AUGUST - 2021
ISSN 2644-2787

pharma TECH OUTLOOK

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Preclinical Expertise from Planning to Production

Developing a brand-new drug is complex, time-consuming, expensive, and daunting, to say the least. This is because the requirements to develop effective medications continue to advance in complex disease areas with unmet medical needs challenging the experts in all disciplines involved, such as cancer, metabolic or CNS diseases. The highest scientific and quality standards are crucial and require a multifaceted approach. To strengthen the chances of successfully completing clinical development leading to the approval of a new drug, the selection of adequate preclinical candidates is of utmost importance. Identifying safe, potent, and effective drug candidates demands thorough preclinical testing, which evaluates aspects of pharmacology, toxicology, toxicopathology, and drug metabolism and pharmacokinetics in in-vitro and in-vivo settings. Nevertheless, merely a small fraction of investigational new drugs tested in clinical trials eventually lead to a marketed product after passing preclinical evaluation. Evidently, there is a need to streamline existing standard preclinical approaches to better emulate the complexity of human disease mechanisms. Besides, the industry is also experiencing a loss of expertise in the last 20 years, and big pharmaceutical organisations are having a hard time deriving the real value from the extracted data in an integrated manner.

This is precisely where PreClinical Safety (PCS) Consultants Ltd is moving the needle. As an integrated drug development company, PCS draws on its rich and unparalleled experience to provide sound strategic and objective scientific input, and their successful operational implementation through testing programmes to ultimately build up a comprehensive basis for a robust risk-benefit assessment. Long-standing operational experience, and strong regulatory background to provide independent expert advisory services in non-clinical drug development are key aspects in the services that PCS provides. The company caters to the needs of pharmaceutical, agro-chemical, chemical and food industries, academic institutions engaged in science and research, business investors and CROs. "We are helping clients to robustly implement the process from the start including the selection of the right places, designing the studies, and working with the CROs to run the studies. We also offer to monitor these studies from a scientific and GLP perspective. Additionally, our group of experts truly help clients write the regulatory documents, defend the programs in terms of development, and accompany them to the regulatory meetings, whether it be in the US or Europe or other places in the world," asserts Dr Stephanie Plassmann, senior expert in non-clinical drug development of PCS.

Dr Stephanie Plassmann, Senior Expert in Non-Clinical Drug Development

A to Z of Preclinical Development

Established in 1989, Switzerland-based PCS comprises a dedicated team of senior experts, each with more than 25 years of continuous hands-on experience and expertise in the field of preclinical drug development, including preclinical pharmacology, toxicology, toxicopathology, DMPK and GLP. At the outset, the company focused on delivering consulting services in histopathology and toxicology. In due course, the dexterity was augmented to comprise the areas of drug metabolism and pharmacokinetics, non-clinical pharmacology and quality assurance (GLP), and was lately further expanded to include clinical pharmacology. The experienced team at PCS also supports regulatory submissions, including the preparation of and participation in meetings with regulatory authorities and the preparation of regulatory documentation such as IBs, INDs, Briefing Documentation and CTD writing according to the ICH standards, covering a broad range of indications. The company has long-standing experience with a wide range of test items used in drug development, including small molecules, herbals or biotechnology-derived products, but also with other materials such as food supplements, chemicals and impurities.

PCS offers a range of services to pharmaceutical companies. For instance, if a particular pharmaceutical company has a question regarding a specific non-clinical issue, the experienced team at PCS notes down an expert opinion and assists the pharmaceutical company to develop and defend adequate strategies to address this challenge. Through such processes, PCS offers guidance to pharmaceutical companies and brings forth a clear understanding of the requirements to be able to pursue clinical development at any stage. "We truly believe in delivering highest quality expertise through our experience. In addition, as there is only a handful of people with good quality experience, we also engage in the development of the field by passing on our expertise through education and training of fellow scientists. We cover all areas of preclinical development, including developmental and reproductive toxicology (DART) as well as juvenile animal studies (JAS)," mentions Dr Stephanie Plassmann. As highest scientific quality and standard is demanded in the complex multidisciplinary process of integrated drug development, PCS supports their clients on a case-by-case basis in close collaboration with their expert teams.

Deploying Outstanding Experience

With innovation at its core, PCS' dedicated team consists of experts with long-standing experience in pharmaceutical development. They gained all their expertise in positions working hands-on in companies conducting preclinical studies in-house, including under GLP, and being integrated members of multidisciplinary project-teams driving pharmaceutical development. "Our team offers unique expertise, which is lost or much less available in many places today, in a broad range of indications and all relevant areas of preclinical drug development, including DART and JAS studies, a field in which only a handful of scientists worldwide have sufficient experience, which is conflicting with an increasing demand for expertise in paediatric drug development," states Dr Plassmann. The value proposition of the company also gets well established with the fact that it is strongly dedicated to provide timely, sound and highest quality support to the projects brought in by the clients. Another aspect that needs to be highlighted is the fact that PCS is highly committed to helping patients suffering from diseases and conditions with a high unmet medical need and has a sound understanding about how resources need to be used in the most efficient manner for bringing drugs on the market in the shortest possible time while maintaining highest quality standards.

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As one of the main purposes of a preclinical safety program is to adequately characterise potential risks for human patients, it is imperative to comprehensively identify potential target organ systems of toxicity as the fundamental basis to further characterise the safety profile in humans. One major factor in this concept is to establish an adequate Maximum Tolerated Dose (MTD) in different types of studies. At the same time, there is no unique scientific definition for an MTD, as it will not only depend on the type and duration of a given study but even different concepts for defining an MTD will be adopted, depending on the regulatory region. PCS' significant experience and direct interaction with regulators over many years in a range of indications act as a benefit for the clients as not only relevant guidelines and regulatory norms are taken into account during the preclinical process, but also real-life scenarios in different contexts. For instance, PCS was involved in a program wherein the client approached PCS to have a word with FDA before starting a phase one trial. Through the formalised process of scientific advice, the team of experts from PCS approached FDA to discuss the available information and paved the way to proceed adopting a robust approach for further development. PCS strongly believes in the concept of close interaction along the way, not only with clients, but also with regulatory agencies, which equally contribute to the complex process of drug development with highly valuable experience and expertise, and therefore encourages clients to interact with regulators in a proactive and transparent manner. In this particular case, with its long-standing experience, the experts panel at PCS detected the loopholes in the studies planned by the CROs, as for instance, the experts panel knew the drill how FDA defines an MTD, to mention one of the key aspects in this case. Not only this, but the PCS team also has the knowledge of how European agencies approach high-dose selection in preclinical studies. Over many years, PCS established itself as a reliable preclinical development partner.

For the future, PCS will continue to encourage young scientists to get involved in this interesting as well as challenging scientific field and also support the development of regulatory guidance documents in the scientific community. "We strongly believe that this proactive engagement will support the future development of medicines for patients in need, and beyond that, we will continue to engage ourselves by publishing book chapters and other publications," concludes Dr Plassmann. Ph