Preparing Pharmaceutical Companies for Major Compliance Requirement Changes

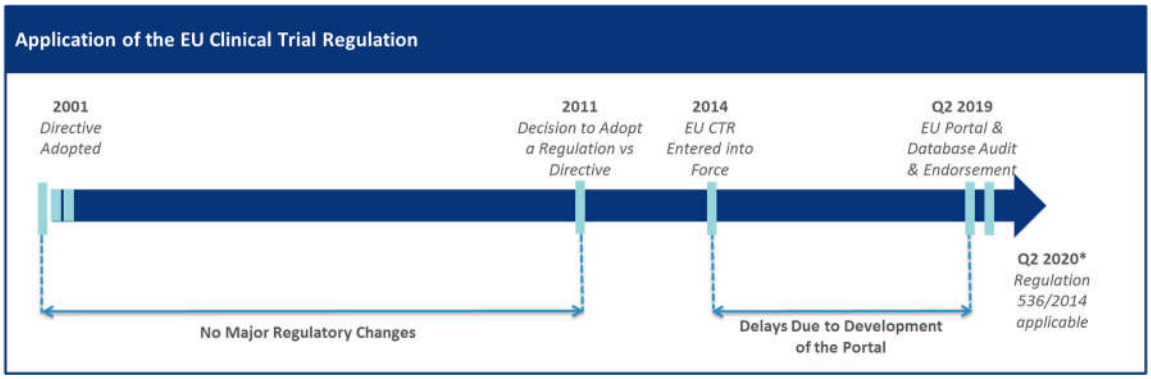
The EU Clinical Trial Regulation is the first major change in legislation in 13 years in how clinical trials are conducted across the European Union.

With the introduction of the EU Clinical Trial Regulation (EU CTR), the European Medicines Agency (EMA) has authored the first major change in 13 years in how clinical trials are conducted within the European Union (EU). When the EU CTR no 536/2014 becomes effective, it will be a legal mandate for all interventional clinical trials of medical products intended for human use. The EU CTR will repeal the 2001 Directive (2001/20/EC), which was not legally mandated and was widely criticized for not fostering a harmonized approach. The intent of the EU CTR is to introduce a single set of EU-wide rules for conducting clinical trials, making the EU more attractive for clinical research.

Transparency is a main tenet of the legislation, with the goal of enabling public access to trial-related information through a centralized EU portal and database. The EU portal will also facilitate submissions and authorization of applications. Key provisions of the EU CTR include:

1) Streamlined procedures for applications and their assessment;
2) Simplified safety reporting;
3) Labeling of inner packaging of small dosage forms;
4) Public access to application dossiers and trial outcomes (with protections for commercially confidential or personal patient data).

Due to complications in developing the portal and database, EMA has pushed back the applicable date of the legislation multiple times since it was initially announced in April 2014. As of the writing of this document, the applicable date is expected to be during the second quarter of 2020 (previously October 2018).



Challenges Abound

To prepare your company for EU CTR –related changes, you must produce scalable, repeatable, and auditable processes.

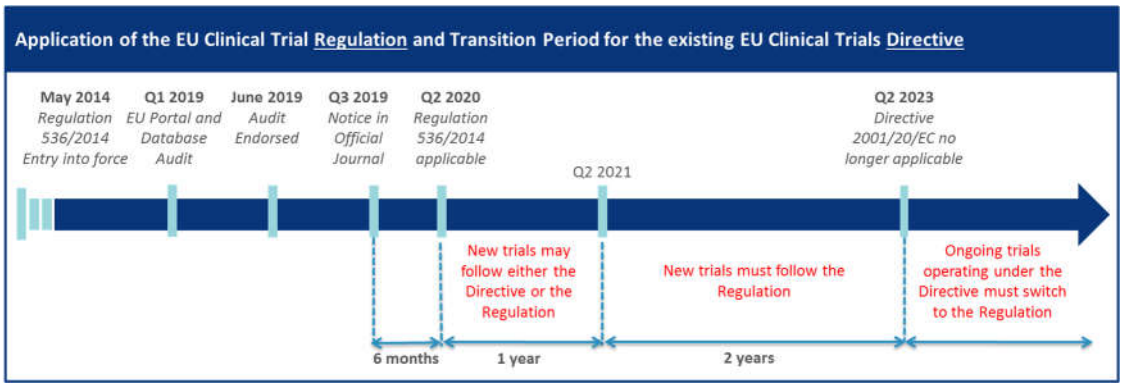
The EU CTR is prompting considerable activity in the healthcare industry due to the magnitude of the changes it requires, and the legal implications thereof. To be compliant, pharmaceutical companies must develop a keen understanding of the new regulation and its exact requirements. Armed with this knowledge, they need to create efficient and effective processes to meet the regulatory needs, including modifying enterprise systems to ensure information is accurately captured and reported.

