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Revised CTIS Transparency Rules

Public consultation on the transparency rules for the operation of the Clinical Trials Regulation (CTR) and its Clinical Trials Information System (CTIS)	3 May 2023 – 28 June 2023
Adoption of revised rules by EMA Management Board	5 October 2023

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1. Introduction

The Clinical Trial Information System (CTIS) has been in use since 31 January 2022 and includes the EU Portal and the EU database established in accordance with Article 81 of the Clinical Trials Regulation (EU) No 536/2014 (CTR), for the exchange of information on clinical trials in the European Union.

A public interface of the EU database is available in line with the requirements of Article 81(4) of the CTR, which also refers to protection of personal data and commercially confidential information (CCI) when providing data and documents to CTIS.

Publicly available information contained in CTIS contributes to protecting public health and fostering the innovation capacity of European medical research, while protection of CCI recognises the legitimate economic interests of sponsors, in line with the CTR.

Legal basis for CTIS transparency rules

Recital 67 of the CTR states that the information in the EU database should be public, unless specific reasons require that a piece of information should not be published.

Specific justifications for not publishing certain information considered as confidential are set out in Article 81(4) of the CTR. According to that Article, confidentiality is justified on any of the following grounds:

- (a) protecting personal data in accordance with Regulation (EC) No 45/2001¹;
- (b) protecting commercially confidential information, in particular through taking into account the status of the marketing authorisation for the medicinal product, unless there is an overriding public interest in disclosure;
- (c) protecting confidential communication between Member States in relation to the preparation of the assessment report;
- (d) ensuring effective supervision of the conduct of a clinical trial by Member States.

The transparency rules implemented in CTIS at the time of the launch of the system in January 2022 were defined in a document adopted by the EMA Management Board in 2015: [Appendix, on disclosure rules, to the "Functional specifications for the EU portal and EU database to be audited - EMA/42176/2014"](#). The document referred to the publication of the clinical trial application (CTA) dossier provided in CTIS, and all the clinical trial information submitted during the trial life cycle, with the exception of the quality related documents, financial arrangements and some supervision related information.

After the launch of CTIS, experience has been gained on the publication of structured data fields² and documents provided by the users, with protection of commercially confidential information (CCI), possible, particularly for sponsors, by using either a deferral mechanism implemented in CTIS to delay the publication of certain data and documents or on redaction of elements considered CCI. Protection of personal data, when contained in the documents submitted in CTIS, applies irrespective of the use of deferrals and should occur at all times in the published documents.

Learning from the experience with the use of the system and in order to listen to the feedback from CTIS users and the general public, an eight-week public consultation was held between May and June 2023 on the revision of CTIS transparency rules with the aim of simplifying the implemented rules

¹ Regulation (EC) No 45/2001 repealed by the EUDPR, Regulation (EU) 2018/1725

² Structured data fields are the fields populated by the users in CTIS, these can be free text fields or fields with predefined values to choose.

while maintaining protection of personal and confidential data and maintaining high levels of transparency, particularly in the interest of patients. The revised transparency rules build on that experience and feedback.

The revised CTIS transparency rules are without prejudice to individual requests for access to additional information or documents under the CTR which will be assessed by the Agency or requests to access documents under Regulation (EU) 1049/2001³.

2. CTIS transparency rules implemented at the time of the launch of the system

CTIS transparency rules defined in the document 'Appendix on disclosure rules', referred to the publication of the almost complete clinical trial application dossier, as well the clinical trials information provided during the trial life cycle, while requiring users to protect personal data and CCI.

To protect personal data that might be available in the documents submitted in CTIS, an option to upload a document version 'for publication' and a corresponding version 'not for publication' has been implemented in the system. Experience has shown that the 'not for publication' document option has been used to protect also CCI, in addition to personal data, if included in the documents.

Of note, document versions 'for publication' and 'not for publication' are to be used in CTIS only depending on the document content, and whether protection of personal data (and CCI) is necessary.

