Changing the Narrative of First in Human Oral Drug Development: The SMART Advantage

In the intricate realm of pharmaceutical development, First Human Dose (FHD) studies represent a pivotal juncture, replete with complexities yet essential for advancing patient safety and drug efficacy. These early-stage clinical trials aim to establish safety and refine the dose to minimise adverse events (AEs) with potentially some indication of efficacy. Traditional drug development pathways for solid oral formulations are often characterised by their transactional nature, contributing to prolonged timelines. Recognising the critical balance between expediency and safety, PCI Pharma Services (PCI), a world-leading CDMO, and CRO, Worldwide Clinical Trials provide an innovative end-to-end partnership designed to navigate the FHD process with unmatched efficiency from drug formulation, and clinical supply through to trial execution and study management.

In FHD development, formulating a drug is just the beginning. Other essential elements include executing Phase 1 trials with precise bioanalytical assessments, effective participant recruitment, and meticulously planned trial designs. These studies rely on healthy volunteers and expert teams to conduct detailed pharmacokinetic/pharmacodynamic (PK/PD) analyses, which are crucial for positioning the novel drug for success in subsequent phases. This article will cover the importance of the partnership between CROs and CDMOs and how their individual capabilities have the power to expedite clinical trials and increase efficiency.

Transforming FHD with Drug in Capsule Technology and Pristine Supply Management

CDMOs have the unique opportunity to proactively recognise areas of improvement in the development and manufacturing process and implement innovative solutions to combat hurdles. PCI identified a way to transform their client's studies and expedite the pathway into the FHD study phase with their Supply Management and Readiness Team (SMART) of development, manufacturing, and supply management experts. SMART is not only an acronym but a reflection of its mission to guarantee the timely provision of solid oral medications for Phase 1 clinical studies. SMART FHD transcends conventional oral drug development and stability study delays by eliminating early-stage formulation development to deliver strategic operational advantages, including a managed operational package and pivotal distribution options. This approach can propel drugs into the early clinical phase months or even a year ahead of traditional methods.

With SMART FHD, all that is needed from the client is the delivery of a sufficient volume of drug substance, and PCI can manage the rest. The critical difference is the streamlined drug-in-capsule (DiC) process that requires less back-and-forth on developing and optimising the drug formulation, moving a molecule to the clinical phase more quickly. In addition, there's no need to add the potential for delays and higher costs from managing multiple vendors.

Comprehensive Solution Providing Time and Financial Savings

The SMART FHD plan offers a seamless package from the availability of the drug substance to delivery at the clinical site. The package provides a ready-made bundle of DiC development and flexible manufacturing, stability program management, packaging and labelling for clinical demand, regulatory dossier compilation, distribution, and clinical supply management.

The SMART approach is optimal for FHD studies as it provides the flexibility needed for dose-ranging studies. Eliminating time-consuming processes and delays over formulation options and having the drug product supply available before any regulatory and clinical site approvals enables an FHD trial to start months faster.

SMART FHD distinguishes itself by providing a white-glove partnership instead of standard transactional manufacturing services. The holistic oversight capabilities encompass material management and inventory planning enhanced by strategic distribution capabilities through Canada for North American studies. Access to this facility circumvents typical IND filing delays but also facilitates an expedited supply chain, significantly reducing time to trial. The predetermined package and unique supply chain remove delays that would otherwise add unnecessary time and increase costs.

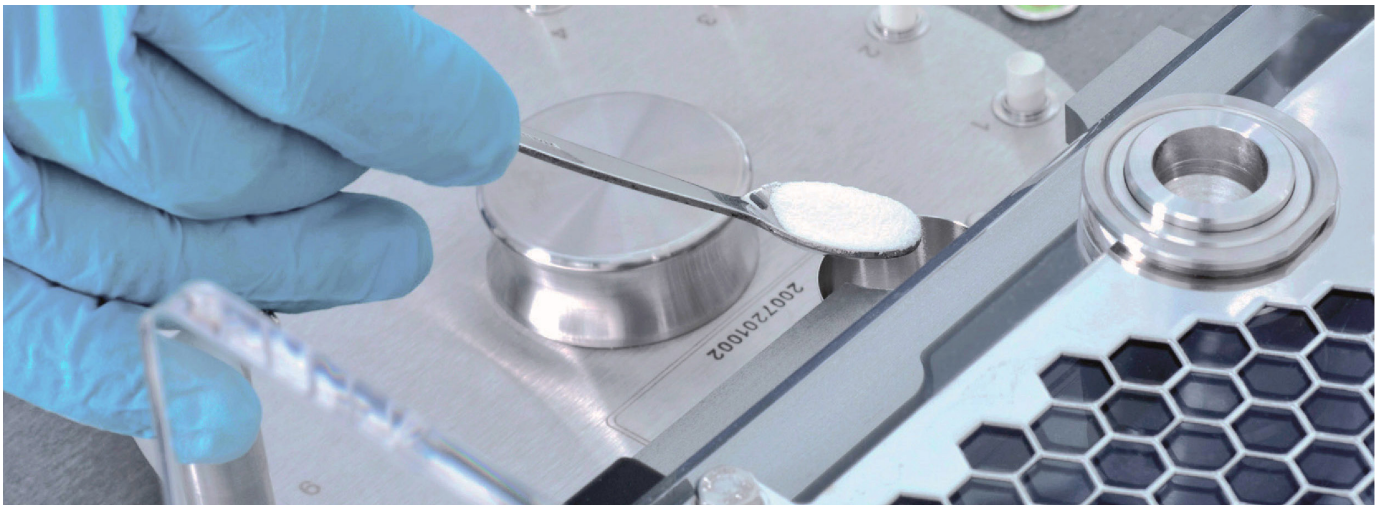
The Power of Partnership – The CRO & CDMO Relationship

