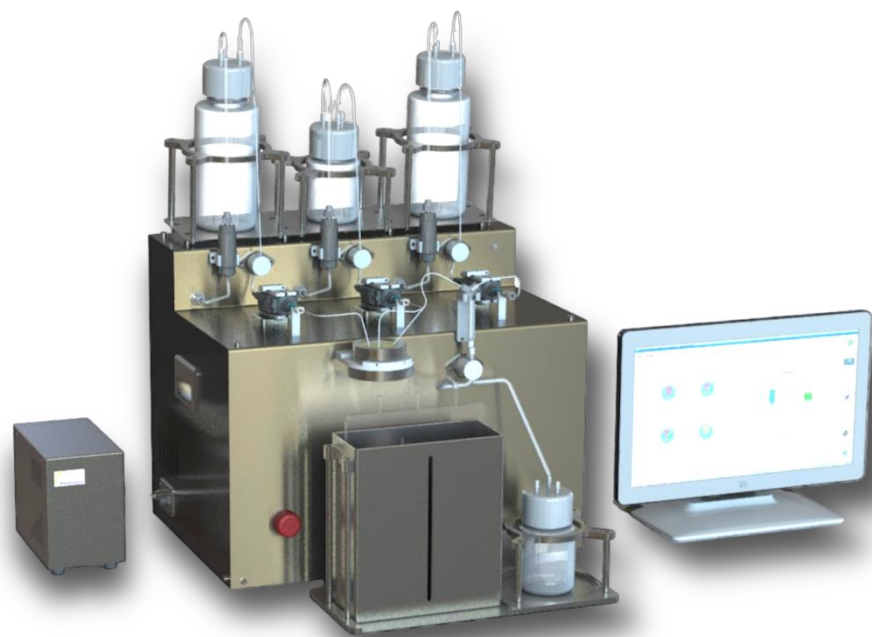


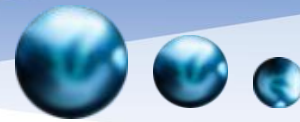
# NanoGenerator<sup>®</sup> MAX Nanoparticle Synthesis System



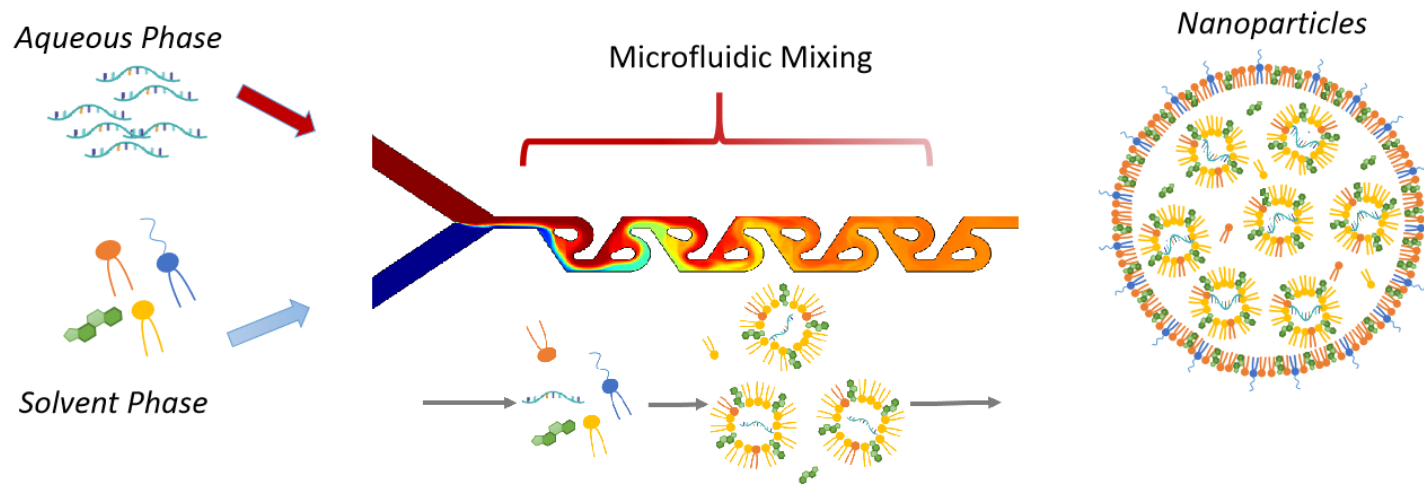
PreciGenome






Mar 2024

# What are Lipid Nanoparticles?

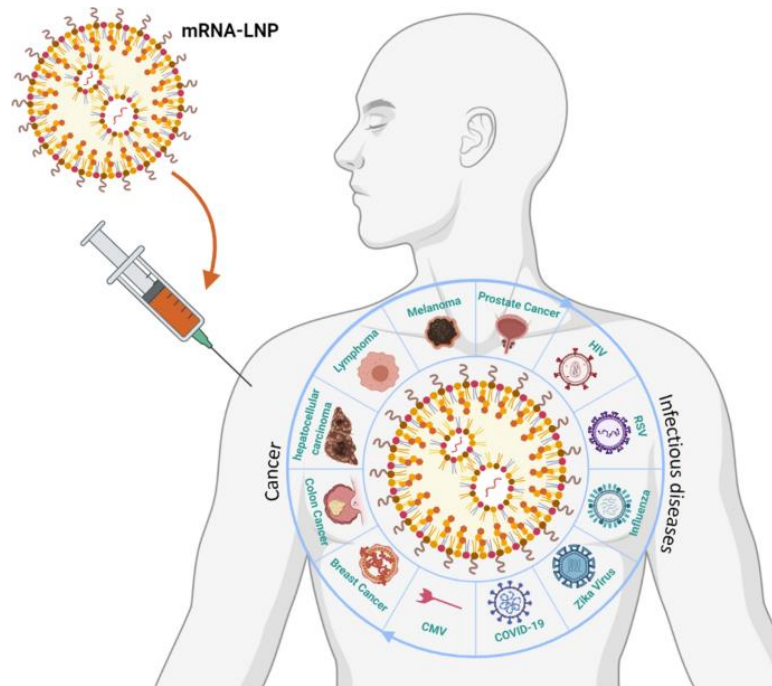
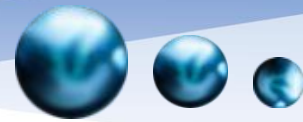


Lipid nanoparticles (LNPs) are self-assembling structures of natural or synthetic lipids in an aqueous environment.



