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ACT EU multi-stakeholder platform annual meeting

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Contents

Introduction

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Collaboration and innovation are key to improving the clinical trials environment in the European Union (EU)/European Economic Aera (EEA). This is recognised by the Accelerating Clinical Trials in the EU (ACT EU) initiative, which, through its multi-stakeholder platform (MSP), aims to foster dialogue and strengthen engagement between stakeholders to transform the clinical trial landscape in the EU and achieve the vision of better, faster and more optimised clinical trials for EU citizens.

Such transformation entails both challenges and opportunities, and it is vital for stakeholders to adapt, learn, and evolve within this new landscape. ACT EU brings stakeholders together in an optimal environment to support the transformation of clinical trials in Europe.

Over the last decade, the relative number of clinical trials conducted in the EU has declined and a quantum leap is required to reverse this trend. The commitment and efforts of the European authorities to ensure the effective implementation of the Clinical Trials Regulation (CTR) and realise the potential of ACT EU are tangible and the long-awaited MSP is a clear sign of progress made. However, the current European clinical trial environment is still not competitive enough when compared to other global regions, and this affects both patients and industry.

As stated in the recent report "The future of European competitiveness" led by Mr. Mario Draghi, former European Central Bank President, who was tasked by the European Commission to prepare a report of his personal vision on the future of European competitiveness, "*regulators should aim to boost the attractiveness of the EU for conducting clinical trials and to expedite access to markets for novel medicines*". Additionally, the report "Much more than a market", written by Mr. Enrico Letta, former President of the Council of Ministers of the Italian Republic and Secretary of the Democratic Party, recognises that "*an effective regulatory framework for conducting clinical trials is essential for the competitiveness of the most innovation-intensive aspects of the EU's pharmaceuticals sector*" and that "*regulatory differences between Member States pose a significant challenge in this regard*".

It is therefore a crucial time for the EU and the health sector. The opportunities represented by the upcoming reform of the EU pharmaceutical legislation and the biotech act foreseen by the EC should encourage Member States to examine/scrutinise the current state of the national and EU clinical trial landscape, and lead the transformation of clinical trials in Europe by reducing divergencies in requirements between Member States and barriers to innovation, attracting investments and retaining talents.

National Competent Authorities (NCAs) are aware of the barriers and challenges stakeholders face when conducting clinical trials in Europe. There is a strong commitment to providing greater flexibility and adapting the system to address these challenges, ensuring the successful transformation of clinical trials across the region.

Through ACT EU, the European Medicines Agency (EMA), the EC and the Heads of Medicines Agencies (HMA), together with key stakeholders (patients, academia, industry, healthcare professionals and funders), can realise the shared vision of delivering a better and more competitive clinical trial environment in the EU.

Session 1

Looking back - Overview of ACT EU delivery to date

Moderators: Peter Arlett (EMA), Marianne Lunzer (AGES, CTCG)

Key messages

- ACT EU has already delivered important achievements, including support for the CTR implementation, by increasing transparency through publication of clinical trial information via the Clinical Trials Information System (CTIS), enhancing support for non-commercial sponsors and strengthening the dialogue between stakeholders, regulators and ethics committees.
- Consolidated advice pilots aim to further streamline clinical trial processes by enhancing the collaboration between regulators, leading to harmonised advice and improved applications.
- The establishment of the multi-stakeholder platform advisory group (MSP AG) enables a defined process to fill the gap between regulators and stakeholders.
- Among the key priorities identified by the MSP AG are: the effective implementation of the CTR, necessitating enhanced coordination and harmonisation of best practices among NCAs and ethics committees; the resolution of interface challenges with other relevant regulations (i.e. *in-vitro* diagnostics [IVDR] AND medical devices [MDR] regulations); and the simplification and increase of flexibility of clinical trial processes (including assessment timelines), reduction of operational barriers, streamlining of CTIS and enabling of risk-based approaches.

