15 November 2023
EMA/75374/2023

Accelerating Clinical Trials in the EU (ACT EU): Priority areas for possible EU-level funding to support the transformation of the European clinical trials environment.

The purpose of this paper is to identify areas of work under ACT EU that could be proposed to receive EU funding according to the governance of the respective EU funds that could be mobilised (HORIZON EUROPE, EU4Health; etc.) and the relevant European Research Partnerships established with EU Member States and other stakeholders under Horizon Europe.

Executive summary

The European Commission (EC), Heads of Medicines Agencies (HMA),and the European Medicines Agency (EMA) agreed, in the margins of the ACT EU 2022 annual meeting, that to achieve the objectives of ACT EU, some degree of additional EU public funding complementing national mechanisms would be required. An analysis of funding opportunities within the programme was therefore undertaken to identify those areas which could most benefit from such funding.

These areas cover: Supporting academic sponsors conduct of multinational clinical trials, and Delivering a clinical trials data analytics research agenda.

The ACT EU Steering Group (ACT EU SG) agreed at its September 2023 meeting that these two areas should be supported by adequate funding to enable their realisation, and deliver benefits for EU public health. Different approaches to funding should be considered subject to the state of play of each initiative, the duration of the support needs, the nature of the support required and the lead-times for securing financial support. Based on these considerations the ACT EU SG agreed that the support to non-commercial sponsors, and the delivery of a clinical trials data analytics research agenda should be considered for EU-level funding programmes and the relevant European Research Partnerships established with EU Member States and other stakeholders under Horizon Europe.

These proposals will need to follow the procedures set in place for requesting and/or applying for funding via the appropriate funds and programmes in question.

Background

ACT EU is the EU clinical trials transformation initiative launched in January 2022 by European Commission (EC), Heads of Medicines Agencies (HMA) and the European Medicines Agency (EMA). The initiative, which builds on the momentum of the Clinical Trials Regulation (EU) 536/2014 and Clinical Trials Information System (CTIS), aims to deliver on the recommendations of the European Medicines Regulatory Network (EMRN) strategy to 2025 and the European Commission's Pharmaceutical strategy for Europe to foster innovation in clinical trials.

To deliver on these recommendations, ACT EU has a number of objectives which aim to optimise the EU environment for clinical research (see Annex I). To establish ACT EU and its objectives, ten key priorities for 2022-2026 were initially identified (see Annex II), which are the backbone for the delivery of the programme benefits. An additional priority action to address the fast set up and initiation of adequately sized, multinational clinical trials in the context of public health emergencies has since been agreed.

One of the key principles for ACT EU is to leverage external initiatives including networks, funding mechanisms, communications, etc. To date, ACT EU has been supported exclusively through matrix working of experts of its founding organisations with some programme management and meeting support from EMA. However, it is understood that to fully realise the potential benefits of ACT EU, external funding will be required for some of the actions. It is also acknowledged that in order to catalyse the transformation of the EU clinical trials environment a limited number of high impact priorities should be identified, which could be put forward for consideration by EU-level funding programmes and other funding mechanisms.

The type of funding needed will depend on the state of play of each initiative, the duration of the support needs, the nature of the support required and the lead-times for securing funding.

In response to this, the activities within the ACT EU priority actions have been reviewed to identify those areas where funding could make a substantial positive impact in changing the EU clinical trials environment. These areas are described in the following sections.

Supporting academic sponsors conduct of multinational clinical trials

The current environment for clinical trials is challenging, however, Europe has an extensive healthcare infrastructure able to support clinical research, with a high level of academic medicine. About 40%[1] of clinical trials are sponsored by academia, often small and nearly all mono-national and about 60% by pharmaceutical industry.