-  Cationic/ionizable lipid
-  Structural lipid
-  Cholesterol
-  PEGylated lipid
-  Nucleic acid payload

# RNA-LNP Therapeutics and Vaccines

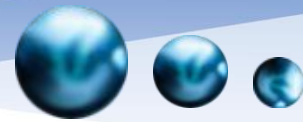


Name	Disease	Encoded antigen	Administration route	ClinicalTrials.gov identifier	Phase
<b>Infections</b>					
mRNA-1273	SARS-CoV-2	Spike	i.m.	NCT04470427	III (EUA and CMA)
BNT162b2	SARS-CoV-2	Spike	i.m.	NCT04368728	III (EUA and CMA)
CVnCoV	SARS-CoV-2	Spike	i.m.	NCT04652102	III
mRNA-1647	Cytomegalovirus	Pentameric complex and B glycoprotein	i.m.	NCT04232280	II
mRNA-1388	Chikungunya virus	Chikungunya virus antigens	i.m.	NCT03325075	I
CV7202	Rabies virus	G glycoprotein	i.m.	NCT03713086	I
<b>Cancer</b>					
mRNA-5671/V941	Non-small-cell lung cancer, colorectal cancer, pancreatic adenocarcinoma	KRAS antigens	i.m.	NCT03948763	I
mRNA-4157	Melanoma	Personalized neoantigens	i.m.	NCT03897881	II
mRNA-4650	Gastrointestinal cancer	Personalized neoantigens	i.m.	NCT03480152	I/II
HARE-40	HPV-positive cancers	HPV oncoproteins E6 and E7	i.d.	NCT03418480	I/II

Kiaie, S.H., Majidi Zolbanin, N., Ahmadi, A. *et al.* Recent advances in mRNA-LNP therapeutics: immunological and pharmacological aspects. *J Nanobiotechnol* **20**, 276 (2022).

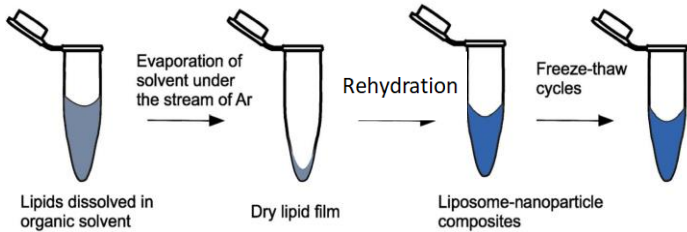
[Nature Reviews Materials](#) volume 6, pages1078–1094 (2021)

# Lipid Nanoparticle Synthesis Methods



## Conventional Methods

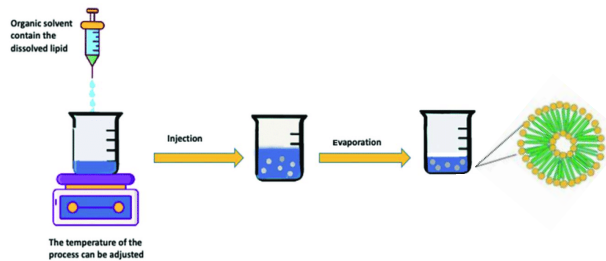
### A Film hydration



- Established method
- Versatile method

- High consumption of the organic solvent
- High PDI
- Lack of reproducibility
- Need for additional downsizing step
- Difficulties in scaling-up

