European Federation of Pharmaceutical Industries and Associations

Enabling the use of randomized pragmatic trials in the EU

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Objective and background

Objective

- Share general insights from EFPIA position paper on randomised pragmatic trials (RPTs)
- Discuss how we can collaboratively identify solutions with relevant stakeholders (e.g. patients, healthcare providers, regulators, drug developers and other organisations e.g. Transcelerate)

➢ So that we can create an EU ecosystem which is more conducive for the conduct of RPT through **the use of pragmatic elements[1], enabling operational flexibilities and building a learning loop**

Background

- *An EFPIA position paper on Randomised pragmatic trials to generate high-quality real-world evidence for regulatory decisions* was released in June 2023. The paper outlines key considerations and proposals including a demonstration project to help us better understand the barriers and how to address them.

[1]See PRECIS-2 tool: designing trials that are fit for purpose. K Loudon et al. 2015 (link)

Why is it important to revisit the concept of pragmatic trials?

- The concept of pragmatic trials is not new, yet very few contributed evidence for regulatory decision

- Global efforts to support the generation of **high-quality RWD** and therefore **RWE** e.g. standardised data format to minimise variability in data collection

- The opportunity of generating evidence from randomised pragmatic trials[1] so that we can reduce confounding and bias using RWD sources e.g. EHR, registries

- A more **patient-centric** study design than traditional trials
  - Collect data from the "real patient", i.e. a **more inclusive and diverse patient population** and therefore increased external validity of the results
  - Collect **patient-relevant outcomes** while **lowering the burden** on participants (e.g. less visits)
  - Enable **broader participation of patients** in clinical trials that would normally not have access to the traditional clinical sites, e.g. because they live far away

- An opportunity to **simplify the conduct of clinical trials and accelerate drug development**

[1]Recent example: RECOVERY – Randomised Evaluation of COVID-19 Therapy [resource on the internet]. [cited 2023 Jun 4]. Available from: https://www.recoverytrial.net/.

How do we define pragmatic trials?

From EU guidance on post-authorisation efficacy studies[1]:

> ''*Pragmatic trials examine* ***interventions under circumstances that approach real-world practice****, with more heterogeneous patient populations, possibly less-standardised treatment protocols and* ***delivery in routine clinical settings*** *as opposed to a research environment. Minimal or no restrictions may be placed on modifying dose, dosing regimens, co-therapies or co-morbidities or treatment switching'*

Questions for discussion:

- Does this remain a good baseline definition?
- Is more awareness needed on what is a pragmatic trial?
- Do we need global alignment on the definition?

[1]Scientific guidance on post-authorisation efficacy studies. EMA/PDCO/AT/CMDh/PRAC/CHMP/261500/2015. link

Possible regulatory settings for the use of randomised pragmatic trials

Regulatory settings (i.e. type of regulatory decisions)

- Approval of **new indications** for a product with an established safety profile (i.e. post-authorisation)
- Provide **evidence** (safety or effectiveness) for **post-authorisation measures** (PAMs) - for example, could be part of the confirmatory strategy for a medicinal product which received conditional approval.
- In exceptional situations (e.g. outstanding benefit with high-quality data in an unmet medical need setting) for marketing authorisation of a new medicinal product

Key considerations and learning opportunities (1)

- **Patients centric**
  - Enable the use of:
    - outcomes and endpoints that are captured in clinical practice
    - aligning schedule of assessments with clinical practice
    - simplified informed consent
- **Data, methods, and statistics**
  - Explore when simplified safety reporting makes sense
  - Explore how to utilise standardised data (through Standard Setting Organizations) and methodological approaches in analysing data from a pragmatic setting
  - Identification of appropriate data sources and Electronic Health Record (EHR)-facilitated trials and registries
  - Interoperability of data between healthcare delivery settings and traditional trial data
  - Randomisation in routine care and other related methods (e.g. cluster randomisation)

Key considerations and learning opportunities (2)

- **Operational**
  - In an already strained healthcare system need for operational simplification for existing and new sites , e.g. simplified procedures, drug supply delivery and funding (e.g. co-pay systems)
  - Data extraction from EHRs (e.g. automation)
- **Regulatory; alignment across stakeholders**
  - Reach global agreement on the definition of pragmatic trials
  - Agreement on appropriate clinical and regulatory setting when RPT can be used
  - Translating highly conceptual principles into practice e.g. fit-for-purpose, risk proportionate, quality by design while ensuring patient safety and data integrity
  - Enabling low interventional trials in the EU
  - Inclusion of RWE in product information; understand what constitutes sufficiently robust RWE

We propose the development of demonstration project(s) to collectively identify solutions

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Thank you