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TOPICAL FEATURE

A Comprehensive Workspace for All Clinical Trials: The Clinical Trial Information System (CTIS) in Europe – Opportunities for Medical Writers

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ABSTRACT

This article introduces the Clinical Trial Information System (CTIS), which is the mandatory workspace for sponsors, authorities, and ethics committees to authorize and supervise all clinical trials in Europe. It describes the key features of the system, its mechanics, and the associated processes including the transparency requirements. Working with CTIS offers opportunities for regulatory medical writers in ensuring compliance, efficiency, and effective communication across the clinical trial life cycle. From crafting high-quality cover letters to writing and managing responses and producing lay language documents, medical writers are well-positioned to contribute their expertise in this collaborative and time-sensitive environment.

BACKGROUND

With the launch of the Clinical Trial Information System (CTIS) on January 31, 2022, the legal framework of the Clinical Trial Regulation (CTR) 536/2014 became fully applicable in the European Union (EU) and the European Economic Area (EEA).[1] On this date, the use of CTIS became mandatory for new clinical trials and, after January 30, 2025, for all clinical trials. CTIS is the single entry point for submitting clinical trial applications (CTAs) in the EU and EEA and handles all aspects of clinical trial conduct: initial submission for authorization, evaluation, approval, updating trial conduct, maintenance, ending, and uploading of clinical trial results and clinical study reports.

The system is to be used for all trials of all clinical phases (I to IV) in patients and healthy volunteers. In addition, CTIS also handles authorization and maintenance of so-called low-intervention trials, that is, trials with authorized medicinal products within the limits of their marketing authorizations (article 2 (2)(3) of the CTR).[1]

CTIS simplifies clinical trial application assessments across EU and EEA member states by enabling a single, centralized submission instead of individual country submissions. It also fulfils CTR transparency requirements by making key trial documents publicly accessible online. Developed to improve efficiency, digitalization, transparency, innovation, and patient safety, CTIS provides the necessary data and documents for competent authorities and ethics committees to evaluate and oversee trials.

Although CTIS improves clinical trial administration, approval and oversight remain the responsibility of the individual member states, not a central agency like the US Food and Drug Administration (FDA) in the United States. The European Medicines Agency (EMA) supports the process by offering infrastructure, guidance, and training but does not assess or oversee trials. Instead, a Reporting Member State (RMS) leads and coordinates the evaluation for all participating member states (Member States Concerned, MSCs).

Because of this set-up, harmonization between the different national competent authorities (NCAs) is key for the efficiency of the system. The coordinative work among NCAs is done by the Clinical Trials Coordination Group (CTCG), a working group established by the Heads of Medicines Agencies (HMA). Guidance on CTIS processes is provided by the CTCG, the European Commission, and EMA.

WHAT IS CTIS AND WHO ARE THE MAIN PLAYERS?

CTIS is best characterized as a collaborative workspace for the stakeholders involved in authorization, maintenance, and results reporting of clinical trials in the EU and EEA. There are 3 major areas: the sponsor workspace, the authority workspace, and the public website that provides in-depth information about all clinical trials in EU and EEA. In the sponsor workspace, sponsors apply for initial CTAs or for modifications of authorized trials. Sponsors issue notifications about trial events to maintain approval and submit Annual Development Safety Update Reports, (DSURs), summary results, and clinical study reports. In the authority workspace, NCAs and ethics committees (ECs, the European counterpart of Institutional Review Boards) evaluate initial CTAs and modifications thereof, issue Requests for Information (RFIs), and maintain oversight over clinical trial conduct by responding to notifications (eg, updates on trial status).

