European Federation of Pharmaceutical Industries and Associations

# Session 1: Current challenges in clinical development and regulatory decision-making

## Stakeholder: Industry








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# Challenges of Clinical Development in DMD

## Patient & Study Heterogeneity

### Patient Population

Rare disease with a highly heterogeneous patient population

### Disease Staging

Disease staging is not accepted as well as other diseases

### Clinical Endpoints

Varied endpoints used across multiple studies, not necessarily designed for trials or to show increased efficacy over SOC

## Trial Execution & Ethics

### Disease Progression

Although relatively fast progressing disease, it can take years to decline, with ethical limits on duration of placebo

### Therapy Impact

Novel therapies may limit future options of experimental treatment, especially in the context of rare disease

# How could Real World Data help to plan or design clinical trials?

## Clinical Trial Simulation

Use advanced simulation tools repeatedly to optimize trial designs, inclusion criteria, and overall study duration.

## Optimized Study Design

Inform key trial protocols including sample size statistics, enrichment strategies, stratification, and patient populations.

## Early-Stage contextualisation

Establish a reliable source of comparison for internal decision-making and creating early-stage supportive clinical evidence.

## Planning Challenges

- Restricted Data Access requiring investment early in life cycle
- Variable Inconsistency in fragmented sources
- Confounding & Missing baseline covariates

# How can RWD help to analyse or interpret clinical trials?

## Comparator Arms

Provide comparator arms for open-label or shorter duration studies to build supportive clinical evidence and/or offer ethical controls after placebo periods end.

## Endpoint Validation

Validate and contextualize clinical endpoints against disease natural history data to establish significance.

## Modelling long-term outcomes

Use historical registry data to map shorter-term trial endpoints to predict effect on longer-term disease milestones like loss of ambulation.

# How can RWD help in the post-approval space?

### Real World Safety

Evidence required by Regulators to support marketing authorisation approval, to address emerging safety concerns & to refine the eligible population in the label.

### Real World Efficacy & Durability

To inform the benefit-risk of a drug in a real world setting including long-term functional durability (e.g., delayed loss of ambulation or respiratory decline). Evidence required by Regulators to support marketing authorisation approval/renewal & label refinement.

### Comparator Cohorts

Use real world data to contextualise long-term outcomes (e.g. background rates or via matched cohort designs).

### Describe Treatment Use

Describe use of treatment in real world setting (e.g. characteristics of exposed patients, timing of use in patient journey).

# Overall Core Challenges

### Fragmented Data

Patient records *within* registries are not centralised, leading to lag times. Data is not standardised *between* registries, limiting sample sizes.

### Restricted Access

Restricted access to patient level data. Patient-level data is critical for propensity scores and regulatory filings.

### Variable Consistency

Inconsistent variable collection across sources (e.g., corticosteroid dosing and loss-of-ambulation definitions).

### Loss to Follow-Up

Incomplete tracking of reasons for patient loss to follow-up impacts downstream analysis and estimands.

### Unmeasured Confounding

A core set of baseline and time-varying covariates (like genotype and comorbidities) is required for robust statistical analysis.

### Data Quality & Density

Wider visit windows, less dense collections, and missing data entries compared to clinical trials.

### Operational Burden

High burden on sites and risk of patient loss to follow-up over very long-term, non-interventional studies.

### Interoperability & Safety

Most registries do not collect necessary variables for assessing safety and lack reporting mechanisms.