ACT EU update: the journey so far

Since its inception, the ACT EU initiative supports stakeholder groups across the clinical trials environment. Key deliverables of the programme include a mapping of the clinical trial landscape defining different responsible parties in the clinical trial, support of CTR implementation via regular consultation with CTIS users through tailored surveys, sharing information on transitional requirements, and ensuring monthly measurement of KPIs.

Equally significant is the support for non-commercial sponsors developed in cooperation with the Clinical Trials Coordination Group (CTCG). This collaboration has resulted in the creation of an interactive map outlining important initiatives of Member States and the establishment of a dedicated regulatory helpdesk for CTR- and CTIS-related matters.

Additional key focus areas of the programme are the support provided to the modernisation of Good Clinical Practice (GCP) with the International Council for Harmonisation (ICH) E6 revision, the enhancement of clinical trial data access and analysis, the alignment of clinical trial methodology guidance and the development of training materials.

The improvement of clinical trial processes during public health emergencies and the promotion of collaboration and harmonisation between stakeholders are also important activities within the workplan. All these activities are delivered through multi-stakeholder engagement, where possible.

Consolidated advice on clinical trials

Two pilots on consolidated advice on clinical trials, launched in June 2024, aim to increase harmonisation of the scientific advice and of technical, regulatory advice by promoting collaboration across the European medicines regulatory network (EMRN).

The consolidated scientific advice pilot coordinated between EMA's Scientific Advice Working Party (SAWP) and the CTCG supports sponsors and applicants in preparing and submitting marketing authorisation and/or clinical trial applications in the EU/EEA. The pre-clinical trial application (CTA) pilot, coordinated by CTCG, offers consolidated technical and regulatory advice on CTA dossiers prior to submission into CTIS. Future collaboration with ethics committees could be envisaged to further enhance harmonisation.

These pilots represent a valuable opportunity to further strengthen dialogue, ensure consistency in decision-making, and streamline the processes. Practical benefits for applicants include early validation opportunities and targeted guidance on combined studies involving medical devices.

New CTIS transparency rules: from policy to reality

The revised CTIS transparency rules facilitate earlier publication of key documents and structured data of clinical trials. The availability of lay summaries of trial results also contributes to improve availability of essential information to the general public, including a diverse and heterogeneous patient population. This level of transparency enables health care professionals and patients to make informed decisions when participating in studies or stay up to date on the results of specific studies. The level of openness achieved so far has fostered greater trust and engagement in clinical research, reflecting the tangible benefits of enhanced transparency.

The MSP Advisory Group and stakeholder feedback

Stakeholder representatives of ACT EU's MSP AG enable a broadly inclusive mechanism facilitating the dialogue between stakeholders (i.e. patients/consumers, healthcare professionals, academia, funders, industry EU trade organisations), regulators and ethics committees. As part of the MSP AG activities, a survey on stakeholder challenges and priorities was conducted. By jointly discussing key priorities and challenges, the platform aims to help identify solutions that can contribute to a more competitive clinical trial ecosystem and the timely availability of better and fairer treatments for patients across the EU.

Among the priorities identified, the MSP AG raises as critical the implementation of the CTR, which calls for increased coordination and harmonisation of best practices among NCAs and ethics committees, and addressing the interface challenges with the IVDR and MDR. The Advisory Group also highlighted fundamental challenges that need to be addressed, such as the simplification and flexibility of clinical trial processes, including assessment timelines, reducing operational barriers, simplification of CTIS, and enabling risk-based approaches, as well as building training capacity and education, safeguarding sustainability of clinical trial funding mechanisms, promoting multinational trials, and encouraging greater global harmonisation and standardisation of decision-making processes. Additionally, stimulating early regulatory interaction, supporting the use of innovative designs and real-world data, and facilitating the use of standard EU templates are important points to be addressed.

The sense of urgency in addressing the issues presented here, and the need to leverage the full potential of the MSP AG to collectively address them, is fully acknowledged. he development of the revised ACT EU workplan, setting priorities for the next couple of years, will be informed by the stakeholder priorities identified.

