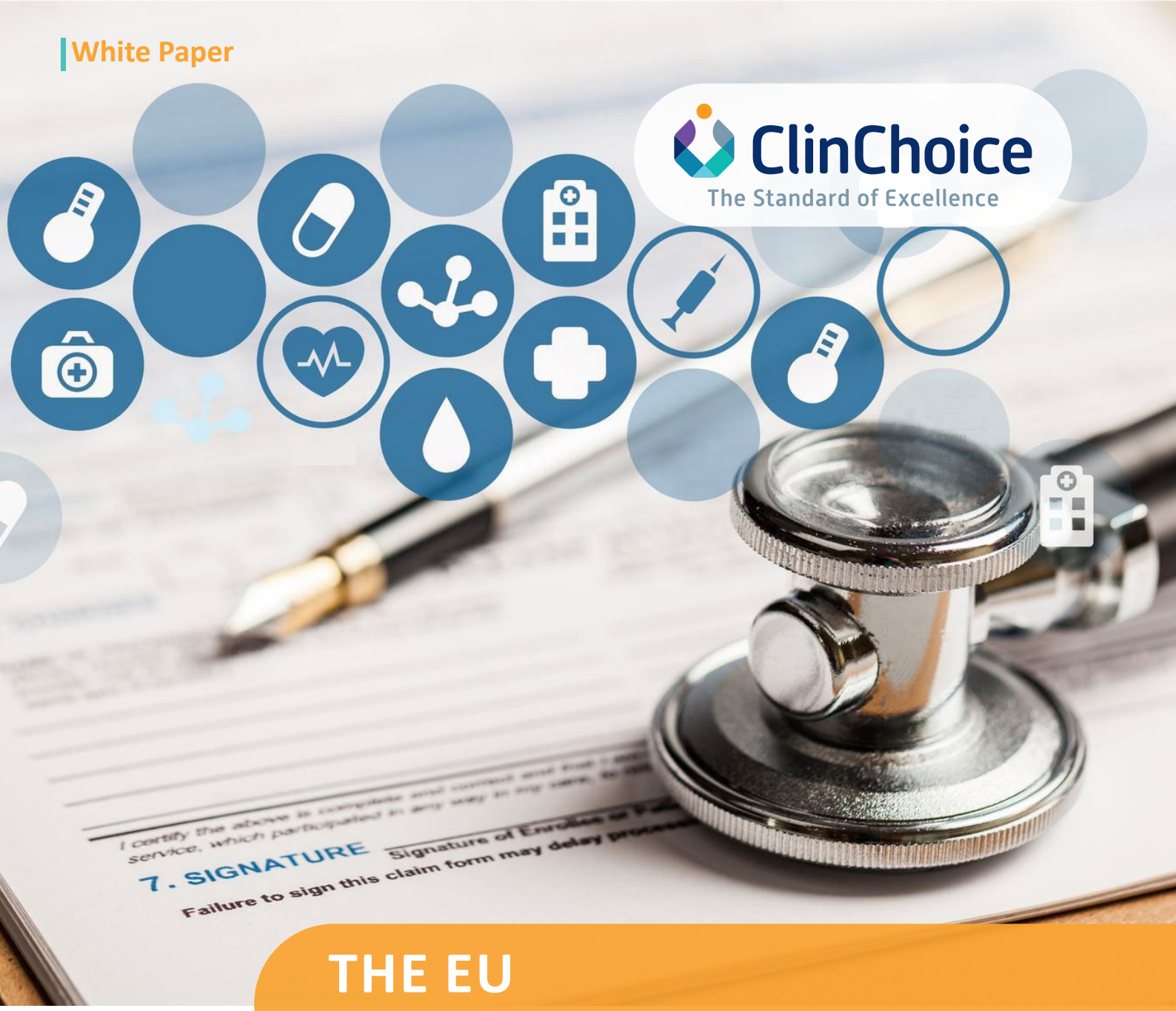
White Paper



THE EU CLINICAL TRIALS REGULATION

What You Need to Know

December 2023

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Introduction – SIGNIFICANT CHANGES UNDER REGULATION

As of 31 January 2022, the EU Clinical Trials Regulation No 536/2014 (CTR) became applicable in all EU/ European Economic Area (EEA) Member States replacing the EU Clinical Trials Directive (2001/20/EC) (CTD). On the same day, the Clinical Trials Information System (CTIS), go-live version was opened for users to submit clinical trials on medicinal products for human use under a coordination authorisation procedure.

