SCENARIO SHEET

Sterling

Bridging the gap between technology transfer and process scale-up

THE SITUATION

When starting any API development project, one crucial question is top of mind: will the process successfully scale? Many newly developed processes may work in the lab, when producing several milligrams or grams, but can prove difficult or impossible to execute at the plant scale.

When an early phase project is transferred to an outsourced partner for further development and scale-up, scalability challenges can require scientists to modify the process significantly. When limited background information on the project is available, addressing the issues at hand can be even more challenging. An experienced partner takes the time to ensure any new process is robust, scalable, and reproducible, while finding tangible solutions to challenges or inefficiencies that can present hurdles down the line.

THE CHALLENGES

Knowledge gaps

Many times, a project is transferred for development with very raw processes that may have been developed in medicinal chemistry labs, leaving limited data and background information to draw from. Addressing these knowledge gaps requires a development partner to examine the existing processes provided in collaboration with the customer. From there, scientists can surface and rectify any issues that impede scalability, whether they are high volumetrics, safety concerns, limited raw material availability, high energy requirements, or other factors.

Impurity formation

One key challenge that impedes scalability in an early phase process is the formation of unanticipated impurities, which can come from unstable intermediates that decompose or lead to side reactions. When impurities arise that have not already been identified and addressed by the customer, the development partner must determine their identities, assess what is causing them, and evaluate their impact on the process or final product. If impurities are present in unsafe concentrations or negatively affect product yield, scientists must seek effective ways to mitigate them.

Process inefficiency

If scientists determine that an early phase process will work as defined as it scales, there may still be opportunities to improve efficiency, yield, sustainability, and other important factors during early phase development. For example, the introduction of an alternative solvent can reduce waste over time, or scientists can adjust certain reaction parameters to increase the reaction rate. Scientists may be able to address some of these considerations early on to save time and costs in the long run, but it requires deep knowledge of the specific process and expertise in process optimisation.

The Sterling solution

Recognising the importance of both theoretical knowledge and practical implementation, we leverage our expertise spanning early phase development through to commercial manufacturing to seamlessly bridge the gap between technology transfer and scale-up.

Hands-on process evaluation

When taking on a new early stage process, we perform a thorough evaluation and pressure test the process internally to determine whether it will work as described. This not only allows us to establish whether it will successfully scale, but also allows us to look at opportunities for improvements like enhanced efficiency and yield and identify any shortcomings or hurdles. In addition to testing the initial process, we test and validate process optimisation strategies in real-world conditions to assess their effectiveness.

If we encounter challenges in the process, we outline strategies for improvement and share actionable solutions with the customer. For example, if a process generates significant amounts of CO^2 that can create a risk of explosion, we may utilise an alternative combination of reagents that retains a similar pH value while avoiding the production of gas.

Collaborative approach

Close collaboration across our internal teams, our other specialised global facilities, and our customers enables us to work together towards a successful project outcome. For example, when it comes to cross-site collaboration, if a highly potent product or intermediate is involved, we can leverage the expertise of the high-potency team at our Wisconsin site to implement stringent containment measures and assess scalability.

As we work with our customers, we remain fully transparent amid any issues we encounter, working with them to find solutions that meet their needs, whilst considering market demand, budget, compliance, and other key factors.

Full-lifecycle perspective

At Sterling, we pair end-to-end capabilities from initial process design to commercialisation with deep expertise in process optimisation, allowing us to support a wide range of project requirements. This not only allows for a seamless transition from development to manufacture, but also enables us to proactively anticipate challenges and inefficiencies, then define strategies to address them. For instance, if a process transferred in from a client has issues of scalability, either due to degradation of intermediates or creation of impurities during reaction, we develop a more feasible alternate route which is economical, scalable, high yielding and affords intermediates with excellent purity without the need for column purification.

Enviromental responsibility

We also consider environmental impact across the entire molecule lifecycle, and look for ways to maximise environmental efficiency wherever possible. For example, in early stage development, we may leverage an alternative solvent that is greener, while during manufacture, we take care to carefully treat and properly dispose of any waste that is produced.

"Our approach to process optimisation is unique because it combines the best of theoretical optimisation and practical implementation. While some organisations specialise in one or the other based on the stages of the molecule lifecycle they support, our expertise from initial development to full commercialisation affords us a unique perspective. This enables us to make tech transfer as seamless as possible for our customers while making suggestions for continuous improvement."

- Joel Annor-Gyamfi
Senior Research Scientist

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