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Clinical Trials Transformation

Sponsor Frequently Asked Questions

Clinical Trial Information System (CTIS) Frequently Asked Questions (FAQs) on the Sponsor’s workspace

Version 1.0

The CTIS operational guidance for sponsors is the Sponsor Handbook. The present document complements it with the most Frequently Asked Questions (FAQs) on the topic.

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Clickable table of contents

Click on a section to jump to a stage of the trial lifecycle[1]. See also **6. CTIS training and support**

1. Pre-submission steps
- Access to EMA applications (CTIS, OMS, EV, XEVMPD)
- Sponsor and other organisation(s) registration in OMS
- Medicinal product registration in XEVMPD
- CTIS user management: Organisation-centric vs Trial-centric
- User roles in CTIS ('role matrix')

2. Apply for a CT authorisation
- CTIS publication rules
- Clinical trial application data fields and documents
- Form and Part I
- Protecting IMPD-Q confidentiality when the Sponsor is not the Product Owner or Substance Owner
- Part II
- Search, view and download a CT or CT application

3. Evaluation Phase
- Evaluation steps, outcome and timetable
- Notices and alerts
- Respond to a Request for Information (RFI)

4. Conduct a clinical trial
- Notify on trial events (e.g. CT start, start of recruitment)
- Create and submit an Additional Member State application (AM)
- Create and submit a Substantial Modification application (SM)
- Notify on Unexpected event, Urgent safety measure, Serious breach and Third-Country Inspectorate Inspection
- Submit an Annual Safety Report (ASR) and respond to ASR RFI

5. End the CT & submit results
- Notify the end of a CT
- Interim results, Summary of results and Lay person Summary of results
- Submit the Clinical Study Report (CSR) and update it

Open the Sponsor Handbook

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[1] Note that not all stages are reflected, only those ones where the most common FAQs were asked

Table of contents

Clickable table of contents 2

Introduction 10

1. Pre-submission steps 11

Access to EMA applications (CTIS, EV, XEVMPD) 11

1.1. How can users update their EMA account personal information? 11

1.2. What shall I do with my EMA credentials when I leave my company? 11

1.3. What to do if our Sponsor Admin or CT Admin leaves our company without terminating their account? 11

1.4. Can multiple CTIS users share the same email address (e.g., a shared mailbox)? 11

Sponsor and other organisation(s) registration in OMS 11

1.5. If a site was created locally in CTIS before it was available in OMS, does it need to be replaced in the application once it is available in OMS? 11

Medicinal product registration in XEVMPD 12

1.6. How can I obtain the EU Medicinal Product number (EU MP number)? 12

1.7. If a non-authorised medicinal product was already entered in XEVMPD by another sponsor, does a new sponsor need to enter it again? 12

1.8. If there is an authorised trial in CTIS using a certain investigational medicinal product (IMP), can another sponsor submit another trial application with the same IMP? 12

1.9. If the protocol identifies the IMP only by substance name and allows for different pharmaceutical forms and strengths, what should be selected from XEVMPD? Can the ATC code level be used? 12

1.10. How can a trial with individually manufactured products with different compositions (e.g. patient-specific peptides) be submitted in CTIS if each product must be entered separately in XEVMPD? 12

1.11. Which comparator(s) should be registered in CTIS if the protocol allows any standard-of-care medication without specifying the exact product(s)? 13

1.12. If an authorised active substance is used in a trial, do manufacturing-site changes require registering a new development medicinal product in XEVMPD? What about changes to the product itself? 13

1.13. XEVMPD appears to be accessible only via Windows. Is there a solution for organisations using Mac computers? 13

CTIS user management: Organisation-centric vs Trial-centric 13

1.14. Can an organisation switch from a trial-centric approach to an organisation-centric approach? 13

User roles in CTIS (‘role matrix’) 13

1.15. In the ‘User Administration’ tab, what is the difference between ‘employer’ and ‘organisation name’? 13

1.16. How can an organisation working for several sponsors (e.g. Contract Research Organisation, CRO) manage roles? 14

1.17. Can a user modify their own role in CTIS? 14

1.18. What happens if a user does not enter their employer details in CTIS? 14

1.19. Which trials can CT Admins see when having an 'all trials' scope? 14

1.20. If a Sponsor Admin leaves the organisation, how can a new Sponsor Admin be assigned? 14

1.21. What happens if a role is assigned under the wrong sponsor organisation? 14

1.22. Why do users with the Application Submitter role have no permissions to view or download the Part II Final Assessment Report (FAR)? ... 14

1.23. Is there an export functionality in the User Administration tab to view the assigned roles per user? ... 15

1.24. Is it possible to know the identity of sponsor users who created applications in CTIS? ... 15

2. Apply for a CT authorisation ... 15

CTIS publication rules ... 15

2.1. Which type of justification should be provided for the category type? ... 15

2.2. How should trials in public health emergency settings and trials in emergency situations be treated in terms of categorisation? ... 15

2.3. Can the Member States raise a Request for Information (RFI) on the trial category at time of validation or assessment part I of the initial application (IN)? ... 15

2.4. When will sponsors know if the proposed trial categorisation is accepted? ... 16

2.5. How can the trial category be modified after the submission of the IN? ... 16

2.6. Will MSC comment on the extent of the redaction done in the CTIS documents version ‘for publication’? ... 16

2.7. Will RMS/MSC compare document version ‘for publication’ vs ‘not for publication’? ... 16

2.8. How should documents with track changes be submitted to CTIS? ... 16

2.9. When submitting applications on a ‘historical’ trial, do sponsors need to ensure that clean versions of all documents not subject to publication are present in the system? ... 17

2.10. Which CTIS documents require a signature? ... 17

2.11. In which CTIS documents are personal data (name and surname of individuals) expected to be included? ... 17

2.12. If an MSC requests it, can the signature page of the protocol be submitted only as a ‘not for publication’ document in CTIS? ... 18

2.13. May sponsors mark/highlight personal data in documents ‘not for publication’? ... 18

2.14. May sponsors mark/highlight the text that they consider CCI in documents ‘not for publication’? ... 19

2.15. How can dose details be prevented from CTIS disclosure in case they are considered CCI? ... 19

2.16. Is it possible not to disclose patient-facing documents publicly? ... 20

2.17. What should I do if an application’s document that contains CCI and/or Personal data is published? ... 20

2.18. What should I do if an application’s structured data field (e.g. trial dose, or trial design) that contains CCI and/or Personal data is published? ... 20

2.19. In case any ‘for publication’ document is updated (e.g. through an SM), does any previous version of the same document remain public? ... 20

2.20. Does the submission of results documents trigger the publication of historical trials’ documents submitted prior to 18 June 2024? ... 20

Clinical trial application data fields and documents ... 21

2.21. What is the difference between the ‘Add document’ button on the right and the ‘Update’ icon? What about the ‘+’ icon? ... 21

2.22. How can the language of an already uploaded document be changed? ... 21

Form and Part I ... 21

2.23. Does the person named in the ‘Statement of compliance with Regulation (EU) 2016/679 (GDPR)’ need to be a CTIS user or have accepted the JCA? ... 21

2.24. What to do in case the inclusion and exclusion criteria are too long to be all included in the relevant CTIS application field? 21

2.25. When does a trial conducted in a third country need to be reported on EudraCT? And when on CTIS? 22

2.26. When a sponsor plans to include subjects under 18 years old in a trial submitted to CTIS, must the trial be covered by a PIP? 22

2.27. Why do the ‘Individual Participant Data (IPD) Sharing Statement’ fields appear blank? 22

2.28. What is the purpose of the section ‘Contact point for the Union’, and how should it be completed for sponsors established outside the EU? 22

2.29. How should a platform trial that includes both Clinical Trials of Investigational Medicinal Products (CTIMPs) and non-CTIMP arms be managed in CTIS? 22

2.30. Is it mandatory to enter dosage information for Auxiliary Medicinal Products (AxMPs), even when their dosage may be at the physician’s discretion? 23

2.31. How should dose units be reported for topical medicines in the product section of CTIS? 23

2.32. In case the product owner (PO)/Substance Owner (SO) of the IMP is also the sponsor of another ongoing EU/EEA trial, can the sponsor refer to that trial? 23

Protecting IMPD-Q confidentiality when the Sponsor is not the Product Owner or Substance Owner 23

2.33. In case the PO/SO of the IMP is not sponsor of an EU/EEA trial, how can IMPD-Q information be inserted in CTIS, without being visible to the sponsor of the trial? 23

2.34. How can an ‘IMPD-Q only application’ be created and submitted? 24

2.35. How is the process of evaluation of an IMPD-Q only application? 26

2.36. How can an SM affecting the quality aspects of the IMPD be created and submitted? 27

2.37. How can an AM to the Sponsor trial be created and submitted? 29

2.38. Can an IMPD-Q application be submitted for an ATMP and/or biological IMP? 31

2.39. If the PO/SO of an IMPD-Q only application has changed does the IMPD-Q only application need to be withdrawn and resubmitted, or is a new IMPD-Q only application needed? 31

Part II 31

2.40. Should a site suitability document be provided for each trial site, or can a unique document be submitted for the whole MSC? 31

2.41. How can satellite sites, where specific trial activities are performed, be inserted and linked to the main site in CTIS? 31

2.42. How can the planned number of subjects be inserted per site in CTIS? 31

2.43. Does CTIS provide an audit trail or tracked-change history for trial sites in Part II? .. 31

Search, view and download a CT or CT application 32

2.44. CTIS displays documents across multiple pages, which makes it difficult to search for specific documents. How will this be improved? 32

2.45. Is it possible for CTIS to provide a list of approved documents, to support TMF or Investigator Site File requirements? 32

3. Evaluation Phase 32

Evaluation steps, outcome and timetable 32

3.1. Why can Part II conclusions be issued before Part I conclusions? What is done to prevent such cases? 32

3.2. When an application is ‘Authorised with conditions’, what actions must the sponsor take to obtain full authorisation? 32

3.3. If a trial is ‘authorised with conditions’ in CTIS, does this status change to ‘authorised’ once the conditions are fulfilled? 33
3.4. For an initial Advanced Therapy Medicinal Product (ATMP) application affected by the winter clock stop, how should the maximum assessment timeline be calculated? 33
3.5. The maximum CTR timeline is 106 days (or 156 days for ATMPs), why do some assessments take longer? 33
3.6. Is the winter clock stop scheduled every year? What are the dates, and is it mandatory for all applications? 33
3.7. If questions arrive late on a Friday, does the assessment clock start immediately, or can it begin on the next working day? 33
3.8. Why is the timetable not modified when RFI responses are submitted earlier than the deadline? 33
3.9. Are shorter review periods of some MSCs reflected in the timetable? 33
3.10. If the approval date shown in CTIS differs from the date indicated in an attached conclusion letter, which date should be considered the official approval date? 34
3.11. Does the sponsor receive a decision letter when an application (IN, SM) is authorised? 34
Notices and alerts **34**
3.12. Is there any way to retrieve Notices & Alerts data (e.g., via Application Programming Interface (API) or export) for reporting purposes? 34
3.13. Tacit approvals do not generate a CTIS notice or alert. Can this be changed in the future? 34
Respond to a Request for Information (RFI) **34**
3.14. My trial has lapsed because I did not reply to an RFI as per deadline. How can I resubmit my application without having to do it all over? 34
3.15. Can emails requested by MSCs as part of an RFI be uploaded in CTIS? 35
3.16. If the maximum 12-days RFI response period is extended because the due date falls on a public holiday, CTIS may still issue an automated reminder earlier. To which date should the sponsor refer? 35
3.17. When downloading the RFI considerations, is it possible to see them categorised per topic? 35
3.18. Can RFI response timelines be extended? 35
3.19. Can additional rounds of Part I RFI be issued after the first RFI due date in CTIS? 35
3.20. Why may RFI response deadlines fall on national holiday in several EU countries, including the RMS and MSC? 35
3.21. What to do if due to an RFI, additional documents need to be updated that do not belong to the same part of the RFI (e.g., the Informed Consent Form needs updates as a consequence of protocol updates)? 36
3.22. When responding to an RFI, a new version of a document must be created and uploaded to replace the previous one. If a typo or another error is identified in the newly uploaded version, can I delete it and upload a corrected file? 36
3.23. Sometimes the RFI validation occurs more than 5 days after RFI response submission. How is this possible? 36
3.24. Can a sponsor contact the RMS (e.g., to ask questions about RFIs)? 36
3.25. Is it possible to remove a document that was submitted as a supporting document during an RFI response? 36
3.26. Can a Sponsor receive RFIs during the winter clock stop? And can an RFI deadline fall within this period? 36
3.27. For how long are all versions of RFIs accessible once the trial is ended? 37

3.28. When responding to multiple considerations within the same RFI, different considerations may require different updates to the same document, how should the sponsor proceed? 37
3.29. Can I answer each consideration with a unique document that includes the answers for all considerations received for the RFI? 37
3.30. Is there a limit to how many RFIs can be submitted during the validation and assessment phases? 37

4. Conduct a clinical trial 37

Notify on trial events (e.g., CT start, start of recruitment) 37

4.1. What happens if notifications are not entered within 15 days? 37
4.2. If no subject is included within two years of the IN authorisation, how can the sponsor avoid a trial expiration? 37
4.3. If a sponsor decides not to proceed with an authorised clinical trial, is a notification of End of Trial (EoT) required in CTIS? 37
4.4. In a complex cohort trial, should sponsors report the Start of Recruitment (SoR) and end of recruitment (EoR) per cohort? Or should sponsors only report the SoR of the first cohort and the EoR of the final cohort? 38
4.5. If the trial protocol includes a planned pause in recruitment, should it be reported to CTIS? 38
4.6. How can an EoR be reported after the EoT notification? For example, if recruitment remains open after the Last Patient Last Visit (LPLV), with no additional participants enrolled. 38
4.7. Should the EoR date be the same for all MSCs? 38
4.8. Is it mandatory to update the number of subjects per MSC after the EoR? 38
4.9. Are notifications for temporary halt or EoT required after an MSC imposed a corrective measure to suspend or revoke a trial? 38
4.10. Can a Temporary Halt notification be limited to recruitment only, or does it always apply to both recruitment and patients' visits? 39
4.11. If a study is temporarily halted, is it still possible to submit an SM, an AM or a NSM? 39
4.12. If a study is temporarily halted, is it possible to submit a safety notification (e.g., Serious Breach) or an inspection report? 39

Create and submit an Additional Member State application (AM) 39

4.13. Can sponsors create multiple AM drafts at the same time, or must they wait until one AM is authorised before creating another? 39