According to the above mentioned 'Appendix on disclosure rules', protection of CCI was also enabled via the use of a deferral mechanism with different options based on a categorisation of trials, acknowledging that clinical trials are different and contain different CCI, depending on the development phase of the investigational medicinal product being used.

Categorisation of trials has been the basis for defining the applicable deferral timelines allowing sponsors to request to publish the relevant clinical trial information not at the time of the application decision, but rather at the end of the deferral period (a variable number of years after trial end in EU/EEA), the submission of summary of results or clinical study reports, whatever occurred earlier. This allowed, for certain types of trials, deferral of publication of key clinical trial documents, including the protocol, for up to 7-years from the end of the trial in the EU/EEA.

The categorisation of trials, as defined in the Appendix of disclosure rules, and that will remain in place under the revised CTIS transparency rules for CTIS, covers:

1. Category 1 trials - Pharmaceutical development clinical trials:

- Phase I clinical trial in healthy volunteers or patients;
- Phase 0 trial - in healthy volunteers or patients, without therapeutic or prophylactic intent;
- Bioequivalence and bioavailability trials;
- Similarity trials for biosimilar product including those conducted in patients where efficacy endpoints are used to determine biosimilarity, where pharmacokinetic and or pharmacodynamic studies are not possible;

³ https://www.europarl.europa.eu/RegData/PDF/r1049_en.pdf

- Equivalence trial for combination products or topical products where a pharmacodynamic or efficacy endpoint is used to determine equivalence, and where pharmacokinetic and or pharmacodynamic studies are not possible.

2. Category 2 trials - Therapeutic exploratory and confirmatory clinical trials:

- Phase I and phase II integrated clinical trial;
- Phase II clinical trial;
- Phase III clinical trial.

3. Category 3 trials - Therapeutic use clinical trials:

- Phase III and phase IV integrated clinical trial;
- Phase IV clinical trial and low interventional clinical trials.

3. Need for revision of CTIS transparency rules

Since the launch of CTIS in 2022, the deferral functionalities have proven to be complex from an information management and data security perspective, which has led to some uncertainties in the use of CTIS when deferrals were applied. The deferral functionality, foreseen in the 'Appendix on disclosure rules' and implemented at the time of the launch of the system, will continue to remain in place until a new CTIS public website, implemented in line with the revised CTIS transparency rules, is available.

The CTIS transparency rules implemented at the time of the launch of CTIS, with extensive publication of data and documents, published even if provided as optional attachments to information already captured in the structured data field, and not focussed and tailored to the documents of interest for patients and clinical researchers, mixed with complex system functionalities, has had an impact on the use of the system.

The derogations for the disclosure of documents in paragraphs (c) and (d) of Article 81(4) of the CTR allows Member States competent authorities to protect confidential communication between Member States in relation to the preparation of the assessment report or to ensure effective supervision. These derogations have been in use since system launch and as a result draft assessment reports are not published, nor is information on planning of supervision activities (i.e. GCP inspections).

For certain other documents currently published via CTIS, redaction is applied to protect CCI, in line with the provisions of Article 81(4)(b).

It should be noted that extensively redacted documents, in their published version, are of limited utility to stakeholders, including patients.

4. Stakeholders view on CTIS transparency rules

4.1. EU Survey

Feedback provided by users revealed some challenges, in respect of the applicability of the publication requirements, combined with the use of a new IT system with functionalities implemented in line with the timelines defined in the CTR, and with the management of documents whose content had not yet been adjusted to sufficiently adapt to the new requirements on publication.

The feedback provided by CTIS users was collected via multiple consultations on CTIS transparency aspects, including on a survey initiated in 2022 under ACT EU Priority Action (PA) 2 on the identification of the main obstacles of the successful implementation of the CTR.

As a result of the collected users' feedback, the European Commission, the Heads of Medicines Agencies and EMA agreed that a change in the CTIS transparency rules was needed, to improve users' experience and easy access to the relevant clinical trial information.

4.2. Outcome of the 2023 public consultation on the revision of CTIS transparency rules

The objective of the public consultation held during May and June 2023, was to review the transparency rules for CTIS considering the experience with the use of the system and allowing the publication of clinical trial information for the benefit of the patients, thereby supporting access to treatments and innovation.

