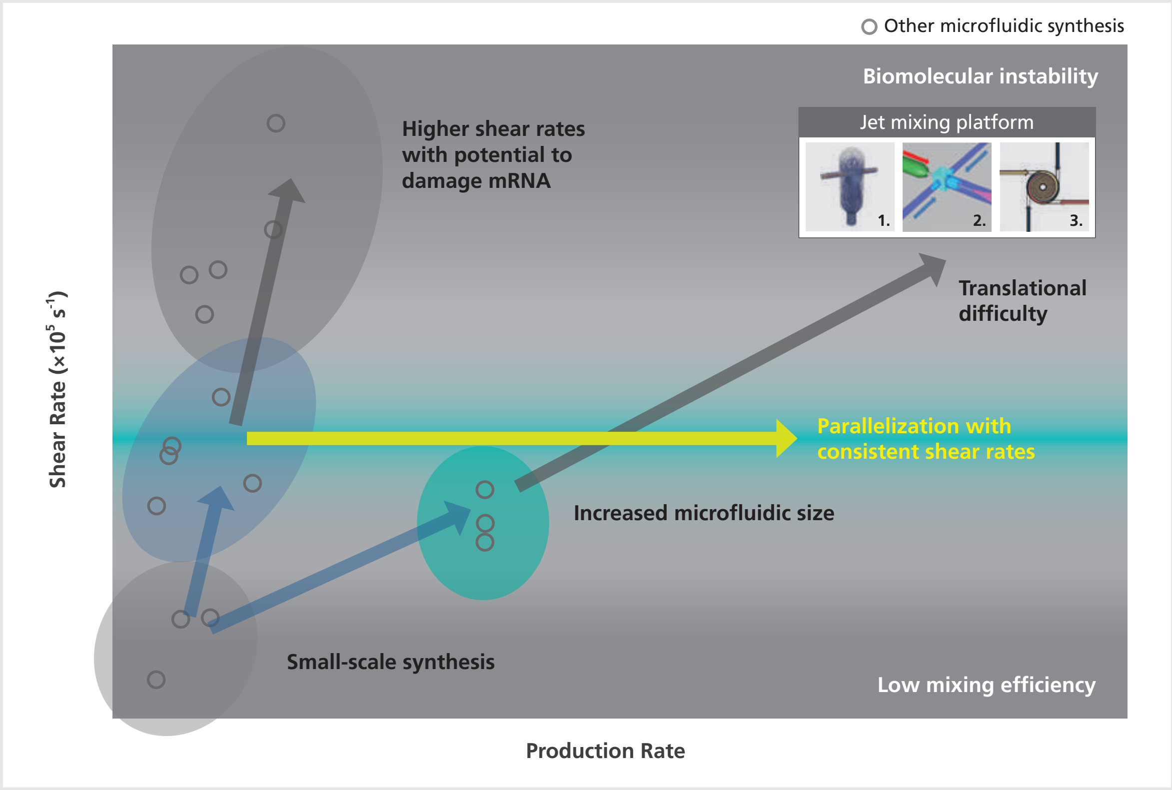
NanoCalibur™

The Scalable Nanoparticle Synthesis System

Lab-scale discovery and preclinical to GMP manufacturing

MEPSGEN

Shear and Production Rates for Stable and Scalable Production of mRNA-LNPs



1. Nie, et al., *ACS, 2019.* **2.** Lim, et al., *ACS nano, 2014.* **3.** Feng, et al., *J. Transl. Med., 2019.*

Maintaining controlled shear rates within the optimal range across production scales—from small to large volumes—is critical for high-quality mRNA-LNP synthesis

- Scaling up mRNA-LNP production by increasing flow rates often leads to excessive shear (e.g., as can be the case with jet mixing-based formulation systems), which can compromise biomolecular stability and therapeutic integrity. On the other hand, channel enlargement strategies typically require re-optimization of synthesis protocols, limiting broad applicability.

Microfluidic parallelization reduces the shear stress imparted to precursor materials during synthesis

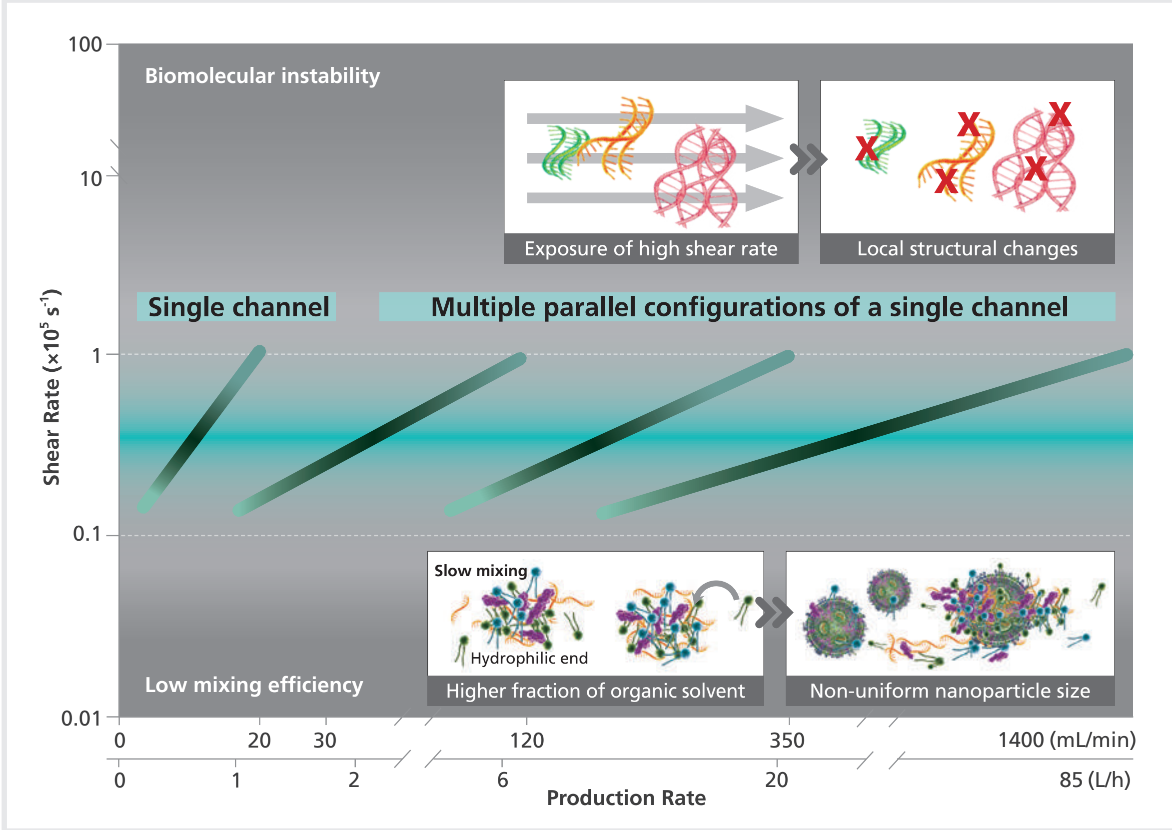
- NanoCalibur™ distributes the flow of aqueous and organic precursor solutions (e.g., those containing mRNA) across multiple pathways and ensures that shear stress applied to payloads (e.g., mRNA) remains that preserve mRNA integrity.

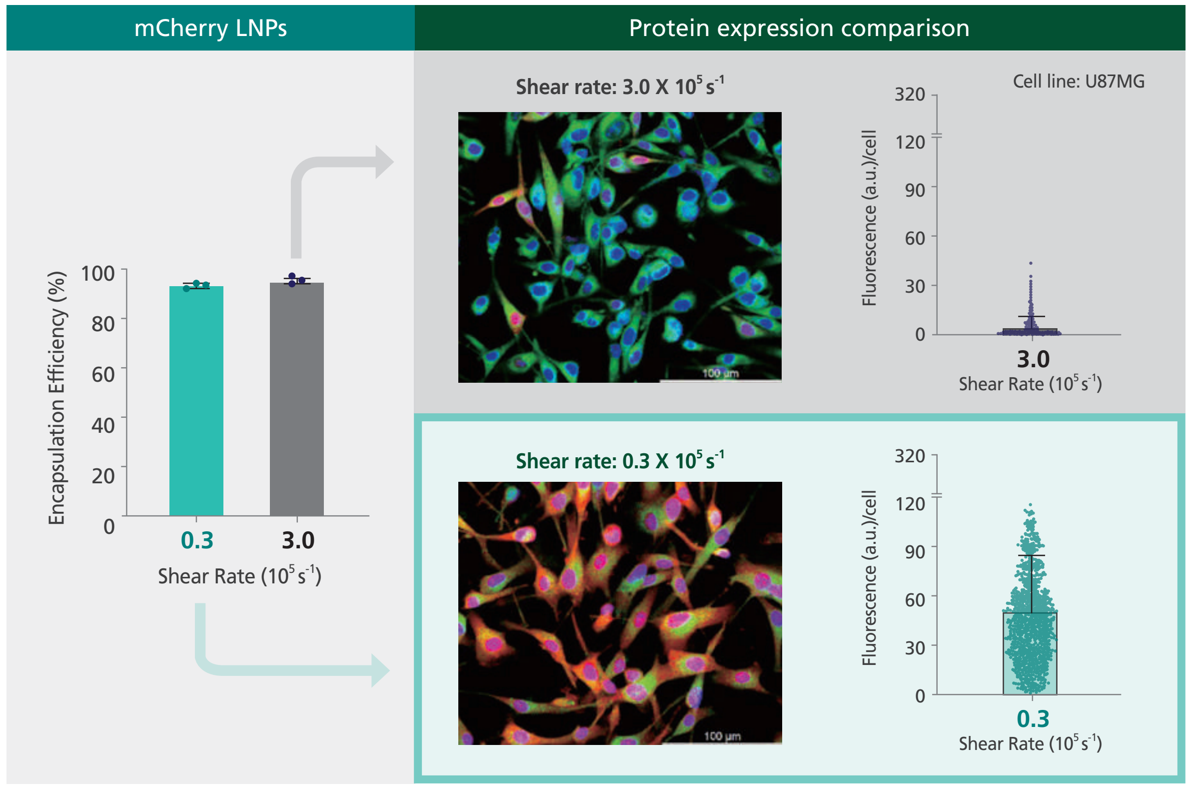
Shear rate-mediated mRNA-LNP synthesis can boost the high stability of mRNA

