2024

Whitepaper

Patent Filing Considerations in View of Revised EU Clinical Trials Regulation Transparency Rules

Authored by

Karen Ng, Associate, European and UK Patent Attorney, J A Kemp

James Biddlecombe, Business Transformation and CTR Lead, DLRC

Summary

Introduction

The transparency requirements of the EU Clinical Trials Regulation present a complex intellectual property challenge requiring a nuanced approach to patent protection of clinical trial-related inventions. This white paper aims to provide some patent filing considerations and highlights the importance of engagement and co-ordination of the legal and regulatory teams early on, and throughout the life cycle of clinical trials, to optimise patent filing opportunities.

Protecting information related to innovations in clinical trials

Information related to innovations in clinical trials may form the basis of a patentable invention. A patentable invention may relate to the drug under investigation in the clinical trial, such as the structure, formulation or dosage of the drug, or method of making the drug. Alternatively, a patentable invention may relate to the clinical trial design, such as the administration schedule, administration route or the particular group of patients being treated.

In the context of documents that have to be submitted to the relevant authorities in the course of a clinical trial, information related to innovations may be present in documents submitted as part of the clinical trial application. Examples of such documents include the investigator's brochure, the protocol and its synopsis, informed consent form and patient documents. Once the clinical trial is approved and underway, information related to innovations may be in the data found in the study progress reports, such as the interim report or the final report.

Under the transparency requirements of the EU Clinical Trials Regulation (CTR), all clinical trials have to be registered and authorised in the Clinical Trials Information System (CTIS) before they commence, and information related to the clinical trials has to be published throughout the course of the clinical trials at the earliest opportunity. The rules on information that has to be published on CTIS have been revised recently. Vital information on clinical trials will continue to be made available to the public early in the trial life cycle. However, the amount and timing of information that is to be published as well as the mechanism of protecting certain information, including information related to innovations, are now different (see Appendix).

The EMA implementing guidelines provide that Commercial Confidential Information (CCI) is to be understood as any information:

- that is not publicly available; and
- whose disclosure may undermine the legitimate economic interest or competitive position of the concerned entities, e.g. clinical trial sponsors or marketing authorisation applicants/holders or service providers.

The CTR exempts certain information from disclosure requirements, including information related to innovations which falls under the category of Commercial Confidential Information (CCI). CCI may include, according to EMA's Guidance:

- Composition of excipients in the drug formulation;
- Information on the synthesis of the active substance, or manufacturing and control processes of the drug;
- Future development plans for treatment of other indications;
- New biomarkers, novel methodologies, or innovative analytical methods;
- Daily dose and maximum dose of drug in clinical trial.