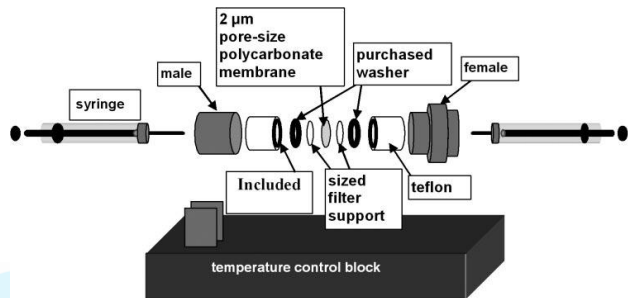
### B Solvent injection



- Simple and fast
- Scaling-up possibility
- Controllable

- Exposing to organic solvent
- High PDI
- Stability problem

### C Extrusion

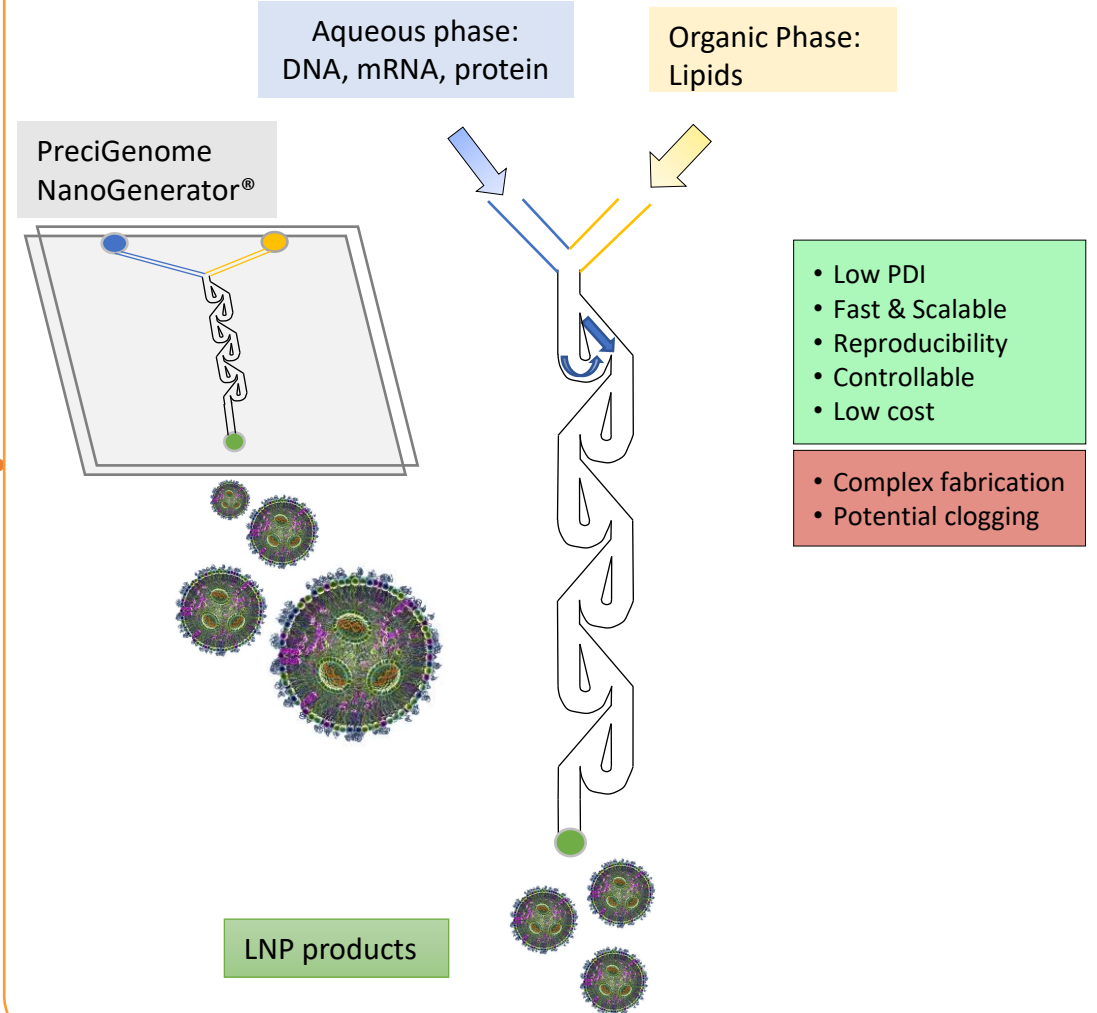


- Established method
- Uniform and homogenous formulation

- Possible clogging of the membrane pores
- Difficulties in scaling up

Nanomaterials, Volume 11, 2021, 3440

## Microfluidic Mixing

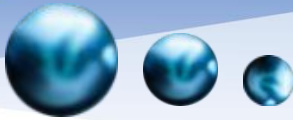


- Low PDI
- Fast & Scalable
- Reproducibility
- Controllable
- Low cost

- Complex fabrication
- Potential clogging

VS.

# NanoGenerator® - Nanoparticle Synthesis System



## FLEX-S



## FLEX-S PLUS



- Flex-S: 0.1 – 2 ml
- Flex-S Plus: High-throughput discovery & screening

## FLEX-M



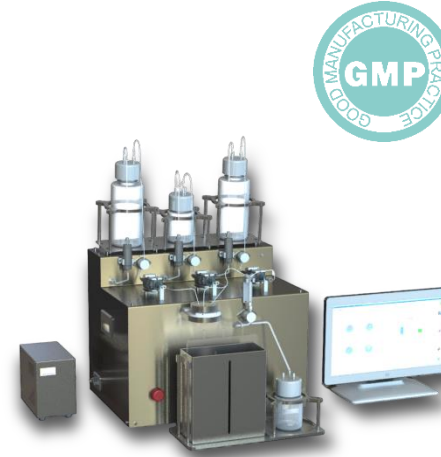
- Flex-M: 1 – 12 ml

## PRO



- Pro: 2 – 200 ml

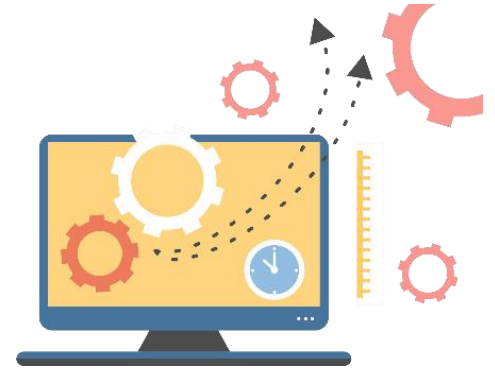
## MAX



Clinical development  
GMP certified manufacturing

- MAX: 50ml – 1L
- MAX (40L/h): >20L

## OEM



Custom design and OEM solutions  
GMP certified manufacturing

- >400 L throughput



DISCOVERY & SCREEN

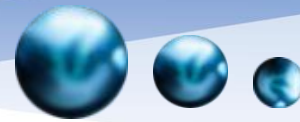
PRE-CLINICAL DEVELOPMENT

CLINICAL  
DEVELOPMENT

CUSTOM SOLUTION



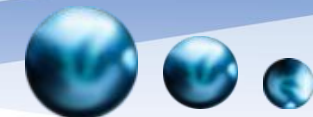
# NanoGenerator® MAX — Intro



- The NanoGenerator® Max is designed for clinical and commercial production. Two versions are available:
  - RUO: Preclinical applications
  - cGMP: Clinical and commercial production
- Two flow kits are available with different supported throughput:
  - 4.8 L/h flow kit: 50 mL – 1 L
  - 40 L/h flow kit: >20 L

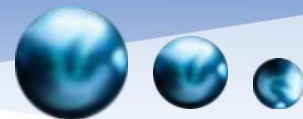


# NanoGenerator® MAX — Spec



Model	NanoGenerator® MAX			
	RUO flow kit 4.8 L/h	GMP flow kit 4.8 L/h	RUO flow kit 40 L/h	GMP flow kit 40 L/h
cGMP compliance	N/A	Yes	N/A	Yes
Software (21 CFR Part 11 compliant)	Optional	Yes	Optional	Yes
Throughput	50 ml – 1 L		> 20 L	
Total flow rate	1.2 – 4.8 L/h		Up to 40 L/h	
Flow rate ratio	1:1 – 9:1		1:1 – 5:1	
Inline dilution	1:1 – 5:1			
Size range	40 – 200 nm			
PDI	0.05 – 0.2			
Encapsulation efficiency	Up to 99%			
Payload	DNA, mRNA, siRNA, protein, small molecules, etc.			
Dimension (L × W × H)	620 × 380 × 430 mm			
Weight	50 Kg		65 Kg	

# NanoGenerator® MAX — Contents



## Instrument:

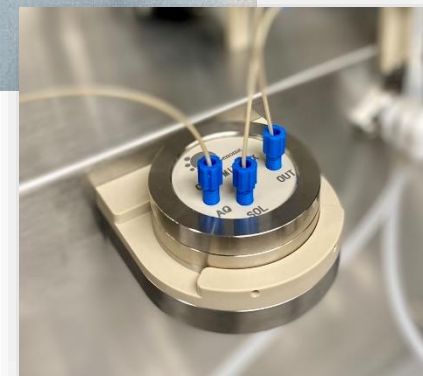
- Pneumatic system
- Valves
- Flow rate sensors
- Consumable kit
- Monitor (optional)
- Pumps (optional)