The changes to be implemented in CTIS, following the feedback of the public consultation, aim at simplifying the transparency rules to make the system less complex, more efficient and user-friendly, ensuring an improvement in the users' experience, reducing burden for the users and still maintaining public access to clinical trials information, in line with the aim of the CTR.

The CTR acknowledges the possibility to protect clinical trial information on justified grounds. In the new rules this is translated on the publication of key clinical trial information of relevance for the public.

The feedback collected during the public consultation was provided by 204 stakeholders, including sponsors, CROs, academia, national competent authorities, ethics committees, health care professionals, and patients organisations.

The consultation response showed stakeholders interest in:

- The publication of structured data fields including details of trial design, product and sponsor details, and notifications;
- Publication of essential documents from part I and part II of the clinical trial application dossier, as well as clinical trial results including clinical study reports;
- Considering use of deferral mechanism in case of high number of documents to be published (as redaction only would be, otherwise, too burdensome for users).

5. Revised CTIS transparency rules

Publication of clinical trials information will be in place through a revised CTIS public website. The revised CTIS transparency rules include:

- Publishing clinical trials information (i.e. structured data fields and documents), relevant for the public and corresponding to the needs of patients and clinical researchers in the EU/EEA;
- The implemented changes will help the public to easily identify the published information by reducing the complexity of information in the CTIS public website and providing easy searching in the structured data fields;
- Rationalising the amount of documents that are published to reduce complexity and workload for users engaged in the necessary redactions;

- Removing the deferral mechanism for every trial category, in combination with reducing the publication of documents to only those essential to patients and researchers, will deliver much earlier publication of key documents (including protocols), as well as significant system simplification.

It is important to note that the following principles remain in place under the revised CTIS transparency rules:

- Classification of trials under one of the three applicable categories is retained, but no longer in connection with the use of deferrals;
- No changes are foreseen on the earliest possible timeline for publication of data and documents, as this remains the time of the clinical trial application decision issued by the Member States Concerned, whether this is a positive or negative decision. This is in line with the requirements of Article 81(5) of the CTR stating that no data from a clinical trial application dossier shall be publicly accessible before the decision on the clinical trial has been made, unless there is an overriding public interest;
- Overriding public interests apply only in exceptional circumstances, on an *ad hoc* basis, when the public interest in having information made publicly available may outweigh considerations that the same information should remain confidential;
- In addition, information on applications which did not reach the decision phase, have lapsed, or have been withdrawn by the sponsors or have been considered not valid during evaluation, will continue to be exempted from publication;
- No changes are foreseen on CTIS being a data provider to the WHO International Clinical Trials Registry Platform (ICTRP). The clinical trial information published via CTIS public website will continue to feed the WHO ICTRP (with the revised rules continue to fully satisfy the WHO data requirements for public registries);
- No changes are foreseen for the clinical trials information contained in EudraCT for trials that have been authorised under Directive 2001/20/EC (CTD), and published via the EU Clinical Trial Register that will continue to be in place, nor for the transitional arrangements of clinical trials from the regime of CTD to CTR;
- No changes on the possibility for EMA to edit – on justified grounds - public information, for example in case of unintended disclosure of clinical trials information containing CCI.

5.1. Revised publication rules for structured data fields in CTIS:

The structured data fields include a compilation of fields that are populated by the users directly in CTIS, these include fields with predefined values, as well as free texts. They include information on trial title, study design, inclusion and exclusion criteria to take part to the trial, primary and secondary endpoints, details on the investigational medicinal product used in the trial, clinical investigator sites in the Member States where the trial is conducted, as well as sponsor's contact details. These structured data fields also allow to capture information on the authorisation status of the trial and relevant dates, such as those related to start of trial and recruitment of patients in the Member States. Of note, structured data fields cannot be redacted, so CTIS users should not include any personal data or CCI in such fields.

The revised CTIS transparency rules applicable to the structured data fields are described in Annex I to this document.