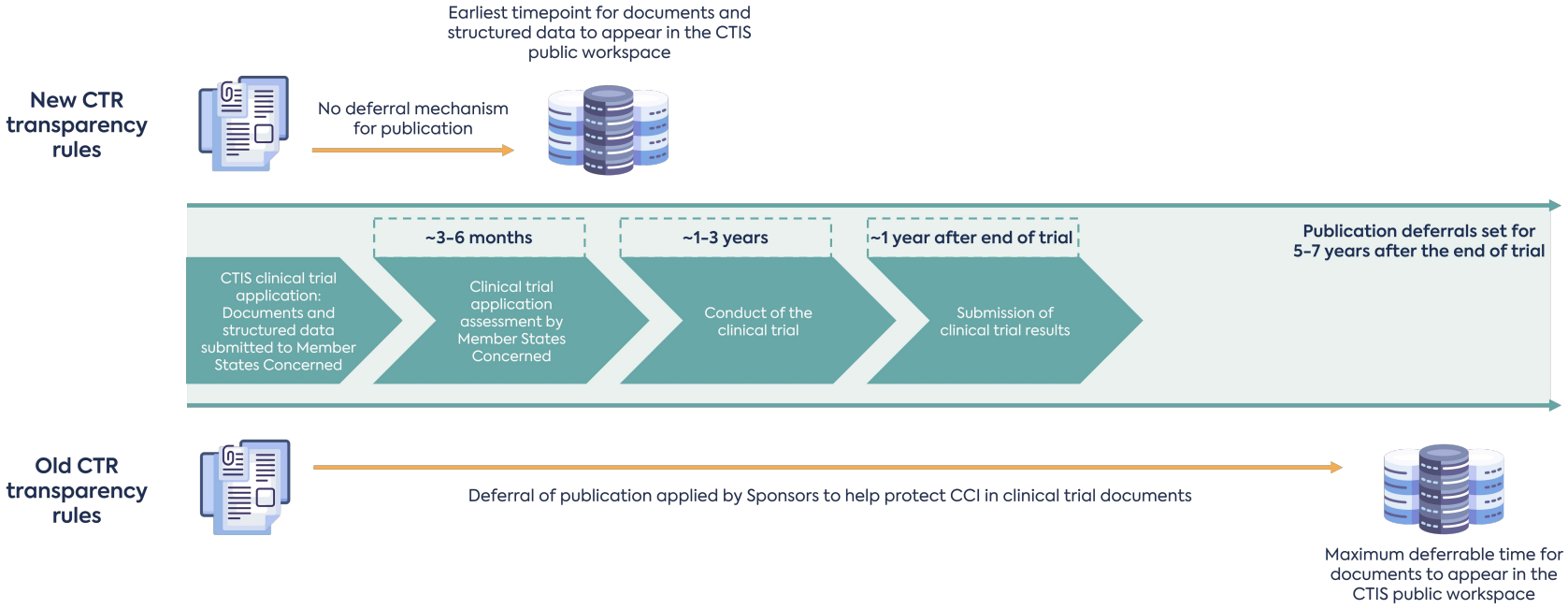
CCI can be redacted from documents submitted and subsequently published in CTIS provided that this information is not already in the public domain. For some structured data fields that are mandatory for registering a clinical trial in CTIS, the applicant may enter 'dummy data' in the related fields if that information is considered to be CCI. For example, in the structured data fields for daily dose / maximum daily dose in CTIS, the user may enter '00'; grounds for which must be clearly stated in the cover letter. However, it is likely to be difficult to omit CCI that is part of the trial title for example. It is the responsibility of the clinical trial sponsor to protect their commercial data and to ensure that clinical trial documents and structured data within CTIS application form are redacted appropriately per the applicable CTR transparency requirements.

Prior to the revised transparency rules, a deferral mechanism was available to protect CCI. The deferral mechanism allowed delayed publication of certain documents, e.g. trial protocol and investigator's brochure (IB), for up to 7 years after the end of the clinical trial. This deferral mechanism is no longer an option under the revised transparency rules (Figure 1).

Hence, similar to the situation under the old transparency rules, unless sponsors decided to protect CCI, that information will be published as part of the documents and structured data in CTIS according to the revised timeline. For example, information such as clinical trial title, drug details, dose, treatment duration and patient eligibility criteria will be published as soon as a decision on a clinical trial application is made, with the exception of Category 1 trials in Adults only (no PIP).

The key difference under the revised transparency rules is that sponsors can no longer rely on delayed publication of entire documents to protect CCI. Instead, redaction is now the main mechanism for protecting CCI. Hence, there is now a shift in the planning and management of CCI. Sponsors will have to decide what pieces of information they consider to be redactable CCI early on in the trial life cycle. Effective implementation and management would be essential in ensuring that the relevant information can be consistently redacted in every document that is submitted for publication in CTIS, and omitted from the structured data in CTIS, where possible, throughout the trial life cycle, until the redaction/omission is deemed no longer necessary.

Figure 1: Timeline showing evolution of publication rules under CTR



Patent filing strategy

To assess the patentability of an invention claimed in a patent application, the claimed invention is compared to information that is publicly available before the patent application is filed, and that information is referred to as prior art. A patent will be granted only if the claimed invention is new and inventive over the prior art (for example the claimed invention would not have been obvious, or has an advantage that would not have been expected, from the prior art), and is sufficiently disclosed in the patent application.

A patent will be granted if the claimed invention is:

- new,
- inventive - for example, the claimed invention would not have been obvious, or has an advantage that would not have been expected, from the prior art, and
- sufficiently disclosed in the patent application - for a medical use invention this requires information or evidence supporting the effectiveness of the treatment.

Sponsors have control over what information about their clinical trial is in the prior art to the extent that they can protect CCI from disclosure under the CTR transparency requirements as explained above, and choose when to file their patent application. However, a further consideration is whether data from the clinical trial needs to be included in the patent application to support the patentability requirements.

