Considerations for Participation in PPP Projects: Learnings from the Critical Path for Parkinson’s Consortium

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Critical Path Institute: A Public-Private Partnership

• Acts as a trusted, neutral third party
• Convenes scientific consortia of industry, academia and government for sharing of data and expertise
  ✓ The best science
  ✓ The broadest experience
  ✓ Active consensus building
  ✓ Shared risk and costs
• Enable iterative FDA/EMA/PMDA participation in developing new methods to assess the safety and efficacy of medical products

Regulatory endorsement of novel methodologies and drug development tools
<table>
<thead>
<tr>
<th>AKI/Neph</th>
<th>Acute Kidney Injury/ Nephrotoxicity</th>
<th>ePRO Consortium</th>
<th>Electronic Patient-Reported Outcome Consortium</th>
<th>PRO Consortium</th>
<th>Patient-Reported Outcome Consortium</th>
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<tr>
<td>BmDR</td>
<td>Biomarker Data Repository</td>
<td>FA-ICD</td>
<td>Friedreich’s Ataxia Integrated Clinical Database</td>
<td>PSTC</td>
<td>Predictive Safety Testing Consortium</td>
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<td>CDRC</td>
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<td>Huntington’s Disease Regulatory Science Consortium</td>
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<td>CPAD</td>
<td>Critical Path for Alzheimer’s Disease</td>
<td>IBD</td>
<td>Inflammatory Bowel Disease</td>
<td>RDCA-DAP</td>
<td>Rare Disease Cures Accelerator – DAP</td>
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<td>CPP</td>
<td>Critical Path for Parkinson’s Disease</td>
<td>INC</td>
<td>International Neonatal Consortium</td>
<td>RD COAs</td>
<td>Rare Disease Clinical Outcome Assessments</td>
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<td>CPTR</td>
<td>Critical Path to TB Drug Regimens</td>
<td>MSOAC</td>
<td>Multiple Sclerosis Outcome Assessment Consortium</td>
<td>T1D</td>
<td>Type 1 Diabetes Consortium</td>
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<td>Critical Path for Sickle Cell Disease</td>
<td>PKD</td>
<td>Polycystic Kidney Disease</td>
<td>TB-PACTS</td>
<td>TB-Platform for Aggregation of Clinical TB Studies</td>
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<td>DCC</td>
<td>Data Collaboration Center</td>
<td>PMD</td>
<td>Pediatric Medical Devices</td>
<td>TOMI-T1D</td>
<td>Trial Outcome Markers Initiative in T1D Consortium</td>
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Critical Path Institute Regulatory Successes

**ALZHEIMER'S DISEASE**
- FDA & EMA endorsed AD clinical trial simulation tool
- EMA qualified model-based AD biomarker
- FDA & EMA letters of support
  - Model-based AD biomarkers and pre-dementia clinical trial simulator

**MULTIPLE SCLEROSIS**
- EMA qualified PerFO measure
  - Test battery for all forms of MS

**POLYCYSTIC KIDNEY DISEASE**
- EMA & FDA model-based qualified Total Kidney Volume (TKV) imaging biomarker
- FDA letter of support
  - TKV imaging biomarker
- FDA designated reasonably likely surrogate marker for PKD trials (TKV)

**PARKINSON'S DISEASE**
- FDA letter of support
  - PD imaging biomarker
- EMA qualified model-based PD imaging biomarker

**TUBERCULOSIS**
- EMA qualified translational drug development platform

**PATIENT-REPORTED OUTCOME MEASURES**
- FDA COA qualification
  - Symptoms of Major Depressive Disorder Scale
  - Non-Small Cell Lung Cancer Symptom Assessment Questionnaire
  - Asthma daytime and nighttime symptom diaries

**PREDICTIVE SAFETY TESTING**
- EMA, FDA & PMDA qualified non-clinical kidney safety biomarkers
- FDA qualified clinical kidney safety markers
- Six FDA & EMA letters of support

**TYPE 1 DIABETES**
- EMA letter of support for model-based islet autoantibodies biomarker for trial enrichment

**FDA**
- Qualification Decisions
- Fit-for-Purpose Endorsement
- Letters of Support

**EMA**
- Qualification Decisions
- Letters of Support

**PMDA**
- Qualification Decision
Critical Path for Parkinson’s (CPP) Consortium

- CPP was launched in 2015 with a major goal to develop tools to quantify disease progression
- Successfully acquired and integrated patient level data from >11000 PD patients
- Qualification of imaging biomarker for enrichment of trials in early PD
- Current CPP focus is regulatory endorsement of PD drug disease trial model
- Digital Drug Development Tools (3DT) team was launched under CPP with the goal of advancing regulatory readiness of digital health technologies in early PD studies

