Jonas Nilsson

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HIGHLIGHTS

Ph.D. Organic Chemistry, Linköping University, Sweden

Leads a team of synthetic chemists working on process development

Leads planning and execution of projects for GMP custom process chemistry development

Works as software engineer, developing tools for internal workflows

Internal mentor for process development and GMP chemical development

SUMMARY

Jonas leads a team of chemists working on process development and optimization.

AREAS OF EXPERTISE

- Organic chemistry
- Process development
- Software engineering
- Impurity tracking

What is the role of process development?

We focus on process development, optimization, and scale-up transfer to production, including robustness testing. Our work is critical for successful manufacturing and a robust supply of drug substances and products. We look at things that need improvement and adaptation to our equipment. It may be that the process is not mature enough to be run at a sufficiently large scale and further

"We investigate even the smallest deviation. If you have a small deviation and don't understand it — and just shrug your shoulders and move on — it will be a very big problem in the end."

development is needed. After we complete development, we make a demo batch to have everything ready for production.

How do you ensure a smooth tech transfer?

We create a mini-production environment in our R&D facility to evaluate the intended process. We include engineers, analytical and QC teams to mimic real production. This is how we find out when you scale up and identify anything that may have been missed. After discussing these items and finding that we have a 'go' decision for the process, all the documentation will be signed off and released, and the transfer to production is complete

How does the Cambrex culture impact clients?

Every project has its core team with an engineer, analytical chemist, project manager, chemist, and QA representative. That team stays together right through the transfer process from R&D to production, and if applicable, through validation and commercialization.

We create a demo batch, working closely with the engineers and analytical teams throughout the production. The lead chemists have a lot of knowledge about our production equipment, and vice versa, the engineer acquires a lot of knowledge about the processes before we go into the transfer to production. This knowledge is attained by close collaboration and plant "dry-runs" prior to the demo batch. These integrated teams work very closely together with an open structure and very little hierarchy.

What services do you provide to clients?

Our services include process development, optimization and scale-up transfer to production, robustness testing, and optimization of processes. We also do manufacturing, as well as analytical services, analytical validation, process validation, and then transfer to a validated process for commercial production.

What types of projects do you work on?

A typical development project is a new product prior to commercial production. The project could be either partially or fully developed or a very early-stage process that needs to be developed, optimized, checked for robustness, and improved in many ways. It could also be mature products that have a developed process that has been on the market for several years—and it's just a process transfer. We need to do process adaptation to our equipment and maybe plan and prepare for a validation with all the required documentation.

How would you describe your team?

We have a very dedicated team. Every chemist takes pride in making the best effort to meet and exceed customer expectations to generate add-on value. The experience of owning and developing the process together with the customer is a key differentiating factor at Cambrex.

How far along are clients when you start working with them?

Typically, new clients are in late phase two or early phase three, and they need to have a certain amount of material produced on their behalf to use for clinical studies. We get the process, start out with the familiarization, which means we run through it according to the customer's RFP, and then we begin development. We look at things that need improvement and adaptation to our equipment. Following the development, we do a demo batch to prepare everything for production.

The demo batch is initiated once all the documentation is generated to create a mini production in our R&D facility with the intended process. We include the engineers, the analytical and QC team for release — everyone required to make it mimic real production and discover when you scale up and what things you have missed. After we have discussed these items, the documentation is signed off and released, and the transfer to production is complete.

This is the part where the R&D development process stops, and we transfer the process to production. Production then initiates their preparations for large-scale production. The chemists will still be on the project, supporting the engineer and the production all the way through to release and delivering it to the customer.

What are the key factors for successful process development?

The key to understanding a process and having a robust method is to look at all the details. Even small deviations need to be understood. If you have a small deviation from the normal, don't understand it, and just shrug your shoulders and move on, it may later become a big problem. Therefore, being detail-oriented and thoroughly knowledgeable about the process keeps our customers returning to Cambrex.

How do you handle deviations?

There are probably a hundred small key items you learn about the process you use during production to facilitate things, mitigate risk, and instruct the operators. Being detail-oriented is a lot of help when we have deviations — they always happen in production. Things may not always go exactly as planned, and if you stand there without a thorough understanding of the process, you may not be able to solve problems within short notice and mitigate risks. But if you have a broader understanding and more general knowledge about the process, you can immediately root out plausible causes for the deviation, and you can have a much quicker handling of the solution to mitigate the risk for future production, avoiding delays in delivery and improving quality of the end product.

What keeps clients coming back to Cambrex?

We have a long track record of very pleased customers. The way we are detail-oriented and dedicated to the project itself makes Cambrex a very good candidate in the industry. We have a very good transfer process from R&D to production — a demo batch where we work very closely with the engineer as part of an integrated transfer process.

We also work closely with engineers and analytical teams from development all the way through production. Our engineers fully understand the processes before we go into the transfer to production. Integrated teams working very closely together mean we have an open structure and very little hierarchy. Every project has its core team with the engineer, analytical chemist, project manager, chemist, and a QA representative, and we have this core team that is working very fluently and without any barriers between themselves.

What are some challenges you and your team face?

Process development is an evolving process. Changes at one end may affect the outcome in the other. Impurities that form during the process needs to be identified, assessed, and tracked to ensure purging before the end product and product quality.

During development, you find key items that need to be assessed. It may not even work as intended on large scale, you need to change things such as solvents, concentrations, or reaction temperatures. Optimization is like an evolution process. Then obviously, if we find severe issues with anything from supply of raw materials to things that really don't work at scale at all, we need to go back to the drawing board and propose to change the synthetic route or change the order of steps and do further ground development.

Our ultimate challenge is to optimize the process and make it scalable and robust. Typically, we need to scale up processes that we have from our clients to a much larger scale than they have ever been running before. We need to take into account things that may not have been considered before, such as heat transfer, ability to stir, filterability, and other things that are very scale dependent and most likely need further optimization. We may also need to optimize on capacity, how many kilograms you can produce per volume so you actually can fit more product into your reaction train.

The other key area is quality. One core item with quality is impurities. From the early start of any product, in any development, we gather information about impurities and how they track in the process from step to step. We keep this in our in-house impurity tracking software as a database so we know all the impurities, their fate, how they purge, and how well they can be removed to get a good quality API.

What role does your team play in scaling up?

Scale-up is one of the core things we work on, looking at the filterability, cake compressibility, heat transfer and many other items. When you have an exothermic reaction, how much heat is evolved? Can you transfer that heat out from the reactor when you have a larger scale? We have to balance that with the time aspects. Typically, a lab distillation may take half an hour and 24 hours in production on a 12 cubic meter scale. You need to assess product stability when you do scale up and ensure that you simulate these conditions that you would have in a true production environment.