KPMG

Trials and Tribulations – The new EU CTR

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Context

How life sciences companies can mitigate the challenges of the new EU Clinical Trials Regulation, accelerate their R&D, and become more competitive.

Set to go live on the 31 of January 2022 the European Union Clinical Trial Regulation 536/2014 (EU CTR) will be a massive change to clinical trials across the EU.

With only a few months to go, this raises the big question: Are you ready?

Aiming to “simplify and harmonise the administrative provisions governing clinical trials in the Union”(1) the EU CTR will replace the existing Clinical Trial Directive (Directive 2001/20/EC) once the EU portal Clinical Trials Information System (CTIS), goes live at the end of January 2022.

This is sure to cause significant challenges for sponsors. A transition period has been set but if you are not ultimately compliant with the #EUCTR, you cannot perform clinical trials within the EU.

While the Clinical Trial Directive helped to improve the quality of data and safety of participants, the need for a new regulation was driven by several factors. Between 2007 and 2011, there was a 25 percent decrease in the number of applications for clinical trials within the EU, an increase in the costs of clinical trials, and a 90 percent increase in the average waiting time.(2)

Additional criticism included slow trial implementation, a shift from independent academic trials to those mostly led by large pharmaceutical companies, less data was being evaluated, there were delays in launching multi-national trials, and fewer patients were treated in therapy optimisation trials. To name just a few.(3)

Overall, the goal of the new regulation is to make the EU an attractive place to conduct clinical research (that is, to make it more efficient and harmonised across Member States) while delivering a strong focus on patient safety and transparency. The regulation requires simpler, consistent rules for trials within the EU, and specific information must be made available to the public.(4)

This last point is an important one, as noted by Glenis Willmott, former Member of the European Parliament “For too long, unflattering studies on new medicines have gone undisclosed. Around half of all trials are never published… It is vital we know about negative outcomes".(5)

Note:
(1) https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=celex%3A32014R0536
(2) https://www.ema.europa.eu/en/documents/presentation/presentation-clinical-trials-regulation-why-when-what-how-s-giraud_en.pdf
(3) https://bo.dgho.de/publikationen/stellungnahmen/gesetzesvorhaben/eu_verordnung_klinische_pruefungen/EU%20Direktive%20Klinische%20Pruefungen%2020100108.pdf
(4) https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/clinical-trials-regulation
(5) https://www.europarl.europa.eu/news/en/press-room/20131220IPR31630/clinical-trials-clearer-rules-better-protection-for-patients

Increased efficiency, safety, and transparency

By boosting the efficiency of trials within Europe, the regulation also aims to encourage research and innovation, and reduce the amount of duplication and repetition of studies through a coordinated submission and assessment process across Member States.

This includes a harmonised digital submission and assessment process, better collaboration, information sharing, and decision making, plus increased transparency of clinical trial information (with various exceptions such as personal data protection).

All the while helping to ensure the highest safety standards for EU clinical trial participants.

In short, the EU CTR is intended to reduce delays, lower cost, and limit administrative and regulatory burdens. All to make it easier for life sciences companies to conduct trials for Investigational Medicinal Products (not devices, surgery, etc.) for human use across member states.

The new regulation in detail

Key changes

Compared with the Clinical Trial Directive, the EU CTR differs in several ways.

- Instead of national complex application and approvals (multiple submissions for one trial plus individual submissions to the National Competent Authority and Ethics Committees), there will be a single e-submission to all Member States Concerned (MSC).
  - Within this, there are several application types – initial application, substantial modification application, non-substantial modification application, and additional MSC application.
- All communication will be via the Clinical Trials Information System.
- Questions received from regulatory authorities (RFI) must be actioned within 10 -12 calendar days. Previously this varied between countries but was much longer . More on this later.
- Within the Clinical Trial Directive, public access to data was limited, however, with the EU CTR the public can access extensive information (public disclosure) about clinical trials.
- A ‘substantial amendment’ is now called a ‘substantial modification’, which requires a similar, but shorter, application process as the original application.