Create and submit a Substantial Modification application (SM) 39

4.14. When downloading SM documents from CTIS, the system exports all documents (including the IN and all previous SMs). Can the download be limited to only the documents authorised within the specific application? 39
4.15. Is it possible to submit a Part II SM (to add new sites in MSC) and an AM at same time? 39
4.16. When creating an SM, if sponsors choose 'Part I & Part II', are all MSCs automatically included? Can the selected MSCs be changed before submitting the SM? 40
4.17. Is it possible to create a draft Part I-only SM and later modify the application to Part I & Part II without cancelling the draft? 40
4.18. If a trial has ended in the RMS, but an SM Part I & Part II is planned in other MSCs, will the RMS be able to conduct the Part I assessment and raise validation and assessment RFIs? 40

Notify an Unexpected Event, an Urgent Safety Measure, a Serious Breach and a Third-Country Inspectorate Inspection 40

4.19. If a trial is halted for reasons unrelated to safety, should this still be reported as an urgent safety measure? 40

4.20. Is there any guideline or template to follow for the documents submitted with an Urgent Safety Measure or Unexpected Event notification? 40

Submit an Annual Safety Report (ASR) and respond to ASR RFI 41

4.21. Under Clinical Trials Directive 2001/20/EC (CTD) the clinical trial participants subject identifier (ID) was provided in ASRs. Is it correct that, under CTR, the subject ID should no longer be provided? 41

4.22. Can an ASR be submitted while other applications (e.g., SMs or AMs) are under assessment? 41

4.23. If a study is temporarily halted, is it still possible perform ASR submissions? 41

4.24. Can a department name and shared mailbox be used as the ASR contact details? What about contact details of a CRO? 41

4.25. After submitting an ASR in CTIS, is it possible to change it, or to upload additional documents? 41

4.26. What happens if a sponsor misses the deadline to respond to an ASR RFI? 42

4.27. Can other sponsors view other ASRs that were submitted in CTIS? 42

5. End the clinical trial and submit results 42

Notify the end of a CT 42

5.1. After submitting the EoT notification in CTIS, is it necessary to submit any further NSMs for site closures? 42

5.2. How is the overall EoT reported in CTIS? 42

5.3. Can a trial for which an EoT notification was submitted be re-opened? 42

Interim results, Summary of results and Lay person Summary of results . 42

5.4. What is the difference between interim and intermediate summary of results and when should they be submitted? 42

5.5. What are the requirements for posting interim results for trials that were transitioned from the Clinical Trial Directive? 43

5.6. Are interim results to be uploaded in the same section as the final summary of results? 43

5.7. Are interim results published on the CTIS public website? 43

Submit the Clinical Study Report (CSR) and update it 43

5.8. What should be the content of a CSR submitted to CTIS? 43

5.9. How to deal with the situation when the same CSR document is subject to transparency requirements in CTIS and under policy 0070? 44

5.10. In case the CSR review under Policy 0070 is not finalized within 30 days of the MA decision, what is the suggested wording for the 'for publication' version of my trial's CSR? 44

5.11. When should a CSR be submitted to CTIS but not under policy 0070? 45

5.12. When is the CSR submission functionality enabled in CTIS? 45

5.13. Does the submission of a CSR trigger the publication of other documents in CTIS? .. 45

5.14. What to submit to CTIS in case by the 30 days deadline only an interim CSR is available, because the trial is still ongoing? 45

5.15. Is it allowed to redact entire pages of the (interim) CSR to protect CCI? 45

5.16. Is the CTIS submission of a CSR required when submitted in the MAA as part of variations, line extensions, etc.? 45

5.17. In case the MAA is withdrawn, should the CSRs included in the MAA be submitted to CTIS? 46
5.18. If the MAA includes several versions of Clinical Study Protocol (CSP), SAP, CRF, should they all be submitted to CTIS together with the CSR? 46
5.19. If the initial MAA includes several versions of CSR (based on multiple Data Cut Offs), is only the current (latest version) of the CSR included in the initial MAA expected to be submitted to CTIS? 46
5.20. Is it possible to only submit to CTIS the version 'for publication' of the CSR? 46
5.21. How to approach blinding redactions when a study has not yet been unblinded at the time of publication? Can the applicant ask to defer the submission of a CSR to CTIS? 46
5.22. If the same clinical trial is referenced in two separate MAA procedures, should both CSRs be submitted to CTIS? 46
5.23. Can a CSR be submitted to CTIS in languages other than English? 47
5.24. If a trial was completed under the CTD in some Member States but was transitioned to CTIS for others, is the submission of the CSR expected? 47
5.25. Could documents such as study protocol that are submitted to CTIS when applying for a trial authorisation have a higher level of redaction compared to the same documents published later as part of a CSR on CTIS or under Policy 0070? 47

6. CTIS training and support 47

6.1. What are the resolution timelines for the CTIS Service Desk? 47
6.2. What is the best way for users to communicate their suggestions on CTIS future improvements to the EMA? 47
6.3. Does the EMA still recommend that users avoid working with CTIS during maintenance windows? 47

7. History and summary of changes of the Sponsor FAQs 48

Annex I: acronyms and definitions 49

Introduction

The EMA Clinical Trials Information System (CTIS) Sponsor Frequently Asked Questions (FAQs) provides clinical trial (CT) sponsors representing pharmaceutical industry, SME (small and medium-sized enterprises), academia, research organisations and other clinical trial sponsor organisations with answers to the most frequently asked questions they may have when creating and submitting clinical trial information to the Member States of the European Union/European Economic Area (EU/EEA) through the CTIS.

This document is based on questions frequently raised to EMA by sponsors during CTIS events such as Walk-in Clinics, Bitesize Talks, and through the EMA CTIS Service Desk. It serves as complementary document to the Sponsor Handbook, which is the main operational guidance for sponsors when using CTIS. Note that the following two documents may also be consulted when looking for answers to frequent questions on CTIS and the Clinical Trial Regulation (EU) No 536/2014, hereinafter ('CTR'):

- the Clinical Trial Regulation Questions and Answers (CTR Q&A)
- the FAQ document listed among the 'Key document list' of the Clinical Trials Coordination Group (CTCG) page

The CTIS processes which are the topics of the present FAQs document are displayed through the Clickable table of contents. The summary of changes of the present document can be found in chapter 7. . Annex I: acronyms and definitions can be consulted for acronyms and definitions.

Important notice: the views expressed in this FAQs document are not legally binding. The European Court of Justice is the only authority that can give an authoritative interpretation of Community law. This document aims at informing on the technical aspects of the CTR with a view to facilitating its implementation.

It is foreseen that this FAQs is updated on a regular basis as soon as new information becomes available.

1. Pre-submission steps

Access to EMA applications (CTIS, EV, XEVMPD)

1.1. How can users update their EMA account personal information?

Users can update their personal information (e.g., name, e-mail or other details) by submitting a request through the specific EMA Service Desk on the EMA Account details update. For more information, refer to the relevant Identity and Access Management (IAM) FAQs document.

1.2. What shall I do with my EMA credentials when I leave my company?

Any time you leave a company you first need to assign the appropriate roles to your replacements (e.g. Sponsor Admin, CT Admin). Afterwards, you may disable your current EMA account as it is linked to your current company. Proceed as follows:

1. Log in to EMA Account Management.
2. Go to 'Manage Identity'
3. Select 'Terminate Account'
4. Tick the user agreement and click 'Confirm'

Alternatively, you can raise a ticket to the EMA CTIS Service Desk to disable your account. Afterwards, when you join a new company, you must register a new EMA Account following the steps described in the 'Create an EMA Account' guide.

1.3. What to do if our Sponsor Admin or CT Admin leaves our company without terminating their account?

The former Sponsor Admin/CT Admin keeps receiving new Admins requests, and no one else in the company can get the Admin role, because the person receiving the requests cannot approve them. In such cases, the organisation should nominate an active employee to request the External Organisation Administrator role via EMA Account Management (see section 1.5.1.1. of the Sponsor Handbook). Once granted, the External Organisation Administrator can manage organisational roles, including Sponsor Admin and CT Admin assignments.

1.4. Can multiple CTIS users share the same email address (e.g., a shared mailbox)?

No. Each CTIS user must have an individual account linked to a personal email address. Shared mailboxes are not permitted.

Sponsor and other organisation(s) registration in OMS

1.5. If a site was created locally in CTIS before it was available in OMS, does it need to be replaced in the application once it is available in OMS?

No. If the site information was already submitted to CTIS and no changes have occurred on it since then, no update is required. The site details should only be updated if there is a change (e.g. a change in the site address). In such cases, the updated information must be retrieved from Organisation Management Service (OMS) and reflected in CTIS.

Medicinal product registration in XEVMPD

1.6. How can I obtain the EU Medicinal Product number (EU MP number)?

The EU MP number is a unique identifier (EV Code) assigned to a medicinal product within the XEVMPD database. Sponsors may obtain the EV Code of an authorised medicinal product directly through the XEVMPD user interface (see section 1.4 of the Sponsor Handbook), by contacting the product owner or by submitting a request to the XEVMPD Service Desk. The EV Code of a non-authorised ('development') medicinal product is visible in the XEVMPD database user interface to the organisation that submitted the product information in the XEVMPD and it is also made publicly available upon trial authorisation on the CTIS public portal for most of trial categories (refer to Table I of Annex I to the Guidance document on how to approach protection of personal data and commercial confidential information while using Clinical Trials Information System (CTIS)

1.7. If a non-authorised medicinal product was already entered in XEVMPD by another sponsor, does a new sponsor need to enter it again?

Yes. Each sponsor must enter information for the non-authorised ('development') medicinal product separately in XEVMPD. This is also in case the non-authorised product is used in a clinical trial that was already authorised in CTIS. The system assigns a different product number (EU MP number) for each sponsor, even if the product is identical. There is no automatic link between entries.

1.8. If there is an authorised trial in CTIS using a certain investigational medicinal product (IMP), can another sponsor submit another trial application with the same IMP?

If the IMP is an authorised medicinal product, the same IMP may be used in multiple clinical trials by different sponsors. There is no limitation in CTIS on the number of clinical trials that reference the same authorised IMP. From a CTIS functionality perspective, different sponsors may reference the same authorised IMP in separate clinical trial applications. Where a sponsor is not the product owner, any contractual or legal arrangements between the sponsor and the product owner must be addressed outside CTIS, as these are not governed by CTIS functionality.

1.9. If the protocol identifies the IMP only by substance name and allows for different pharmaceutical forms and strengths, what should be selected from XEVMPD? Can the ATC code level be used?

Yes. When adding an authorised product in CTIS, users may search in XEVMPD by product details, active substance, or ATC code. Where an authorised medicinal product available in the EU/EEA is used in a clinical trial, an ATC code (level 3, 4, or 5) linked to the active substance(s) may be selected to cover the permitted forms and strengths.

1.10. How can a trial with individually manufactured products with different compositions (e.g. patient-specific peptides) be submitted in CTIS if each product must be entered separately in XEVMPD?

For individually manufactured products, sponsors may reference the final product substance in CTIS instead of entering each individual starting material. Note that unauthorised products can only be entered in CTIS if both product and substance number are provided. See the principles described in *Process map 2* of the XEVMPD submission guidance for sponsors. Sponsors may also contact the XEVMPD Service Desk for guidance.

1.11. Which comparator(s) should be registered in CTIS if the protocol allows any standard-of-care medication without specifying the exact product(s)?

All IMPs, including comparators, must be registered in CTIS. Where standard-of-care medications is not specified in the protocol and the trial is multinational, sponsors may either: register the comparator at ATC code level, allowing each Member State to use the locally relevant standard-of-care option; or register all possible products and use the exclusion function to indicate which products apply to each Member State.

1.12. If an authorised active substance is used in a trial, do manufacturing-site changes require registering a new development medicinal product in XEVMPD? What about changes to the product itself?

Changing the manufacturing site of an already authorised product does not require a new product registration in XEVMPD. However, if the product itself is modified (e.g., changes to the pharmaceutical form, active substance, or its dosage) this is considered a new development product. In such cases, it must be registered in XEVMPD (refer to section 2.4.5.1. of the Sponsor Handbook).

1.13. XEVMPD appears to be accessible only via Windows. Is there a solution for organisations using Mac computers?

As of 10 February 2026, XEVMPD can be accessed by registered users via the **XEVMPDweb**, which is an upgraded version of the XEVMPD user interface . This upgraded version is a browser-based solution, which can be used in various browsers and operating systems without the need for ActiveX and/or Internet Explorer Tab. It is however recommended that users use Microsoft Edge or Google Chrome as these are, in line with the EMA's IT policy, the browsers for which support can be provided by EMA's IT department. Please note that the user interface is however not optimised for tablets and smartphones.

CTIS user management: Organisation-centric vs Trial-centric

1.14. Can an organisation switch from a trial-centric approach to an organisation-centric approach?

Yes. An organisation may switch from the trial-centric approach to the organisation-centric approach at any time (refer to section 1.5. of the Sponsor Handbook). After the change, all trials can be overseen and managed centrally under one administration.

User roles in CTIS (‘role matrix’)

1.15. In the ‘User Administration’ tab, what is the difference between ‘employer’ and ‘organisation name’?

When Administrators access the ‘User Administration’ tab when assigning roles as per section 1.7.1. of the Sponsor Handbook, they see that for each person the ‘employer’ and the ‘organisation name’ are specified. The ‘employer’ is the organisation the person works for (i.e. the one with which the person has a formal working relationship). The ‘organisation name’ is the authority/sponsor organisation that assigns the person a role to conduct clinical trial activities on their behalf. The employer and the organisation may be the same entity or different ones.

1.16. How can an organisation working for several sponsors (e.g. Contract Research Organisation, CRO) manage roles?

Users employed by a CRO must specify their CRO as their employer in CTIS and can be assigned roles for multiple sponsors. CTIS supports managing different affiliations through role requests and appropriate role-scope assignment. Any user, including those working at CROs, can request a role to work in a trial in CTIS. The request must then be processed by the relevant Sponsor Admin or CT Admin, see section 1.7.1. of the Sponsor Handbook.

1.17. Can a user modify their own role in CTIS?

In principle, users cannot modify their own roles. They may request new roles, but these must be approved or assigned by an administrator. However, users with CT Admin - trial level role can revoke their own role on the specific trial.

1.18. What happens if a user does not enter their employer details in CTIS?

Missing employer information makes it difficult for administrators to confirm a user's organisational affiliation, particularly in CRO environments. Users must enter their actual employer (e.g., the CRO), not the sponsor they are working on behalf of.

