3 May 2023
EMA/212507/2021
European Medicines Agency

Interim guidance document on how to approach the protection of personal data and commercially confidential information while using the Clinical Trials Information System (CTIS) version 1.0

Table of contents

Acronyms

Acronym	Description
Art. 29 WP	The Article 29 Working Party was set up under Article 29 of Directive 95/46/EC. The Art. 29 WP is the independent European working party that dealt with issues relating to the protection of privacy and personal data until 25 May 2018 (entry into application of the GDPR).
ASR	Annual Safety Reporting
CCI	Commercially Confidential Information
CTs	Clinical Trials
CTIS	Clinical Trials Information System
CTR	Clinical Trials Regulation or Regulation (EU) No 536/2014 of the European Parliament and of The Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC.
EC	European Commission
EEA	European Economic Area
EMA	European Medicines Agency, also referred to hereafter as the Agency
EU	European Union
EUDPR	Regulation (EU) 2018/1725 of the European Parliament and of the Council of 23 October 2018 on the protection of natural persons with regard to the processing of personal data by the Union institutions, bodies, offices and agencies and on the free movement of such data, and repealing Regulation (EC) No 45/2001 and Decision No 1247/2002/EC (European Data Protection Regulation)
EUPD	European Union Portal and Database
GCP	Good Clinical Practice
GDPR	Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation)
IAM	Identity Access Management
MA	Marketing Authorisation
MAA	Marketing Authorisation Application
MAH	Marketing Authorisation Holder
MSs	Member States
MSC	Member State Concerned
NCAs	National Competent Authorities

Acronym	Description
OMS	Organisation Management Service
RFI	Request for information
RMS	Reporting Member State
XEVMPD	Extended EudraVigilance Medicinal Product Dictionary

Definitions

In this guidance document the following definitions apply:

Definition	Description
Aggregated data	Data about several individuals that have been combined/grouped to present general trends or values without identifying (either directly or indirectly) individuals within the data generated for statistical or research purposes.
Anonymisation	The process of rendering personal data anonymous as described in recital 16 of the EUDPR and recital 26 of the GDPR i.e., 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.
Anonymous data (also called as anonymised)	Information which does not relate to an identified or identifiable natural person or personal data rendered anonymous in such a manner that the data subject is not, or no longer, identifiable.
Article 29 Data Protection Working Party (Art. 29 WP)	The 'Article 29 Working Party' is the short name of the Article 29 Data Protection Working Party established by Article 29 of Directive 95/46/EC. It provided the European Commission with independent advice on data protection matters and helped in the development of a harmonised implementation of data protection rules in the EU Member States. As of 25 May 2018, the Article 29 Working Party ceased to exist, and has been replaced by the European Data Protection Board (EDPB).
Clinical trial information submitted to CTIS	Data (captured in structured data fields) and documents submitted to CTIS in the context of a clinical trial application, during the evaluation of an application and during the clinical trial life cycle including the supervision of the clinical trial and the clinical trials results.
Commercially Confidential Information (CCI)	Any information submitted to CTIS which is not in the public domain, or publicly available, and where disclosure may undermine the legitimate economic interest or competitive position of the owner of the information.[1]
Data	'Data' means any digital representation of acts, facts or information and any compilation of such acts, facts or information, including in the form of sound, visual or audio-visual recording (Article 2 of Data Act).
Database	An organized collection of data stored as multiple datasets.
Dataset	A dataset is a structured collection of data. A table where each column represents a particular variable, and each row corresponds to a different record is an example of a dataset[2].
Data controller (or controller)	"Controller' means the natural or legal person, public authority, agency or other body which, alone or jointly with others, determines the purposes

[1] HMA/EMA recommendations on transparency approved in November 2010 - Recommendations on release of information with regard to new applications for medicinal products before and after opinion or decision on granting of a marketing authorisation (EMA/484118/2010)

[2] See AEPD-EDPS joint paper on 10 misunderstandings related to anonymisation, https://edps.europa.eu/data-protection/our-work/publications/papers/aepd-edps-joint-paper-10-misunderstandings-related_en

Definition	Description
	and means of the processing of personal data; where the purposes and means of such processing are determined by Union or Member State law, the controller or the specific criteria for its nomination may be provided for by Union or Member State law.' (Article 4(7) of Regulation (EU) 2016/679). or, as applicable to the entity in question ''Controller' means the Union institution or body or the directorate-general or any other organisational entity which, alone or jointly with others, determines the purposes and means of the processing of personal data; where the purposes and means of such processing are determined by a specific Union act, the controller or the specific criteria for its nomination can be provided for by Union law.' (Article 3(8) of Regulation (EU) 2018/1725).
Data minimisation principle	'Personal data shall be adequate, relevant and limited to what is necessary in relation to the purposes for which they are processed.' (Article 5(1)(c) of Regulation (EU) 2016/679 and Article 4(1)(c) of Regulation (EU) 2018/1725).
Data processor (or processor)	''Data processor' means a natural or legal person, public authority, agency or other body which processes personal data on behalf of the controller.' (Article 4(8) of Regulation (EU) 2016/679 and Article 3(12) of Regulation (EU) 2018/1725).
Data protection principles	Regulation (EU) 2016/679 and Regulation (EU) 2018/1725 prescribe adherence to 7 data protection principles, i.e.: • Lawfulness, fairness and transparency • Purpose limitation • Data minimisation • Accuracy • Storage limitation • Integrity and confidentiality (security) • Accountability
Data subject	'An identified or identifiable natural person to whom personal data relates. An identifiable natural person is one who can be identified, directly or indirectly, in particular by reference to an identifier such as a name, an identification number, location data, an online identifier or to one or more factors specific to the physical, physiological, genetic, mental, economic, cultural or social identity of that natural person.' (Article 4(1) of Regulation (EU) 2016/679 and Article 3(1) of Regulation (EU) 2018/1725). Data subjects applicable to CTR and CTIS are: trial participants, CTIS users, principal investigators, sponsor staff, etc.

Definition	Description
Deferral mechanism	Functionality of CTIS to allow CTIS users to delay the publication of clinical trials data and document with the aim to protect commercially confidential information.
Disclosure	The act of making data available to one or more third parties.
EU Clinical Trials Information System (CTIS)	The IT platform, including the EU portal and EU database, that allows the exchange of clinical trials information in the European Union. CTIS interacts with other databases such as IAM (Identity Access Management), XEVMPD (Extended EudraVigilance Medicinal Product Dictionary) and OMS (Organisation Management Service) which are also managed by the Agency.
EU Clinical Trials Information System (CTIS) user	The natural person(s) being granted access to the secure domains of CTIS, that submitted the clinical trial information to CTIS in the context of a clinical trial application, or that has access to the system during the evaluation of an application, or during the clinical trial life cycle including supervision of the clinical trial.
EU Portal and Database (EUPD)	In accordance with Articles 80 and 81, and Recitals 66 and 67 of the Clinical Trials Regulation, the Agency has the obligation, in collaboration with the Member States and the Commission, to set up and maintain both a Clinical Trials Portal, as a single entry point for the submission of data and information relating to clinical trials, and a Clinical Trials Database containing data and information submitted in accordance with that Regulation.
Joint Controller	'Where two or more controllers jointly determine the purposes and means of processing, they shall be joint controllers. They shall in a transparent manner determine their respective responsibilities for compliance with the obligations under this Regulation, in particular as regards the exercising of the rights of the data subject and their respective duties to provide the information referred to in Articles 13 and 14, by means of an arrangement between them unless, and in so far as, the respective responsibilities of the controllers are determined by Union or Member State law to which the controllers are subject. The arrangement may designate a contact point for data subjects.' (Article 26(1) of Regulation (EU) 2016/679) or, as applicable to the entity in question 'Where two or more controllers or one or more controllers together with one or more controllers other than Union institutions and bodies jointly determine the purposes and means of processing, they shall be joint controllers. They shall in a transparent manner determine their respective responsibilities for compliance with their data protection obligations, in particular as regards the exercising of the rights of the data subject and their respective duties to provide the information referred to in Articles 15 and 16, by means of an arrangement between them unless, and in so far as, the respective responsibilities of the joint controllers are determined by Union or Member State law to which the joint controllers are subject. The

