Helix Biotech

Case Study

Transferring from Microfluidics to a Turbulent Mixer

Lipid Nanoparticle Manufacturing

Their Dilemma

A Client came to us with a defined protocol to make lipid nanoparticles (LNPs). This protocol was established on a well-known microfluidics mixer which produced R&D scale particles. The Client determined the route to commercial scalability with a microfluidics-based approach was too costly and logistically difficult. Hence, the Client sought our expertise in LNP manufacturing and to leverage our scalable LNP equipment - the Nova™ nanoparticle manufacturing platform. Ultimately, they wanted us to help determine the feasibility of transferring their formulation process to a turbulent Impinged Jet Mixing (IJM) based approach in a cost and time efficient manner.

Our Solution

Knowledge Transfer: We met with our Client and discussed details regarding their formulation process to better determine how best to proceed with the technology transfer. Important details included formulation composition and ratios, buffers, pH levels, flow rates, N:P ratio, as well as their quality control assays. We wanted to keep as many of these parameters constant to ensure the success of the transfer.

Process Parameter Screening: We began by performing small volume screening runs to minimize the use of expensive client material. With every parameter held constant, we first conducted a total flow rate screening, surveying a total of 8 flow rates ranging from 2 to 20 mL/min. This was done to produce particles of optimal size (<100nm) and polydispersity (PDI, <0.20). Size and PDI were measured after each manufacturing and post-processing step (i.e. dilution, wash step, sucrose addition, sterile filtration, and freeze-thaw). We were able to successfully produce LNPs at a range of total flow rates, but ultimately chose 8 mL/min due to a combination of low size and PDI, high nucleic acid encapsulation efficiency (>90%), and optimal nucleic acid integrity as determined by Agarose Gel.

Verification: Once the optimal conditions were determined, we performed a full-scale run to produce their desired sample volumes. After verifying the samples had similar QC results as the small-scale runs, the samples were shipped to the Client's lab for independent *in vitro* testing and QC.

The Result

We were able to finish our Client's technology transfer project in <3 weeks upon receiving their materials. Afterwards, the Client reported their results and were happy that the particles we produced yielded comparable cell viability and transfection results as LNPs produced by their in-house microfluidics instrument. Ongoing work is now seamlessly underway for straightforward process scaleup development.

Nova™ Benchtop

HELIX BIOTECH