Data present in a patent application can be relied upon to establish an inventive step and may be necessary to meet the sufficiency of disclosure requirements. Whilst data available after the filing date of the patent application (post-published evidence) may also be relied upon, there are situations where data is required in the application itself, for example where inventiveness is based on a surprising result observed in patients.

Filing a patent application when results are available allows the clinical trial data to be included in the patent application (which may help to establish an inventive step), but means there is likely to be more relevant prior art. The prior art may include the clinical trial information published according to the CTR transparency requirements, as well as press releases, publications from parallel clinical trials in other countries, as well as any disclosures by competitors. Moreover, the confidential manner (or lack thereof) under which a clinical trial is conducted may impact on how much clinical trial information will become prior art.

Some prior art may be more relevant than others, depending on what distinguishes the invention from the prior art. For example, if the claimed invention relates to a new drug, a prior art disclosure relating to the structure of the drug would be relevant for novelty, whilst if the claimed invention relates to a new way of using a known drug, prior art disclosure of details and results of an earlier phase clinical trial would be relevant.

Therefore, when considering when to file a patent application, the amount of prior art and the availability of data are important factors to consider. In any given situation, the most appropriate filing strategy will depend on the nature of the clinical trial, what information is already in the prior art, and what aspect of the treatment may be inventive.

Factors for consideration when considering patent filing strategy:

- the nature of the clinical trial,
- what aspect of the treatment may be inventive,
- what information is already in the prior art, and
- what information relating to the invention to be claimed in a patent application will be published under CTR transparency requirements, when will that information be published, and whether that information can be redacted or omitted in CTIS disclosure.

Early patent filing strategy: before clinical trial information disclosure

An invention may be more suited to an early patent filing where clinical trial results are not expected to be important for establishing an inventive step.

For some inventions, inventive step may be established by relying on pre-clinical data. Examples of this may be a new dosing schedule of a known drug based on newly discovered properties of the drug, e.g. new pharmacokinetic and pharmacodynamic profiles. An early filing strategy may be appropriate for such inventions.

Sponsors in this situation could minimise their own prior art by filing a patent application prior to any disclosure of clinical trial information relating to the claimed invention (Figure 2). To minimise the disadvantages associated with having no clinical data in the patent application, the patent application should include pre-clinical data, if available, and an explanation of the mechanistic link between the claimed invention and the treatment.

Late patent filing strategy: filing with clinical trial data

An invention would likely to be more suited for a late patent filing strategy if it relies on data to establish inventive step. The advantages of filing late to include more data in the patent application may outweigh the disadvantages of having more prior art. Examples of inventions that fall into this category include a new combination therapy involving known drugs that work in synergy, or a treatment using a known drug in a new disease indication or patient subpopulation.

Sponsors wishing to protect an invention in this category may wish to wait until clinical trial results are available for inclusion in a patent application before filing the patent application (Figure 2). In the meantime, disclosure of the information related to the clinical trial should be minimised, as such disclosure may be detrimental to a patent application filed after the disclosure.

In particular, sponsors can make use of the mechanisms for protecting CCI from disclosure under the CTR transparency rules explained above. We advise that decisions as to what information constitutes CCI should be made early in the trial life cycle, and this can be coupled with clear dissemination of instructions to all teams involved in managing and running the clinical trial. It would also be important to ensure confidentiality of the trial when it is being conducted to minimise information falling into the public domain. Furthermore, press releases and disclosures at public meetings should be controlled. Clinical trials can take many years to complete. Therefore, such safeguarding mechanisms would have to be put in place early in the trial life cycle, and assessed throughout the trial cycle to determine if any adjustments are needed.