The deadline for the European Commission to implement the CTR was to set up fully functional portal which has workspace for sponsors, National Competent Authorities (NCA) and the European Commission. The portal which allows clinical trials' sponsors to apply with a single application which covers submissions to NCAs, Ethics Committees, and public registration of the clinical trial in all EU/ EEA Member States.

In July 2021, the European Commission announced in the Official Journal of the European Commission that the new portal named Clinical Trials Information System (CTIS) is fully functional and at the same time, ready for use after six months of its publication, on 31 January 2022.

The announcement stated that Members States, Sponsors and Contract Research Organizations (CROs) started preparing intensively for the changes in the clinical trials environment.

Fortunately, the CTR foresees a 3-year transition period for sponsors to use CTIS.

During the first year starting from the CTIS go-live date until 31 January 2023, sponsors were able to choose whether to apply for a new Clinical Trial Application (CTA) under the regime of the CTD, including using EudraCT, national portals or CESP (Common European Submission Portal) or to apply under the new CTR using CTIS.

During the second and third year until 30 January 2025, the EudraCT and CESP will not be available for new CTAs. From 31 January 2023, all new CTAs must be submitted under the CTR using CTIS. CTAs that were submitted under the CTD prior to 31 January 2023, will be able to continue to run and be completed under CTD for an additional two years maximum.

By 30 January 2025, trials submitted under the CTD must either have ended in the EU/EEA or have been transitioned to the CTR via CTIS.

If sponsors are conducting trials authorized under the CTD and have at least one active site in the EU/ EEA on 30 January 2023, and they anticipate that these trials will continue beyond 30 January 2025, they will need to transition them to the CTR before the transition period expires.

However, clinical trials under the CTD that have concluded in all EU/EEA Member States, even if the global end of the trial has not yet been reached, will not require transition.

Additionally, data submitted through the CTIS are collected and stored in the EU database. The CTIS harmonises and simplifies the end-to-end application process over the life cycle of clinical trials, harmonises assessment of safety reporting of trials, accessing electronic reporting of Suspected Unexpected Serious Adverse Reactions (SUSARs) by Sponsors and re-routing to Member States, providing one single decision. In addition, the CTIS offers searchable clinical trial information to the patient, healthcare professional and the general public. The results of clinical trials are shared in the CTIS in layman's language.

This white paper provides information on how to be prepared for the new initial clinical trial authorization and substantial modification procedures under CTR.

Furthermore, it describes how to smoothly perform the transition of ongoing studies into the CTIS. Apart from that, it presents requirements for streamlined reporting and public disclosure of data.

SIGNIFICANT CHANGES UNDER REGULATION

Definitions

The Clinical Trials Regulation has retained some definitions and refined others. For example the definition of “clinical study”: “Any investigation in relation to humans intended: (a) to discover or verify the clinical, pharmacological or other pharmacodynamic effects of one or more medicinal products; (b) to identify any adverse reactions to one or more medicinal products; or (c) to study the absorption, distribution, metabolism and excretion of one or more medicinal products” is similar to the definition in the CTD, but a “clinical trial” is defined more narrowly as a subset of a clinical study. The CTR defines a non-interventional clinical trial as “a clinical study other than clinical trial.”

The CTR introduces new elements like Low-intervention Trial and Auxiliary Medicinal Product. A Low- intervention Trial is defined as a new category of a trial which must fulfil the main conditions mentioned in the Regulation, but requires less stringent rules, for example, regarding insurance, monitoring and Investigational Medicinal Product (IMP) traceability. The precise interpretation of this definition is left to each Member State where an application for authorisation of a clinical trial or of a substantial modification will be submitted (Member State Concerned; MSC). Auxiliary Medicinal Product (AxMP) is defined as a medicinal product used in a clinical trial, for example, for background treatment or rescue medication, but not as an investigational medicinal product.

The CTR uses the term “substantial modification” instead of “substantial amendment” used by CAs and ECs in accordance with the CTD. The two definitions are comparable and cover any changes to any aspect of the clinical trial which is made after notification of a decision, and which is likely to have a substantial impact on the safety or rights of the subjects or on the reliability and robustness of the data generated in the clinical trial.

Initial Authorisation Procedure under CTR

Submission

One of the main aims of the CTR for the authorisation procedure is for the sponsor/applicant to submit one application dossier, including a single set of documents in harmonised format via the CTIS regardless of how many Member States are participating in the trial. Each Member State issues one decision per study.
The CTIS has sponsor workspace (for sponsors, Marketing Authorisation Applicants (MAAs)) and authorities’ workspace (for Member States, European Commission and European Medicines Agency (EMA)). At the sponsor workspace, a sponsor or CRO must create the CTIS User Administrator role in the system, which covers:

- Assigning new role or clinical trial access;
- Amending role or clinical trial access;
- Revoking role or clinical trials access;
- Approving or rejecting user request for role.

