EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Revised CTIS transparency rules and historical trials: quick guide for users

V. 1.7, updated on 19 July 2024, to include slide 17 on SM change of sponsor

CTIS team, Data Analytics and Methods Taskforce (TDA)

An agency of the European Union

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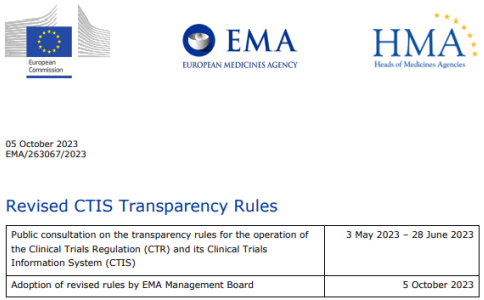
Article 81(4) of Regulation (EU) No. 536/2014: legal basis for the establishment a publicly accessible EU clinical trials database, while protecting commercially confidential information (CCI), personal data (PD) and confidential information on the assessment conducted by MSs

Implementation of revised CTIS transparency rules

Implementation of revised CTIS transparency rules

As of 18 June 2024, the Revised CTIS transparency rules are the publication rules of the Clinical Trial Information System:

- All trials submitted on or after 18 June follow the principles and timelines defined in the revised rules
- Trials submitted to CTIS before 18 June are considered 'historical' and have only their structured data published, see 'historical trials' section



European Commission · EMA EUROPEAN MEDICINES AGENCY · HMA Heads of Medicines Agencies

05 October 2023
EMA/263067/2023

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

Rules are summarised in the Annex 1

to the Guidance document on how to approach the protection of personal data and CCI while using the CTIS

More info is in the Q&A on the protection of CCI and Personal Data, in a dedicated CTIS bitesize talk and in the List of CTIS application fields and documents + notifications fields

Revised rules: modality of disclosure of CTIS trials' information

Chapter 2 of Guidance document on how to approach the protection of personal data and commercially confidential information while using the CTIS

Revised rules: modality of disclosure of CTIS trials' information

The **most recent** authorised application of any trial, as well as any 'not authorised' initial application, is made publicly available as per timelines based on:

- trial category, selected in the 'Form' section as per below table
- population age
- trial phase *(in case of category 2 trials that are integrated phase 1&2)*

Category	Trial type
Category 1 Pharmaceutical development clinical trials	Phase I clinical trials in healthy volunteers or patients Phase 0 trial in healthy volunteers or patients Bioequivalence and bioavailability trials Similarity trials for biosimilars Equivalence trials for combination or topical products
Category 2 Therapeutic exploratory & confirmatory clinical trials	Phase I and phase II integrated clinical trials Phase II clinical trials Phase II and phase III integrated clinical trials Phase III clinical trials
Category 3 Therapeutic use clinical trials	Phase III and phase IV integrated clinical trials Phase IV clinical trial and low interventional trials

Publication of structured data

Table I of Annex 1 to Guidance document, List of CTIS application and notifications fields and documents

Structured data – what will be published & when

Structured data	Category 1		Category 2 integrated p h1&2	Category 2 & 3 *(excl. integr. ph1&2)*
	Paediatrics and/or PIP	**Adults**		
CTIS application fields	First MSC decision	First MSC decision	First MSC decision	First MSC decision
		30 months after EU/EEA End of Trial		
CTIS application fields on dose and treatment duration[1]	30 months after EU/EEA End of Trial			
MSC(s) conclusions and decision outcomes	That MSC decision			
Notifications on trial status and recruitment	As soon as submitted by sponsor			
Notific. on serious breaches, urgent safety measures, unexpected events	After MSC assessment	30 months after EU/EEA EoT & MSC assessment	After MSC assessment	
Corrective measures (suspension, revocation, modification request)	When applied by MSC(s)			

[1]*As a temporary measure, the publication of fields 'strength of product' and 'strength of active substance' has been suspended: further information will follow*

Structured data – what will be published & when

Structured data	Category 1		Category 2 integrated ph1&2
	Paediatrics and/or PIP	Adults	
CTIS application fields populated by the sponsor, including: •Public title (= title in lay terms) •Trial identifiers in registers, protocol code •Phase, medical cond., rare disease, therap. area •Population age, gender •Sponsor details •Details of clinical investigator sites in MSC(s)	First MSC decision	First MSC decision	First MSC decision
Remaining CTA fields populated by the sponsor		30 months after EU/EEA End of Trial	
CTIS application fields[1] on Maximum duration of treatment, Maximum daily dose allowed, Daily dose unit of measure, Maximum total dose allowed, Total dose unit of measure	30 months after EU/EEA End of Trial		