In addition, new requirements include the need for updated packaging and a close look at how your existing IT interfaces with the new CTIS portal and database.

A quick look at the CTIS

Acting as a single-entry point for you to submit clinical trial information, the CTIS utilises two restricted and secured areas – Sponsor and Authority – to support everyone throughout the life cycle of your clinical trial.

All data is to be stored within the system and (subject to transparency rules) made publicly available.

A full description and overview of Sponsor and Authority workspaces can be found on the European Medicines Agency website. For an overall look, refer to the CTIS Sponsor Handbook 2021.

The challenges for the healthcare industry

Put simply, the immense changes that the EU CTR requires will bring substantial challenges. Compliance won't come easily

Not only must you have a full understanding of the regulation, the legal ramifications, and how it must be implemented, you'll need to develop the appropriate processes to ensure you can meet the demands of the new system.

Can your IT systems securely capture and report the necessary critical study milestones for your clinical trial – and can you demonstrate that your organisation has adequate safeguards for data protection? Are your processes scalable, repeatable, and auditable? Is your organisation able to quickly adapt to the new systems and timelines (and if they change in the future)?

Are you prepared for the EU CTR requirements around data transparency, which must be carried out throughout the entire lifecycle of the clinical trial? Every requirement applies to all EU Member States for all trials registered within CTIS and conducted in the EU.

Do you have a strategic plan that considers the risks and can mitigate them? As this is a new regulation using a recently developed IT solution, there are certain to be teething problems.

Are your teams trained on the new CTIS platform and have you defined who exactly is responsible for regulatory submission and reporting?

Size and location matters

Large organisations can expect less impact from the new regulation. More robust and agile technologies, combined with their seasoned regulatory teams or use of outside consultants, are sure to help make the transition more manageable. As is the ability to conduct comprehensive impact assessments. But they still must focus strongly on cross-functional coordination between departments and third parties, including compliance, pharmacovigilance, clinical operations, IT, outsourced services, and more.

For smaller firms and academia, who have fewer resources to contend with the increased administration and costs; let alone training and the development of new processes and technologies; compliance may be a real struggle. If you're not ready, expect your R&D timelines in the EU to be significantly impacted.

The new regulation will also be a challenge for any firms working outside of the European Union. While the United Kingdom was heavily involved in the EU CTR development, post-Brexit they are now developing a UK-specific bespoke system.

To be ready, and fully compliant with the regulation, extensive preparation and planning are required.

A question of timing

As the countdown to launch quickly picks up pace, one specific issue must be addressed very early on; particularly for SME organisations who want to ensure the EU's biotech sector continues to innovate and grow.(6)

Key changes

The 12-day response time for queries or a 'request for information'. This is the absolute maximum time being? available. There is no flexibility.

Let's consider the implications.

You've submitted your trial to 20 EU MSCs. The costs alone were staggering. Development time, setting up the team, training, collating the available data, submitting the trial, fees to each MSC.

Now, every single MSC asks you 50 questions.

You have 12 days to answer. To gather everyone you need. To review each answer. Compile the responses and get everything ready for input into the CTIS. To potentially redact information and have that reviewed.

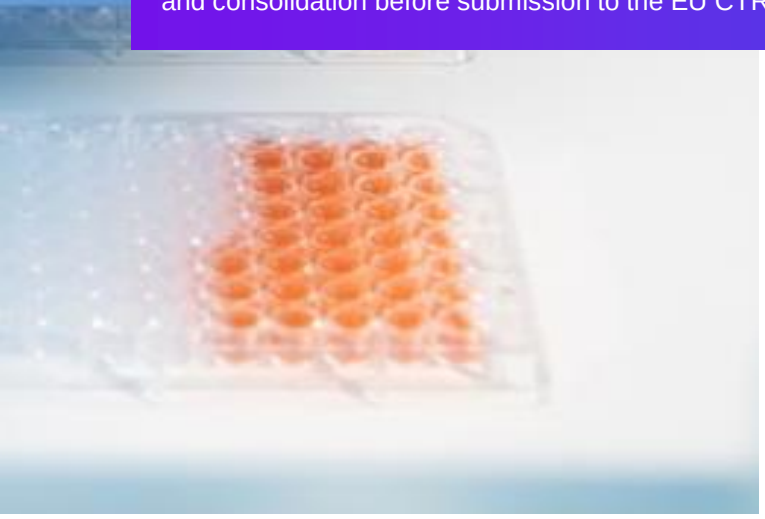
You may also have to translate every response into multiple languages (if not each question as well).

