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TRANSLATION NATIONS: THE CHALLENGES AND OPPORTUNITIES OF THE EU'S NEW CENTRALIZED CLINICAL TRIAL APPROACH

4 WAYS THE UPCOMING EU CLINICAL TRIAL REGULATION WILL IMPACT THE TRIAL PROCESS— AND TRIAL SPONSORS AROUND THE GLOBE

BY LIONBRIDGE LIFE SCIENCES

In this paper, you'll learn:

How a new, centralized EU portal for clinical trials affects trial submissions and authorizations.

How to respond to an increased drive for transparency, which puts the public and the patient in focus.

How to establish efficient and reliable content translation in a region with 24 different official languages.

How trial sponsors can meet challenges head-on with a centralized translation strategy.

THE EU CLINICAL TRIAL LANDSCAPE IS ABOUT TO CHANGE—FOR THE BETTER

May 27, 2014, was a pivotal day for clinical trials in the European Union (EU). On this date, the EU Clinical Trial Regulation (No. 536/2014) was officially published, replacing EU directive No. 2001/20/EC and revamping the way clinical trials are conducted in the region. For international trial sponsors as well as National Competent Authorities and EU member states, this regulation is a game-changer.

The new regulation harmonizes clinical trial requirements throughout the EU by establishing a new Clinical Trials Information System—a centralized portal and database developed and maintained by the European Medicines Agency (EMA) in collaboration with the European Commission and EU member states. Part of the information system will be open to the public subject to new transparency rules.

The primary goal of the Clinical Trial Regulation is to create a more favorable trial environment in the EU through enhanced efficiency, reduced costs and timing, and the highest standards of safety.

The regulation aims to:

- Streamline and standardize application, submission, and approval processes and protocols across all EU member states.
- Increase transparency into clinical research, processes, outcomes, and other trial information through a public database.
- Accelerate timelines—enforced by tacit approval/rejection—while avoiding trial duplication or failed trial repetition.
- Improve trial awareness and understanding among clinicians, health authorities, patients, and the population at-large.
- Foster innovation, coordination, and cooperation across borders to encourage the development of new patient treatments.

CHANGE IS COMING...SOON

The EU Clinical Trial Regulation enforcement date is not yet confirmed. The regulation will take effect six months after the European Commission publishes a notice of completion for the new portal and database. As of this paper's publication, that system is expected to be ready in late 2019, with regulatory enforcement targeted for early 2020 and a three-year transition period to follow.

THE CENTRAL CHALLENGE? A PUBLIC PORTAL OF TRIAL INFORMATION

Central to the new Clinical Trial Regulation is the deployment of the Clinical Trials Information System.

The secure, unified portal and database will be used by trial sponsors and National Competent Authorities within each member state, and it serves as the centralized repository for all clinical trial-related information. The EMA will manage the database and supervise content publication on a public website, keeping the responsibility for trial authorization and oversight in the hands of member states.

For regulators and trial sponsors, a dedicated workspace will be available to prepare, share, and collaborate on data and documents. For the public, the portal provides access to non-confidential information on clinical trials for medicinal products conducted in the EU, in all official EU languages once the system is launched. This enables the population at-large to:

- Review clinical trial statistics and download data and reports.
- Read summaries of trial results in plain, non-technical language.
- Conduct advanced searches of clinical trials and receive site updates.

The Big Opportunity?
A Centralized Translation Plan

Transitioning from the current de-centralized way of managing clinical trial submissions and authorizations to a new approach in which sponsors submit a single dossier to all member states through the centralized EU portal means trial sponsors must:

- Meet shorter review cycles and manage coordinated reviews.
- Refine processes and increase transparency to reduce compliance risk.
- Ensure consistent and swift translations across multiple EU languages.

Over the next several pages, we'll explore how the EU portal may create significant translation challenges for trial sponsors. Yet challenges beget opportunities, and we'll also examine how implementing a global, centralized approach to translations—as opposed to managing translations locally—can help sponsors generate rapid and reliable clinical and plain language content to address the demands of the new Clinical Trial Regulation.

