SMART First Human Dose, with PCI Pharma Services

The core concept of PCI's SMART FHD service offering is simple: to accelerate early phase clinical manufacture and supply. In order to achieve this, PCI has taken three of its flagship services and combined them into a program that ensures a sponsor's valuable API can get to Phase I clinical trials quicker, cheaper and more efficiently than via the traditional development route. Those three services are drug-in-capsule manufacture, using Xcelodose® micro-dosing technology; industry-leading clinical packaging services; and PCI's bespoke clinical program management service, clinicalSMART™.

Service #1: Drug-in-Capsule Manufacture with Xcelodose®
The traditional route through early clinical phase formulation development can be a complex and time-consuming process. Excipient compatibility studies, prototype development, and the associated stability studies themselves can take months to complete before the product can be delivered to the clinic. However, by providing drug in capsule (DIC) manufacturing services using Xcelodose® micro-dosing technology, sponsors can significantly reduce the time it takes to get the first-in-human dose to clinic.

Xcelodose® is a precision powder micro-dosing system that allows API to be filled directly into capsules and vials. This approach removes the need for development of a powder blend, as would be the case for a more traditional development processes. PCI operates both the Xcelodose® 120S and the 600S models, filling up to 120 and 600 capsules per hour respectively, making them ideal for clinical manufacture from early to later stage clinical programs. Additional investments in Xcelohood™ and Xceloprotect™ containment systems further enhances the safe processing of highly potent drug products at our manufacturing facility in the UK.

By eliminating the requirement for pre-formulation activities, excipient compatibility and associated stability studies, as well as simplification of method development processes, Xcelodose® enables products to be manufactured and delivered to clinic up to 6 months faster than the more traditional route. Dosing directly into capsules also helps to reduce the amount of API required, helping to eliminate wastage of often-valuable APIs which is particularly important at the early stages of proof of concept if API is in short supply.

Additionally, Xcelodose® is a fully programmable system, ensuring exceptional levels of accuracy, precision and consistency whilst minimizing wastage of drug substance. Capsules can be filled with API at dosage strengths ranging from 100 µg to 100 mg and beyond, and the weight of each capsule is recorded, allowing traceability of samples that meet GMP requirements. Enabling an optimised filling process compensates for variability in drug powder properties, simplifies method development, and improves data transfer, all of which contributes to greater efficiencies and speed to clinic and patient.

Service #2: Clinical Packaging Services
Manufacturing DIC products containing highly potent APIs can be challenging, and not all CDMOs have the capability to package the same drug product safely on site. In 2022, PCI launched a new highly potent packaging facility (HPPF), located at the same site that hosts our Xcelodose® technology in the UK. Segregated rooms, dedicated HVAC systems, conditioned environments for packaging activities and dust extraction units to remove any airborne particulates from potent APIs ensures the highest level of operator safety and drug product integrity.

Additionally, online HAPA digital printing technology ensures that with just one reel of lidding foil, the facility is able to print artwork for different market requirements on a single packaging line, all within an envelope of very high grade control of airborne particulates. This, in turn, grants sponsors considerable flexibility and reduces waste of pre-printed materials.

This facility is a recent addition to PCI's established global clinical packaging network. With sites in the US, Europe, the UK and Asia Pacific, and full capabilities for the primary and secondary packaging of encapsulated drug substance, PCI's manufacturing activities are well-supported to provide FHD services to sponsors.

Service #3: clinicalSMART™

PCI's clinical Supply Management And Readiness Team (SMART) is a specialist team of Clinical Supplies industry professionals who have over 400 years' collective experience, and who manage clinical drug supply on behalf of clients. Since its inception in 2016, clinicalSMART™ has supported almost 100 clients and over 250 studies globally. Designed with flexibility at its core, clinicalSMART™ is able to support sponsor requirements either throughout the entire study lifecycle, from protocol development through to final destruction of materials, or at certain time points when sponsor teams require additional resources to supplement in-house supply management expertise.