Being able to respond efficiently and rapidly is essential. Because, as per the regulation "Where the sponsor does not provide additional information within the period set by the reporting Member State the application shall be deemed to have lapsed in all Member States concerned."(7)

Yes, *all* member states. Can you afford to resubmit?

What if you're already running a clinical trial

Thankfully, there will be a three-year transition period. However, if you were a part of the Voluntary Harmonisation Procedure, it is being disbanded this October to end in November. Any multi-national trial must align its documentation across all participating Member States, which is likely to require amendments and consolidation before submission to the EU CTR.



Note:
(6) https://www.mckinsey.com/industries/life-sciences/our-insights/infographic-building-the-european-biotech-sector-with-world-class-science-and-innovation
(7) (refer to page 17) https://ec.europa.eu/health/sites/default/files/files/eudralex/vol-1/reg_2014_536/reg_2014_536_en.pdf

Don't wait until tomorrow

What then can make the transition to EU CTR easier?

Because every organisation is different, there can be no one-size-fits-all approach. The following list, however, provides some guidance on where to initially focus your attention. For a truly comprehensive analysis of your organisation's readiness for EU CTR – and support to ensure you are fully compliant and ready to go – contact KPMG today!

Build the right team

Clearly define key roles and consider creating a centralised team to manage, operate, and monitor your CTIS interface. With short response times, it is essential that all communications, data entry requirements, and timelines are constantly monitored.

Perform a GAP analysis

Make sure you fully understand the differences between the outgoing Clinical Trials Directive and the new EU CTR – and how it will change areas within your business. Focus on business and technical functions, people and roles, processes, tools, data management, and more.

Review overall business/cross-department / third party regulatory impact

From your people to your technology, how you deal with your data, your current processes – and those of any third-party services – a comprehensive impact assessment can help you see how the new EU CTR requirements differ from what you already have in place.

Review your tech

One thing your GAP analysis and impact assessment should identify is how your technology may be affected by these changes. Can your existing systems easily integrate with the CTIS? Are your clinical trial management systems and document management systems ready to meet the new demands of the EU CTR?

Additionally, create an effective communication strategy to inform everyone in your organisation about required and potential changes – from processes, roles, and technologies. It is also essential to provide comprehensive training about the regulation and the CTIS.

Once your business is ready, it's time to consider how each trial is best conducted.

Be smart about the countries you choose. What languages must be included? National laws to consider? What differences in Informed Consent exist within that country? Don't forget that a negative conclusion by a Reporting Member State can affect all MSCs.

Focus strongly on getting it right the first time. Again, if your submission (and any Substantial Modification application) fails to pass the validation phase with just one MSC it will struggle to proceed.

