



# Critical Path for Parkinson's (CPP) Digital Drug Development Team (3DT)

August 2019

**PARKINSON'S<sup>UK</sup>**  
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# Critical Path for Parkinson's

**Mission:** *To serve as a leading International consortium to collectively advance data driven collaborative research under the advisement of worldwide regulatory agencies*



## Patient-Advocacy Organizations

- Parkinson's Foundation
- Michael J. Fox Foundation
- Davis Phinney Foundation
- The Cure Parkinson's Trust
- **PMD Alliance**
- **Parkinson's UK**

## Academic Institutions

- University of Oxford
- University of Cambridge
- Newcastle University
- University of Glasgow
- Radboud University



- 6 Qualification Decisions
- Polycystic Kidney Disease
  - Predictive Safety Testing
  - Patient-Reported Outcome

- 1 Fit-for-Purpose Endorsement
- Alzheimer's Disease

7 Letters of Support

8 FDA Critical Path Innovation Meetings



- 7 Qualification Decisions
- Polycystic Kidney Disease
  - Tuberculosis
  - Alzheimer's
  - Predictive Safety Testing
  - Parkinson's
  - Multiple Sclerosis

7 Letters of Support

2 EMA Innovative Task Force meetings



- 1 Qualification Decision
- Predictive Safety Testing

- The PD field is in need of optimizing outcome measures of disease progression; digital measures have potential to assess aspects of the disease in a more accurate way or assess aspects of the disease that are not currently measured.
- A number of public, academic and industry activities are implementing DHTs in PD (PPMI, academic research studies [1], industry clinical trials [2,3]); CPP can leverage its unique role in bringing stakeholders together for pre-competitive collaboration and regulatory discussions.

## Overall:

- CPP consortium model, including alignment with regulatory agencies and excellence in data science, is well placed to fill gaps to enable efficiencies in the use of digital health technologies in PD.

1) **Academic:** Silva de Lima AL, Hahn T, Evers LJW, de Vries NM, Cohen E, Afek M, et al. (2017). PLoS ONE 12(12):e0189161.

2) **Industry** – Lipsmeier, F. et al. Movement Disorders (2018). 33(8): 1287-1297

3) **Industry** - Boroojerdi, B., Parkinsonism and Related Disorders, 2019: 61: 70-76

- A subset of CPP member organizations\* have convened to collaborate pre-competitively with the goal of optimizing the efficiency of paths for developing digital tools for PD drug development.
- 3DT is leveraging a prospective study called WATCH-PD (Wearable Assessments in The Clinic and Home in PD), a 12-month multi-center, longitudinal, digital assessment study of PD progression in subjects with early, untreated PD as an exemplar pilot study to collect digital data in an early PD target population for the purpose of facilitating discussion and alignment with regulatory agencies.

\* *Biogen, Takeda, UCB, Merck, Roche, Lundbeck, GSK  
Academic advisors: University of Rochester, Rush  
University, Parkinson's UK, Michael J Fox Foundation*

*Ray Dorsey,  
Principal Investigator*

The primary goal of this study is to **generate a set of candidate objective digital measures** with optimized performance (e.g., improved sensitivity, reduced variability, closing of measurement gaps, etc.) to complement standard clinical assessments in measuring the progression of Parkinson's disease and response to treatment in clinical studies targeting early stages following clinical diagnosis.

A secondary goal is to understand the relationship between standard clinical assessments, research-grade digital tools used in a clinic setting, and more user-friendly consumer digital platforms to **develop a scalable approach for objective, sensitive, and frequent collection of motor and non-motor data in early PD.**

# What Makes 3DT Unique as a C-Path Project?

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- 3DT is focused on engaging regulators early —and collecting data prospectively
- It is built around a pilot study of digital health technologies in a prospective study (the WATCH-PD study in early Parkinson's disease).
- It is not focused on any single biomarker or endpoint, but on the identification of multiple clinically relevant candidate measures for further discussion with regulators

We seek Agency feedback on how to maximize the value of the Wearable Assessments in the Clinic and Home in PD (WATCH-PD) pilot study design in advancing the regulatory maturity of digital technologies to monitor disease progression, in order to optimally inform sponsors on their use in future clinical trials.

