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Q&A on the protection of Commercially Confidential Information and Personal Data while using CTIS

Question and Answers, version 1.4

This Q&A document has been created to provide preliminary guidance to CTIS users on how to protect personal data and commercially confidential information (CCI) in CTIS, the EU database established in accordance with the requirements of Regulation (EU) No 536/2014 (CTR).

The Q&A document has been produced to address a number of questions related to the transparency aspects of CTIS which were communicated by sponsors in response to the ACT EU survey on the CTR (Clinical Trial Regulation (EU) No 536/2014) implementation under ACT EU Priority action 2 (Successful implementation of the CTR). It is foreseen that the Q&A may be updated on a regular basis as soon as new information becomes available.

The Q&A intends to provide more clarity on main aspects that have been discussed with the Clinical Trials Coordination Group (CTCG) and it 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 \(CTIS\)](#) and its [Annex I](#).



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Version 1.2	17 May 2023	<ul style="list-style-type: none"> - Clarification on deferrals section 1 (<i>Italics</i>) - Revised text in Q&A 1.8 - Revised text in Q&A 2.2 - New Q&A 3.3. - Minimum editorial review across the text
Version 1.3	29 November 2023	<ul style="list-style-type: none"> - New section 4 on revised transparency rules - Update text across the document to align with principles of section 4
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Table of contents

1. Deferrals	5
2. Personal Data	7
3. Commercially Confidential Information	8
4. Revised CTIS transparency rules	10
Annex I - Recommended wording for all documents that are no longer subject to publication as per revised CTIS publication rules.....	12

Abbreviations

AR	Assessment Report
ASR	Annual Safety Report
CCI	Commercial Confidential Information
CTD	Clinical Trial Directive 2001/20/EC
CTIS	Clinical Trials Information System
CTR	Clinical Trial Regulation (EU) No 536/2014
CV	Curriculum Vitae
GDPR	General Data Protection Regulation
GMP	Good Manufacturing Practices
IB	Investigator's Brochure
MS	Member State(s)
MSC	Member State Concerned
PD	Personal Data
PI	Principal Investigator
RFI	Request for Information
RMS	Reporting Member State
SM	Substantial Modification
QP	Qualified Person
WHO ICTRP	World Health Organisation International Clinical Trials Registry Platform

1. Deferrals

Please note that clinical trials with a decision issued after mid-August 2022, for which sponsors have requested any type of deferrals in the application form are currently not published in CTIS. This is a temporary measure until the functionalities of CTIS public website will be implemented in line with the requirements of the [revised CTIS transparency rules](#).

In addition, and following the publication of the above mentioned rules, sponsors can consider options on the use of deferrals, as explained in section 4. of this document.

1.1 Will RMS/MSC comment on the trial categorisation only, or also on the proposed deferrals timelines?

It is expected that RMS/MSC will comment mainly on the trial category rather than on the sponsor's proposed timelines for deferrals. However, the possibility to receive more detailed comments on the proposed timelines for deferrals should not be excluded.

1.2 How should trials in public health emergency settings and trials in emergency situations be treated in terms of categorisation/ deferrals?

As provided in Article 17(1) of Regulation (EU) 2022/123, for clinical trials in public health emergency settings¹, the protocol should be made public at the time of the start of trial and the summary of results later on during the trial life cycle. The publication of these documents cannot be deferred.

In principle, clinical trials in emergency situations² fall either under category 2 or 3 (therapeutic intent), since for these trials Article 35 (1)(b) of Regulation (EU) No 536/2014 requires scientific grounds for individual clinically relevant benefit for subjects.³

1.3 Which type of justification should be provided for deferrals?

RMS/MSC will consider the justification provided for the trial category, based on the characteristics of the trial, as the basis for requesting deferrals.

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.

1.4 Will RMS raise an RFI on deferrals at time of validation or assessment part I?

An RFI on deferrals can be raised at any time at validation and assessment of part I, however it is expected to be raised by the RMS primarily at the time of part I assessment.

Of note, deferrals can only be set by the sponsors in an initial application. Once the initial application has been authorised it will not be possible for the sponsor to modify deferrals with subsequent applications, such as substantial modifications.

¹ Clinical trials with medicinal products with the potential to address public health emergencies.

² Emergency situation: first trial specific intervention before signing the informed consent.

³ Article 35 of Regulation (EU) No 536/2014

1.5 When will sponsors know if deferrals have been granted?

Sponsors will know that a deferral 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 deferrals are accepted, they are part of the application evaluation overall.

1.6 Will MSCs apply the same timelines as sponsors for the deferrals of their final ARs/ RFI?

Yes, it is expected that, in principle, the MSCs will apply the same timelines as the sponsors to delay the publication of their assessment reports (conclusion by RMS for Part I, conclusion by MSCs on Part II, respectively) and RFIs sent to the sponsors.

1.7 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/MS might occasionally comment on the extent of the redaction applied by the sponsor to ensure that the principles of transparency are followed⁴.

