Meeting highlights – ACT EU Multi-stakeholder Platform Advisory Group

26 June 2025, 09:30-13:30 (CEST), Webex

Co-Chairs: Maria Jesús Lamas (Regulatory co-chair), Denis Lacombe (Stakeholder co-chair)

1. Opening of the meeting

The co-chairs welcomed participants to the Multi-stakeholder Platform Advisory Group (MSP AG) meeting highlighting the key achievements reached since its launch in 2024 (i.e. identification of 14 key priorities focussing on improving efficiencies and better refining the request for information process and the role of member states). The importance of a legislative framework which enables public health oriented clinical trials was reinforced, noting that this is not presently the case. The need to reduce approval timelines, increase the number of clinical trials, and ensure these remain impactful was stressed.
Due to the co-chairs concurrent availability during the meeting, a representative of the MSP AG secretariat co-chaired the session to ensure continuity throughout.
Through the work of the MSP the main factors representing bottlenecks to clinical trial environment are being recognised and possible solutions discussed.

The agenda and membership updates were briefly presented.

Links to presentations and meeting agenda.

2. Risk-based approached in clinical trials

2.1 Presentation on LICT/ flexible safety reporting

Acknowledging the improvement already brought by the Clinical Trial Regulation (CTR), cases where a broader approach for low-intervention clinical trials (LICT) and flexible safety reporting were presented. In this context the guidance issued by the Danish Medicines Agency (DKMA) on flexible safety reporting was pointed out. The need for a harmonised risk-adapted approach to safety reporting in addition to CTR interpretation harmonisation and production of evidence-based practice with reduced administrative burden for LICT were emphasized.
The importance of clinical expertise in the assessment of the low intervention status, including the evaluation of minimal risk seen in the context of normal clinical practice, were highlighted as critical elements.

2.2 Presentation of OECD framework

OECD Council Recommendation on the Governance of Clinical Trials framework aiming at promoting risk-based and international harmonisation of regulatory approaches to reduce complexities and enhance trials approvals were presented. The presentation highlighted approval frameworks in other

jurisdictions where a simplified approaches involving only ethics approval is taken for non-registration trials i.e. non-IND (US) and non-chiken (Japan). The difference in risk categorisation between the CTR (2 categories) and OECD framework (3 categories) was noted as a factor to be addressed for alignment with other regulatory frameworks.

2.3 Update on revision of the March 2024 Recommendation paper on the use of Auxiliary Medicinal Products (AxMP) in Clinical Trials

The steps undertaken by the Clinical Trials Coordination Group (CTCG) to align the Recommendation paper on the use of Auxiliary Medicinal Products in Clinical Trials with relevant provisions of the CTR were outlined. The feedback provided by commercial and non-commercial sponsors represented in the MSP AG was considered key and represented an example of effective cooperation between regulators and stakeholders.

An important proposal in the paper is that the standard of care as background treatment is considered an AxMP if the standard of care is not modified as part of the clinical trial; this is also applicable for situation where there is no placebo as a comparator in the reference group and the standard of care is the only comparator. Further clarifications on standard of care as background treatment are provided in the paper, with additional simplification proposed on safety reporting.

The MSP AG was informed that, pending the endorsement of CTCG and Clinical Trials Coordination and Advisory Group (CTAG), the paper is expected to be published on Eudralex Volume 10. Guidance for ongoing trials will also be provided.

Q&A session

The MSP AG reached consensus that a pragmatic, risk-based approach to clinical trial oversight should build on existing successful frameworks rather than creating new systems from scratch. The OECD framework was recognised as a solid starting point for this discussion, offering alignment with practices already established in countries such as the US, UK, Japan, and Switzerland.

One key area of agreement was the potential to replace the full Clinical Trial Application (CTA) approval process for low-risk (OECD Category A) trials with a streamlined notification procedure via the Clinical Trials Information System (CTIS). This would require submission of a declaration confirming the risk classification and evidence of ethics committee approval, although such approval is not required by the National Competent Authorities (NCAs).

For Category B trials, the MSP AG supported the introduction of simplified dossiers with less complex protocols and more limited review by National Competent Authorities (NCAs). For high-risk (Category C) trials, it was suggested that NCAs could rely on prior knowledge—either from within their own agency based on previous assessments or from trusted international regulators—to inform their evaluations.

It was emphasised that risk proportionality should apply throughout the full clinical trial spectrum, rather than being limited to low-intervention clinical trials (LICTs) in the post-authorisation phase. This includes drawing on prior knowledge and adopting proportionate approaches to oversight and safety reporting, principles already reflected in ICH E8(R1) and ICH E6(R3). Risk-proportionality to enable a regulatory focus on higher-risk studies was supported.