Definition	Description
	arrangement may designate a contact point for data subjects.' (Article 28(1) of Regulation (EU) 2018/1725).
Personal data	''Personal data' means any information relating to an identified or identifiable natural person ('data subject'); an identifiable natural person is one who can be identified, directly or indirectly, in particular by reference to an identifier such as a name, an identification number, location data, an online identifier or to one or more factors specific to the physical, physiological, genetic, mental, economic, cultural or social identity of that natural person'. (Article 4(1) of Regulation (EU) 2016/679 and Article 3(1) of Regulation (EU) 2018/1725).
Special categories of personal data	Personal data revealing racial or ethnic origin, political opinions, religious or philosophical beliefs, or trade union membership, and the processing of genetic data, biometric data for the purpose of uniquely identifying a natural person, data concerning health or data concerning a natural person's sex life or sexual orientation. (Article 9(1) of Regulation (EU) 2016/679 and Article 10(1) of Regulation (EU) 2018/1725).
Personal data breach	''Personal data breach' means a breach of security leading to the accidental or unlawful destruction, loss, alteration, unauthorised disclosure of, or access to, personal data transmitted, stored or otherwise processed'. (Article 4(12) of Regulation (EU) 2016/679 and Article 3(16) of Regulation (EU) 2018/1725).
Process, processes, processing	''Processing' means any operation or set of operations which is performed on personal data or on sets of personal data, whether or not by automated means, such as collection, recording, organisation, structuring, storage, adaptation or alteration, retrieval, consultation, use, disclosure by transmission, dissemination or otherwise making available, alignment or combination, restriction, erasure or destruction'. (Article 4(2) of Regulation (EU) 2016/679 and Article 3(3) of Regulation (EU) 2018/1725).
Pseudonymised, pseudonymisation	''Pseudonymisation' means the processing of personal data in such a manner that the personal data can no longer be attributed to a specific data subject without the use of additional information, provided that such additional information is kept separately and is subject to technical and organisational measures to ensure that the personal data are not attributed to an identified or identifiable natural person'. (Article 4(5) of Regulation (EU) 2016/679 and Article 3(6) of Regulation (EU) 2018/1725).
Publishing	The act of making data publicly available.
Redaction	Masking of text in a document by applying a permanent and unremovable overlay, rendering the text unreadable.
Re-identification	The process of analysing data, or combining it with other data, with the result that individuals become identifiable.

Definition	Description
Re-identification risk (or re-identification likelihood, risk of re-identification)	The re-identification risk (or likelihood) is the probability in a given dataset of re-identifying an individual, by turning anonymised data back into personal data through the use of data matching or similar techniques.[3]
Study subject, trial participant	'An individual who participates in a clinical trial, either as a recipient of an investigational medicinal product or as a control'. Article 2(17) of Regulation (EU) No 536/2014. Use is made in the guidance of the term 'trial participant' as an equivalent to 'trial subject/study subject'.
Version of the document 'for publication'	The version of the document provided in CTIS by the users which should not contain commercial confidential information (CCI) and personal data[4]. It is the responsibility of the user to ensure that this version does not contain such information.
Version of the document 'not for publication'	The version of the document provided in CTIS by the users which may contain personal data insofar that this is necessary for the purposes listed in Article 81(2) of the Clinical Trials Regulation and/or commercial confidential information (CCI).

[3] See AEPD-EDPS joint paper on 10 misunderstandings related to anonymisation, https://edps.europa.eu/data-protection/our-work/publications/papers/aepd-edps-joint-paper-10-misunderstandings-related_en.
[4] With the exceptions defined by the present guidance

1. General information

1.1. Introduction

The European Clinical Trials Regulation (EU) No 536/2014[5] (hereinafter 'the Clinical Trials Regulation' or 'CTR') repeals Directive 2001/20/EC on clinical trials[6] (CTs) and establishes a harmonised approach to the submission, assessment, supervision and reporting of clinical trials information with the implementation of consistent rules throughout the European Union (EU)/European Economic Area (EEA) Member States (MSs).

The Clinical Trials Regulation aims to foster innovation through: harmonised content of clinical trial applications submitted to the Member States for assessment, increased collaboration between the Member States on the assessment of clinical trial applications, and to increase transparency and availability of information on clinical trials and their results. Publicly available information foreseen by the CTR should contribute to protecting public health and fostering the innovation capacity of European medical research, while recognising the legitimate economic interests of sponsors and protecting personal data.

In accordance with Recitals 66 and 67 and Articles 80 and 81 of the Clinical Trials Regulation, the Agency, in collaboration with the Member States and the European Commission (EC), has the obligation to set up and maintain an EU Portal as a single entry point for the submission of data and documents relating to clinical trials, and a EU Database containing the data and documents submitted via the EU Portal. The EU Clinical Trials Portal and Database are jointly referred to as the EU Portal and Database (EUPD).

To ensure transparency of clinical trials, the EU Database should be publicly accessible and data should be presented in an easily searchable format.

The EU database is a key instrument to ensure transparency of clinical trial information. The database serves as the source of public information on assessed clinical trial applications, clinical trials conducted from the time of decision, until the submission of summary their results. Access to this information is fundamental to enable trust in the clinical research conducted in the European Union.

The EUPD and associated workspaces provide MSs, the European Commission, the Agency, sponsors and applicants[7] of a marketing authorisation with an effective network to streamline and facilitate the preparation of the flow of information for the authorisation and supervision of clinical trials in the EU/EEA.

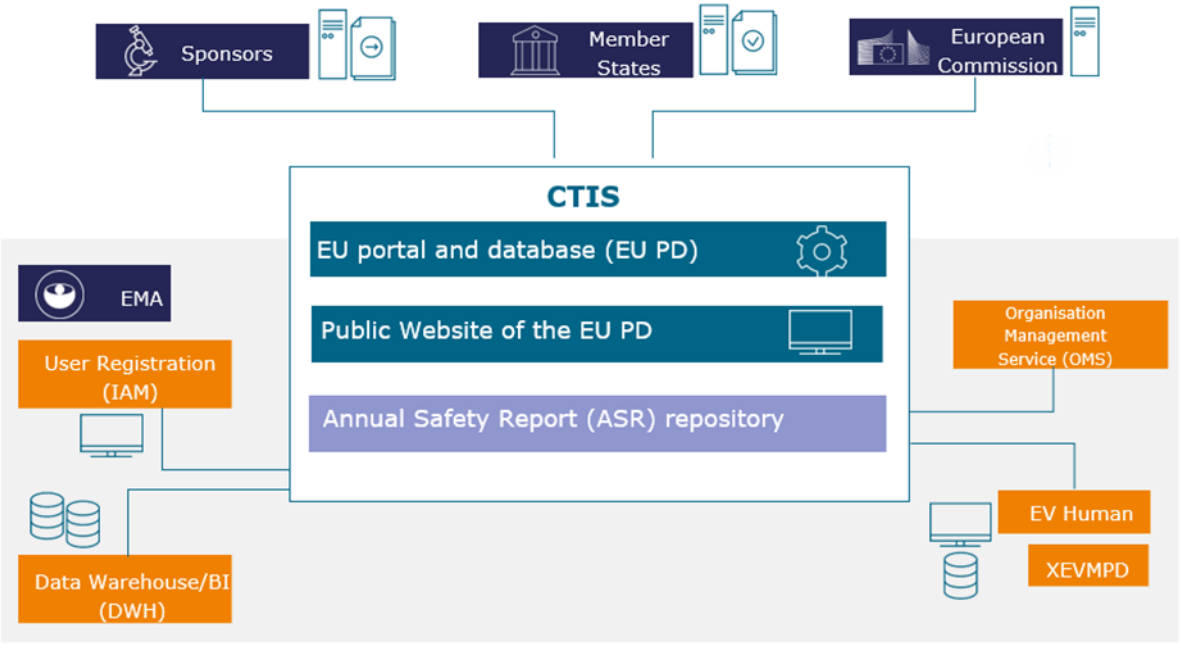
The EUPD, that enables the submission and storing of clinical trial information, is one of the two components of the Clinical Trials Information System (CTIS) in addition to the module for submission of the Annual Safety Reports (ASRs). Throughout the document reference is made to the use of CTIS overall.