To get access to the CTIS, all users need to register by themselves in the EMA Identity and Access Management System (IAM). Users receive their login credentials, a default role that allows them to access the CTIS and perform a limited number of activities like to request a role or update personal profile. In order to perform clinical trial activities for the particular study, the CTIS User Administrator needs to assign in the system, the CT Admin who can be assigned to specific trial or all clinical trials for the organization. CTIS User Administrator or CT Admin can assign user to study specific role in the CTIS.
In addition, sponsors need to create the Sponsor Admin role on their CTIS account. This role has full control over monitoring the workflow of the clinical trial and can also assign new roles for specific clinical studies for its organization.

The assigned user with the role, for example, "submitter" can submit the harmonised format of the application dossier for the clinical trial simultaneously to all Member States where a clinical trial is going to be conducted. The application dossier should consist of:

- Part I Scientific Review – to be assessed jointly by all MSCs; and
- Part II Ethical Review – to be assessed by each MSC's Ethics Committee separately

The required content of the application dossier is presented in **Table 1.**

Part I (Global, Scientific Review) Refers to Annex I of CTR (Sections B to J, Q)	Part II (National, Ethical Review) Refers to Annex I of CTR (Sections K to R) Information per Mem ber State Concerned
Cover Letter	Recruitment arrangements specific for the MSC
EU Application Form	Subject Information, Informed Consent Form, and Informed Concerned Procedure - in national language
Protocol	Suitability of the Investigator-specific for the MSC
Investigator's Brochure/ Summary of Product Characteristic (SmPC)	Suitability of the facilities-specific for the MSC
Documentation relating to compliance with GMP for the investigational medicinal product (MIA, QP, CoA)	Proof of Insurance cover or indemnification-global or local
Investigational Medicinal Product Dossier (IMPD)	Financial and other arrangements
Auxiliary medicinal product dossier, if applicable	Proof that data will be processed in compliance with Union Law on Data protection
Scientific advice and Paediatric Investigational Plan (PIP), if applicable	
Labels	
EU Legal Representative if sponsor is out from the EU/EEA	
Proof of payment of fee (information per MSC)	

Table 1. List of required documents for the initial application under CTR Annex I, Application Dossier for the Initial Application: https://ec.europa.eu/health//sites/health/files/files/eudralex/vol-1/reg_2014_536/reg_2014_536_en.pdf

The language used for the application dossier should be common in the medical field (i.e., English), but documents addressed to the subjects should be in their national and understood language(s). The CT Admin/User "Submitter" can submit Part I and Part II together, but there is also the possibility for them to submit only Part I for review and approval; Part II may be submitted up to two years after Part I assessment has been completed.

Part II dossier may include recently published by the European Commission, harmonised templates, and documents such as Investigator Curriculum Vitae (CV), declaration of interest, site and facilities suitability, recruitment and informed consent procedure, and payment of compensation.

Using harmonised templates by NCAs or sponsors across all of the EU are not mandatory, but strongly recommended by the European Commission. NCAs inform the applicants whether the harmonized templates are accepted by them, and whether the templates must be translated or if they should use the specific templates published on the NCAs' websites. In the application dossier, the sponsor shall propose one of the MSCs as the Reporting Member State (RMS), which will coordinate the validation and evaluation of the assessment process of the application. There should be one RMS for each study/protocol. If no MSC is willing to be the RMS or more than one MSC is willing to be the RMS, then the RMS should be selected by agreement among the MSCs. In case of only one MSC participating in the clinical trials that MSC will automatically be the RMS. The RMS shall notify the sponsor and, if applicable, other MSCs, that is the RMS within six working days from the submission of the application dossier through the CTIS.

Validation and Assessment

The overall process, when Part I (Scientific Review) and Part II (Ethical Review) are submitted together, consists of two steps: validation and assessment.

The dossier is validated by the RMS within ten days from submission taking into account comments expressed by the other MSCs. If there is no feedback from MSCs the application dossier shall be considered complete. If there is a request for information or any inquiries, the RMS sends a request for information (RFI) to the sponsor and one clock stop is allowed. The sponsor has maximum ten days to respond. The sponsor's failure to reply will lead to the automatic withdrawal of the application in all MSCs. The RMS has five days following receipt of the response to confirm validation to the applicant. If the RMS has not notified the sponsor within five days, the application dossier shall be considered complete.