Major changes breed challenges, including:

- Ambiguity of the intent or details of certain areas of the text;
- Pending guidance from EMA on key areas related to medical safety requirements, serious breach requirements, and the concept of "low-intervention" trials (for which regulatory requirements are lighter, e.g., those comparing medicines already authorized);
- How to account for the cross-functional nature of the changes;
- How to incorporate the additional reporting requirements efficiently while meeting the stricter timelines;
- Determining whether your organization's people, processes, and technology are capable of managing trials during the transitional period where both the the Directive and Regulation may be in place.

When faced with an effort of this magnitude, some companies may be tempted to address these changes with a "band-aid" solution; one that requires minimal effort and organizational change. This would be a mistake, and will result in confusion, and potential corrective measures and audit failures for the business.

To prepare your company successfully for EU CTR changes, you must produce scalable, repeatable, and auditable processes. Acquis is working closely with our pharmaceutical clients to prepare them for the upcoming changes and ensure they are compliant with the EU CTR.



Efforts to address this regulation require cross-functional coordination with a variety of departments including Regulatory, Compliance, IT, Clinical Operations, and the Therapeutic Areas (TAs). Typical questions that arise during these initial discussions include:

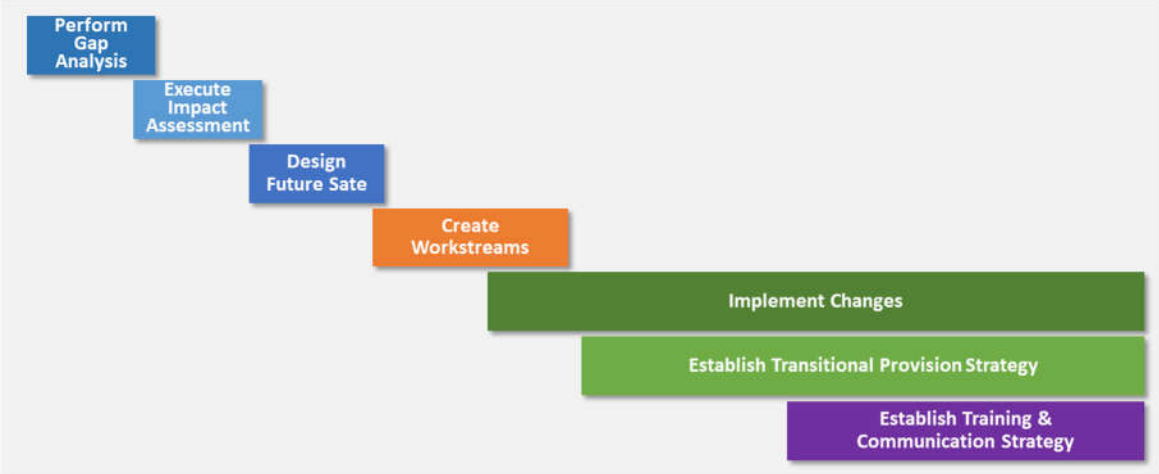
1) What are the major differences between the EU CTD and the EU CTR?
2) How do I build a team that can identify and manage these impacts?
3) How should we approach the transitional period?

A Structured Approach

A strong, cross-functional team is imperative to implementing changes successfully and maintaining compliance.

Acquis recommends a multistep, phased approach to execute business process and system changes successfully. Additionally, the implementation team must be strong, and should include a dedicated project manager, executive sponsorship within the organization, and additional roles representing key stakeholder groups (e.g., Clinical Operations, Regulatory, and Legal).

There are seven major portions of this effort, as depicted and described below.



GAP ANALYSIS

1) Perform a gap analysis between the 2001 Directive and the EU CTR

The purpose of the gap analysis exercise is to understand the differences in requirements between the 2001 Directive and the new EU CTR, as well as understand the major changes the EU CTR will bring to your organization.

How We Help:

- Provide criteria to assist in identifying the individuals / teams required;
- Facilitate the execution of the gap analysis;
- Work with the team to identify the impact business areas (high level).

IMPACT ASSESSMENT

2) Execute an impact assessment

Completing a detailed assessment of the impacts to your organization will allow you to identify how the new requirements differ from the company's current processes, and changes that will be required from people, systems, and processes perspectives.