[5] Regulation (EU) No 536/2014 of the European Parliament and of The Council of 16 April 2014 on clinical trials on medicinal products for human use, and repealing Directive 2001/20/EC.
[6] Directive 2001/20/EC of the European Parliament and of the Council of 4 April 2001 on the approximation of the laws, regulations and administrative provisions of the Member States relating to the implementation of good clinical practice in the conduct of clinical trials on medicinal products for human use.
[7] Note that where this document refers to 'sponsor users' or 'sponsor domain', this may refer to, respectively as applicable, users acting on behalf of marketing authorisation applicants/holders and related user domain areas in the system.

To streamline the use of the already available information stored in other databases managed by the Agency and to promote consistency and standardisation, CTIS consumes data from the following data sources:

- Extended EudraVigilance Medicinal Product Dictionary (XEVMPD);
- Organisation Management Service (OMS);
- Identity Access Management (IAM).

The interface of CTIS with other EMA data sources is shown in the figure below:



1.2. Scope

The CTR brings an unprecedented level of transparency in terms of publication of clinical trials information for trials in the EU/EEA. Access to this information, including trial results, is important to allow prompt recruitment of patients at the side, avoid duplication of efforts and ultimately foster innovation and promote clinical research in the European Union.

This guidance document aims to help CTIS users to navigate through the system functionalities and understand the main principles to be followed to enable protection of personal data and commercially confidential information while using CTIS and publishing clinical trials data and documents.

The following chapters are presented:

- Description of CTIS structure and components, including a description of the functionalities and publication rules for clinical trials information submitted to CTIS (chapter 2);
- Principles to be followed to enable protection of personal data as part of the clinical trial information submitted to CTIS (chapter 3);
- Principles to be followed to enable protection of commercially confidential information (CCI) as part of the clinical trial information submitted to CTIS (chapter 4); To be finalised in version 1.1
- The protection of personal data and CCI in inspection reports (chapter 5). To be finalised in version 1.1

1.3. Legal framework

The CTR sets out requirements for the protection of personal data, CCI and increased transparency of clinical trials in the EU/EEA. These requirements apply to information contained in the EU Database.

Data and documents defined in the CTR are submitted via the EU Portal, stored in the EU Database and subject to the disclosure rules.

Article 81(4) of the CTR states that the EU Database shall be publicly accessible unless, for all or parts of the data and information contained therein, confidentiality is justified on any of the following grounds:

a) protecting personal data in accordance with Regulation (EU) 2018/1725[8];

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.

Recital 68 of the CTR states that: in general the data included in a clinical study report should not be considered commercially confidential once a marketing authorisation has been granted, the procedure for granting the marketing authorisation has been completed, the application for marketing authorisation has been withdrawn. In addition, the main characteristics of a clinical trial, the conclusion on Part I of the assessment report for the authorisation of a clinical trial, the decision on the authorisation of a clinical trial, the substantial modification of a clinical trial, and the clinical trial results including reasons for temporary halt and early termination, in general, should not be considered confidential.

Data from the clinical trial application dossier can be made public after the decision on the clinical trial has been taken (Article 81(5) of the CTR), unless there is an overriding public interest for a particular clinical trial to do so earlier, which applies only in exceptional circumstances where the general public interest in having information made publicly available may outweigh considerations that the same information should remain confidential. Accordingly, only applications on which a decision has been made by a Member State concerned (MSC) will be made public. This applies to any decision outcome, i.e. authorisation, authorisation with condition(s) or whether the authorisation is refused.

Information on initial applications which are only for assessment of Part I of the dossier (Article 11 applications) will not be made public until a Part II has been submitted to the MSC and a decision has been issued by, at least, one of the MSC(s).

Applications which are not validated or those withdrawn by the sponsors before a decision is made will not be made public.

In addition, the following provisions related to the protection of personal data and CCI should be also taken into account as part of the guidance provided in this document.

Data protection related provisions

Article 93 of the CTR expressly makes reference to EU data protection legislation i.e., to the now applicable GDPR with reference to the processing of personal data carried out in MSs (including

[8] Article 81(4) of Regulation EU (No) 536/2014 refers to Regulation (EU) No 45/2001 replaced by Regulation 2018/1725, the EUDPR

processing by the regulatory authorities and ethics committees) as well as sponsors, marketing authorisation applicants or holders and the EUDPR which applies to the processing of personal data by the European Commission and the Agency.

CTR details the need for the protection of personal data as follows:

- Recital 67: *No personal data of data subjects participating in a clinical trial should be recorded in the EU database. The information in the EU database should be public, unless specific reasons require that a piece of information should not be published, in order to protect the right of the individual to private life and the right to the protection of personal data, recognised by Articles 7 and 8 of the Charter (…).*
- Article 56(1): *All clinical trial information shall be recorded, processed, handled, and stored by the sponsor or investigator, as applicable, in such a way that it can be accurately reported, interpreted and verified while the confidentiality of records and the personal data of the subjects remain protected in accordance with the applicable law on personal data protection.*
- Article 56(2): *Appropriate technical and organisational measures shall be implemented to protect information and personal data processed against unauthorised or unlawful access, disclosure, dissemination, alteration, or destruction or accidental loss, in particular where the processing involves the transmission over a network.*
- Article 81(2): *The EU database shall be established to enable cooperation between the competent authorities of the Member States concerned to the extent that it is necessary for the application of this Regulation and to search for specific clinical trials. It shall also facilitate the communication between sponsors and Member States concerned and enable sponsors to refer to previous submissions of an application for authorisation of a clinical trial or a substantial modification (…).*
- Article 81(4): *The EU database shall be publicly accessible unless, for all or part of the data and information contained therein, confidentiality is justified on any of the following grounds:*
  (a) protecting personal data in accordance with Regulation (EC) No 45/2001;
- Article 81(6): *The EU database shall contain personal data only insofar as this is necessary for the purposes of paragraph 2.*
- Article 81(7): *No personal data of subjects shall be publicly accessible.*
- Article 93(1): *Member States shall apply Directive 95/46/EC[9] to the processing of personal data carried out in the Member States pursuant to this Regulation.*
- Article 93(2): *Regulation (EC) No 45/2001[10] shall apply to the processing of personal data carried out by the Commission and the Agency pursuant to this Regulation.*

[9] Replaced by Regulation (EU) 2016/679 (GDPR).
[10] Replaced by Regulation (EU) 2018/1725 (EUDPR).

Commercially Confidential Information (CCI) related provisions

- Recital 68 clarifies that, for the purposes of the CTR, in general the data included in a clinical study report should not be considered commercially confidential once the procedure is finalised.
- For clinical trials intended to be used in a marketing authorisation application in the EU/EEA, Article 37(4) of the CTR requires that the applicant for a marketing authorisation submits the clinical study report to the EU database within 30 days after the day the marketing authorisation has been granted, the procedure for granting marketing authorisation has been completed, or the applicant has withdrawn the application.
- Article 81(4) of the CTR states that: *The EU database shall be publicly accessible unless, for all or part of the data and information contained therein, confidentiality is justified on any of the following grounds: ……..(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.*

Overriding public interest anticipating the publication of clinical trials information is considered as meaning that the general public interest in having information made publicly available may outweigh considerations that the same information should remain confidential. It applies in exceptional circumstances only.