## Consumable Kit:

(Sterilized, Nuclease free, pre-assembled)

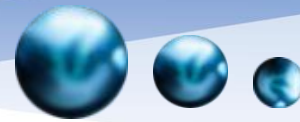


- Sample bottle (aqueous)
- Sample bottle (solvent)
- Sample bottle (dilution)
- Waste bottle
- Bioprocessing bag (collection)
- Tubing & connectors
- Mixing chip





# NanoGenerator® MAX — Software



## Software (21 CFR Part 11) Features:

- Experimental parameter setting
- Experimental recipe save/load
- Real-time pressure/flow rate chart
- Historic experimental parameter tracking
- Historic pressure/flow rate tracking
- System self-diagnostic system
- Real-time flow rate diagnostic system
- Warning system
- Manual & automatic emergency stop system
- User management
- Audit trail
- Zero flow calibration
- Flow sensor maintenance & re-calibration (Service)

**Settings List**

Mode	Configuration	Last Modify
1	default recipe advanced	2023/05/29 13:16:37

**Current Settings (Advanced Mode)**

Default:

Current: default recipe advanced

Buttons: Load, Save, Set as Default, Import, Export, Delete

**Others**

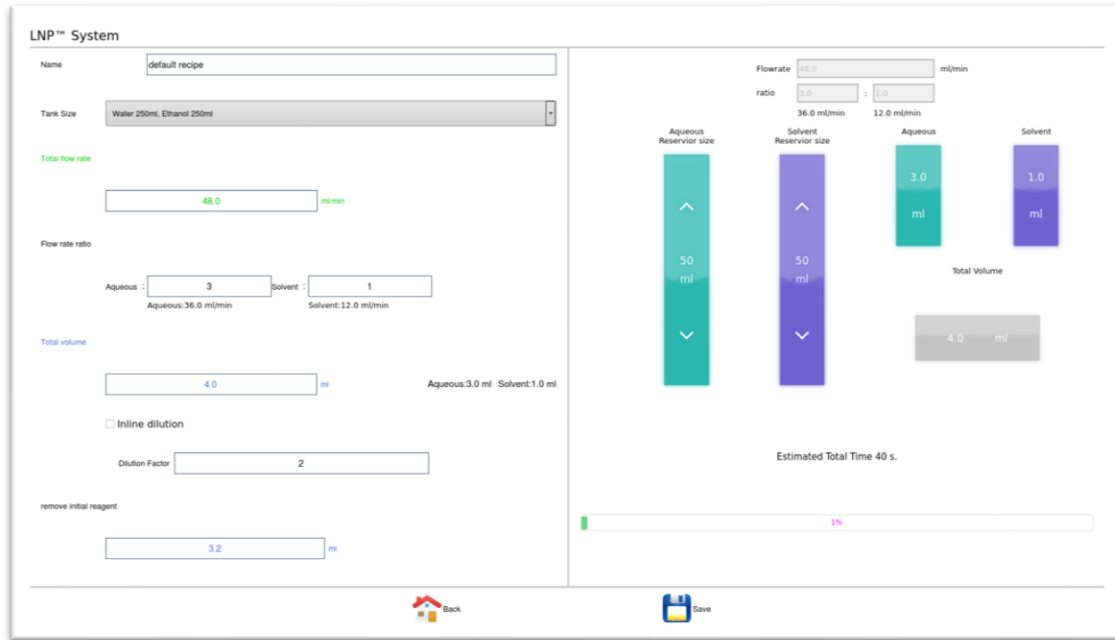
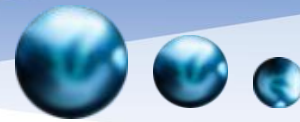
Pressure Unit:  kPa  psi  mBar

Data Export	Software Update
Import Data	Firmware Update
Flow Sensor Calibrating	System Time
Self-Check	About

**Functions**

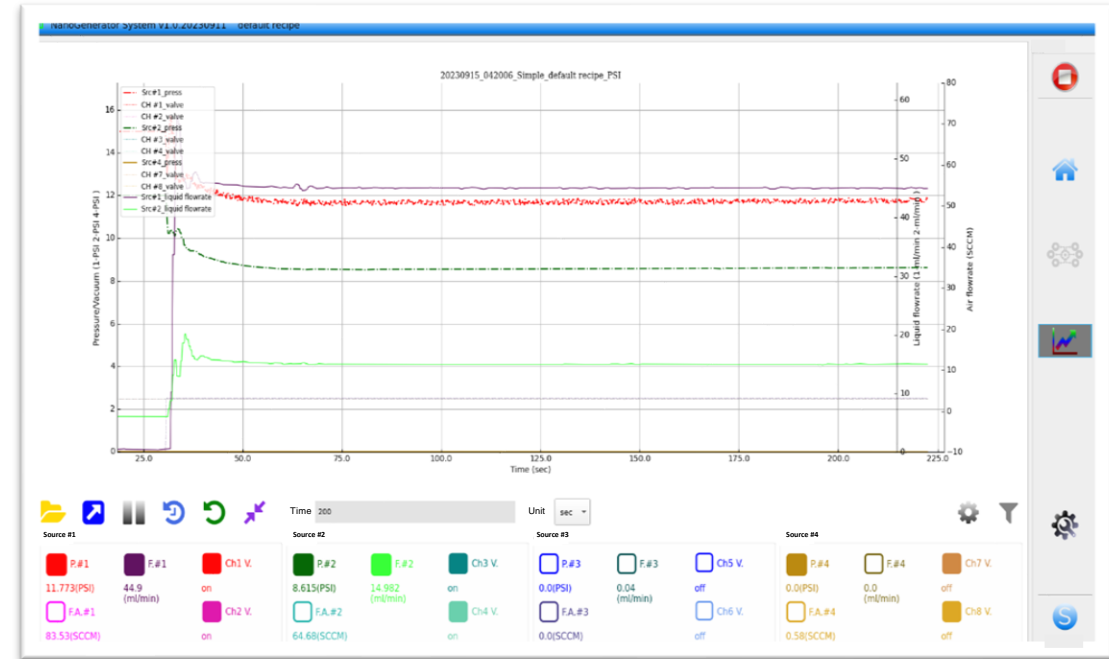
History Data	Zero
User Management	Audit Trail