## *In scope:*

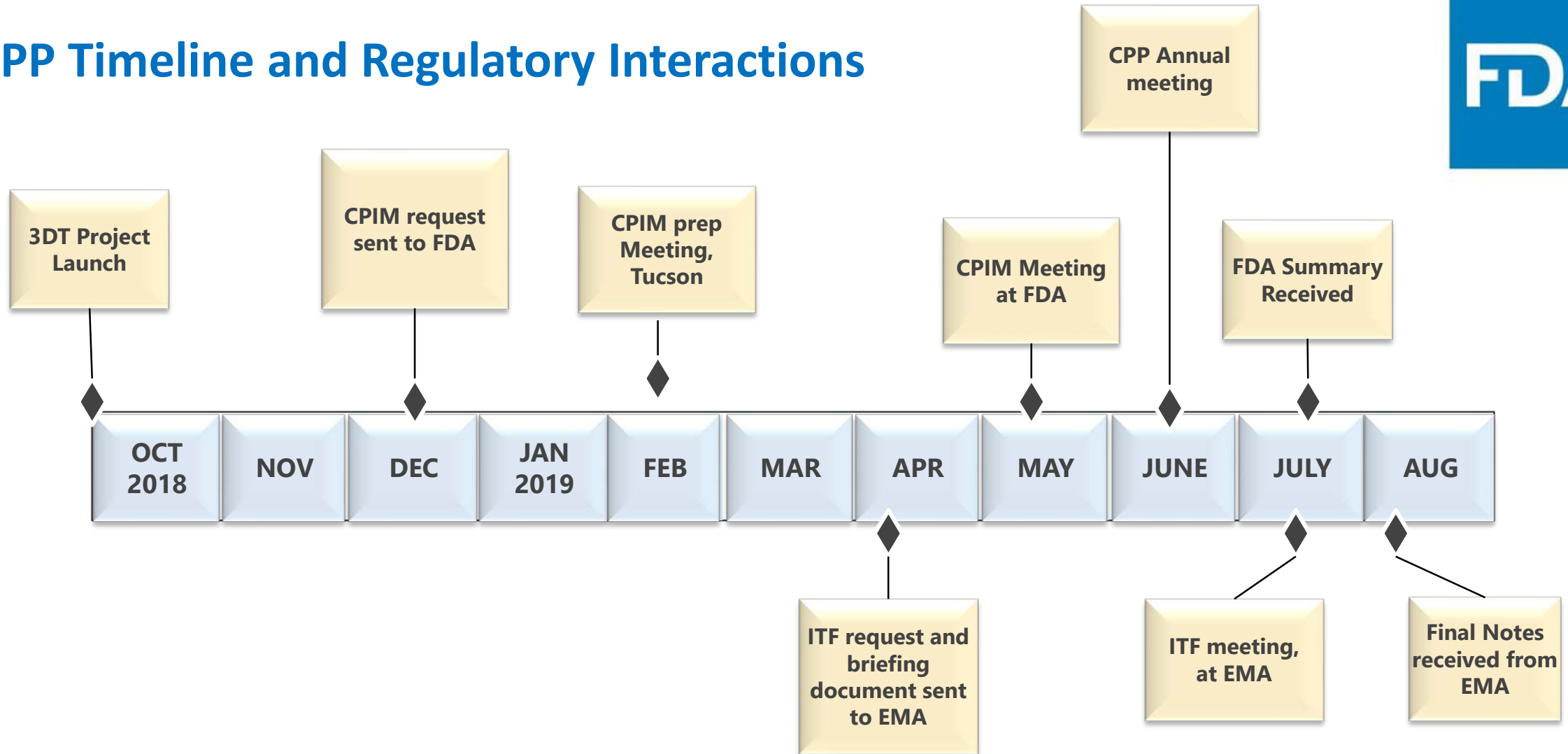
- Maximize the use of WATCH-PD pilot study to identify candidate digital measures for future discussions with regulators

## *Out of scope:*

- Qualification (as biomarker or clinical outcome assessment)
- Device clearance or approval with CDRH, CE Mark certification for medical devices