[1]As a temporary measure, the publication of fields 'strength of product' and 'strength of active substance' has been suspended: further information will follow

Structured data – what will be published & when

Structured data	All categories
Sponsor legal representative details	Never
Any request for information (RFI) and RFI responses	
Validation conclusion details, assessment decision conditions (if any)	
MSC(s) assessment(s) on notifications	
3rd country inspection details	

Publication of documents

Table II of Annex 1 to Guidance document, List of CTIS application and notifications fields and documents

Documents – what will be published & when

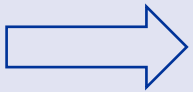
Documents type	Category 1		Category 2 and 3 *including integrated ph1&2*
	Paediatrics and/or PIP	**Adults**	
Protocol, synopsis, patients facing documents	Upon results' submission	30 months after EU/EEA End of Trial	First MSC decision
SmPC, if available	Never		
Subject information and informed consent form			That MSC decision
Recruitment arrangements, *including procedures for inclusion and copy of advertising material*			
Final summary of results, Lay person summary of results	As soon as submitted	30 months after EU/EEA End of Trial	As soon as submitted
Clinical study report, *if available*	As soon as submitted *(requirement: 30 days from MA)*		
All other documents, including any MS document	Never		

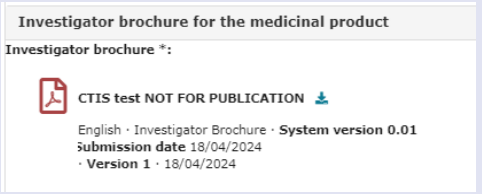
As of 18 June 2024, for any application created before this date

For all those documents that are no longer published (e.g. IB), the system had to remove the former version 'for publication', unless no 'not for publication' version was linked to it

workspace view

before 18/6/24





as of 18/6/24

Examples are in the next slide

Note question 1.9 of Q&A: when submitting a modification application of those trials, sponsors are not requested to re-upload the clean versions of those documents 'not for publication' that are no longer available. Only the clean version and corresponding track-changes version of those documents that have been modified as part of the application should be uploaded, unless MSCs requests further uploads.

Examples

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Before 18 June, sponsor had uploaded:		As of 18 June, Sponsor/MS sees, in the same placeholder:
In slot 'for publication'	and linked to 'not for publication'	
Doc 1 'for publication'	-	Doc 1 (formerly 'for publication')
Doc 1 'for publication'	Doc 1 not for publication	Doc 1 (formerly 'not for publication')
Doc 1 'for publication'	2 or more docs 'not for publication', linked to the same unique document for pub	All 'not for publication' docs *(doc 'for publication' removed)*
Doc 1 For publication Doc 2 For publication (e.g. translation)	Doc 1 'not for publication' Doc 2 'not for publication' (e.g. translation)	Doc 1 (formerly 'not for publication') Doc 2 (formerly 'not for publication' ,e.g. translation)
Doc 1 For publication Doc 2 For publication	Doc 1 'not for publication' linked to doc 1 -	Doc 1 (formerly 'not for publication') Doc 2 (formerly 'for publication')
Doc 1 'for publication' Doc 2 'for publication' Doc 3 'for publication' Doc 4 'for publication'	Doc 1 'not for publication' Doc 2 'not for publication' - -	Doc 1 (formerly 'not for publication') Doc 2 (formerly 'not for publication') Doc 3 (formerly 'for publication') Doc 4 (formerly 'for publication')
Doc 1 'for publication' English Doc 2 'for publication' German	Doc 3 'not for publication' Spanish Doc 4 'not for publication' Italian	Doc 1 (formerly 'for publication' English) Doc 2 (formerly 'for publication' German) Doc 3 (formerly 'not for publication' Spanish) Doc 4 (formerly 'not for publication' Italian)

In some cases, users could still see both 'for publication' and 'not for publication' versions. Note that also in these cases the document is not published.

Historical trials, submitted before 18 June 2024

Section 2.3 of Guidance document on how to approach the protection of personal data and CCI while using the CTIS + specific behaviour of SM change of sponsor

Historical trials: what is published and when

For all those CTIS applications **submitted*** before 18 June 2024:

- the structured data are published for all trials' categories as per revised rules
- **documents are not published** *(this applies to all historical trials, regardless of the previous use of deferrals or publication status)*

The following kinds of CTIS applications **submitted*** on or after 18 June 2024 will trigger publication of those documents that are in scope of the application and of the revised rules:

- Substantial Modifications (part I and/or part II)
- Non-Substantial Modification part II
- Additional Member State (triggering publication of part II docs only)