# NanoGenerator® MAX — Software



Easy-to-use UI to set parameters including:

- Total flow rate
- Flow rate ratio
- Production volume
- Inline dilution factor
- Waste volume

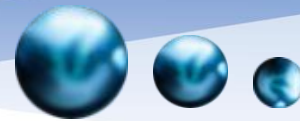


Easy-to-use real-time flow rate /pressure chart including:

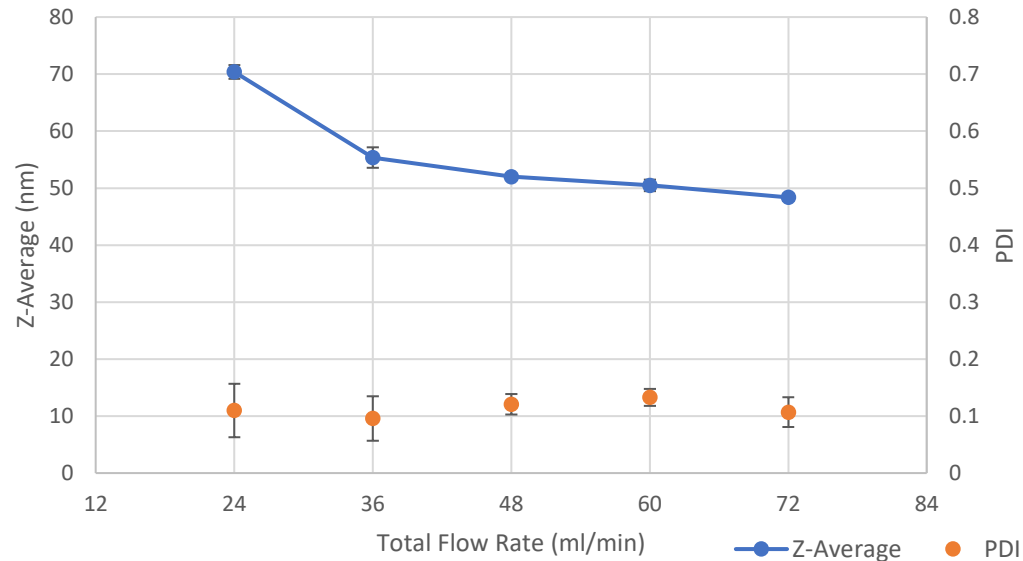
- Flow rate
- Pressure
- Air flow rate

All parameters are tracked for aqueous, solvent, and inline dilution lines

# NanoGenerator® MAX — Performance



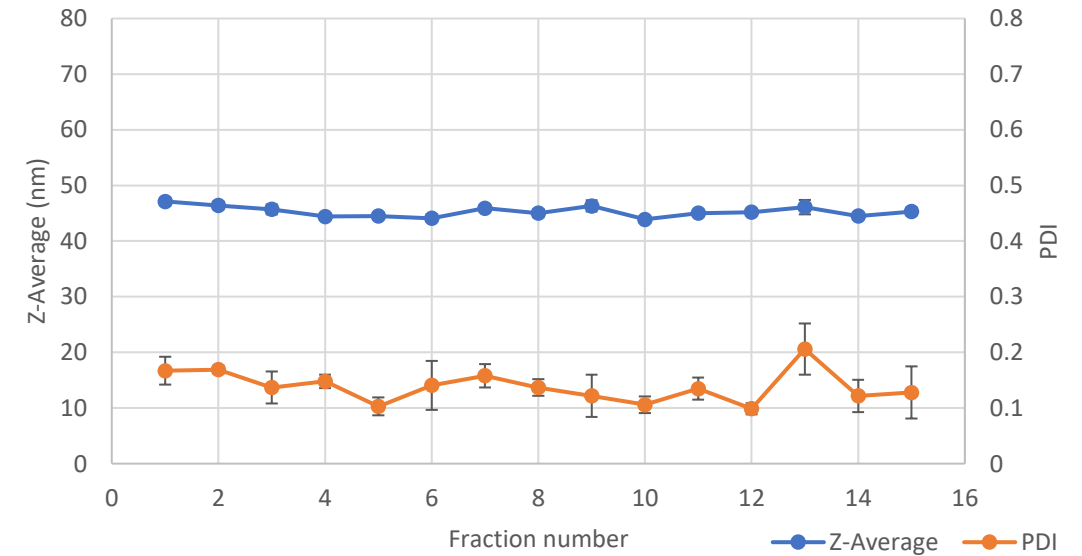
Nanoparticle Size vs. Total Flow Rate



- Nanoparticle size decreases as total flow rate increases
- Size decrease experiences diminishing returns when the flow rate reaches 48 ml/min

Reagents	
Aqueous phase	Sodium acetate buffer (100mM, pH5.2)
Solvent phase	LipidFlex, 15mM in ethanol

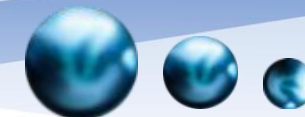
Nanoparticle Size uniformity (50 ml/fraction)



- Throughout the entire production run, there is no significant difference in the nanoparticle size and PDI

Reagents	
Aqueous phase	Phosphate-Buffered Saline (1X, pH7.4)
Solvent phase	LipidDemo, 15mM in ethanol