In the context of inspection reports, the CTR sets out the following:

- Article 53(2): *The sponsor shall submit to the Member States concerned, through the EU portal, all inspection reports of third country authorities concerning the clinical trial.*
  When requested by a Member State concerned, the sponsor shall submit a translation of the report or of its summary in an official language of the Union indicated in the request.
- Article 78(6): *Following an inspection, the Member State under whose responsibility the inspection has been conducted shall draw up an inspection report. That Member State shall make the inspection report available to the inspected entity and the sponsor of the relevant clinical trial and shall submit the inspection report through the EU portal.*
- Furthermore, Article 13 of the Commission Implementing Regulation (EU) 2017/556 of 24 March 2017[11] states (…) *The inspection reports submitted through the EU portal shall not contain personal data of clinical trials' subjects.*

The implementation of the disclosure rules of the Clinical Trials Regulation is without prejudice to the application of Regulation (EC) No 1049/2001[12] and citizens' right to request documents under that Regulation.

[11] COMMISSION IMPLEMENTING REGULATION (EU) 2017/ 556 - of 24 March 2017 - on the detailed arrangements for the good clinical practice inspection procedures pursuant to Regulation (EU) No 536 / 2014 of the European Parliament and of the Council (europa.eu).
[12] REGULATION (EC) No 1049/2001 OF THE EUROPEAN PARLIAMENT AND OF THE COUNCIL of 30 May 2001 regarding public access to European Parliament, Council and Commission documents

2. Rules of clinical trial information in CTIS pertaining to submission and publication

2.1. Introduction

This chapter describes CTIS functionalities implemented to enable protection of personal data and commercially confidential information. Content of this chapter might be impacted by the results of the public consultation on CTIS transparency rules launched in May 2023.

This chapter describes the type of clinical trial information, including data and documents, submitted to CTIS and how this information should be managed to protect personal data and commercially confidential information (CCI), while ensuring publication principles are met.

Principles of protection of personal data and CCI should be followed while using CTIS, as required in the CTR. The clinical trial information flow starts in the CTIS secure domain with a clinical trial application submitted by the sponsor, or delegated entities, to carry out a clinical trial in the EU/EEA and the corresponding evaluation performed by the EU/EEA Member States concerned.

Following the evaluation of the application, a decision is issued by each Member State concerned for the application, on whether the trial is authorised, authorised with conditions or not authorised. After a decision has been issued by the Member States concerned, the data and documents submitted to the CTIS for the trial will be made available to the public, unless the sponsor has applied for a deferral.

Where requested, a deferral will delay the publication of a set of data and documents (e.g. protocol, investigator brochure, informed consent information sheet) for a certain number of months or years after the end of the trial in the EU/EEA or until the publication of the final summary of results.

In case of a 'Not Authorised' initial clinical trial application (CTA) with deferrals, the last MSC decision date will be considered for publication purposes.

Data and documents of an application that are not subject to publication (e.g., IMPD-Q, draft assessment reports, financial arrangements) will not be published after a decision on the application has been reached, regardless if deferrals apply or not for the trial.

After the authorisation is obtained, the trial may then start, and the Member States concerned will supervise the trial running in their territory. After the initial application, other application types may be submitted by the sponsor for the same trial such as substantial modifications to the initial application or the addition of new Member State(s) concerned which are also subject to the assessment and decision from the Member State(s) concerned in question.

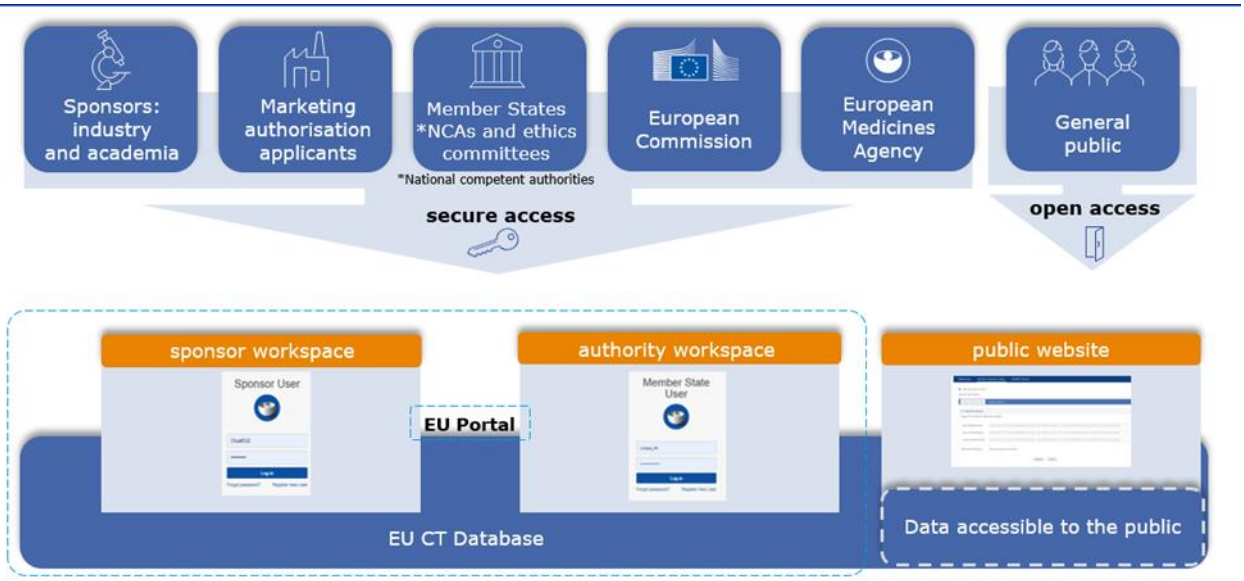
In addition to the above, non-substantial modifications to the content of the application dossier can be applied by the sponsor during the trial life cycle up to its completion, as well as notifications to the Member States concerned by the trial, of events of relevance, such as the occurrence of a serious breach or an urgent safety measure. The Member States concerned supervise the conduct of the trial in their territory with different means, including monitoring and assessing safety reports such as Annual Safety Reporting (ASRs), performing *ad hoc* assessment including for safety related matters, performing Good Clinical Practice (GCP) inspections and having the possibility to apply corrective measures to request modifications, suspend the trial or revoke the trial authorisation, for example.

The sequence of events occurring during the trial life cycle might require the collection and processing of personal data for the purposes set out in Article 81(2) of the Clinical Trials Regulation. Data and documents provided by the users in CTIS may also contain information that is considered commercially confidential. As defined in Article 81(4) of the CTR, personal data of trial participants, as well as other types of personal data, and commercial confidential information are exempted from publication.

Within CTIS secure domains for sponsors and Member States, users can have access to clinical trial data and documents for the trials of their concern. These users are: clinical trial sponsors or delegated parties, marketing authorisation applicants/holders, EU/EEA Member States (encompassing responsible national competent authorities and Ethics Committees), the European Commission and the Agency.

Access to data and documents in CTIS secure domain is managed through the user's profile.

The image below represents the different domains in CTIS, including sponsors and authorities domains with secure access and a public domain.



2.2. Clinical trial information in CTIS and document submissions 'for publication' and 'not for publication'

Table I and table II in the Annex to this document provide an overview of the types of data and documents that are submitted to CTIS by sponsors and Member states users, respectively, during the trial life cycle, from CTA submission to summary of results and clinical study reports, as applicable.

In CTIS, documents can be provided in version 'for publication' and 'not for publication'. The requirements to have both versions will depend on the document type and content and may not be necessary in every instance.

When both versions are required, for example for GMP documentation with signature of the qualified person, as applicable, these documents should be provided at the same time.

The following general principles apply:

- Sponsors should submit high quality documentation to CTIS to enable an assessment by the Member States concerned. The need to have both versions of documents will depend on the document type and whether protection of personal data and/or CCI would be applicable based on document content.
- Except for those document types exempt from publication, for any clinical trial document submitted to CTIS in an initial application or during the trial life-cycle, the document version 'for publication' is to be provided, regardless of whether a deferral for publication will be requested.
- The document version 'for publication' is the one that will be published with timing depending on the deferral rules, as applicable.