TRANSLATION CHALLENGE 1: A POTENTIAL LANGUAGE BARRIER

When the Clinical Trial Regulation goes into effect, EU member states must identify a primary language for clinical trial documentation submitted into the portal. While the EMA encourages member states to select a commonly understood language in the medical field, not every nation can be expected to choose the same language or commit to communicate in English.

While language preferences may vary across EU member states during review of the clinical trial application dossier's scientific content, submission documents intended for trial participants and reviewed by ethics committees will require translation and submission in the local language. Plus, the regulation's amplified focus on transparent public information will inevitably precipitate a rise in translation for patient- and public-facing materials in non-technical language. (More on that later.)

In other words, accurate translations of trial-related content are critical—and trial sponsors would be wise to develop a streamlined, centralized approach in anticipation of the new regulation.

We speak EU: The European Union comprises 28 countries that speak 24 different official languages—all supported by Lionbridge.

Austria	Estonia	Italy	Portugal
Belgium	Finland	Latvia	Romania
Bulgaria	France	Lithuania	Slovakia*
Croatia	Germany	Luxembourg	Slovenia
Cyprus	Greece	Malta	Spain
Czech Republic	Hungary	Netherlands*	Sweden
Denmark*	Ireland*	Poland	United Kingdom*,**

* Lionbridge Life Sciences Center of Excellence

** The new Clinical Trial Regulation will not apply to the UK if/when it leaves the EU, per the June 2016 referendum.

TRANSLATION CHALLENGE 2: A STREAMLINED AUTHORIZATION PROCESS

Under the current EU directive on clinical trials, sponsors seeking to conduct a study in multiple European nations must complete submissions for authorization in each member state separately. This requires organizations to use in-country site managers or clinical research associates, who often prefer to contract local agencies to complete their translation work. Use of multiple local translation vendors, however, can result in varying degrees of linguistic accuracy across a multinational clinical trial.

The new centralized portal eliminates the need for trial sponsors to complete individual submissions for each trial country. Under the new regulation, sponsors will be responsible for a single submission.

Sounds simpler, right? In many ways, it is. And yet preparing a full dossier and tackling translations across official EU languages during member state review puts pressure on sponsors for timely execution, efficient coordination, and consistent content.

A centralized trial authorization process calls for a centralized approach to translations. Working with a single global language services provider can improve consistency and compliance for trial applications while reducing the burdens of working with multiple vendors.

Clinical Trial Dossier

PART 1 EUROPEAN UNION, COORDINATED ASSESSMENT Review by Regulators & Ethics Committees 45 Days /+ 31 Days	← SINGLE SUBMISSION →	PART 2 MEMBER STATE, NATIONAL EVALUATION Review by Ethics Committees Only 45 Days/+ 31 Days
• Cover Letter • EU Application Form • Clinical Trial Protocol • Investigator's Brochure • IMPD • GMP Compliance • AMP Dossier • Scientific Advice/PIP • Labeling	Reporting member state validates submission, completes draft assessment, and coordinates joint review with other member states.	• Recruitment Arrangements • Subject Info/Informed Consent • Suitability of Investigator • Suitability of Facilities • Proof of Insurance • Financial/Other Arrangements • Proof of Fee Payment • EU Law of Data Protection

EU PORTAL

TRANSLATION CHALLENGE 3: AN ACCELERATED REVIEW TIMELINE

As noted above, a centralized Clinical Trials Information System with a single submission will naturally create new efficiencies for trials conducted in the EU. To further streamline the overall process, the new regulation also reduces clinical trial authorization from 60 to 45 days, unless the process is extended (e.g., for trials involving advanced therapy investigational products).

New Clinical Trial Authorization Process

Initial Assessment Phase: 26 days
- Reporting Member State (RMS) provides draft Part 1 of Assessment Report
- RMS circulates draft to all other member states

Coordinated Review Phase: 12 days
- Joint review of trial application based on draft Part 1 of Assessment Report
- Member states provide comments on draft to RMS

Consolidation Phase: Seven days
- RMS finalizes Part 1 of Assessment Report
- RMS submits report to trial sponsor and all other member states
- Report must be finalized within 45 days of validation date

Welcome to the Time-Crunch

A stricter timeframe for validation, assessment, and approval creates a time-crunch for National Competent Authorities and ethics committees, as well as trial sponsors. Due to the coordinated review required across the EU during trial authorization, a greater sense of urgency will be needed not only from the RMS, but from all concerned member states.

