

# Send your LNP product development to lightspeed with the Sunny Suite

## Introduction

Lipid Nanoparticles are changing the face of medicine – from rapid responses to infectious disease, to in-vivo gene editing and targeted protein replacement therapeutics, LNPs are leading the way. Despite their proven clinical success, LNPs still present challenges to the drug developer, among them that the material produced in discovery must be the same as that produced commercially. As a complex, formulated product, this is not always easy, as nuances in the formation of the particles can affect particle size, distribution structure, and in the end, efficacy (Figure 1).

Unchained Labs’ Sunny Suite leads our customers through the whole process of pharmaceutical product development – from the first steps of screening large libraries of formulations, all the way through to the manufacture of clinical materials (Figure 2).

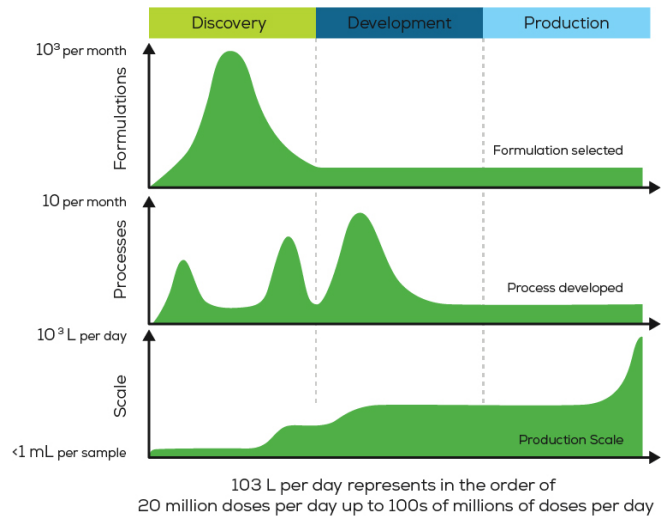


Figure 1: Experimental requirements at the different stages of drug development.



Figure 2: Sunny Suite instruments across the drug development stages.

All the method development and changes in process throughout the lifetime of a product development project can leave you feeling stuck in the mud on the path to production, raising costs and eating time.

To beat the process transfer blues, the Sunny Suite equipment is designed to change with your needs at each step as the product gets closer to realization, whilst maintaining process consistency in between each device, making the transition as easy as possible.

## Surf to seamless scale-up at GMP with Sunbather

Good Manufacturing Practice (GMP) for clinical material comes with its own additional burdens – the software has got to be FDA 21 CFR Part 11 compliant for full traceability, the flow path has to be single-use or clean-in-place (CIP) compatible to avoid bio-contamination, and all the contact materials have to be tested for leachables and extractables to make sure there’s no surprise extra chemicals in there! It’s a high bar to clear, but don’t worry...

Sunbather (Figure 3) is Unchained Labs’ solution to GMP manufacture. Unlike other GMP solutions, Sunbather is designed to require no further optimization from the method already developed on the Sunshine instrument in continuous mode, by exactly maintaining the core system functionalities of each device.

This includes our advanced microfluidic mixing devices, or “Sunnies,” (Figure 4) that let you use the same mixing conditions across the development process, including GMP.

Made from glass with ultra-smooth channels to avoid material build-up, these are as well-suited for running multiple formulations in a screen as they are for long, continuous production runs.

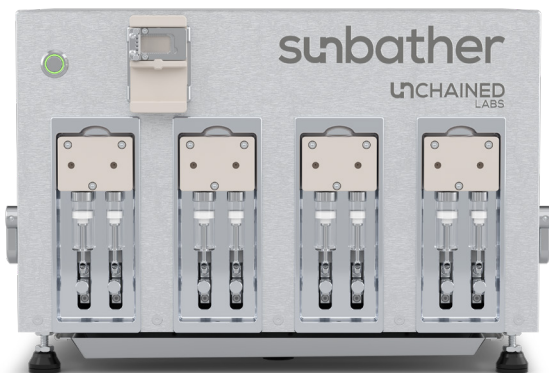


Figure 3: Sunbather, the GMP-ready LNP producer.



Figure 4: Sunny 100X.

Uniquely, the pumping technology is also retained from initial screening all the way to clinical production. Therefore, you know exactly what you are getting from your pump performance, with no additional process development necessary as you shift to manufacture (Figure 5).

This means there is much less danger of process hiccups as you move into GMP manufacture, and makes drastic savings on time, materials and cost (Figure 6).