To date, communication between sponsors and regulators (NCAs and ECs) occurs (almost) exclusively within CTIS. The Notices and Alerts functionality informs sponsors

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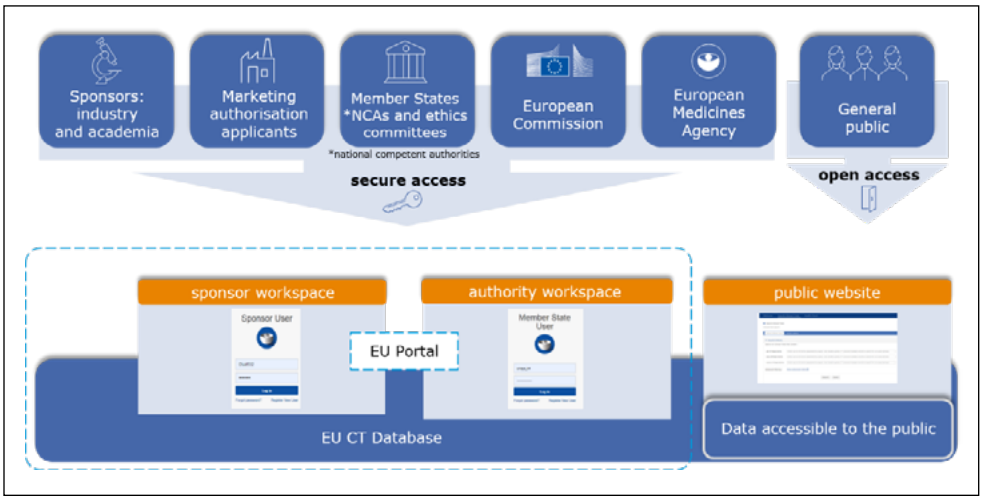

Figure 1. CTIS as a collaborative workspace for authorization, maintenance, and reporting of results of clinical trials in the EU and EEA. CT, clinical trial; CTIS, Clinical Trial Information System; EEA, European Economic Area; EU, European Union. Source: Sponsor Handbook, v6.1, Introduction and general principles.[3]

about required actions. Currently (November 2025), CTIS does not send or receive emails; therefore, constant monitoring is required. This is planned to be changed in Spring 2026, although no precise implementation date has yet been provided. However, even now, in nonroutine cases and for special requests, the different national authorities may also be contacted directly via email.

CTIS BASICS: ENTRY OF DATA AND UPLOAD OF DOCUMENTS, PART I AND PART II

Information is entered into CTIS either as text into data fields or by choosing entries from drop-down lists and by the uploading of documents. For documents that will become publicly available (see section on Transparency), sponsors need to upload 2 versions: first, a redacted version in which all personal protected data (PPD) and the commercially sensitive data (commercially confidential information, CCI) are redacted, that is, blacked out; and a clean, unredacted version of the document. The redacted version will become public according to the CTIS transparency rules, whereas the clean, unredacted version is used in the assessment by authorities and ECs.

To understand the workings of CTIS, it is important to realize the difference between Part I and Part II. Part I comprises documents that pertain to the entire trial (trial-level) such as the study protocol or the investigator brochure (IB) and the quality documentation. These trial-level documents in Part I are complemented by Part II that comprises all documents related to investigator and site qualification, insurance, financial arrangements, the patient information, and the informed consent forms (ICFs).

OVERVIEW OF THE STRUCTURE OF CTIS

Trial entries are made in 4 main tabs or sections in CTIS: the Form section, the MSC section, Part I, and Part II sections.

Form Section

This section comprises the cover letter, the proofs of payment per participating MSC, a statement of compliance with the General Data Protection Regulation 2016/679 (GDPR), and the justification of the trial category. The trial category is important because it drives the disclosure obligations according to the transparency rules (see section on Transparency).

The cover letter should not be mistaken as a formality. In CTIS, it is the only document that the sponsor can use to explain special features of an application. Here, sponsors can convey information that is not available in other documents or in the structured data fields. This may be drug-, trial-, or program-specific information or may concern quality or supply aspects. Some countries require the cover letter both in English and in their national language (Bulgaria, Croatia, Greece, Hungary, Slovakia).[2]

Therefore, the document should be carefully crafted both in terms of content as well as in appearance. A well-written, high-quality cover letter can streamline the assessment process and proactively address potential concerns that would lead to RFIs. To achieve this, the cover letter must be succinct, well-structured, and must effectively summarize the information provided to facilitate efficient processing—skills that are core competencies of regulatory medical writers. Given the appropriate organizational setup, medical writers can ensure consistency and create standards across trials for entire clinical trial programs.

MSC Section

In this section, the sponsor needs to provide the participating countries with their enrollment targets. Here the sponsor also proposes which of the MSCs should become the RMS. Also, the countries in which the trial is conducted outside of the EU and EEA need to be entered along with the total number of patients within and outside of the EEA.

