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Improving EU Clinical Trials: Proposals to Overcome Current Challenges and Strengthen the Ecosystem

What is the issue?

Clinical trials are one of the most critical, expensive and time-consuming stages of the drug development process. An effective and harmonised regulatory framework is essential—not only to maintain the EU's global competitiveness in pharmaceutical innovation, but also to ensure patients with unmet medical needs can access the latest scientific breakthroughs.

Multi-country clinical trials are especially critical, enabling medicine developers in Europe to scale their efforts and compete with global leaders like the US, China and other global competitors. However, ongoing regulatory fragmentation and operational complexity continue to make the EU a less attractive location for conducting clinical research, as also underlined in both Letta and Draghi reports.

What needs to happen?

While several improvements can be made within the existing legislative framework, non-legislative changes alone are insufficient to sustain Europe's long-term competitiveness in clinical research. Greater investment and simplified policy implementation to address the multiple and fragmented regulatory pathways needed to conduct research are essential to build a thriving, future-ready ecosystem. Legislative updates—most urgently to the In Vitro Diagnostics Regulation (IVDR) and Medical Devices Regulation (MDR)—are needed, and the ongoing review process offers a key opportunity to drive meaningful reform. Meanwhile, pilot projects and voluntary processes could enable earlier progress. Initiatives like ACT-EU, MedEthicsEU and CTR Collaborate all contribute to the improvement of the ecosystem; however, their impact has been limited so far to operational short-term actions.

The Clinical Trials Regulation (CTR) has yet to deliver on its full potential. Rather than a full revision, a targeted approach with focused amendments and full implementation across all Member States is needed. These actions must be supported through sufficient resourcing at all levels, particularly to enable efficient coordination and agile decision-making by national authorities. Above all, swift and coordinated action is critical—and for Europe to remain competitive, it must function as a unified region.

What will be the impact?

- **Improved Patient Access**: Earlier access to innovative treatments can lead to better health outcomes for patients in Europe.
- **Stronger Innovation and R&D eco-system**: A higher volume of trials strengthens collaboration across academia, industry, and healthcare, accelerating innovation.

- **Economic Growth and Global Competitiveness**: More clinical trials attract investment, create jobs, and generate revenue for healthcare systems. Increasing EU's share of global trials re-establishes its position as a leading hub for clinical research.

How is the industry working to address this issue?

In early 2024, EFPIA launched its Clinical Trials Strategy 2030+ with the aim of re-establishing Europe as a leading hub for faster, smarter, and more patient-centric clinical trials. We are working closely with other industry associations, patient organisations, academia, and national trade bodies to engage with regulators and policymakers, addressing challenges in the current legislative framework (CTR, IVDR, MDR, etc.) and proactively proposing solutions. Our messages are shared through key platforms such as ACT EU, the COMBINE project/programme, and bilateral discussions with decision-makers. Additionally, there are multiple IHI projects geared toward making the clinical research more effective, inclusive, and patient-centred by improving trial design and conduct, enhancing patient engagement and experience, increasing the efficiency of clinical trials, and addressing health disparities, among others.

Advancing Together: EFPIA's list of proposals

The proposals outlined in this brief are intended as **a starting point for open dialogue.** They reflect EFPIA's vision for faster, smarter, and more patient-centric clinical trials in Europe. We welcome feedback and continued engagement to ensure the EU's future clinical trial framework fosters innovation, safeguards patient safety, and delivers meaningful health outcomes.

Recognising the vital role of a strong clinical research ecosystem, EFPIA remains committed to working collaboratively with all key stakeholders to identify and implement solutions that enhance the efficiency, quality, and attractiveness of conducting clinical trials in the EU.

Further resources

- EFPIA/VE IQVIA report on European Clinical Trials Ecosystem
- Advancing Clinical Trials for European Patients - EFPIA Blog
- EFPIA survey on IVDR implementation impact
- Cross-border access to clinical trials initiative
- Blog: Unlocking cross-border clinical trials for patients in Europe
- EFPIA CTR Report - June 2024

Advancing Together: EFPIA's list of proposals

1) Simplifying the Regulatory System and Making it Fit for Purpose

1. Streamlining Clinical Trial Processes

ENABLE PARALLEL SUBMISSION OF SUBSTANTIAL and NON-SUBSTANTIAL MODIFICATIONS

Issue(s): Inability to submit parallel substantial modifications (SM) to modify an ongoing trial. Inability to update all documentation with non-substantial modifications (NSM). Approvals with conditions requiring a subsequent SM approval before study is allowed to start.

