C-Path in Europe: Moving Global Regulatory Science Forward

20 April 2022

Please be advised this Webinar is being recorded
Welcome

Critical Path Institute is a catalyst for innovation that accelerates the path to a healthier world.
Agenda

1. Welcome Remarks

2. C-Path Overview

3. Alignment with EMA Regulatory Science Strategy to 2025

4. Panel Discussion
What We Do

- Foster development of new evaluation tools to inform medical product development and regulatory decision-making
- Convene scientific consortia of industry, academia, and government for sharing of data/expertise

The best science
- The broadest experience
- Active consensus building
- Shared risks and costs

- Enable iterative EMA/FDA/PMDA participation in developing new methods to assess the safety and efficacy of medical products
- Obtain official regulatory endorsement of novel methodologies and drug development tools
## Active C-Path Consortia & Programs

<table>
<thead>
<tr>
<th>Consortia/Programs</th>
<th>Description</th>
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<tbody>
<tr>
<td>BmDR Biomarker Data Repository</td>
<td>ERA4TB European Regimen Accelerator for Tuberculosis*</td>
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<tr>
<td>CDRC Cure Drug Repurposing Collaboratory</td>
<td>HD-RSC Huntington’s Disease Regulatory Science Consortium</td>
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<tr>
<td>CPAD Critical Path for Alzheimer’s Disease</td>
<td>INC International Neonatal Consortium</td>
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<tr>
<td>CPP Critical Path for Parkinson’s Disease</td>
<td>MSOAC Multiple Sclerosis Outcome Assessment Consortium</td>
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<tr>
<td>CPTA Critical Path to Therapeutics for the Ataxias</td>
<td>PKDOC Polycystic Kidney Disease Outcomes Consortium</td>
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<tr>
<td>CPTR Critical Path to TB Drug Regimens</td>
<td>PredicTox KE PredicTox Knowledge Environment</td>
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<td>CP-SCD Critical Path for Sickle Cell Disease</td>
<td>PRO Consortium Patient-Reported Outcome Consortium</td>
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<tr>
<td>DCC Data Collaboration Center</td>
<td>PSTC Predictive Safety Testing Consortium</td>
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<td>D-RSC Duchenne Regulatory Science Consortium</td>
<td>QuantMed Quantitative Medicine</td>
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<td>eCOA Consortium Electronic Clinical Outcome Assessment Consortium</td>
<td>RDCA-DAP Rare Disease Cures Accelerator - Data and Analytics Platform</td>
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<td>RD-COAC Rare Disease Clinical Outcome Assessment Consortium</td>
<td>T1D Type 1 Diabetes Consortium</td>
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<td>TOMI-T1D Trial Outcome Markers Initiative in T1D Consortium</td>
<td>TTC Transplant Therapeutics Consortium</td>
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<tr>
<td>UNITE4TB Worldwide Accelerator for Tuberculosis*</td>
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* C-Path Ltd
Data Sharing and Aggregation by Area

C-Path Clinical Subject Growth

<table>
<thead>
<tr>
<th>Neuro</th>
<th>Rare</th>
<th>IHP</th>
<th>TSSP</th>
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<tbody>
<tr>
<td>Alzheimer's Disease</td>
<td>38,890</td>
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<td>Huntington's Disease</td>
<td>19,903</td>
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<td>Multiple Sclerosis</td>
<td>15,626</td>
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<td>Parkinson's Disease</td>
<td>15,885</td>
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<td>Duchenne's Muscular Dystrophy</td>
<td>11,442</td>
<td>Sickle Cell Disease</td>
<td>6,240</td>
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<td>Friedreich's Ataxia</td>
<td>1,572</td>
<td>Transplant Therapeutics</td>
<td>24,888</td>
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<td>Rare Diseases</td>
<td>8,087</td>
<td>Type 1 Diabetes</td>
<td>41,096</td>
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<tr>
<td>Neonatal</td>
<td>308,672</td>
<td>Tuberculosis</td>
<td>29,630</td>
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Clinical Data