Part I Section

This section comprises all information that pertains to the entire clinical trial irrespective of participating countries. It is comprehensive and contains key information about the clinical trial in structured data fields and the key clinical documents: the protocol, the protocol synopsis, the IB, and the Investigational Medicinal Product Dossier - Quality (IMPD-Q) and the IMPD Safety and Efficacy. The following sections are of particular importance as they contain information that will become public.

The subsection "Trial information" comprises information on the trial phase, the medical condition, and the therapeutic area investigated, the main (primary) objective, secondary objectives, inclusion and exclusion criteria, and primary and secondary endpoints. The dates of trial start and end within the EEA and globally, and some information on the trial population also need to be provided.

In the "Protocol information" subsection, the trial protocol, the synopsis of the protocol (layperson protocol synopsis and, for some countries, the scientific protocol synopsis), and charters of the Data and Safety Monitoring Board and other trial committees need to be uploaded.

The "Product section" comprises details on the products used either as test or comparator or placebo, or as Auxiliary Medicinal Products, that is, products prescribed by the study protocol that are not part of the study hypothesis. Details of the product characteristics—whether the product is immunological, neurological, and so on—need to be given together with the dosage and administration details. Most importantly, potential CCI on total daily dose, treatment duration, and maximum total dose are to be entered. Here the documents related to quality, that is, documentation of Good Manufacture Practice, the Manufacturing and Import Authorizations, and a Qualified Persons declaration need to be uploaded.

Part II Section

The Part II tab is subcategorized into the different participating MSCs. For each MSC, this section comprises all documents needed for assessing investigator and site suitability, as well as certain statements of compliance. In the subsection "Subject Information and Informed Consent Form," all ICFs need to be uploaded in the local languages of the MSC. Should the ICFs contain any CCI, both a redacted and an unredacted version need to be uploaded. In the section "Suitability of the investigator," the CVs, the Declarations of Interest, and the Good Clinical Practice training certificates need to be provided for all investigators in the country. The filled Site Suitability Form per participating site needs to be uploaded in the section "Suitability of the facilities." Insurance certificates per country come into section "Proof of insurance cover or indemnification." Under "Financial and other arrangements," the country budgets, participant compensation plan, and the compensation plan for the site need to be uploaded. The remaining sections require statements of compliance with the national requirements on data protection and the use of biological samples.

Figure 2. Structure of Part II of CTIS for each Member State Concerned (MSC); each line represents a sub-section for uploading the required documents. CTIS, Clinical Trial Information System. Source: Sponsor Handbook, v6.1, Section 2.4.6[3]

The Processing of an Initial CTA as an Example of CTIS Processes

The first step after the submission of an initial CTA is the selection of the RMS, which coordinates, collates, and consolidates the assessment of predominately Part I and will issue the final decision on Part I.

As the next step, the dossier is validated for completeness. During this phase, the sponsor may receive validation RFIs, which usually have to be responded to within 10 calendar days. Once validation has been passed, both Part I and Part II are evaluated in parallel, Part I predominantly by the NCAs and Part II by the ECs of the MSCs. During the assess-ment phase, authorities can issue RFIs, which need to be responded to within 12 calendar days (or even shorter time-lines). RFIs prolong the overall timeline for authorization by 31 days. Once the assessment is completed, a decision phase commences, after which the final decision is issued by each MSC for their country (Part II) as either authorized, not authorized, or authorized with conditions. The RMS issues a decision for Part I as either approved, approved with conditions, or not authorized.

The RFI Phase

RFIs are notified in the Notices and Alerts tab in CTIS. Although planned for Spring 2026, CTIS does not send alerts via email. Therefore, to best use the response time allocated (12 calendar days or less), sponsors must constantly monitor CTIS for alerts. Hence, sponsors or service providers

(eg, contract research organizations) need to establish an infrastructure that allows monitoring of CTIS during European business hours from Monday to Friday. Once RFIs have been received, the sponsor teams need to start working on the responses immediately and need to prioritize this task above all others. Should the responses not be received by the deadline, the entire CTA will lapse. Resubmission of a CTA is possible, but this will lead to a substantial delay in study approval and additional cost because some national authorities require renewed payment with a resubmission. Providing the responses in time is particularly challenging for changes in key documents such as the trial protocol, IB, IMPD, or the ICFs because not only do the revised documents need to be submitted but also their redacted versions (only for trial protocol and protocol synopses), and, in the case of ICFs, the translated (and potentially redacted) versions for all countries. Medical writers with strong coordinative and managerial abilities can guide multifunctional teams to ensure timely and accurate responses. They may draft responses, maintain editorial oversight, ensure coherence across responses, and critically assess the appropriate level of detail in relation to the question posed.

