the issue is fixed.

13. Issue: In both User Administration and My Roles, the search results are clickable when they should not be, upon clicking an error is displayed. [ADO-334293].

Workaround: There is no workaround until the issue is fixed.

14. Issue: In the Clinical Trial tab of both My Roles and User Administration, roles fail to load from time to time. [ADO-334294].

Workaround: Search button needs to be clicked first.

15. Issue: In the User Administration Safety tab, legacy Enterprise roles are displayed when they should not be. [ADO-334297].

Workaround: Disregard the Enterprise roles shown until the issue is fixed.

16. Issue: In the Personal Profile, the 'My Employer' information is displayed incorrectly. [ADO-334295].

Workaround: There is no workaround until the issue is fixed. Contact the EMA CTIS ServiceDesk for urgent assignments.

17. Issue: When assigning a role, the expected confirmation pop-up window does not appear. [ADO-334300].

Workaround: Verify the assignment before confirming.

18. Issue: An Authority Safety Admin cannot assign a new role scoped to a specific trial. [ADO-334326].

Workaround: Assign also the NOA Admin role to this user.

19. Issue: An Authority Safety Admin can assign roles to users belonging to a different Member State, which must not be allowed. [ADO-334576].

Workaround: Authority Safety Admins should take care to assign roles only to users within their own Member State until the issue is fixed.

20. Issue: When the User Administration screen has many results across many pages, clicking a page number can lead to an error instead of showing the selected page. [ADO-334637].

Workaround: Retry the navigation or narrow the search criteria to reduce the number of result pages.

21. Issue: In the User Administration screen and My Roles screen, the Authorised Date is not consistently formatted (all dates should be DD-MM-YYYY). [ADO-334640].

Workaround: There is no workaround until the issue is fixed.

22. Issue: Across the User Administration and My Roles screens, several advanced-search filters and sort options do not work correctly. The affected fields vary by tab and workspace (e.g. email, role, organisation name/ID filters, and sorting by role, status, employer or 'authorised from'). [ADO-332298] [ADO-332301] [ADO-333301] [ADO-332702] [ADO-333155] [ADO-328836].

3. New Safety Module on ASR

This section contains known issues related to the Safety module, including the saMS overview, saMS selection, SG lookup, ASR and Notice centre screens.

1. Issue: In the SG Lookup tab, the search function is unable to retrieve entries that contain blank values in the searched field. [ADO-284330].

Workaround: Use alternative populated search fields to locate the entry until the issue is fixed.

2. Issue: In the SG-CT screen, three Active Substance Low-Level (AS LL) IDs are displayed for a trial, one of which is not actually associated with that clinical trial (it belongs to a different product within the same substance group). [ADO-284345].

Workaround: There is no workaround until the issue is fixed. Verify the correct product/substance association in the CT product section.

3. Issue: In the saMS Selection screen, the MSC filter incorrectly includes Member States with statuses other than 'Authorised', 'Under Evaluation', 'Halted' and 'Suspended' (for example 'Revoked' or 'Ended'), producing unexpected results. [ADO-288480].

Workaround: Verify results by checking the CT status directly, as the filter may return SGs linked to CTs with ended or revoked MSCs.

4. Issue: When a saMS notification event is triggered, the resulting email is displayed differently in the Outlook desktop application compared with the Outlook web interface. The web interface display is the intended reference. [ADO-289792].

> **Workaround:** There is no workaround until the issue is fixed. Refer to the Outlook web view for the correct layout.

5. Issue: In the Notice Centre and saMS Selection search filters, the 'X' on the date filter does not consistently clear the selected date, and after opening and closing the date selector the control can become unresponsive until another input field is clicked. [ADO-295606].

> **Workaround:** Click on another input field to restore the date selector or reload the screen to reset the filters.

6. Issue: An issue has been reported affecting the display of Trial Phase | Population(s) information in the Safety module. [ADO-295615].

> **Workaround:** There is no workaround until the issue is fixed.

7. Issue: When an EMA Admin performs a saMS correction or retrigger, the 'selecting entity' shown in the saMS Selection screen is not the correct one. [ADO-295619].

> **Workaround:** There is no workaround until the issue is fixed.

8. Issue: When a document upload exceeds the maximum 50 MB limit, the file-size message displayed to the user is misleading. [ADO-315216].

> **Workaround:** Ensure uploaded files are within the 50 MB limit; split large documents if necessary.

9. Issue: Documents that are downloaded lose their original file name. [ADO-316527].

> **Workaround:** There is no workaround until the issue is fixed. Rename downloaded files manually if needed.

10. Issue: Occasionally, a notification can take an unexpectedly long time before it is displayed in the Notice centre. [ADO-319019].

> **Workaround:** There is no workaround until the issue is fixed. Refresh the Notice Centre if an expected notification is not shown.

11. Issue: After the DAR is shared, comments are not visible in the ASR assessment until the page is manually refreshed. [ADO-325225].

> **Workaround:** Refresh the page to display the comments.

12. Issue: When filtering by Active Substance on the SG-CT screen, the search fails. [ADO-326785].

> **Workaround:** Use alternative search filters until the issue is fixed.

13. Issue: In the SG Lookup screen, applying a filter on the Main Status field and searching returns 'There are currently no data to display', even when matching records exist. [ADO-326788].