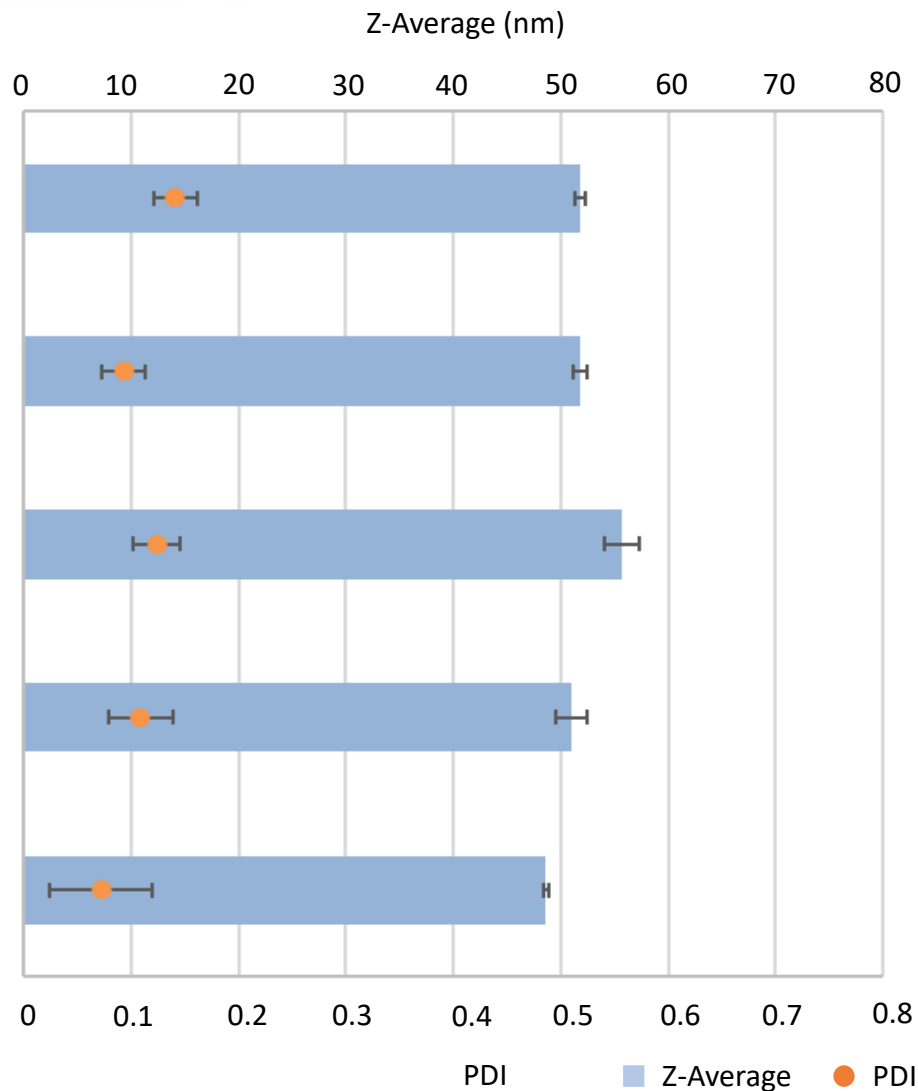
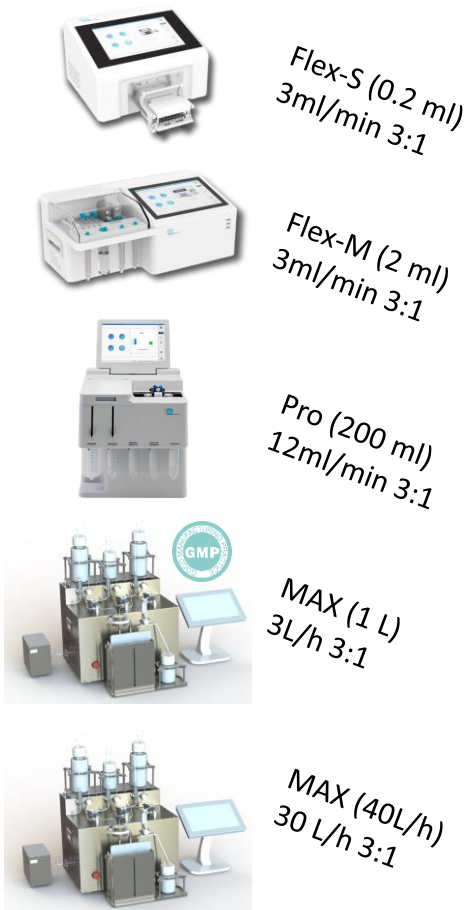
# NanoGenerator® — Scale Up



DISCOVERY &  
SCREEN

PRE-CLINICAL  
DEVELOPMENT

CLINICAL  
DEVELOPMENT

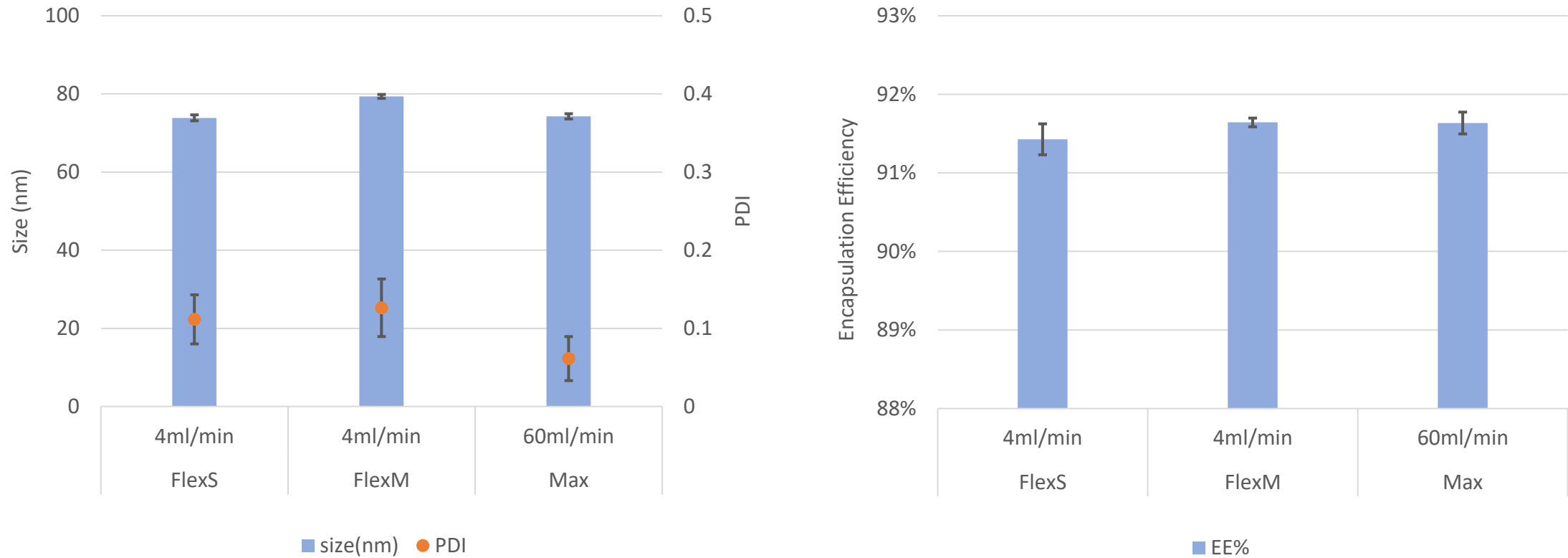
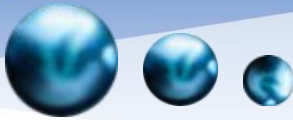