Once the validation process is completed, Parts I and II are assessed in parallel within 45 calendar days and up to 76 calendar days if there are any questions requiring an extension.
Assessment of Part I and Part II submissions is carried out as follows:

- Part I Assessment: Scientific Part

In case of a multinational trial all MSCs must collaborate in the evaluation and the 45 days reporting period is then divided as follows:

- Initial assessment: within 26 days the RMS submits an initial Part I draft assessment report to MSCs (in case of trials involving an advanced therapy or a biotechnology medicinal product, the RMS extends the period by 50 days);
- Coordinated review: within 12 days MSCs review and provide comments to the RMS;
- Consolidation: within seven days the RMS consolidates the input from MSCs.

The RMS, considering issues raised by MSCs, may extend the reporting period up to 31 calendar days. Only the RMS can request for information (RFI) from the sponsor. The sponsor has maximum 12 calendar days to respond. Lack of response is considered as withdrawal of the application in all MSCs.

The sponsor's responses are sent to all MSCs for joint coordinated review and the MSCs provide feedback to the RMS within 12 calendar days. The RMS consolidates the input from MSCs within seven days and prepares the final assessment report.

- Part II Assessment: Ethical Part

Part II covers aspects typically examined by Ethics Committees and is conducted separately by each MSC

individually for its own territory. Each MSC shall complete its assessment of Part II within 45 calendar days from the validation date.

To obtain and review additional information from the sponsor the Ethics Committee (EC) or the National Competent Authority on behalf of the EC, may issue RFI and at the same time extend the initial assessment up to 31 calendar days. All MSCs and ECs have the same deadlines but, independently and separately, can request for additional information. The sponsor gets maximum 12 calendar days to reply. In case of lack of responses, the clinical trials submission will be withdrawn in all MSCs. Within the 31 days' extension and after receiving sponsor's responses, each MSC has 19 days for final assessment of ethical review.

Decision

The Regulation says that within five days of the final Part I assessment report or Part II assessment by each MSC, whichever is later, a single decision must be communicated to the sponsor. The Ethics Committee review may encompass aspects addressed in Part I (Scientific) and Part II (Ethical) of the assessment report. The final decision is made after Part I and Part II assessments are completed. The clinical trial may be found acceptable or acceptable subject to conditions, or it may be refused for all MSCs. The overall process of initial authorisation under the CTR is illustrated in Figure1.