Recent events including the COVID-19 pandemic have demonstrated a relative absence of EU impactful multi-state trials and analysis of clinical trial applications continues to show registration of a preponderance of small single member state studies. There is an opportunity to reverse this trend by boosting support to non-commercial sponsors to conduct multi-national clinical trials. This opportunity is mirrored in the Clinical Trials Regulation (EU) No 536/2014, which states that "…. *experience also shows that a large proportion of clinical trials are conducted by non-commercial sponsors. Non-*

[1] EudraCT data between 2005-2020

commercial sponsors frequently rely on funding which comes partly or entirely from public funds or charities. In order to maximise the valuable contribution of such non-commercial sponsors and to further stimulate their research but without compromising the quality of clinical trials, measures should be taken by Member States to encourage clinical trials conducted by those sponsors". Additionally, the need for funding was strongly and repeatedly expressed by diverse stakeholders during the Multi-stakeholder platform (MSP) kick-off workshop on 22-23 June 2023.

Throughout the lifecycle of a clinical trial there are numerous areas where academic sponsors benefit, or could benefit, from support; below are some examples:

- During trial preparation
    - coordination of funding and support navigating EU research infrastructure,
    - identification of collaborators,
    - support for investigator-directed activities (site visits, investigator trainings),
    - access to data to analyse feasibility of study design,
    - regulatory, contractual and ethics requirements support,
    - scientific support e.g. protocol writing and methodological design,
    - waiver of fees e.g. for scientific advice
- During trial conduct
    - regulatory support for CTIS submissions and ethics committee interactions,
    - support for pro-active management of the ongoing trial,
    - monitoring,
    - support for results reporting
    - adverse event reporting,
    - support for recruitment and retention, clinical services, data collection,
    - support for inspection fees, scientific advice fees.

There are multiple EU funded initiatives and organisations at EU level supporting academic sponsors, such as ECRIN, the European Clinical Research Infrastructure Network that supports the conduct of multinational clinical trials in Europe and EATRIS, the European Infrastructure for Translational Medicine. Other initiatives include the STARS (Strengthening Training of Academia in Regulatory Science) project, now concluded, with a number of Strategic recommendations from the STARS project to foster academic drug development.

To foster impactful clinical trials in the academic setting, long-term support services across the EU, to complement those delivered by stakeholders such as ECRIN and EATRIS, must be improved. ACT EU could deliver on this ambition by developing a scheme, which together with existing initiatives, national support mechanisms for non-commercial clinical trials the EMA Academia Collaboration Matrix and the EU-IN activity, will bolster clinical research in this field.

The extent and long-term nature of the support needed by academics across the EU, makes this area a suitable candidate for *ad hoc* mechanisms to leverage funding available at EU and at MS level.

Delivering a clinical trials data analytics research agenda

To optimally design, set up, run, and report on clinical trials, we need to understand which clinical trial designs are successful. This includes success in terms of recruitment, approval, and generation of quality data, but also success in the support of marketing authorisation decisions and support of down-stream decision-makers such as HTA bodies and payers. Currently, the planning and design of individual clinical trials is not informed by a profound understanding of historical clinical trial experience. Furthermore, taking a broader view than just design, there are other gaps in knowledge which could similarly be addressed by having a more complete view of historical experience. This was recognised by patients and consumer representatives during the Multi-stakeholder platform (MSP) kick-off workshop on 22-23 June 2023, where repeated and explicit calls were made for better use and sharing of data on clinical trials.

Therefore, an ACT EU multi-stakeholder workshop is being planned in the first quarter of 2024 to identify gaps in knowledge which could be addressed by access to data, data analytics, and funding. The workshop will collect a broad set of use cases from stakeholders. The workshop will also inform stakeholders of data standardisation efforts as part of ICH M11, and gather needs to maximise opportunities offered by access to structured data. The outcome of the workshop will be collated into a research agenda which could be delivered through competitive funding calls. Delivering the research agenda would demonstrate the public health and innovation business case of clinical trial data analytics and create a shared focus for Network and stakeholder research efforts.