*CPP includes 25 academic scientific advisors as partners*
CPP has Integrated Data from >11000 people with Parkinson’s From Around the World

Observational Cohorts
- PPMI
- Oxford Discovery PD
- Tracking Parkinson’s
- ICICLE
- CamPaIGN

Randomized Controlled Clinical Trials
- PRECEPT
- DATATOP
- ELLDOPA
- ADAGIO
- FS-1
- CONFIDENT-PD
- SP-513 (Rotigotine)
- SP-512 (Rotigotine)
- SUREPD-Ph2
- FS-Too

CPP Unified PD Clinical database
Future model of Parkinson’s therapies

Parkinson’s - Not all one flavor

Personalized Medicine targeted treatments
Case Example: Parkinson’s Imaging Biomarker

Qualification opinion - Molecular neuroimaging of the dopamine transporter as biomarker to identify patients with early manifest Parkinsonism in Parkinson’s disease

Qualification opinion on dopamine transporter imaging as an enrichment biomarker for Parkinson’s disease clinical trials in patients with early Parkinsonian symptoms

29 May 2018
EMA/CHMP/SAWP/765041/2017
Committee for Medicinal Products for Human Use (CHMP)

Qualification opinion on dopamine transporter imaging as an enrichment biomarker for Parkinson’s disease clinical trials in patients with early Parkinsonian symptoms

FDA Gives a Nod for Alzheimer’s and Parkinson’s Biomarkers

03 Apr 2015
In the age of the Internet, don’t you love it when you get a real letter? Especially a letter
CPP is changing the landscape

Selecting more appropriate subjects for clinical trials will reduce the numbers needed and make trials more efficient.

~20% reduction in sample size by excluding biomarker negative subjects
Biomarker Strategies for Regulatory Success

**Retrospective** data collection with **Prospective** biomarker data analysis

**Consortium Collects:**
- Key patient-level data
- Including clinical trials, registries, and longitudinal observational studies
- From academic laboratories, industry, and/or government agencies

- Enable statistical analysis to support biomarker qualification
- May also be used to develop quantitative drug development platforms
Newest example of CPP’s impact

Precompetitive Consensus Building to Facilitate the Use of Digital Health Technologies to Support Parkinson Disease Drug Development through Regulatory Science


Digital Biomarkers
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CPP Digital Drug Development Tool (3DT) Objective:
Advance regulatory maturity for The use of DHTs in PD clinical trials

https://www.karger.com/Article/FullText/512500
Engage Regulatory Agencies Early and Often

EMA initiatives to support drug development

What do we provide?

2. Innovation Task Force (ITF) platform and meetings

ITF Briefing Meeting Report

Critical Path Institute Ltd, Critical Path for Parkinson’s (CPP) Consortium

Briefing meeting held at the European Medicines Agency (EMA) on 15th July 2019.

The objective of the ITF briefing meetings is to provide for a preparatory discussion on scientific and regulatory topics relevant to the development of new medicinal products and technologies complementing and reinforcing existing formal procedures.

EMA: Innovative Task Force suggested taking a stepwise approach. Identify a small, well-defined meaningful measure and come back to them with a focused data-driven path for a future Scientific Advice and potential for qualification.

FDA: The appropriate FDA review divisions will continue to have iterative, disease-specific discussions with CPP, including strategies for establishing meaningful clinical endpoints.
What is Needed for Success in the Future?

Current state

Medical practitioners aspire for prodromal diagnosis

Clinicians & drug developers aspire to enrol large diverse patient cohorts at minimal cost to validate studies

Patients want to increase their quality of life

Success

Voice of the patient

Regulators

Clinicians

Device vendors

Engineers, data scientists, statisticians

Patient-centric outcomes
- Improved quality of life
- Patient centric digital biomarker

Data sharing
- Reduce duplication of effort
- Clinical and technical validation through data harmonisation

Data Standards
- Increase data interoperability and data management
- Data used beyond its purpose of collection

Global Collaboration
- Reduce discrepancy between research utility & clinical value

Stephenson et al., Digital Progression Biomarkers as Novel Endpoints in Clinical Trials: A Multistakeholder Perspective, J. Parkinson’s Disease, in press
Summary

• Addressing gaps in new treatments for diseases of high unmet need require precompetitive collaborations and focus on regulatory science

• To enable improved success, efficiency and sense of urgency it has been suggested that new WARP SPEED strategies are needed for success in age related neurodegenerative diseases
  - Enhanced global collaboration
  - Data sharing has to be transformed and far easier than now
  - Focus on patients needs to be front and center
  - All stakeholders need to be fully onboard with collaboration
  - Expanding the term precompetitive beyond where it is now
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  Maria Tome, Corrine de Vries, Spiros Vamvakas

- **People living with Parkinson’s, the hidden pandemic**