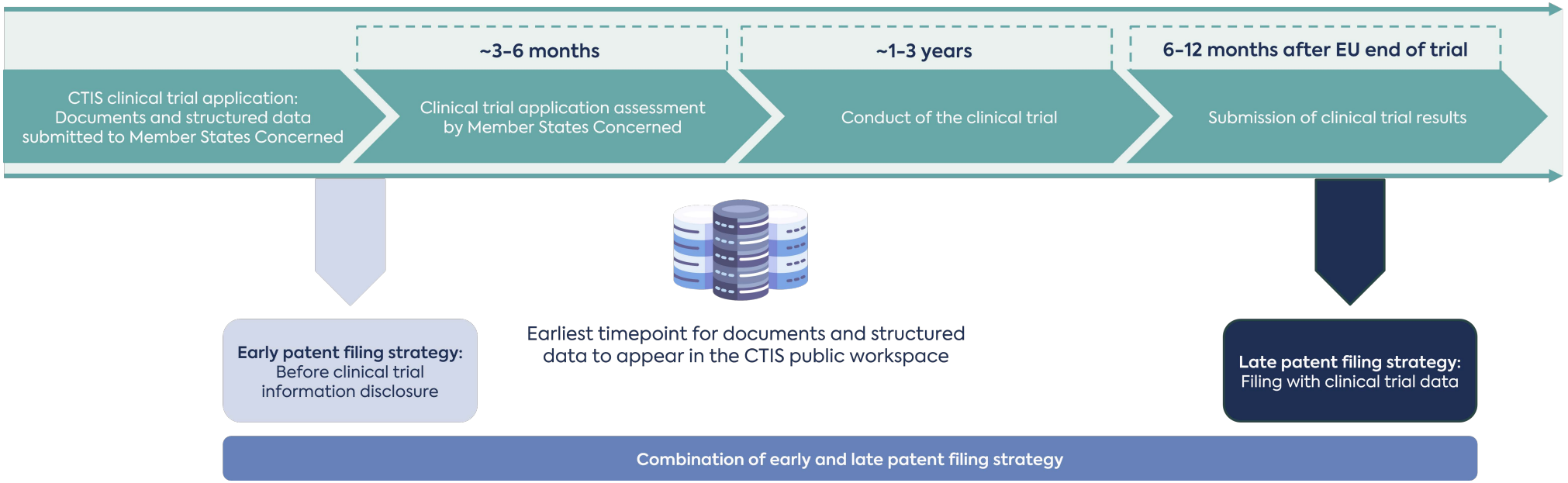
There may sometimes be unintentional disclosures or instances where public disclosure of the clinical trial information cannot be avoided. In these cases, sponsors would have to rely on arguments during prosecution of the patent application to overcome any objections based on such disclosures. Appropriate arguments would depend on the nature of the invention and the nature of the disclosures. For example, it may be possible to argue that a disclosure is not novelty-destroying for the claimed invention because the disclosure does not allow any conclusion to be drawn regarding the success of the claimed invention, such as the

success of a proposed treatment. It may also be possible to argue that a disclosure is not prejudicial to inventive step of the claimed invention because the disclosure would not provide any expectation of achieving the advantages demonstrated in the patent application. However, such arguments are likely to be difficult to formulate if the disclosure is a press release published just before the filing of the patent application describing positive data from the clinical trial, or is a clinical trial results summary document that is made publicly available as soon as it is uploaded to CTIS [this is applicable to all categories of clinical trials except for category 1 trials in adults only (no PIP), see Appendix].

Figure 2 – Patent filing strategies visualised in relation to a typical clinical trial application and conduct timeline

Combination of early and late patent filing strategy

There is no "one-size fits all" patent filing strategy. There may be instances where it is unclear whether an early or a late filing strategy would be preferable. Some sponsors may wish to adopt both early and late filing strategies (Figure 2), and see which works. However, depending on the timing of the filings, an earlier filed patent application will be published 18 months after filing and so may be prior art against the later filing. This may be particularly problematic if the earlier filing discloses information that is redacted from documents published in CTIS. Sponsors are therefore advised to seek advice from their legal team before deciding on their patent filing strategy.



Conclusion

Premature publication of clinical trial information related to innovations may jeopardise patent filing opportunities. It is therefore important to understand what and when clinical trial information will be made publicly available under the CTR transparency rules, and what actions can be taken by sponsors to prevent clinical trials information related to innovations becoming prior art that may prejudice patenting an invention. Sponsors are advised to engage with their legal and regulatory teams early on in the clinical trial life cycle to devise strategies to navigate through the complexity of the patent system in view of the transparency requirements of the CTR.

Appendix

Timing of information that is to be published in CTIS public workspace for a clinical trial

This is not an exhaustive list of data that is to be published under the CTR revised transparency rules, rather the list of documents and data that bear direct relation to a patent filing application strategy.