Impact: These issues significantly affect the feasibility and operational efficiency of clinical trials, especially innovative, multi-arm trials where design-driven modifications are anticipated. Approval of a substantial modification can take over three months, effectively limiting sponsors to just four SMs per year.

Updating CTAs with NSMs is currently limited to a few document types. As a result, discrepancies can occur between the versions held by sponsors and those in CTIS, complicating document reconciliation.

The lack of flexibility forces sponsors to bundle modifications, which delays necessary updates—such as Investigator Brochure (IB) revisions—until a bundled submission is prepared and approved.

Conditional approvals requiring subsequent SMs can delay trial initiation by more than 90 days, leading to a total start-up time of up to 196 days or more from initial Clinical Trial Application (CTA) submission.

Option(s): Amend Article 2(2)(13) of the CTR definition of substantial modification and align CTIS functionality to allow parallel submission of SMs where appropriate.

Short-term workaround: Until this is possible, enable parallel submissions for selected modifications (e.g. IB updates, Investigational Medicinal Product Dossier (IMPD) amendments, and new Member State additions).

Allow sponsors to submit non-substantial updates to any approved document in the dossier at any time, making CTIS a reliable "source of truth" for multinational/international trials. *(Note: This is primarily a CTIS/Member State implementation issue, not a legislative one. Sponsors remain responsible for determining whether a change is substantial.)*

Establish a mechanism where a conditional approval (e.g. tied to a predefined and agreed documentation change) can be addressed by the sponsor through a self-service update in CTIS (e.g. via an NSM as per Article 81.9).

Consider legislative or guidance updates to clarify the status of the ability of the trial to start where an authorisation subject to conditions is issued, given that CTR text that: "An authorisation of a clinical trial subject to conditions is restricted to conditions which by their nature cannot be fulfilled at the time of that authorisation."

STRENGTHEN THE ROLE OF THE REPORTING MEMBER STATE

Issue(s): Reporting Member States (rMS) are not sufficiently empowered to play a lead role that enables reliance and harmonisation among Member States (MSs). In multi-country trials, during both the validation and assessment phases, sponsors may receive a large number of Requests for Information (RFIs)—many of which are duplicative, contradictory, or unclear.

Under the CTR, the rMS does not hold a strong coordinating role to ensure consistency in trial requirements across MSs. Additionally, submitting a second application with nearly identical documentation (e.g. for a new indication of the same drug) involving a different mix of MSs can trigger a completely new set of RFIs. This also applies when adding a new MS to an ongoing trial, where additional RFIs are often introduced—even when the trial has already been approved by several other MSs—leading to unplanned substantial modifications (SMs).

Some MSs have also introduced requirements beyond the scope of the EU CTR, in some cases through national legislation. Conversely, others enforce a kind of "hyper-compliance" with the CTR by requesting additional protocol language confirming adherence to specific CTR articles (e.g. stating that SUSARs will be

reported according to Article 42). However, sponsors already commit to conducting trials in compliance with applicable legislation and ICH GCP. Requiring EU- or MS-specific protocol text in an international protocol adds no regulatory, safety, or data quality benefit—but significantly increases documentation maintenance burdens. When multiple MSs request their own specific wording, it can also reduce the usability of the protocol for its primary end user—the Investigator.

Impact: These challenges make conducting multi-country and international trials in the EU burdensome and unpredictable. They result in the inefficient use of resources across the ecosystem and introduce avoidable delays in trial initiation. As a consequence, the spirit of the EU CTR—which aims to streamline and harmonise trial processes—is undermined. Instead, sponsors are often forced to develop 'bespoke' protocols tailored to individual countries, adding unnecessary complexity and administrative burden. This significantly reduces the EU's attractiveness as a destination for running multi-country clinical trials.

Option(s):

Empower the rMS and promote greater reliance: Enhance the authority of the rMS to coordinate and lead assessments, ensuring greater recognition and reliance by Concerned Member States (MSCs) and additional MSs, as applicable. Allow for change of the rMS during the trial lifecycle under specific circumstances (e.g. when the trial does not proceed in the original rMS post-authorisation).

Improve coordination and, potentially, centralisation: Increase coordination and – to the extent possible - centralisation of both regulatory and ethics review processes. Establish reinforced coordination mechanisms between national ethics committees and a single EU-level decision for the Member States concerned in the authorisation of multi-country clinical trials.

Streamline and harmonise documentation and review: Enable the use of cross-referral to previously approved core documentation with minimal or no reassessment in subsequent applications. Ensure only critical grounds for non-acceptance are raised, in line with the intended scope of the CTR. Strengthen Article 14 to reinforce the scenarios and process for handling disagreements between MSs.