5.2. Revised publication rules for documents submitted in CTIS:

The documents to be published should be redacted to protect CCI and personal data, if this is needed depending on the document content. Documents are published at the time of decision in case they are part of a clinical trial application dossier or at the time of submission into the database, as applicable.

For documents to be published, CTIS offers the possibility to use a document version 'for publication' for redacted documents and a document version 'not for publication' that may contain personal data and CCI, as needed for the scientific and regulatory review carried out by the Member States. Documents that will not be published via the CTIS public website will be uploaded in CTIS secure domain only with a document version 'not for publication'.

The revised CTIS transparency rules focus on publication of clinical trials documents that are more impactful for patients and clinical researchers, and are described in Annex I to this document.

The Guidance document on protecting personal data and CCI while using CTIS⁴ and its Annex⁵ should be consulted for practical instructions when using the system.

6. Implementation

The simplifications introduced by the revised CTIS transparency rules aim to guarantee access to clinical trial information in a faster and more efficient way. Reduced system complexity helps to improve users' experience, especially for multinational trials requiring provision of numerous documents.

Following adoption by the EMA Management Board, the new transparency rules will be implemented in the CTIS system including its public portal.

Whilst the Agency will endeavour to finalise implementation by the second quarter of 2024, the effective date of completion of the process and application of the new rules will be communicated to CTIS users in due course and prior to the date when they will become applicable.

⁴ [Guidance document on protection of personal data and commercially confidential information \(CCI\) in CTIS \(europa.eu\)](#)

⁵ [Annex I to the guidance document \(europa.eu\)](#)

Annex I : Revised CTIS transparency rules

Trial category	Type of information	Timing of publication
Category 1 trials - if the trial is conducted in paediatric population and/or if part of a paediatric investigational plan (PIP)	Structured data fields	
	Structured data fields* populated by the sponsor in the CTA dossier: <i>* Product details in category 1 trials in paediatric population and/or part of a PIP, namely daily and maximum dose allowed with units of measures, maximum treatment duration, product strength: not published at time of decision as impacting sponsor's legitimate economic interest or competitive position, including in respect of patent applications, as that information is considered CCI</i>	At the time of the decision on the CTA issued by the Member States Concerned (MSC) The first MSC issuing the decision triggers the publication of the trial in CTIS public domain
	Structured data fields on the outcome of the evaluation performed by the EU/EEA MSC: <ul style="list-style-type: none"> conclusion on part I and part II of the application, with the corresponding dates decision on the application with the corresponding decision date 	At time of the decision issued by that MSC
	Notifications for start of trial, start of recruitment, end of recruitment, end of trial including early termination, temporary halt benefit/risk related or not, restart of trial and restart of recruitment	As soon as the notification is submitted by the sponsor
Notifications of serious breaches, urgent safety measures, unexpected events, as applicable	After the MSC have assessed the notification submitted by the sponsor	

Trial category	Type of information	Timing of publication
Category 1 trials – if the trial is conducted only in adult population	Some structured data fields populated by the sponsor in the CTA dossier, including: <ul style="list-style-type: none"> • Trial title in lay terms • Trial identifiers in registers, protocol code • Therapeutic area, medical condition, rare disease • Population age, gender • Sponsors details • Details of clinical investigator sites in MSC 	At the time of the decision on the CTA issued by the Member States Concerned (MSC) The first MSC issuing the decision triggers the publication of the trial in CTIS public domain
	Remaining structured data fields populated by the sponsor in the CTA dossier	30 months after the end of trial in the EU/EEA
	Structured data fields on the outcome of the evaluation performed by the EU/EEA MSC: <ul style="list-style-type: none"> • conclusion on part I and part II of the application, with the corresponding dates • decision on the application with the corresponding decision date 	At the time of the decision issued by that MSC
	Notifications for start of trial, start of recruitment, end of recruitment, end of trial including early termination, temporary halt benefit/risk related or not, restart of trial and restart of recruitment	As soon as the notification is submitted by the sponsor
	Notifications of serious breaches, urgent safety measures, unexpected events, as applicable	30 months after the end of trial in the EU/EEA and provided that the Member States Concerned have assessed the notification submitted by the sponsor