The achievements presented, as well as those planned to be delivered in the near future, underline the commitment of the ACT EU initiative to continue building a streamlined, innovative and resilient clinical trials environment that meets the diverse needs of the research community.

Session 2

The current landscape for clinical trials in Europe - ACT EU and beyond

Moderators: Isabelle Clamou (EC), Stan van Belkum (HMA, CCMO)

Key messages

- CTR implementation metrics show progress with increased submission rates for initial and transitioning applications. Nevertheless, metrics in regions such as the United States (US) and China are growing more rapidly, leading to a decrease in EEA's global share of trials.
- Initiatives like CTR Collaborate and COMBINE, as well as cooperation with MedEthicsEU and CTAG, are working to improve the trial approval process and trial design, harmonise best practices, streamline the interface between legislations and enhance patient involvement. These activities are a foundation, but further efforts are essential to effectively tackle the pressing challenges within the EU clinical trials environment, with further work needed to achieve true harmonisation, patient-centric approaches and a future proof EU trial ecosystem.
- The ACT EU initiative and MSP are essential channels to promote dialogue and cooperation between all stakeholders, regulators and ethics committees.
- Patient-centricity and meaningful patient involvement in clinical trials development/design remain key priorities. Achieving this requires harmonisation, embedding clinical research in healthcare systems, prioritising quality over quantity in measuring success, and ensuring flexibility, proportionality and pragmatism (e.g. in oncology and rare diseases), alongside robust training and leveraging of opportunities offered by artificial intelligence and emerging technologies.

Summary of presentation and panel discussion

What do the numbers tell us?

In the clinical trial ecosystem, monitoring trends is essential for understanding the performance of established systems. Current metrics on the implementation of the CTR show stable submission rates for initial applications and an upward trend for transitioning applications.

Recent months have shown a temporary decline in multinational trial submissions, which might be due to developers focusing their efforts on transitioning applications to the CTR. However, signs of recovery are evident as more trials are transitioning to the CTR.

According to a recently published report by industry stakeholders, the global clinical trials ecosystem is generally evolving, with the US and China experiencing significant growth. In contrast, Europe has seen a relative decline in its global share of trials over the past decade. Moreover, the number of participants enrolled in clinical trials in the EU/EEA has decreased, diverging from global trends of growth. These findings underscore the need for Europe to address challenges in trial approval, setup and recruitment to maintain competitiveness and ensure clinical trials are distributed evenly across the region.

Analysis of the metrics allows for a better understanding of Europe's evolving role in the global clinical trials landscape and can inform relevant legislative and regulatory actions (such as investing in innovation and clinical trials attractiveness) that can foster a more robust ecosystem.

Exploring the dynamics of partner collaboration with ACT EU

ACT EU collaborates with key partner initiatives, such as the CTCG-led CTR Collaborate , the European Commission led COMBINE project, and work done with the MedEthicsEU group and the Clinical Trials Coordination and Advisory group (CTAG), in an effort to tackle challenges and enhance the clinical trial environment in the EU.

The CTR Collaborate initiative promotes faster and better clinical trials in Europe by fostering trust, collaboration and a shared understanding between NCAs and ethics committees. Through workshops (such as the recent multi-stakeholder event on key priorities) and the assessor round table meetings, CTR Collaborate facilitates discussions on operational aspects of the CTR.

Patient centricity in clinical trials continues to be a key area of focus for stakeholders, regulators and ethics committees. This is reflected in the recent initiative launched by the CTCG to promote patient involvement in clinical trial design. Together with key stakeholders' groups, the initiative aims at establishing a mechanism to increase patient participation in the entire clinical trial lifecycle, including the design stages.

Ensuring a harmonised approach to the implementation of the CTR between NCAs and the European Commission is a key priority reflected in the CTAG activities.