Limit divergent national requirements: The CTR should explicitly prohibit MSs from requesting documents or content beyond what is listed in Annex I (CTA) and Annex II (SM). Strengthen the language in Articles 25(1) and 25(2) (final paragraphs) to reinforce that no additional content can be required by MSs beyond the defined annexes. Limit the ability of MSs to raise "considerations" to only significant issues impacting risk-benefit, trial integrity, or CTR compliance. If a new MS is added, the same approach should be applied, i.e. allowed to disagree with the rMS's existing decision in cases where new data raise significant grounds for objection.

Support and institutionalise best practices: Urgently prioritise delivery of Clinical Trial Coordination Group (CTCG) and Accelerating Clinical Trials in the EU (ACT EU) initiatives, with support from the Clinical Trials Coordination and Advisory Group (CTAG), to promote harmonisation toward best practice, avoiding a drift toward the most conservative standards. Make adherence to best practice guidance developed by CTCG and CTR Collaborate mandatory via legislation, including empowering rMS to remove unnecessary RFIs. Ensure best practice guidance is easily updatable to support innovation, as referenced in the legislative text.

Legislative amendments to support these reforms: Amend recitals (6), (22) and Articles 5(3), 6(5), 6(8), 8(1), 8(2), 14(5), 14(6), 17(1), 17(2), 18(4), 18(6) to (a) strengthen reliance on rMS assessments for both NCAs and Ethics Committees and (b) enhance coordination mechanisms led by the rMS. Update Article 79 to strengthen Union controls for consistent and pragmatic implementation, e.g. by changing the wording from "may" to "will" to reflect mandatory enforcement.

IMPROVE CTIS AND FUTURE-PROOF DIGITAL SOLUTIONS

Issue: The Clinical Trials Information System (CTIS) has been developed with overly strict business rules that limit the flexibility required for efficient clinical trial review and approval. These rules are based on narrow interpretations of the CTR and restrict the system's ability to adapt quickly—particularly in areas such as timelines and the submission of substantial modifications. Moreover, digital solutions across Europe are often developed in silos, with varying levels of maturity and limited interoperability. This fragmented

approach slows down progress, complicates integration with EU-wide platforms like CTIS and EUDAMED, and undermines efforts to create a seamless, efficient regulatory environment for clinical research.
Impact: Rather than supporting the implementation of the CTR, CTIS is effectively dictating it, hindering the agility needed at this stage of the regulation's evolution. This rigidity is increasing the resource burden on both sponsors and authorities, compromising operational efficiency across the ecosystem.
In addition, the fragmented digital landscape across Europe—where systems are developed in isolation, progress at different speeds, and lack consistent maturity—further compounds the issue. The lack of interoperability between national systems and EU-level platforms disrupts data flows, slows down decision-making, and leads to inefficiencies and inconsistencies in trial oversight and execution.
Option(s): Accelerate implementation of CTIS simplification proposals, particularly those aimed at easing business rules that currently limit system flexibility, enabling interoperability with other systems, such as EUDAMED.
Allow MSs to roll back CTIS decisions where appropriate, introducing needed flexibility in regulatory processes.
Build on the success of the safety module by developing additional modules (e.g. a product module, communication module) to support the concept of simplification and adaptability.
Enable easy downloading of approvals and approved document versions to support both EU and third-country inspections, improving oversight and operational transparency.
In addition, launch a resourced and funded project to develop digital systems that support modern clinical research, including (but not only) cloud-based platforms, interoperable data flows and required support for dynamic regulatory reviews and reliance-based approaches.

ESTABLISH CLEAR AND FLEXIBLE COMMUNICATION ROUTES

Issue: Under the CTR and CTIS, sponsors lack direct contact with assessors and are unable to clarify RFIs or other questions related to the CTA. This includes situations where clarification prior to submission—especially on potential conditional approvals—would prevent unnecessary delays or confusion. Currently, communication must go through generic National Competent Authority (NCA) email inboxes, often requiring a minimum of 24 hours for a response—even as the 12-day response deadline continues to count down. As a result, the opportunity for meaningful dialogue is very limited.
Impact: Unclear RFIs often cannot be adequately resolved, leading to incomplete or insufficient responses that may not satisfy assessors. This can result in conditional approvals, even when the issues could have been easily addressed by the sponsor or principal investigator with direct clarification. Ultimately, this lack of communication leads to approval delays and a lengthier process.
Option(s): Amend the CTR to establish a direct communication channel allowing sponsors or investigators to contact ethics or NCA assessors. NCA contact points should be able to provide timely responses and, where necessary, connect the sponsor with the appropriate assessor to resolve technical or scientific questions efficiently. Also, explore options for a dedicated "communication module" within CTIS to facilitate structured, real-time exchanges between sponsors and assessors, particularly for clarifying RFIs and addressing potential conditions prior to submission.

