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Exploratory analysis on funding to support academic sponsors conduct multi-national clinical trials

1. Problem statement

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 (non-commercial sponsors), however these trials are often small and nearly all mono-national.

The vision of the European regulators is to place the EU at the forefront of a patient-centred clinical trials, including non-commercial ones. Non-commercial trials are central for changing practice, improving standards of care, in public health emergencies when immediate action is needed, and as a complement to clinical trials conducted by commercial sponsors.

2. Background

Through the ACT EU Steering Group, the European Commission services (EC), Heads of Medicines Agencies (HMA), and the European Medicines Agency (EMA) agreed that to achieve the objectives of ACT EU, additional EU funding to support non-commercial sponsors, complementing national mechanisms, is required. See: ACT EU priority areas for possible EU-level funding (europa.eu)

This paper provides proposals for areas for EU-level funding which could further complement already existing financial support under Horizon Europe or EU4Health projects in addition to national funding. The results of the mapping of support to investigator initiated clinical trials undertaken by the ERA4Health partnership, has been taken into consideration in the drafting of this proposal, as has the output of the STARS project.

This proposal does not imply any commitment to the final content of either the Horizon Europe or ERA4Health work programmes, nor of the EU4Health Work Programme.

During the development of these proposals, the ACT EU Multi-stakeholder advisory group (MSP AG) was consulted to identify the most critical areas for supporting non-commercial sponsors conduct multi-national clinical trials, and to highlight any significant gaps in the proposals (see annex 1 for further detail). The MSP AG broadly agreed with the proposals; encouraging clinical research network development and collaboration was identified as the most critical area which could benefit from funding. This aligns closely with the ideas emerging during the development of this paper.

[1] EudraCT data between 2005-2020

The ACT EU workplan and associated network initiatives will address additional areas of importance identified by stakeholders.

3. Funding needs

A shortlist of concrete proposals is presented below:

3.1. Development of a Member State Network of national helpdesks

i ***Problem statement***: The provision of national support to non-commercial sponsors is known to be heterogeneous across the EU, and often not at the same level as the support available to commercial sponsors. To better understand the landscape a survey by the CTCG was conducted in 2023. The survey revealed different degrees of support ranging from very limited to broad offerings covering among others, scientific advice, helpdesk support, dedicated webpages, regulatory and ethics requirements support or CTIS submissions support among others. Analysis indicates highly heterogenous support across NCAs. To enable the conduct of multi-national trials in the academic setting across the whole expanse of the EU, NCAs need to be better equipped to support these sponsors, benefitting from the good practice found in some MSs.

ii ***Proposal***: Development of a capability and capacity building project based on twinning to incentivise the expansion of existing support structures within NCAs, leading to the creation of a network of national helpdesks. The project would envisage a cooperation mechanism between NCAs that have more developed non-commercial support offering to help upgrade those NCAs that are less advanced, by offering training activities and sharing of best practices. Links with the network of Horizon Europe National Contact Points that provide information about EU-funding should be explored.

iii ***Benefits***:

- A network of national helpdesks would enable informal early communication with academia within each NCA;
- A network of national helpdesks would enable robust, consistent and high quality support to academic sponsors across the EU, facilitating the conduct of more multi-national clinical trials;
- A network of national helpdesks could help bridge the gap between national support infrastructure to more European support;
- A network of national helpdesks would enable the creation of a well-trained taskforce to support the training of non-commercial sponsors in regulatory science;
- A network of national helpdesks would foster long-term relationships between NCAs.

3.2. "Train the trainer" regulatory science training programmes for academia

i ***Problem statement***: Progressing projects into clinical development is often challenging for academic drug researchers, in part owing to a lack of knowledge regarding regulatory requirements and skills for navigating the regulatory system. As part of the STARS surveys academic researchers identified that support available from local organisations such as research centres or innovation hubs are the most important and practical source of information, rather than the support provided by NCAs.

Building on the STARS outputs, and as part of the ACT EU priority action developing a clinical trials training curriculum, an analysis of training needs for academia is currently under development. Following the completion and the dissemination of the analysis to relevant stakeholder groups, we expect that it will be leveraged by other initiatives and entities/organisations inside or outside of the European Regulatory Network (EMRN) for the support and development of future training/guidance for academics in the area of clinical trials.

ii ***Proposal***: Development of a "train the trainer" programme where European regulatory agencies support national academia actively offering training activities to local organisations such as research centres or innovation hubs, which can in turn provide support to local academic researchers. A "train the trainer" programme anchored at the NCA level would benefit from being anchored within a network of national helpdesks. It should be noted, however, that training initiatives are already in place across a number of Member states. Proposals should take into consideration existing initiatives in order to avoid duplication.

iii ***Benefits***:

- NCAs could facilitate the exchange of training experts and materials among the participants and establish collaborations;
- Harmonisation of activities and networking across NCAs would enable sharing and continuous updating of tools and resources, thus enabling academia training capacity and sustainability in the future;
- The training network could be integrated with the activities of ACT EU (academia regulatory helpdesk development and development of CT training curriculum), and facilitate bidirectional exchanges on academic training needs and availabilities;
- The "train the trainers" concept would facilitate outreach to a wider target, especially where an expertise centre for consultations at universities is established, which could support further dissemination of information;
- Enable academics to better engage with the European Medicines Regulatory Network after gaining better knowledge of regulatory requirements and new methodologies/guidance in order to generate and collect reliable and robust data which are fit for regulatory decisions/licensing submissions;
- Increased awareness and use of regulatory support tools.