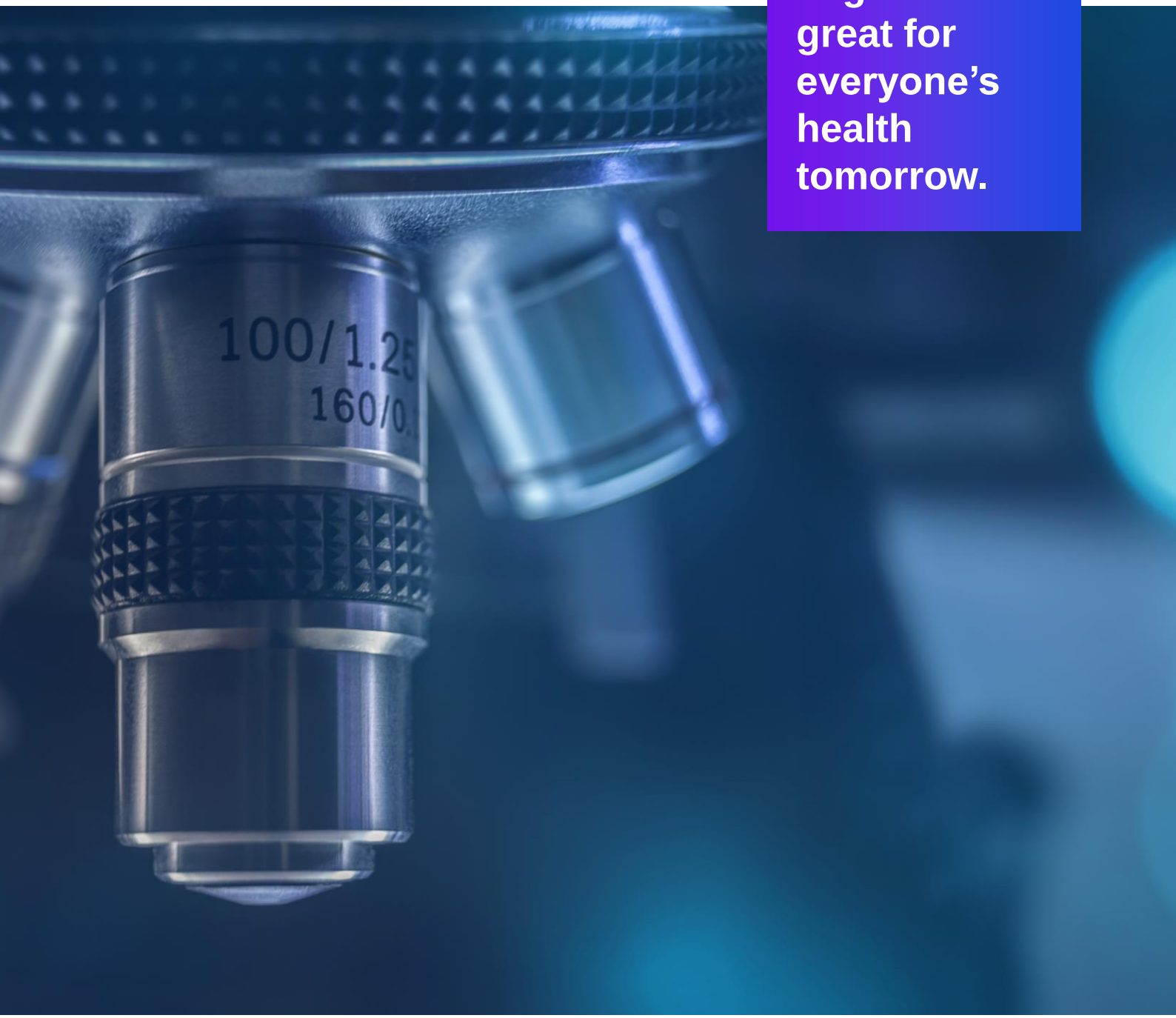
Finally, get your timing right. You must closely coordinate applications and synchronise processes and internal and external teams. A missed timeline can have a hugely negative impact (such as a lapsed application).

One for all, all for one

There is little doubt that the aim of the EU CTR to increase the efficiency and transparency of clinical trials in Europe will have a significant impact on regulatory authorities and anyone conducting a clinical trial. Not to ignore the potential benefit to EU countries.

But the challenge to get ready is significant. KPMG can help you to navigate the issues and ensure you're complaint.

What's good for your business today just might be great for everyone's health tomorrow.



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