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Clinical Trials Information System (CTIS) List of known issues for Sponsor Users

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Introduction

The purpose of this document is to describe issues known to occur in the sponsor workspace of CTIS. These issues have been identified mainly through use of the CTIS test environments, CTIS training environment (CTIS Sandbox) and CTIS production environment in various activities including e.g. testing, training, organisation model exploration or use in practice. The document also describes workarounds to apply, where possible, should those issues occur.

The document is structured in sections based on CTIS functionalities. The issue is numbered and described followed by an explanation of a workaround. In addition, each item is connected to a number ("[CTCS-xxxxx or SD-xxxxxx]"). This number is unique and is used by EMA to identify and track the issue from reporting to resolution.

EMA aims to publish updates of this document as frequently as necessary once issues are resolved or if new issues would be identified.

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1. Application Creation/Preparation on documents and data

This section contains issues that sponsor users may encounter when creating a new clinical trial application, or substantial or non-substantial modifications or other subsequent actions or while uploading or downloading some documents.

1. **Issue:** In some cases, the sponsor users cannot upload the document "Proof of payment (not for publication)" in the Form tab after a Member State concerned has been added in the Member State Concerned tab. [CTCS-22809]

   Workaround: If the user encounters this issue, they can delete all uploaded document(s) in the Proof of payment section, save the section using the Save button or by pressing the padlock, then reload the page (either by navigating out of the application or pressing refresh button in the browser). Then, the user can upload all documents again.

2. **Issue:** Member State and Sponsor users may be prevented to download the document 'Content labelling of IMP's' and assess its content when this document is linked to a product. [SD-658262]

   Workaround: There is no workaround. Member State or Sponsors users need to notify the CTIS service desk to apply a technical workaround on their behalf. The Member State should not raise a consideration for the sponsor to attach a new document as this will not fix the problem.

3. **Issue:** When a sponsor associates a co-sponsor to a clinical trial application, the users from the co-sponsor organisation with roles with the scope "all trials" have access to all details of the clinical trial where the co-sponsor is recorded. In particular, all of the co-sponsor's users that have the roles Q-IMPD Preparer, Q-IMPD Submitter, or CT Admin will have access to the quality documents such as the IMPD-Q, Scientific Advice – restricted, and Part I Assessment report – quality, RFIs and RFI responses to IMPD-Q. [CTCS-22534]

   Workaround: The lead sponsor should only associate a co-sponsor to an application if they are ensured that all users from the co-sponsor are allowed to have access to the information of this clinical trial. Otherwise, the sponsor user should not associate a co-sponsor and should instead include the co-sponsor details in the protocol and in the cover letter.

4. **Issue:** There are occasions when, after selection of an authorised medicinal product, the active substance details including the substance name and its EV code are not populated in CTIS. [CTCS-22890]

   Workaround: The user is advised to rely on the authorised medicinal product and to ignore the fact that the active substance details are not rendered in the user interface.

5. **Issue:** When responding to an RFI, the user can upload a supportive document (general section) for which the system incorrectly displays the red statement "document will not be publicly accessible", however this document will be published. When uploading a document to a quality consideration response, the system incorrectly displays the statement "document will be publicly accessible"; this is incorrect as the documents for quality considerations are not published. [CTCS-20567]

Workaround: The sponsor user should disregard these statements and can confidently upload the document as required.

6. **Issue:** When responding to an RFI Part II, the user may not be able to edit Part II if some of the other Member State concerned have already decided on the application. [CTCS-22231][SD-685709]

   Workaround: The user should upload any documents that may need to be updated with the RFI consideration responses.

7. **Issue:** When the user uploads a document in CTIS with special characters in the title, after the document is saved, it is not possible to download the document. [SD-648208]

   Workaround: The user should avoid uploading documents with special characters in the title. If such a document is already uploaded, the user can access it when downloading the entire application through the summary page of the clinical trial

8. **Issue:** The specific combination of the roles Part I viewer + QIMPD preparer is not working as expected; the user is able to upload documents for different sections in Part I e.g. protocol, IB, synopsis, study design, PIP. [CTCS-22846]

   Workaround: The issue is caused by the combination of these two roles because a user with only one of the roles is not able to perform these additional actions. There is no workaround until the issue is fixed.