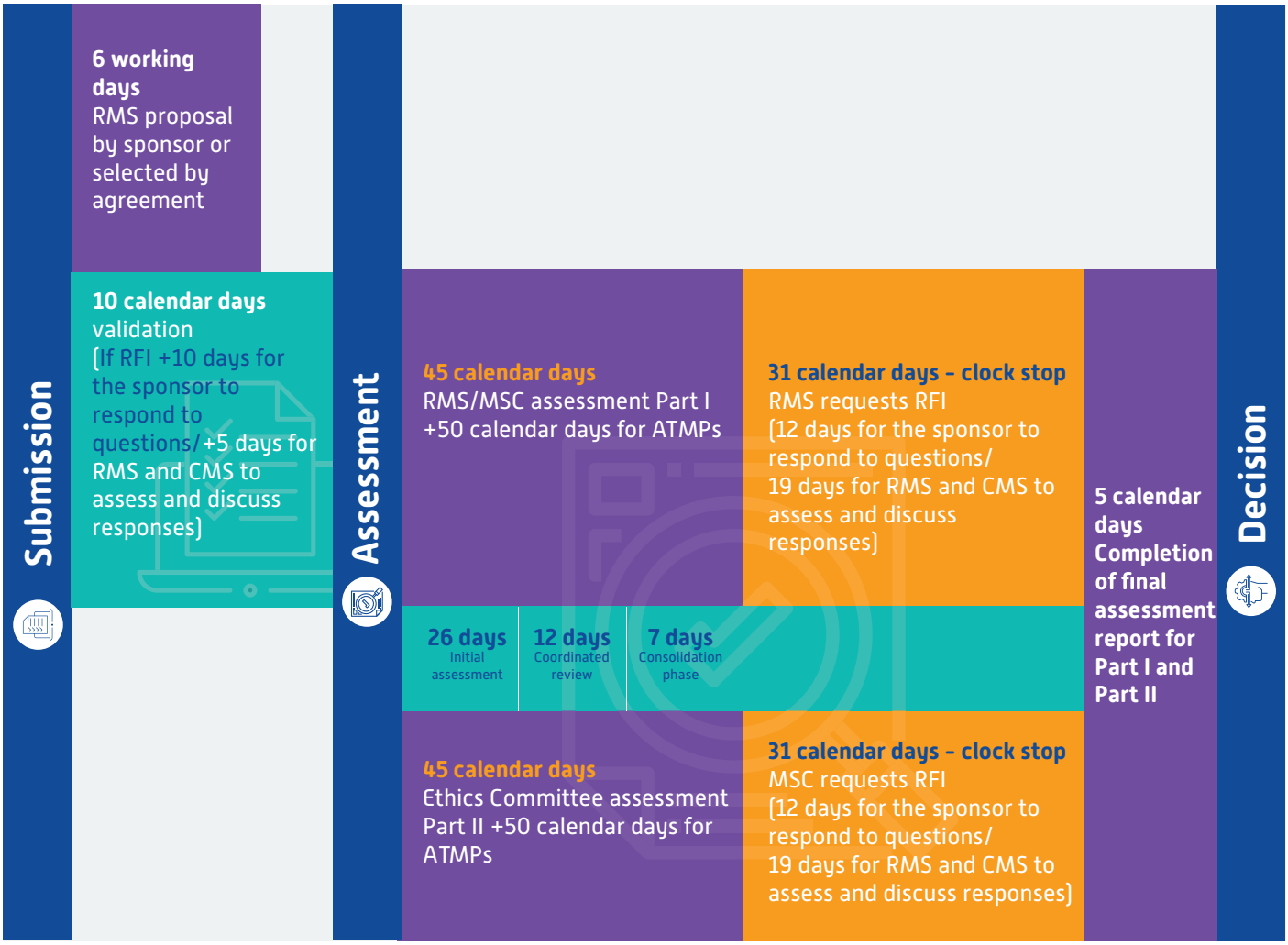

Figure 1. An overall process of Initial Authorisation Procedure under CTR Chapter II, Authorisation Procedure for a Clinical Trial: https://ec.europa.eu/health//sites/health/files/files/eudralex/vol-1/reg_2014_536/reg_2014_536_en.pdf

If a MSC does not give its decision within the regulated timeframe, then the conclusion of the RMS Part I assessment report will automatically be considered as MSC decision. Where the conclusion of the RMS regarding Part I of the assessment report and clinical trial is not acceptable, that conclusion shall be deemed to be the conclusion of all MSCs.

A MSC can refuse to authorise a clinical trial if it disagrees with the conclusion of the RMS regarding Part I or an Ethics Committee can issue a negative opinion in a MSC. The MSC shall provide for an appeal procedure in respect of such refusal.

Individual Member States may decline to participate in a trial even when others have already accepted it. The application can be withdrawn at any time by the sponsor, up to the reporting date, but only if withdrawn in all MSCs.

Resubmission of the clinical trial is possible in the MSC in which the study has been refused, but it will be considered as a separate new Clinical Trial Application with a new EU CT number.

Substantial Modification Procedure

According to the CTR, only substantial modification needs approval prior to implementation. A substantial modification may affect a change to Part I, Part II or to both parts of the submitted application dossier. The RMS for the authorisation of a substantial modification shall be the same RMS as for the initial authorisation procedure. If the substantial modification concerns only Part I (e.g., Protocol, Investigator's Brochure, or IMP Dossier), the RMS in cooperation with MSCs shall validate the application within six calendar days. If there are any questions, the sponsor will get a maximum ten days to provide a response and the RMS five days to confirm the validation. The assessment report shall be completed within 38 calendar days or 69 calendar days in case of request for additional information to the sponsor. Within five days, each MSC shall communicate to the sponsor their decision on substantial modification.

In cases where the substantial modification concerns only Part II (e.g., recruitment arrangement, additional site in a MSC) only the MSC, is involved in the assessment. The same timeframes apply for Part II as for PartI, including 19 days for ethical review.

When the changes affect both Parts I and II (e.g., change of main objective of the clinical trial or addition of a trial arm, or placebo group), both will be run in parallel with the same timeframe. As is the case with initial authorisation, the RMS will take the responsibility for coordinating the validation and evaluation of the assessment process of the application.

Addition of a Member State

After a clinical trial has received the initial authorisation decision, the sponsor may apply to the same RMS for adding another Member State. The procedures are the same as for initial submission. The CT Admin/user "Submitter" must submit Part I and Part II through the CTIS for MSC evaluation, comments, or disagreement to the clinical trial. The submission shall be done through the CTIS and the MSC shall notify its decision to sponsor within 52 calendar days or 83 calendar days depending on whether comments have been raised and require an answer from the sponsor.