1.19. Which trials can CT Admins see when having an 'all trials' scope?

CT Admins with the scope 'All Trials' can see all clinical trial applications under the relevant sponsor, including those created by other CT Admins.

1.20. If a Sponsor Admin leaves the organisation, how can a new Sponsor Admin be assigned?

It is advised to have at least two Sponsor Admins per organisation. If only one was in place and that person leaves, a new Sponsor Admin must be registered through EMA's IAM system (refer to section 1.5.1.1. of the Sponsor Handbook). See also question 1.2. on actions to take when leaving the company.

1.21. What happens if a role is assigned under the wrong sponsor organisation?

Administrators must select the correct sponsor when assigning roles, particularly in CROs working with multiple organisations. An incorrect sponsor assignment can cause unintended disclosure of confidential information, including personal data.

1.22. Why do users with the Application Submitter role have no permissions to view or download the Part II Final Assessment Report (FAR)?

This is a matter of how user permissions are defined and implemented in CTIS. Application submitters can view only the Part I FAR except quality. Thus, this user cannot view the Part I FAR Quality and Part II FAR. A possible solution is to provide the user with an additional role that allows to view and download the Part II FAR (see section 1.6.4. of Sponsor Handbook).

1.23. Is there an export functionality in the User Administration tab to view the assigned roles per user?

No, an export function is not available at the moment, it is planned as a future improvement. Currently, only a manual review of the roles is possible.

1.24. Is it possible to know the identity of sponsor users who created applications in CTIS?

No. Due to General Data Protection Regulation (GDPR) requirements, CTIS does not disclose user-specific details. In addition, the EMA CTIS Service Desk cannot provide information on which user initiated a draft application for an organisation, or which user submitted the application. Sponsor users should instead contact their Sponsor Admin or CT Admin for assistance.

2. Apply for a CT authorisation

CTIS publication rules

Most of the following FAQs are taken from the 'Q&A on the protection of Commercially Confidential Information and Personal Data while using CTIS' (EMA/898965/2022, version 2.2 of 13 December 2024). Some FAQs were merged or slightly rephrased for clarity purposes. The present section of this FAQs fully replaces the mentioned Q&A, and should be read in conjunction with the Guidance document on how to approach protection of personal data and commercial confidential information while using Clinical Trials Information System (CTIS) (hereinafter 'Guidance document') and its Annex I.

2.1. Which type of justification should be provided for the category type?

The RMS/MSC(s) will consider the justification provided for the trial category, based on the characteristics of the trial, as the basis for evaluating the appropriateness of the category assigned. The justification should be in line with definitions provided in Table V of Annex I to the Guidance document. Sponsors should consider that when a protocol sets out a multiphase or adaptive design that falls in both category 1 and 2, the trial should be treated according to category 2.

2.2. How should trials in public health emergency settings and trials in emergency situations be treated in terms of categorisation?

As provided in Article 17(1) of Regulation (EU) 2022/123, for clinical trials in public health emergency settings[2], the protocol should be made public at the time of the start of trial and the summary of results within a timeline set by the EMA. The publication of these documents cannot occur at a later point in time. In principle, clinical trials in emergency situations[3] fall either under category 2 or 3 (therapeutic intent), since for these trials Article 35 (1)(b) of the CTR requires scientific grounds for individual clinically relevant benefit for subjects.

2.3. Can the Member States raise a Request for Information (RFI) on the trial category at time of validation or assessment part I of the initial application (IN)?

It is expected that the Reporting Member State (RMS)/Member State Concerned (MSC) could comment on whether the assigned trial category is appropriate, based on the information on the trial phase that is provided by the sponsor throughout the IN. An RFI on the trial category can be raised at any time during validation and assessment of Part I; however, it is expected to be raised by the RMS primarily at the time of Part I assessment.

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[2] Clinical trials with medicinal products with the potential to address public health emergencies.

[3] Emergency situation: first trial specific intervention occurs before signing the informed consent.

Currently, trial categorisation can only be set by the sponsors in an IN. **Once the IN has been authorised it will not be possible for the sponsor to modify the trial category with subsequent applications**, including a substantial modification applications (SMs), see question 2.5. .

2.4. When will sponsors know if the proposed trial categorisation is accepted?

Sponsors will know that a category is granted if no RFIs are raised in that respect during evaluation (validation/assessment Part I) or if the issues raised with RFI are addressed in a satisfactory fashion by the sponsor (e.g., no further issues raised on the matter). There is no specific mechanism to flag in the system that the trial category is accepted, it is part of the overall application evaluation.

2.5. How can the trial category be modified after the submission of the IN?

A change of trial category may be accepted if it is explicitly requested in a RFI issued during the assessment of the IN. Currently it is not possible to change the trial category through a SM: once the IN is authorised, it is no longer possible to change the category of a trial.

2.6. Will MSC comment on the extent of the redaction done in the CTIS documents version 'for publication'?

Sponsors are responsible for the level of redaction applied in the documents uploaded in CTIS. However, in addition to the scientific and regulatory review of the documentation provided in a CTA or other documents, RMS/MSC might occasionally comment on the extent of the redaction applied by the sponsor to ensure that the principles of transparency are followed[4].

2.7. Will RMS/MSC compare document version 'for publication' vs 'not for publication'?

RMS/MSC are not responsible for verifying the level of redaction applied by sponsors in the documents uploaded in CTIS. However, they might occasionally comment on the extent of the redaction applied by the sponsor and compare the two versions to ensure that the principles of transparency are followed. Protection of CTIS personal data is described in the CTIS Joint controllership arrangement (JCA). In principle, Commercially Confidential Information (CCI)-related redactions should be performed taking into account the timelines for disclosure of each document, that vary depending on trial development phase and population age, as defined in the revised CTIS transparency rules. Specific guidance on the management of personal data and CCI in CTIS is provided in the Guidance document and its Annex I.

2.8. How should documents with track changes be submitted to CTIS?

Documents with track changes should be uploaded in CTIS to clearly illustrate the scope of a revision applied in a document as a reply to a RFI or as part of an SM. **Users should use the '+' icon** in order to upload them (not the 'add document' button), since they are associated to documents already present in the application. In case of documents subject to publication, the 'not for publication' version

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[4] Article 94 (2)(a) of the Regulation (EU) No 536/2014 refers to application of penalties including non-compliance with the provisions laid down in the Regulation on submission of information intended to be made publicly available to the EU database.

(without track changes and unredacted) of the relevant 'for publication' document should also be uploaded in the same way (see question 2.21.).

2.9. When submitting applications on a 'historical' trial, do sponsors need to ensure that clean versions of all documents not subject to publication are present in the system?

Trials submitted before 18 June 2024 could be showing only documents in track changes for those type of documents that are no longer subject to publication, as described in the quick user guide: the clean versions of those documents might have been in the corresponding 'for publication' placeholders, which are no longer available.

When submitting an SM, a Non-Substantial Modification application (NSM) or an Additional Member State application (AM), sponsors are not requested to re-upload the clean versions of those documents 'not for publication' that are no longer available. Sponsors should upload only the new clean version and corresponding track-changes version of those documents that have been modified as part of the application. Sponsors should also not submit any other previous versions of deleted documents.

Note that, however, in case those clean versions of deleted documents would be necessary to assess the new documents in scope of the application, MSCs may request to provide them within the application.

2.10. Which CTIS documents require a signature?

Signatures should never be included in documents submitted to CTIS that are subject to publication.

With regards to documents that are not subject to publication, a signature should be provided for the Qualified Person (QP) declaration for good manufacturing practice (GMP) (Part I) and the Suitability of sites document (Part II). In addition, Member States specific requirements for signatures include:

- **Hungary:** Suitability of the principal investigator documents (CV)
- **Portugal:** Suitability of the principal investigator documents (CV and declaration of interests), Proof of insurance certificate
- **Romania:** Proof of payment
- **Slovakia:** Suitability of the principal investigator documents (CV and declaration of interests)

Further clarification on this matter are provided in question 1.4 of the CTR Q&A: 'Importantly, electronic submission of the CTA to CTIS by the sponsor is regarded as equivalent to signing the document in accordance to Annex I.3. CTR is a regulation, which is directly applicable and ensures complete harmonisation of the sector, national laws should be set out to support its full implementation'.

Sponsors should be mindful of the requirements for signed documents that are part of the trial master file (TMF), as applicable.

Further information on the management of personal data in CTIS is provided in the Guidance document and its Annex I.

2.11. In which CTIS documents are personal data (name and surname of individuals) expected to be included?

Personal data (e.g., names and surnames, and also contact details) should be generally included exclusively in those CTIS documents that are not subject to publication as per the Revised CTIS transparency rules. Personal data should be normally redacted if included in documents that are subject to publication. Exceptions apply to those data that are disclosed as a structured data field in the CTIS public portal (i.e., Principal Investigator's name and surname): refer to section 3.3.1 of the Guidance document.

In the documents that are not subject to publication, principles of data minimisation apply to personal data (see section 3.4 of the mentioned Guidance document). However, these data could be needed during the scientific and regulatory review conducted by the MSC and therefore the following names and surnames of certain roles are expected to be included:

- Principal investigator on the CV
- QP on the GMP declaration
- The person issuing the site suitability document
- Data Safety Monitoring Board (DSMB) composition on the charter or applicable document
- Minimum amount of sponsor staff in the protocol
- GDPR compliance statement to be provided under the CTIS 'form' section, in line with available template

Personal data of trial participants may only appear, as applicable, in CTIS document versions 'not for publication' and encompass personal data in a pseudonymised format (e.g., clinical trial subject ID) as well as indirect identifiers such as weight, height, age, gender, etc. These personal data are to be anonymised in the document version 'for publication' (refer to section 3.3.2 of the Guidance document).https://accelerating-clinical-trials.europa.eu/document/download/6a0b836f-4779-4bb9-9584-1ce504a9ae38_en?filename=guidance-document-how-approach-protection-personal-data-commercially-confidential-information-while_.pdf

2.12. If an MSC requests it, can the signature page of the protocol be submitted only as a 'not for publication' document in CTIS?

Yes, if requested by a MSC, the signature page may be submitted exclusively as a 'not for publication' document. Note that signature pages are generally not required to be submitted, in line with the data minimisation principles outlined in the Guidance document and with question 1.4 of the CTR Q&A.

2.13. May sponsors mark/highlight personal data in documents 'not for publication'?

No. Currently, in the document version 'not for publication' it is not necessary to mark those personal data that were anonymised/redacted in the version 'for publication'.

In the document version 'for publication' any personal data needs to be anonymised/redacted, as applicable, in line with section 3 of the Guidance document.

In all documents that are not subject to publication, in line with the data minimisation principle (see section 2 of the Guidance document), sponsors should limit the presence of personal data to only those ones that are necessary for MSC(s) assessment (see question 2.11.).

2.14. May sponsors mark/highlight the text that they consider CCI in documents ‘not for publication’?

No, this is not necessary. However, in case the sponsors wish to flag what they consider CCI in the documents ‘not for publication’, they could place red border boxes around the text as indicated below. The corresponding text in the document version ‘for publication’ should be redacted with black background boxes. Redacted text and the black background redaction box (that covers the redacted text) should neither be searchable nor allow further editing. This is not mandatory and can be done only for information to the Member State.

Example:

a) Documents ‘not for publication’ mark in a text content that is considered CCI with red border boxes

b) Documents ‘for publication’ [redacted]

It is important that the version of the documents ‘not for publication’ is readable and ready to be used for MS assessment.

Application of redaction in the version ‘for publication’ should be done with scrupulous judgment. It should be considered that extensive redaction in the document versions ‘for publication’ would go against the spirit of transparency of the CTR. The redacted documents have to remain meaningful to the public, including potential trial participants and health care professionals.

2.15. How can dose details be prevented from CTIS disclosure in case they are considered CCI?

Medicinal products’ and active substances’ details of trials falling into category 1, as well as those of integrated phase 1 and 2 trials falling under category 2 are subject to publication 30 months after the end of the trial in the EU/EEA, in line with the Revised CTIS transparency rules.

In some instances, for any trial category dose details may be considered to be CCI. In such instances, sponsors can include ‘dummy data’ (e.g. 00 digits) in the related structured data field(s) of CTIS.

The full information on the posology should, however, be provided to the Member States for assessment in the document version ‘not for publication’ and can be redacted in the corresponding documents to be published.

This approach would be acceptable only on **justified grounds,** i.e., when the sponsor proves that the specific information on the posology is not in the public domain and constitutes patentable matter, the disclosure of which before a patent application is filed (typically, after the completion of the trial and during the trial readout) would jeopardise its protection.

The grounds for considering dose details as CCI should be clearly documented in the cover letter of the application.

Note that sponsors should not include CCI or personal data in any other CTIS free text fields that are subject to publication as per column H of the CTIS applications fields document and the Notifications, ASR and Results document; the use of ‘dummy data’ (e.g. XX) is possible, if needed and it does impact the understanding of the document’s content.

2.16. Is it possible not to disclose patient-facing documents publicly?

In some cases, written agreements between the sponsor and the third-party service provider expressly establish that patient facing documents (e.g., patient questionnaires) cannot be disclosed publicly. In those cases, it is possible for the sponsor to upload in the 'for publication' placeholder a document where a justification for not disclosing the patient facing document is provided. In the placeholder 'not for publication' the document with its full content should be uploaded to allow the Member State(s) assessment.

2.17. What should I do if an application's document that contains CCI and/or Personal data is published?

You are responsible to replace the relevant 'for publication' document with a document that can be disclosed in public view as soon as possible. To do so, you can:

- **create and submit a NSM**: the NSM will replace the previous application overnight; for a quicker publication, you may contact the EMA Service Desk, once you have submitted your NSM.
- *if it is not possible to submit a NSM due to an ongoing assessment or other draft applications*, you may contact the EMA Service Desk for a provisional arrangement. In this case, note that you are still required to perform the relevant update through the draft/ongoing application (e.g. RFI response) or through a subsequent NSM as soon as it becomes feasible; after this, you will need to inform the EMA Service Desk that such update was performed.

To perform the update, you can use the 'update' functionality of the relevant 'for publication' document that you need to replace (see section 2.3.1.1. of the Sponsor Handbook), adding an explanation in the 'comment' section. In case, instead, you would like to remove the 'for publication' document to replace it, note that all the 'not for publication' versions of the document need to be removed (refer to section 5 of the List of known issues and workarounds for specific instructions).

