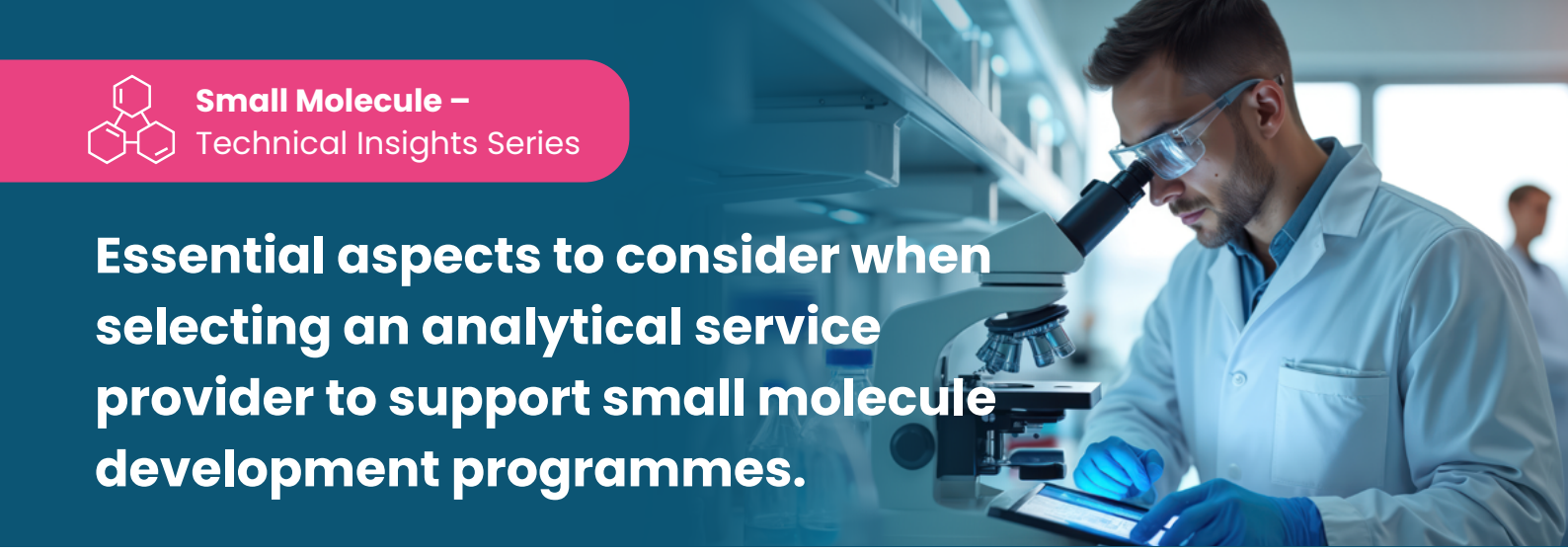
Small Molecule –
Technical Insights Series



Essential aspects to consider when selecting an analytical service provider to support small molecule development programmes.

Introduction

As part of our small molecule insights interview series, we review the 'Essential aspects to consider when selecting an analytical service provider to support small molecule development programmes''. This interview with Dr Mark Creswell (Head of Formulated Products) from Lucideon Ltd aims to establish what challenges outsourcers may face during early product development studies, how choice of service provider may help to reduce project risk and what value can service providers add as part of the overall project team.

Mark is a Chartered Chemist specialising in synthetic and materials chemistry, sol-gel chemistry, formulation science, and controlled release technologies. He splits his time between directing the Formulations team on active projects, assisting the commercial team in scoping new projects and contributes to the development of Lucideon's iCRT technology platform (controlled release of actives and ingredients) and research programmes.

1. Please can you provide an overview of the typical steps involved to develop suitable analytical methods to support new product developments and method improvement activities?

It is always best to start with the end goal in mind; define the product's critical quality attributes and what the appropriate acceptance criteria are in relation to the desired endpoint. From here, it becomes much easier to work backwards to define the critical milestones during method development.

Given the complexity of the projects Lucideon typically supports, the next step would be a literature review to ensure the current state-of-the-art for a specific technique/test method. This would also involve dialogue with the client team, sharing knowledge on the behaviour and physicochemical properties of the active ingredient or the product in question. An effective literature search and planning phase goes a long way in defining the key parameters and boundaries for the initial method development trials which follow.

Aspects including evaluation of techniques, sample preparation methodologies, mobile phase composition, detector selection, column type etc would all be considered and evaluated.

These investigations are often performed as design of experiment (DoE) studies. This brings two benefits: it enables a deeper understanding of the working design space and, even at an early stage, starts to build the framework for a quality by design (QBD) approach.

Optimised parameters are often found empirically, but if not, these can be identified by mathematical modelling of the design space. Once optimised parameters are identified, keeping in mind the pre-defined acceptance criteria initially established, a series of mock validation experiments are then carried out to ensure that the developed method holds up to the required scrutiny. Success at this stage may then lead to method validation to ICH Q2(R2) standards where required.

2. What are the frequent challenges that occur during method development activities and how can these be de-risked at project outset?

There are typically two significant challenges in our experience.

I) Quantitatively extracting or isolating the components of interest from the sample matrix.

Particularly in an environment where more complex formulations and sample matrices are being developed to provide best-in-class performance or novel technologies. This is a technical challenge and can be overcome by having early and full oversight of the sample matrix and its constituent materials. Deep expertise in materials chemistry and DoE approaches to sample preparation can streamline this process.