MedEthicsEU, a group of national representatives of medical research ethics committees in the EU/EEA, was launched in February 2024, following agreement reached during the ACT EU multi-stakeholder platform meeting (22-23 June 2023). The creation of this group recognises the need for a discussion platform to promote more integrated reviews of clinical trials and to align and promote best practices among ethics committees and across Member States. To enable true alignment, MedEthicsEU contributes to other initiatives such as CTR collaborate, COMBINE and the ACT EU priority action on clinical trials in public health emergencies.

COMBINE, launched in June 2023, is another initiative to address the regulatory complexities of combined studies involving medicinal products, medical devices and *in vitro* diagnostics. The first phase of the project involved extensive stakeholder collaboration to analyse the problem and identify potential solutions. The results of this analysis, including the recommendations and next steps, are available in the published report. COMBINE is now working on a dedicated programme to implement the identified recommendations.

Stakeholders welcome the initiatives and activities presented, as well as the progress made, particularly in providing support to ensure cooperation, streamline and harmonise procedures and facilitate the interface between legislative frameworks. The current activities and initiatives are regarded as a foundation, but further efforts are essential to effectively tackle the pressing challenges within the EU clinical trials environment. A patient-centred approach to clinical trial development and meaningful patient involvement across the clinical trials ecosystem must remain priorities. To achieve these goals, the focus should be on true harmonisation, embedding clinical research in healthcare systems and prioritising quality over quantity in measuring success. The need for flexibility, proportionality and pragmatism, where appropriate (such as, for example, in oncology and rare diseases) is critical, alongside the development of robust

training programmes. Additionally, leveraging the opportunities offered by artificial intelligence and emerging technologies must be integral to future activities.

It is essential to avoid working in silos and to continue promoting the collaborative dialogue between stakeholders, regulators and ethics committees through the ACT EU MSP to sustain progress and drive meaningful change in the EU clinical trial landscape.

Session 3

A brighter future for clinical trials in the EU: continuing the journey

Moderators: Martin O'Kane (EFPIA), Anton Ussi (EATRIS), Amelia Hursey (Parkinson's Europe), Tarec El-Galaly (EHA)

Key messages

- Establishing Europe as a competitive and attractive region is the shared vision of all stakeholders, and the political discussion at the level of the European Commission confirms clinical research and clinical trials as key priorities.
- Once all current foundational blockers are resolved, quality of life, accessibility and sustainability should be the main targets for innovative trials in Europe.
- The global clinical trials ecosystem needs to be included in the European debate, with appropriate metrics to monitor progress and inform legislative/regulatory changes.
- Open dialogue and cooperation between all stakeholders and relevant regulatory authorities is the main enabler for change.
- The importance of addressing existing challenges before focusing on new areas was emphasised. Harmonisation, simplification and flexibility for specific therapeutic areas (e.g. oncology, rare diseases) are identified as key priorities.

Summary of key presentations and panel discussion

The EU's political drive for clinical trials

Establishing Europe as an attractive region for clinical trials is politically important, and the support to clinical research is an integral part of the current and future agenda of the European Commission. Ongoing initiatives and programmes, such as Horizon scanning, EU4Health, ACT EU, the reform of the EU pharmaceutical legislation and the upcoming biotech act, are expected to further strengthen the EU clinical trial ecosystem, as reflected in the political agenda of the new commission and recommended in the Draghi and Letta reports mentioned in the introduction.

Beyond the political discussion, it is clear that establishing Europe as a competitive region is pivotal for patients and stakeholders. A key benefit for all citizens is that an attractive trial ecosystem will promote investment in Europe, leading to job creation and increased wealth.

Addressing stakeholders' challenges – what's next

The feedback received from stakeholder consultations through the CTR survey, input from the MSP AG and CTR Collaborate confirms the need for critical improvements to the current processes and systems, in order to realise the vision of Europe as a hub for innovative and attractive research and clinical trials.

Significant priorities for stakeholders include fully addressing the challenges posed by the implementation of the CTR, including streamlining the legislative interface with MDR and IVDR), providing adequate support for investigator-initiated trials and creating a welcoming environment for novel methodological approaches and innovation. These challenges were prioritised by stakeholders based on urgency, with the expectation that the most urgent issues will be addressed within 12 months or whenever possible. These priorities will be further analysed by the regulators and, where possible, integrated, in a timely manner, into the activities of ACT EU, CTR Collaborate, CTAG and MedEthicsEU in accordance with their respective mandates.