<table>
<tr><th>Data within the clinical trial application</th><th>Category 1:
Adult only (no PIP)</th><th>Category 1:
Paediatrics and/or PIP</th><th>Category 2:
Integrated phase 1 / 2</th><th>Category 2 and 3:
Excluding integrated phase 1 / 2</th></tr>
<tr><td>CTIS application form structured data fields (maximum daily dose, duration of treatment, total dose, units of measure)</td><td colspan="3">30 months after the EU/EEA end of trial</td><td>The first decision on the clinical trial application by a Member State Concerned</td></tr>
<tr><td>Protocol, protocol synopsis, and patient facing documents</td><td>30 months after the EU/EEA end of trial</td><td>When the final summary of results are submitted</td><td colspan="2">The first decision on the clinical trial application by a Member State Concerned</td></tr>
<tr><td>Recruitment arrangements (including procedures for inclusion and copy of advertisement materials)</td><td colspan="2" rowspan="2">Not made public</td><td colspan="2" rowspan="2">The decision on the clinical trial application by the Member State Concerned</td></tr>
<tr><td>Subject information and Informed Consent Form</td></tr>
<tr><td>Study notifications on serious breaches, urgent safety measures, unexpected events</td><td>30 months after the EU/EEA end of trial</td><td colspan="3">After the Member State Concerned assessment</td></tr>
<tr><td>Intermediate results</td><td colspan="4">Not made public</td></tr>
</table>

Final Summary of Results and Layperson Summary of Results	30 months after the EU/EEA end of trial	As soon as these documents are submitted in CTIS
Clinical Study Report as part of a Marketing Authorisation Application	As soon as this document is submitted in CTIS	

Meet the experts

Karen Ng

Associate, European and UK Patent Attorney, J A Kemp

Karen plays an active role in advising and managing patent portfolios for a wide variety of clients, from startups to large multinational corporations. In particular, she has experience of managing large, complex portfolios of patent families, including those covering clinical candidates and platform technologies. She has expertise across a wide range of disciplines, including cell and gene therapies, antibodies, vaccines, biomarkers, and diagnostics. Karen is based in J A Kemp's Oxford office.

James Biddlecombe

Business Transformation and CTR Lead, DLRC

James's journey with the EU CTR started in 2017, working at the EMA in the CTIS business team. Over the last seven years, he supported the development of the regulation and guidance, the development of CTIS, and has supported clients with CTR readiness and CTA submissions. He has supported clients in getting them ready for the CTR Go-Live through training, redesign of operating models, and updates to processes and procedures. More recently, he supports clients with strategic direction for trials submitted under the CTR and helps to navigate EU CTR guidelines and ensure CTA document compliance with the regulation.

J A Kemp

J A Kemp is one of the largest UK and European patent and trade mark attorney firms, with offices in London, Paris, Oxford, Cambridge, and Munich. Their attorneys draft, file and prosecute patent and trade mark applications in the UK, Europe and internationally. The firm works for a huge variety of clients, from startups, spinouts and SMEs through to some of the largest corporate clients and most prestigious academic institutions in the world. J A Kemp is also renowned and respected as one of the leading opposition practices in Europe and has the sector specialist attorney capabilities required to secure and protect the most complex IP portfolios.

DLRC

DLRC is an award-winning consultancy team of >80 highly qualified, experienced regulatory professionals operating from our offices in the UK, Germany, and US. With a deep commitment to excellence, we are dedicated to helping clients navigate the complex regulatory landscape of the life science industry. We develop and execute innovative phase-appropriate regulatory strategies, providing comprehensive support from early development to post-licensing activities for medicinal products and medical devices. Our team comprises consultant experts in nonclinical, CMC, clinical and MedTech from pharmaceutical, medical device and regulatory agency backgrounds. We have proudly served companies of all sizes and backgrounds in various regulatory jurisdictions.

Contact us

J A · K E M P

enquiries@jakemp.com

jakemp.com

J A Kemp

+44 20 3077 8600

DLRC

hello@dlrcgroup.com

www.dlrcgroup.com

DLRC Regulatory Consultancy

UK: +44 (0)1462 372 472

EU: +49 (0)89 44489 311

US: +1 617 851 1438