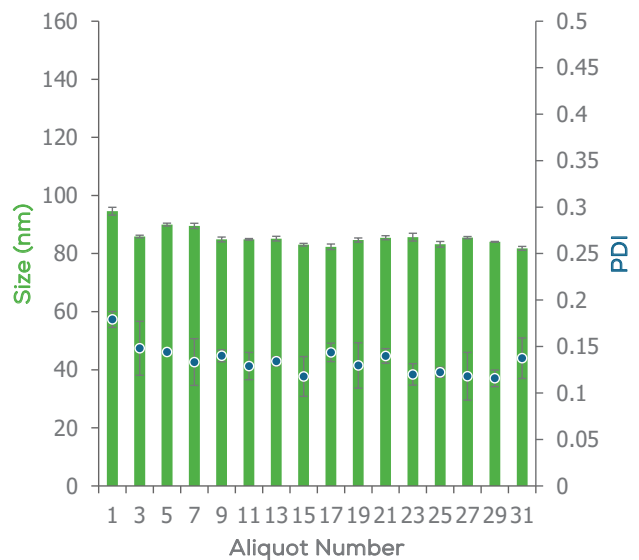
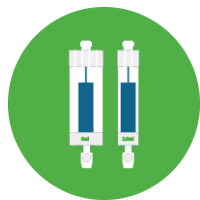


Figure 5: Aliquot of a continuous production run on Sunshine using a Sunny 490 Trident T to optimize particle production before transfer to GMP.



Microfluidic mixing gives excellent control over your process throughout development and manufacture.



The same super accurate pumping technology works across your Sunny Suite instruments, so no more tricky transfers.



Our highly reliable process means fewer wasted batches, and saves time and money.



Provided with all necessary traceability documentation for regulatory compliance.



Excellent service and support, from installation and training through to after-care product support.



Combining these benefits means you get your life-changing vaccines and therapeutics to market faster than ever before.

Figure 6: Sunbather benefits.

Sunbather uses a fully replaceable wetted flow-path (with accompanying extractables data provided), comprised of pump valves, syringes and tubing, and a GMP-Sunny of your choice, to eliminate the chances of batch contamination. Replace the whole flowpath run-to-run, or clean in place with a cleaning protocol – the choice is yours. The control unit is a touch screen kiosk perfect for a production environment, with 21 CFR Part 11 compliant software for full process traceability. The software is designed for ease of use, with minimal training necessary (Figure 7).

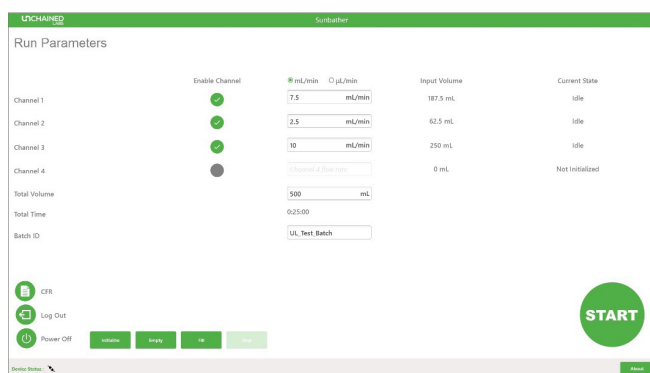


Figure 7: Sunbather’s easy-to-use software interface.

Just hook up your bioprocessing bags, plug in the flow rates developed from your Sunshine continuous runs, and set it going to produce as much nanoparticle suspension as you need, with no fuss.

## Put poor process control in the shade with a Sunny

Our microfluidic Sunnies are more than just simple mixing channels. Each one is made of chemically inert glass, which has a channel surface roughness of just  $\pm 5$  nm, compared to injection molded chips that typically have values of  $\pm 1-3$   $\mu$ m!

Their careful design allows for thorough, controlled mixing. Various mixing geometries mean your mixing can be suited to your exact application and the flow rates that you need for your particular product and your process.

The Sunny is compatible with each of the Sunny Suite systems, and is used with Sunbather along with all the tubing, fittings and syringes (for the pump channels) needed to run the device whilst minimizing contamination risk. The flowpaths come with the necessary documentation for material traceability and accountability, and Sunbather is available with a full warranty, IQ/OQ and maintenance packages so you know we’ve got your back.

## Reliable results so you can relax

The excellent microfluidic reproducibility means you know you can go from one development stage to another with the same excellent control over the process, so you know your batch will be up to scratch when it's time to manufacture.