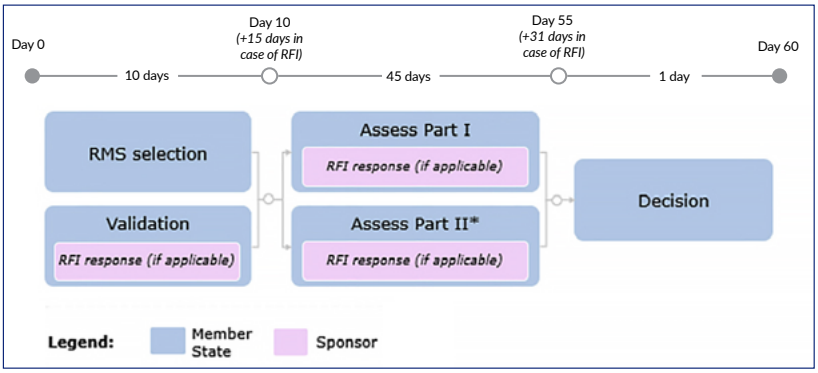

Figure 3. Timelines for an initial Clinical Trial Authorization (CTA) submission. RFI, Request for Information; RMS, Reporting Member State. Source: Sponsor Handbook, v6.1, Section 3.1.1.[3]

Timelines for an Initial CTA

The CTR mandates certain timelines for the processing of clinical trial applications, and therefore, CTIS works according to standard timelines (Figure 3). However, actual timelines from submission to decision will depend on the number of RFIs received and the speed with which the sponsor provides responses. Although the standard timeline for an initial CTA is 60 days, it is common that it takes 100 to 130 days from submission to decision. In the most recent performance assessment of CTIS, the median time from submission to approval for an initial CTA was 108 days.[4]

Standard timelines are also available for substantial modifications (50 days without any RFIs) or the addition of a member state (52 days without any RFI).[3]

Transparency

Transparency about clinical trials was a key motivation behind the legal framework of the CTR. Initially, CTIS aimed to make nearly all trial documents and structured data fields public, except for the quality dossier (eg, IMPD-Q). However, this approach created significant complexity and workload, requiring sponsors and authorities to redact and upload versions of documents containing PPD or CCI. To address these challenges, revised transparency rules were introduced on June 18, 2024, shifting to a focused transparency approach. Under this model, only key documents are made public, and they are published earlier. Publicly available documents include the trial protocol, protocol synopsis (layperson protocol synopsis and, for some countries, the scientific synopsis), ICFs, patient-facing materials (published at authorization), and the lay and scientific summaries of results (published 12 months after trial completion). Clinical study reports are made public once the trial was part of a marketing authorization procedure, regardless of its outcome. The scope and timing of publication depend on the trial category (Table 1).

Table 1. Disclosure Categories and Clinical Trial Types
Source: Revised CTIS Transparency Rules and Historical Trials: Quick Guide for Users, v1.9, modified.[5]

Category	Trial Type
Category 1: pharmaceutical development clinical trials	• Phase 0 clinical trials in healthy volunteers or patients • Phase I clinical trials in healthy volunteers or patients • Bioequivalence and bioavailability trials • Similarity trials for biosimilars • Equivalence trials for combination or topical product
Category 2: therapeutic exploratory and confirmatory clinical trials	• Phase I and phase II integrated clinical trial • Phase II clinical trials • Phase II and phase III integrated clinical trials • Phase III clinical trials
Category 3: therapeutic use clinical trial	• Phase III and phase IV integrated clinical trials • Phase IV clinical trial and low interventional trials
Pediatric trials	• All trials involving minors

The revised transparency rules grant some protection of data and documents for Category 1 trials by delaying

the publication of key information and documents to 30 months after the end of the trial (defined as last patient, last visit). For trials of higher categories, the key documents and the key data become available almost instantly with the first decision of an MSC.

