Recent Advances in High Throughput Experimentation (HTE) and Flow Chemistry: Webinar FAQs

HTE Questions

Q: What's the advantage of this HTE platform?

A: *Thanks for asking. We have rich experience of condition screenings of 80K of reactions and we have our own condition design for each type of reactions, or even for different types of substrates. In order to solve the challenging chemical reactions, we not only use the successful experiences, but we also summarized the most failed substrates and do further analysis of functional group effect, try the newly reported catalysts or extensive variables combinations. At the same time, we also use new techniques, new types of reactions to try different ways to make the target from different starting material or reactions.*

Q: We feel very interested in your HTE service; how can we use this service?

A: *We support all the on-going projects in WuXi for free, it's an added value of other synthesis collaboration with WuXi. We'll use all the technology platforms we must accelerate the project progress. If there's individual request of HTE service, we will provide FTE or FFS quote.*

Q: Can you also do photoredox screenings in your HTE service? What's the reaction number scales you can run?

A: *We also do photoredox screening, and we have different kinds of reactors for screenings, like 96 well plate, LED strips, Penn optical reactors, we can run ~400 reactions a day. As the example I just showed in the slides, we flexibly try photoredox and metal catalysis at the same time if we believe this C-C bond formation can be realized from different strategies.*

Q: What's the success rate of all the reaction screenings?

A: *The average success rate is about 60%. And the success rate will be different for different types of reactions. The Buchwald couplings account for the most reactions in our condition screening work, and the Buchwald coupling could be very challenging due to the highly functionalized substrates, and condition screenings often necessary. The success rate of Buchwald couplings could be less than 60%, which is often lower than other coupling reactions.*

Q: What's the material amount needed for a round of reaction screening?

A: *HTE screening is a technique using miniaturized parallel reactions to explore as many conditions as possible with limited precious project substrates. The reaction scale can be run at 5 umol or smaller, the material cost for each screening can be as less as 10-20 mg, then you can identify the most optimal conditions quickly.*

Q: How's the reproducibility of condition screening reaction scale to following synthesis scale?

A: *Reproducibility is always a problem we are concerned about. We use chembeads coated catalysts solid dispensing to minimize the errors in the reaction weighing, and also use prefilled plate to save the manually weighing step. We transfer the screening experimental procedures with many details as we can to the project team. We also do <1g scale ups for the project team for sensitive reactions, especially photoredox reactions. HTE is a special technique and our HTE team have very collaborative relationships with chemists in the project teams to work together in the final target's fulfillment.*

Q: Any experience in polymerization processes used in API, polyelectrolytes or similar.

A: *The number of reaction types we have currently in HTE platform is more than 40, but the capability of polymerization process optimization is not yet established. We'll start to do some reference search and potential needs investigation of polymerization process optimization.*

Q: Is much of this HTE work performed published in the literature?

A: *We never publish any HTE results and we don't have the plan either. Our platform provides condition optimization service to all the clients' projects having collaborations with WuXi AppTec, in terms of reducing time line, improving reaction efficiency. We have intenal research to discover optimized condition systems of challenging type of substrates for some reaction types, in order to improve the success rate of reaction optimizations and provide more efficient supports to all the projects. However, any research work has never been published.*

Flow Chemistry Questions

Q: What is the general workflow of doing flow, from small scale to big?

A: *We start with analyzing the batch results, to identify what the challenges are in the reaction. Most common issues are related to safety and selectivity, of which flow chemistry can be a good solution. We check whether solid will be formed, and we evaluate reaction parameters including*

flow rate, temperature, and pressure. If a solid is formed, depending on its property, we can sometimes use CSTR to run the flow. Next, we can do upscaling from small-to-big, or use parallel reactors.

Q: How to evaluate and handle possible solid formation in flow?

A: *For requested reactions that have never been performed in batch, we do quick batch reactions to see whether a solid forms. If yes, one solution is to use CSTR. Other common methods to consider (in parallel) include diluting the reaction mixture, changing solvents, and changing reagents.*

Q: How long would it take to optimize one reaction?

A: *Approximately 1-2 days to optimize one reaction and delivery its target molecule in the early phase. For more detailed parameter screening, the timeframe would be a bit longer.*

Q: As clients, how do we get access to the flow chemistry service at WuXi AppTec?

A: *Flow chemistry in the early phase is a complimentary service within our chemistry division for supporting existing client projects. We are also happy to discuss our flow chemistry service with non-clients. If you need more process-intensive flow chemistry (especially toward large scale), our STA team can meet this demand.*

Q: What is the direction of future development?

A: *We are looking at transforming more chemistry from batch into flow, to explore the boundaries of flow chemistry. We are also working to improve the standardization of hardware, and to establish digital communication between devices.*