Furthermore, failure of regulators or trial sponsors to comply with validation and review windows will lead to tacit approval or rejection of the application dossier. Should a sponsor fail to complete the dossier within the validation window, the application will be rejected for all trial countries—resulting in a trial startup delay. Member states and trial sponsors must comply with timelines to complete their assessments or submissions of additional information to avoid delays or re-submissions.

Consider the joint review process, now limited to just 12 days, and the commensurate implications of language translation along the way. If the RMS coordinating the assessment review across all member states operates in a language other than English, there may be an urgent need to translate trial documents or communication during cross-country review to ensure an effective and timely assessment of the application.

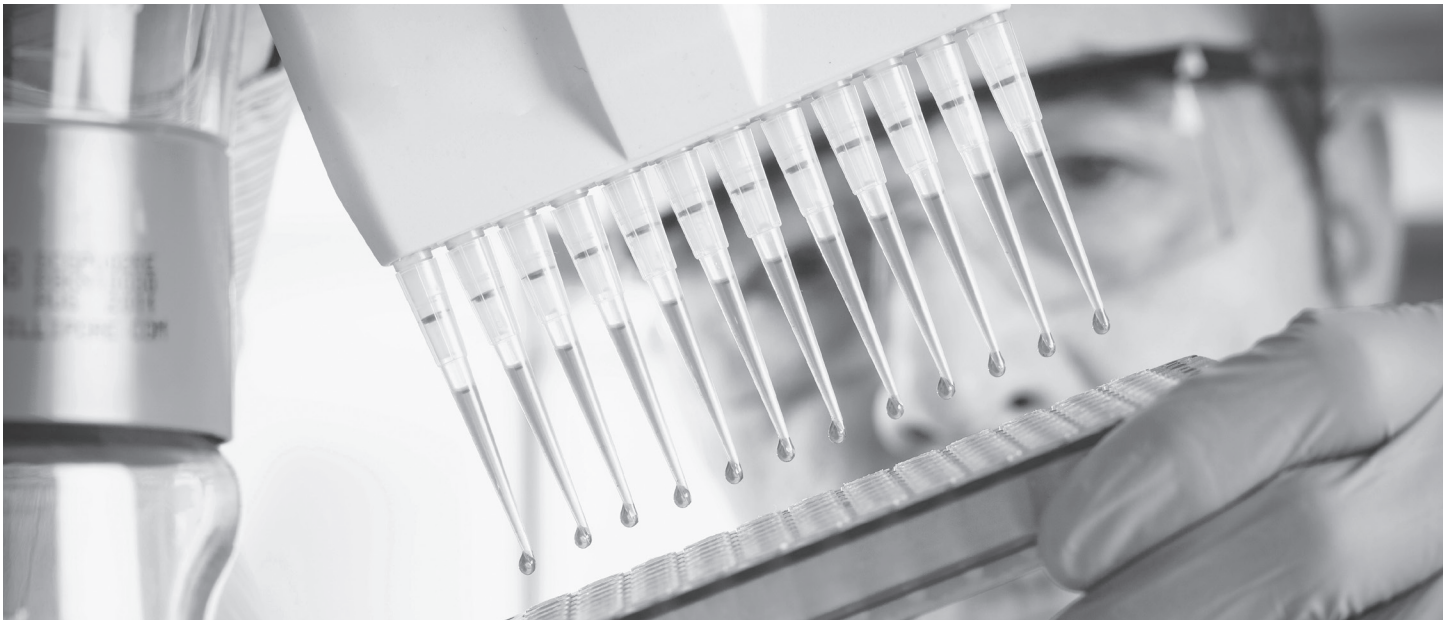
At the moment, the linguistic implications of the new authorization process and the new Clinical Trial Regulation are not fully known. It is certain, however, that the European Union has a declared multilingual policy in which EU citizens have the right to use any of the EU's 24 official languages.