- In principle no alteration of the documents content should occur in the document versions 'for publication' and 'not for publication', where the difference should be only personal data and commercially confidential information being redacted.

  Protection of personal data of trial participants should be done with the available anonymisation techniques that might require modification of the text, as redaction might not be the preferred options to use in that case.

Considerations on protection of personal data:

- Personal data, if needed during the scientific and regulatory review carried out by the Member States concerned, should be provided in the document version 'not for publication'. This will enable the Member States Concerned to have all the necessary information for evaluation. Principles of minimisation should however be followed when providing personal data, only as needed in light of Articles 81(6) referring to 81(2) of the CTR.
- Personal data in the document version 'for publication' should be anonymised, for the purpose of public disclosure except the name and surname of the principal investigator at the clinical site(s), of the head of the clinic/institution or other responsible person issuing the statement of suitability of the facility, of the sponsor legal representative[13] and of the persons signing the clinical study reports, in line with the requirements of the Appendix, on disclosure rules, to the "Functional specifications for the EU portal and EU database to be audited - EMA/42176/2014".
- Signatures, if available in documents uploaded in CTIS, should not be disclosed in the document version 'for publication'.
- There is no equivalent of having a version 'for publication' and 'not for publication' in the structured data fields populated by the CTIS users, as these fields cannot be redacted. Therefore, sponsors and Member States users should be mindful of this aspect when populating structured data fields, for example in RFI and RFI responses, using the data minimisation principles to protect personal data, as applicable.

Considerations on protection of CCI:

- In general, the data included in a clinical study report should not be considered commercially confidential once a marketing authorisation has been granted, the procedure for granting the marketing authorisation has been completed or the application for a marketing authorisation has been withdrawn. In addition, the main characteristics of a clinical trial, the conclusion on Part I of the assessment report for the authorisation of a clinical trial, the decision on the authorisation of a clinical trial, the substantial modification of a clinical trial, and the clinical trial results including reasons for temporary halt and early termination, in general, should not be considered confidential[14].

  It should be noted that for category 1 trials, the sponsor may opt to have main characteristic (structured data fields and documents) deferred for publication to the time when the final summary of results are made public.
- Deferral mechanism can be used to protect CCI. Alternatively, CCI can be redacted, where applicable, in the document version 'for publication'.

[13] The role of the sponsor legal representative is clearly defined in Article 74(1) of the CTR: ''Where the sponsor of a clinical trial is not established in the Union, that sponsor shall ensure that a natural or legal person is established in the Union as its legal representative.''
[14] Recital 68 of the Clinical Trials Regulation

- Nonetheless CCI should be available in the document version 'not for publication' as needed for Member State evaluation and therefore should not be redacted. Therefore, the version of a document 'not for publication' should be considered as the original, integral version of the document containing all information required for the assessment by the Member States concerned.
- There is no equivalent of having a version 'for publication' and 'not for publication' in the structured data fields populated by the CTIS users, as these fields cannot be redacted. Therefore sponsors and Member States users should be mindful of this aspect when populating structured data fields, for example in RFI and RFI responses, to protect commercially confidential information, if applicable. The CTIS functionality allows for the submission of required information in the secure domain and provides users access depending on their user profile, thus protecting personal data and the legitimate economic interest of sponsors for what concerns CCI.

More details on what should be protected in the version of the documents 'for publication' in relation to personal data and CCI, can be found in chapter 3 and 4 of this document, respectively. – Note chapter 4 of the document will be published in version 1.1. of this guidance document.

2.3. Use of the deferral mechanism and publication rules

The deferral mechanism in CTIS has been introduced to provide sponsors and Member States with the possibility to delay the publication of clinical trial information with the objective to protect CCI. Publication rules in CTIS are set out in the document Appendix, on disclosure rules, to the "Functional specifications for the EU portal and EU database to be audited - EMA/42176/2014", describing three categories for clinical trials depending on the trial phase and clinical development of the medicinal product(s) being tested.

More details on trial categories and applicable deferrals depending on the category can also be found in tables III and IV in the Annex to this document.

Deferrals requested by sponsor users

Considerations on deferrals acceptability:

- When submitting the initial application, the sponsor has the possibility to apply for a deferral or not. The extent of the deferral, for the data and documents deferred, and consequent timing for publication of the clinical trial data and documents depends on the selected trial category[15]. Any justification to be provided by the sponsors when requesting deferrals should be on the selection of the trial category. Deferrals can only be set with an initial application and cannot be modified with subsequent applications for the remainder of the trial life cycle.
- The assessment performed by the RMS/MSC on an initial application takes into account whether the trial category chosen is correct depending on the trial phase and the clinical development status of the medicinal product(s) being tested. It is expected that RMS/MSC will comment mainly on the trial category rather than on the sponsor proposed timelines for deferrals. However the possibility to receive more detailed comments on the proposed timelines for deferrals should not be excluded.
- In case of integrated trial phases or adaptive study design, i.e. phase I / II trials, phase II/III trial category should be treated in line with the higher designation, for example sponsors should

[15] Category 1 trials includes: phase 1 trials, FIH, BE/BA and bio similarity trials. Category 2 includes: phase II and phase III. Category 3 includes: phase IV trials. More details on the Appendix of disclosure rules and tables III and IV of this document.

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.[16]

- Sponsors will know that a deferral is granted if no RFIs are raised in that respect during the initial application evaluation or if the issues raised with RFI are addressed in a satisfactory fashion by the sponsor (e.g. no further RFI 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. Therefore, by authorising the initial application the Member State also authorises the deferral timelines as deferrals are part of the CTA and apply to the remainder of the trial life-cycle.
- If there is disagreement with the sponsor proposed deferrals the RMS may ask the sponsor to apply changes to the deferral settings via a request for information (RFI) on Part I. RFI on deferrals may be raised both 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. Via the RFI mechanism sponsors and MSC can communicate on the selected deferral settings. As an ultimate measure the sponsors can withdraw their application in case of any reported issues with the proposed deferrals settings.
- If a sponsor does not apply for a deferral, the document version 'for publication' will be published at the earliest opportunity, namely: time of the decision. For example, in case of a multinational initial clinical trial application, the publication will occur as soon as the first MSC issues its decision, i.e. authorise, authorise with conditions, not authorise the application.

Considerations on trials were deferrals are not accepted:

- For category 1 trials that are conducted in paediatric population or are included as part of a paediatric investigational plan (PIP) it is not possible to defer the publication of: main characteristics of the trial, notifications, summary of results, including for an intermediate data analysis, and layperson summary.
- For clinical trials in public health emergency settings[17], 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 situations[18] fall either under category 2 or 3 (therapeutic intent), since for these trials Article 35 (1)(b) of the Clinical Trials Regulation requires scientific grounds for individual clinically relevant benefit for subjects.[19]

Considerations on deferrals and publication aspects:

- Regardless if deferrals are selected by the sponsor, the sponsor has the obligation to submit in CTIS a document version 'for publication'. A document version 'not for publication' may also be submitted based on the document type and document content, as long as the protection of CCI and personal data is necessary.
- This rule is also applicable to the documents provided by the Member States Concerned.
- Note that two versions will not always be needed, it will depend on documents type and content, i.e. if no CCI/PPD protection required, only a 'for publication' version will be necessary.
- The structured data fields and the document version 'for publication' are the one published at the designated time, meaning at the time of decision of an application, or months/years after the end

[16] Section 4.3.3. paragraph 3 of Appendix, on disclosure rules, to the "Functional specifications for the EU portal and EU database to be audited - EMA/42176/2014''.
[17] Article 17 of Regulation (EU) 2022/123
[18] Emergency situation: first trial specific intervention before signing the informed consent
[19] Article 35 of Regulation (EU) No 536/2014

of the trial in the EU/EEA or at the time of publication of the final summary of results, depending if a deferral is applicable. The document version 'for publication' should not contain personal data and should not contain information that would still be considered 'commercially confidential' at the time of publication.