It is important to note that substantial problems beyond the CTR also require attention. In particular, the legal contract work between sites and between countries in Europe, including data sharing and collaboration agreements, can significantly hinder progress, sometimes even more so than trial regulations themselves. Increased regulatory attention is needed in this area. In this context, regulation is needed which allows for the development and promotion of overarching standard contract drafts that are widely accepted, while still allowing for necessary changes under exceptional circumstances. The current process of contract negotiation is a substantial burden for investigators and adds significant cost.

Stakeholders stress the importance of first resolving current challenges before focusing attention on other areas. The need to harmonise, simplify and allow flexibility for certain therapeutic areas (e.g. oncology, rare diseases) are flagged as key pillars.

According to stakeholders, it is time to focus on meaningful, diverse and inclusive trials that enable all patients across the EU, including traditionally underserved/underrepresented populations, to contribute to clinical research and benefit from innovative medicines. The key to success lies in better designed trials, harnessing innovation opportunities of pragmatic trials and building sustainable patterns and funding. All of these priorities can only be addressed by further strengthening the dialogue and cooperation between all stakeholders.

WHO global guidance for more effective and equitable clinical trials

The World Health Organization (WHO) guidance for best practices for clinical trials provides an overview of key scientific and ethical considerations and best practices that can strengthen the global clinical trials ecosystem. International cooperation is another important aspect that needs to be included into the European debate in order to overcome design barriers and ensure stronger clinical research ecosystems via monitoring, evaluation and learnings. Also in this case, collaboration and engagement among stakeholders is key.

In terms of what characterises a welcoming clinical trial environment, all stakeholders believe in the need for a cultural shift which should build on the simplification and capacity already captured in the ACT EU programme. This shift should aim to remove barriers, leverage European expertise to focus on more complex trials, achieve fit-for-purpose innovation and develop a strategy that considers patient participation, diagnostic aspects and healthcare

sustainability. A key element of this cultural shift should be a focus on minimising research waste by designing robust trials that generate high-quality evidence to inform decision-making.

The formation of dedicated focus groups within the MSP where all stakeholders can work on concrete solutions, with a focus on quality rather than quantity, is a suggestion widely supported by stakeholders.

Successfully embedding clinical research as part of healthcare

One of the elements that contributes to the success of clinical trials is their integration into the healthcare system. In this context, Spain has been at the forefront of embedding clinical trials in the clinical setting and recognising the importance of a robust national health system, patient involvement, ethics and transparency.

When looking to the future and identifying determinants for success, overcoming the aforementioned challenges posed by legislative changes is seen a necessary step enabling efficiency, harmonisation, simplification and improved timelines.

Global benchmarking is suggested to address "real society" needs, including ensuring accessibility to innovative, effective and evidence-based medicines to all patients, including those with rare conditions, and sustainability of the health systems across Europe.

From the theory to the practice, how will we measure success?

Monitoring and measuring the clinical trials environment are critical to understand the impact of ACT EU and associated initiatives. Key metrics for evaluation should include measuring EU attractiveness, timely/faster access to treatments, impact of clinical trials.

The proposed measures are expected to provide tangible benchmarks for assessing progress and refining strategies in the EU clinical trial ecosystem.

Stakeholders highlighted additional metrics and points for reflection, such as the focus on patient experience, measuring the impact of clinical trials on quality of life and measuring academic research.

Furthermore, stakeholders emphasised the importance of looking beyond the quantity of trials to the quality of the evidence generated, and specifically whether the trial is able to answer the research question and inform a public health or regulatory decision.

