Are You Ready for the EU Clinical Trial Regulation No. 536/2014?

The European Medicines Agency (EMA) is set to apply a new clinical trial regulation designed to encourage sponsors to conduct trials across the EU: EU Clinical Trial Regulation 536/2014. The new regulation defines consistent rules for conducting clinical trials throughout the EU whilst minimizing individual Member State (MS) interpretation. It also makes information on authorization, conduct and results of every EU Clinical Trial publicly available. The regulation is applicable for Investigational Medicinal Products (IMPs) for human use and does not apply to non-interventional studies without medicinal products such as devices or surgery, etc.

The EU Clinical Trial Regulation 536/2014 simplifies the application process by harmonizing it across EU MSs. Here's a snapshot…

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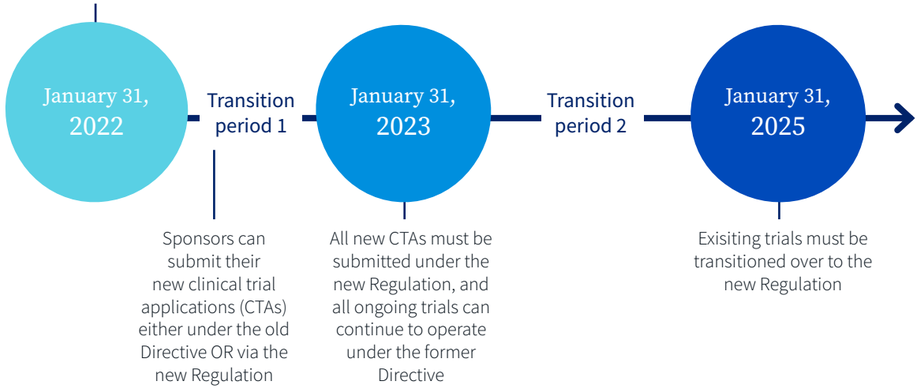
When Will This Happen?

The regulation (which, although technically was adopted and went into force in 2014), is finally applicable on January 31, 2022, with a three-year transition period.



How It Works

A central portal, the Clinical Trial Information System (CTIS) is used to upload, consult on and review CTAs. One application dossier is submitted to all MSs involved in the trial, covering both regulatory and ethical aspects.

The review is conducted in two parts, but leads to a single decision across the EU. The rules on protecting subjects and on information transparency are harmonized across all MSs, and suspected unexpected serious adverse events are reported centrally.

Single Dossier (Regulatory Authority/Ethics Committee)

Across the EU, sponsors submit their CTAs via a single submission portal.

Part I Documents — Scientific

A single, reporting MS selected by the Sponsor reviews the Core Documents and coordinates reviews by all concerned MSs

- Cover letter
- EU application Form
- Protocol
- Investigator's brochure
- GMP-related documentation
- Investigational Medicinal Product Dossier (IMPD)
- Auxiliary Medicinal Product Dossier
- Scientific Advice and Paediatric Investigation Plan (PIP)
- Content of labelling of the IMP
- Proof of payment

Part II Documents — National

Each MS concerned assesses national/local aspects

- Recruitment arrangements
- Subject Information, Informed Consent Form and informed consent procedure
- Suitability of the investigator
- Suitability of the facilities
- Proof of insurance or indemnification
- Financial and other arrangements
- Proof that data will be processed in compliance with union law on data protection
- Proof of payment fee

EU Portal (CTIS)

All material stored in the Clinical Trial Information System (CTIS) is open to public view except as agreed upon, Personal Protected Data, commercially confidential information and confidential communiques between MSs.