1.8 Will RMS/MS compare document version 'for publication' vs 'not for publication'?

RMS/MS 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 personal data is described in the [CTIS JCA](#) and applies regardless of the use of deferrals in the system.

In principle, CCI-related redactions should be avoided in case a deferral has been requested. CCI can be protected by way of redaction **or** requesting a deferral, only one of the two mechanisms shall be used by the sponsor to comply with the CTR transparency principles.

It is acknowledged though that, in limited situations, specific pieces of information (e.g., of quality nature in the trial protocol) could still be considered CCI after the deferral period elapses, and consequently their redaction would be acceptable even in documents subject to deferral requests.

1.9 How should documents with track changes be submitted in CTIS?

Documents with track changes should be provided to the Member States to clearly illustrate the scope of the revision applied in the documents content. These documents can be submitted in an application in reply to a request for information (RFI) or as part of a substantial modification. Member States expect these documents to be uploaded **only** in the slot 'not for publication'.

A clean version of the final text of the documents should be uploaded in CTIS in the slot 'for publication', as applicable for published documents and as recommended in section 4 of this Q&A, with no personal data or commercial confidential information included.

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.

2. Personal Data

2.1 Which CTIS documents require a signature?

For documents uploaded in CTIS in a clinical trial application dossier, a signature should be provided for the Qualified Person (QP) declaration for 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)

Please also consider further clarification on this matter provided in [Eudralex Volume 10, COM 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'*.

Any signed document should be provided in the CTIS dossier placeholder 'not for publication', and content redacted in the placeholder 'for publication' for those documents in line with the revised CTIS transparency rules (see section 4 of the present document). Please consult [training module 12](#) for additional information.

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

2.2 Name and surname of individuals – where are they expected to be included?

Only the name and surname of applicable persons are required on the following documents in a clinical trial application dossier submitted to CTIS:

- 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](#)

Any document containing personal data (e.g., names and surnames, and also contact details) should be provided in the CTIS dossier placeholder 'not for publication' and personal data redacted in the placeholder 'for publication' for those documents in line with the revised CTIS transparency rules (see section 4 of the present document).

Please note that the document versions uploaded in the slot 'not for publication' should be clean documents, without any redaction. Redacted documents should be submitted only in the slot 'for publication'.

Name and surname of the principal investigator and the person issuing the site suitability document are not to be redacted in line with [Appendix on disclosure rule](#). Please consult [training module 12](#) for additional information.

2.3 Under Directive (2001/20/EC) the clinical trial participants subject identifier (ID) was provided in Annual Safety Reports (ASRs). Is it correct that as per Regulation (EU) No 536/2014 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 Volume 10 - Clinical Trials Regulation (EU) NO 536/2014 questions & answers, point 7.33 (366 and 367): [regulation5362014_qa_en.pdf \(europa.eu\)](#)

For more information on data protection in CTIS please consult also:

- CTIS Joint controllership arrangement (JCA):
https://www.ema.europa.eu/en/documents/other/joint-controllership-arrangement-regard-clinical-trials-information-system-ctis_en.pdf
- Questions and answers on the JCA:
https://www.ema.europa.eu/en/documents/other/questions-answers-joint-controllership-arrangement-data-protection-matters-related-use-clinical_en.pdf

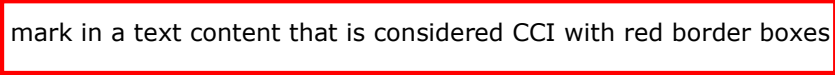

3. Commercially Confidential Information

3.1 May sponsors mark/highlight the text that they consider CCI in documents 'not for publication'?

Yes. In case the sponsors wish to flag what they consider CCI in the documents uploaded in CTIS, they can mark the text with red border boxes. The sponsor could place red border boxes around the text in the non-redacted document to clearly indicate what they consider as confidential information.

Of note the version of the documents 'not for publication' should be readable and ready to be used for MS assessment. 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.

Example:

- a) Documents 'not for publication'  mark in a text content that is considered CCI with red border boxes
- b) Documents 'for publication' 

Application of redaction 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.

It needs to be emphasized that the redacted documents have to remain meaningful to the public, including potential trial participants and health care professionals.

3.2 How will the Member States ensure that CCI is not inadvertently published through MS responses and assessments?

The CTIS contains multiple safeguards to protect the inadvertent publication of CCI or personal data. The system ensures that information classified as quality-related within considerations, RFIs and assessment reports is never published. In addition, member states users are aware of the need for correct categorisation of their considerations in the system and that the MSC published documents and structured data should be carefully phrased.

The system also automatically excludes certain types of documents from publication for example, draft assessment reports, annual safety reports, ad hoc assessment forms and related documents, ensuring these documents and assessments will never become public.

Furthermore, assessors will be aware of those pieces of information highlighted as CCI in the document version 'not for publication' and take this into account to avoid that such information is not accidentally disclosed in the assessment report or RFI.