II) Compressed timelines for method development and thereafter the method validation.

A product development project will often have a critical milestone or deliverable already in mind, but frequently the time taken to set up the contractual and commercial agreements takes far longer than anticipated. This ultimately has the effect of compressing the time available for the experimental work to be completed. The worst-case outcome is that the original deadline is missed or the method developed is later found to lack robustness, such that issues surface later during the product development pipeline. This challenge can be mitigated by encouraging partners to engage early in the initial phases of the relationship development.

3. As a service provider, what are the key pieces of information you require from an outsourcer at project initiation to establish a strategy for method development that will meet scientific, regulatory and programme requirements?

One of the most important pieces of information we require from our clients is shared visibility of key programme milestones. This helps to keep stakeholders happy on both sides of the fence. It is key that our clients share all relevant technical insight regarding the active/material/product physicochemical properties and characterisation work carried out, as well as previous related development activities.

4. How critical is it that a service provider has particular experience and expertise with the characterisation of certain types of dosage forms?

Prior experience with specific dosage forms is of paramount importance. The key defining features of each dosage form can lead to rapid and robust choices for key method aspects such as sample preparation methods, choice of analytical technique, and common excipients used and their potential for interaction with different types of APIs. Knowing which elements are most critical to the specific regulatory requirements for each dosage form can also help to facilitate the method development process.

5. What are the key differences between companies that provide testing services and those that provide development and consultancy services to support product development activities?

Lucideon operate at both ends of this spectrum and across everything in between. Testing services are an important part of the process when speed and reliability are the key factors in enabling the pipeline progression to move forward. Established methods and workflows, ideally under a robust quality management system, are the key pieces for successful collaborations for testing services.

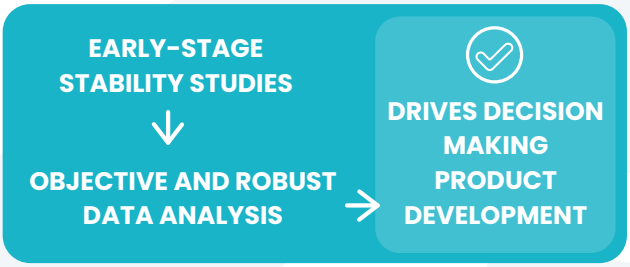
The successful implementation of development and consultancy services, however, relies on different attributes in both culture and mindset. Depth of institutional knowledge and an effective problem-solving approach are the most important factors. Challenges are almost always guaranteed to arise during method development programmes, and companies that are successful at method development are those that are most effective in overcoming challenges as they arise.

6. Why are consultancy services to support method development so important to support early phase development?

The depth of knowledge and breadth of exposure to a range of actives, products, and dosage forms that a consultancy offering brings provides the background to enable effective support during the early phase. This is the stage where the number of unknowns in a system is at its maximum, and addressing this systematically requires an effective problem-solving approach. A consultancy-based service provides the ideal setting to tackle these early challenges most effectively.

7. How can service providers support project teams from a data analysis and interpretation perspective, considering early phase stability data and shelf-life extrapolation?

Service providers offering an objective and robust data analysis during early-stage stability studies are important for driving decision-making during product development. Extracting meaningful trends, recognising variability, and applying the right statistical models to predict long-term performance allows teams to build confidence in their shelf-life projections. By approaching product stability analysis objectively and as an iterative learning process, service providers can de-risk pharmaceutical product development.



8. Can you provide any examples of where a consultative approach to analytical strategy can help a client to reduce project timelines or reduce both short- and longer-term cash burn?

A consultative approach relies on deeper and more meaningful relationship building between the parties. In this way, the engagement should always be more collaborative with both parties working towards a shared vision of the successful outcome. This transparency helps to frame the challenge more openly, leads to more effective sharing of prior knowledge and enables more realistic expectations of progress milestones to be forecast. In turn, this fosters a 'right first time approach' to the development programme, which in most cases enables better management of the project budget and milestones and reduces the need for costly and delaying iterations.

9. What types of challenges do you personally like to be involved with and why?

On a personal level, the projects I've most enjoyed being involved with are those that have deeper complexity and require input from all of our different technical teams. Lucideon have broad technical expertise across not only analytical sciences, but also microbiology, cell biology, formulation science and materials chemistry at a wider level. It is fantastic to see those different groups come together and work towards a common goal of helping our customers arrive at the desired successful outcome.

10. Partnerships are essential for any project to succeed. Can you provide an insight as those factors which enable successful partnerships?

Early engagement between the relevant technical subject matter experts is important. Irrespective of the efforts of the commercial and business teams, it is the experts on the ground who will dictate the success of a programme. Two-way transparency between the parties is also an important factor. An openness to discuss in a pragmatic way project progress and the potential challenges and mitigations helps to build a relationship that is productive. Most importantly, it is essential to recognise that these projects rely on establishing a partnership rather than being approached as a transactional engagement.

LUCIDEON

Lucideon is a global materials technology company providing contract R&D, analytical testing, and consultancy to the pharmaceutical industry. They help drug developers, manufacturers, and CDMOs accelerate innovation, ensure regulatory compliance, and solve complex product challenges. Their services include analytical services, materials expertise, regulatory testing, failure analysis, and R&D collaboration.

Lucideon's solutions are tailored to each individual client to ensure they fit individual challenges, rather than relying on off-the-shelf services.