The group also discussed practical implementation challenges. Although many academic trials do not qualify as LICTs, the primary benefit of risk-adapted approaches—particularly simplified safety reporting—was recognised by academic stakeholders. However, it was noted that many academic sponsors conduct few trials in their careers and may lack the expertise to implement risk adaptations effectively. To address this, a straightforward tool such as a checklist was proposed to guide protocol development and risk assessment decisions.

Simplification of the trial dossier was identified as feasible within the current legal framework, provided that documentation remains aligned with CTR requirements. However, responsibility lies with sponsors to ensure protocol quality and provide appropriate justification for any proposed risk adaptations.
Related discussions included the role of pragmatic trial designs, their definitions, and the use of real-world data to inform regulatory decision-making. The group expressed interest in further exploring the acceptability of pragmatic elements and corresponding risk adaptations in clinical trial conduct, potentially through a dedicated workshop.
In this context, participants discussed the importance of clearly defining the key areas to be addressed in a forthcoming workshop on risk-based approaches. This could include support for the ongoing revision of the 2017 recommendation paper on risk-proportionate approaches in clinical trials. There was broad agreement on the urgency of updating relevant guidance, ensuring effective trial oversight across all risk categories, and leveraging prior regulatory knowledge to increase efficiency and facilitate reliance among authorities.
The current Clinical Trials Regulation (CTR) framework was seen as providing a solid foundation for risk-based adaptations. However, it was acknowledged that the established CTR timelines—designed to support coordinated multinational assessments—can sometimes obscure the fact that risk-based assessment is already occurring. Challenges remain in accelerating timelines for individual trials due to a lack of coordination tools. While there was no clear consensus on the need to accelerate timelines for LICTs using authorised products, it was agreed that faster timelines are particularly critical in early-phase trials to improve Europe's global competitiveness. Nevertheless, the MSP AG concluded that this issue should be treated separately from the risk-based approach discussion.
To further examine these topics, the MSP AG supported the establishment of a dedicated focus group to analyse practical experiences using real-world case studies. The findings would inform the upcoming workshop and feed into the revision of the 2017 guidance document.
Lastly, the Clinical Trials Coordination Group (CTCG) informed the MSP AG that the Danish guidance referenced during the meeting had already been incorporated into the CTCG's Questions & Answers on safety-related matters, updating Section 7 of the Commission's Q&A on safety in Eudralex Volume 10 (link). Ensuring broad dissemination of such updates was seen as critical—particularly to ensure that academic sponsors are well informed and aware of the flexibilities already available to them under the CTR.

Actions arising:

- MSP AG secretariat to define scope and objective of focus group and launch call for nominations (action taken).

3. Update on Public Health Emergencies (PHEs)

3.1 Update from Emergency Task Force (ETF)

An update was provided on the scientific advice procedure for clinical trials authorisations under the remit of the ETF targeted to specific pathogens during preparedness phase or during declared emergency situations. The process ensures interlinks and harmonisation with clinical trial experts from national competent authority and ethics assessors (from the Public Health Emergency Ethics Advisory Group (PHE EAG)).

The importance of applicants providing the required information during the IRIS application process was stressed. This information includes the identification of the pathogen and a declared emergency, the identification of the relevant member states, and advice for clinical trial authorisations. This ensures the involvement of all relevant member states and ethics committees.

3.2 Update from ACT EU Priority Action on Clinical Trials in PHEs

The MSP AG was provided with an update on the activities linked to managing clinical trials in PHEs, confirming the establishment of the PHE EAG which is expected to strengthen the collaboration between ethics committees and regulators during scientific advice procedures.

The group was also updated on the ongoing activities relating to the simplification of the clinical trial application (CTA) package and on the drafting of a guideline on regulatory flexibilities for the conduct of clinical trials during PHEs, for which a public consultation is planned at the end of the year.

Related information: Report of the Joint ETF - ACT EU PA on CTs in Public Health Emergencies Workshop (November 2024)

Q&A session

The MSP AG welcomed the developments presented, in particular the establishment of a central EAG. The group expressed interest in further exploring ethical considerations—such as those related to human challenge studies—and in drawing lessons from the ETF-PHE EAG experience. In this context, the importance of building experience through collaborative discussions on both scientific and ethical aspects of complex trial designs was underlined. There was hope that sponsors would soon submit scientific advice applications, enabling practical engagement on these issues.
It was clarified that the initiatives being explored under ACT EU and with the ETF are, at this stage, intended for exceptional circumstances arising from a public health emergency (PHE), where rapid actions and procedural simplifications are essential to expedite trial approval. However, the need to develop mechanisms for triggering faster, simplified approaches even before the formal declaration of a PHE was recognised as an important area for further consideration.

4. Update on stakeholder initiatives / proposals

4.1 Pilot programmes for innovative designs and co - partnership models

A proposal of launching 2 pilot programmes to enhance the adoption of innovative clinical trial designs and co-sponsorship models, especially in paediatric research, was presented suggesting the adoption of sandbox models. These are particularly relevant in the fields of paediatrics and rare diseases, where traditional clinical trial models often face significant challenges related to small patient populations, ethical constraints, and limited commercial incentives. We suggested focusing on three key areas where sandbox approaches could provide tangible benefits: Co-Sponsorship Models, Targeted Funding for Academic Studies, Innovative Study Designs.

