C-Path's Role in IHI Call 4: Enhancing Rare Disease Clinical Trials

This memo outlines how C-Path can contribute as a key strategic regulatory partner to the Innovative Health Initiative's (IHI) call 4,
"Establishing novel approaches to improve clinical trials for rare and ultra-rare diseases."
We encourage potential partners to review the memo and reach out as early as possible to rdcadap@c-path.org with interest.

On 27 July 2023, the Innovative Health Initiative (IHI) published a Call for Proposals for Topic HORIZON-JU-IHI-2023-04-02-two-stage titled, "Establishing novel approaches to improve clinical trials for rare and ultra-rare diseases."

The principal aim of this topic is to develop capacities and capabilities to execute innovative trial designs, but also plan to identify solutions to address scientific gaps as well as technical and operational challenges, and to collaborate/find synergies with relevant existing initiatives to establish a new, dedicated, rare disease specific and sustainable infrastructure. The project is expected to support innovation and optimise drug development for rare diseases with high unmet medical needs by focusing on clinical trials conducted for small populations and clusters of diseases with commonalities.

This document provides information for how Critical Path Institute (C-Path) and the Rare Disease Cures Accelerator-Data and Analytics Platform (RDCA-DAP®) may be involved in relevant proposals.

As mentioned in the Rare Disease Moonshot recommendations, projects at all stages of the development need to contribute to regulatory approvals to address the unmet medical needs of the rare disease community in a timely manner and in a way that is meaningful to patients. The development of existing and new predictive tools and methods that would qualify as Drug Development Tools (DDTs) require regulatory and data science strategies at design and planning stage to accelerate implementation of novel technologies, innovative trial design and the use of Real-World Evidence (RWE) in study design and medicines developments. C-Path's RDCA-DAP, funded by FDA, provides a centralised and standardised infrastructure to support and accelerate rare disease characterisation, with the goal of accelerating therapy development across rare diseases. RDCA-DAP promotes the sharing of data and encourages regulatory-grade standardisation of data collection for analytics, accelerating the understanding of disease progression, clinical outcome measures and biomarkers that capture clinically meaningful changes, and facilitates the development of regulatory-grade mathematical models of disease and innovative clinical trial designs.

Given C-Path's leadership role in the RDCA-DAP initiative, whose mission aligns closely with the Topic HORIZON-JU-IHI-2023-04-02-two-stage Call, it would be considered highly advantageous for C-Path to participate in decisions regarding the orientation of the work programme, the development of research protocols, and the discussion and dissemination of the results for the IHI Call. **This role would require C-Path to be involved early in the proposal design and preparation, as well as relevant work package(s).**

Intentions to propose C-Path's involvement in a project are welcome and should be communicated as early as possible to rdcadap@c-path.org so C-Path can ensure its level of involvement is closely aligned with its

strategic priorities in rare disease research. A non-exhaustive list of C-Path rare diseases focus areas is available in Annex I.

Annex I: C-Path rare diseases focus areas (non-exhaustive):

- Rare neurodegenerative disorders: Amytrophic Lateral Sclerosis, Fronto Temporal Dementia, Friedreich’s Ataxia, Spinocerebellar Ataxia, Progressive Supranuclear Palsy, Huntingon’s Disease
- Rare dystrophies: Duchenne Muscular Dystrophy, Limb Girdle Muscular Dystrophy, Fascioscapulohumeral Muscular Dystrophy
- Rare kidney disorders: Polycystic Kidney disease
- Rare epilepsies and neurodevelopmental disorders
- Rare mitochondrial disorders
- Rare metabolic disorders
- Rare hematological disorders and rare cancers: Sickle Cell Disease