Closing remarks

Maria Jesús Lamas (AEMPS), Denis Lacombe (EORTC)

The discussions highlighted the significant progress made through ACT EU and its partner initiatives, including support for CTR implementation, the development of the CTIS system, and increased transparency of data and documents. The establishment of MedEthicsEU and the ongoing pilots for scientific advice have contributed to improved harmonisation across Europe. These advancements represent critical steps in creating a more cohesive, efficient, and patient-centered clinical trials ecosystem.

However, as the challenges reported by stakeholders indicate, work remains to fully address the issues of simplification, capacity building, and harmonisation. The feedback received highlights the need for a more streamlined and pragmatic approach to clinical trial processes, ensuring that the evolving regulatory framework supports the diverse needs of different therapeutic areas, such as oncology and rare diseases.

The shift from focusing on the quantity of trials to prioritising the quality of evidence remains a central cultural change needed to create a more welcoming and effective clinical trials environment in Europe. This transition is vital for ensuring that clinical trials generate meaningful insights that contribute to better patient outcomes.

The multi-stakeholder platform (MSP) continues to serve as an essential vehicle for open dialogue, bringing together a wide range of perspectives to drive meaningful change. The feedback gathered from stakeholders will be integrated into the ACT EU workplan and other relevant initiatives, allowing for the continued refinement of the clinical trials framework.

In summary, while challenges persist, the progress made through ACT EU and its partner initiatives signals a positive trajectory. The ongoing collaboration between stakeholders provides a strong foundation for the further evolution of the clinical trials landscape in Europe, with the ultimate goal of creating a more efficient, harmonised, and patient-centered system.

Glossary

ACT EU	Accelerating Clinical Trials in the EU
AEMPS	Agencia Española de Medicamentos y Productos Sanitarios
AGES	Austrian Agency for Health and Food Safety
CCMO	Central Committee on research Involving Human Subjects
CTA	Clinical trial application
CTAG	Clinical Trials Coordination and Advisory Group
CTCG	Clinical Trials Coordination Group
CTIS	Clinical Trials Information System
CTR	Clinical trials regulation
EATRIS	European infrastructure for translational medicine
EC	European Commission
EEA	European Economic Area
EFPIA	European Federation of Pharmaceutical Industries and Associations
EHA	European Haematology Association
EMA	European Medicines Agency
EMRN	European medicines regulatory network
EORTC	European Organisation for Research and Treatment of Cancer
EU	European Union
GCP	Good Clinical Practices
HMA	Heads of Medicines Agencies
IVDR	In-Vitro Diagnostics Regulation
MDR	Medical devices regulation
MSP	Multi-stakeholder platform
MSP AG	Multi-stakeholder platform Advisory Group
NCA	National Competent Authority
SAWP	Scientific Advice Working Patry
US	United States
WHO	World Health Organisation

More information

The Accelerating Clinical Trials in the EU (ACT EU) initiative aims to develop the European Union further as a competitive centre for innovative clinical research. ACT EU seeks to deliver on the clinical trial innovation recommendations of the European medicines agencies network strategy and the European Commission's Pharmaceutical strategy for Europe.

ACT EU builds on the Clinical Trials Regulation (CTR) and Clinical Trials Information System (CTIS) launched on 31 January 2022. The European Commission, EMA and Heads of Medicines Agencies launched ACT EU in January 2022 and run the initiative together, establishing a steering group in March 2022. The programme's strategy paper features dedicated priority action (PA) areas that are the basis for the ACT EU workplan. The updated workplan highlights ACT EU's areas of focus over the next two years, reflecting the feedback received through the Multi-Stakeholder Platform (MSP) advisory group and other channels:

- The operation of the Clinical Trials Regulation.
- Maximising the impact of clinical trials.
- Clinical trials in public health emergencies.
- Clinical trial analytics, training and communication remain integral to ACT EU's work, interlinked with all other activities. The workplan also outlines the fundamental role of ACT EU regulatory partners involved in clinical trials, working together to improve the landscape for clinical research in the European Union. The workplan is reviewed on a regular basis and revised to better address stakeholder priorities, as identified by the MSP Advisory Group.

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