2.18. What should I do if an application's structured data field (e.g. trial dose, or trial design) that contains CCI and/or Personal data is published?

Consult columns O and P of the CTIS applications fields document to see through which kind of application the relevant data can be modified. If a NSM is sufficient, refer to question 2.17. If an SM is necessary, you may contact the EMA Service Desk for a provisional arrangement while you modify your data through the SM.

2.19. In case any 'for publication' document is updated (e.g. through an SM), does any previous version of the same document remain public?

Only the latest submitted version of each trial's application and therefore 'for publication' document is made publicly available on the CTIS public portal. This applies to the IN as well as to any SM or NSM.

2.20. Does the submission of results documents trigger the publication of historical trials' documents submitted prior to 18 June 2024?

No. The submission of layperson summary of results, of summary of results and/or the Clinical Study Report (CSR) does not trigger the publication of clinical trial application documents that were submitted before the implementation of the revised CTIS transparency rules (18 June 2024). Those documents will remain unpublished.

Clinical trial application data fields and documents

2.21. *What is the difference between the 'Add document' button on the right and the 'Update' icon? What about the '+' icon?*

When drafting any kind of application (sections 2.3., 4.2, 4.3, 4.8 of the Sponsor Handbook):, the **'Add document' button should only be used to upload a new document** for which no earlier version is already present in the trial's dossier. A document added through the 'Add document' button should not replace a previously submitted document. The **'Update' icon should be used for uploading a new version of an existing document** (that was previously submitted) when replacing the document during an RFI reply (section 3.3.1 of the Sponsor Handbook) or during an SM/NSM (sections 4.3, 4.8 of the Sponsor Handbook): for this reason, only one single document can be uploaded as 'draft' in a specific slot.

The '+' icon that is displayed on the right of those documents subject to publication allows sponsor users to upload a 'not for publication' version of a document that was uploaded 'for publication': this version should only uploaded in case the 'for publication' version contains redacted CCI and/or Personal data that are to be disclosed to the MSC(s) to allow a proper assessment (for example, track changes versions of a document modified through an SM). More information on cross systems bottons and icons can be found in section 2.3.1. of the Sponsor Handbook.

2.22. *How can the language of an already uploaded document be changed?*

Once a document is uploaded in CTIS, its language can be changed through clicking on the pencil ('Edit') icon. Note that this cannot be done when responding to an RFI: in this case, the language can be updated when updating documents through a subsequent SM/NSM. If a document contains multiple languages, users are advised to include a brief description of the document content and clearly specify all languages included in the comments field.

Form and Part I

2.23. *Does the person named in the 'Statement of compliance with Regulation (EU) 2016/679 (GDPR)' need to be a CTIS user or have accepted the JCA?*

No. Although the template mentioned in section 2.2 of the Sponsor Handbook requires a named person, this individual does not need to be a CTIS user or have accepted the JCA. It is for the sponsor to determine, in accordance with its internal procedures, who is an appropriate representative to be named on the GDPR statement, and to mention this person in the document.

2.24. *What to do in case the inclusion and exclusion criteria are too long to be all included in the relevant CTIS application field?*

The list of inclusion and exclusion criteria can be extensive, and it may not always be feasible to include all criteria in the structured CTIS application fields. Sponsors may therefore include key inclusion and exclusion criteria in the relevant CTIS application field, based on their assessment of which criteria are essential to highlight. All inclusion and exclusion criteria should be fully described in the submitted protocol.

2.25. When does a trial conducted in a third country need to be reported on EudraCT? And when on CTIS?

A trial conducted **solely** in a country that is not in the EU/EEA (third country) needs to be reported in EudraCT if it is part of an agreed Paediatric Investigation Plan (PIP) or is in scope of Article 46 of the Paediatric Regulation (EC) No 1901/2006. If a PIP/Art 46 trial is conducted in the EU/EEA as well as outside of the EU/EEA, this trial needs to be reported on CTIS only. More information is available in section 'Questions about third country trials' of the EudraCT FAQs.

2.26. When a sponsor plans to include subjects under 18 years old in a trial submitted to CTIS, must the trial be covered by a PIP?

A paediatric trial is any trial that includes at least one subject under 18 years old. Under Regulation (EC) No 1901/2006, a PIP (or a waiver) is required for any EU marketing authorisation application (MAA), line extension, or new indication for product that could potentially be used in the paediatric population. For further information on PIPs, refer to the Paediatric investigation plans EMA webpage. A sponsor conducting clinical trials intended to support a marketing authorisation and including subjects under 18 years old should generally be covered by an agreed or approved PIP, unless a waiver or deferral applies. Sponsors should ensure that the PIP decision (including any waiver or deferral) is reflected in CTIS by completing the 'Paediatric information' section of the application and referencing the relevant EMA decision number.

2.27. Why do the 'Individual Participant Data (IPD) Sharing Statement' fields appear blank?

The 'IPD Sharing Statement' fields are a requirement of the WHO Trial Registration Data Set which was introduced in CTIS on the 30 April 2024 (see section 2.2 of the Sponsor Handbook). For applications authorised before the introduction of these fields, those fields appear as blank: for those trials, the fields can be updated through the submission of a NSM. Further details on this field are provided in section 2.2 of the Sponsor Handbook and in the CTIS applications fields document.

2.28. What is the purpose of the section 'Contact point for the Union', and how should it be completed for sponsors established outside the EU?

These are the contact details that need to be used by the EU/EEA regulatory authorities in case of required contact with the sponsor. This contact point should always be in the EU/EEA, including for sponsors that are not established in the EU/EEA. As authorities may use this information to contact sponsors about ongoing applications, including time-sensitive topics, it is advised that the provided email address is actively monitored and can respond quickly.

2.29. How should a platform trial that includes both Clinical Trials of Investigational Medicinal Products (CTIMPs) and non-CTIMP arms be managed in CTIS?

Non-CTIMP arms cannot be assessed within CTIS. The CTR applies only to those parts of a trial that meet the definition of a clinical trial, namely the investigation of a medicinal product. Treatment modalities that do not involve an IMP fall outside the scope of the CTR and are therefore assessed under the relevant national or EU legislation applicable to those interventions. Depending on the Member State, the oversight of these non-CTIMP components may be conducted by the same or by separate national competent authorities (NCAs) and/or ethics committees (ECs).

2.30. Is it mandatory to enter dosage information for Auxiliary Medicinal Products (AxMPs), even when their dosage may be at the physician's discretion?

Yes. When AxMPs are required to be recorded in CTIS, all mandatory AxMP fields must be completed, irrespective of physician's discretion. There is no system workaround to omit these fields, as their completion is required to ensure traceability within CTIS. Sponsors should consult the Recommendations on the use of Auxiliary Medicinal Products in Clinical Trials to determine when an AxMP is required to be included in CTIS.

2.31. How should dose units be reported for topical medicines in the product section of CTIS?

Currently, 'other' is the only available dose unit for topical medicines. EMA has acknowledged this limitation and an improvement on this might be added in the future.

2.32. In case the product owner (PO)/Substance Owner (SO) of the IMP is also the sponsor of another ongoing EU/EEA trial, can the sponsor refer to that trial?

If the PO/SO of the new IN ('daughter trial') is also a sponsor of another clinical trial ('mother trial') with the same IMP that is ongoing under the CTR, and those criteria listed in question 2.15 of the CTR Q&A are met (e.g. similar population), a cross-reference to the mother clinical trial should be made via the function 'Associated clinical trials'. Note that it is required that all MSC(s) of the daughter trial are also MSC(s) of the mother trial. In addition, in case there are various products in a trial, the sponsor can cross-reference medicinal products from different trials in the same application. They do not need to cross-reference a trial that has all the same products.

Protecting IMPD-Q confidentiality when the Sponsor is not the Product Owner or Substance Owner

CTIS does not include the functionality for the submission of a quality document part of the IMPD by a third party independent from the sponsor's CTIS user administration. The present section needs to be read in conjunction with question 2.15 of the CTR Q&A. It contains instructions to follow to address the case where the sponsor is not the product owner (PO) or substance owner (SO) of the IMP and should not have access to the quality IMPD (IMPD-Q), or to any associated documents and considerations raised by MSC(s) via requests for information (RFI) in order to protect CCI belonging to the PO/SO. Note that that for biological products the IMPD-Q only approach is not possible: see question 2.38.

2.33. In case the PO/SO of the IMP is not sponsor of an EU/EEA trial, how can IMPD-Q information be inserted in CTIS, without being visible to the sponsor of the trial?

In case the PO/SO is not a sponsor of a clinical trial in the European Economic Area (EEA), two applications can be submitted in parallel to CTIS:

- The **sponsor submits the Sponsor trial IN application excluding** all data and documents related to the **IMPD-Q** part
- The **PO/SO creates** and manages a so called '**IMPD-Q only application'** which is then submitted as an IN Part I only, see question 2.34.

Both applications need to be submitted at the same time, refer to point 125 of the CTR Q&A. The **IMPD-Q only application** is complementary to the Sponsor trial IN application submitted by the sponsor, and it **is not** to be considered as **an application** per se. After conclusion of Part I assessment, the IMPD-Q only cannot be subject to issuing a decision since it **does not include part II in the application**, and, consequently, **is not made public**.

Note that in case the IN application of the Sponsor trial would need to refer to more products/substances for which the quality part is commercially confidential, and all those products/substances belong to the same PO/SO, it is possible for the PO/SO to include more IMPD-Q products in the same IMPD-Q application.

2.34. How can an 'IMPD-Q only application' be created and submitted?

The PO/SO should first be registered in Organisation Management Service (OMS), in order to be able to create an IMPD-Q application as IN: see section 1.2 of the Sponsor Handbook. Afterwards, the PO/SO can refer to section 1.5.1.1 of the Sponsor Handbook to know how to gain the Sponsor Admin user role, and to section 1.7.1. how to assign themselves the CT Admin user roles, and to the sponsor the 'Application submitter' role.

The below steps describe how to create and submit an 'IMPD-Q only application'. Those steps can all be performed with two operational models:

- Solely by the PO/SO with a 'CT Admin' user role, or
- Collaboratively between PO/SO and Sponsor namely by:
    - A PO/SO user (responsible for filling in the IMPD-Q and quality-related information in the IMPD-Q only application) and
    - A sponsor user (responsible for all remaining parts and submitting the IMPD-Q only application) with an 'Application submitter' role assigned by the PO/SO user.

This latter operational model is possible, since the 'Application submitter' role cannot view any data fields or documents related to 'Quality', but can submit them, ensuring that the PO/SO's confidential information remains fully protected. More information on roles can be found in section 1.6 of the Sponsor Handbook. Note that assigning the sponsor an 'Application submitter' role is not mandatory and it depends on the agreements between sponsor and PO/SO.

	Step to perform on the IMPD Q only application	PO/SO needed Role(s)	*Sponsor needed Role (optional)*
1.	The **PO/SO user registers in OMS**: see section 1.2 of the Sponsor Handbook		
2.	The PO/SO user gains the **role** of 'Sponsor Admin' and assigns a PO/SO CT Admin, following the organisation centric approach (see section 1.5.1 and 1.7.1. of the Sponsor Handbook)	Sponsor Admin	
3.	**PO/SO CT Admin creates a new IN with 'IMPD-Q only application' in the title**, and under their ORG-ID as 'Sponsor' (see section 2.3 of the Sponsor Handbook)	CT Admin (all trials)	

	Step to perform on the IMPD Q only application	PO/SO needed Role(s)	*Sponsor needed Role (optional)*
4.	*If the collaborative operating model is needed (see above explanation), PO/SO CT Admin assigns the Sponsor with the 'Application Submitter' role for the created IMPD-Q only application*	*CT Admin (all trials)*	
5.	**PO/SO or the Sponsor's Application submitter fills in the IN Form, MSC, Part I (excl. Q-IMPD)** Refer to instructions provided in paragraph 125 of CTR Q&A on how to fill in data fields and documents for this IN and consult the 'Best practice guide naming of documents in CTIS', available in the 'Key document list' section on the CTCG page. Of note: - *in case the Sponsor is granted the 'Application submitter' role for the IMPD-Q only application*, the PO/SO should not include any product confidential information in these parts of the application, as they would be visible to the Sponsor - the **cover letter** should not mention any confidential product details, but a statement as specified in point 125 of CTR Q&A - **mandatory information that should be completed is listed in point 125 of CTR Q&A**. All other mandatory fields should be completed with 'IMPD-Q-only' for text fields or '0' for numeric fields - placeholder documents should be used for all mandatory documents that are not applicable - in Part I '**Sponsor' section contact details** of the PO/SO should be provided. Note: although the contact information in this section should be the ones of the PO/SO, the PO/SO does not become a sponsor under the CTR. Their responsibilities are limited to those for the IMPD-Q and the correspondence with the MSs, as defined in the contractual agreement with the sponsor. Therefore, in case the PO/SO is not established in the EU/EEA, an EU legal representative is not required. **Part II of the IN is NOT filled in**.	CT Admin	*Application Submitter (specific trial)*
6.	**The PO/SO fills in the IN Part I (Q-IMPD)** Refer to instructions provided in **paragraph 125 of CTR Q&A on how to fill in data fields and documents** for this IN and consult the 'Best practice guide naming of documents in CTIS', available in the 'Key document list' section on the CTCG page. Of note: *in case the Sponsor is granted the 'Application submitter' role for the IMPD-Q only application*, in addition to the IMPD-Q data and documents, the PO/SO must upload **any product document other than the IMPD-Q** (e.g. Manufacturing and Importation Authorisation, or in the QP declaration), also under the IMPD-Q	CT Admin or IMPD-Q Preparer	

	Step to perform on the IMPD Q only application	PO/SO needed Role(s)	*Sponsor needed Role (optional)*
	document type, and **not under their standard CTIS document types**, when they contain or constitute product confidential information.		
7.	PO/SO or the Sponsor's Application submitter submits the IMPD-Q only application **as a Part I only application** on the same day as the application for the Sponsor trial.	CT Admin	*Application Submitter (specific trial)*

2.35. How is the process of evaluation of an IMPD-Q only application?

The IMPD-Q only application is evaluated **in parallel with the relevant IN application of the Sponsor trial** (see question 2.33.). In case an RFI is issued for the IMPD-Q-only application, a corresponding one is also raised for the IN application of the Sponsor trial (not on the Quality part), that is managed by the Sponsor to keep the evaluation timelines of both procedures aligned. The PO/SO and the Sponsor are required to respond to both RFIs to prevent lapsing of either application, although no content is expected in the response to the matching RFI which was raised only for administrative purposes. The below steps describe **how to manage the RFI responses** during the evaluation of an IMPD-Q only application and on the visibility of the part I conclusion.