The emphasis on timelines, combined with the number of official languages in the EU, makes precise document translations invaluable. Without a reliable, responsive, and centrally-managed language service provider, trial sponsors could see the tick of approval turn into the tock of denial.

Tighter Deadlines Require Tighter Collaboration

An expedited authorization process—on top of the sheer scale of this multilingual, multi-country undertaking—means all stakeholders will need to communicate faster and collaborate better. Member states across the EU must work together in the same, interdependent regulatory timeframe. Regulatory authorities and ethics committees within each country must establish practices that facilitate cooperation during the assessment phase. Trial sponsors must respond quickly and accurately to avoid tacit rejections, re-submissions, or delays in trial start.

In a union with 28 nations and 24 official languages, collaboration is king.



TRANSLATION CHALLENGE 4: A DRIVE FOR GREATER TRANSPARENCY

Another key focus of the new regulation is the public disclosure of trial information through the portal. The European Commission wants to make clinical research more accessible to the public, so summaries of trial results—including a separate one written in plain language and intended for non-medical laypersons—must be submitted within one year of the end of the trial[1].

Trial sponsors potentially face penalties if they do not meet regulatory requirements for transparency. The new Clinical Trial Regulation requires member states to implement rules on penalties for lack of compliance with publication on the EU database.

This shift amplifies transparency of clinical research and creates a new reality for the scientific community.

Language is Now a Regulatory Objective

Plain language summaries, made available in the official language of each country in which the study is conducted, are designed to improve patient understanding of the clinical research process, medicines, and trial outcomes. Although these summaries are not new to clinical investigations, their legal enforcement is—and that requires sponsors to integrate summaries into their quality management systems and to dedicate budget and resources to clinical trial disclosure activities.

Translation of plain language summaries into local language is a critical step in effective global communication of trial results, and sponsors must develop efficient processes to achieve compliance. Sponsors need to develop high-quality translations, and all local language versions should align with the master summary while incorporating unique principles of health literacy, numeracy, and cultural literacy.

READ MORE

For more information on the value of high-quality translations for plain language summaries, please read our whitepaper:
Successfully Authoring and Translating Plain Language Summaries

CHANGE IS GOOD—
SO ARE CHALLENGES

The new EU Clinical Trial Regulation brings with it new challenges—especially during the transition phase. Stringent timelines. Swift approvals. Streamlined processes that require seamless solutions. In response, trial sponsors may need to adjust workflows and internal responsibilities to accommodate the EU's centralized authorization process.

While the regulation's enforcement date is still to be determined, savvy trial sponsors will grapple with these challenges sooner than later to ensure effectiveness and compliance. A smooth transition to the new regulatory framework will require sponsors to:

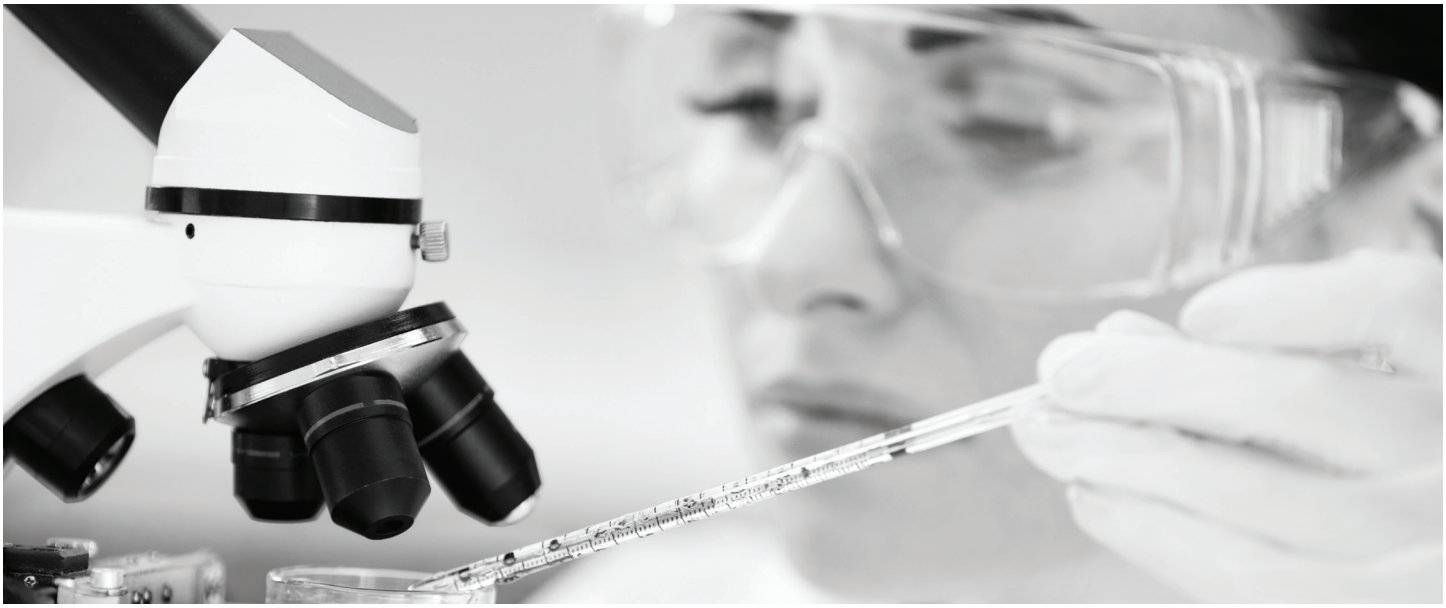
- Complete a full analysis of the regulation's operational impact.
- Develop a detailed plan for implementing the required process changes.
- Properly train all parties involved in the plan so they are ready for day one.