- Nanoparticle size is consistent across different production volumes if using optimal flow rates
- Mixing mechanism is the same for all PreciGenome instruments
- Production can be scaled up from discovery & screening to preclinical & clinical trial production

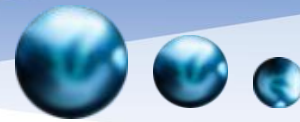
Reagents	
Aqueous phase	Sodium acetate buffer (100mM, pH5.2)
Solvent phase	LipidFlex, 15mM in ethanol



# NanoGenerator® — Scale Up



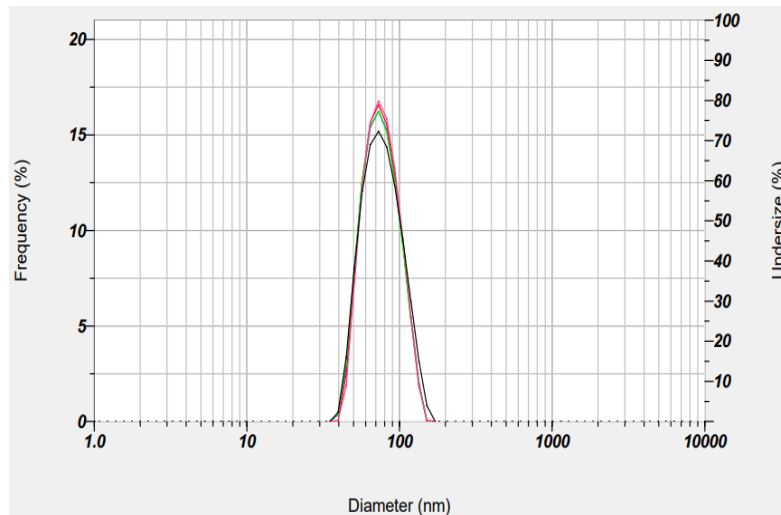
Reagents	
Aqueous phase	Sodium acetate buffer (100mM, pH5.2)
Payload	RNA (~600 nt)
Solvent phase	LipidFlex RNA-LNP kit



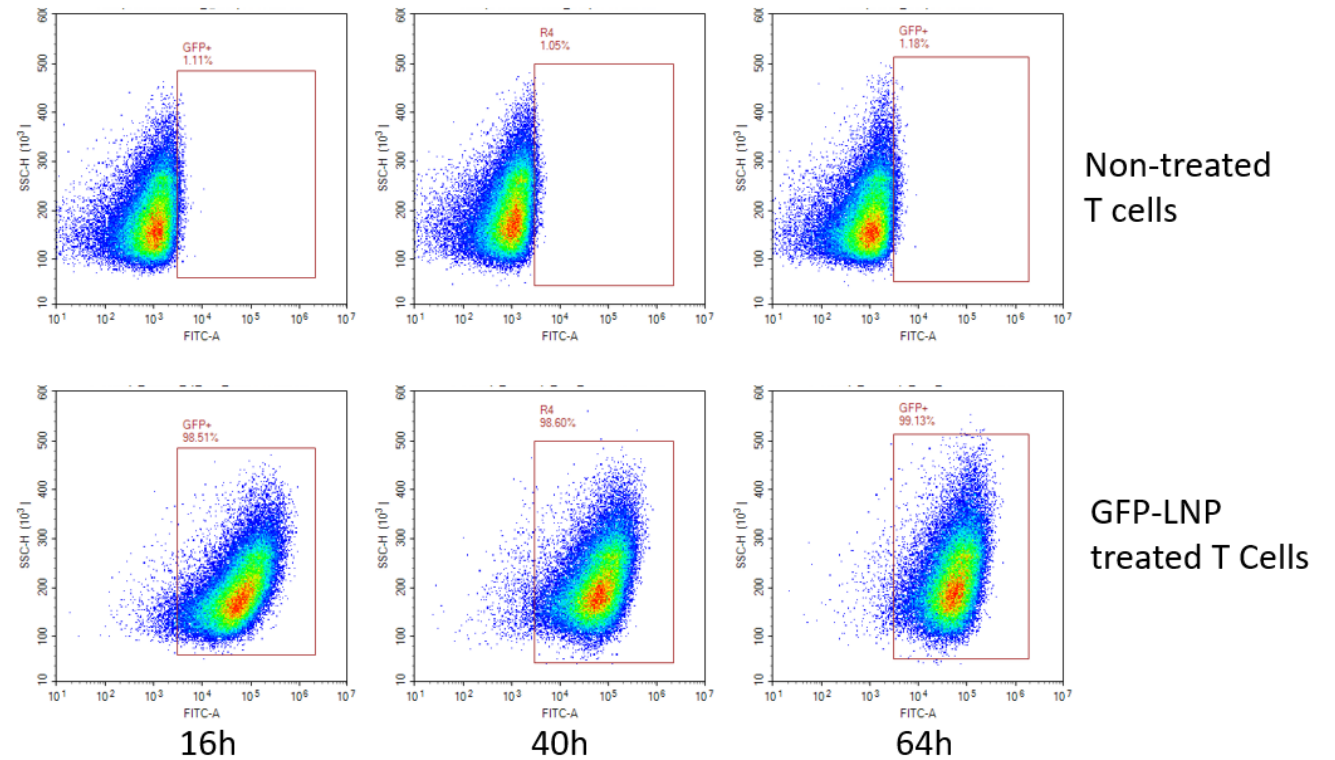
## eGFP mRNA Lipid Nanoparticles

Z-Average Diameter: 67.3 nm

PDI: 0.106

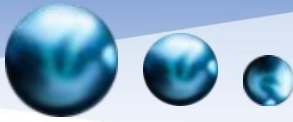


**Figure 1.** mRNA(eGFP)-LNP Synthesized by NanoGenerator. Average diameter is 67.3 nm. PDI is 0.106. Encapsulation efficiency is 94.5% (Ribo Green RNA Quantification Kit).