- Although physicochemical properties and encapsulation efficiencies of mRNA-LNPs remain consistent across shear conditions, excessive shear rate during formulation damages mRNA and lead to reduced protein expression and in vitro efficacy.

NanoCalibur™ enables scalable mRNA-LNP production across a wide range of production rates by maintaining controlled shear conditions, ensuring uniform and stable nanoparticles with intact mRNA encapsulation.

Nanoparticle Production Under Controlled Shear Rates Prevents RNA Damage





Blue: Nucleus, Green: Cytoskeleton, Red: mCherry

NanoCalibur™ Product Lines and Technologies

NanoCalibur™ provides unprecedented solutions with advanced microfluidic technologies to formulate various types of nanoparticles (NPs) with precisely defined properties and tunable scalability.

NanoCalibur™ Lab	NanoCalibur™ GMP	NanoCalibur™ Commercial
		
Small-scale synthesis for discovery and preclinical	GMP level production for preclinical and clinical	GMP to Commercial
2.5 - 20 mL/min	Up to 6 L/h (Expandable)	Up to 100 L/h with multiple PMS chips (Customizable)

Microvortex mixing patterns engineered to formulate nanoparticles

- These scalable single chip units support a range of throughputs from discovery to preclinical studies with >95% mixing efficiency for uniform synthesis.

Microfluidic synthesis chip parallelization for scalable production

- Microfluidic parallelizations in the PMS-cMPA and PMS-cSMR chips, as employed by NanoCalibur™, enables scalable and reproducible nanoparticle production by maintaining consistent microfluidic patterns and controlled shear rates—preserving payload integrity and supporting clinical and GMP-scale production.

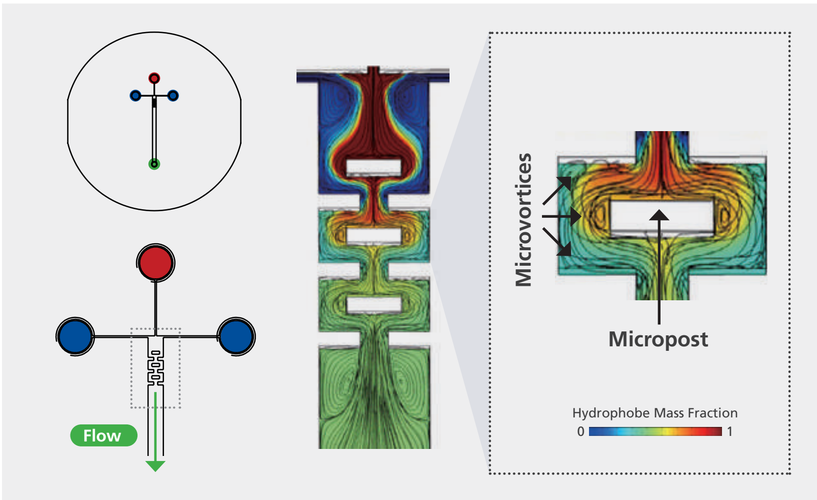
MPA : Dean vortex-induced mixing

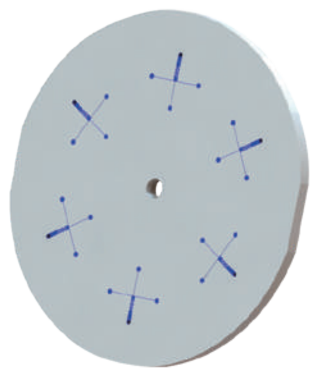
* PMS: Parallelized Microfluidic Synthesis