With such a heightened focus on effective and timely communication via the portal, sponsors should consider a plan that both evaluates organizational readiness and uses the new regulation as an impetus to improve their communication efficiency.

"It's encouraging to see that the new EU regulation emphasizes language as an important aspect of clinical trials, and that it requires language to be understandable both in the scientific community and for the public.

I hope clinical trial sponsors adjust to a centralized approach to translation with the EU's implementation of a single submission system, and that they will realize the benefits—translation consistency, cost-efficiency, swift turn-arounds—they can achieve from working with a single global language partner."

Pia Windelov, Director of Product Strategy,
Lionbridge Life Sciences



A PARTNERSHIP WITH THE GLOBAL LANGUAGE EXPERT

As we've explored, many forthcoming big regulatory changes are connected by a common thread: content translation.

To support the new processes prompted by the Clinical Trial Regulation, sponsors should work with a trusted translation partner that can act as a centralized resource for multi-EU country patient locations. A global leader that can quickly scale based on project timelines while also helping you to streamline communications and control costs. A linguistic expert that can provide consistent content across all languages, so you can effectively communicate to regulators, study participants, site staff, and the population at-large.

Lionbridge Life Sciences is ready to be your partner for the challenges ahead. As the world's most experienced language service provider in life sciences, we can help your organization develop a comprehensive translation strategy that increases efficiency, improves compliance, and reduces costs. Lionbridge will:

- Collaborate closely with your team to meet tight deadlines.
- Provide accurate translation in any official EU language.
- Offer clinical and linguistic expertise for plain language communications.
- Deliver translation projects at scale, with speed, and with your complete confidence.

LET'S TALK TRANSLATION

Our experts are ready to better understand what your organization needs ahead of the new Clinical Trial Regulation—so we can tackle these challenges together.

GET STARTED.

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Footnotes

1. https://ec.europa.eu/health/sites/health/files/files/eudralex/vol-10/2017_01_26_summaries_of_ct_results_for_laypersons.pdf

All other references from: https://www.ema.europa.eu/en/human-regulatory/research-development/clinical-trials/clinical-trial-regulation

About Lionbridge

Lionbridge partners with brands to break barriers and build bridges all over the world. For more than 20 years, we have helped companies connect with global customers by delivering marketing, testing and globalization services in more than 300 languages.

Through our world-class platform, we orchestrate a network of 500,000 passionate experts in 5,000-plus cities, who partner with brands to create culturally rich experiences. Relentless in our love of linguistics, we use the best of human and machine intelligence to forge understanding that resonates with our customers' customers. Based in Waltham, Mass., Lionbridge maintains solution centers in 27 countries.

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