Streamlined Reporting

Under the CTR, the sponsor submits all Suspected Unexpected Serious Adverse Reactions (SUSARs) through the dedicated new module of the EudraVigilance. The EudraVigilance clinical trial module for the electronic reporting of SUSARs is upgraded in the CTIS. Upgraded module is a part of CTIS in accordance with Article 40 to 44 of the CTR and is maintained by the EMA. The EMA will forward the safety information electronically to all MSCs. The Annual Safety Report (ASR) (Development Safety Update Report (DSUR)) should be submitted through the CTIS. SUSARs reporting should be shared with the Ethics Committees, but some countries agreed that SUSARs will be not reported and reviewed by ECs. This task will be managed only by NCAs. The European Commission published Implementing Regulation (EU) 2022/20 setting up the rules and procedures on the cooperation of the Member States in safety assessment of clinical trials. The Regulation (EU) 2022/20 applied on 31 January 2022, on the same day as Date of Application (DoA) of the CTR and CTIS go-live version.

Implementing the regulation harmonizes rules concerning MS cooperation in assessing information reported to the relevant Ethics Committee. The EMA is also a controller of the CTIS and is responsible for avoiding unnecessary duplication between the EU database and the EudraCT and EudraVigilance databases.

The safety reporting via upgraded EudraVigilance module in the CTIS is effective on 31 January 2022. It streamlines safety reporting and end-to-end electronic solution for safety reporting of clinical trials. The CTR has kept the same timeframes for reporting SUSARs and ASRs as specified under the CTD: fatal and life- threatening SUSARs - as soon as possible and in any event not later than seven days after the sponsor became aware of the reaction; other SUSARs - within 15 days; and ASR - yearly.

The CTD had no provisions to notify the CA/EC of the start of a clinical trial(first patient first visit; FPFV). The only requirement was to inform the CA/EC about: the end of the trial (within 90 days);
a temporary halt and early termination (within 15 days). The CTR requires harmonised reporting of all clinical trial lifecycle events by obligating the sponsor or his delegated user (e.g., Contract Research Organisation (CRO)) to notify each MSC within 15 days of all events listed in Table 2. The notification of events must be managed through the CTIS.

Notification to be submitted	Timeframe permitted
Start of the trial in each MS	Within 15 days
Inclusion of first patient in each MS	Within 15 days
End of recruitment in each MS	Within 15 days
End of trial in EEA to all MSC	Within 15 days
Early termination to each MSC	Within 15 days
Global end of trial (including third world countries) to all MSCs	Within 15 days
Temporary halt and reason to each MSC (max. 2 years)	Within 15 days
Restart clinical trial after temporary halt to each MSC (SM when halt was due to safety)	Within 15 days
Restart recruitment	= Restart clinical trial
Unexpected events	Within 15 days
Serious breach report	Within 7 days
Urgent safety measures	Within 7 days
Third country Inspectorate inspection	No timelines

Table 2. Clinical trial lifecycle: notification of events within 15 days (CHAPTER VI, START, END, TEMPORARY HALT, and EARLY TERMINATION OF A CLINICAL TRIAL): https://ec.europa.eu/health//sites/health/files/files/eudralex/vol-1/reg_2014_536/reg_2014_536_en.pdf

Public Disclosure of Data

Prior to 1 May 2004 when EudraCT database was established, clinical trial information was confidential and available only to Member States' Competent Authorities, the EMA, and the European Commission. After 21 July 2014, it became mandatory for sponsors to post clinical trials results in the EudraCT database. According to the CTR, the EU database should contain all relevant clinical trial information submitted through the CTIS. The information must be available publicly and includes: inclusion and exclusion criteria; main objectives and endpoints; the start and end dates of patient recruitment; and the trial end date. However, subject personal data cannot be entered into the CTIS. To protect an individual's right to privacy and rights to personal data protection, some information regarding clinical trials need to be anonymised. To maintain confidentiality, certain documents must be submitted in two versions: one for publication (redacted) and one for non-publication (not redacted).

In October 2023, the EMA (European Medicines Agency) adapted revised transparency rules for CTIS, including its public portal. The implementation of the new CTIS public website is planned for the second quarter of 2024. The effective date of completion and application of the new rules will be communicated to CTIS users before they become applicable.

Prior to the technical implementation of the revised rules on the CTIS public website, certain information will not be published. For Part I, the IMPD (Investigational Medicinal Product Dossier) IMPD Quality and correspondence with authorities regarding this document will remain confidential. Similarly, for Part II, financial and other arrangements with principal investigators and/or sites will not be disclosed. Therefore, the submission of redacted versions of these documents is not required.