- Organic Phase Inlet
- Aqueous Phase Inlet
- Outlet

MPA X1

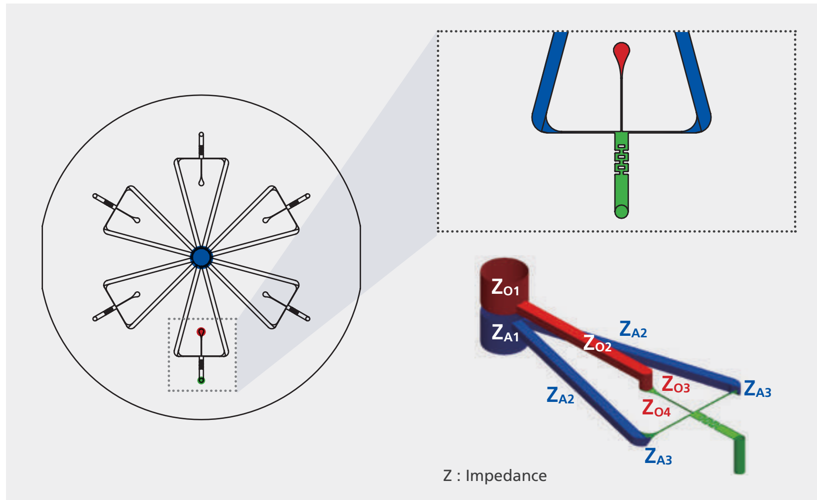
NanoCalibur™ Lab





PMS-cMPA X16

NanoCalibur™ GMP

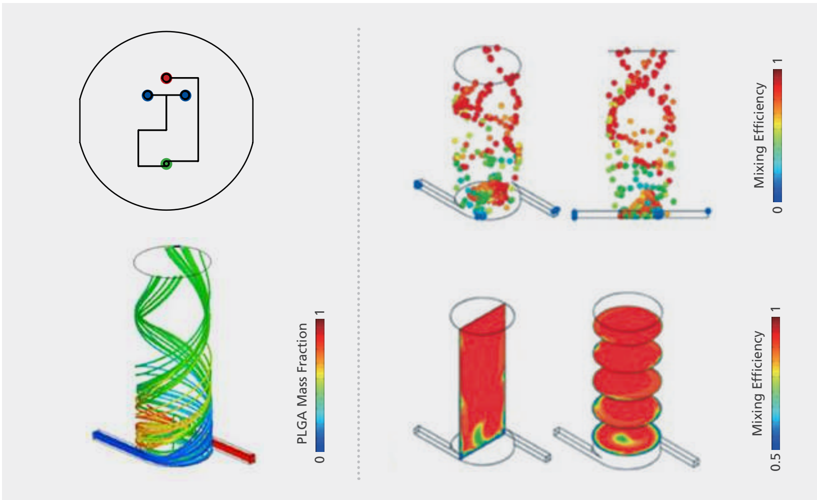


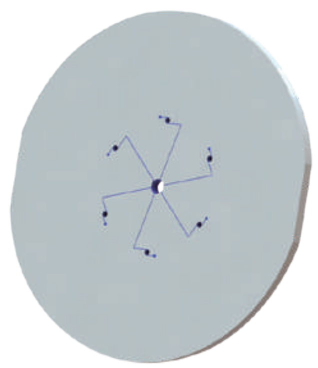
SMR : Swirling vortex-induced mixing

- Organic Phase Inlet
- Aqueous Phase Inlet
- Outlet

SMR T1

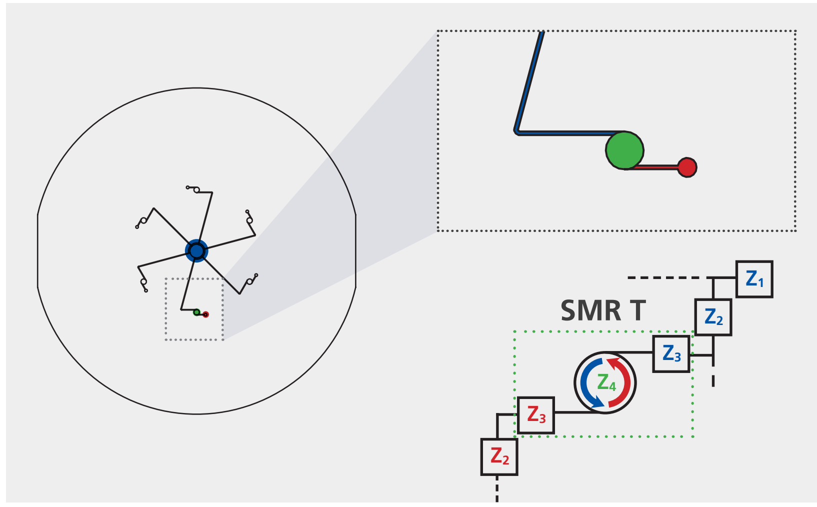
NanoCalibur™ Lab





PMS-cSMR T16

NanoCalibur™ GMP



NanoCalibur™ Lab

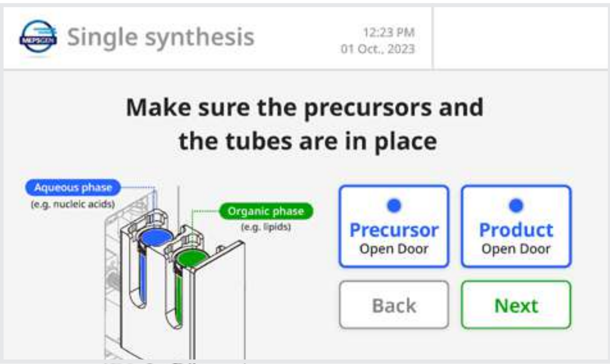
The system offers user-friendly operation, making lab-scale synthesis and the development of new drug-loaded nanoparticles more accessible. It supports production rates ranging from 2.5 to 20 mL/min (0.15 to 1 L/h).

❶ Closed-loop feedback control system and computerized manufacturing

- High-precision flow control is enabled via closed-loop pressure regulation for robust manufacturing.
- The continuous feedback loop implemented into the microfluidic synthesis chip immediately responds to any fluctuations that may affect the quality of the produced nanoparticles.

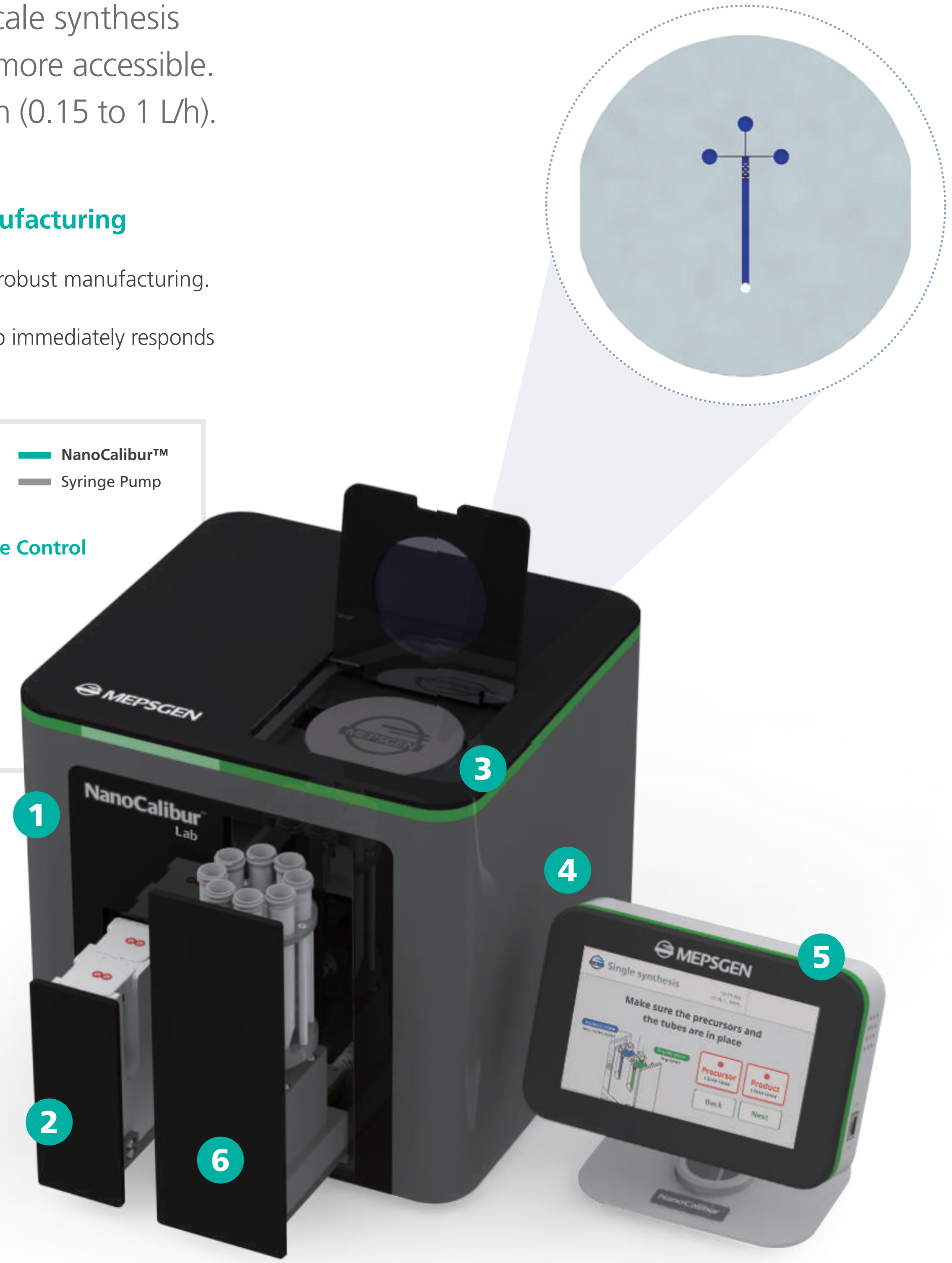
❷ User-friendly precursor preparation

- Automated operation with no syringe or tubing bundles makes it easier and more reliable for small-scale nanoparticle synthesis.



mRNA : 0.004 to 0.3 mg/mL

Lipid : 0.6 to 13 mg/mL



❻ Product multi-tube holder for multiple syntheses

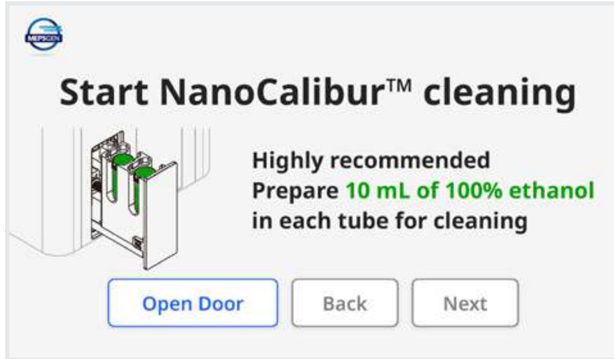
❸ Microfluidic synthesis chip made of stainless steel (SUS 316L)

- Reusable, semi-permanent chip eliminates need for laborious chip replacement before each synthesis

※ Disposable plastic chip available (Optional)

❹ Chip cleaning protocol

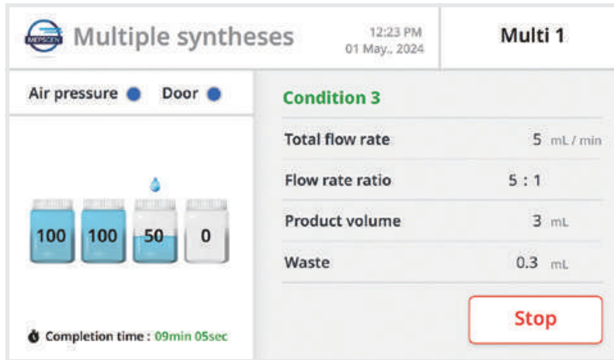
- Built-in cleaning protocols ensure that the chips are ready for synthesis



❺ Touchscreen display

- User-friendly interface allows easy control and monitoring of nanoparticle synthesis

※ Optimized conditions pre-set in Library:
FRR (Flow Rate Ratio) = 1:5.5
TFR (Total Flow Rate) = 5.2, 10.4, 19.8 mL/min

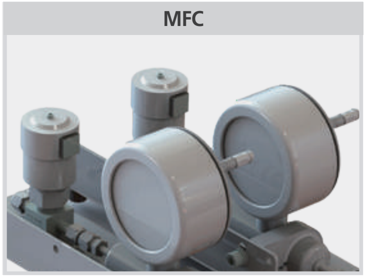


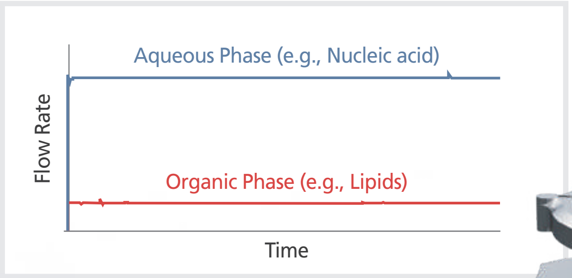
NanoCalibur™ GMP

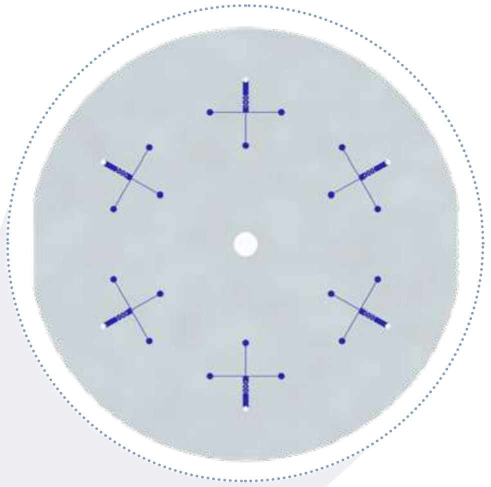
This novel and robust nanoparticle production system offers integrated synthesis and cleaning processes that support R&D, from preclinical animal studies to clinical trials.