How We Help:

- Facilitate the creation of current state end-to-end process maps;
- Develop a template to perform a detailed impact assessment;
- Work with business owners from the affected business areas that were identified during the gap analysis to capture all procedure, system, and organizational impacts of each article;
- Collate and finalize the output of this critical step; a detailed listing of all affected systems, procedural documents, and data / definition changes.

FUTURE STATE DESIGN

3) Develop the future state design

During this step, future state process flows are created, and a roadmap is developed that showcases the future state design.

How We Help:

- Facilitate workshops and brainstorming sessions to define the future state;
- Work with teams to leverage the current state process flows documented in Step 1 and update them to include the required changes identified in Step 2. The future-state should include affected procedural documents and templates as well as affected systems. Roles and responsibilities should be clearly defined by function.

ESTABLISH WORKSTREAMS

4) Establish workstreams to manage the implementation

Understanding what needs to be changed is critical, and identifying the right set of people to implement the identified changes is of utmost importance.

How We Help:

- Create a project management team that can bring the workstreams together, drive project deliverables, and manage the various workstreams;
- Develop a steering committee, including executive sponsorship, to help set project strategy and direction. The steering committee should comprise leadership across the various affected business areas;
- Identify appropriate workstreams (consisting of leads, standing members, and SMEs) that are aligned with the identified impacts to manage the implementation of those changes;
- Facilitate the creation of workstream charters that clearly outline the workstream objective, scope, team, and key deliverables.

IMPLEMENTATION ACTIVITIES

5) Implement all required changes

Implementing the required changes includes updating all processes and systems to be EU CTR compliant . This is the longest phase of the project and is iterative in nature, as new information is brought forward by EMA, and workstreams may need to pivot.

How We Help:

- Partner with workstream leads to drive deliverables and meet milestones;
- Develop a project plan template and partner with workstream leads to develop workstream-specific project plans;
- Track dependencies, both internally to the other project workstreams, and externally across ongoing initiatives within the organization;
- Develop a risk and issues log, and facilitate the escalation of issues to the project steering committee and executive sponsorship as needed;
- Facilitate the connection to the local countries, and related processes. Work with the local regulatory teams to ensure the most stringent laws (global vs. local) are followed.

TRANSITIONAL PROVISION STRATEGY

6) Determine the transitional provision strategy

A crucial step for companies is to determine how clinical trials will be run during the transitional period. For one year after the applicable date, companies will be able to start new trials on either the Regulation or the Directive. After that one-year period, all new trials will need to follow the Regulation. Companies then have an additional two years to transition studies that are following the Directive, and that will be ongoing at the end of that two-year period, to follow the Regulation. In total, the transitional period will be three years.

How We Help:

- Help to identify the stakeholders that will need to provide input into the transitional strategy (e.g. leadership, TAs, study teams, etc.);
- Facilitate defining the overall strategy for new trials. This includes obtaining the answers to several key questions:
    - Will certain trials be selected as pilots and roll out using the EU CTR before all trials begin using the regulation?
    - Will trials begin using the EU CTR in a waved approach?
    - Will all trials begin using the EU CTR at once?
    - Will the strategy be different depending on phase of study or Therapeutic Area?
- Facilitate defining the strategy for converting existing trials from the Directive to the EU CTR. This includes obtaining the answers to several key questions:
    - Will trials be converted at the compound level?
    - When will trials start to convert?
- Engage with the TAs early in the process to obtain insight on which trials will be good candidates for potential pilots. Obtain a high-level understanding of the TA strategy to ensure that the transitional strategy fits with business strategy and needs.

TRAINING & COMMUNICATION

3) Create an effective training and communication strategy

An often overlooked element of any project is the change management approach. To implement change effectively, you must ensure that all required changes are appropriately communicated throughout the organization, and that all affected roles have been provided sufficient training to meet all Regulation requirements.

How We Help:

- Facilitate the development of a strong training program and comprehensive communication plan that aligns with the approach the company pursues for the transitional strategy. This may influence whether a company decides to leverage just in time training or creates a comprehensive mandatory curriculum.
- Work with teams to leverage the current state process flows documented in Step 1 and update them to include the required changes identified in Step 2. The future-state should include affected procedural documents and templates as well as affected systems. Roles and responsibilities should be clearly defined by function.

Time for Action

Does your company currently conduct trials in the EU or does it plan to in the future? Are you ready to be compliant with this Regulation, including assessing the impact to your organization, devising, and then executing a plan for implementation? Ramifications of not meeting regulation requirements include potential corrective measures and audit findings. For more information on how Acquis can support your organization, please contact us for a consultation.

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