Prior the launch of the new CTIS public website, Sponsors have the option to apply for deferral in the pub-

lication of clinical trials information in the CTIS. Deferral requests must be submitted only with the initial Clinical Trial Application. For instance, for Phase II and III studies, sponsors may request to defer the publication of the study protocol for up to 5 years after the end of the trials in the EU/EEA.

Upon the launch of the new go-live CTIS public website, the deferral mechanism will be removed. This decision aims to provide patients with access to key data and documents as early as possible, enhancing awareness of potential treatment options. However, certain documents, such as protocols, patient-facing documents, SmPC (Summary of Product Characteristics), subject information and informed consent forms, and recruitment arrangement documents will never be published. Additionally, all other documents including IMPD Q, IB and Member State documents, will also remain confidential.

The outcome of a clinical trial will also be published in the CTIS. The sponsor shall submit a summary of the results of the clinical trial to the CTIS within one year from the end of a clinical trial in all MSCs (as set out in Annex IV of the CTR). It shall be also accompanied by a summary written in a manner that is understandable to laypersons and translated into the Member State's national language (as set out in Annex V).

In addition, when clinical trials are intended to be used for obtaining a marketing authorisation for the medicinal product, the marketing authorisation applicant shall submit to the CTIS, the Clinical Study Report (CSR) within 30 days after "*the day the marketing authorisation has been granted, the procedure for granting the marketing authorisation has been completed, or the applicant for marketing authorisation has withdrawn the application.*"

3-YEAR TRANSMISSION PERIOD

By 30 January 2025, all clinical trials authorised under the CTD and only with active clinical trials without ongoing document assessments in any EU/EEA countries are eligible for transition. In the context of transition, an "active site" is defined as one where the last subject visit or trial-specific intervention is scheduled to occur on or after 30 January 2025.

The primary aim of transitioning clinical trials from the CTD to CTR is to streamline the administrative process and minimize assessments by Member States to meet the minimum requirements.
There are essential principles for transitional trials:

- No reassessment of previously assessed documents.
- No requirement for template updates.
- No retrospective creation of a site suitability form.

Before transitioning a study, sponsors should consider three possible scenarios:

Scenario 1: If key documents (e.g., Protocol, IB, or IMPD) have already been approved in all relevant Mem-

ber States under the CTD, the sponsor can transition to the CTR by submitting a Clinical Trial Application (CTA) to CTIS without needing a substantial amendment under the CTD. The sponsor should declare the approval of these documents in all relevant Member States under the CTD in a cover letter via CTIS.

Scenario 2: If there are minor substantial or non-substantial differences in these documents across Member States (e.g., related to subject population age groups or administrative details), a consolidated version may be transitioned as a single new version, without prior submission under the CTD. The sponsor should declare that no substantial content differences exist beyond these minor discrepancies.

Scenario 3: In cases where there are significant substantial differences among Member States regarding the Protocol, IB, or IMPD, a substantial amendment (under the CTD) should be submitted to NCAs and Ethics Committees in the Member States where the trial is ongoing. This is necessary to harmonize these aspects of the documents across Member States before transitioning the trial to the CTR.

Moreover, the estimated timeline for the transition process to the CTR, including validation, assessment, and decision phases, may range from 22 to 60 calendar days. The validation process takes 10 calendar days, including six working days for RMS selection in the case of multinational studies. Additional Part II documents may be requested for some studies, with a 10-day period provided for the sponsor to respond.

The assessment phase may take seven calendar days if there are no requests for further information from MSCs. A decision from each Member State in the EU should be issued within five days.

After receiving the decision, the sponsor should submit the first substantial modification via CTIS for Part I and/or Part II to align with CTR requirements. Part I should be completed for the relevant dossier elements, and non-redacted versions should be replaced with versions for publication at the time of the first substantial modification application. For Part II, the sponsor should complete the relevant dossier elements, excluding the retrospective creation of a site suitability statement. There is no requirement to upload new template documents for trial procedures that have already been completed.

CONCLUSION

Without a doubt, the Clinical Trials Regulation changes the rules for authorisation of all phases (I-IV) of clinical trials on medicinal products for human use. It harmonises and centralises the processes from the start to the end of clinical trials. In addition, the information relating to clinical trials becomes publicly available.

An independent CTIS audit, improving usability, quality, and stability of the CTIS successfully finished, and on 31 July 2021, a major CTIS milestone had been reached. This allowed the European Commission to publish the full functionality of the CTIS, and the same announced on 31 January 2022 as the date of CTR application in the EU/EEA countries. To prepare everyone from the clinical trials environment, the EMA has published the CTIS Sponsor Handbook, providing key guidance, technical information and references for sponsors and collaborating organisations. Moreover, the EMA was hosting several webinars on how end users can prepare for CTIS.