- The document version 'not for publication' is the original, integral version containing all the information required by Member State Concerned to perform the assessment, and it is not published. It may contain personal data if necessary in accordance with Article 81(6) referring to the purposes listed in Article 81(2) of the CTR and it may contain CCI in order to allow for the evaluation of the application carried out by a Member State Concerned.
- In case both document versions 'for publication' and 'not for publication' are to be submitted, these documents should be submitted at the same time in CTIS secure domain as part of a clinical trial application, and during the clinical trial life cycle. The document version 'for publication' is the first one to be uploaded then optionally followed by the version not for publication by clicking on (+) icon next to the document. More information on this can also be found in CTIS training module 10.
- CTIS functionality to have document version 'for publication' and 'not for publication' is depicted below.

Certain documents in CTIS are never published, for example: quality related documentation and quality assessment reports, financial arrangements, supporting documentation to a sponsor opinion on a corrective measure or a sponsor's response to an *ad hoc* request for information raised by the RMS/MSC, are categorised in CTIS as document 'not for publication'. ASRs are also exempted from publication rules and submitted in line with the requirements of chapter VII of the CTR.

Considerations on modification of a clinical trial dossier and deferrals:

- Sponsors can modify structure data fields and document content to an application Part I and Part II while the application (of any type: initial, substantial modification, addition of a MSC) is under evaluation and if an RFI has been raised in that respect. If needed, via the RFI responses sponsors can update or permanently delete documents (of any type) in a CTA, that are within the scope of the RFI raised. Document versions submitted in a particular application type but superseded while responding to an RFI will not be published, leading to the publication only of the latest submitted version.

  Once a decision is issued on the application, it will no longer be possible for the sponsor to modify the structured data and documents content in that application, even if publication has not yet occurred because of the deferrals authorised.

- Substantial modifications can be submitted during the trial life cycle when changes are likely to substantially impact on the safety or rights of the subjects or on the reliability and robustness of the data generated in the clinical trial. These substantial modifications are subject to Member States concerned assessment and decision.

  All applications are subject to the same publication rules and applicable deferral of publication set during the initial clinical trial application, as described in the Appendix on disclosure rules for CTIS[20]. For application types requiring a decision (initial application, subsequent substantial modifications or additions of a new member state concerned) once the decision has been granted 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. For non-substantial modifications data and document versions are subject to publication once the submission has been made.

- Sponsors can also submit notifications (e.g. serious breaches, unexpected events, etc..) and summary of results. Also for these documents, in case an update is done, a new version can be submitted. It should be noted that in case there are several document versions 'for publication' due to the updates done, then all the submitted versions of the documents 'for publication' will be available in the public domain.

- After a decision has been issued on a clinical trial application the Agency will be the only party able to amend publication of published information and modify documents content on the CTIS secure domain, on justified grounds and on the basis of protection of personal data and CCI.

Deferrals applied by Member States users

If a sponsor applies for a deferral which is granted by the MSC during the evaluation, then the RMS and MSC can defer the publication of the RFI raised and certain documents for the same time period as selected by the sponsor. It is expected that, in principle, the RMS/MSCs will apply the same timelines as the sponsors to delay the publication for the elements of their concern.

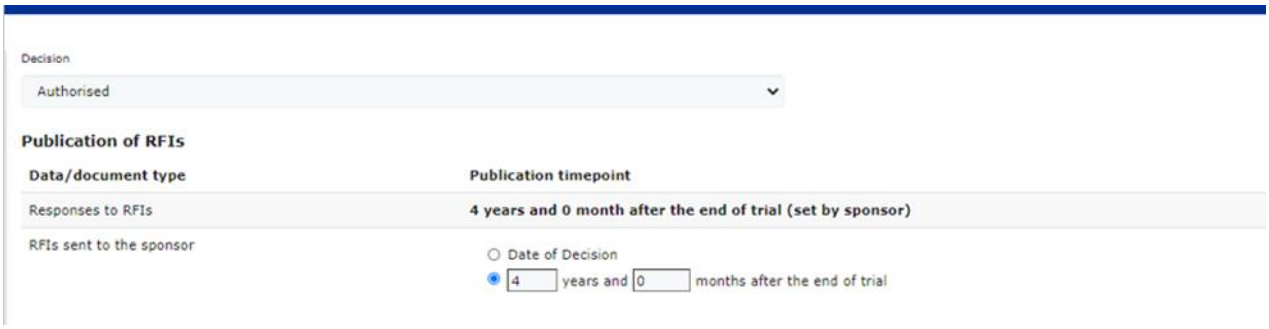
More specifically:

- The **RMS** can defer the publication of information for **Part I**, in relation to request for information (RFI), the final assessment reports and conclusions;

- The **MSC** can defer the publication of information for **Part II**, in relation to request for information (RFI), the final assessment reports and conclusions.

This is defined in the CTIS by each of the Member states concerned at the time of issuing a decision where Member States are presented with the deferrals values selected by the sponsors **as default** setting, please see the screenshot below for illustration purpose, also showing that not necessarily the maximum timelines for deferrals have to be selected by the sponsors and consequently by the Member States (4 years in this case).

[20] https://www.ema.europa.eu/en/documents/other/appendix-disclosure-rules-functional-specifications-eu-portal-eu-database-be-audited_en.pdf



The following principles apply:

- The publication of the considerations of RFIs sent to the sponsors, and any documents provided with an RFI, can be deferred by the MSC/RMS in line with the deferral timelines requested by the sponsor for their responses to such RFI.
- The publication of MSCs/RMS assessment reports and conditions can be deferred in line with the deferral timelines requested by the sponsors for the protocol and summary of scientific advice, investigator's brochure and investigational medicinal product dossier for safety and efficacy (IMPD S&E).
- Exceptionally, if MSC/RMS wish to deviate from the timelines proposed by the sponsors for the deferrals, they will inform the sponsor in advance via the RFI including a rationale for the necessary changes for deviation. As an ultimate measure the sponsors can withdraw their application in case of any reported issues with deferrals settings.
- The deferral of publication of structured data fields and documents for a clinical trial will conclude:
  - When the agreed timelines for publication are reached for the respective trial category (e.g. 7 years after the end of the trial in the EU/EEA, or the publication of final summary of results)

    or
  - The trial results are used in any marketing authorisation application in the EU/EEA and a clinical study report (CSR) has been submitted to CTIS for this trial. In that instance, the submission of the CSR for this trial in CTIS, and its subsequent publication, will trigger the publication of the deferred data and documents, as applicable, even if the deferral timelines have not yet been met.

Further details on the use of the deferral functionality to protect commercial confidential information is provided in chapter 4 of this guidance document. (To be finalised in version 1.1. of the document)

3. Management of personal data in structured data fields and in documents submitted to CTIS

3.1. Introduction

The protection of personal data processed in CTIS is a joint responsibility of the EMA, the European Commission, the Member States (including National Competent Authorities and Ethics Committees) and commercial, non-commercial organisations including academia acting as sponsors of clinical trials and marketing authorisation applicants/holders. This joint responsibility is documented in the Joint Controllership Arrangement (JCA) for CTIS (europa.eu), which includes in Annex II the EMA Data Protection Notice, addressed to data subjects namely CTIS users, sponsors, principal investigators, trial participants and that explains the purpose of the processing of personal data, the way CTIS collects, handles and protects personal data, how the information is evaluated and the rights of data subjects in relation to their personal data.

The processing of personal data in CTIS, entailing the collection, publication and archiving of clinical trial information in documents and structured data fields is necessary for the management and functioning of the Agency and the performance of its tasks carried out in the public interest mandated by Union law, as joint controller of the CTIS, which includes the EU Portal and Database, for the effective materialisation of the objectives of the Clinical Trials Regulation. Therefore, this data processing by the Agency is lawful under Article 5(1)(a) of the EUDPR and justified on the grounds of public interest.