Trial category	Type of information	Timing of publication
Category 2 and 3 trials	Structured data fields* populated by the sponsor in the CTA dossier: <i>*Product details in integrated phase I/II CTAs, falling in category 2, namely daily and maximum dose allowed with units of measures, maximum treatment duration, product strength: not published at time of decision as impacting sponsor's legitimate economic interests or competitive position, including in respect of patent applications as that information is considered CCI.</i>	At the time of the decision on the CTA issued by the Member States Concerned (MSC) The first MSC issuing the decision triggers the publication of the trial in CTIS public domain
	Structured data fields on the outcome of the evaluation performed by the EU/EEA MSC: <ul style="list-style-type: none"> conclusion on part I and part II of the application, with the corresponding dates decision on the application with the corresponding decision date 	At the time of the decision issued by that MSC
	Notifications for start of trial, start of recruitment, end of recruitment, end of trial including early termination, temporary halt benefit/risk related or not, restart of trial and restart of recruitment	As soon as the notification is submitted by the sponsor
	Notifications of serious breaches, urgent safety measures, unexpected events, as applicable	After the Member States Concerned have assessed the notification submitted by the sponsor

Trial category	Type of information	Timing of publication
For all trial categories	<ul style="list-style-type: none"> Request for information (RFI) raised by the Member States Concerned at the time of validation and assessment of part I and part II, and the corresponding sponsors' RFI responses; Details (i.e., name, surname, telephone number, e-mail address) of the sponsor legal representative; Assessment performed by the Member States concerned on the notifications reported by the sponsors. 	Never published
For all trial categories	Corrective measures (suspension, revocation and request for modification of an application)	Published when applied by the Member States Concerned
Documents		
Category 1 trials – if the trial is conducted in paediatric population and/or if part of a paediatric investigational plan (PIP)	Protocol, synopsis and including patients facing documents, if available	Together with the final summary of results, as soon as the results are submitted in CTIS
	Final summary of results, with a layperson summary	When submitted in CTIS
Category 1 trials - if the trial is conducted only in adult population	Protocol, synopsis and including patients facing documents, if available	30 months after the end of the trial in the EU/EEA
	Final summary of results, with a layperson summary	Submitted in CTIS secure domain (expected within 12 months from the end of trial in the EU/EEA) and published 30 months after the end of trial in the EU/EEA

Trial category	Type of information	Timing of publication
Category 2 and 3 trials	<ul style="list-style-type: none"> • Protocol, synopsis and including patients facing documents, if available • Summary of medicinal product characteristics (SMPC), if available • Informed consent form and patient information sheet • Recruitment arrangements, including procedures for inclusion and copy of advertising material 	<p>At the time of the decision on the CTA issued by the Member States Concerned (MSC)</p> <p>The first MSC issuing the decision triggers the publication of the trial in CTIS public domain</p>
	Final summary of results, with a layperson summary	When submitted in CTIS
For all trials categories	Clinical study report (CSR), if available, in case trial results are used in a marketing authorisation procedure	When submitted in CTIS
For all trials categories	<ul style="list-style-type: none"> • Assessment reports (draft and final) for part I and part II • Decision letters for the clinical trial application • GCP inspection reports • Documents provided with corrective measures, including sponsors' opinion • Documents provided with RFI and RFI responses • Documents provided with an <i>ad hoc</i> assessment • Union Control plans and corresponding reports 	Never Published
Note for all trial categories	<p>All applications are subject to the same publication rules. Applications require a decision (i.e., initial applications, subsequent substantial modifications or applications for the addition of a new Member States Concerned). Once the decision on the application has been issued, the latest data and document versions are subject to publication, while data or document versions superseded during the application evaluation, via one or multiple RFI responses, are not published.</p> <p>For non-substantial modifications data and document versions are subject to publication once the submission in CTIS has been made.</p>	