Let's walk through a process then, using the Moderna Spikevax formulation as a commercially relevant example, with FLuc mRNA as the cargo. Starting with Sunscreen, we're looking for a formulation that produces stable particles with good transfection efficiency. In the research stage, you'll be running hundreds of different formulations, which Sunscreen is perfect for with its high-throughput, fully automated 96-well plate format. The reusable microfluidic chip and small sample sizes (from as low as 100  $\mu$ L/ input) help you cut your costs, too! To see what 96 formulations in a day could look like for you, check out the App Note ["Accelerate your LNP formulation screening with Sunscreen's automated microfluidic technology."](#)

When you are happy with one formulation, (or, as it may be, 10 or 20 formulations), Sunshine helps shine a light on the best process to use as you start to optimize your product. Sunshine allows rapid formulation and process prototyping, with larger and more flexible sample volumes, from ~1 mL up to fully continuous manufacture. Just select your winning screening formulation, run samples in protocol mode for optimization, then move on to continuous mode, to make large volumes of your most promising candidates.

Once you've done that, it's just a hop and a skip to move to GMP manufacture with Sunbather – no optimizing necessary. Just use one of the Sunbather Flowpath Packs that matches with your Sunshine configuration and go for it.

To show how easy the path to GMP manufacture can be, we've produced the same formulation, at the same conditions, across all of our devices. Starting with Sunscreen, we collected 800  $\mu$ L of mFLuc-LNPs, using the Sunny 490 Trident T at 12 mL/min. We ran the same formulation on Sunshine with a 1.5 mL collection volume, then

transitioned the Sunshine to continuous mode and produced 20 mL of mFLuc-LNP suspension. Finally, the same formulation and conditions were used with Sunbather, to produce 60 mL of LNPs in a GMP appropriate process.

All these samples were analyzed for consistency, measuring particle size, PDI (Figure 8) and EE% (Figure 9) – showing excellent reproducibility across the sunny suite range, with unbeatable ease and convenience.

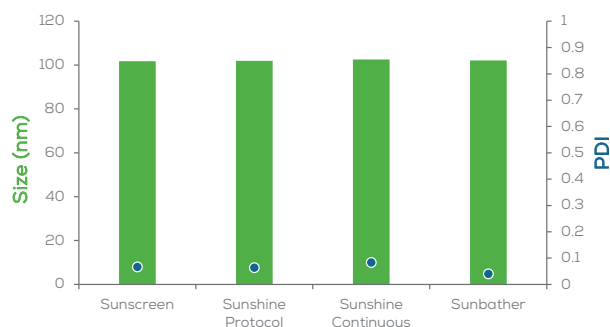


Figure 8: Comparison of LNPs sizes produced on different Sunny Suite instruments.

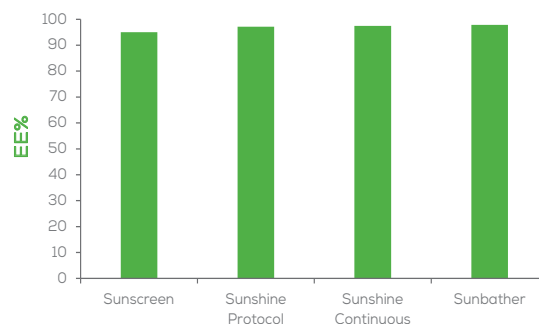


Figure 9: Comparison of LNP Encapsulation Efficiency (EE%) produced on different Sunny Suite instruments.

The high-performance continuous syringe pumps will keep on pushing out material for as long as you need them to, with consistent, reliable performance. We've produced liters of material here, so you can be sure that Sunbather can get the job done for you.

## Join the crew

As if that wasn't game-changing enough, Unchained Labs also helps you free up your quality control workflow. Stunner, the first-in-class Rotational Angle Dynamic Light Scattering (RADLS) system, allows you to analyze the quality of your material.

With a 96-well plate format input you can churn through samples rapidly, and at only 2  $\mu$ L per sample, with a minimum of wasted material. Combined with simultaneous total RNA quantification and particle concentration, there is no better solution to ensure your particles are hitting their Critical Quality Attributes of size, distribution, concentration and RNA content (Figure 8).

## Get ready to breeze through to GMP

From formulation screening to clinical manufacture, this is GMP made as easy as it can be. Reducing the time, cost and failure rate of your development processes, Unchained Labs helps you get the best version of your product to market as quickly as possible.



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