9. **Issue:** When a temporary halt is submitted, in the CT summary screen, the end of trial date is updated with the temporary halt date. [CTCS-21083]

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

10. **Issue:** For the transition of a trial previously authorised under the Clinical Trials Directive, the user may be able to submit an initial application that does not contain a valid EudraCT number. [CTCS-22853]

    Workaround: The user should verify that the EudraCT number is correct and complete (i.e. valid) before submission.

11. **Issue:** When the user submits a new multi-trial Substantial Modification, the system does not account for the winter clock stop (winter clock stop period from 22 December to 8 January inclusive) when assigning the due date for the task. [CTCS-22810]

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

12. **Issue:** When the user drafts a Substantial Modification for which the change is to take place for several trials (multi trials SM application), and the user tries to include more than one trial at the same time, the system displays an error message. [CTCS-23344]

Workaround: Include the trial for the Multi-Substantial Modification one by one

13. **Issue:** When the user drafts a Substantial Modification for which the change is to take place for several trials (multi trials SM application), can delete products in Part I and Investigator brochure document. [CTCS-22810]

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

14. **Issue:** When the user wishes to restart a trial which is halted in one or more Member States concerned and submits a Substantial Modification application with the reason "restart of trial", the system asks for the "anticipated restart trial date" for each Member State concerned, including for those in which the trial is not halted. [CTCS-22793]

    Workaround: To complete the Substantial Modification, the user can provide a fictitious date for the Member States concerned in which the trial is not halted. This fictitious date does not have an impact on the trial in Member States concerned where the trial was not halted.

15. **Issue:** When adding a Non Substantial Modification Part I (NSM-Part I) to trials with an Additional Member State concerned that has not decided on the application, the NSM-Part I includes this Member State concerned under the application section of the summary overview when in fact only the authorised Member States concerned should be displayed. [CTCS-22537]

    Workaround: The user should wait for the decision on the Additional Member State concerned application before creating and submitting an NSM-Part I.

16. **Issue:** The document "agreement from another sponsor (not for publication)" submitted by the sponsor is not available to the Member State concerned in the Associated Clinical Trials section of the Part I tab in the authority workspace, nor in the downloaded zip file. [CTCS-22812]

    Workaround: The sponsor user should provide this document, if required, within the cover letter placeholder and ensure that they select the option "not for publication".

17. **Issue:** After the initial application is authorised, and a Substantial Modification is created, and a Member State concerned has responded with an RFI, incorrect header information may display for all draft applications (e.g. showing draft applications as under evaluation, displaying a Substantial Modification as an RFI). [CTCS-21772]

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

18. **Issue:** In the rare event that the sponsor has created a draft Substantial Modification application and they respond to an RFI with the creation of a subsequent draft version of the initial application, the sponsor may be prevented from accessing their draft Substantial Modification application. [CTCS-22634]

    Workaround: The user should submit their RFI response before attempting to work further on their draft SM.

19. **Issue:** If the user adds the same substance to the application more than once and adds different details for the medical device per each substance, the system saves the medical device information under the first IMP. [CTCS-22802]

    Workaround: The medical device can be defined in the structured data only for the first IMP from the Role until this issue is fixed. The sponsor can provide additional information on the medical device in the documentation provided to the Member State Concerned.

20. **Issue:** When Overall Trial Status is "Halted" and a second draft Additional Member State concerned application is added, the translations added to the first Additional Member State concerned application are visible in the draft second Additional Member State concerned application. [CTCS-22653]

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

21. **Issue:** In the section "Full trial information", the system does not display the number of subjects per Member State concerned. [CTCS-22593]

    Workaround: The user should view the number of subjects per Member State concerned by clicking on the respective applications.