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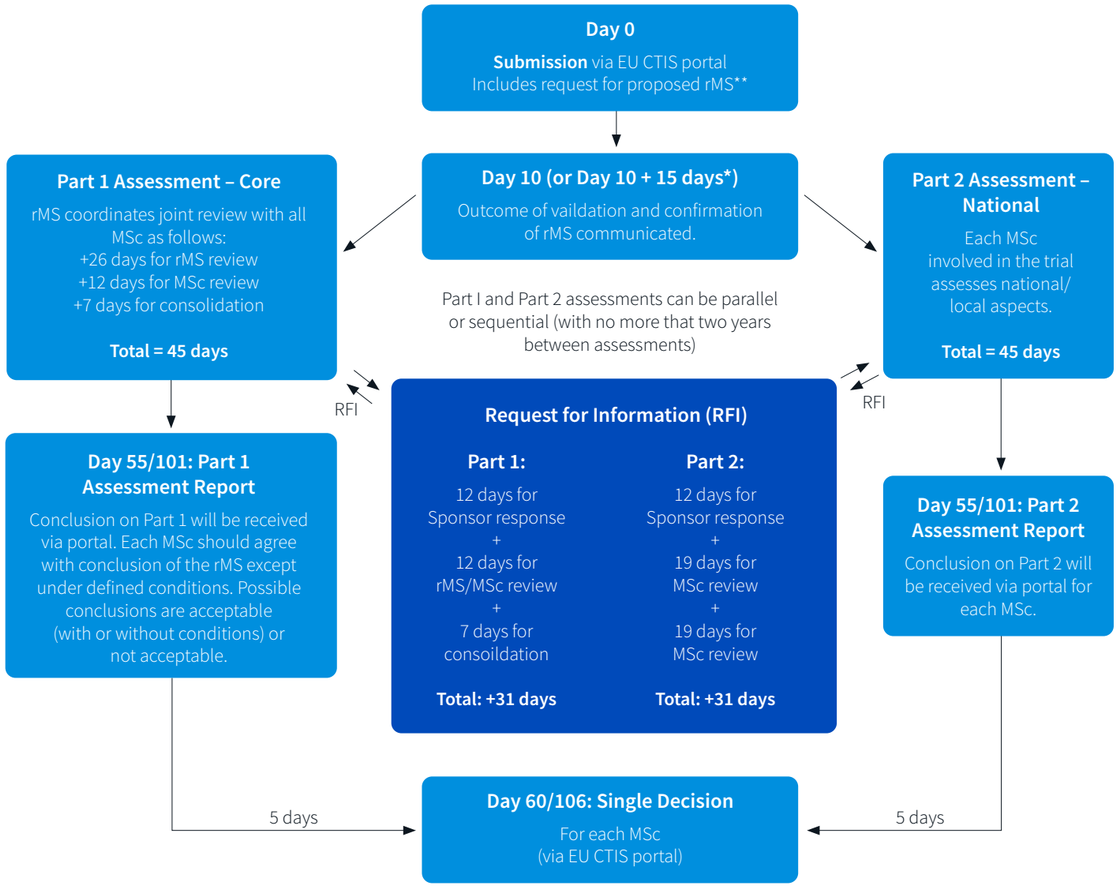
How Long It Takes

The timeline for initial submission to approval is predictable – between 60 and 106 days for a standard IMP. **Applicants have up to 12 calendar days to respond to requests for information** as the application progresses. If you miss a response deadline, the application is considered lapsed. Should an MS fail to meet an interim deadline, it will constitute tacit approval of that stage of the process.



rMS: Reporting Member State
MSc: Member State Concerned
* = +15 days for addressing validation: 10 days for Sponsor to repspond +5 days for rMS decision.
** = Overall assessment can be increased by rMS for a further 50 days in the case of advanced therapy products and biologics (for purpose of consulting with experts).
*** = The rMS shall notify the Sponsor, and if applicable, other MSc' within 6 days from submission of the dossier.

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What It Means for You

The new process is not without challenges for Sponsors and has far-reaching implications for everything from selecting the optimal submission strategy to your ability to respond to queries within the time allotted. You should be prepared to adopt new Standard Operating Procedures (SOPs) around each of these areas:

- **Public Access to Information:** You may need to upload two different versions of material – one that is available for review by the MSs and one that is redacted for public consumption.
- **Serious Breaches:** The notification timeline is seven days.
- **Trial Master File Retention:** Master files must be retained for 25 years.
- **IMP Manufacture and Labelling:**
  - Requirement for period of use to be listed on immediate packaging.
  - Expiry date extension re-labelling at site may be performed only by authorized personnel.
    - Expiry date extension re-labelling of immediate packaging needed in addition to expiry date extension re-labelling of outer packaging.
- **Query Responses:** Requests for information must be answered within 2 - 12 calendar days.
- **Regulatory/Ethics Submissions:** A single submission will cover Regulatory as well as Ethics Committee submissions.
- **Transition of Trials:** All ongoing trials must be transferred to the new Regulation through CTIS by January 31, 2025.
- **Inspection Reporting from Outside the EU:** Inspection reports of third-country authorities concerning the clinical trial are to be submitted through CTIS to MSs.
- **Safety Reporting:** Annual Safety Reports must be submitted through CTIS.

How Labcorp Drug Development Can Help

Labcorp brought together an internal task force consisting of 80 professionals across multiple functions. They performed gap analyses and established various workstreams to prepare for the EU Clinical Trial Regulation 536/2014 implementation date. Our Project Managers, Clinical Operations and Regulatory Submissions Teams are intimately familiar with the new requirements and are ready to help you craft and execute the most appropriate submission strategy for your asset.

Learn more about how Labcorp can help you adopt the new Regulation in your clinical program at drugdevelopment.labcorp.com

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