	Step to perform for the IMPD Q only application	PO/SO needed Role(s)	*Sponsor needed Role (optional)*
1.	**PO/SO or the Sponsor's Application submitter** views RFI through the Notices & Alerts tab	CT Admin or IMPD-Q Preparer	*Application Submitter (specific trial)*
2.	**The PO/SO adds supporting doc to Part I IMPD-Q RFI** Note that any product related consideration is raised by the RMS classified as 'Quality' to maintain confidentiality and any RFI supporting document related to the product, should be therefore uploaded under 'Sponsor supporting document – Quality' section.	CT Admin or IMPD-Q Preparer	
3.	**PO/SO or the Sponsor's Application submitter changes CTA Part I IMPD-Q through RFI response**. Of note: *in case the Sponsor is granted the 'Application submitter' role for the application*, the 'RFI response - Changes to the application dossier' document cannot contain product confidential details, but should make reference to the 'Sponsor supporting document - Quality' uploaded by the PO/SO.	CT Admin	*Application Submitter (specific trial)*

	Step to perform for the IMPD Q only application	PO/SO needed Role(s)	*Sponsor needed Role (optional)*
4.	**PO/SO or the Sponsor's Application submitter submits response to RFI** on Part I IMPD-Q	CT Admin	*Application Submitter (specific trial)*
5.	**PO/SO or the Sponsor's Application submitter** views Part I Conclusion – Quality AR	CT Admin or IMPD-Q Preparer (seeing the conclusion AR)	*Application Submitter (specific trial) (sees the conclusion only, not the AR)*

Since the IMPD-Q only application is a Part 1 only application, **it will remain under evaluation** and it lapses after 2 years (see section 2.5 of the Sponsor Handbook). If this happens, a resubmission of the IMPD-Q application is not required, unless an SM impacting the IMPD-Q only dossier information, or an AM is needed (see questions 2.36. and 2.37.).

In case the related IN of the Sponsor trial is 'not valid', is lapsed, is concluded 'not acceptable' or decided 'not authorised', the IMPD-Q only application procedure also needs to be terminated through a withdrawal of the application. This allows the existing information in the IMPD-Q-only application to be re-used in subsequent applications keeping the same EU CT number 'XXXX-XXXXXX-XX-NN' while incrementing only the resubmission sequence (NN: -00, -01, -02…).

2.36. How can an SM affecting the quality aspects of the IMPD be created and submitted?

In case, the substantial modification affects exclusively the content of the Sponsor trial and not IMPD-Q aspects, a resubmission of the IMPD-Q only application **is not required**, even if corresponding data fields, e.g. inclusion/exclusion criteria sections, are affected.

However, **if a substantial modification affecting the quality aspects of the IMPD** is needed:

- The formerly created IMPD-Q only application is **withdrawn and resubmitted** with the needed changes, as an IN Part I only application (see question 2.34.)
- The **sponsor submits an SM to the main application** of their trial to classify the change of the quality part of the IMPD as an SM

The steps to perform in case an SM to the IMPD-Q only application is needed are below.

	Steps to perform for the IMPD Q only application	PO/SO needed Role(s)	*Sponsor needed Role (optional)*
1.	**The PO/SO or the Sponsor's Application submitter withdraws the IMPD-Q only application**	CT Admin	*Application Submitter (specific trial)*
2.	**The PO/SO creates a resubmission of the IMD-Q only application as IN** (in parallel with SM of sponsor trial) with the existing latest information populated and EU CT number 'XXXX-XXXXXX-XX-NN' incremented with the next resubmission sequence (NN: -00, -01, -02…).	CT Admin (all trials)	
3.	*If needed, PO/SO CT Admin assigns the Sponsor again with the 'Application Submitter' role for the resubmitted IMPD-Q only application*	*CT Admin (all trials)*	
4.	**The PO/SO or the Sponsor's Application submitter fills in IN Form, MSC, Part I (excl. Q-IMPD**) Refer to instructions provided in paragraph 125 of **CTR Q&A** on how to fill in data fields and documents and consult the 'Best practice guide naming of documents in CTIS', available in the 'Key document list' section on the CTCG page. Of note: - *in case the Sponsor is granted the 'Application submitter' role for the application*, the PO/SO should not include any product confidential information in these parts of the application, as they would be visible to the Sponsor - the cover letter should not mention any confidential product details, but a statement as specified in paragraph 125 of CTR Q&A - the 'Modification description' section should not describe any confidential product details, but make reference to any Summary of changes document that is uploaded directly under the IMPD-Q document type to retain confidentiality **Part II of the IN is NOT filled in.**	CT Admin	*Application Submitter (specific trial)*
5.	**The PO/SO fills in the IN Part I (Q-IMPD**) Refer to instructions provided in **paragraph 125 of CTR Q&A** on how to fill in data fields and documents and consult the 'Best practice guide naming of documents in CTIS', available in the 'Key document list' section on the CTCG page. An additional document with tracked changes from previously submitted version should be included to facilitate the assessment of this application. Of note: *in case the sponsor is granted the 'Application submitter' role for the application*, in addition to the IMPD-Q data and	CT Admin or IMPD-Q Preparer	

	Steps to perform for the IMPD Q only application	**PO/SO needed Role(s)**	***Sponsor needed Role (optional)***
	documents, the PO/SO must upload **any product document other than the IMPD-Q**, e.g. Manufacturing and Importation Authorisation, or in the QP declaration, **also under the IMPD-Q document type,** and not under their standard CTIS document types, in case they contain CCI.		
6.	**The PO/SO or the Sponsor's Application submitter submits the IN resubmission of the IMPD-Q only application** on the same day as the SM application for the Sponsor trial.	CT Admin	*Application Submitter specific trial)*

Submission, evaluation, RFI responses, and withdrawal remain with the same tasks and responsibilities as described in question 2.35..

2.37. How can an AM to the Sponsor trial be created and submitted?

In case an AM to the Sponsor trial is needed:

- The formerly created IMPD-Q only application is **withdrawn and resubmitted with the relevant RMS and only the additional member state(s)** selected in the 'Form' section, as an IN Part I only application (see question 2.34.). Existing other MSC(s) that are also part of the Sponsor trial should not be included
- The **AM to the Sponsor trial** is submitted by the sponsor **in parallel** with the resubmission of the IMPD Q only application. See question 2.15 of the CTR Q&A for further information on this submission.

Note that the IN of the IMPD-Q only application will only be evaluated by the additional member state(s) and the Reporting Member State, but not by the others: for this reason, **it needs to contain only the additional member state(s) and the RMS**, and not the others, see step 5 below.

In addition, in this case it is not possible to change from an IMPD-Q application to a cross-reference application. This is to ensure that all Member States receive the same documents for review and follow the same procedure.

Steps to perform on the IMPD-Q only application in parallel to the AM submitted on the Sponsor trial:

	Step to perform on the IMPD Q only application	**PO/SO needed Role(s)**	***Sponsor needed Role (optional)***
1.	**The PO/SO or the Sponsor's Application submitter withdraws the IMPD-Q only application**	CT Admin	*Application Submitter (specific trial)*
2.	**The PO/SO creates a resubmission of the IMD-Q only application as IN** (in parallel with AM of sponsor trial) with the	CT Admin (all trials)	

	Step to perform on the IMPD Q only application	PO/SO needed Role(s)	*Sponsor needed Role (optional)*
	existing latest information populated and EU CT number 'XXXX-XXXXXX-XX-NN' incremented with the next resubmission sequence (NN: -00, -01, -02…).		
3.	*If needed, the PO/SO CT Admin assigns Sponsor again with the 'Application Submitter' role for the resubmitted IMPD-Q only application*	*CT Admin (all trials)*	
4.	**The PO/SO or the Sponsor's Application submitter fills in the Form section**. Note: - *in case the Sponsor is granted the 'Application submitter' role for the application*, the PO/SO should not include any product confidential information in this part of the application, as they would be visible to the Sponsor - the cover letter should include a statement as specified in point 125 of CTR Q&A and a brief AM description, where no product confidential information is specified	CT Admin	*Application Submitter specific trial)*
5.	**The PO/SO or the Sponsor's Application submitter fills in the MSC section with RMS and additional MSC(s),** while existing MSC(s) should be deleted	CT Admin	*Application Submitter(specific trial)*
6.	**The PO/SO or the Sponsor's Application submitter fills in IN Form, MSC, Part I (excl. Q-IMPD**) This IN should be filled in with identical data and documents as to those that were included in the application withdrawn in step 1. **Part II of the IN is NOT filled in.**	CT Admin	*Application Submitter (specific trial)*
7.	**The PO/SO fills in the IN Part I (Q-IMPD**) This IN should be filled in with identical data and documents as to those that were included in the application withdrawn in step 1.	CT Admin or IMPD-Q Preparer	
8.	**The PO/SO or the Sponsor's Application submitter submits the IN resubmission of the IMPD-Q only application** on the same day as the AM application for the Sponsor trial.	CT Admin	*Application Submitter (specific trial)*

Submission, evaluation, RFI responses, and withdrawal remain with the same tasks as described in question 2.34. .

2.38. Can an IMPD-Q application be submitted for an ATMP and/or biological IMP?

It is not possible to submit an IMPD-Q only application for biological medicinal products or ATMPs. In these cases, the sponsor submits this information in the main application and no IMPD Q application is needed. As per question 2.15 of the CTR Q&A: 'The scenario that a substance owner (SO) submits the IMPD-Q for the drug substance (DS) part as 'IMPD-Q-only' and the drug product (DP) part is submitted in the sponsor trial is only possible if the applicable product legislation allows this (e.g. where a drug substance master file is allowed)'.

2.39. If the PO/SO of an IMPD-Q only application has changed does the IMPD-Q only application need to be withdrawn and resubmitted, or is a new IMPD-Q only application needed?

From a technical perspective, it is not possible to change the sponsor of an application by resubmitting it. Therefore, the appropriate action would be to submit a new application with the new PO and mention the change of PO in the cover letter.

Part II

2.40. Should a site suitability document be provided for each trial site, or can a unique document be submitted for the whole MSC?

Sponsors must provide one site suitability document per trial site. Submitting a single document per country is only appropriate when there is only one site in that country.

2.41. How can satellite sites, where specific trial activities are performed, be inserted and linked to the main site in CTIS?

The CTR does not define the concept of a 'satellite site', therefore, CTIS does not allow ''satellite sites'' to be formally linked to a main site. However, it is possible to register more than one location per site in OMS, where applicable (e.g., when primary trial activities take place at one location and certain supportive activities are conducted at another): see section 1.2.1. of the Sponsor Handbook. All registered locations can be selected and added in CTIS, provided they are available in OMS.

In addition, trial sites can be manually entered in CTIS as local registration, see section 2.4.3. of the Sponsor Handbook.

2.42. How can the planned number of subjects be inserted per site in CTIS?

CTIS allows only to enter the planned number of subjects per country. Currently, the number of subjects cannot be entered per site. The discrepancy with Annex I M.64 of the CTR is acknowledged. If requested by MSCs, sponsors may need to provide this in a Part II document (e.g., site list), and reference it in the cover letter or supporting documentation.

2.43. Does CTIS provide an audit trail or tracked-change history for trial sites in Part II?

CTIS is designed to support the assessment and supervision of clinical trials in the EU but is not intended to serve as an archiving system with a comprehensive audit trail or tracked-change view for trial site changes. While documents related to closed sites remain accessible in previous application versions, CTIS is not intended to replace the TMF, sponsors are responsible for maintaining complete and up-to-date site records in their TMF.

Search, view and download a CT or CT application

2.44. CTIS displays documents across multiple pages, which makes it difficult to search for specific documents. How will this be improved?

CTIS does not currently provide filtering, sorting, or searching functionalities for lists of documents, nor does it offer a downloadable table of contents. In the future, it is foreseen that CTIS will allow users to download an .xls/.csv file with the list of trial documents and their associated metadata; users will therefore be able to find the relevant document in the file. The timeline for implementing this improvement has not yet been confirmed.

2.45. Is it possible for CTIS to provide a list of approved documents, to support TMF or Investigator Site File requirements?

Currently, while it is possible to consult document details at country level within CTIS, these details are not available in a downloadable format. Sponsors are encouraged to apply clear and consistent naming conventions when uploading documents, as this facilitates identification of approved documents when downloading application files and related assessment reports. In the future, CTIS will provide a functionality to download a standalone list of documents with associated metadata (see question 2.44.). For archiving reasons (i.e., TMF), users might use the browser's built-in print functionality and print out CTIS user interface including details (i.e., metadata) that cannot be retrieved from the download functionality. Snapshots from certain CTIS user interface could be used for that purpose too.

3. Evaluation Phase

Evaluation steps, outcome and timetable

3.1. Why can Part II conclusions be issued before Part I conclusions? What is done to prevent such cases?

CTIS reflects the requirements of the CTR, where a parallel assessment of Part I and Part II is foreseen: see chapter 3 of the Sponsor Handbook. Member States have drafted best practices outlining that Part II conclusions should be issued only after the Part I conclusion has been finalised. However, in situations where the Part II assessment deadline is reached before the Part I conclusion is finalised, the MS needs to register the Part II conclusion earlier to prevent a tacit conclusion for Part II.

3.2. When an application is 'Authorised with conditions', what actions must the sponsor take to obtain full authorisation?

The sponsor should fulfil the conditions specified by the MSC(s) to obtain full authorisation of their trial. Member States are responsible for clearly specifying in the condition text what is required by the sponsor to fulfil the condition, when and how (e.g., SM) the sponsor should submit the required information in CTIS, and whether or not this should be done before the trial can start. If this is not clear to the sponsor, the sponsor can contact the Member States for clarification.

3.3. If a trial is 'authorised with conditions' in CTIS, does this status change to 'authorised' once the conditions are fulfilled?

No, when a trial is recorded as 'Authorised with conditions' in CTIS, this status remains for the entire duration of the trial. There is no update of the status to 'Authorised' after conditions are met. The trial is still considered authorised, and MSCs may take corrective measures if the conditions are not fulfilled.

3.4. For an initial Advanced Therapy Medicinal Product (ATMP) application affected by the winter clock stop, how should the maximum assessment timeline be calculated?

For ATMP applications, the standard assessment timeline may be extended by up to 50 days to allow for consultation with experts, in accordance with the CTR. The winter clock stop period (16 days) is excluded from the calculation of the regulatory assessment timeline.