**Figure 2.** GFP(+) positive population of control (non-treat) and EGFP mRNA LNP treated primary T cells at 16, 40 and 64 hours. Cells were stained (1:50) using Biolegend 7-AAD Viability Staining for 10 minutes. Gating: First select for individual cells (excluding doublets). Then select for the healthy cell population. Then select for viable cells by excluding cells which are positive for 7-AAD. Gate for FitC-A channel (GFP)

# Why PreciGenome?



## High Performance & Efficiency



- Tunable size (40-200 nm)
- Low PDI (0.05-0.2)
- High encapsulation efficiency

## Open Platform



- Upgradable system
- Transferable microfluidic chips

## Scalable Throughput



- Low volume for screening (Flex-S)
- Medium volume production (Flex-M)
- High volume production (Pro, MAX-GMP)

## Simple Operation



- Simple setup
- Compact size
- Intuitive UI w/ touchscreen

## Cost Effective

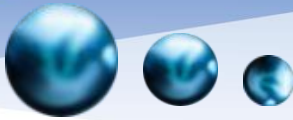


- Affordable configuration
- Lower cost per run

## Custom Support



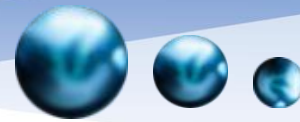
- Demo, Training and Support
- Extended Warranty
- Hot swap option
- Local US company



- **Manual**
- **Standard Operation Procedure (SOP)**
- **Warranty (1 year)**
- **Documentation related to cGMP compliance (cGMP version)**
  - ✓ Installation qualification, operational qualification, performance qualification
  - ✓ Report of consumable items
  - ✓ Chemical compatibility report of consumable items
  - ✓ Report of endotoxin test
  - ✓ Report of RNase/DNase free test
  - ✓ Report of sterilization test
  - ✓ Report of ethylene oxide residue test
  - ✓ 21 CFR Part 11 report
  - ✓ Electromagnetic compatibility report
  - ✓ Report of safety regulations
  - ✓ Other reports by requesting



# Appendix II



PurePower Medical Suzhou Purepower Medical Technology Co.,Ltd

### Sterility Test Report

No.: QT/QG/Q01-01 No. 020230724-01

Product Name	GMP Consumable Bag	Type	Sample	Lot No.	Sample
Sample ID	1, 2, 3, 4	Sterilization Lot No.	202307220101	Test Date	2023-07-24
Inoculation Method	<input type="checkbox"/> Membrane Filter <input checked="" type="checkbox"/> Direct Inj.				
FTM Lot No.	FTM-230724				
TSB Lot No.	TSB-230724				
Positive Strain	Staphylococcus aureus				

Test Result:

Culture Medium	Sample ID	1	2
FTM 30 - 35°C	1	-	-
	2	-	-
	3	-	-
	4	-	-
TSB 20 - 25°C	1	-	-
	2	-	-
	3	-	-
	4	-	-

Incubation Temperature (°C): 37

Dish No.: 1

Incubation Time: 24h, 48h

Average: ✓

Conclusion: ✓/Com

Remark: ✓

Notice: Put the "P" in the "C"; in the "Re"

Tested by/Date: Yu Yanwei 2023

PurePower Medical Suzhou Purepower Medical Technology Co.,Ltd

### EO Residual Test Report

No.: QT/QG/Q04-02 No. 020230731-01

Sample Name	GMP Consumable	Type	Sample
Lot No.	Sample		
Sample No.	Sample		
Test Date	2023		

### Extractables Test Report

**Report title** The Extractables Study Report of Nanoparticle Synthesis System Consumables Kit

**Report number** EL-REP-23-019.01-E

**Project No.** N/A

**Customer** PreciGenome LLC

**Address** 2176 Ringwood Ave. San Jose, CA, 95131, USA

**Testing laboratory** Centre Testing International Pinchuang (Shanghai) Co., Ltd.

**Testing laboratory address** 1351 Wanfang Road, Minhang District, Shanghai

Underwriters Laboratories (UL LLC) IEC/EN Safety Report

UL Solutions

Model: PG-SYN-G

Device Description: NanoGenerator™ Max Nanoparticle Synthesis System

Applicant: PreciGenome LLC

Manufacturer: Same as Applicant

Manufacturing Facility(ies): Suzhou Precige Unit 202, Building

Report No.: E526160-D1003

Report (Re) Issue Date: 2023-12-06

Base Standard(s): EN 61010-1:2011

Additional Standards: N/A

Report Types: This report covers the Safety evaluation above.

Test Report issued under the responsibility of: UL Solutions

### TEST REPORT IEC 61010-1

Safety requirements for electrical equipment for measurement, control and protection parts

Report Number .....: E526160-D1003

Date of issue .....: 2023-12-06

Total number of pages .....: 1

Name of Testing Laboratory preparing the Report .....: UL Solutions

Applicant's name .....: PreciGenome LLC

Address .....: 2176 Ringwood Ave, San Jose, CA, 95131, USA

Test specification: IEC 61010-1

Standard .....: IEC 61010-1

Test procedure .....: In-house

Non-standard test method .....: N/A

TRF template used .....: IEC 61010-1

Test Report Form No. ....: IEC 61010-1

Test Report Form Originator .....: UL Solutions

Master TRF .....: 4790895205-2.1-1

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This report is not valid as a CB Test Report and appended to a CB Test Certificate.

General disclaimer: The test results presented in this report are for information only. This report shall not be reproduced, except in full, without the prior approval of the General Manager. This verification is subjected to the governance of the General Conditions of Services, printed overleaf.

UL Solutions

### Statement of Compliance

UL-CCIC Company Limited  
No. 2, Chengwan Road, Suzhou Industrial Park, Suzhou 215122, China  
T: +86-512-6808 6400  
F: +86-512-6808 4099

Project No.: 4790895205-2.1

Applicant: PreciGenome LLC

Address of Applicant: 2176 Ringwood Ave, San Jose, CA, 95131, USA

Product Description: NanoGenerator™ Max Nanoparticle Synthesis System

Model No.: PG-SYN-G

Test Standard: EN IEC 61326-1:2021

Test Report Number(s): 4790895205-2.1-1

Issue Date: 2023-08-26

CE

Leon Wu  
Leon Wu  
UL-CCIC Company Limited.

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