# CPP Timeline and Regulatory Interactions



## Key:

3DT = digital drug development tool team

CPIM = Critical Path Innovation Meeting

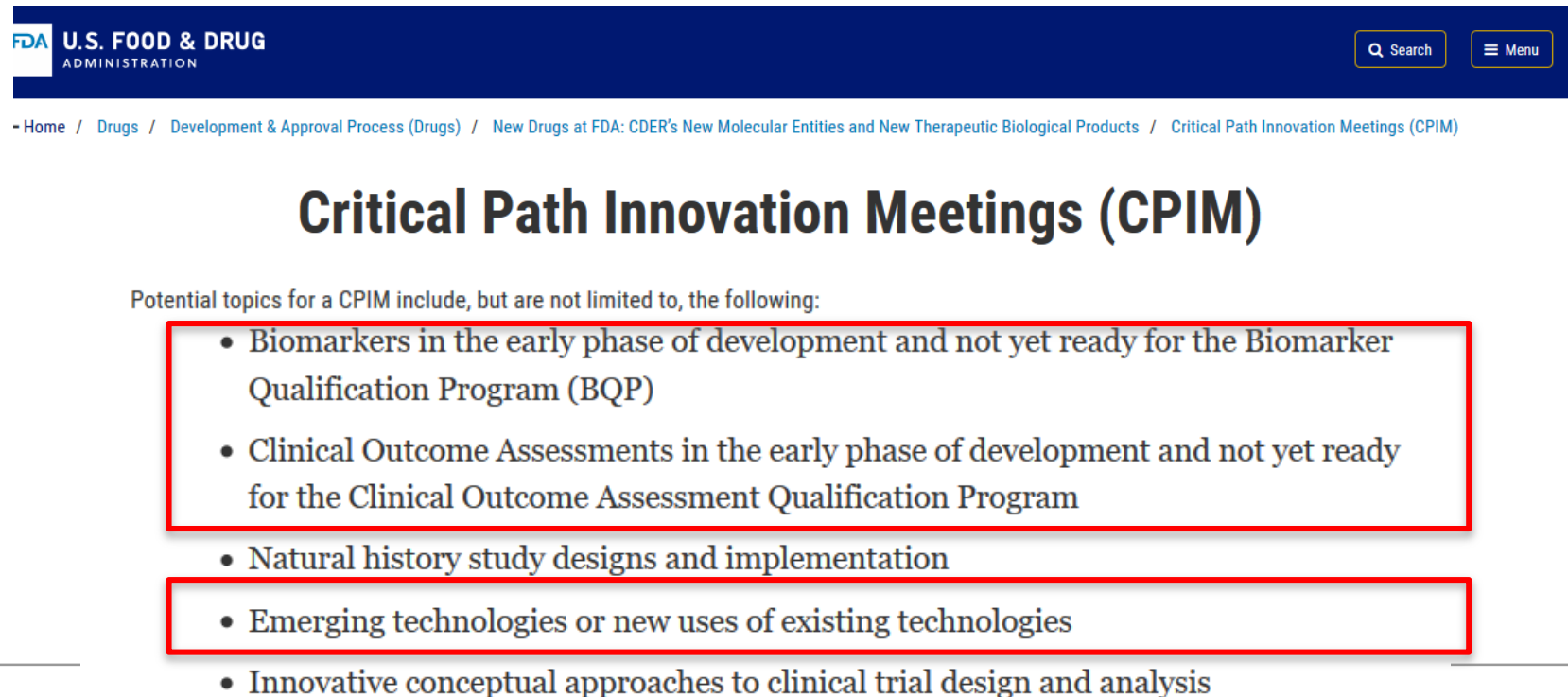
ITF = Innovative Task Force Meeting



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SCIENCE MEDICINES HEALTH

# What is a Critical Path Innovation Meeting (CPIM)?

- A forum to meet with the FDA to discuss innovative drug development approaches
- The goals of the CPIM are to discuss a methodology or technology proposed by the meeting requester and for CDER to provide general advice on how this methodology or technology might enhance drug development.
- Not all requests are accepted
- Meetings are informal and advice is non-binding



The screenshot shows the FDA website header with the logo and navigation links. Below the header is a breadcrumb trail: - Home / Drugs / Development & Approval Process (Drugs) / New Drugs at FDA: CDER's New Molecular Entities and New Therapeutic Biological Products / Critical Path Innovation Meetings (CPIM). The main heading is "Critical Path Innovation Meetings (CPIM)". Below this, a paragraph states: "Potential topics for a CPIM include, but are not limited to, the following:". A list of five topics follows, with the first two and the last one highlighted by red boxes in the original image:

- Biomarkers in the early phase of development and not yet ready for the Biomarker Qualification Program (BQP)
- Clinical Outcome Assessments in the early phase of development and not yet ready for the Clinical Outcome Assessment Qualification Program
- Natural history study designs and implementation
- Emerging technologies or new uses of existing technologies
- Innovative conceptual approaches to clinical trial design and analysis

### Well attended by wide range of FDA staff from across the agency

- Office of Medical Policy (OMP)
- Division of Neurology Products (DNP)
- Clinical Outcomes Assessments (COA)
- Office of Biostatistics (OB)
- Office of Science Policy (OSP)
- Center for Devices and Radiological Health (CDRH)
- Center for Biologics and Evaluation Research (CBER)
- Office of Clinical Pharmacology (OCP)
- Office of Business Informatics (OBI)

*36 FDA participants  
in person, 18 remote*

# What is an Innovation Task Force Meeting (ITF)?

## EMA initiatives to support drug development



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### What do we provide?