3.5. The maximum CTR timeline is 106 days (or 156 days for ATMPs), why do some assessments take longer?

The CTR allows up to 106 days for standard CTAs assessments and up to 156 days for ATMPs (additional 50 days). Longer elapsed timelines may result from the winter clock stop (e.g., 23 Dec – 7 Jan), weekends/holiday (up to 20 days), or in case there are any technical issues. The assessment timeline adheres to Euratom rules: refer to section 3.1 of the Sponsor Handbook.

3.6. Is the winter clock stop scheduled every year? What are the dates, and is it mandatory for all applications?

The winter clock stop is mandatory every year and applies from 23 December to 7 January (clock stops at 22 December 23:59:59 and restarts on 8 January 00:00:01, see section 3.1 of Sponsor Handbook). It applies to the evaluation of any application and cannot be opted out. Sponsors may continue to submit applications and responses to RFIs during this period; however, MSC(s) evaluation timelines are paused. The sponsor may also submit notifications, including the safety ones, which will then be assessed by the MSC(s) once the clock stop period has ended. During the clock stop period, MSCs may still perform tasks, but their assessment timelines remain frozen.

3.7. If questions arrive late on a Friday, does the assessment clock start immediately, or can it begin on the next working day?

The clock starts at the time the submission is made, including Friday evening. There is no functionality in CTIS to defer the clock start to the next working day.

3.8. Why is the timetable not modified when RFI responses are submitted earlier than the deadline?

The guidelines describe CTIS as a dynamic workflow where early completion of certain tasks could recalculate subsequent deadlines and, in some cases, even shorten the maximum timelines. Those cases are listed in section 3.1 of the Sponsor Handbook. Answering RFI earlier than the date set by the MSCs does not change the timelines, only completing MSCs tasks earlier changes them: see question 3.23. .

3.9. Are shorter review periods of some MSCs reflected in the timetable?

No. Even though some Member States may internally commit to reviewing applications within shorter timelines (e.g., for mono-national applications), these timelines are not visible in CTIS. The legal deadlines established by the CTR apply across all MSCs, and only those are reflected in the system's calendar. However, this information may be shared with the sponsor by the MSCs via other means.

3.10. If the approval date shown in CTIS differs from the date indicated in an attached conclusion letter, which date should be considered the official approval date?

Sponsors should rely on the approval date recorded in CTIS, as this is the official date under the CTR. Differences may occur because decision letters can be created and signed on different dates.

3.11. Does the sponsor receive a decision letter when an application (IN, SM) is authorised?

The CTR (and therefore CTIS) do not require MSCs to issue a signed decision letter for an authorised IN or SM. Sponsors can access the outcome through CTIS, including structured data and the mandatory assessment reports. Some MSC(s) may upload a signed letter on a voluntary basis.

Notices and alerts

3.12. Is there any way to retrieve Notices & Alerts data (e.g., via Application Programming Interface (API) or export) for reporting purposes?

No. There is currently no public API available for accessing Notices & Alerts, and CTIS does not offer an export function (e.g., .xls or .csv) for Notices & Alerts.

3.13. Tacit approvals do not generate a CTIS notice or alert. Can this be changed in the future?

Tacit approvals do not trigger a CTIS notification. Sponsors must manually check the application status in CTIS. Future improvements on this aspect may be considered, however no change is planned yet.

Respond to a Request for Information (RFI)

The present section is applicable to RFIs raised during the evaluation of **any CTIS application** (IN, AM and SM, see sections 2.3., 4.2, and 4.3 of the Sponsor Handbook).

3.14. My trial has lapsed because I did not reply to an RFI as per deadline. How can I resubmit my application without having to do it all over?

In such cases, the application must be resubmitted in accordance with Section 2.7.2 of the Sponsor Handbook: sponsors are not required to restart the entire submission process, and it is not necessary to upload all documents again (only metadata can be modified if needed). In addition, **documents do not need to be amended solely to update the last two digits of the EU CT number**, as outlined in the 'Best practice guide naming of documents in CTIS', available in the 'Key document list' section on the Clinical Trials Coordination Group (CTCG) page.

3.15. Can emails requested by MSCs as part of an RFI be uploaded in CTIS?

Emails containing relevant regulatory communication may be submitted as 'Not for Publication' documents only. This is to comply with GDPR and CTIS transparency rules; more information is available in the Guidance document.

3.16. If the maximum 12-days RFI response period is extended because the due date falls on a public holiday, CTIS may still issue an automated reminder earlier. To which date should the sponsor refer?

The correct due date is the one of the RFI in the evaluation tab. This generally corresponds to the one of the automated reminder. Sponsors should always **check the due date of the RFI in the evaluation tab** in order to avoid the application to lapse.

3.17. When downloading the RFI considerations, is it possible to see them categorised per topic?

Once raised, sponsors have the possibility to download the RFI considerations. However, with the current design of CTIS, it is not possible to categorise them: all considerations on different topics (e.g., Informed Consent Forms (ICFs), CVs, site suitability) appear in the same list. The downloaded file can be sorted or analysed offline to allocate questions to the appropriate sponsor team members.

RFI documents can also be downloaded individually using the blue download icon next to each of them.

3.18. Can RFI response timelines be extended?

RFI timelines are defined by the CTR and **cannot be extended**. It is important to submit the RFI response on time to prevent the application from lapsing. Sponsors are encouraged to submit mature, high-quality dossiers to minimise the need for an RFI. If additional time is required to respond to questions or provide requested documents, sponsors could opt to withdraw and resubmit the application with the RFI questions already addressed. In exceptional circumstances, the application could be authorised under conditions.

3.19. Can additional rounds of Part I RFI be issued after the first RFI due date in CTIS?

Additional rounds of Part I RFIs after the first RFI due date can only be issued under exceptional cases, and solely when necessary to avoid a refusal of the clinical trial authorisation.

3.20. Why may RFI response deadlines fall on national holiday in several EU countries, including the RMS and MSC?

The system is designed to exclude weekends but not national holidays. This decision was made by Member States, acknowledging that sponsors are located globally, and considering that a single EU-wide holiday calendar was not feasible. In addition, the reference calendar (see section 3.1 of Sponsor Handbook) is only applicable to Member States tasks, and not sponsor's actions (e.g. RFI response due date).

3.21. What to do if due to an RFI, additional documents need to be updated that do not belong to the same part of the RFI (e.g., the Informed Consent Form needs updates as a consequence of protocol updates)?

CTIS unlocks only the part of the dossier to which an assessment RFI relates. Both Part I and Part II can therefore be unlocked at the same time only if RFIs are issued in parallel or with overlapping timelines. If additional documents (such as Informed Consent Forms in Part II) need revision because of changes requested in Part I, the MSC must issue a corresponding RFI for the relevant part. If no such RFI is issued, these documents cannot be updated during the ongoing assessment and must instead be submitted after authorisation as an SM (SM Part II). Please note that an RFI issued in the validation phase does unlock both Parts of the application, regardless of the scope of the considerations.

3.22. When responding to an RFI, a new version of a document must be created and uploaded to replace the previous one. If a typo or another error is identified in the newly uploaded version, can I delete it and upload a corrected file?

It is possible to delete a document that has been incorrectly uploaded when preparing a response to an RFI. However, if the document is a 'for publication' file with an associated 'not for publication' version, deletion is only possible once the associated 'not for publication' document has been removed (see specific instructions on section 5 of the List of known issues and workarounds). In such cases, users should first delete the 'not for publication' document or discard the draft RFI response and restart the preparation process.

3.23. Sometimes the RFI validation occurs more than 5 days after RFI response submission. How is this possible?

According to Article 5 of the CTR, once a response to a validation RFI is submitted, the RMS has 5 days to complete validation. However, when an RFI is issued, CTIS automatically extends the validation timeline by 15 days, regardless of the sponsor's actual response date. The timeline is not recalculated based on early responses. Also, although the RMS may complete validation earlier, CTIS continues to display the full extended deadline.

3.24. Can a sponsor contact the RMS (e.g., to ask questions about RFIs)?

Yes, sponsors can contact the RMS using publicly available Member States contact points and contact points listed in Annex III of the CTR Q&A.

3.25. Is it possible to remove a document that was submitted as a supporting document during an RFI response?

A document cannot be removed once it was included in an RFI response that was already submitted.

3.26. Can a Sponsor receive RFIs during the winter clock stop? And can an RFI deadline fall within this period?

A sponsor may receive RFIs during the winter clock stop and they can submit responses to RFIs. However, the response deadline cannot fall within the clock stop period. The purpose of clock stop is to extend the overall timeline pausing the evaluation timelines for MSCs, not to pause communication, see question 3.6..

3.27. For how long are all versions of RFIs accessible once the trial is ended?

CTIS retains all information, including structured data and documents, for at least 25 years from their submission. This applies also to all RFI versions, which are all retained in CTIS. Superseded RFI versions remain accessible and are archived in each document's history.

3.28. When responding to multiple considerations within the same RFI, different considerations may require different updates to the same document, how should the sponsor proceed?

The sponsor should upload a single revised version of the document addressing all considerations. Clarifications can be described in the response text boxes corresponding to each question.

3.29. Can I answer each consideration with a unique document that includes the answers for all considerations received for the RFI?

This is technically possible. However, MSCs may prefer individual responses for each consideration: depending on the topic, the assessment of responses to single considerations may be easier to perform.

3.30. Is there a limit to how many RFIs can be submitted during the validation and assessment phases?

The system allows multiple RFIs to be issued during the validation and assessment phases. Although best practice encourages issuing a single consolidated RFI, additional rounds may be sent when necessary. Note that only the first round of RFI affects the evaluation timelines, not further rounds: see section 3.3. of the Sponsor Handbook.

4. Conduct a clinical trial

Notify on trial events (e.g., CT start, start of recruitment)

4.1. What happens if notifications are not entered within 15 days?

CTIS does not prevent sponsors to submit notifications late. However, failure to submit notifications within 15 days is a non-compliance with the CTR which could be raised during inspections.

4.2. If no subject is included within two years of the IN authorisation, how can the sponsor avoid a trial expiration?

To avoid a trial from expiring, the sponsor must **submit an SM to extend the recruitment start date**, and this SM must be authorised prior to the 2-year deadline (see section 4.3.3. of the Sponsor Handbook)**.** Only the SM authorisation (not the submission) determines whether the extension is valid**.**

4.3. If a sponsor decides not to proceed with an authorised clinical trial, is a notification of End of Trial (EoT) required in CTIS?

An authorised trial that has not started within two years after the authorisation date will automatically expire in CTIS. This change of status occurs automatically in the system and does not require any action or notification by the sponsor. However, if the clinical trial has started (i.e., the start of the clinical trial has been notified in CTIS), and the sponsor subsequently decides not to continue the trial, the sponsor must submit an EoT notification to CTIS in accordance with the CTR.

4.4. In a complex cohort trial, should sponsors report the Start of Recruitment (SoR) and end of recruitment (EoR) per cohort? Or should sponsors only report the SoR of the first cohort and the EoR of the final cohort?

In CTIS it is only possible to report the SoR and EoR per MSC but not per subprotocol or cohort per MSC. There is also no suitable placeholder to submit cohort-specific information in a NSM. Therefore, in CTIS, sponsors can enter only the SoR of the first cohort and the EoR of the last cohort. However, it is mandatory for complex clinical trials (CTTs) to provide an overview of the status of each cohort per Member State when a SM is submitted. In this overview, those cohort-level details can be provided. More information on complex trials can be found in the 'Complex clinical trials (CCTs) – Questions and answers' available in the 'Key documents list' section on the CTCG page.

4.5. If the trial protocol includes a planned pause in recruitment, should it be reported to CTIS?

A planned pause described in the protocol must be reported as an EoR in the relevant MSC. Once recruitment resumes, the sponsor must submit a Restart of Recruitment notification within 15 days for each MSC.

4.6. How can an EoR be reported after the EoT notification? For example, if recruitment remains open after the Last Patient Last Visit (LPLV), with no additional participants enrolled.

According to the guidance provided in the FAQ document listed in the CTCG Key Documents list, the sponsor should select an EoT date that occurs after the LPLV date in all MSCs. CTIS does not permit an EoT date that precedes the EoR in any country. The sponsor should justify the selected EoT date by including explanatory supporting documentation in CTIS.

4.7. Should the EoR date be the same for all MSCs?

Each MSC should be notified individually when recruitment ends in their territory. If the same date applies across more MSCs, they can all be selected in the 'notifications' section and a single notification can be sent by the sponsor (see section 4.1.1 of the Sponsor Handbook).

4.8. Is it mandatory to update the number of subjects per MSC after the EoR?

There is no requirement under the CTR to update the planned number of participants in the application's MSC section. The actual number of participants needs to be reported in the summary of results.

4.9. Are notifications for temporary halt or EoT required after an MSC imposed a corrective measure to suspend or revoke a trial?

If an MSC has imposed a corrective measure **suspending** the CT, a temporary halt notification is not needed. The sponsor will need to submit an SM, as per MSC instructions. Afterwards, the MSC will revert the status to authorised. If an MSC has imposed a corrective measure **revoking** CT authorisation, the sponsor needs to submit the end of trial notification to the relevant MSC (see section 5.1 of the Sponsor Handbook), and then to upload the summary of results and lay person summary of results.

4.10. Can a Temporary Halt notification be limited to recruitment only, or does it always apply to both recruitment and patients' visits?

A temporary halt may be limited to recruitment only. Further details are in section 10 of the CTR Q&A.

4.11. If a study is temporarily halted, is it still possible to submit an SM, an AM or a NSM?

When a trial is temporarily halted it is possible to submit an SM and an AM. With regards to the NSM, this cannot be submitted if the trial is a mononational trial: in this case, the sponsor should wait for the restart of the trial. For multinational trials halted in some but not all MSCs, an NSM is possible on Part I, and on Part II for the non-halted MSCs.

4.12. If a study is temporarily halted, is it possible to submit a safety notification (e.g., Serious Breach) or an inspection report?

Yes. If a study is temporarily halted, any safety notification can be submitted, as well as an inspection report.

Create and submit an Additional Member State application (AM)

4.13. Can sponsors create multiple AM drafts at the same time, or must they wait until one AM is authorised before creating another?

Multiple AM drafts can be created in parallel, and multiple AM can be submitted in parallel. AMs are mutually exclusive, do not depend on each other and can be approved at different times. However, **sponsors should avoid creating SM or NSM drafts when an AM application is already in draft or under evaluation**, as the MSC being added will not be included as MSC in the SM/NSM. In addition, structured data and documents added during the AM would be missing from the SM/NSM, and this results in missing translations or misalignment with the concerned MSCs: see section 4 of the Sponsor Handbook.