2. Enhancing Efficiency of Assessments and Approvals

MOVE TOWARDS PRODUCT BASED TRIAL SUBMISSIONS: CROSS-REFERENCE AND RELIANCE ON APPROVED DOCUMENTATION

Issue: Under the current submission model, sponsors must file a separate application for each clinical trial, including a full set of documents—even when the same Investigational Medicinal Product (IMP) and associated safety and quality documents have already been submitted for another trial in the region. Key documents like the IB and IMPD are re-submitted repeatedly, despite being applicable across multiple trials for the same product, and any modifications need to be submitted trial by trial. Moreover, each submission

is reviewed independently by different MSs, leading to inconsistent feedback and assessments regarding benefit-risk and quality, and revealing a lack of harmonisation.

Impact: This approach results in duplicative submissions, fragmented reviews, and redundant document maintenance, often producing divergent outcomes for the same product. It risks having parallel trials operating under different document versions, creating inefficiencies for both sponsors and NCAs. Despite the CTR referencing cross-referencing mechanisms, the full potential of this provision has not been realised in its implementation.

Option(s): The following proposals support a shift toward a Core Dossier model, enabling product-based trial submissions. This approach would transform trial review processes, embed reliance on prior assessments, and reduce duplication. The concept has been discussed with the CTCG and other stakeholders, who have shown interest and openness to its adoption.

- Single Portal Submission (Article 5(1)): Clarify procedures for submitting core documents through a unified portal and explore integration with other EMA systems.
- Reinforce Reliance Mechanisms: Article 4: Enable European Commission review of Part I (Article 4), ensure all concerned MSs (cMS) jointly review (Article 6), restrict reassessment by additional MSs for already approved core documents (Article 14) and consider implementing acts for Quality-assessing MS (qaMS) for quality documents, IB-assessing MS (IBaMS) for IBs, building on the Safety-assessing MS (saMS) model
- Substantial Modifications (Article 18, Q&A Q3.5): Amend to allow updates to core documents that would automatically apply across all related trials, eliminating the need for multiple identical SMs.
- CTIS Enhancements: Update business rules to allow cross-referencing of previously approved documents and remove blocking mechanisms that prevent submissions when another SM is ongoing.
- Ethics Review (Part II): Explore a central “core” ethics review, with national-specific adaptations, based on reliance or coordination led by an rMS.
- Combined Clinical Trials Coordination: Implement an “All-in-One” submission and assessment pathway, inspired by COMBINE Project 1, to integrate clinical trials with clinical investigations and performance studies. Ensure coordination of ethics committees and notified bodies within this framework. Minimise fragmentation, streamline processes, and reduce duplication.

CONVERGENCE OF REGULATORY PATHWAYS FOR RESEARCH APPROVALS (medicine, device/diagnostic, radioprotection, GMO etc).

Issue: Clinical research involving investigational medicinal products (IMPs), in vitro diagnostics (IVDs), medical devices (MDs), genetically modified organisms (GMOs), and radioprotection (etc.) is subject to multiple, often disconnected regulatory pathways, each with distinct timelines, requirements, and systems. The interaction between the various legislative texts (e.g. CTR, IVDR, MDR) is interpreted differently across MSs, leading to inconsistent application and a fragmented regulatory environment.

Impact: This lack of convergence creates a confusing, inefficient, and delayed approval process for developers, particularly when conducting integrated or combined trials. The need to navigate separate systems with varying timelines significantly slows down research progress and creates additional administrative burden, undermining the EU’s attractiveness as a destination for complex, multi-disciplinary clinical research.

Option(s): Establish an overarching requirement that all regulatory approvals linked to a clinical trial involving an IMP be processed within the same timeframe and submitted through CTIS. This would create a single-entry point for developers, enabling parallel feedback and coordinated outcomes from all relevant authorities via a “one-stop shop” model.

Create a “regulatory orchestrator” for clinical trials involving integrated solutions. This body would enable cross-disciplinary scientific exchange, coordinate the review and decision-making across all domains (e.g. medicine, device, diagnostic, GMO, radioprotection) and act as a central oversight mechanism for harmonised interpretation and dispute resolution.