Q&A session

It was discussed that the current challenges hindering the implementation of innovative trial designs are not rooted in the Clinical Trials Regulation (CTR) itself, which in fact permits both innovative

design approaches and co-sponsorship models. However, the limited uptake of these options may be attributed to a lack of training and regulatory expertise.
The administrative complexity of conducting such trials appears to stem more from challenges in the approval process—particularly when dealing with substantial modifications in master protocols involving multiple investigational medicinal products (IMPs)—as well as from operational issues at local clinical sites. In some cases, the reported reluctance of regulators to accept data from trials incorporating innovative elements, such as decentralised components, was highlighted as a barrier.
While CTIS was not seen as a major obstacle, the potential benefit of improved registration options for diverse trial models was acknowledged. The MSP AG took note of the ongoing drafting of CTIS guidance on the submission of substantial modifications and welcomed this development.
The proposal to include more structured data fields in CTIS, in order to prevent under-reporting of innovative trial designs, was also noted. Finally, suggestions for pilot programmes will be considered in the context of the upcoming revision of the ACT EU workplan and prioritisation process.

5.Updates from ACT EU and partners

5.1 Update on upcoming ACT EU workshop on external controls

The MSP AG was informed about the workshop organised by the Methodology Working Party (MWP) on 3rd of November related to the "Use of external controls for evidence generation in regulatory decision". The aim of the workshop is to explore with relevant stakeholders' potential use of external controls in the regulatory setting and discuss related methodological challenges.
The MSP AG (industry; academia) was invited to contribute to this event with nomination for the scientific programme committee.

Action arising:

- MSP AG to provide 2 nominations for the scientific programme committee by 16th of July 2025.

5.2 Update on policy development at the EU level

The MSP AG noted the overview of EU programmes, policies and strategies in support of clinical research and competitiveness.
The European Life Science Strategy recommendations, drafted following a public call for evidence, were outlined noting the emphasis on new approach methodologies, the enhancement of clinical trials with regulatory simplification and digitalisation, and the focus on Advanced Therapies Medicinal Products (ATMPs), rare disease, crisis preparedness and supply chain resilience.

The key features and timelines for the EC proposal for a Biotech Act and for a revised pharmaceutical legislation were noted.

Q&A on policy development at the EU level

In terms of policy development, it was clarified that, even if there is a diversity in projects and legislative frameworks, interlinks and relevant project coordination to strengthen regulatory convergence are being conducted in accordance with relevant priorities.
Clarifications were provided on the market protection modulation foreseen in the revised pharmaceutical legislations confirming its applicability to regulatory market protection rather than regulatory data protection.

5.3 Update on patient involvement project

An update on the CTCG project to deliver meaningful review of patient involvement in design and conduct of clinical trials was presented. The work included consultation with regulators, ethics committees and relevant stakeholder groups. The need to establish a clear framework for involvement, provide clear guidance, allow flexibilities for specific cases and identify incentives was flagged.
A reflection paper is planned to be drafted over the summer and consultation with stakeholders is envisaged before finalisation (estimated February 2026).

Q&A on patient involvement project

The MSP AG welcomed the update on the patient involvement project and appreciated the opportunity to be further consulted on the draft reflection paper.
The group briefly discussed proposals to incentivise patient-centricity and involvement. Suggestions included referencing patient involvement in public assessment reports or clinical trial approvals, as well as engaging patients early in protocol development and throughout the entire product lifecycle—at appropriate and meaningful moments—while safeguarding their wellbeing. The use of financial incentives was raised, particularly in light of limited resources in academic settings and the challenges in identifying lay persons and patient advocates.
The importance of fostering dialogue with research funders was emphasised, to embed patient involvement in funding proposals from the outset. Training initiatives to help patients become more research-aware were also suggested, alongside collaboration with the Patients and Consumers Working Party.
Demonstrating the added value of patient involvement throughout all phases of development was considered essential, while ensuring it does not become a "tick-box" exercise or perceived as an administrative burden. The group debated whether engagement should occur at the level of each individual trial or more strategically at the programme level. However, concerns were noted that delayed engagement at the development stage may contribute to inefficiencies and setbacks.
Finally, the group highlighted the importance of viewing patient engagement—including that of vulnerable and underrepresented populations—not only as a responsibility, but also as a source of learning, competitive advantage, and mutual benefit. It was noted that patient involvement in paediatric trials remains uncommon and should be further encouraged.

Closing remarks

The co-chairs closed the meeting by thanking participants for their contributions and engagement. Actions arising will be followed up as needed.
Next meeting 18th September 2025 (virtual) | Deadline for topic submissions: 11th July 2025