Create and submit a Substantial Modification application (SM)

4.14. When downloading SM documents from CTIS, the system exports all documents (including the IN and all previous SMs). Can the download be limited to only the documents authorised within the specific application?

There is currently no functionality to filter documents by version or submission type. When downloading an SM, NSM or AM, all historical documents are also included in the export. In the future, it is foreseen that CTIS will allow users to only download the documents of the specific application. The timeline for implementing this improvement has not yet been confirmed.

4.15. Is it possible to submit a Part II SM (to add new sites in MSC) and an AM at same time?

Yes. Part II SM and parallel AMs not affecting the same MSC can be submitted in parallel. See the table in section 4 of the Sponsor handbook that summarises the allowed submissions whilst there are other ongoing evaluations.

4.16. When creating an SM, if sponsors choose 'Part I & Part II', are all MSCs automatically included? Can the selected MSCs be changed before submitting the SM?

When sponsors select 'Part I & Part II' all MSCs are initially included by default. The sponsor needs to select the countries for which Part II needs to be included: this is a must in the draft creation step when including part II (see section 4.3.2. of the Sponsor Handbook). If an MSC is not selected for part II at the time of creation of the SM, it cannot be added later in the draft (in this case the sponsor needs to create again the SM to add additional countries for Part II). However, any Part II MSC can be excluded at the time of submission if it was included in the draft at the time of creation.

4.17. Is it possible to create a draft Part I-only SM and later modify the application to Part I & Part II without cancelling the draft?

No. The scope selected when creating the SM draft (Part I only, Part II only, or Part I + Part II) cannot be changed once the draft has been created as per section 4.3.2. of the Sponsor Handbook. If a Part I–only SM draft needs to be expanded to include Part II, the sponsor must cancel the draft and create a new SM with the correct scope. Although this generates a new SM number, it has no functional impact in CTIS. When uncertain about the scope at the time of creation, sponsors are advised to select 'Part I + Part II' and decide the final scope at submission, see question 4.16..

4.18. If a trial has ended in the RMS, but an SM Part I & Part II is planned in other MSCs, will the RMS be able to conduct the Part I assessment and raise validation and assessment RFIs?

Under the CTR once a Member State has been agreed to be the RMS for a trial, it remains in charge for the entire trial lifecycle. In CTIS, the RMS will no longer be reflected in the assessment overview for a subsequent SM, however the RMS will still be involved in the assessment of the Part I SM. The RMS will receive Part I tasks for the SM validation and evaluation, including the ability to issue RFIs. However, the RMS will not receive Part II or enter their national decision, as these are managed by the MSC(s) participating in the assessment in which the clinical trial is not ended.

Notify an Unexpected Event, an Urgent Safety Measure, a Serious Breach and a Third-Country Inspectorate Inspection

4.19. If a trial is halted for reasons unrelated to safety, should this still be reported as an urgent safety measure?

An Urgent Safety Measure is required only where immediate action is necessary to protect the safety of trial subjects. Where a halt is not safety-related, the submission of an urgent safety measure is not appropriate. In case of an incident that might influence the benefit-risk balance of the medicinal product, an unexpected event notification should be submitted in line with Article 53 of the CTR.

4.20. Is there any guideline or template to follow for the documents submitted with an Urgent Safety Measure or Unexpected Event notification?

While for Serious Breaches sponsors should submit a document in line with the Guideline on reporting serious breaches and Appendix III b – Information to be submitted with a notification of a serious breach, other notifications such as Urgent Safety Measures and Unexpected Events do not have a reference guideline. For those notifications, submitting a document is optional as long as information included in the structured data fields of the notification is exhaustive.

Submit an Annual Safety Report (ASR) and respond to ASR RFI

4.21. Under Clinical Trials Directive 2001/20/EC (CTD) the clinical trial participants subject identifier (ID) was provided in ASRs. Is it correct that, under CTR, the subject ID should no longer be provided?

ASRs should only contain anonymous information, namely information which does not relate to an identified or identifiable natural person or to personal data rendered anonymous in such a manner that the data subject is not or no longer identifiable.

A subject identifier is pseudonymised information, in accordance with Article 4(5) of Regulation (EU) 2016/679, and should therefore be excluded in the ASRs. Additional clarification on provision of the Worldwide Unique Case Identification Number (case ID) and the trial ID, rather than the subject ID, is provided in question 7.34 of the CTR Q&A.

For more information on data protection in CTIS sponsors can consult also the CTIS JCA and the relevant Questions and answers on the JCA.

4.22. Can an ASR be submitted while other applications (e.g., SMs or AMs) are under assessment?

Yes, the CTR does not prevent the submission of an ASR while other applications are under assessment: CTIS therefore allows these procedures to run simultaneously. However, in the case of a 'change of sponsor SM' (see section 4.4 of the Sponsor Handbook), it is recommended to wait until this SM is approved before submitting the ASR to avoid system errors.

4.23. If a study is temporarily halted, is it still possible perform ASR submissions?

Yes. Temporary halt does not restrict ASR submissions.

4.24. Can a department name and shared mailbox be used as the ASR contact details? What about contact details of a CRO?

CTIS allows the use of a department name and a shared mailbox in the 'Contact details for ASR submission' of the 'Sponsor information' section (see section 4.13.1 of the Sponsor Handbook). In addition, it is recommended to include the name of an individual contact person who can be reached directly by the authorities for any clarifications or follow-up actions. If a CRO or legal representative submits the ASR on behalf of the sponsor, their contact details and a shared mailbox must be provided in the contact section of the ASR form.

4.25. After submitting an ASR in CTIS, is it possible to change it, or to upload additional documents?

Following the initial ASR submission, sponsors cannot change the ASR submitted and its related documents on their own initiative. Additional documentation can only be provided if requested by a MSCs within a RFI during the assessment process. If the sponsor wants to update the ASR while there is no active RFI, they to contact the saMS (Safety Assessing Member State).

4.26. What happens if a sponsor misses the deadline to respond to an ASR RFI?

When the saMS creates an RFI in the context of an ASR, the due date for the sponsor's reply is set to 14 days by default, although the saMS may define a different due date (see section 4.13.3. of the Sponsor Handbook). If the Sponsor does not respond by the specified deadline, the RFI will expire; however, the workflow does not stop, and the **sponsor must still submit a response to the RFI as soon as possible**. If the sponsor foresees that the RFI cannot be responded to in time, they should contact the Member State to request an extension.

4.27. Can other sponsors view other ASRs that were submitted in CTIS?

No. Sponsors can only view and manage their own ASRs in CTIS. Information submitted by other sponsors is not visible due to confidentiality and regulatory access controls within the system.

5. End the clinical trial and submit results

Notify the end of a CT

5.1. After submitting the EoT notification in CTIS, is it necessary to submit any further NSMs for site closures?

No. Once the EoT notification has been submitted in CTIS, the trial is considered closed in the system. As a result, no further NSMs, including those related to site closures, are required.

5.2. How is the overall EoT reported in CTIS?

The EoT is submitted separately by the sponsor for each MSC. Once the final MSC has submitted its EoT notification, CTIS automatically designates the trial as ended in the EU/EEA: this date triggers the timeline for submitting the summary results. In case a trial is also ongoing in third countries, then the global End of trial date shall be notified to CTIS, in line with Art 37(3) of the CTR.

5.3. Can a trial for which an EoT notification was submitted be re-opened?

In CTIS it is not possible to re-open a trial once an EoT notification has been submitted for a MSC. If reopening is needed, for example, if a protocol amendment extending recruitment is planned, sponsors may consider a workaround (e.g., withdrawing the EoT notification, see section 4.1.1.1. of the Sponsor Handbook), however alignment with the concerned authorities is required before any action is taken.

Interim results, Summary of results and Lay person Summary of results

5.4. What is the difference between interim and intermediate summary of results and when should they be submitted?

The terms 'interim' and 'intermediate' have the same meaning in CTIS and both refer to the assessment of results while the trial is ongoing. 'Interim' refers to the stage of the analysis (as in interim or final analysis), whereas 'intermediate' refers to the completeness of the dataset (as in intermediate or full data). If the clinical trial protocol specifies a date for an intermediate (or interim) data analysis, a summary of that analysis must be submitted to CTIS within one year of the data cut-off date: refer to question 6.6. of the CTR Q&A, where exceptions to their submission requirement are listed. If no intermediate data analysis is specified in the protocol, interim results do not need to be submitted unless explicitly requested by the RMS. This also includes interim results that are for internal administrative purpose only and are not foreseen by the protocol. The required content is defined in Annex IV of the CTR and must be limited to the endpoints included in the interim analysis as described in the protocol.

5.5. *What are the requirements for posting interim results for trials that were transitioned from the Clinical Trial Directive?*

For trials that have been transitioned to CTIS, interim results must be submitted to CTIS. This includes trials with interim analysis completed prior to transition but the 1-year due date falling after transition. If the interim results were already posted in EudraCT before the transition because their due date for submission was falling before the transition date, they can remain there and do not need to be re-submitted to CTIS. More information on EudraCT can be found in the EudraCT uploaded Frequently Asked Questions.

5.6. *Are interim results to be uploaded in the same section as the final summary of results?*

Yes. The interim summary of results is uploaded in the same section as the final summary of results: see section 5.2.3. of the Sponsor Handbook. In case the trial is ongoing, those results are automatically classified as 'intermediate.' In case the trial is ended, to submit the interim results sponsors need to select 'Intermediate Results' from the dropdown menu.

5.7. *Are interim results published on the CTIS public website?*

No. The interim summary of results is never made public in CTIS according to CTIS Revised transparency rules. As per section 5.2.3. of the Sponsor Handbook, the wording 'for publication' displayed by the system refers to the final summary of results and never to the intermediate summary.

Submit the Clinical Study Report (CSR) and update it

In addition to the frequently asked questions received on CSR submission under the CTR, some of the questions of this section provide clarification on those cases where the same CSR is subject to transparency requirements in both CTIS and under the EMA Policy 0070 on clinical data publication.

5.8. *What should be the content of a CSR submitted to CTIS?*

In line with Art 2(2)(35) of the CTR the content of the CSR submitted to CTIS should be based on Annex I, Part I, Module 5 of DIR 2001/83/EC. The CSR should contain all sections of the CSR body as defined in ICH E3, Structure and Content of Clinical Study Reports (Sections 1 to 15) and the 3 appendices identified as being of the most relevant for the interpretation of the study results (16.1.1 Protocol & protocol amendments, 16.1.2 Sample case report form, 16.1.9. Documentation of statistical methods).

The above applies to both versions 'for publication' and 'not for publication' (which may contain CCI and personal data) of a CSR that was part of a marketing authorisation dossier submitted through a centralised authorisation procedure or a national authorisation procedure.

5.9. How to deal with the situation when the same CSR document is subject to transparency requirements in CTIS and under policy 0070?

In the context of centralised authorisation procedures, the Marketing Authorisation (MA) applicant submits the anonymised CSR to the EMA for review in line with the requirements of EMA Policy 0070 (called 'version 1' for the purposes of this document). Once the EMA review is completed, the agreed **anonymised version of the CSR** (called 'version 2' for the purposes of this document), along with other clinical documents covered under the scope of EMA Policy 0070, will be published on the Clinical Data Publication (CDP) portal. For any CSR that should be submitted both to CTIS and under EMA Policy 0070, **applicants should submit to CTIS, within 30 days of the MA decision** (or of withdrawal of the application, as applicable):

- A **'for publication' version**, with redacted personal data and CCI as applicable, that is the **document already reviewed under the Policy 0070** ('version 2'), if available. **Alternatively**, in cases where the EMA review under Policy 0070 has not yet been finalised, applicants should submit in the CTIS section 'for publication' of the CSR a **document with standard wording including a reference to the Policy 0070 CSR** (see question 5.10.).
- A **'not for publication' version of the CSR**, that corresponds to the original version, unredacted and with content in line with question 5.8.

5.10. In case the CSR review under Policy 0070 is not finalized within 30 days of the MA decision, what is the suggested wording for the 'for publication' version of my trial's CSR?

In case the anonymised CSR is still under Policy 0070 review by day 30 following the MA Decision (see question 5.9.), in the 'for publication' version of CTIS, the MA applicant may submit a company headed document with the following suggested wording:

> The present Clinical Study Report (CSR) of EMA procedure number *[insert as applicable EMEA/H/C/00XXXX/XXXX/, VR number or equivalent procedure number]* is (will be) published on the Clinical Data Publication website (https://clinicaldata.ema.europa.eu/web/cdp/search) once its anonymised version becomes available. Users can identify the clinical data document package by logging into the website and entering one or more of the following details in the advanced search functionality:
>
> **Product name**: *[trade name]*
>
> **Active substance name / International Nonproprietary Name (INN)**: *[INN]*
>
> **Marketing authorisation holder/applicant**: *[company name]*
>
> **Procedure type**: *fill in as applicable [Initial Marketing Authorisation]/[Line Extension]/[Extension of indication]/[Workshare]*
>
> Once the relevant clinical data document package has been identified and opened, the CSR documents can be found under the section 'Clinical study reports'. The file names of these documents contain the following study identifier: *[insert the relevant number as included in the electronic file name of the CSR submitted for review under Policy 0070]*

Note that the 'not for publication' version of the CSR should not have the above suggested wording: its content should be in line with the requirements mentioned in the response to question 5.8..

5.11. When should a CSR be submitted to CTIS but not under policy 0070?

Note that CSRs included in MA applications submitted via national authorisation procedures (decentralised, mutually recognised procedures and national procedures) are not subject to Policy 0070 publication requirements; however, they fall within the scope of submission to CTIS under the CTR. For those CSRs, the standard wording referenced in the response to question 5.10. cannot be used.

5.12. When is the CSR submission functionality enabled in CTIS?

The CSR submission functionality becomes available once the trial is authorised.

5.13. Does the submission of a CSR trigger the publication of other documents in CTIS?

No. The CSR is published as soon as it is submitted in CTIS for all trial categories, including category 1. However, this does not trigger the publication of any other document or data, which will continue to follow the timelines defined in the Revised Transparency Rules. Note that for category 1 trials conducted on paediatric population, the study protocol documents that were submitted as 'for publication' before the trial's authorisation, are published upon submission of summary of results and/or layperson summary of results (see refer to Table II of Annex I to the relevant Guidance document).