22. **Issue:** In the associated clinical trials, when adding a EudraCT trial, the sponsor's name is available in the search box but not when the information is saved in the general tab that contains the list of associated trials. [CTCS-22949]

    Workaround: This information can be consulted in CTIS if the search pop up is opened or directly in the clinical trials register of the EudraCT database (clinicaltrials.eu).

23. **Issue:** In the Part I study design period section, during the drafting of an application, the information related to the roles blinded to the participants' treatment is not displayed properly when the pop-up is opened again. The information is saved but is not visible in the period details pop-up. [CTCS-21055]

    Workaround: The blinded roles to the participants' treatment can be seen on the main screen, and actions can be completed, saved and confirmed on the main screen. Also, the roles are properly saved and displayed in the authority workspace.

24. **Issue:** In the medical condition when searching by MedDRA is it not possible to search by classification code. [CTCS-21992]

    Workaround: To search by classification code, the user needs to type a term name, then clear and then type again the classification code.

25. **Issue:** In the deferrals section after adding years and months when a draft application is saved, when returning to deferrals those fields do not become enabled and the user is unable to correct the values if needed. [CTCS-20652]

    Workaround: Set the deferral as date of decision and try again to set the date and months. That way the deferrals are again editable.

26. **Issue:** In a specific scenario where an additional Member State concerned application is created and the user attempts to submit it without a cover letter, when the user then uploads the cover letter and tries to submit it again, multiple invalid validation errors are displayed. [CTCS-21447]

    Workaround: It is possible to proceed by clicking on the submit button again.

27. **Issue:** When a non-SM Part I only is submitted with updates to documents in an authorised CT, the documents table in Full Trial Information does not show the documents added in Non-SM. [CTCS-22886]

    Workaround: It is possible to consult these documents in the application.

28. **Issue:** When the Part I document 'Content labelling of IMP's' is linked to a product, the document cannot be deleted. [SD-622201]

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

29. **Issue:** In a draft application, when the user clicks on the button 'Cancel' to cancel the application, a pop-up window is displayed which has an 'x' in the upper corner that allows the user to close the pop-up window. If the user clicks on that 'x' in the upper corner, the pop-up closes but also the draft application is automatically cancelled. In the same manner, the Amend role assignment action is confirmed when the user clicks to close the "Amend" confirmation pop-up window using the 'x'. [SD-637630] [CTCS-23076]

    Workaround: Users should not use the 'x' functionality but only click on 'cancel' or 'confirm' in the pop-up windows throughout the system.

30. **Issue:** When the user verifies that a draft application has all mandatory fields completed by clicking on the "Check" button, the system may not highlight some fields that have not been completed. [SD-635524] [CTCS-21199]

    Workaround: The user should verify manually that the fields for the telephone and the email address have been completed correctly for the third party organisation(s) included in the application. Also, the user should verify that they have provided the scientific and public contact points as these are mandatory fields.

31. **Issue:** When RFIs are raised during any evaluation process (validation, Part I or Part II) for any type of application, a response to RFI due alert is not generated for the sponsor to inform them that there are some days remaining to submit the response to the RFI. [CTCS-19185] [CTCS-18132]

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

32. **Issue:** When none of the Member States Concerned authorise a trial, and then one of them reverts the decision to "Authorise with Conditions", this information is not displayed in "Full trial Information" [CTCS-23307]

    Workaround: The user should navigate to the initial application to review the decision on the application.

33. **Issue:** The "CT Admin" and/or the "Application Submitter" for a specific trial cannot create substantial or non-substantial modification applications on the trial over which they have been granted the role. [SD-684187]

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

2. Authorisation and supervision of clinical trials

This section contains known issues related to the sponsor's activities for the application where the sponsor interacts with or responds to the Member State assessment of their application.

1. **Issue:** The user cannot associate Active Substance(s) in an unexpected event notification form. [CTCS-22816]

   Workaround: The user can use the free-text field "Other" to enter information about the Active substance(s).