In particular, at the interface between CTR, IVDR, and MDR, establish a single, integrated accountable body tasked with ensuring harmonised, science-based interpretations of regulatory requirements, resolution disputes, overseeing Notified Bodies (NBs) to promote consistency, enhancing coordination between medicines and MD/CDx pathways and providing integrated scientific and regulatory advice for combined trials involving medicinal products, integrated device-drug combination (iDDC) products, and IVDs.
Simplify procedural touchpoints across the regulatory framework to make it easier for all innovators—academic, industrial, or public sector—to navigate EU requirements. This would help attract R&I investment that leverages the EU's existing expertise, infrastructure, and scientific excellence.

EXPEDITING ASSESSMENT REVIEWS TIMELINES

Issue: Although the EU Clinical Trials Regulation (CTR) defines maximum timelines, Member States (MSs) often default to using the full time allowed to assess and decide on applications. For example, the CTR permits an additional 50 days for the assessment of advanced therapy medicinal products (ATMPs) and other biotechnology products "for the purpose of consulting with experts." However, some MSs apply this extension systematically, rather than as an exception. In addition, when sponsors respond faster than required during specific steps of the process (e.g., responding to RFIs), the time saved is not carried forward, but instead added to the next phase for MSs—resulting in no net gain in overall timeline.
Impact: Because maximum timelines are routinely applied, average CTA approval timelines in the EU now exceed 110 days, compared to 30–60 days in other global regions. *(Please note that timelines vary across MSs and for therapeutic areas).* This significantly affects the EU's competitiveness. In global multi-country trials, delays in EU approvals may lead to fewer European patients participating due to earlier enrolment in other regions.
For ATMPs, the inconsistent and automatic addition of 50 days to the timeline further discourages innovation by making Europe a less attractive region for advanced therapies.
The absence of a clear process to request expedited reviews gives the impression that the EU is slow and unresponsive, particularly in areas of high public health interest.
Option(s): Shorten timelines in the CTR, establishing a 60-day maximum for CTA approval. This would be feasible if reliance on the rMS is effectively implemented. Specific streamlining opportunities include reducing rMS confirmation and validation to a combined 15-day maximum (Article 5), limiting concerned MS (cMS) assessment to 30 days (Articles 6 & 7) and requiring decisions within 1 day of the reporting date or assessment conclusion (Article 8). Also, consider developing and promoting EU-level fast-track procedures for priority studies.
Introduce Key Performance Indicators (KPIs) to encourage MSs to complete reviews within 60 days, a globally competitive benchmark. MSs should make every effort to expedite reviews, including avoiding unnecessary delays, such as the 5-day buffer in Article 8(1) and issuing decisions promptly once assessments are complete.
Amend Article 6(7) to restrict automatic use of timeline extensions for ATMPs and other regulated products under Annex 1 of Regulation (EC) No 726/2004.
Legislate flexible criteria for expedited review eligibility. This could include designations such as PRIME status, Orphan Drug Designation (ODD), Public health emergencies, Paediatric or other high public health benefit studies.

APPLY RISK PROPORTIONALITY AND RISK BASED APPROACHES

Issue: The low-interventional trial concept under the CTR does not enable a truly risk-based approach to trial review and conduct. Its only practical benefit is reduced requirements for insurance coverage. In practice, sponsors are still required to submit the same volume of documentation and are frequently met with a high number of RFIs—comparable to those in standard interventional trials.
Impact: The regulatory burden of CTA submission and review is disproportionate to the actual risk posed to patients. The CTR does not differentiate between trials using market-authorised IMPs) and higher-risk investigational products, treating all trials uniformly. This undermines efficiency and creates unnecessary

administrative load for both sponsors and authorities as well as investigators running these types of studies. Lower-risk trials, particularly those involving well-characterised, authorised products, should be evaluated through a streamlined process and conducted in a risk-proportionate way.

Option(s): Integrate risk categorisation into the CTR, aligning with the OECD framework. This should include reduced documentation requirements for low-risk trials, simplified or limited review pathways and consideration to exempt lowest-risk trials from NCAs involvement entirely. Allow minor updates to any documentation to be submitted as NSMs, with the sponsor responsible for determining the level of significance.

Amend and clarify legislation: adapt Recitals (11) and (12) and Article 2(3) and introduce a new definition establishing categories of risk-based trial types.

Apply the risk-based approach also to combined clinical trials and clinical investigations/performance studies (CI/PS) involving low-risk MDs or IVDs:

- Enable a proportionate and streamlined submission process, reducing regulatory burden on sponsors, NCAs, and Ethics Committees.
- Clarify acceptance of MDs/IVDs approved in other jurisdictions for use in medicinal product clinical trials, to facilitate innovation and access.
- Remove Performance Study Application (PSA) requirements for CE-marked IVDs used according to their intended purpose; in these cases, ethical concerns around sampling procedures should be addressed by Ethics Committees, not IVD regulatory authorities.