❶ Precise flow control by integrated mass flow controller (MFC)

- The continuous feedback loop integrated into the microfluidic system ensures that synthesis conditions remain consistent throughout the production process.
- Enhanced control allows for real-time monitoring and adjustment of flow conditions, facilitating immediate responses to any fluctuations that may affect the product quality.







❷ Durable precursor containers for large-scale nanoparticle production

- Maximum pressure of up to 7 bar (101.5 psi) applicable with stainless steel (SUS 316L)

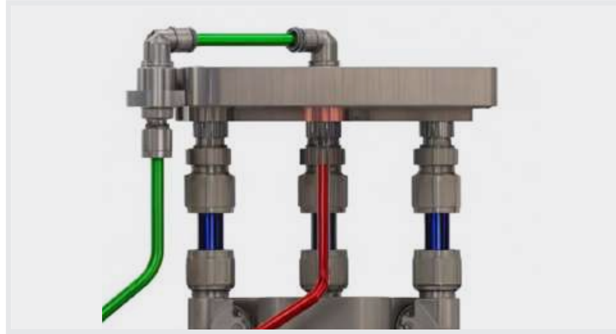
❸ Other features of NanoCalibur™ GMP

- Ensuring stable productivity at a liters-per-hour scale through high precision flow control and PMS based synthetic chips
- Clean in place (CIP), without relocation or disassembly, to ensure GMP compliance with product quality standards

❹ Microfluidic synthesis chip made of stainless steel (SUS 316L)

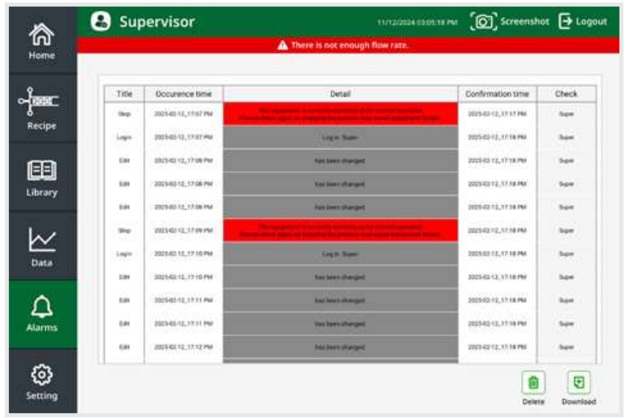
- Reusable, semi-permanent chip eliminates need for laborious chip replacement before each synthesis

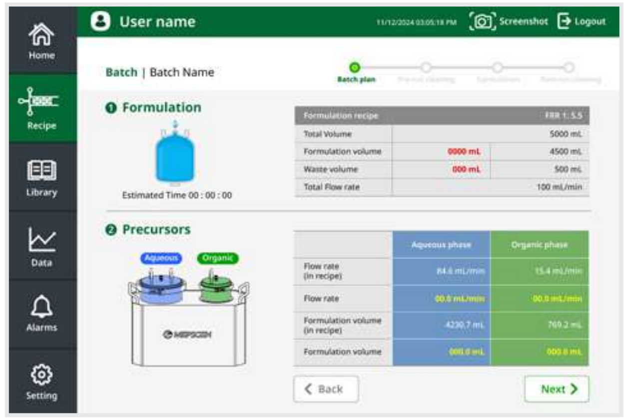
※ Disposable plastic chip available (Optional)



❺ Logs and user control

- Save all processes as document records
- User-specific administrative records

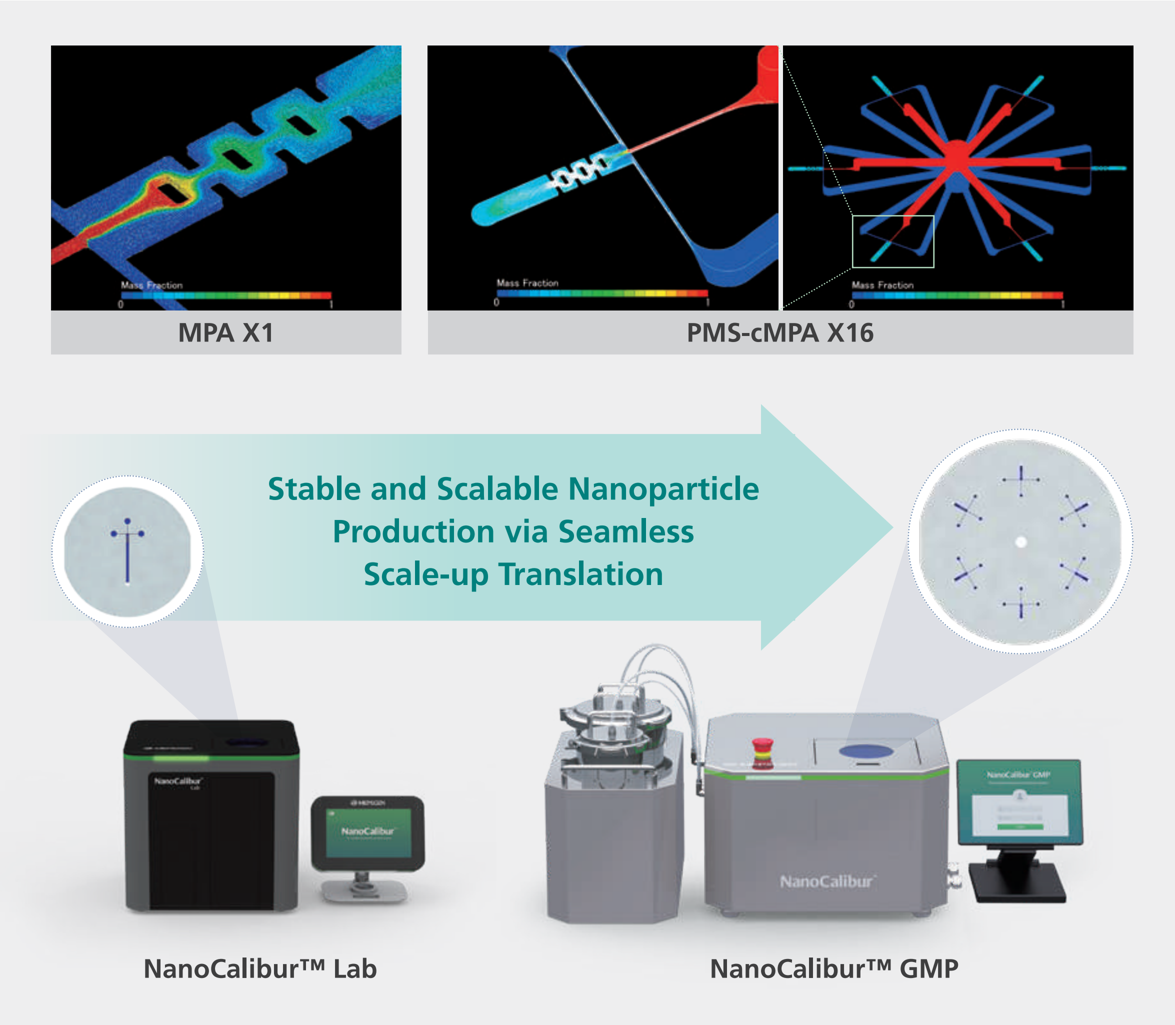




❻ Network

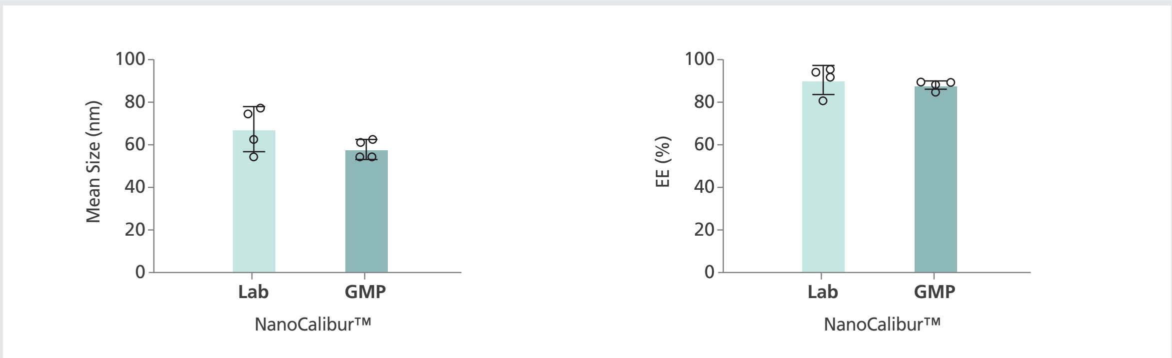
- Built-in Wi-Fi and Ethernet network for seamless data export and firmware upgrades at no additional cost