In addition, the Member States, the European Commission, the commercial, non-commercial organisation including academia acting as sponsors of clinical trials and marketing authorisation applicants/holders, are also joint controllers in the CTIS. They are legally obliged to collect and upload relevant documents in the CTIS. Therefore, the data processing by the Member States and the European Commission also relies on the lawful ground of public interest under Article 6(1)(e) of the GDPR and Article 5(1)(a) of the EUDPR, respectively.

In the case of sponsors and marketing authorisation applicants/holders their activities in CTIS and the related personal data processing is necessary for compliance with their legal obligations under the Clinical Trials Regulation in accordance with Article 6(1)(c) of the GDPR.

In the context of transparency of clinical trials in CTIS, to protect the rights of trial participants to private life and the right to the protection of personal data, Article 81(7) of the CTR sets out that no personal data of trial participants shall be publicly accessible, which is further reinforced by Article 81(4) of the CTR that states that the CTIS shall be publicly accessible except where justified to protect the confidentiality of personal data.

Personal data, including special categories of personal data of trial participants, should only be provided in CTIS as strictly necessary to allow for the scientific and regulatory assessment of the documents submitted to Member States.

Chapter 2.1 of the EMA Privacy Statement (Annex II of the CTIS JCA), referring to the personal data in documents provided by the joint controllers in CTIS, states the following: 'Should any of these documents contain personal data, as applicable and as required in light of Article 81(2) of Regulation (EU) No 536/2014, this can be provided in the version of the documents 'not for publication'. The version of the documents 'for publication' should not contain personal data.'

To ensure that no personal data are made public these data should be anonymised, in the versions of documents 'for publication' with the following exceptions:

- In documents that are submitted in a clinical trial application dossier this principle **does not apply** to the following personal data as this information is required to be in the public domain as defined in the Appendix on disclosure rules[21]:
  - the name and surname of the principal investigator and address of the clinical trial site;
  - the name and surname of the head of the clinic/institution, or by some other responsible person, declaring the status of compliance of the clinical trial site;
  - the name and surname of the sponsor legal representative, as defined in Article 72 of the CTR for sponsors that are not based in the European Union.
- Contact details provided in CTIS for the principal investigator and the sponsor legal representative should be professional contact details or functional contact details and they will be published via the applicable structured data fields. These contact details should, therefore, not be redacted, or otherwise anonymised, in the documents uploaded in CTIS.
- In the clinical study report (CSR) submitted in CTIS by the marketing authorisation applicant/holder the principle of protection of personal data **does not apply** to the individual signing the CSR, whose names and surnames, but not the signatures, should be available in the document version 'for publication'[22].

In addition to the EMA data protection notice, Tables I and II in the Annex to this document should be consulted for a more detailed description of the documents submitted via CTIS and the type of personal data that they might typically contain.

3.2. The principles of anonymisation

Anonymisation refers to 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 (Recital 26 of GDPR and Recital 16 of EUDPR). The processing of such anonymous information is not subject to the provisions of the GDPR/EUDPR.

To determine whether a natural person is identifiable, account should be taken of all the means reasonably likely to be used, such as singling out, either by the controller or by another person to identify the natural person directly or indirectly. To ascertain whether means are reasonably likely to be used to identify the natural person, account should be taken of all objective factors, such as the costs of and the amount of time required for identification, taking into consideration the available technology at the time of the processing and technological developments (Recital 26 of GDPR and Recital 16 of EUDPR).

The Article 29 Working Party has issued an Opinion on Anonymisation Techniques[23]. The Opinion discusses that the effectiveness of anonymisation techniques should be checked against three criteria:

i. is it still possible to single out an individual,

ii. is it still possible to link records relating to an individual, and

iii. can information be inferred concerning an individual?[24]

[21] https://www.ema.europa.eu/en/documents/other/appendix-disclosure-rules-functional-specifications-eu-portal-eu-database-be-audited_en.pdf
[22] See section 4.2.5 of the Appendix on disclosure rules
[23] Opinion 05/2014 on Anonymisation Techniques, 0829/14/EN WP216, available: https://ec.europa.eu/justice/article-29/documentation/opinion-recommendation/files/2014/wp216_en.pdf
[24] Ibid, Executive Summary.

The Opinion also recognises that the use of one individual anonymisation technique alone may not meet with certainty, in every instance, the criteria of effective anonymisation. However, some of the criteria may be met in whole or in part by a given anonymisation technique, therefore a combination of techniques should be carefully applied together to enhance the robustness of the outcome.[25]

Combination of anonymisation techniques could be used, for example, in clinical study reports. For documents part of the CTA, which are expected to contain mainly direct identifiers, redaction would be most likely the anonymisation technique of choice.

An anonymisation report describing the anonymisation techniques used is not expected to be provided in CTIS, unless specifically requested.

When establishing a process for ensuring an adequate level of anonymisation, the following factors may be considered:

- the likelihood of re-identification being attempted;
- the likelihood the reidentification would be successful;
- the anonymisation techniques which are available to use; and
- the quality of the data after anonymisation has taken place and whether this will meet the needs of the organisation (and the public) using the anonymised information. For example, once the anonymisation has been completed, an analysis of the interpretability of the anonymised data and information could be carried out to ensure they still remain meaningful and having utility for the public.

3.3. General principles on anonymisation of personal data in the documents version 'for publication'

In the context of CTIS, it is paramount to differentiate between:

a) **Personal data, other than those of trial participants**, such as of staff of the sponsor and of the marketing authorisation applicant/holder, qualified person for GMP documentation, principal investigators, etc.

and

b) **Personal data of clinical trial participants**.

Regarding anonymisation of personal data in CTIS, the following principles should be taken into account:

- Anonymisation of personal data in the documents submitted to CTIS 'for publication' should occur outside of CTIS and be applied consistently across all documents.
- The publication of documents in CTIS can occur at the time of decision on an application, or later on in case deferrals are applied (see chapter 2).
- Where only one version of a document is provided in CTIS secure domain, namely the version 'for publication' this version will be subject to publication and used for review by the MSC(s), in the absence of a version 'not for publication'.

[25] Ibid, Section 5.2.

- It is the sole responsibility of CTIS users to ensure the quality, accuracy and adequacy of anonymisation applied and that the document versions 'for publication' are anonymised in accordance with the applicable process agreed within their organisation.
- CTIS does not automatically verify if anonymisation has been applied in the version of documents intended for publication.
- When progressing with the submission of the documents via CTIS, the authorised user confirms that the recording, storage and publication of the documents in question are in accordance with Union data protection legislation. A dedicated template is available for use[26].
- The Agency, as the system administrator, holds the power to delete corrupted, incorrect, or unlawfully processed data, including removing information from CTIS public domain. This refers to requests for removal raised by the parties[27] that uploaded the document in CTIS. Such requests can be raised by contacting the dedicated EMA service desk[28].
- In addition, EMA can delete incorrect information identified in the public domain, in which case EMA will inform the party that has provided the document, that an amendment to the published document is needed. The Agency, or other joint controllers in accordance with the joint controllership arrangement, can also edit the inaccurate or outdated information contained in the CTIS secure domain to comply with Union data protection legislation.
- The Agency, the European Commission, the Member States, commercial and non-commercial organisations, including academia acting as sponsors and/or marketing authorisation applicants/holders, have joint responsibilities in submitting clinical trial data and documents in accordance with the Clinical Trials Regulation and Union data protection legislation. They also have joint responsibilities towards the data subjects and should have clear, defined processes in place to deal with any personal data breaches.
- Other shared aspects of CTIS falling under the joint controllership scheme, such as the handling of data subjects' rights, is addressed in a published joint controllership arrangement (JCA) for CTIS.[29]

3.3.1. Anonymisation of personal data other than those of trial participants in the documents version 'for publication'

Personal data of individuals including names and surnames are captured, as applicable, in CTIS structured data fields and related documents in the version 'not for publication' and should be anonymised in the document version 'for publication'.