<table>
<thead>
<tr>
<th></th>
<th>Studies</th>
<th>Participants</th>
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<tbody>
<tr>
<td>Neuro Rare IHP TSSP</td>
<td>354</td>
<td>532,504</td>
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<tr>
<td>Polygenic Kidney Disease</td>
<td>4,422</td>
<td>11,084</td>
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<tr>
<td>Rare Diseases</td>
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C-Path Core Competencies

Core Competencies
- Biomarkers
- Clinical Outcome Assessments
- Regulatory/Development Science
- Modeling and Analytics
- Data Management and Standards

Unmet Medical Need

Concentration Area
- Neuroscience
- Immunology and Inflammation
- Infectious Diseases

Bedrock Foundation: Unique Neutral Convener

DDTs and Other Solutions
- Safety Science
- Rare/Orphan Diseases
- Pediatrics

DDTs and Other Solutions
Key Milestones of Collaboration in Europe

2008
Parallel EMA/FDA qualifications for safety biomarkers as drug development tools

2012
London office and C-Path Global established

2013
10 year Anniversary Meeting with EMA

2018
Dublin office and C-Path Ltd. established

2020
New contract with Innovative Medicines Initiative (IMI)

2020
Former CHMP Chair, Dr. Salmonson appointed to C-Path Board of Directors

2020
ERA4TB and UNITE4TB international consortia launched

2022
Non-profit office in Amsterdam launches
Agenda

1. Welcome Remarks

2. C-Path Overview

3. Alignment with EMA Regulatory Science Strategy to 2025

4. Panel Discussion
C-Path in Amsterdam

Mission

• Leveraging and developing C-Path US and European activities in a complementary operational setting to facilitate global collaboration and harmonisation
• Strengthen C-Path relationship with EMA and EU Member States
• Strengthen and develop collaboration with European key stakeholders in the DDT, Data Management and Standards, and Regulatory Science

Industry partners
Academic experts
Regulators (FDA)
Patient groups
Nonprofit members

Industry partners
Academic experts
Regulators (EMA)
Patient groups
Nonprofit members
C-Path Operational Model - Impact

C-Path Unmet needs Horizon Scanning

Decision Point

Pre-PPP Assessment
~12-18 months

Decision Point

Operational Consortium

Impact

1. Synergies with EMA RSS 2025
2. EMA x C-Path webinars & workshops
3. Education and trainings

1. EU contribution beyond individual capacity
2. Focused contribution and optimized resource input
3. EU goals integrated in a global strategy

1. EU fit for purpose DDTs
2. Global data strategy
3. Sharing knowledge and learnings with the EU network

Industry Partners
A
B
C

C-Path Precompetitive Neutral Ground

FMA
FDA
PMDA

Patients

Academia
## C-Path Alignment with EMA RSS to 2025

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<th>EMA RSS Goals</th>
<th>Example C-Path efforts</th>
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"Critical Path Institute"
C-Path Alignment to EMA RSS H1 Goals

Goal 1

Catalysing the integration of science and technology in medicines development

- Support developments in precision medicine, biomarkers and ‘omics’
- Support translation of advanced therapy medicinal products (ATMPs) into patient treatments
- Promote and invest in the PRIority MEdicines scheme (PRIME)
- Facilitate the implementation of novel manufacturing technologies
- Create an integrated evaluation pathway for the assessment of medical devices, in vitro diagnostics and borderline products
- Develop understanding of, and regulatory response to, nanotechnology and new materials in pharmaceuticals
- Diversify and integrate the provision of regulatory advice along the development continuum
Regulatory Successes in Drug Development Tools

**FDA**
- 7 Qualification Decisions
- 7 Letters of Support
- 1 Fit-For-Purpose Endorsement

**EMA**
- 8 Qualification Opinions
- 8 Letters of Support

**PMDA**
- 1 Qualification Decisions

*Global endorsement of actionable solutions accelerates and de-risks medical product development.*
Goal 2

Driving collaborative evidence generation and improving the scientific quality of evaluations