It is to be noted that, until the implementation of the technical changes in CTIS, the Member States may already follow the principles of the revised CTIS transparency rules, as detailed in section 4 of this Q&A, and upload a page with the wording suggested in Annex I of the present document in the slot 'for publication' of all documents that are no longer subject to publication in line with the revised rules, such as final assessment reports, decision letters, etc.

3.3 How can dose details be protected from disclosure from CTIS for certain trials category falling within category 2?

The main characteristics of medicinal products used in clinical trials falling under **category 2** are subject to publication rules after a decision on the clinical trial application is issued by the first Member State concerned.

These main characteristics also include structured data fields on daily dose allowed and maximum dose allowed for the medicinal product under investigation. In some instances, depending on the trial

development phase, 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.

This might be applicable for example to integrated phase I/phase II trials that are to be marked in CTIS as category 2 trials. The grounds for considering dose details as CCI should be clearly documented in the cover letter of the application.

3.4 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.

4. Revised CTIS transparency rules

4.1 How to deal with clinical trials applications being submitted in CTIS before the implementation of the revised transparency rules into CTIS?

In the period of time from adoption of the revised rules until their technical implementation in the system, for initial clinical trials applications, sponsors may already follow the principles of the revised rules, providing a version 'for publication' and 'not for publication' **only for the documents in scope of the revised transparency rules (as detailed in [Annex I of the document](#))**, and upload in the slot 'for publication' for those documents that will no longer be subject to publication, a page with the wording suggested in **Annex I** to this Q&A.

The unredacted version of the documents to be assessed must be provided in the slot 'not for publication', in order to allow a proper evaluation of the dossier by the Member States.

Making use of the principles of the revised transparency rules prior to their implementation in CTIS, the burden of redaction to CTIS users is reduced. This should translate in **refraining from requesting deferral**, as CCI will be protected by redaction in the documents in scope of publication.

Publication of clinical trials information in CTIS public website will therefore increase, as well as in the WHO ICTRP, for which CTIS is a registered data provider.

Regarding the other applications submitted during the trial life cycle prior to the implementation of the technical changes, such as substantial modifications and the addition of a new MSC, sponsors should

consider the preferred approach on protection of personal data and CCI, with the aim to decrease burden depending on the status of the trial, i.e. for example whether deferrals are already in place.

The principles of the revised transparency rules may be followed also for documents produced by the Member States, for which the same wording suggested in **Annex I** to this Q&A should be used in the documents slot 'for publication', for example for assessment reports, decision letters, etc.. and as detailed in section 3 above.

CTIS users are reminded that personal data and CCI still continue to be protected in RFI and RFI responses, as the fields cannot be redacted and continue to be published until implementation of technical changes in CTIS, as per revised transparency rules.

4.2 Will the revised transparency rules be applied retrospectively to existing trials, including trials with deferrals, that have already been submitted in CTIS?

Once that the new CTIS public website will be launched, the 'historical' trials (i.e. trials submitted to CTIS before the new transparency rules are implemented, whether publicly available or not, and with/without deferrals) will follow the publication principles detailed below:

- **Structured data fields:** the structured data fields for all trials' categories of historical trials will be published in line with the timelines and principles of the revised transparency rules;
- **Documents:** all documents contained in applications submitted to CTIS before the implementation of the technical changes **will not be published**. This applies to all historical trials in the system, and regardless of the previous use of deferrals or publication status.

Documents in scope of publication, as detailed in Annex I of the revised rules, provided in applications, or trial results, submitted to CTIS after the implementation of the technical changes, will be published in line with the timelines and principles of the new rules.

For example if a Substantial Modification (SM) part I of an historical trial that had a deferral in place on the protocol is submitted in CTIS after the implementation of the revised rules with the purpose of updating the Investigator's Brochure (IB), the sponsor should consider redaction of the protocol and synopsis, as applicable, to protect personal data and CCI as the protocol and synopsis will be subject to publication under the new rules.

4.3. How to deal with transition of clinical trials from CTD to CTR according to the new CTIS transparency rules?

Sponsors are encouraged to transition clinical trials from CTD to CTR based on available existing [guidance](#) document.

In particular, transparency aspects of transitional trials are described in question 11 of the guidance, clarifying that the documents to be published for transitional trials are the protocol, subject information sheet and informed consent form.

At the time of submission of subsequent modifications, the dossier can then be updated with the documents for publication falling within the scope of the revised transparency rules, e.g., synopsis and recruitment arrangements. For these documents the same principles of Q&A 4.1 of this document apply.

Annex I - Recommended wording for all documents that are no longer subject to publication as per revised CTIS publication rules

A page can be uploaded in the slot 'for publication' of all documents that are no longer subject to publication as per revised CTIS publication rules, with the following recommended wording:

The present document is no longer subject to publication in line with [revised CTIS transparency rules](#). Further information is provided in section 4 of the 'Q&A on the protection of Commercially Confidential Information and Personal Data while using CTIS' published on the [ACT EU website – Implementation of the Clinical Trials Regulation](#).