It does so by collating all key information from external parties (such as trial design, drug stability, and recruitment assumptions) and utilising in-house expertise to develop optimal supply strategies. Whether it's working with client's internal teams in a consultative role, or assuming full ownership of supply chain management, clinicalSMART™ services are immediately available, preventing the need to recruit new staff, delivering the agreed contracted hours per month as required by the client.

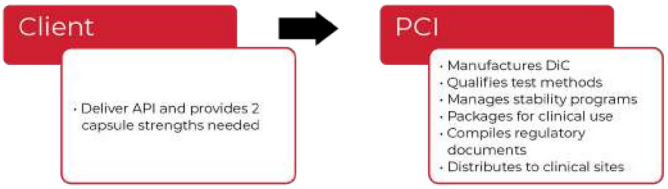
Established in 2016, clinicalSMART™ addressed the industry's growing need for integrated clinical supply management services. At that time, the two highest ranking therapeutic areas in terms of clinical trial cost per patient were haematology and oncology, with a median cost of over $200k and over $100k respectively.[1] As of December 2023, there were 187,957 registered interventional clinical trials using drug or biologic therapies, up from 174,669 in September 2022.[2] Considering the sheer numbers involved here, any delays, miscommunications or errors in the clinical trials management process would be extremely costly in financial terms, not to mention the most important factor: the risks to the patients themselves.

In addition to clinical supply chain management, clinicalSMART™ is also able to initiate RFQ document writing to support outsourcing requirements on a client's behalf. After reviewing key study assumptions and estimates in order to establish an initial study plan, the RFQ and relevant supporting documentation is prepared for the client; due to a thorough knowledge and evaluation of the study requirements, a high level of accuracy within the quotation is assured. As with the study plans, RFQs are then submitted to the clinicalSMART™ team for peer review, drawing on the vast experience within the team to ensure a high level of accuracy.

Regardless of the level of CSM involvement contracted to the client, the critical objective remains the same: to provide a seamless, integrated clinical supply service at the level required by the client, at any stage or throughout the study lifecycle, whilst leveraging PCI's extensive experience in this area of expertise.

To gain maximum benefit from clinicalSMART™ it is recommended that services are contracted as early as possible, preferably prior to study start up. This enables the PCI CSM to collate and analyse key information from external study stake holders, and to review the protocol, the drug stability, the availability of comparators in the marketplace, the countries involved in the study, the labelling and distribution strategy, and recruitment projections.

This comprehensive assessment will help the clinicalSMART™ CSM identify the most efficient kit design and create an initial packaging forecast, which can be modified as changes arise. The CSM will also ensure the forecast is 'fit for purpose' by assessing it against the potential drug utilisation in the IRT.



The PCI CMS will typically review the IRT specifications and recommend initial shipment triggers and re-supply values, ensuring best use of available drug product, adjusting values when live study data becomes available, and when changes arise from unplanned protocol revisions, or variance between projected vs actual site activity. This enables the PCI CSM to flag potential supplies risks, and present corrective measures.

A Combined Program: SMART FHD Services

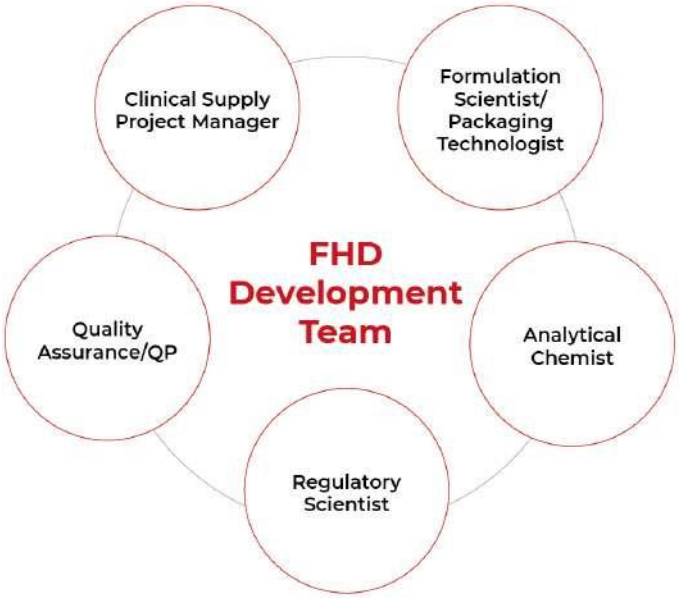
PCI's SMART FHD service consists of a dedicated CMC development team capable of rapidly transitioning a drug product from candidate selection to first human dose clinical trials.