3. Clarifying Roles and Responsibilities

DEFINE AND ALIGN ROLES AND RESPONSIBILITIES OF ETHICS COMMITTEES AND NATIONAL COMPETENT AUTHORITIES

Issue: The roles and responsibilities of regulatory authorities and Ethics Committees are not standardised across EU Member States. This inconsistency leads to divergent practices in how clinical trial applications are reviewed, contributing to inefficiencies and confusion for sponsors.

Impact: The lack of harmonised delineation between regulatory and Ethics bodies increases procedural challenges. Sponsors must navigate varied requirements and review practices in each Member State, increasing the administrative burden and compromising the consistency, efficiency, and predictability of the clinical trial approval process. This goes against the spirit of the CTR.

Option(s): Standardise/clearly delineate the responsibilities of regulatory authorities and Ethics Committees during the application review process. Successful examples of this are the Swiss and UK systems where the remit of review for each body is clearly defined (either in legislation or via Memorandum of Understanding).

More centralisation and coordination of regulatory and ethics bodies' review both at national and European level is required, including mandatory use of standardised pan-EU templates to provide consistency and predictability on submission expectations and assessment outcomes.

Accelerate alignment of ethical requirements through the MedEthicsEU initiative, with closer oversight and support from the European Commission. Importantly, ensure that the work of Ethics Committee members is financially supported and should not rely on voluntary time commitment in certain MS.

Encourage pilot projects based on best practice models (e.g. Denmark, Belgium), where Ethics Committees are actively seeking to improve their processes. These pilots could form the basis for collaborative frameworks supporting faster and more reliable Part II assessments.

Propose a clarifying annex to Article 4 of the CTR, which would provide detailed delineation of the responsibilities of NCAs (for Part I assessment) and ethics committees (for Part II), ensure that Part I and Part II reviews remain distinct but coordinated, with limited overlap and mandate that RFIs resulting from overlapping assessments be raised jointly to prevent duplication and inefficiency.

4. Fostering Innovation

ENABLING INNOVATIVE TRIAL DESIGNS, METHODS, AND TECHNOLOGIES (e.g. platform trials, decentralised trials, digital endpoints)

Issue: Since the CTR was adopted in 2014, clinical research methodologies have evolved significantly. There is a growing need to review the CTR for potential roadblocks to innovative trial designs and technologies—while maintaining enough regulatory flexibility to accommodate future innovations and ensure the framework remains future-proof.

One of the challenges is the lack of clarity around the regulatory status and requirements for Digital Health Technologies (DHTs)—particularly when digital endpoints are included in trial design during early-stage development. Depending on the DHT's intended purpose and function, different EU legislative frameworks and authorities may apply, creating uncertainty for developers.

Impact: Sponsors and developers face significant uncertainty in navigating the regulatory landscape for novel trial designs, technologies, and methods. There is a lack of consistent, clear guidance on how innovative approaches—such as decentralised models, platform protocols, or digital endpoints—will be assessed and accepted by Competent Authorities and Ethics Committees. Requirements often vary from one Member State to another, leading to inconsistent expectations and application outcomes.

This inconsistency extends to the site level, where uptake and operational readiness for implementing innovative methods can differ greatly. As a result, sponsors struggle to design and execute trials that are both regulatory-compliant and operationally feasible across multiple jurisdictions.

Option(s): Review and amend the CTR and associated guidance to remove structural and interpretative barriers to innovative trial designs, methods, and technologies. Specific attention should be given to enabling flexible implementation of platform trials, decentralised trials, and digital endpoints within a harmonised framework.

Launch a sandbox or (regulatory) incubator initiative, where novel trial designs and digital innovations can be safely tested in real-world conditions. This environment would allow early engagement with key stakeholders, enabling joint exploration and resolution of regulatory uncertainties. Lessons learned from these pilots should be systematically gathered, analysed, and shared publicly, with a view to improving transparency, promoting adoption, and ensuring alignment across the EU. At the same time, ensure that outcomes from the sandbox / incubator initiatives feed into the ongoing update of regulatory guidance and best practice documents, making the system more responsive and better equipped to handle emerging methodologies.

Conduct a dedicated pilot program—co-led by EMA (ACT EU) and interested Member States (possibly via a public-private partnership like IHI)—to support adaptive and platform trial designs, clarify regulatory expectations for DHTs and digital endpoints and promote harmonised decision-making across Competent Authorities and Ethics Committees.

Provide fit-for-purpose regulatory criteria for DHTs, especially in early development stages, to avoid requiring CE marking prematurely.