- Leverage non-clinical models and 3Rs principles
- Foster innovation in clinical trials
- Develop the regulatory framework for emerging clinical data generation
- Expand benefit-risk assessment and communication
- Invest in special populations initiatives
- Optimise capabilities in modelling, simulation and extrapolation
- Exploit digital technology and artificial intelligence in decision making
Advancing Drug Development in Rare Disease

Examples of modelling in Duchenne muscular dystrophy (DMD) from C-Path’s Duchenne Regulatory Science Consortium (D-RSC)

- **DMD Progression Models and Building CTS Tools**
  - Data and Quantitative Model-Based Drug Development Approach to Clinical Trial Simulation (CTS) Tools

- **GLDH Qualification as Safety Biomarker for DMD Clinical Trials**
  - Collaboration with C-Path’s Predictive Safety Testing Consortium (PSTC) on Safety Biomarker Qualification for Glutamate Dehydrogenase (GLDH)

- **Master Protocol for Duchenne Adaptive Platform Trial**
  - Complex Clinical Trial Design in Rare Diseases

**Impact**
- Learnings from the DMD CTS platform have been used by industry sponsors in trial design for new therapeutic candidates.

**Clinical trial simulation (CTS) platform for DMD**
- First-ever comprehensive collection of models for five clinically meaningful outcome measures across the continuum of DMD.
Development of Novel Digital Measures for Clinical Trials in PD

- **Need**: Better outcome measures for assessment of progression of Parkinson’s disease (PD)
- **Solution**: Critical Path for Parkinson’s (CPP) Digital Drug Development Tools (3DT) initiative

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**FDA Critical Path Innovation Meeting (CPIM)**

- 2019 - 3DT launched
- 2020 to today
- **Future Vision - digital measure(s) for use in clinical trials**

**EMA Innovation Task Force (ITF) Meeting**

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**Digital technologies for medicines: shaping a framework for success**

Regulatory agencies can provide advice to support developers of digital technologies for medicines use, but what are the best strategies to maximise the chance of a successful regulatory interaction? Here, EMA and industry representatives comment on the experience so far.

_Francesca Cerreta, Armin Ritzhaupt, Thomas Metcalfe, Scott Akin, João Duarte, Michael Bremgren & Spiros Vassilakos_

_Nat Rev Drug Discovery 19(9): 573-574, 2020_
C-Path Alignment to EMA RSS H3 Goals

Goal 3

- Contribute to HTA’s preparedness and downstream decision making for innovative medicines
- Bridge from evaluation to access through collaboration with payers
- Reinforce patient relevance in evidence generation
- Promote use of high-quality real-world data (RWD) in decision-making
- Develop network competence and specialist collaborations to engage with big data
- Deliver improved product information in electronic format (ePI)
- Promote the availability and support uptake of biosimilars in healthcare systems
- Further develop external engagement and communications to promote trust and confidence in the EU regulatory system
Chronic Heart Failure (CHF) Working Group (WG) in the Patient-Reported Outcome (PRO) Consortium

- **WG objective:** Qualification by FDA of an activity monitor-based endpoint measure for use in assessing clinical benefit in CHF treatment trials
- **Project goal:** Identify variables obtainable via activity monitors that can be used to derive efficacy endpoints that adequately reflect meaningful aspects of day-to-day physical activity for persons with CHF

**Conducted Concept Elicitation Interviews**
- Generated qualitative evidence of important day-to-day physical activities and performance dimensions
  - **Light/moderate physical activities:** cleaning, cooking, laundry, self-care, gardening
  - **Walking:** shopping, appointments, exercise
  - **Dimensions:** duration, frequency, intensity, distance

**Convened an Advisory Panel**
- Advisory panel meetings (1 Dec 2021 and 16 Mar 2022)
- Built on WG’s study results, other research, and literature
- Identified candidate metrics for assessing clinical benefit and deriving endpoints
  - Step counts (walking)
  - Activity counts (general activities)

**Future Vision**
- Alignment among WG sponsors, C-Path, and FDA on specific metric(s) to move forward for Qualification Plan submission to FDA
• **Metabolic disorders**
  - Analysis of baseline characteristics of patients in the PKU registry from NPKUA
  - Evaluation of the Foundation of Prader-Willi Research data from hyperphagia questionnaires