2. **Issue:** The user can create a restart of trial notification for a halted trial due to an issue with the Benefit/Risk and submit it without having received an authorisation to re-start the trial. [CTCS-22403]

   Workaround: The user should not submit a re-start of trial notification if the halt was due to Benefit/Risk before they have received a positive Substantial Modification authorisation to re-start the trial.

3. **Issue:** In an initial application, where the Part II Assessment RFI has lapsed, the overall trial status may still display as "Under evaluation" when in fact the application has lapsed. [CTCS-22748]

   Workaround: The overall trial status will display as lapsed once the Reporting Member State concludes on the Part I assessment. Users are advised to always check the individual Member State concerned trial status.

4. **Issue:** When the CT admin provides the end date of the trial and the projected date for the summary results (which must be within 12 months of the end of the trial) as part of the end of trial notification for a mono-national trial and multinational trial, the system assumes that the results

will be provided over 12 months after the end of the trial and requests a justification for the delay. [CTCS-22888]

Workaround: The user can select the reason "other" and provide the justification that the results are to be provided within 12 months of the end of the trial.

5. **Issue:** When the user updates the 'Notification supporting documentation' document, the updated document is displayed in the previous version of the Unexpected Event notification. [CTCS-22635]

   Workaround: The user should navigate to the previous version to see any updated documentation, until this issue is fixed.

6. **Issue:** At this moment there is no possibility for the member state to disable to winter clock stop during the evaluation of a clinical trial application. [CTCS-11646]

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

3. Communication between Sponsor and Member States

This section contains the issues related to the RFI functionality that sponsor users might face when performing the "Change Application" process.

1. **Issue:** When the user changes the application in response to an RFI, more than one version of the 'Content labelling of the IMPs' document can be uploaded. The system should not allow this action and an error message should be displayed stating "Only one document version of a document can be uploaded in draft. Please remove the previous version before uploading a new one." However, this error message may not in fact display. [CTCS-22700]

   Workaround: Sponsor users should only upload the new version that they wish the Member State concerned to review.

2. **Issue:** In the response to an RFI, when the user changes the application and they lock the Member States concerned section, if the user navigates out of the application and navigates back to the Member State Concerned tab to unlock the section, the section cannot be unlocked. There is an error message displayed. [SD-645818]

   Workaround: Following the above steps the error will be displayed and the user will not be able to unlock the section. The user needs to wait approximately 45 minutes and log back into the application to be able to unlock the Member State Concerned tab without receiving the error message.

3. **Issue:** In the summary tab, under application details, the statement "considerations are pending to be consolidated" appears despite the fact that all consolidated considerations are already concluded. [CTCS-20694]

   Workaround: The message disappears when manually refreshing the page. The workflow is not impacted and it is possible to proceed with CT tasks. It is only the auto-refresh that is not present.

4. **Issue:** When the RFI is sent in Validation phase, in the Conclusion sub-section, it is displayed that the application is valid although the Reporting Member State has not yet submitted the conclusion to the validation and has yet to complete the task. [SD-671125] [CTCS-20643]

   Workaround: The user should ignore this label and proceed as normal.

5. **Issue:** After sharing an Ad-hoc assessment, if any changes are applied and a new RFI is created, the RFI number should be recorded with a sequential number unique to that RFI. However, this is not the case and the RFI number can be the same for distinct RFIs associated with the same ad hoc assessment. [CTCS-23085]

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

4. Locking mechanism

This section contains the known issues related to the lock mechanism and the problems with data/document refresh while there are parallel users working at the same time.

1. **Issue:** When two users are working at the same time and one of them locks one RFI and uploads one document, the other user is not able to see the uploaded document from the first user. [CTCS-22804]

   Workaround: The second user should wait for the first user to complete the task before refreshing the system (using F5) and then will be able to see the newly uploaded document.

5. Publication

This section describes the known issues related to the CTIS Public Portal and publication processes of trial-related information.