The European Commission published harmonised templates and documents to support sponsors of clinical trials when submitting Part II elements of the application under the CTR.

A number of clinical trials guidance documents in Volume 10 of the EudraLex 10-volume collection of rules governing medicinal products in the EU are being revised and updated by the European Commission to bring them in line with the changes required by the CTR. The European Commission updates progressively Questions and Answers Document - Regulation (EU) 536/2014 and discusses some inconclusive questions with the Expert Group on Clinical Trials.

As of 31 January 2022, the Clinical Trials Regulation became applicable automatically for all EU Member States. Preparing for the changes was a challenge not only for sponsors or CROs but also for Member States. They had to set up communications between the National CA and the Ethics Committee, and to execute ethical review of the trial for the entire territory. The CTR does not give instructions on how to manage cooperation with the Ethics Committees. It says only that each MS is responsible for ensuring the Ethics Committee meets CTR timelines and procedures for the ethical assessment Part II.

Furthermore, the sponsors and CROs must take into consideration some aspects of transitional trials from the CTD to CTR. They should start preparations for submitting the applications early enough before 30 January 2025.

In addition to revising the transparency rules, the EMA will require sponsors to provide fewer documents that necessitate redaction of confidential commercial information (CCI) and personal data. This change is expected to expedite the preparation of the Clinical Trial Application (CTA) dossier. Removing the deferral mechanism will grant patients earlier access to information, facilitating the prompt initiation of trials and enrollment.

To ensure easier access to pertinent clinical trial information, the revised CTIS transparency rules will introduce a more user-friendly CTIS public website. Changes are intended to simplify access to information for clinical trial stakeholders, increase awareness of possible treatment options, rationalise the amount of clinical trial data that needs to be published and eliminate deferrals, resulting in earlier access to important documents.

Many sponsors have relied on the deferral mechanism to delay publication of clinical trial documents with minimal redactions of CCI. As a result, ClinChoice recommends that sponsors may need to revise their internal procedures for managing CCI and fulfilling their transparency obligations under the CTR. Sponsors also should ensure that all personnel involved in the submission of clinical trial applications are appropriately trained on the requirements of the new CTIS transparency rules ahead of entry into application of these rules in 2024.

The revised CTIS transparency rules are expected to apply in the second quarter of 2024, once their technical implementation in the CTIS has been finalised.

The EU CTR ushered the EU and EEA countries into a new era, in the way clinical trials are conducted for sponsors, Member States, CROs and especially for patients whose rights, safety, dignity and well-being will be better protected. Sponsors and their delegated users should become familiar with CTR requirements explained in this white paper for initial authorization, substantial modification, reporting safety information, notification of clinical trial events and plan properly for the transition of ongoing clinical trials from CTD to CTR.

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David joined the company in 2018 as Regulatory Services Director. He has more than 33 years of leadership experience in the pharmaceutical and medical device industry within the regulatory affairs and compliance space.

He has held positions of increasing responsibility with sponsors and service providers of various sizes, including large, global OEM's/sponsors, consultancies and a global CRO, as well as virtual, small, mid, and large-sized enterprises.

He has worked with clients in ASEAN/APAC, EMEA and The Americas, and certainly with FDA and the global Health Authorities with product portfolios covering multiple therapeutic areas and medical specialties.

He is providing the global regulatory capabilities and regulatory intelligence support for clients and collaborating with our internal stakeholders. In addition, to being a professional member with industry associations, advisory boards, prolific speaker at industry events, he navigates the regulatory landscape throughout the product life cycle and regulatory crisis management. In addition, David is responsible for the development and launch of new services in the regulatory and strategic consulting space.

This white paper was collaboratively crafted with the assistance and input on behalf of fellow colleagues from the Regulatory Services team.

About ClinChoice

ClinChoice is a leading full-service clinical CRO offering high-quality solutions to pharmaceutical, biotechnology, medical device and consumer products clients. We contribute to a safer and better world by helping our sponsor clients accelerate drug and device approvals to market. We do this by combining our 25 years of proven quality and results with expertise in 30+ therapeutic areas, a flexible approach, and dedicated teams who enable rapid startups and fast timelines.

Our commitment to the highest quality standards, flexibility, and timeline fulfillment has earned us and our clients consistent results. We provide services for the full development lifecycle to a wide range of clients, large and small, including six of the top 10 pharmaceutical companies, as well as small to midsize biotechnology companies. For us, our record of quality means consistency, accuracy and reliability. For you, it means a reliable partner and quality results.

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