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# Global biotech convergence and international regulatory convergence

# EMA leadership of ICMRA to address regulatory challenges at global level

- EuropaBio welcomes and values the leadership role EMA has played at ICMRA
- The ICMRA platform of global regulators and stakeholders has been effective in highlighting best practices through sharing of experience in the assessment of clinical trial designs, evidence gathering and regulatory assessment.
- ICMRA has been important for promoting transparency and knowledge sharing
- ICMRA collaborations have enabled work towards increasing the efficiency and effectiveness of regulatory processes and decision-making
- We encourage EMA to remain actively engaged at ICMRA and would be interested to hear in which areas EMA believes ICMRA will be most useful moving forward

# Building on the EMA OPEN pilot and increasing international collaboration in other areas

- EuropaBio welcomes the OPEN pilot – increasing international collaboration and knowledge-sharing with non-EU regulators to the benefit of all patients
- Initiative is limited to the evaluation of COVID-19 vaccines and therapeutics and involves a small selection of regulatory authorities
- EuropaBio recognises the value of additional expertise to the EU network; participation of which non-EU regulators to be discussed with the MA applicant
- EuropaBio suggests involving industry in the analysis of the OPEN pilot and its evolution after the pandemic

# International alignment on ATMP long-term follow-up (LTFU)

- A global risk-based and flexible approach is needed for LTFU
- Unclear if there is global harmonisation on duration of studies
  - EU: Case by case; up to 15 years for integrating vectors or where potential for latency
  - US
    - 15 years for integrating vectors
    - Up to 15 years when potential for latency, persistent infection, genome editing
    - Up to five years for AAV vectors
- Flexibility needed for LTFU evidence to meet needs of multiple stakeholders
  - clinical trials/extension, PAES, PASS, registries and/or RWE
  - global approach to acceptability of data sources/methodologies would be useful
- LTFU periods can present unique logistical challenges (patients, HCPs, sponsors)
  - Patients may choose not to participate in LTFU, drop out or relocate
  - Health care professionals (study investigator or primary care physician) may change
  - Development of best practices is recommended to ensure that patients remain engaged over the course of potentially lengthy follow-up timeframes

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# Preparing the regulatory environment for the next wave of innovative products

# Innovative clinical trial design

## Introduction/Background

- Innovation in clinical trial design transformed evidence generation in drug development, even more during Covid-19 pandemic
- New clinical trial designs raises many questions, change our approach to conducting and assessing clinical trials
- Europe is facing increasing competition from other regions in the race for medical excellence & guidance

## Call for harmonisation & cooperation

- Opportunities to harmonize across regulatory agencies in Europe and align with other international regulatory agencies on CCT guidelines, recommendations and best practices
- Use the learnings from FDA CID to develop a pilot programme for CCTs in Europe
- Capabilities required for complex and innovation in clinical trial in regulatory agencies and Industry: maximise the ways of working within and across the EU regulatory agency network

## Plea for streamlined operations

- Pre-CTA engagement process for CCTs has been very helpful to Industry
- How best to define the end of study for CCTs, simplifying the process to add new IMPs in platform trials, not mandating IDMCs for early development protocols and minimising the number of times country specific protocols are needed
- Opportunity to use a common Master screening protocol to serve a number of registrational platform trials
- Alignment on the scope of modelling & simulation details required to support a CCT design

# Digitally enabled trials & Decentralised trials

## Introduction /Background

- Digital technologies are transforming healthcare & dug development: improve participant access, engagement, trial-related measurements, and/or interventions, enable randomized intervention allocation → It makes innovation more patient-centric
- Harmonisation is still required to support incorporation of digital technologies in clinical trials

## Current challenges

- Lack of regional and global harmonization, which limits the potential to conduct global clinical trials consistently (i.e. it requires country-by-country adjustments, which overcomplicate operations, creates inefficiency and reduces options for participants)
- Impact of changing the location of an assessment (e.g. from clinic to home), and determining whether comparability should/needs to be demonstrated to Health Authorities, appropriateness of procedures being conducted from a patient's home
- Limited acceptance of digital endpoints as primary endpoints in clinical trials: limited opportunities to get input from EU regulators

## Most pressing needs

- Regulatory flexibilities used during Covid, by the EMA and MSs, not to be revoked in their entirety, but rather reviewed individually with a full risk/benefit analysis be performed on each, to concretely assess the potential for long-term implementation
- EMA guidance on validation requirements for primary endpoint data, when collected via different visit models
- Support regarding IMP shipments to patients homes from a central hub/depot, shipped at the request of the investigator site (Within MS AND across EU MSs)

# Single-arm trial considerations

- Rare diseases are orphan diseases with high unmet medical need in very small populations of patients
  - Conduct of randomized clinical trial programs (e.g., vs. placebo) is unethical and often infeasible
  - Well conducted, controlled, single arm studies measuring efficacy and safety as change from baseline are accepted regulatory alternatives to randomized studies
  - Opportunities for use of multi-dimensional data sources to support interpretation of clinically meaningful results of single-arm studies include natural history historical controls, consortium and other real-world data sources, post-approval registry data
- There is EuropaBio member interest in developing a framework that would set out scenarios where single-arm studies would have a role in drug development and regulatory decision making

# Towards maintaining regulatory adaptations introduced during the COVID-19 pandemic

- Adopting innovative regulatory approaches
  - staged submission of scientific evidence to support accelerated regulatory assessment and speed up patient access
  - rapid scientific advice
  - remote inspection alternatives

- Value of using digitalisation tools
  - ePI can improve access to up-to-date product information on medicines
  - centralised agreement to use a single language pack (rather than agreement at a Member State level)
  - remote source data verification in clinical trials