→ ***documents** in scope of publication **should be redacted accordingly***

Warning: 'SM part I change of sponsor' triggers publication of part I documents: see slide 17

**the date determining whether a trial is 'historical' or not, is the submission date, not the date of creation of your draft*

Historical trials: what is published and when

NSM and AM applications done on 'historical trials' do not trigger the publication of part I documents: this is because through these two kinds of applications, it is not possible for sponsors to update and therefore redact those documents in scope of publication

→ ***for an application that is submitted to CTIS on any 'historical' trial,*** *the* ***documents*** *in scope of publication that are feasible to be modified through the application are going to be published and* ***should be redacted accordingly***

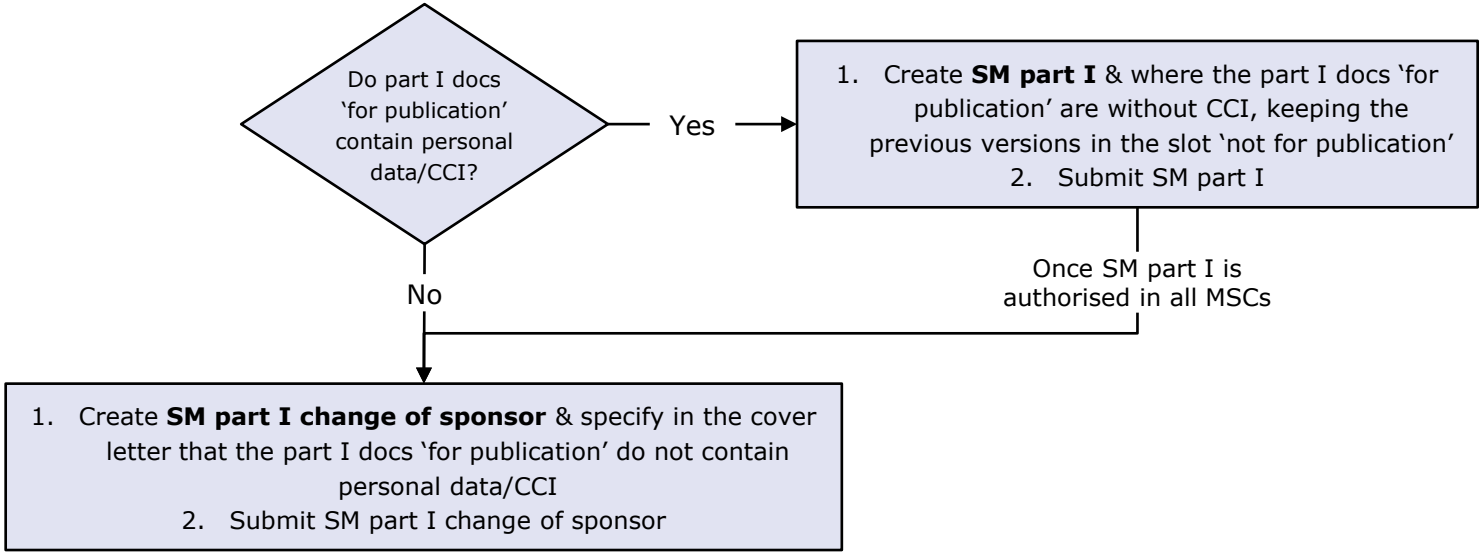
Example: an initial application submitted before 18 June 2024 will have the latest version of its structured data published on 18 June 2024 while its documents were not published; if, on this trial:

- A SM-1 is submitted, with the purpose of updating the IB: protocol and synopsis will be published as per revised rules and should be redacted accordingly. Note: part II documents will not be published
- A NSM-1 is submitted: this triggers an update of the structured data and not of any document
- A NSM part 1&2 is submitted: this triggers publication of part II documents only & update of all structured data fields.
- A SM part I change of sponsor is submitted: this will trigger publication of part I documents, see next slide

Note: submission of trial notifications or results do not trigger publication of application's documents of the same trial.

SM part I change of sponsor* triggers publication of part I docs

For a trial submitted to CTIS before 18 June 2024:



For questions: contact the Reporting Member State (RMS)

* Specific SM that allows the change of the Sponsor's ORG ID

Reference documentation

ACT EU – Implementation of clinical trial regulation website

Reference documentation

- Revised transparency rules
- Quick guide for users
- Guidance document on how to approach the protection of personal data and commercially confidential information (CCI) while using CTIS and its Annex I
- Q&A on the protection of CCI and Personal Data while using CTIS
- List of CTIS application fields and documents (with publication details)
- List of CTIS notifications fields and documents (with publication details)
- CTIS Bitesize talk on the transparency rules