Table 2. Publication of Clinical Documents According to the Revised Transparency Rules

<table>
<tr><th colspan="3">Category 1</th><th rowspan="2">Category 2 and 3 incl. integrated ph 1&2</th></tr>
<tr><th>Document Type</th><th>Pediatrics and/or PIP</th><th>Adults</th></tr>
<tr><td>Protocol, synopsis, patients facing documents</td><td>Upon results submission</td><td>30 months after EU/EEA End of Trial</td><td rowspan="2">First MSC decision</td></tr>
<tr><td>SmPC, if available</td><td colspan="2" rowspan="3">Never</td></tr>
<tr><td>Subject information and informed consent form</td><td rowspan="2">That MSC decision</td></tr>
<tr><td>Recruitment arrangements, incl. procedures for inclusion and copy of advertising material</td></tr>
<tr><td>Final summary of results, Lay summary of results</td><td>As soon as submitted</td><td>30 months after EU/EEA End of Trial</td><td>As soon as submitted</td></tr>
<tr><td>Clinical study report, if available</td><td colspan="3">As soon as submitted</td></tr>
<tr><td>All other documents, incl. any MS document</td><td colspan="3">Never</td></tr>
</table>

EEA, European Economic Area; EU, European Union; MS, member state; MSC, member states concerned; PIP, Pediatric Investigational Plan; SmPC, Summary of Product Characteristics. The table was copied as provided in the source document without any changes.Source: Revised CTIS Transparency Rules and Historical Trials: Quick Guide for Users.[5]

For all documents in scope, a redacted version and a clean version need to be uploaded. For trials of category 2 or above, this also entails redacted versions of the ICFs in each of the languages in which the trial is conducted.[6]

Lay Language Documents

The CTR introduced 2 lay language documents: the layperson protocol synopsis and the lay summary of trial results.[2,7] Medical writers with expertise in lay language communication are well positioned to create, edit, and oversee these documents. In particular, the layperson protocol synopsis is often time-sensitive because it must be translated into the languages of the participating countries beforte submission. Medical writers with experience in this area can ensure that the documents are clear, accessible, patient-focused, and delivered within timelines. Developing templates and standards either for all trials of a company or for specific trial programs improves efficiency. Furthermore, because the transparency aspects are constantly evolving, medical writers with a background in disclosure and transparency can support study teams in achieving compliance while avoiding disclosure of commercially sensitive information.

CTIS Public Portal Including the Clinical Trial Map

CTIS enables public access to key information of some 10,373 trials (as of November 2025) that are conducted in the EU and EEA (https://euclinicaltrials.eu/search-for-clinical-trials/?lang=en). After substantial improvement in September 2024, the updated search functionality permits both a basic search and an advanced search. The portal can be searched for indication or disease studied, trial phase, trial status (recruiting, started, ended), sponsor, participant type, and many more. The search can be done in all 26 languages of the countries of the EU and EEA. Users can access a summary of the trial, the full trial information (objectives, eligibility criteria, endpoints), the trial documents (according to the transparency rules), trial results (lay results summary and scientific results summary), and the locations of the study centers where the trial is conducted, including the names and phone numbers of the principal investigators and the sponsor. In addition, information on serious breaches, unexpected events, urgent safety measures, and temporary halts is available. Users can directly download all the information about a particular trial from the public website.

In March 2025, the latest feature of this website, an interactive map for all clinical sites in Europe, was released (https://euclinicaltrials.eu/search-for-clinical-trials/trial-map/?lang=en&EUCT=2025-520743-33-00). The map displays all of EU and EEA and can be searched for a specific condition, recruiting trials, and trial locations. Details of the trials identified, including the site address, full name of the trial, condition studied, and contact details of investigators can be viewed. Clicking on the European Clinical Trial Number (EU CT number) will take the reader to the full record of the trial in the CTIS public portal (see Figure 4 on next page).

Since October 2025, the map is available in all 26 languages of the EU and EEA countries.