Examples of research projects/topics that might benefit from funding:

- Linking clinical trial design with the outcome of marketing authorisation applications.
- EU projects to develop, track, and validate innovative clinical trial methods (including complex CT and DCT).
- Elaborating the methodology behind clinical trial safety monitoring, establishing scientifically sound foundations.
- Projects that fill evidence gaps for treatment/clinically relevant questions for European public health priorities e.g., Beating Cancer.
- The development of a clinical trials dashboard to present information on EU clinical trials, building on but not limited to data from CTIS.

The extent and long-term nature of the support needed to deliver a clinical trials data analytics research agenda, makes this area a suitable candidate for *ad hoc* mechanisms to leverage funding available at EU and at MS level.

Conclusion and next steps

Two areas have been identified as having significant potential for positive impact on the European clinical trials environment, which if adequately funded, would contribute to fostering the development of new and innovative medicines, from the early phases of clinical research all the way to the patient. These are: supporting academic sponsors to conduct multi-national clinical trials and delivering a clinical trials data analytics research agenda.

Following feedback from the ACT EU Steering Group, next steps will include elaboration of the proposals based on a mapping of existing funding mechanisms and further engagement with potential funding programmes managed by the European Commission and the relevant European Research Partnerships established with EU Member States and other stakeholders under Horizon Europe.

Annex I

ACT EU objectives

1. Optimise the EU environment for clinical research in Europe, whilst maintaining high-level participant protection, data robustness and transparency, by:
    a. Strengthening leadership and coordination on clinical trial authorisation and execution.
    b. Optimising ethical oversight and further integrate ethics committees into the clinical trial and medicines regulatory lifecycle.
    c. Supporting the conduct of large-scale multinational clinical trials with broader geographical scope.
    d. Reducing administrative burden and increasing efficiency.

2. Strengthening clinical trials that deliver decisional evidence for unmet medical needs, rare diseases, and on vaccines and therapeutics for public health crises and pandemics, ensuring support for HTA bodies as well as for academic and SME sponsors.

3. Heighten the impact of European clinical trials through excellent and coordinated scientific advice as a complement to trial authorisation and to support marketing authorisation and access throughout the medicine lifecycle.

4. Engage all stakeholders to proactively deliver inclusive patient-oriented medicines development and delivery across populations.

5. Ensure a clear and unified European position on clinical trials in strategic matters at the international level.

6. Build capacity in all aspects of drug development and regulatory science through, amongst others, research collaboration and training with academia.

Annex II

ACT EU Priority actions

1. Map existing initiatives and develop a governance rationalisation strategy (aligning different expert groups and working parties in the EMRN and ethics infrastructure).
2. The successful and timely implementation of the CTR and its implementing acts.
    - Develop KPIs and dashboard to track performance of the European clinical trials environment.
    - Including the promotion of larger, multinational trials, specifically in the academic setting.
3. Establish a multi-stakeholder platform, including patients, after stakeholder analysis.
4. Implementing the GCP modernisation informed by the development of guidance at ICH.
5. Analyse clinical trial data leveraging academic, non-profit, European, and international initiatives, improving the impact of policymaking and funding on research outputs to support evidence-based decision making.
6. Plan and launch a targeted communication campaign to engage all enablers (including data protection experts, academia, SMEs, funders, HTA bodies, healthcare professionals).
7. Reinforce the coordination between scientific advice on CT approval and CT design and link to the methodologies working party domain.
8. Develop and publish key methodologies guidance e.g., on AI/ML impacted CTs, complex trials, decentralised CTs and IVDR/CTR interface (to strengthen links between innovation and scientific advice fora).
9. Successfully establish CT safety monitoring and bridge to the EU4Health Joint Action and start its integration into a pre- and post-marketing safety monitoring framework.
10. Deliver a clinical trials training curriculum including modules on drug development and regulatory science with links to universities and SMEs (serving as an educational 'ecosystem').