2) Accelerating Site Activation and Operational Readiness

ACCELERATE SITE ACTIVATION FOR CLINICAL TRIALS

Issue: The process of setting up clinical trial sites in Europe is often slow and fragmented, involving multiple administrative, legal, and operational steps that differ across institutions and countries. Contract negotiations, ethics approvals, staff training, and logistics (like equipment, IT access, and data systems) frequently occur in a sequential rather than parallel fashion, causing unnecessary delays. Moreover, many hospitals lack dedicated research support teams, and standard operating procedures (SOPs) are either absent or inconsistent.

Impact: These delays significantly hinder the ability to initiate trials quickly, especially in time-sensitive areas like oncology, infectious diseases, or rare conditions. Sponsors may deprioritise certain regions due to long timelines, resulting in fewer trials and reduced access for patients. For sites that do participate, sluggish start-up can affect recruitment targets, budget timelines, and trial viability, ultimately undermining Europe's attractiveness as a destination for cutting-edge research.
Option(s): Accelerating site readiness requires a combination of standardisation, proactive planning, and dedicated resources. Creating EU-level or national templates for contracts and SOPs, investing in site readiness programs, and promoting pre-approved trial networks or research-ready hospitals can dramatically reduce timelines. Parallel processing of legal, ethical, and operational steps—supported by digital tools—can further speed up activation. Strengthening partnerships between sponsors, CROs, and hospital research offices, and ensuring research is recognised as a priority within clinical settings, are also key to sustainable improvements.

BUILDING HIGH-PERFORMING CLINICAL TRIAL NETWORKS AND CENTERS OF EXCELLENCE

Issue: Europe currently lacks a cohesive network of interconnected, high-performing clinical trial sites, accessible to both commercial and non-commercial sponsors. Trial infrastructure remains fragmented, with limited coordination between hospitals, research centers, and Member States. Access to sites is inconsistent, and many centres operate without shared standards, centralised onboarding processes, or sustainable funding.
Moreover, few sites are designated as centres of excellence or specialisation, and when such designations exist, they are not uniformly recognised or integrated across borders. The absence of single points of entry, centralised contracting, or joint ethics review further slows down trial implementation and limits scalability—especially in cross-border or multicentre studies.
Impact: This fragmentation delays site selection and trial start-up, particularly in complex or specialised trials (e.g., rare diseases, paediatrics, oncology, advanced therapies). It limits patient access to innovative treatments, especially in regions outside traditional trial hubs. Also, it undermines the EU's ability to rapidly launch large-scale, coordinated trials, which is critical for pandemic preparedness and health security (i.e. we should build on COVID-19 lessons learnt). It discourages commercial sponsors, who may deprioritise Europe in favour of countries with faster and more streamlined networks (e.g., the US, UK).
Option(s): Establish interconnected clinical trial networks across Member States with a single point of entry for sponsors, centralised ethics approval and contracting and a common infrastructure standards and procedures.
Promote and fund the development of centres of excellence and specialisation, ensuring they are visible, interoperable, and open to both commercial and non-commercial research.
Support the creation and maintenance of "ever-warm" clinical trial networks—infrastructure that remains continuously prepared to initiate trials rapidly, regardless of therapeutic area or sponsor type.
Ensure clinical research is embedded as a strategic priority within national healthcare systems, with networks sustainably resourced, not reliant on fragmented project-based funding.
Actively engage industry as a partner in building and sustaining high-performing networks, leveraging its ability to bring trials, co-invest in infrastructure, and support network maturation.
Facilitate real-time knowledge exchange across centres, especially those working on innovative trial designs (e.g. platform, decentralised, adaptive).
Integrate these networks into broader EU health preparedness frameworks, recognising them as critical infrastructure for clinical response in pandemics and public health emergencies.

3) Supporting People's Awareness, Understanding, and Engagement in Life Sciences

1. Improving Awareness and Understanding of Clinical Trials

IMPROVING AWARENESS, TRAINING, AND ENGAGEMENT IN CLINICAL TRIALS

Issue: Despite the vital role clinical trials play in advancing medicine, public awareness and understanding of clinical research remain low. Many patients are unaware of trials as a care option or misunderstand what participation entails. Similarly, healthcare professionals often receive limited training on the conduct of clinical research, patient communication about trials, or how to integrate trials into their practice. This lack of research literacy affects both demand (patient interest) and supply (professional engagement).

Impact: As a result, clinical trials often suffer from slow recruitment, low diversity, and unequal geographic access. Patients who might benefit from innovative treatments may never hear about trials, while clinicians may lack confidence or time to refer them. This not only delays research but also contributes to health inequities, as certain populations remain underrepresented in evidence generation. The disconnect between research and routine care limits Europe's ability to leverage its full patient and provider base.