The identifiers which are expected to be provided in CTIS documents are further described in the ACT EU Q&A[30] on CTIS transparency aspects. More specifically the name and surname of applicable persons are required in the following documents:

- Principal investigator on the CV
- Qualified Person (QP) on the GMP declaration

[26] https://health.ec.europa.eu/system/files/2022-09/compliance_reg2016_679_template_en.pdf
[27] Deletion of incorrect/corrupted documentation should not occur on routine basis but rather on justified grounds to remove corrupted/unlawful information. This should not be seen as an instrument for modification / protection of personal data or commercial confidential information provided by CTIS users that retain the ultimate responsibility
[28] https://servicedesk.ema.europa.eu/
[29] https://www.ema.europa.eu/en/documents/other/joint-controllership-arrangement-regard-clinical-trials-information-system-ctis_en.pdf
[30] ACT EU Q&A on the protection of Commercially Confidential Information and Personal data while using CTIS, version 1.1, 27 March 2023, https://www.ema.europa.eu/en/documents/other/questions-answers-protection-commercially-confidential-information-personal-data-while-using-ctis_en.pdf

- The person issuing the clinical trial 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 provided under the CTIS 'form' section, in line with available template

Specifically, for signatures the ACT EU Q&A clarifies that the only CTA documents to be signed are the suitability of the site and the QP declaration per GMP, in addition to few MSs specific requirements for Part II. Signatures should always be anonymised in the document version for publication.

The anonymisation of personal data can be achieved by applying redaction as the sole anonymisation technique. Redactions can be performed by using any available tool which ensures that the redacted information is irreversibly blacked out by applying a permanent and unremovable overlay and, at the same time, making the redacted text unreadable in the document.

Redaction of pre-specified identifiers, e.g., names, surnames, telephone numbers, can be done manually and/or automatically with software functionalities which enable the user to identify the pre-specified identifiers intended for redaction. Redaction would be the anonymisation technique of choice for personal data of individuals other than those of trial participants.

As previously described the following exceptions apply to names and surnames that should be disclosed in the document version 'for publication':

- Names and surnames of principal investigators, legal representative of the sponsors, head of the clinic/institution or other responsible person issuing the statement of suitability of the facility, which are subject to publication as explained in sections 4.2.2 and 4.2.4 of the Appendix on disclosure rules[31].
- The full name (not signatures) of the sponsor and coordinating investigator signatories of the clinical study report and the identities of the principal investigator(s) who conducted the trial, which are subject to publication as explained in sections 4.2.5 of the Appendix on disclosure rules[32].

All contact details, e-mail addresses and telephone numbers of the above mentioned individuals should be their professional contact details or provided in CTIS as functional contact details. Private contact details should not be provided in structured data fields in CTIS and if included in the documents should be redacted in the published documents.

Personal data of the author of a document, included as part of the metadata of a file, should equally be removed prior to uploading the document in CTIS secure domain and subsequent publication of the document. Instructions are available in dedicated CTIS training material, Module 02 – Guide on CTIS common features[33].

3.3.2. Anonymisation of personal data of trial participants in the documents version 'for publication'

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

[31] Appendix, on disclosure rules, to the "Functional specifications for the EU portal and EU database to be audited - EMA/42176/2014", https://www.ema.europa.eu/en/documents/other/appendix-disclosure-rules-functional-specifications-eu-portal-eu-database-be-audited_en.pdf
[32] Idem.
[33] Section 3 in training module 02: clinical-trials-information-system-ctis-common-features-ctis-training-programme-module-02_en.pdf (europa.eu)

number) 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'**.

The following elements should be considered when applying anonymisation in the documents to be published:

- **The choice of anonymisation techniques**[34]

In the context of CTIS, no specific anonymisation methodology to protect personal data of clinical trial participants is prescribed, acknowledging that each anonymisation technique has its own strengths and weaknesses. The robustness of each anonymisation technique is based upon the anonymisation criteria and will help in identifying the most suitable technique (or combination of different techniques) to establish an adequate anonymisation process for a given document.

- **Data utility**

Personal data of trial participants could be present in document version 'not for publication' (e.g. notification of serious breaches, unexpected events or urgent safety measures, clinical study reports). It should be noted that it is equally important to preserve **data utility** in the public version of the documents, as much as possible, whilst ensuring adequate anonymisation. Moreover a quantitative approach to the measurement of the risk of re-identification could be favoured.

- **The sensitivity of the data**

The specificities of the relevant data should be taken into consideration when selecting the most appropriate anonymisation technique(s). For example, clinical trials conducted on rare diseases and/or on small populations may carry a high risk of re-identification of trial participants. A thorough risk assessment should be performed for such scenarios and the anonymisation of personal data should be adapted to the identified risk. Moreover such an approach is also applicable to genetic information and low frequency events (e.g. rare events, extreme values, unusual treatments, pregnancy outcomes).

For a more detailed description of the available anonymisation techniques and their strengths and weaknesses please refer to Article 29 Working Party Opinion on Anonymisation Techniques. The same principles will apply to the protection of personal data of trial participants in the documents submitted to CTIS.

3.4. The principle of pseudonymisation applicable in the version of documents 'not for publication'

The documents uploaded in CTIS may contain personal data in a pseudonymised format. Mostly frequently included one is the clinical trial subject ID number. For the reasons presented above the clinical trial subject ID number should not be disclosed in the document version 'for publication'. It should be adequatly anonymised by employing appropriate anonymisation techniques.

The pseudonymisation of personal data can reduce the **risks** to the data subjects concerned (e.g. trial participants). Pseudonymisation refers to processing of personal data in such a manner that the personal data can no longer be attributed to a specific data subject without the use of additional information, provided that such additional information is kept separately and is subject to technical and organisational measures to ensure that the personal data are not attributed to an identified or identifiable natural person (Article 4(5) of GDPR and Article 3(6) of the EUDPR).

[34] The EMA Guidance on the implementation of Policy 0070 https://www.ema.europa.eu/en/documents/regulatory-procedural-guideline/external-guidance-implementation-european-medicines-agency-policy-publication-clinical-data_en-3.pdf

Practically, pseudonymisation consists of replacing one attribute (typically a unique attribute) in a record by another. When pseudonymisation is used alone, the natural person could still be identified indirectly. Therefore, pseudonymisation reduces the linkability of a dataset with the original identity of a data subject, but when used alone will not result in an anonymised dataset. Thereby, pseudonymisation is not an anonymisation technique but a useful security measure.

Personal data which have undergone pseudonymisation and which could be attributed to a natural person by the use of additional information, should be considered to be information on an identifiable natural person, therefore data protection rules still apply.

3.4.1. Personal data of trial participants, including pseudonymised personal data, in the documents version 'not for publication'

Personal data of trial participants which could appear, as applicable, in CTIS document versions 'not for publication' encompass personal data in pseudonymised format (e.g. clinical trial subject ID number) and indirect identifiers such as weight, height, age, gender, etc. Such personal data may be contained in CTIS secure domain and if provided should only be included in the document version 'not for publication'.

A non-exhaustive list of documents that may contain personal data of trial participants is provided below:

- Investigator Brochure
- Paediatric Investigational Plan
- IMPD sections on Safety and Efficacy
- Unexpected event reports and supporting information
- Urgent safety measure reports and supporting information
- Serious Breach Reports and supporting information
- Clinical study reports
- Assessment reports
- Inspection reports

It should be noted that the principle of data minimisation should be followed when providing pseudonymised personal data of trial participants in the documents 'not for publication' in CTIS secure domain. The use of personal data of trial participants should be proportionate. The clinical trial documents should include sufficient level of details to permit for the scientific evaluation and include sufficient data to evaluate the benefit/risk profile of the investigational medicinal product(s) used.