1. **Issue:** The supportive documentation submitted by the sponsor within the overall section of the RFI may not be published as per the system specifications. [CTCS-22012]

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

2. **Issue:** For all trials including several Member States concerned, the Reporting Member State is not identified in the public website. [CTCS-22892]

   Workaround: There is no workaround until the issue is fixed. Trial details for all Member States concerned and the reporting Member State are displayed on the public website, only the identification of which Member State is the reporting Member State is not displayed.

3. **Issue:** In some cases, authorised multi-national trials with two Member States concerned display with the status "Under evaluation" for one of the Member States concerned in the public portal. [CTCS-22806]

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

4. **Issue:** When clicking the "Last" page on Search results on the public portal, no clinical trials are displayed on-screen. [CTCS-22654]

   Workaround: Click on the actual page number instead of clicking on the "Last" button.

5. **Issue:** From 15.7.2022 information related to a limited set of clinical trials was prematurely published on the public website of the EU Clinical Trial Information System (CTIS) portal.

Based on available findings, it has been confirmed that information on requests for information or the reports related to Part I or Part II assessment were inadvertently made available on the public portal which is not in accordance with the established transparency rules. These documents were published earlier than the deferral rules allowed it. link

It has been confirmed that the protocol, the investigator brochure and Investigational Medicinal Product Dossier (IMPD) were not published, which is in accordance with the established deferral transparency rules. link

Immediate mitigation action was taken on 9 August 2022 to suspend access to the published trials on the public website of the EU CTIS portal. As a consequence, external users cannot currently view or search for public trials.

EMA is working to solve this issue and will reactivate the public search functionality of the euclinicaltrials.eu website once it is ensured that no publication in breach of the disclosure rules takes place again.

6. Other Issues

This section includes the known issues that do not fall under the above categories.

1. **Issue:** When the product name is longer than 100 characters the Annual Safety Report record cannot include the product and this prevents the validation of the Annual Safety Report and its submission. [CTCS-22893]

   Workaround: If this issue is encountered, please contact the service desk for a resolution.

2. **Issue:** When a user that is following the trial-centric approach creates a draft initial application, the user cannot assign roles to other users. [CTCS-22792]

   Workaround: It is recommended that the user creates the new organisations in the Organisation Management System (OMS). If the organisation is created through CTIS, the CT Admin will have to perform all the functions required within that Clinical trial.

3. **Issue:** The sponsor cannot create Organisation via CTIS when creating a new CT application, adding a clinical trial site or adding a legal entity. [SD-631869] [CTCS-23332]

   Workaround: It is recommended that the user creates the new organisations in the Organisation Management System (OMS).

4. **Issue:** The "search for organisation" feature, which is an integration with the Organisation Management System (OMS), **does not support non-Latin characters**. [CTCS-22798]

   Workaround: The users should search using the organisation ID code. Alternatively, the search can also be done using Latin characters only.

5. **Issue:** The user is not able to remove a location associated with an organisation by accessing the relevant functionality in CTIS. [CTCS-22595]

   Workaround: It is recommended to request any organisation change directly in the Organisation Management System (OMS).

6. **Issue:** When the user receives an email from CTIS, the EMA phone number and address are outdated [CTCS-22925].

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

7. **Issue:** In the Notice & Alert dashboard, when sorting by "Title of the Notice/Alert" some notices are displayed later than they should, according to the alphabetical order, as capitals are displaying before small letters. [CTCS-21212]

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

8. **Issue:** In the Notice & Alert dashboard advanced search, in the field "Title of the Notice/Alert" the predictive search is not returning dedicated workspace specific notices and alerts. [CTCS-19133]

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

9. **Issue:** Sponsor and Authority users navigate to Notices & Alerts Tab and search for the "Validation conclusion recorded" notice for Substantial Modification, then click on the notice and the user is not redirected to the correct section. [CTCS-23319]

   Workaround: The information can be consulted in the Evaluation section.