5.14. What to submit to CTIS in case by the 30 days deadline only an interim CSR is available, because the trial is still ongoing?

In this case, the 'interim' CSR version should be submitted, according to the CTR, within the deadline of 30 days from the MA decision (or of withdrawal of the application, as applicable). The applicant is in this case not legally required to submit the final version of the CSR (once available), unless this final version is submitted in support of further changes to the terms of MA (see question 5.16.). However, note that submitting a final version is technically possible and encouraged in the interest of transparency towards the public.

5.15. Is it allowed to redact entire pages of the (interim) CSR to protect CCI?

When redacting a CSR, the Marketing Authorisation Applicant must ensure a proper balance between protecting CCI and personal data, while maintaining data utility for the public. Redacting entire pages is generally not acceptable unless it is the only way to guarantee the protection of CCI and personal data.

5.16. Is the CTIS submission of a CSR required when submitted in the MAA as part of variations, line extensions, etc.?

Yes, Article 37(4) of the CTR establishes the principle that any CSR, on the basis of which a MA is granted or refused or the application for the same MA is withdrawn, should be submitted via CTIS within 30 days of the MA decision or MAA withdrawal. Therefore, **any change to the terms of such MA based on a new version of the CSR with new clinical data** should be subject to the same obligations as the initial MA (see also section 4.6.3., page 27 of the Guidance document). In CTIS, MA applicants need to upload CSRs through clicking on 'Add document' in the CSR section. Multiple versions of a CSR can be uploaded in the same placeholder and their 'for publication' versions will be subject to publication. Note that, when submitting the CSR version referred to variation/line extension, **the**

structured data field to be filled in the CSR section of CTIS need to refer to the variation/line extension and no longer to the initial marketing authorisation.

5.17. In case the MAA is withdrawn, should the CSRs included in the MAA be submitted to CTIS?

Yes. The requirements laid down in Art 37(4) of the CTR foresee the submission to CTIS of all CSRs included in MAAs submitted in EU/EEA via any authorisation route, including those applications which are withdrawn during the assessment stage of the MAA, or those for which the outcome was negative.

5.18. If the MAA includes several versions of Clinical Study Protocol (CSP), SAP, CRF, should they all be submitted to CTIS together with the CSR?

If in the MAA there are several versions of the protocol and of the SAP, all versions should be included in the CSR Appendixes 16.1.1 and 16.1.9, in line with ICH E3 for MAA requirements. For the CRF, the most current (the latest version of all unique pages) is expected.

5.19. If the initial MAA includes several versions of CSR (based on multiple Data Cut Offs), is only the current (latest version) of the CSR included in the initial MAA expected to be submitted to CTIS?

Yes. The latest CSR version and appendixes is the one that need to be submitted to CTIS.

5.20. Is it possible to only submit to CTIS the version 'for publication' of the CSR?

The version 'not for publication' should also be submitted within the legal timelines, in case in the corresponding 'for publication' version there are redactions or anonymisations. In case the 'for publication' version does not contain any redactions or anonymisations, then only this version is sufficient and no 'not for publication' version should be submitted to CTIS.

5.21. How to approach blinding redactions when a study has not yet been unblinded at the time of publication? Can the applicant ask to defer the submission of a CSR to CTIS?

It is not possible to ask to defer the submission of the CSR. The CSR versions 'for publication' and 'not for publication' need to be submitted to CTIS within 30 days from marketing authorisation decision on the product, or of its withdrawal, as per the CTR. For the 'for publication' version the applicant can submit a CSR with the necessary redactions to protect the blinding of the study. Once the unblinding occurs, for transparency reasons the applicant is then required to submit a further version of the CSR to CTIS, where the blinding redactions are removed.

5.22. If the same clinical trial is referenced in two separate MAA procedures, should both CSRs be submitted to CTIS?

The CSR and appendices should be uploaded separately for each MAA, under the same CTIS trial. CTIS gives the possibility of uploading multiple 'for publication' and 'not for publication' documents in the same location through the 'Add document' button. The most recent MA procedure's CSR should be the one referenced in the structured data fields.

5.23. Can a CSR be submitted to CTIS in languages other than English?

In the CTR there is no reference to language requirements for CSR, so the MA applicant/holder can submit CSRs in languages other than English.

Note that in the context of centralised authorisation procedures, the applicant is required to provide the English version of the document, which is also foreseen and published under EMA Policy 0070. This document is the one that should also be submitted to CTIS (or referenced to, see question 5.9.).

5.24. If a trial was completed under the CTD in some Member States but was transitioned to CTIS for others, is the submission of the CSR expected?

In case a trial that was part of a MAA was transitioned to CTIS, even if in only some Member States, the submission of the relevant CSR to CTIS is required since the trial is now under CTR requirements.

5.25. Could documents such as study protocol that are submitted to CTIS when applying for a trial authorisation have a higher level of redaction compared to the same documents published later as part of a CSR on CTIS or under Policy 0070?

Yes, this is possible as CCI may be time dependent: information considered CCI at the time of approval of the CTA may not be considered CCI anymore after the MA procedure is concluded.

6. CTIS training and support

6.1. What are the resolution timelines for the CTIS Service Desk?

The EMA CTIS Service Desk prioritises urgent technical support tickets, particularly those involving blocking issues or risks related to publication of CCI or personal data. Resolution timelines depend on the urgency and impact of the issue, in line with the applicable Service Level Agreements (SLAs). These timelines are visible within the Service Desk portal once a ticket is submitted. For urgent situations (e.g., risk of trial lapse), users may contact the EMA Service Desk directly by phone in addition to submitting a ticket.

6.2. What is the best way for users to communicate their suggestions on CTIS future improvements to the EMA?

Users can contact the product owners representing stakeholders or submit well-justified and clearly described requests via the EMA CTIS Service Desk.

6.3. Does the EMA still recommend that users avoid working with CTIS during maintenance windows?

Yes. The EMA continues to recommend that users do not log in or perform any work in CTIS during planned maintenance windows, listed under Planned system interruptions, since any data entered during these periods may be lost.

7. History and summary of changes of the Sponsor FAQs

This FAQs document has been developed by the EMA and it based on questions frequently raised to EMA by sponsors during CTIS events such as Walk-in Clinics, Bitesize Talks, and through the EMA CTIS Service Desk. In addition, it replaces other Q&A documents on CTIS (the Q&A on the protection of Commercially Confidential Information and Personal Data while using CTIS, and the Q&A – Clinical Trials Information System (CTIS) and Clinical Trials Regulation (CTR)). It was reviewed in collaboration with representatives from academia, industry, and Member States. It is regularly updated, particularly to reflect changes in CTIS functionalities.

Document version and publication date	Changes introduced in the text
1.0, 26 March 2026	First version of the document.

Annex I: acronyms and definitions

See also 'Definitions' Article 2 of CTR, EMA General Glossary of regulatory terms and EMA Medical Terms Simplifier.

Acronym	Definition
AM – Addition of a Member State concerned application	Refer to Article 14 of the CTR and to definition of CT application.
ASR - Annual Safety Report	Document on the monitoring and evaluation of the evolving safety profile of an IMP and the mitigation of potential risks. When submitting an ASR, the following two terms are mentioned, in step 2: **Novel-novel combination**: a combination of two or more innovative (investigational) medicinal products, neither of which has been authorised or thoroughly studied before, either individually or in combination **New combination**: a new pairing (or grouping) of already known/authorised medicinal products that have not previously been studied together in a clinical trial. Even though the individual components are not innovative per se, their combined use introduces a novel therapeutic strategy that requires separate evaluation for safety and efficacy.
ATC code - Anatomical Therapeutic Chemical code	International classification system for medicines that is maintained by the World Health Organisation (WHO).
ATMP - Advanced Therapy Medicinal Product	Medicine for human use that are based on genes, tissues, or cells, offering ground-breaking new opportunities for the treatment of disease and injury.
AxMPs – Auxiliary Medicinal Product	Article 2 (8) of the CTR defines an AxMP as 'a medicinal product used for the needs of a clinical trial as described in the protocol, but not as an investigational medicinal product'. Therefore, AxMPs are medicinal products that fall within Article 3(3) of Directive 2001/83/EC, as they are used for the needs of a clinical trial, while not falling within the definition of IMPs as defined in Article 2 (5) of the CTR.
CCI - Commercially confidential information	Information whose publication might prejudice the commercial interests of individuals or companies to an unreasonable degree. The Agency cannot disclose commercially confidential information unless there is an overriding public interest in disclosure.
CRO - Clinical Research Organisation	A contract research organisation, also called a clinical research organisation is a service organisation that provides support to the pharmaceutical and biotechnology industries in the form of outsourced pharmaceutical research services (for both medicinal products and medical devices).
CSR - Clinical Study Report	Report of an individual study of an investigational medicinal product, in which the clinical and statistical description, presentations, and analyses are integrated.

Acronym	Definition
CT - Clinical trial	Refer to Article 2(2)(2) of the CTR.
CT application - Clinical Trial Application	A request (made by the sponsors) for the authorisation (by the Member States concerned), to perform an action related to clinical trials conducted in the EU. It can be a request to start a clinical trial (IN), the extension of a clinical trial to another MSC territory and subjects (AM), or to perform an important modification to an already started CT.
CTCG - Clinical Trials Coordination Group	The CTCG is a European Heads of Medicines Agencies (HMA) working group of experts in the classification, assessment, and oversight of clinical trials from National Agencies. This working group also promotes harmonisation of clinical trial assessment decisions and administrative processes across the national competent authorities (NCAs). More information here.
CTD - Clinical Trial Directive 2001/20/EC	Former Clinical Trials' legislation applicable in the EU, repealed by the Clinical Trial Regulation (EU) 536/2014.
CTIS - Clinical Trial Information System	Online system for the regulatory submission, authorisation, and supervision of clinical trials in the EU/EEA. CTIS acts as the single-entry portal in the EU/EEA for all trials on investigational medicinal products involving human subjects. Trial data and documents are accessible on the CTIS public website.
CTR - Clinical Trial Regulation (EU) 536/2014	EU pharmaceutical legislation aiming to harmonises the processes for assessment and supervision of clinical trials throughout the EU. On 31 January 2022, the Regulation repealed the Clinical Trials Directive (EC) No. 2001/20/EC and national implementing legislation in the EU Member States, which regulated clinical trials in the EU until the Regulation's entry into application. More information here.
CV	Curriculum Vitae
EC - Ethics Committee	Refer to Article 2(2)(11) of the CTR.
EEA - European Economic Area	Economic area composed of Member States of the EU and three countries of the European Free Trade Association (EFTA) (Iceland, Liechtenstein, and Norway; excluding Switzerland).
EMA - European Medicines Agency	Agency of the EU responsible for the scientific evaluation, supervision, and safety monitoring of medicines in the EU, as well as for the maintenance and further development of the CTIS. More information here.
EoR – End of Recruitment	The act of stopping recruitment of subjects in an MSC.
EoT – End of Trial	The last visit of the last subject, or a later point in time as defined in the protocol (as per Article 2(26) of the CTR).
EU - European Union	Supranational political and economic union of 27 member states that are in Europe.

Acronym	Definition
EU CT number - EU Clinical Trial number	Trial identifier code, unique to each clinical trial conducted in CTIS.
EU MP number - EU Medicinal Product number	A unique number (EV Code) assigned by the XEVMPD to each medicinal product record successfully inserted in the dictionary; it is used to identify this medicinal product in the XEVMPD.
EV - EudraVigilance	Refer to definition here.
GDPR	General Data Protection Regulation
GMP	Good Manufacturing Practices
IAM – Identity and Access Management	User registration system that provides individuals with access to the applications that are managed by the EMA, including CTIS, XEVMPD, OMS, EV.
ICF – Informed Consent Form	
IMP - Investigational Medical Product	Refer to Article 2(2)(5) of the CTR.
IMPD - IMP Dossier	Dossier that provides information related to the quality of an IMP (IMPD Q), and to the Safety and Efficacy (IMPD S and E).
IN - Initial Clinical trial Application	Refer to definition of CT application. The elements to be included in the application dossier for an IN are defined in Annex I of the CTR.
IPD – Individual Patient Data	Raw data collected from each individual participant in a study.
JCA – Joint Controllership Arrangement	The Joint Controllership Arrangement describes the allocation of respective roles, responsibilities and practical arrangements between the parties for compliance with their respective data protection obligations as part of the authorisation and supervision of clinical trials in CTIS.
MAH/MAA - Marketing Authorisation Holder/MA Applicant	The company named on the Marketing Authorisation for a medicinal product in a country or in the EU/EEA, or the applicant of a marketing authorisation for a medicinal product.
MSC - Member State Concerned	An EU Member State that has received a CT application for its assessment and therefore is responsible for its assessment. Refer to Article 2(2)(12) of the CTR.
NCA - National Competent Authority	National regulatory agency in an EU Member State.
NSM - Non-Substantial Modification	A change implemented to a Clinical trial with the purpose of correcting information that is not expected to have a substantial impact on the safety or rights of the subjects or on the reliability and robustness of the data generated in the Clinical trial. Refer to Article 81(9) of the CTR.

Acronym	Definition
OMS - Organisation Management Service	EMA management system managed providing a single source of organisation data, such as their names and addresses. More information here.
PIP - Paediatric investigation plan	A paediatric investigation plan (PIP) is a development plan aimed at ensuring that the necessary data are obtained through studies in children, to support the authorisation of a medicine for children. More information here.
QP	Qualified Person
RFI - Request for Information	CTIS functionality through which the MSC(s) ask sponsors to provide additional information in the context of validation and assessment of a CT application, ad hoc assessments, corrective measures, and ASR.
RMS - Reporting Member State	Member State Concerned with a leading role in the assessment of Part I of a CT application and in the monitoring of a CT during the clinical trial lifecycle
saMS – Safety Assessing Member State	The Member Sate performing the coordinated assessment of the ASR.
SM - Substantial Modification	Refer to Article 2(2)(13) of the CTR and to definition of CT application
SoR – Start of Recruitment	The date of the first visit of the first subject, as required by article 36(2) CTR.
TMF – Trial Master File	The collection of essential documents that is used by sponsors, CROs and investigators/institutions for the management of the trial and by monitors, auditors, and inspectors to review and verify whether the sponsor and the investigators/institutions have conducted the trial in line with the applicable regulatory requirements and the principles and standards of GCP
XEVMPD - eXtended EV Medicinal product data dictionary	Data base that stores and provides quality data on authorised or investigational medicinal products to CTIS. This information is requested to sponsors when filling out a clinical trial dossier/application.