The ability to manufacture DIC dosage forms, a robust clinical packaging network and the expertise of PCI's clinicalSMART™ team is a powerful combination of services which ensures that early phase drug products reach FHD clinical trials as quickly and efficiently as possible. Driving this service offering is PCI's SMART FHD team, which consists of experienced Clinical Supply Managers, Regulatory Scientists, Formulation Scientists, Packaging Technologists, Analytical Chemists and Quality Assurance/QPs who collectively have hundreds of years of industry experience.

This experienced group will oversee all drug development preparation activities plus regulatory and clinical trial supply management, reducing clinical trial preparation from up to two years to possibly just a few months, as outlined below.

PCI's SMART FHD team provides sponsors with a development path to FHD clinical trials that is shorter than traditional routes by a matter of several months, potentially reducing the time to market by a matter of years. The SMART FHD team achieves this by:

- Developing and manufacturing minimum and maximum DIC dosages;
- Qualifying test methods and conducting a bracketed stability protocol including packaging, storage, and testing, and providing reports throughout;
- Bottling and labeling the drug product for clinic use;
- Compiling all CMC information to support regulatory submission;
- Providing QP release of the clinical drug product;
- Managing the sponsor's inventory and distributing the drug product for clinical use;
- Supplying project management support services to organise and oversee all aspects of the development project.



The "white glove" service that SMART FHD team provides encompasses a number of benefits to sponsors, which include, but are not limited to:

- Rapid access to clinical data;
- Removal of traditional drug development from the critical path;
- Significant financial savings;
- Reduction of time delays and financial investments linked to multiple development activities;
- Flexibility of supply from clinical Phase I, through to Phase IIa and possibly beyond;
- Quality Assurance, QP, Regulatory and Analytical support from dedicated teams within PCI.

The Future of SMART FHD

The value of PCI's SMART FHD service offering is twofold. Firstly, it enhances a handful of PCI's existing service offerings to create a symbiotic operation for sponsors whose drug product is entering early phase clinical trials. In doing so, it displays PCI's ongoing commitment to providing sponsors with fast, efficient services which deliver their valuable drug product to patients around the globe. SMART FHD's continued excellence in providing seamless, integrated services aligns perfectly with the wider organisation's goal of providing true end-to-end CDMO services for clients around the globe. If you would like to learn more about SMART FHD

and how it may assist you in your clinical goals, please get in touch today.

REFERENCES

1. https://www.statista.com/statistics/1197095/clinical-trial-cost-per-patient-by-therapy-area/
2. https://www.clinicaltrials.gov/ct2/resources/trends#TypesOfRegisteredStudies

Ed Groleau

Ed Groleau, Director, Clinical Supply Chain for North America at PCI Pharma Services, has over 30 years of experience in the Pharmaceutical industry. He joined PCI Pharma Services in 2018 and became the director of his group in 2019. Ed leads the Supply Management And Readiness Team (SMART) at PCI where his team partners with clinical trial sponsors to provide any clinical supply management services from protocol development through destruction. Prior to PCI, Ed worked in numerous departments at Eli Lilly, spending 15 years in various laboratories before moving into the Clinical Trial Supplies group in 2003. In 2011 he became part of a highly integrated CM&C team responsible for overseeing the development of compounds from discovery through the proof-of-concept stage. In 2016 Ed moved to Elanco, Lilly's animal health division, where he established a global clinical trial supplies group for developing companion and food animal projects.

Email: edward.groleau@pci.com

Website: www.pci.com
Email: talkfuture@pci.com