Training and Online Resources

EMA and the CTCG have invested themselves heavily in providing appropriate training both for sponsor and authority users. The training opportunities provided comprise step-by-step guidance, videos, Q&As, and many more. The training material is generally of good quality and visually appealing. Currently, there are 2 websites with references to training material. One is called Clinical Trials Information System

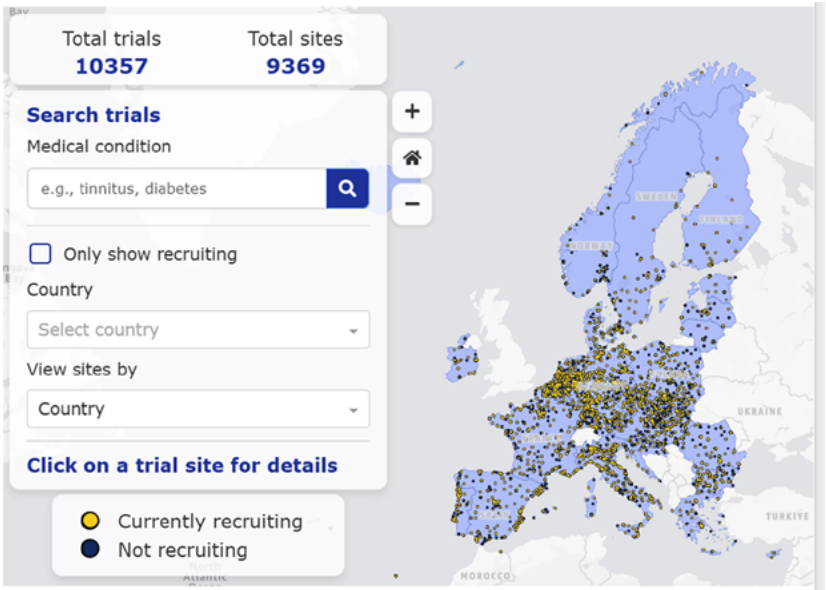

Figure 4. Screenshot of the Interactive European clinical trials map (November 13, 2025). Source: https://euclinicaltrials.eu/search-for-clinical-trials/trial-map/?lang=en&EUCT=2025-520743-33-00

(CTIS): Training and Support (https://www.ema.europa.eu/en/human-regulatory-overview/research-development/clinical-trials-human-medicines/clinical-trials-information-system-ctis-training-support), which comprises a link to the handbook for clinical trial sponsors, information on the protection of personal data and commercially confidential information (transparency rules), and additional reference materials for CTIS users.

The other training resource is called "Clinical Trials Information System (CTIS): online training modules for authorities (https://www.ema.europa.eu/en/human-regulatory-overview/research-development/clinical-trials-human-medicines/clinical-trials-information-system-ctis-training-support/clinical-trials-information-system-ctis-online-training-modules-authorities). It also provides a link to the CTIS Sponsor Handbook, to training material on the "Common functionalities for all registered users," and to the training material for the authorities.

The recently (November 2025) updated CTIS Sponsor Handbook covers the key topics for the use of CTIS and acts as a very good starting point. It provides active hyperlinks to references and further supporting material that EMA regularly updates. Additionally, EMA hosts public meetings such as "Walk-in Clinics" for stakeholder questions and "Bitesize Talks" focused on specific CTIS topics. Dates and details are available on the CTIS Training and Support website.

OPPORTUNITIES FOR MEDICAL WRITERS

The process of achieving clinical trial authorization through CTIS is highly interactive and requires collaboration across multiple functions within a company. Regulatory Affairs typically handles Part I documents, Clinical Operations oversees Part II documents, Trial Supply Management takes care of the labels, and Clinical Development/Medicine provides details on the investigational medicinal products. Regulatory medical writers, who enjoy collaborative environments and close networking, are well-suited to the tasks involved in this process.

CTIS presents a wealth of opportunities for regulatory medical writers to apply their knowledge, collaborative skills, and expertise in communication. Because all aspects of clinical trial authorization are always time critical, medical writers must be able to work well under pressure. From crafting high-quality cover letters to managing responses and producing lay language documents, they can make significant contributions. However, whether their expertise is used will ultimately depend on the organizational set-up of the company and its flexibility in redefining responsibilities across the traditional realms of activity.

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