Seamless Translation Using the NanoCalibur™



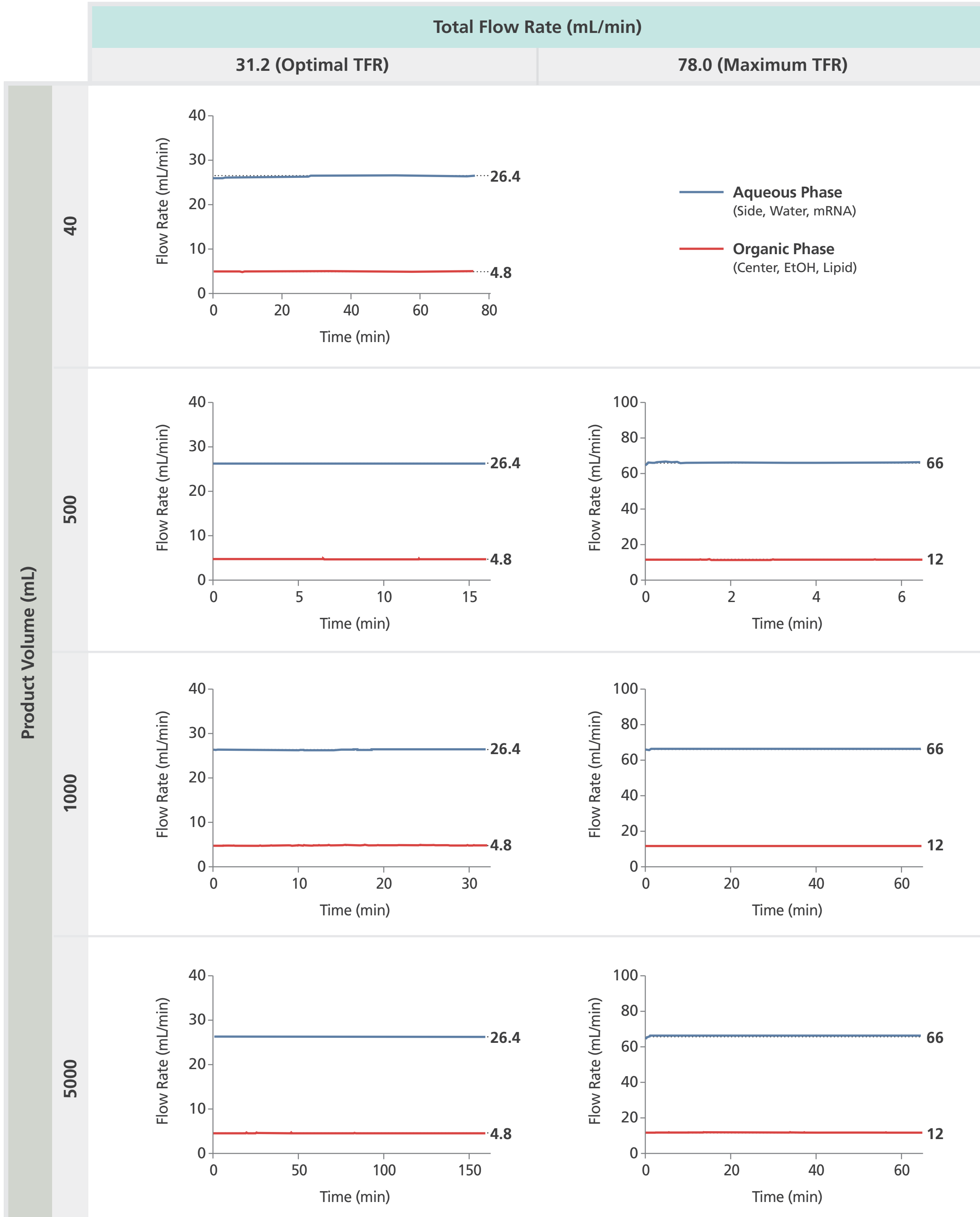
Seamless scalability from Lab to GMP

- mRNA-LNPs synthesized using the NanoCalibur™ Lab during early-stage research retain key physicochemical properties—such as hydrodynamic size and >90% encapsulation efficiency—when scaled up with the NanoCalibur™ GMP.



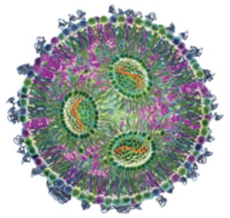
Precise flow rate profiles via closed-loop feedback control

- The system maintained flow rate deviation within 3% under all tested operating conditions—including varying total flow rates (TFR) and target product volumes—demonstrating the precise feedback control performance of NanoCalibur™ GMP.



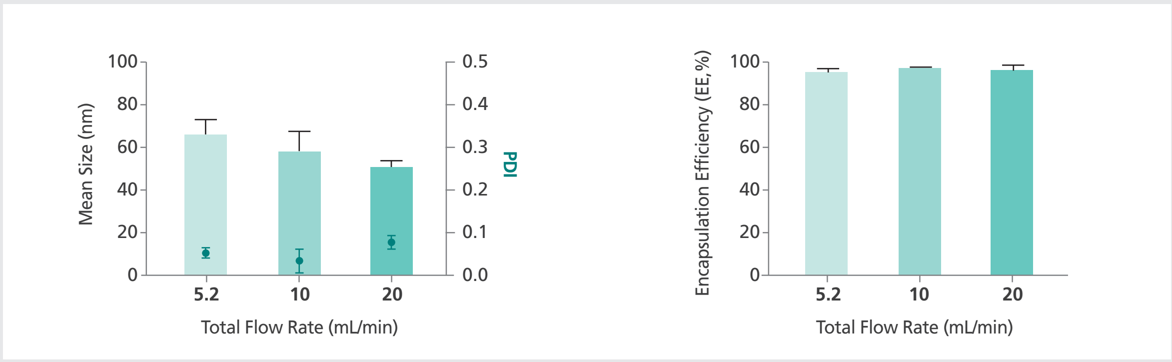
Case Studies:

Lipid Nanoparticle (LNP)



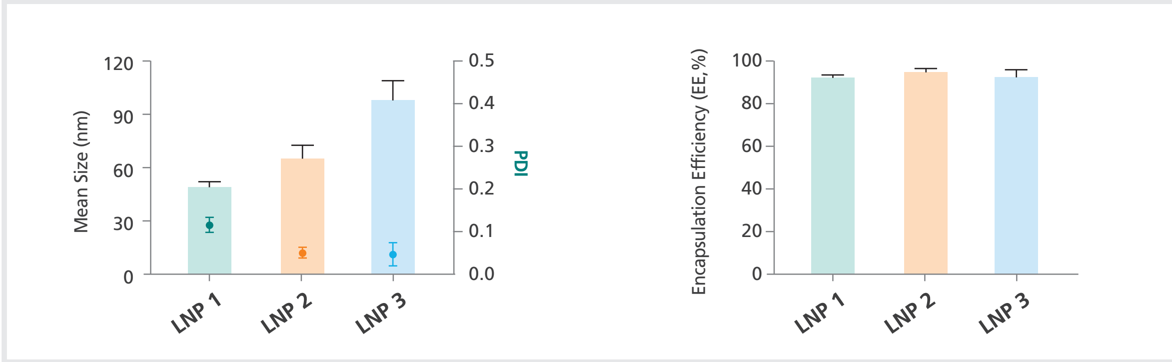
Uniform production of high mRNA encapsulated LNPs

- The size of LNPs decreases from 70 nm to 50 nm as the total flow rate increases. The PDI remains below 0.1. In addition, the encapsulation efficiency (EE) exceeds 95%.



