



EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

Foster innovation in clinical trials

Underlying actions

EMA's Regulatory Science Strategy to 2025 – Human Stakeholder Workshop

Chaired by Bruno Sepodes, CHMP and Anja Schiel, SAWP on 19 November 2019
Presented by Francesca Cerreta, Safety and Efficacy, EMA



An agency of the European Union





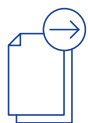
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Foster innovation in clinical trials



Drive adoption of practices that facilitate Clinical Trial Authorisation, GCP and HTA acceptance



Critically assess the clinical value of new and emerging endpoints and their role in facilitating patients' access to new medicines



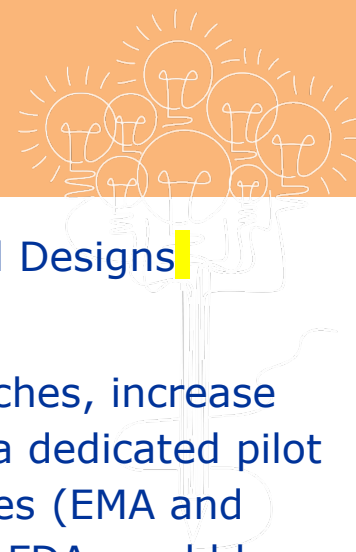
Work with stakeholders to encourage collaborative clinical trials



Collaborate with international partners in ongoing initiatives such as the Clinical Trial Transformation Initiative.



Work with stakeholders to encourage complex collaborative clinical trials



- Develop a new strategic initiative on Complex Innovative Clinical Trial Designs (including adaptive design and master protocols).
- Facilitate use and acceptability of such innovative clinical trial approaches, increase the regulators experience by allowing submission of case studies via a dedicated pilot programme and address different concerns from Regulatory Authorities (EMA and NCAs), Ethics Committees, HTAs. International collaboration with the FDA would be beneficial.
- It is important to avoid a situation where seamless trials were possible in one regulatory jurisdiction but not in the other.

Work with stakeholders to encourage complex collaborative clinical trials



- Ensure Clinical Trial Regulation does not prevent the advance of innovative designs.
- Administrative processes must also be streamlined for innovation in clinical trials to be realised. Delays to protocol amendments due to administrative processes could significantly impact the ability of the innovative trial design to add efficiency.
- The current system for substantial amendments slows down clinical trials in the EU without providing benefits to patient. Adapting, this paradigm has the largest potential to fundamentally change the regulatory system.
- Adopting a pragmatic approach to allowing parallel substantial modifications under the Clinical Trial Regulation, to facilitate operation of complex trials.



Work with stakeholders to encourage complex collaborative clinical trials



- Advance global coordination on the topic, for example via ICH deliberation on CCTs
- Developing guidance on approaches such as the use of Bayesian methods for design and analysis, hierarchical modelling for borrowing historical control, synthetic control arms, etc.



2. Establish a multi-stakeholder, neutral platform, to enable new approaches to clinical studies and to transform EU as a preferred location for innovative clinical research



- Global partner collaboration, e.g. Clinical Trial Transformation Initiative and ICH to drive global multi-stakeholder alignment around medicine development
- Work with CTFG to support clinical trial innovation and maintain competitiveness of the clinical trial environment in the EU.
- Ensure upcoming CT regulation is not preventing advance of innovative designs (e.g. allowing parallel substantial modifications)
- Stakeholders should work on defining patient centricity...should ensure that the CT model adapts to patient needs from a scientific and operational perspective for example allowing decentralised CTs using patient-centric endpoints.



2. Establish a multi-stakeholder, neutral platform, to enable new approaches to clinical studies and to transform EU as a preferred location for innovative clinical research

- EMA engagement in multi-stakeholder frameworks on endpoint development and usage
- Use of opportunities for stakeholder interaction to share information on innovative trial designs, including aligned understanding of best practises, concerns and limitations to ensure that this area continues to progress.
- While discussion of innovative designs is an option via the Innovation Task Force, EMA could initiate a pilot programme that would allow for broader discussion and shared learning relating to novel designs.





2. Establish a multi-stakeholder, neutral platform, to enable new approaches to clinical studies and to transform EU as a preferred location for innovative clinical research

- Support the organisation of high-quality clinical trials by participating in the training of clinical investigators and facilitating the transfer of knowledge to MS with fewer experience in conducting clinical research for regulatory purposes, as "applied regulatory science" programme.
- The EU-PEARL project will become a reference for the regulatory authorities to assess the efficacy of this instrument in the era of personalized medicine.
- Play a positive role with funders to support administrative aspects of clinical academic research.



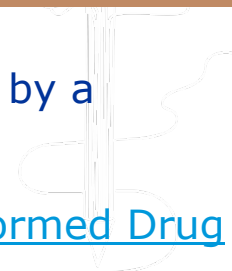


3. Drive adoption of novel practices that facilitate clinical trial authorisation, GCP and HTA acceptance



Development pathways

- The activities to advance innovation in clinical trials must be accompanied by a modernization of GCP.
- Consider a platform for information sharing like US FDA MID-3 ([Model Informed Drug Discovery](#))





3. Drive adoption of novel practices that facilitate clinical trial authorisation, GCP and HTA acceptance



Digital

- Advance acceptance of digital endpoints.
- Modelling and simulation and extrapolation in clinical trials e.g. in silico trials, needs to incorporate RWD, natural history, and/or observational data.
- In silico clinical trial could help to reduce, refine, and partially replace real clinical trials.
- Reflect on scope and quality criteria of RWD; Should be cautious using this data to establish clinical effectiveness due to high confounding.





4. Critically assess the clinical value of new and emerging endpoints and their role in facilitating patients' access to new medicines



Endpoints

- Global regulatory alignment on uses of integrated endpoint approaches, where combined data on mutually supportive outcome measures can support efficacy.
- Engage with patient organisations e.g. when developing novel endpoints.
- Allow decentralised CTs using patient-centric endpoints.
- Consider publication of evidentiary considerations for the development of surrogate endpoint markers.
- Revise clinical guidelines to allow for digital technology endpoints.



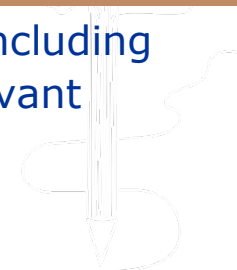


4. Critically assess the clinical value of new and emerging endpoints and their role in facilitating patients' access to new medicines



RCTs

- Raise the bar with strong evidence requirements for marketing approval including comparative trials against standard of care treatment, using clinically relevant endpoints including quality of life and overall survival.
- New clinical trial designs are needed to respond to the new patient needs.
- Strengthen the scientific rigour and relevance of RCT's used in the MAA evaluation.
- Gender differences and other relevant subgroups (such as the elderly) must be reflected in RCT.
- Push the methodology of pivotal randomised controlled trials toward a pragmatic approach through regulatory guidelines.





Any questions?

Further information

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