3.3. Encouraging clinical research network development and collaboration

i ***Problem statement***: A lot of effort needs to be invested for starting up a clinical trial. The challenge is exacerbated by the fact that many academic clinical researchers conduct a single clinical trial in their career, as a qualification exercise, constituting a lost opportunity for the European clinical research ecosystem. Having clinical research networks that are running trials all the time can be useful. They are particularly needed for being able to react quickly with testing of interventions in case of a public health emergency. The idea is to pivot ongoing trials within an active clinical research network towards trials addressing the public health emergency when it occurs.

Disease-specific investigator networks to facilitate collaboration, capacity building, and recruitment at the investigator level, together with disease-agnostic clinical trial unit (CTU) networks to support single sponsors with operational aspects can help build up a clinical research workforce that is continually involved in trials and in care, for advancement of clinical studies and European public health.

Apart from the need to create and/or strengthen such networks, feedback from stakeholders indicates that there is a lack of awareness of existing multinational clinical research networks, how to join them, and what they have to offer.

ii ***Proposal***: Supporting collaborative European networks of clinical researchers with healthcare professionals, where gaps in coordination of clinical research exist, with the aim to facilitate the development of new drugs and other interventions, optimise their use and build capacity for the implementation of multinational clinical trials. Taking inspiration from the Collaborative Network for European Clinical Trials in Children (conect4children) and the European Clinical Research Alliance on Infectious Diseases (ECRAID), sustainable, integrated European networks, clustered by therapeutic areas or major public health topics, could support the delivery of efficient and swift clinical trials across all conditions and phases of the drug development process, partly through enhancing collaboration with specialist and national networks. Where relevant, such networks could support the response to public health emergencies by pivoting ongoing (platform-)trials to testing interventions addressing the emergency.

iii ***Benefits***:

- Contribute to the efficient implementation of trials, adopting consistent approaches, aligned quality standards and coordination of sites at national and international level;
- Facilitate EU collaborations with specialist and national networks;
- Creation of an ever-warm clinical research workforce;
- Promote education and training;
- Contribute to clinical research on a larger scale by bringing together different stakeholders;
- Within the always active clinical research networks just mentioned one would expect that the different functions for carrying out clinical trials are well developed.

3.4. Development of a standard site agreement and other templates

i ***Problem statement:*** Site agreement negotiations between the trial sponsor and sites, and translations into local languages, represent a major bottleneck for academic research. This operational constraint has a negative impact on the start of a clinical trial, which is exacerbated in the case of a public health emergency. Other contracting arrangements also pose issues for non-commercial sponsors, such as setting up agreements with commercial sponsors, material transfer agreements (MTA), data ownership agreements or Freedom-to-Operate (FTO) analysis.

ii ***Proposal:*** funding for the development of a project to create a suite of templates with standard clauses to address diverse contracting requirements. Work packages could include a pan-European site agreement template, allowing for electronic signature for all parties, and translation into all European languages; standard clauses for contracting with commercial sponsors, MTA standard clauses, data ownership templates and FTO analysis templates.

Under ACT EU, work is ongoing to prepare the European clinical trials environment to implement an expedited, harmonized authorization procedure that allows for timely start, and flexible conduct of multi-national, impactful clinical trials during public health emergencies for rapid deployment of medical counter measures. As part of this activity, consideration is being given to the development of templates for site agreement with the trial sponsors and for biological sample agreements on material transfer. Proposals should therefore take into account any outputs from this activity.

iii ***Benefits***:

- Reduction in time between clinical trial approval and first patient entered into the study, ultimately reducing overall time to complete study;
- Improved use of resources with academic institutions, contributing to a renewed mindset regarding multistate research;
- Common understanding of what is being shared (e.g. data, biological materials) facilitating faster set up of clinical trials, in particular in public health emergencies;
- Increased data sharing maximizing transparency and public accountability.

4. Considerations for leveraging existing infrastructure services

There remains a need to provide additional support for carrying out clinical trials by academic sponsors. The European research infrastructure ECRIN was created with this in mind. It is supported by 13 countries including two non-EU Member States, thus missing out on a large section of Europe. In some instances, there is support at national, regional or institutional level. The level of support is variable, with only a few organisations able to provide the full range of services. A mapping of support to investigator initiated clinical trials has been undertaken by the ERA4Health partnership. One should consider leveraging existing services in the best possible manner. There might also be scope to coming up with new types/structures to support academic

sponsors of clinical trials. Key demands for new tools to be created are that they build on existing structures as much as possible to avoid duplication and wasting of precious resources. The set up must be as light as possible and avoid unnecessary bureaucracy. New ways of carrying out medical research through the use of health data (with the European Health Data Space legislation on the final stretch of being adopted), and new trial methodologies must be considered in such an exercise.

5. Recommendations

These proposals are put forward to EU research policy makers, including the Commission, for consideration for funding programmes. These target the strengthening of clinical research networks and infrastructure support, developing a Member State Network of national helpdesks, EU-wide regulatory science programmes, and pan-European standard site agreement templates.

Annex I - MSP AG consultation participants

- Cancer Patients Europe
- CoLAB TRIALS
- European Academy of Neurology (EAN)
- European Association of Nuclear Medicine (EANM)
- European Clinical Research Infrastructure Network (ECRIN)
- European Federation of Pharmaceutical Industries and Associations (EFPIA)
- European Haematology Association (EHA)
- European infrastructure for translational medicine (EATRIS)
- European Network of Excellence for Paediatric Research (TEDDY)
- European Organisation for Research and Treatment of Cancer (EORTC)
- Innovative Health Initiative Joint Undertaking (IHI JU)
- KKS Network, KKSN/ KKS-Netzwerk e. V.
- Parkinson's Europe
- University Medical Center Utrecht
- Vaccines Europe

Other respondents

- Innovative Therapies for Children and Adolescents with Cancer (ITCC)
- University of Evora