Option(s): Raising awareness and building research capacity requires coordinated investment in education, training, and communication. For the public, this means trusted, transparent information campaigns, co-developed with patients, that demystify trials and promote informed decision-making. For healthcare professionals, clinical research should be embedded in medical education, with ongoing training and professional recognition of research roles. Creating a culture that values research as part of care, and supports professionals with time, tools, and incentives, will be key to bridging the gap between trials and the real world.

Linking electronic health data in the EHDS with recruiting trials in the EMA trial map system would enable physicians to be alerted to possible trials that match their patient's diagnosis. This could then be discussed with the patient as part of the overall treatment concept, benefitting patients as well as accelerating trial recruitment in Europe. Furthermore, certain interfaces with local and national repositories should be considered to provide a more comprehensive set of relevant information and to make more effective use of the data available in EMA's trial maps.

2. Enhancing Access to Clinical Trials

ENABLE EASIER CROSS-BORDER ACCESS TO TRIALS

Issue: Patients and healthcare professionals across Europe face significant challenges when attempting to access clinical trials in another EU country. This is especially problematic for rare and paediatric diseases, where patients often need to travel to specialised hospitals or clinicians that may not be available in their home country.

Despite the importance of cross-border trial access, the current Directive on cross-border healthcare (2011/24/EU) does not address clinical trial participation. As a result, European patients are not guaranteed access to trials outside their country of residence, even when no suitable options exist domestically.

Impact: The absence of a dedicated EU legal framework for cross-border clinical trial participation means that each case must be negotiated individually, often requiring substantial administrative, logistical, and financial effort by both patients and investigators. This not only limits access to potentially life-saving treatments but also discourages sponsors from conducting trials in Europe for conditions with small, hard-to-reach patient populations.

To address this, EFPIA and EFGCP launched the EU-X-CT initiative in 2023 (*Borders Should No Longer Be Barriers*), a multi-stakeholder collaboration aimed at enabling cross-border access to clinical trials. The initiative has drafted a set of high-level recommendations, currently under public review, that could serve as practical guidance for all actors involved in allowing cross-border trial participation.

Facilitating this access would encourage more European-based trials for rare diseases, paediatrics, and advanced therapies (such as ATMPs and gene therapies), and improve patient equity and research inclusivity.

Option(s): Firstly, support from the European Commission for the EU-X-CT initiative and its multi-stakeholder recommendations is essential. This support could include explicit reference to cross-border trial access in upcoming legislation, such as the proposed Biotech Act.
Secondly, issue EU-level guidance to clarify the application of existing laws and provide direction for patients and healthcare professionals, sponsors and investigators, Ethics Committees, liability insurers and healthcare providers. The EU-X-CT recommendations could serve as a strong basis for such guidance. Given the current legal vacuum, this is a matter of urgency.
Thirdly, identify the best legislative pathway to formally regulate cross-border access to clinical trials – and begin the process of writing legislation, whether that means revising the Cross-Border Healthcare Directive (2011/24/EU) or consider including relevant provisions within the Biotech Act or a new legislative instrument.

EMBED CLINICAL TRIALS INTO MEDICAL CARE

Issue: Embedding clinical trials into routine medical care is hindered by fragmented healthcare and research systems, regulatory complexity, and a lack of interoperable infrastructure. Hospitals often lack the dedicated resources—staff, funding, and digital tools—needed to support trials alongside daily care delivery. Regulatory and administrative burdens, despite reforms like the Clinical Trials Regulation, remain significant and inconsistently applied across EU Member States.
Impact: This fragmentation limits patient access to innovative therapies and delays evidence generation in real-world clinical environments. As a result, clinical trials are often concentrated in select academic centers, excluding many patients—especially those from rural or underserved areas. The lack of integration also slows the adoption of new, evidence-based practices into routine care, reducing health system responsiveness and contributing to inequities in care quality and outcomes across Europe.
Option(s): To address these challenges, Europe must invest in creating a research-enabling environment across all healthcare settings. This includes funding dedicated trial infrastructure in hospitals, simplifying administrative procedures, and developing interoperable IT systems that support both care and research. Europe could introduce a KPI to increase the percentage of patients that participate in clinical trials from medical care to aim to increase the current approximate 4% and target 10%. The overview on all clinical trials in EU in EMA's trial map offers a unique advantage and opportunity to match EU patient's data in the EHDS with potential trials in their vicinity. Finally, strengthening EU-wide collaboration and shared learning among Member States, including building on good practice examples will be essential to make trials more accessible, efficient, and impactful.

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