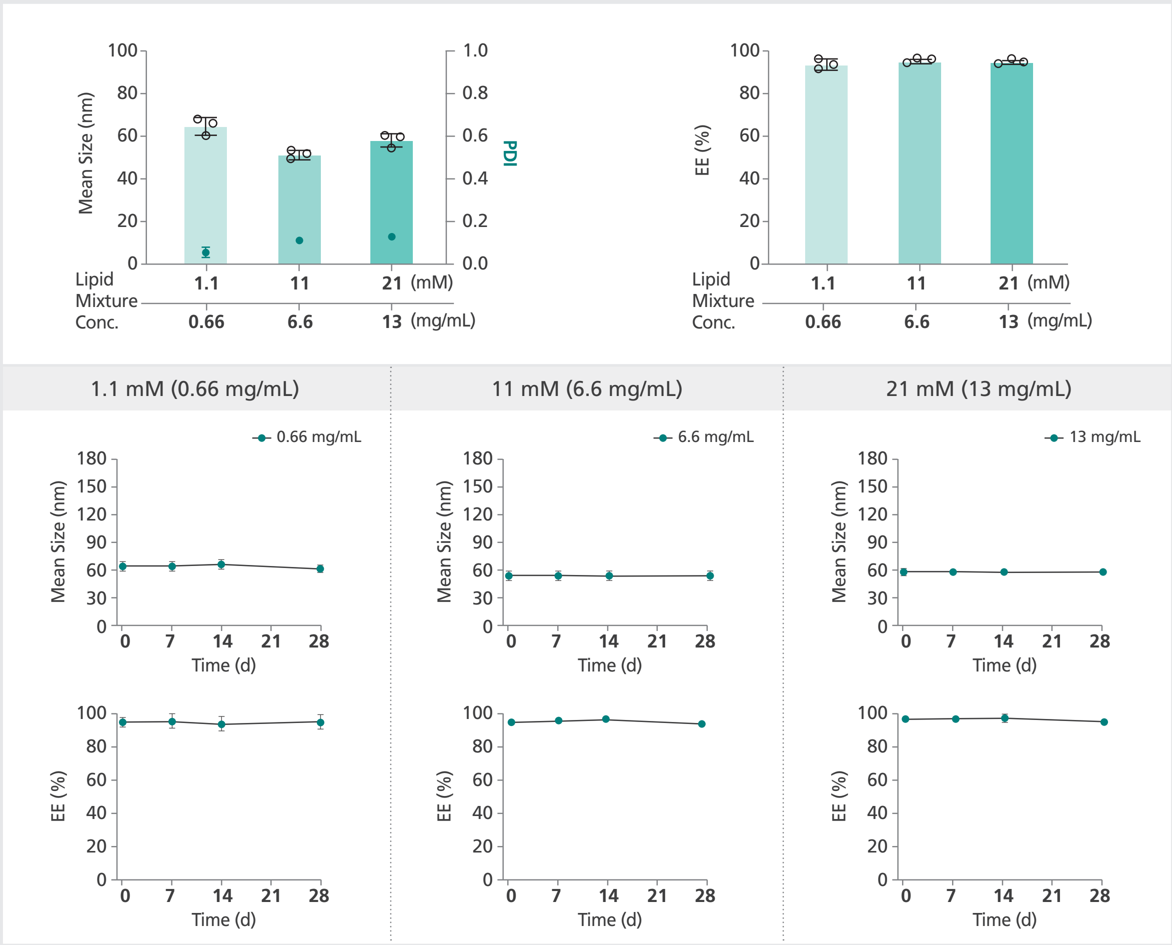
Size-controllable production of mRNA LNPs

- The size of LNPs (40–100 nm) can be controlled by adjusting the composition of precursor lipids, with encapsulation efficiency exceeding 95%.



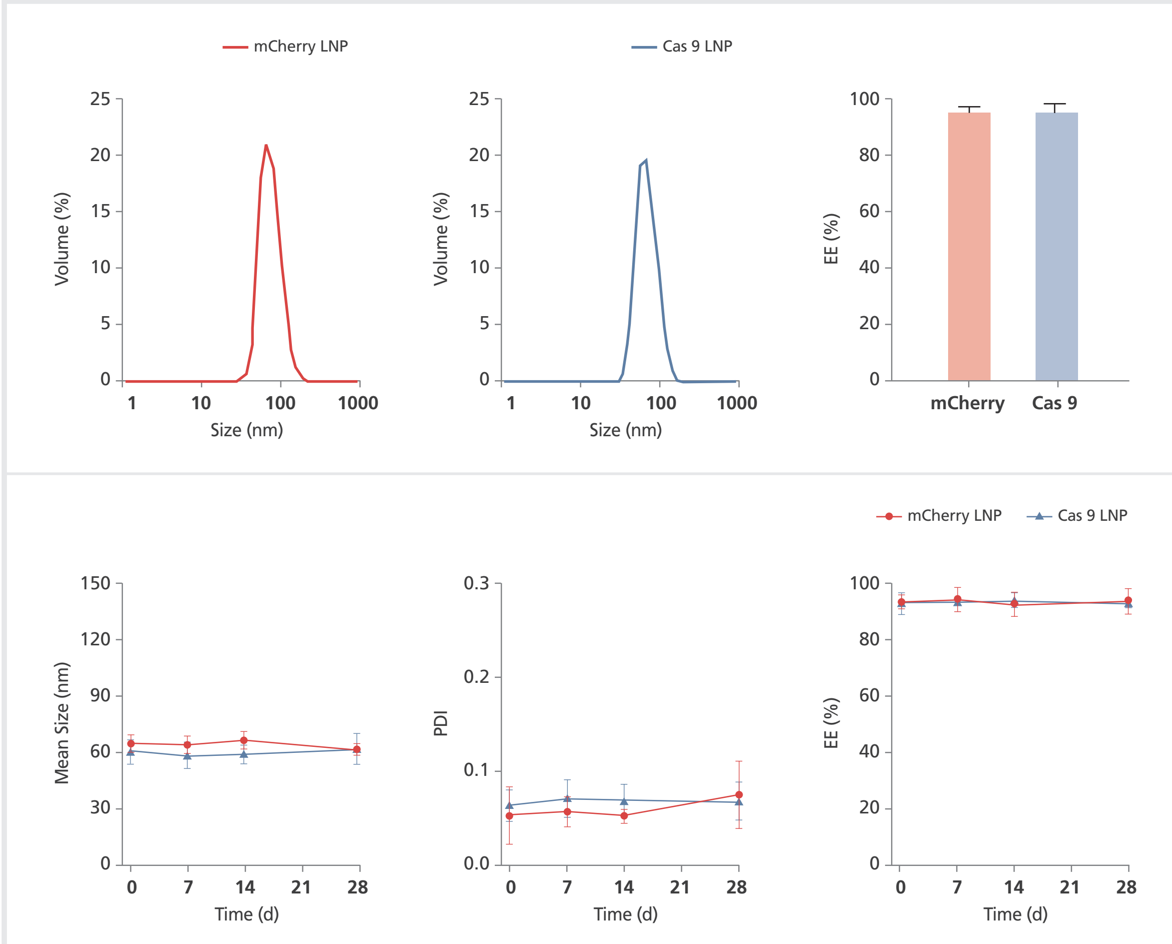
Highly stable sizes and encapsulation efficiencies depending on lipids concentration

- mCherry LNPs synthesized with varying concentrations of lipid mixtures exhibited a highly uniform size and an EE exceeding 95%. Stability assessments confirmed that both the size and EE of mCherry LNPs were maintained in solution for four weeks at levels comparable to those observed immediately after synthesis.



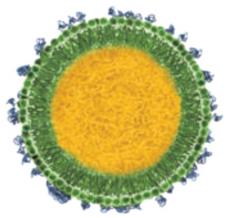
High stability in particle size and encapsulation efficiency across different payloads

- Both the size and encapsulation efficiency of mCherry LNPs and Cas9 LNPs synthesized with high mixing efficiency (>95%) are maintained for four weeks in solution.



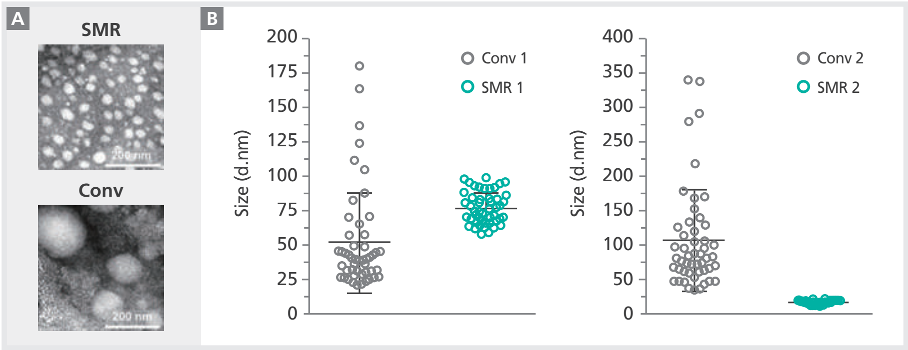
Case Studies:

Lipid-Polymer



Production of uniformly sized lipid-polymer

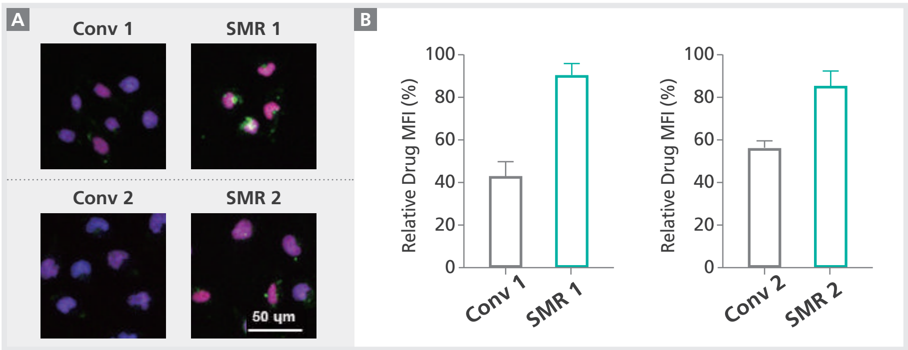
• The nanoparticles produced by SMR T1 showed a higher size uniformity than the nanoparticles produced by conventional manual synthesis.



