Evolving Solutions to Optimize Clinical Trial Decentralization

The benefits offered by decentralized trials are driving wider adoption of this approach to clinical research. The introduction of novel solutions to facilitate adherence can support decentralized trials and mitigate potential concerns surrounding reduced patient-physician touchpoints. Now that PPD is part of the Thermo Fisher family, it is uniquely positioned to provide new, fit-for-purpose solutions to help sponsors create a better patient experience and realize the benefits of decentralized trials while assuring that those studies yield high-quality data.

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Decentralization is Here to Stay

Hybrid trials — combining a mixture of site-based and decentralized solutions — are experiencing explosive growth.[1] With the hybrid model, it is possible to conduct aspects of the trial remotely, supporting a better patient experience while still conducting the aspects that require in-person interactions at clinical trials sites. As new modalities and personalized medicines become an industry focal point, this shift to decentralization represents an exciting evolution in the clinical trial landscape and has the potential to bring more lifesaving drug products to patients — faster. Because hybrid trials prioritize patient-centricity, they also have the potential to increase patient retention and reach otherwise unrepresented patient groups.

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The industry's wider adoption of both existing technologies and recent innovations has supported the growth of hybrid trials. In an effort to find ways of reducing patient burden — without sacrificing data quality — these technologies have been incorporated into new and evolving trial designs that include assessments through TeleVisits, wearable devices that provide real-time patient data, and even reconsidered endpoints. The space continues to rapidly evolve at nearly every level.

The broader industry push toward patient centricity is guided by the expectation that reduced patient burden — including regular travel to the clinical trial site — will lead to faster screening and recruitment and greater participation and retention, which can be highly beneficial in terms of increasing the diversity and representativeness of clinical trials, a crucial and historically overlooked consideration. Overall, the hope is that decentralization will make it possible to implement clinical studies more quickly and cost-effectively.

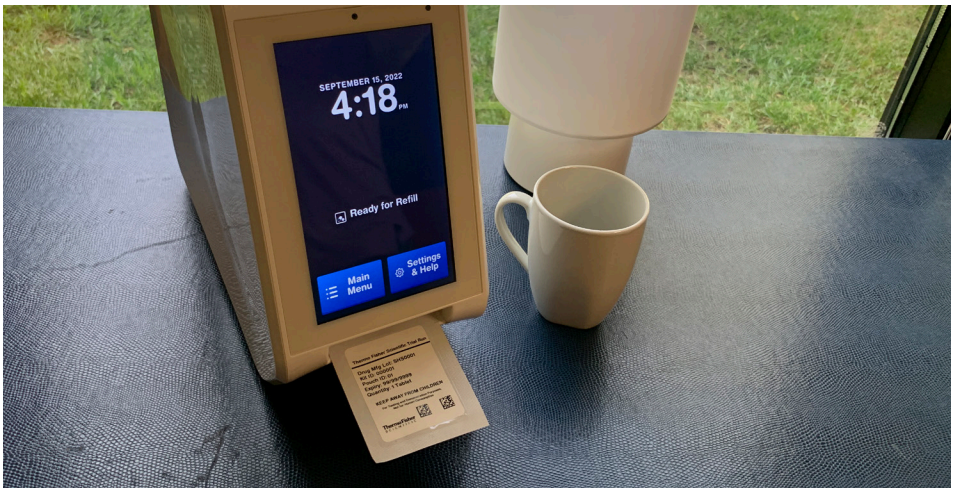
Balancing Participation and Adherence

Traditional site-based trials leverage designs to support patient adherence. In the most extreme cases, where a patient must receive treatment every day under supervision — "direct observational therapy" — 100% adherence can be consistently achieved. For example, the success of early HIV treatments can be partially attributed to clinical trials with direct observational therapy. Today, this approach is used in developing countries for the treatment of tuberculosis and other infectious diseases that require that strict regimens be followed.

Achieving a level of successful adherence in decentralized or hybrid trial models require new approaches to validate whether patients are participating as per protocol — taking their medication as prescribed, making self-observations, performing certain activities, and so on — and help mitigate any potential uncertainty.