#### 2. Innovation Task Force (ITF) platform and meetings

- meetings are free and provide an open environment for a dialogue with experts
- a multidisciplinary group that includes **scientific, regulatory and legal competences**.
- provide regulatory advice to applicants on the eligibility to Agency procedures as a medicinal product
- **increase awareness and learning** in emerging therapies and technologies at the Agency

### What can it be used for?

- a discussion platform **for early dialogue** with applicants to proactively identify scientific, legal and regulatory issues **of emerging therapies and technologies** (e.g. growth factors, gene and cell therapy, any significant therapeutic innovation in PD;)

[http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general\\_content\\_000334.jsp&mid=W0b01ac05800ba1d9](http://www.ema.europa.eu/ema/index.jsp?curl=pages/regulation/general/general_content_000334.jsp&mid=W0b01ac05800ba1d9)

*“Drug Development in Parkinson’s disease: The regulatory perspective, and how can we help coping with the bottlenecks”*

*Presented by: Pavel Balabanov, MD PhD  
Human Medicines Evaluation Division,  
Scientific and regulatory management department,  
CNS and ophthalmology*

## IN-PERSON ATTENDEES

- ITF coordinator, Science & Innovation Support
- Head of Science & Innovation Support
- Head of Scientific Advice
- Head of Central Nervous System & Ophthalmology
- Biostatistics & Methodology Support
- Evaluation Procedures Division

**12 EMA participants**

## REMOTE ATTENDEES

- Scientific Advice
- Central Nervous System & Ophthalmology
- Surveillance & Epidemiology
- Regulatory Affairs
- Clinical, Immunologicals/Biologicals, Pharmacovigilance and Risk Management  
Medicines and Medical Devices Agency, Austria

- Complimentary of the concept of coming to regulators early with a consortium approach focused on a defined prospective study
- Looking at motor, non-motor, and mood-related symptoms is critical
- Recommendation to assess the patient's perspective of how they function and feel through interviews and quality-of-life measures
- Establishment of normative databases from metrics that will be collected with wearables is very important
- Suggestion that it may be beneficial to enroll subjects at the earliest point possible in their disease progression to identify sensitive measures that are uniquely applicable to early PD

- Questions around at-home data collection (issues with patient adherence with the proposed hardware and potential environmental factors)
- Concerns around data quality (e.g., importance of raw data, software/firmware updates, dealing with missing data, transparency of algorithms)
- Data analysis, including comparators and assessment of novel measures, and the importance of context in home-based monitoring

- WATCH-PD study sponsors have integrated some feedback into plans going forward
- Other members find value in learning how to address regulatory concerns and expectations in ongoing and planned studies employing digital devices
- Feedback may have impact on other initiatives
  - Personalized Parkinson's Project (Netherlands)
  - PPMI (Michael J Fox Foundation, Ken Marek)



Bloem *et al.* *BMC Neurology* (2019) 19:160  
<https://doi.org/10.1186/s12883-019-1394-3>

BMC Neurology

STUDY PROTOCOL

Open Access

The Personalized Parkinson Project:  
examining disease progression through  
broad biomarkers in early Parkinson's  
disease



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R. C. Helmich<sup>1</sup>, B. P. van de Warrenburg<sup>1</sup>, L. J. W. Evers<sup>1,9</sup>, J. int'Hout<sup>10</sup>, T. van de Zande<sup>11</sup>, T. M. Snyder<sup>2</sup>,  
R. Kapur<sup>12</sup> and M. J. Meinders<sup>13</sup>



**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.

## Conclusions

- CPP's 3DT effort has made significant progress on the goal of reaching a shared understanding of the open regulatory and scientific issues in the use of digital health technologies as endpoints in PD clinical trials, using the WATCH-PD study as a case example
- By seeking regulatory agency feedback on how to maximize the value of the WATCH-PD pilot study in advancing the regulatory maturity of these digital technologies, multiple sponsors have been informed on issues to attend to for optimizing the use of DHTs in future clinical trials.
- CPP consortium model including alignment with regulatory agencies and data core competencies is well placed to fill gaps to enable efficiencies in the use of digital health technologies as drug development tools in PD
- If you have interest in joining CPP and becoming part of the 3DT initiative, please reach out to Diane Stephenson ([dstephenson@c-path.org](mailto:dstephenson@c-path.org); 520-382-1405)