A) Morphologies of nanoparticles were observed by TEM to compare the obtained nanoparticles (Conv vs. SMR). **B)** Representative size distribution of nanoparticles measured from TEM images. (Conv 1, SMR 1 and Conv 2, SMR 2 differ in their drug/polymer ratios.)

Production of drug-loaded lipid-polymer

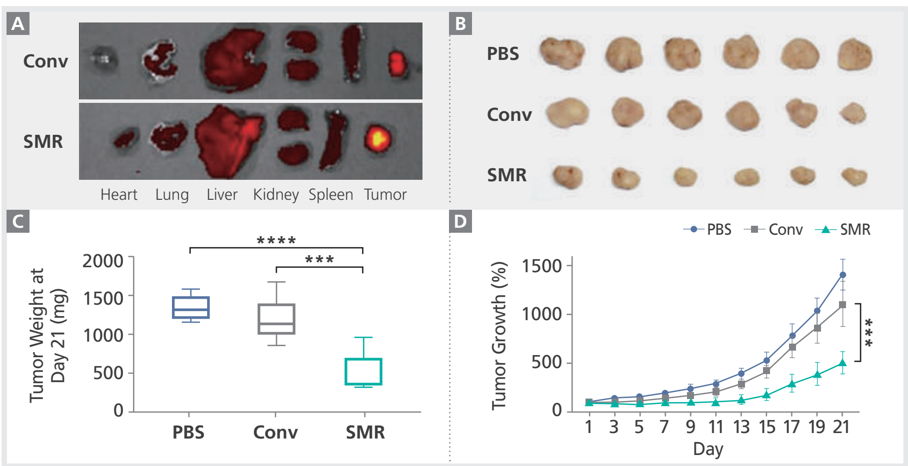
• The nanoparticle manufacturing technology enables the mass scale production of highly uniform nanoparticles with high drug encapsulation efficiency.



A) Fluorescence images of Daoy cell showing cellular uptake of drug (Doxorubicin)-polymer nanoparticles for 4 h. **B)** Relative drug and polymer mean fluorescence intensities (MFI).

Therapeutic effect of drug-loaded lipid-polymer in vivo

• The drug-loaded lipid-polymer produced by SMR T1 exhibited higher cellular internalization efficiency and a stronger anti-tumor effect in tumor-bearing nude mice compared to nanoparticles produced by conventional synthesis.

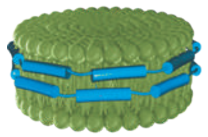


A) Representative images of drug accumulation in major organs at 24 h after intravenous (i.v.) injection. **B)** Images and **C)** Weights of tumors dissected from each group at day 21. **D)** Tumor growth after intravenous injection of each drug-polymer nanoparticles.

Jung *et al., Advanced healthcare materials,* 2020

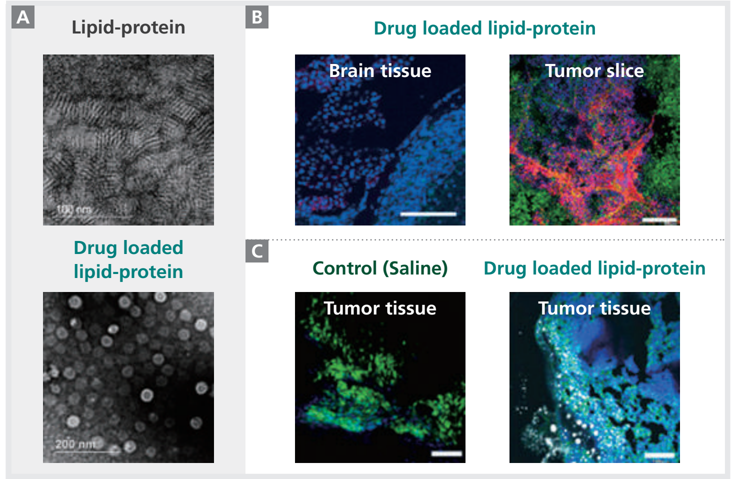
Case Studies:

Lipid-Protein



Production of uniformly sized lipid-protein

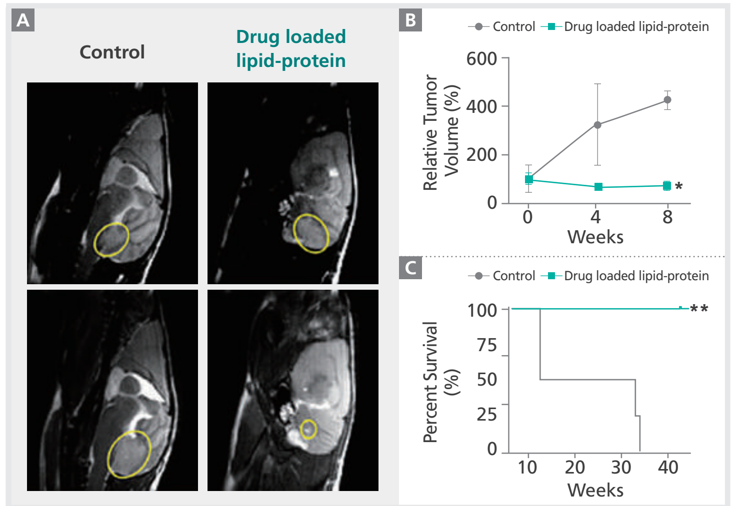
• The uniformly synthesized lipid-protein demonstrated excellent drug encapsulation and validated high targeting efficiency via protein to the target site.



A) TEM images of lipid-protein and drug loaded lipid-protein. **B)** Image of GFP-expressing SmoA1 MB organotypic tumor slice culture upon the treatment of drug loaded lipid-protein. **C)** Localization of lipid-protein in the GFP-expressing medulloblastoma (MB) cells in a sonic hedgehog (SHH) MB mouse model upon i.v. injection.

Anti-cancer effect of drug loaded lipid-protein

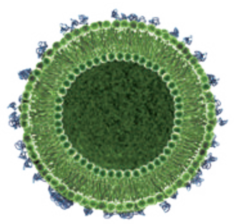
• The uniformly synthesized drug loaded lipid-protein successfully penetrated the receptor-mediated blood-brain barrier and selectively accumulated in brain tumor tissue, exhibiting significantly enhanced anti-cancer efficacy compared to the control group.



A) MRI scans of MB-bearing Patched (PTC) knockout mice brain before and 4 weeks after the i.v. injection. **B)** Relative tumor volume of MB before and after the injection. **C)** Percent survival of SHH MB-bearing PTC mice injected with saline and drug loaded lipid-protein.

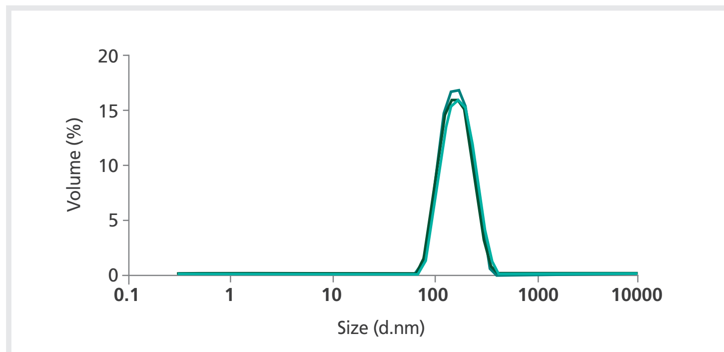
Kim, Jinhwan, *et al. Proceedings of the National Academy of Sciences* 117.39 (2020): 24205-24212.

Liposome



Uniform liposome production

• Liposomes synthesized by MPA X1 exhibit a PDI of less than 0.2, demonstrating excellent uniformity.