New adherence measurement methods — for example, smart packaging combined with remote monitoring, including text messages containing alerts or phone calls made to participants — enable investigators to deeply understand how each patient is exposed to the study drug, to provide confirmation that each patient is dosed correctly, and to manage some of the potential risks. Additionally, acquiring more information about specific dosing behavioral problems allows the sponsor and CROs to offer specific, not-too-intrusive interventions to patients to help correct them, and patients tend to be responsive to these tailored interventions.

The right trial design and the application of adherence technologies and techniques are among the solutions that can reduce or eliminate concerns surrounding perception of decentralization and its fewer human touchpoints. Ultimately improving a patient's exposure to the study drug in compliance with the protocol, these innovative adherence measurement solutions could be seen as an insurance policy.



Adherence data can be used not only for their primary purpose — to confirm and/ or maximize patient adherence — but also to improve future protocol designs and processes and the procedures used to implement hybrid and fully decentralized studies.

Significant Opportunities for New Trial Designs

In support of increased patient-centricity, pivoting from a preventative focus to the collection of adherence data could also provide deeper insights into patient behaviors. Those data can be used not only for their primary purpose — to confirm and/ or maximize patient adherence — but also to improve future protocol designs and processes and the procedures used to implement hybrid and fully decentralized studies.

The biggest resistance to adoption of these adherence tracking technologies is that they generate data that are very different from the passive methods traditionally used (diary entries and pill counts). It has been shown that the overestimation of drug exposure in most trials using existing methods is 15% over time compared with what is determined using passive adherence methods.[2] That 15% is typically accounted for by adding more patients to trials. We are on the journey, but the implementation of comprehensive adherence techniques may make it possible to require fewer patients in trials in the near future.

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PPD and Thermo Fisher Scientific: Innovating Adherence Measurement Solutions

Since the 2021 acquisition of PPD by Thermo Fisher Scientific, they have been working closely together to offer a comprehensive suite of world-class services across the clinical development spectrum. From scientific discovery, through assessing safety, efficacy, and healthcare outcomes and managing clinical trial logistics, to the development and manufacture of drug products, we are continuing to find new ways to connect the capabilities across the combined company to further help our customers accelerate innovation and drive productivity. Together, the teams are establishing a portfolio of decentralized and adherence technologies — including medicine packages and devices that measure the date and time of a medication event for each delivery method.

Creating and offering solutions to optimize adherence remotely is just one piece of the broader PPD DCT Ecosystem, a collection of people, partnerships, technology, services, and resources that presents a comprehensive and holistic solution to overcome the new and evolving complexities inherent to decentralized clinical research. The DCT Ecosystem removes the rigidity associated with traditional trial design and keeps the focus on the patient and innovation, by combining a portfolio of digital and decentralized services, including:

- TeleVisits
- Wearables
- Direct-to-/direct-from-patient shipments
- Remote monitoring
- Virtual sites
- Mobile sites
- Home healthcare and nursing
- eCOA
- eConsent
- eSource
- Patient concierge
- Our DCT PI/site network

We are supporting our customers by providing a comprehensive ecosystem of qualified solutions to ensure that each sponsor has access to the right portfolio of solutions for any given trial. By doing so, we are enabling more effective decentralized trials that offer the benefits of improved patient experience, easier recruitment, and greater retention while also ensuring high levels of patient adherence. ■

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Tim Rich is a vice president and one of the founding members of PPD Digital, PPD's decentralized business unit. He leads the consultancy, innovation, and strategy group who are driving forward the adoption of decentralization while bringing forward innovative new solutions. Prior to his appointment, Rich was a member of the biotech operational leadership group. In this role, he provided strategic direction, leadership, and management across multiple divisions and therapeutic areas by utilizing his 20 years of experience in project delivery that covers a wide range of indications, including complex rare disease and gene therapy programs. Rich joined PPD in 2006 in project management and has progressed to his current leadership role. His experience spans all elements of global project management, portfolio management, development operations, and client relationship roles.

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John Musaus, MS, MBA, is the Head of Medication Adherence and Biomarker Measurement at Thermo Fisher Scientific. He has been working in the field of remote measurement of patient adherence and biomarker data for >10 years with a focus on the solutions that measure drug dosing histories and the platforms that analyze and leverage the data across the healthcare value chain. John is also the Founder and Executive Director of the Adherence Measurement Institute, a non-profit organization that works with academic researchers from around the world who are interested in integrating remote measurement solutions into their research designs. He has a BS in biological systems engineering from Virginia Tech, and an MBA from Cornell University.

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