Traditionally, the relationship between CDMO's and CRO's is very transactional or even non-existent if the client doesn't make that initial introduction. Once the drug is shipped by the CDMO there's often little to no communication between the two parties. Collaborating with a CDMO and CRO in tandem presents a strategic opportunity to move through the lifecycle of a novel drug investigation efficiently. By having in-house Clinical Supply Managers, the CDMO can maintain that connection and prepare clients for the next phase of their clinical trial. This partnership offers a more complete package that goes from drug substance all the way to clinical data for phase I trials and potentially beyond.

PCI and Worldwide together provide a comprehensive service beginning with drug formulation and dosing through PK/PD and healthy volunteer recruitment and testing, allowing for reduced costs and increased speed to market. Overall, a shared vision and aligned leadership between PCI and Worldwide function to streamline the FHD process across the board.

Excellence in Pharmacokinetic/Pharmacodynamic Studies, Site Selection and Patient Recruitment

Worldwide's PK/PD capabilities enhances the drug development process from start to finish. At our state-of-the-art manufacturing facility, specialised teams analyse PK/PD data in a bioanalytical lab and review it thoroughly to ensure a deep understanding of the relationship between kinetic and dynamic components. Having an experienced team behind a study provides rigorous and accurate data



on drug interactions with target engagement and efficacy, saving time and money when moving forward in trials. This preemptive analysis also helps avoid delays later in the research, particularly concerning dosage adjustments.

Engaging with Worldwide's PK/PD services for drug trials streamlines the development process, from initial dose planning to dose escalation in later trials. This efficiency is partly due to automated bioanalytic capabilities that reduce the risk of inaccuracies that traditionally arise during manual testing and partially from the expertise of the scientific staff. Worldwide has an extensive automation suite with various liquid handling workstations and microplate management systems. Beyond, Worldwide's resources and capacity allow for state-of-the-art instrumentation to cover all drug discovery needs, spanning high-throughput mass spectrometry, Spectramax, MSD, Microlab Star, and liquid scintillation counter and oxidiser, which supports radiolabeled absorption metabolism and excretion (AME) studies. When combining the automated lab capabilities with staff that average more than 15 years of bioanalytical experience, the opportunities for research increase exponentially. The team prioritises data integrity, traceability, quality control, and on-time records, touting a 100% sponsor audit pass rate and a clean record for regulatory inspections. When working with Worldwide, you can expect direct and individualised attention from the in-house PK and biostatistics staff with the added assurance of knowing that their lab space is GLP and Part 11 compliant.

Whilst managing a novel drug investigation can at times be stressful, leveraging Worldwide's expertise in drug discovery minimises common challenges, particularly in solid dose formulation. where expertise extends beyond the lab to include site selection and patient recruitment, adding value to clinical projects and helping to sidestep potential setbacks and unnecessary stress.

Worldwide delivers continued excellence in early-phase drug development through expertise in precision targeting of nuanced patient populations and maintaining the highest quality standards of scientific and operational acumen. Worldwide collectively provides a wide range of support throughout Phase 1 drug studies beyond PK/PD in their expansive network of sites and participant recruitment, leveraging their highly differentiated contributions to the drug development industry. The innovation expands beyond participant recruitment; the intentionally located 200-bed facility close to their cutting-edge bioanalytical lab facilitates rapid data output that you can trust and position your drug to lead the industry.

Unique Innovation with an Opportunity for Expansion: The Future of Drug Development

PCI is looking forward with the SMART FHD initiative, which promises to set a new standard in the market for solid oral medications. With PCI's innovative SMART FHD offering and Worldwide's expertise in Phase 1 trial execution, together we provide a comprehensive solution that encompasses every aspect of development to get you from a molecule to clinical data available in the fastest time possible.

Looking forward, PCI also plans to revolutionise the pharmaceutical landscape by increasing the scale of this offering enabling a commercialisation strategy with a DiC formulation. By avoiding the delay and expense of formulating, there is the potential to reach the market years ahead of the traditional model with significant cost savings. Additional enhancements to the program are investigating the expansion of the SMART concept to include sterile injectable dosage forms.

Worldwide Clinical Trials

Worldwide Clinical Trials (Worldwide) is a leading global contract research organisation (CRO) partnering with biotechnology and pharmaceutical companies to advance new medications. Services include bioanalytical lab services, Phase I–IV clinical trials, and real-world evidence studies, specialising in neuroscience, oncology, rare diseases, and cardiometabolic disorders.

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Ed Groleau has over 30 years of experience in pharmaceutical drug development on both the pharma and vendor sides. The first half of his career was spent in various laboratories from analytical method development, to solid state characterization and polymorph screening, to stress degradation and chemical characterization. He left the labs and moved into clinical supplies in 2003 providing all aspects of CSM support to maintain clinical programs. He joined PCI in 2018 and became Sr. Director of PCI's Supply Management And Readiness Team (SMART).