> **Workaround:** Use alternative search filters until the issue is fixed.

14. Issue: After opening an ASR-related notice via its hyperlink, the user is taken to the ASR assessment screen and cannot navigate back to the Notice Centre using the menu (the user stays on the assessment screen). This occurs only when arriving via the hyperlink. [ADO-327621].

Workaround: Refresh the page and navigate to the Notice Centre directly rather than via the hyperlink.

15. Issue: The 'New CT added to SG' notice and its email contain a typo in the header text. [ADO-327625].

Workaround: No action required; this is a cosmetic text issue that does not affect functionality.

16. Issue: The 'Blanks only' checkbox in the ASR search filters provides no clear benefit and its purpose is unclear, which may confuse users. [ADO-327791].

Workaround: No action required; the checkbox can be left unused.

17. Issue: In the ASR Detail and Assessment views, the active substance name is shown instead of the product name for IMPs whose product name is not null, and the IMP string is split incorrectly, inflating the apparent number of products. [ADO-327925].

Workaround: Consult the original CT application for accurate IMP product-name information.

18. Issue: In the 'Select another organisation' pop-up, the City field appears empty even though a value is present in the underlying organisation record. [ADO-327928].

Workaround: Verify the city value in the organisation record; the data is present despite the empty display.

19. Issue: A mandatory field is indicated only by text and not by the standard red-box highlight, making the requirement less visible. [ADO-328198].

Workaround: Ensure all mandatory fields are completed regardless of highlighting.

20. Issue: When uploading a document, the document version of type x.yy is incorrectly not allowed. [ADO-328274].

Workaround: Record the document version differently.

21. Issue: In the CTs-per-SG overview, the 'Other CT SGs' column is missing for combipack products. [ADO-328556].

Workaround: There is no workaround until the issue is fixed. Consult the product details for the full substance-group information.

22. Issue: An MSC country is displayed twice (duplicated) in the ASR Assessment screen. [ADO-330274].

Workaround: The duplicate display can be disregarded; it does not affect the assessment.

23. Issue: There is a typographical error in Section 2 of the DAR/FAR (i.e. ‘benefict’ instead of ‘benefit’). [ADO-331154].

Workaround: No action required; cosmetic text issue.

24. Issue: In the Safety module search, filtering by Sponsor and by Trial Phase / Population(s) does not work or works only partially. [ADO-332726].

Workaround: Use alternative search fields until the issue is fixed.

Annex II: Acronyms and definitions

Acronym	Definition
API	Application Programming Interface
AS HL - Active Substance High Level	High-level active substance used to identify and group related active substances in CTIS.
AS LL - Active Substance Low Level	Low-level active substance associated with an Active Substance High Level in CTIS.
ASR - Annual Safety Report	Report submitted annually by the sponsor in accordance with Article 43 of Regulation (EU) No 536/2014 to provide an evaluation of the evolving safety profile and benefit-risk balance of the investigational medicinal product(s).
CT - Clinical Trial	Clinical trial as defined in Regulation (EU) No 536/2014.
CTIS - Clinical Trial Information System	The single-entry point for sponsors and Member States for the submission, assessment, authorisation, supervision and transparency of clinical trials in the European Union and European Economic Area.
CTR - Clinical Trials Regulation	Regulation (EU) No 536/2014 on clinical trials on medicinal products for human use.
DAR - Draft Assessment Report	Preliminary assessment report prepared by the saMS and shared with the MSC the coordinated ASR assessment.
DSUR - Development Safety Update Report	ICH E2F annual safety report on which the Annual Safety Report submitted under the Clinical Trials Regulation is based.
EC	European Commission
EEA	European Economic Area
EMA	European Medicines Agency
EU	European Union
EU CT number - EU Clinical Trial number	Trial identifier code, unique to each clinical trial conducted in CTIS.
EV-CTM - EudraVigilance Clinical Trial Module	Module of EudraVigilance supporting clinical trial safety reporting.
FAR - Final Assessment Report	Final report adopted by the Safety Assessing Member State following the coordinated assessment of an Annual Safety Report.
ICH	International Council for Harmonisation
IMP - Investigational Medicinal Product	Medicinal product being tested or used as reference in a clinical trial.
MedDRA - Medical Dictionary for Regulatory	International standardised medical terminology used for coding and reporting medical information.

Acronym	Definition
Activities (MedDRA)	
MS - Member State	A Member State of the European Union/European Economic Area.
MSC - Member State Concerned	Member State in which the clinical trial concerned is authorised.
PT - Preferred Term	MedDRA Preferred Term associated with a safety concern.
RFI - Request for Information	Request issued during the assessment process requiring the sponsor to provide additional information or clarification.
RMS - Reporting Member State.	Member State leading the assessment of a clinical trial application.
saMS - Safety Assessing Member State	Member State that assesses the information contained in ASRs submitted in accordance with Article 43 of the CTR, leading the safety assessment of a Substance Group.
SG - Substance Group	Grouping of related active substances for the purpose of safety assessment
SM - Substantial Modification	A substantial modification as defined in Article 2(13) of Regulation (EU) No 536/2014
XEVMPD - eXtended EudraVigilance Medicinal Product Dictionary	European database containing information on medicinal products to support regulatory and pharmacovigilance activities.