NanoCalibur™ Products

Sales and service

Instruments

Semi-permanent chips
(MPA X, SMR T, and the PMS)

- Optimal synthesis conditions of representative nanoparticles provided and updated
- Operating software updated

Offering lines

NanoCalibur™ Lab

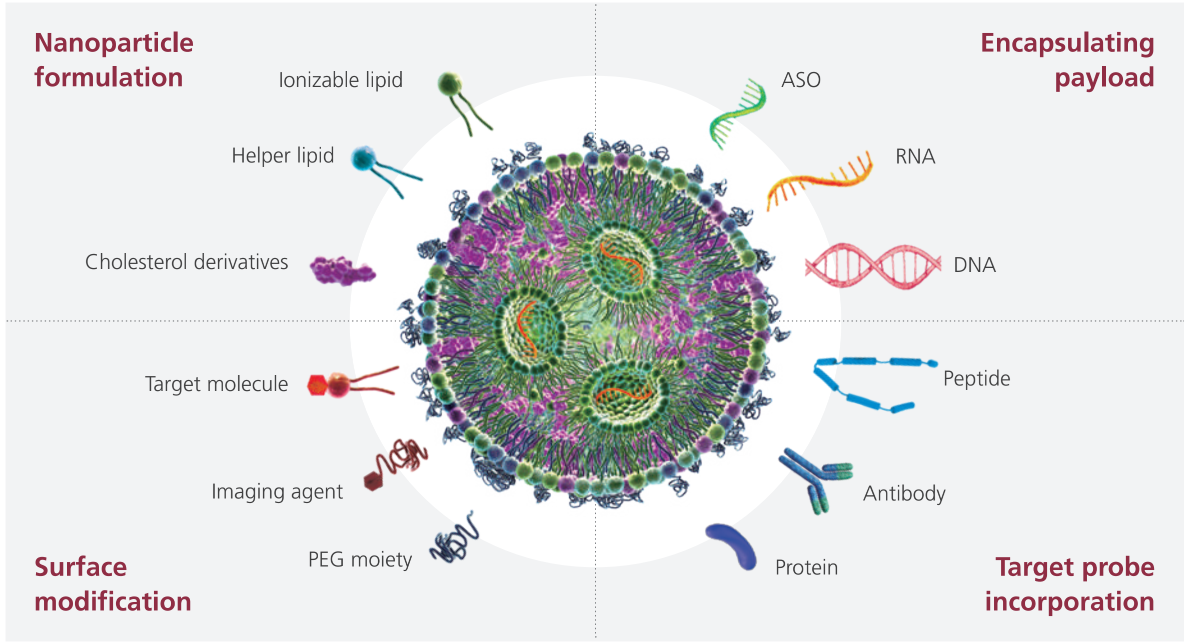
Research laboratories and academic institutions that are developing nanoparticle-based vaccine and therapeutics.

NanoCalibur™ GMP & Commercial

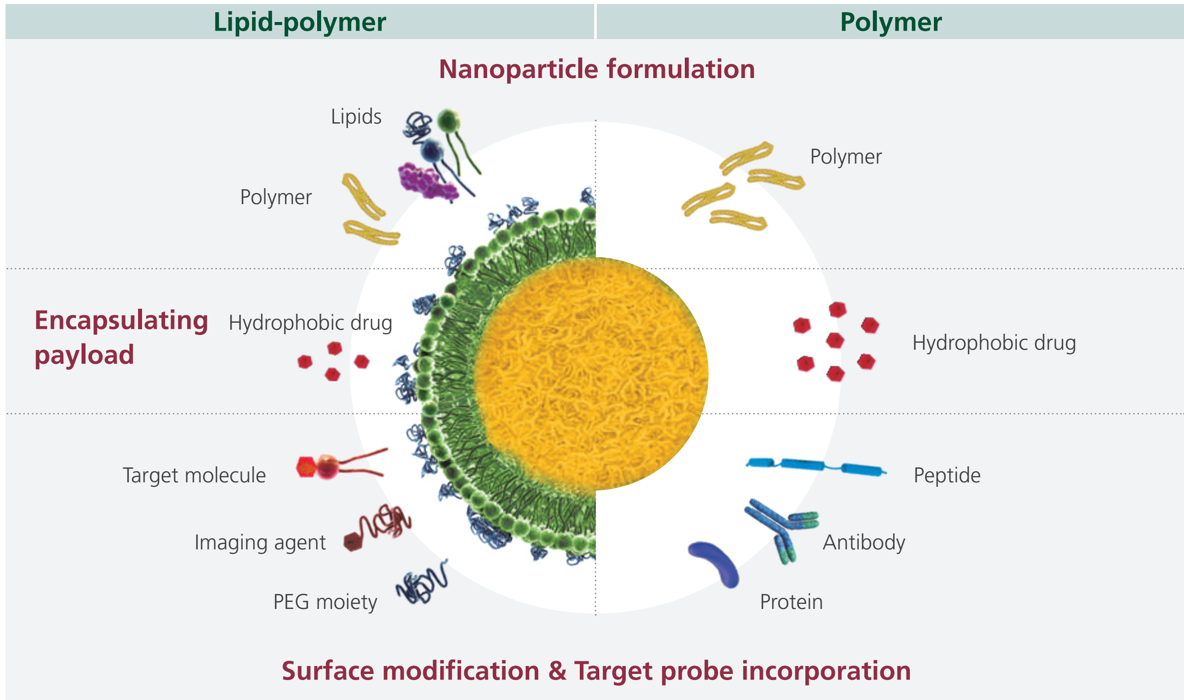
GMP manufacturers that require large-scale production for preclinical studies, clinical trials, and commercial processes.

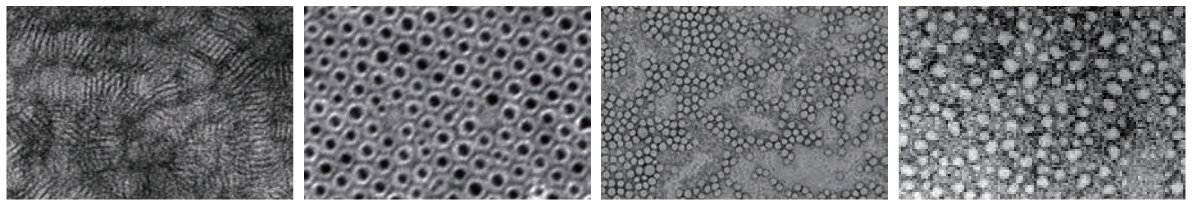
Nanoparticle Formulation Service

LNP formulation



Polymeric nanoparticle formulation





Specifications

NanoCalibur™ Lab

General	Model			NanoCalibur™ Lab
	Size (W x L x H)	Main body		320 x 320 x 310 mm
		Control pad		210 x 140 x 200 mm
	Container	Precursor container	Aqueous phase	50 mL conical tube (recommended fill volume: up to 45 mL)
			Organic phase	50 mL conical tube (recommended fill volume: up to 45 mL)
		Product container	Product & waste	15 mL conical tube
	Weight	Main body		21 kg
		Control pad		2 kg
	Power consumption			230 W
Operating requirement	Electrical power			100 to 230 V (50/60 Hz)
	Gas composition and pressure conditions			100% N_2, 4 to 10 bar
	Operation pressure			4 bar
Environmental	Operating temperature			15 to 35 °C
	Relative humidity			20 to 80 %
	Storage temperature			-10 to +60 °C
	Storage humidity			10 to 60 %
Technical	Production rate	Total flow rate		2.5 to 20 mL/min (0.15 to 1 L/h)
		Product volume per run		3 to 90 mL (Maximum tube capacity)
	Formulation information of precursors (N/P ratio 2-10)	Total lipid concentration		0.6 to 13 mg/mL
		Nucleic acid concentration		0.004 to 0.3 mg/mL
		Minimum amount of initial mRNA		0.007 mg
	Flow control			PID control
	Flow control resolution			0.1 mL/min
Interface	Display			7 inch, 1024 * 600 pixel
	Touchscreen			Capacitive touch
	Connection			USB 2.0, LAN

NanoCalibur™ GMP

General	Model			NanoCalibur™ GMP
	Size (W x L x H)	Main body		500 x 500 x 283 mm
		Control pad		280 x 200 x 90 mm
		Precursor container	Aqueous phase	Ø200 x 350 mm (5 L)
			Organic phase	Ø150 x 200 mm (1 L)
		Precursor housing holder		480 x 300 x 230 mm
	Weight	Main body		54 kg
		Control pad		2 kg
		Precursor container	Aqueous phase	9 kg
			Organic phase	4 kg
		Precursor housing holder		4 kg
	Power consumption			90 W
Operating requirement	Electrical power			100 to 230 V (50/60 Hz)
	Gas composition and pressure conditions			100% N_2, 4 to 7 bar
	Operation pressure			Up to 6 bar
Environmental	Operating temperature			15 to 35 °C
	Relative humidity			20 to 80 %
	Storage temperature			-10 to +60 °C
	Storage humidity			10 to 60 %
Technical	Production rate	Total flow rate		15 to 100 mL/min
				1 to 6 L/h
	Flow control			PID control
	Flow control resolution			0.1 mL/min
Interface	Display			11.6 inch, 1920 * 1080 pixel
	Touchscreen			Capacitive touch
	Connection			USB 2.0, LAN

Chip MPA X1, SMR T1

General specification	Diameter	100 mm
	Weight	<1 kg
	Main component	SUS 316L stainless steel for semi-permanent use

Chip PMS-cMPA X16, PMS-cSMR T16

General specification	Diameter	160 mm
	Weight	3 kg
	Main component	SUS 316L stainless steel for semi-permanent use

Sep.2025

MEPSGEN

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