• **Genetic disorders**
  - Exploration of GNE myopathy cross diseases discovery potential

• **Neurodegenerative disorders**
  - Progressive Supranuclear Palsy (TBD)
  - Dynamics of the modified Friedreich’s Ataxia Rating Scale: population variance, placebo affect and clinical meaningfulness

RDCA-DAP is an initiative led by Critical Path Institute in collaboration with FDA and NORD
C-Path Alignment to EMA RSS H4 Goals

Goal 4

- Implement EMA's health threats plan, ring-fence resources and refine preparedness approaches
- Continue to support development of new antibacterial agents and their alternatives
- Promote global cooperation to anticipate and address supply problems
- Support innovative approaches to the development, approval and post-authorisation monitoring of vaccines
- Support the development and implementation of a repurposing framework

Addressing emerging health threats and availability/therapeutic challenges
Global Partnerships to Address Global Health Threats

CDRC Stages

Framework

Prioritization

- Repurposing

Pre-Clinical

- AI mining

Real-World Data

- EHRs, clinical reports

Clinical Trials

- Embedded in clinical practice

Guidelines

- Professional societies

Policy

- Pathway for submission

Legislation

- Changing the landscape
  - Maximize use of existing medicines
  - New incentivizes for expanded use of existing generic drugs
  - Establish a new pathway for non-industry drug sponsors
  - Affect policy changes

- Challenges to repurposing drugs
  - No financial incentives to expand drug labels
  - Labeling changes must be initiated by drug sponsor
  - Intellectual property/patent protections
C-Path Alignment to EMA RSS H5 Goals

Goal 5

- Develop network-led partnerships with academia to undertake fundamental research in strategic areas of regulatory science
- Leverage collaborations between academia and network scientists to address rapidly emerging regulatory science research questions
- Identify and enable access to the best expertise across Europe and internationally
- Disseminate and exchange knowledge, expertise and innovation across the network and to its stakeholders
1. **Model-informed Drug Development training courses**
   - 8 modules with focus areas in:
     - Introduction to drug development and regulatory science
     - Foundation of MIDD
     - Model-informed decision making in drug development
     - Future Considerations including Digital Health, RWD/RWE, and AI/ML
     - E-learning environment, web-based learning management system (LMS)

2. **Regulatory Science Graduate Certificate program**
   - 9 courses total (3 of which are led by C-Path scientists)
     - Drug Discovery, Development, and in the Market
     - Development and Innovation: Biologics, Devices, and Diagnostics
     - Regulatory Science Case Study Project

3. **Strengthening Training of Academia in Regulatory Science (STARS) Global Conference – 19 May 2022**
   - Session on “Excellence in Regulatory Science”
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Acknowledgements – Regulatory Science team

Huong Huynh, PhD
Director, Regulatory Science

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Senior Project Manager

Kimberly Ward Barowicz
Project Manager

Bri Sullivan
Project Coordinator
Panel Discussion

Ralf Herold, MD
Senior Scientific Officer
Taskforce Regulatory Science and Innovation at EMA

Lada Leyens, PhD
Global Regulatory Lead
Clinical Trial Innovation and Digital Health at Roche

Dimitrios Athanasiou, MBA
PDCO Member at EMA – EURORDIS Board,
Member in World Duchenne Organization,
European Patients Forum Greek Patient Association

Franz Koenig, PhD
Associate Professor
Medical University of Vienna

Klaus Romero, MD, MS
Chief Science Officer
Executive Director of Clinical Pharmacology

Cécile Ollivier, MS
EU Regulatory Science Advisor (US)
Board of Directors (Netherlands)

Tomas Salmonson, PhD, MSc
Board of Directors (US)
Board of Directors (Netherlands)
Closing Remarks

• Timely global compatibility can only be achieved through collaboration

• Regional multistakeholders platforms need appropriate regional fundings to be able to develop global consensus

• C-Path is a neutral convener committed to moving Regulatory Science forward and will focus for the next 5 years on developing such global platform in areas with great impact for the patients
Thank you.

Please complete the webinar survey.