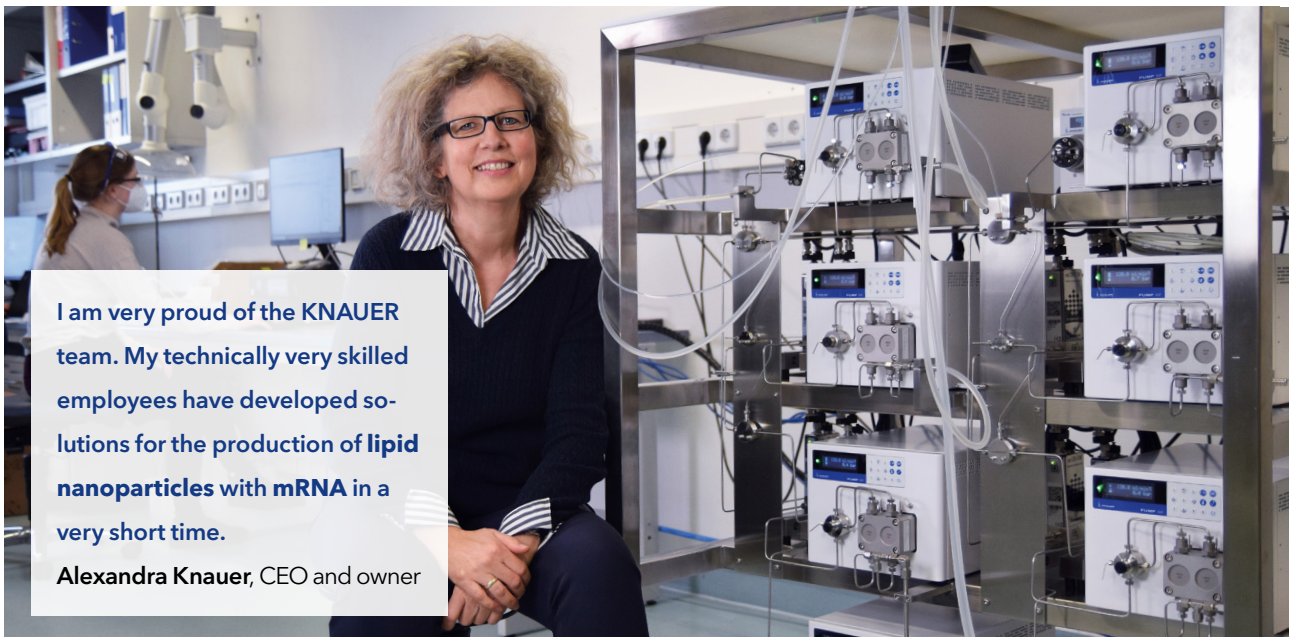


Science Together



think **LNP.** | think **KNAUER.**

Impingement Jets Mixing Skids for high flow production of nanoparticles (LNP, microemulsions, etc.)



I am very proud of the KNAUER team. My technically very skilled employees have developed solutions for the production of **lipid nanoparticles with mRNA** in a very short time.

Alexandra Knauer, CEO and owner



www.knauer.net/LNP

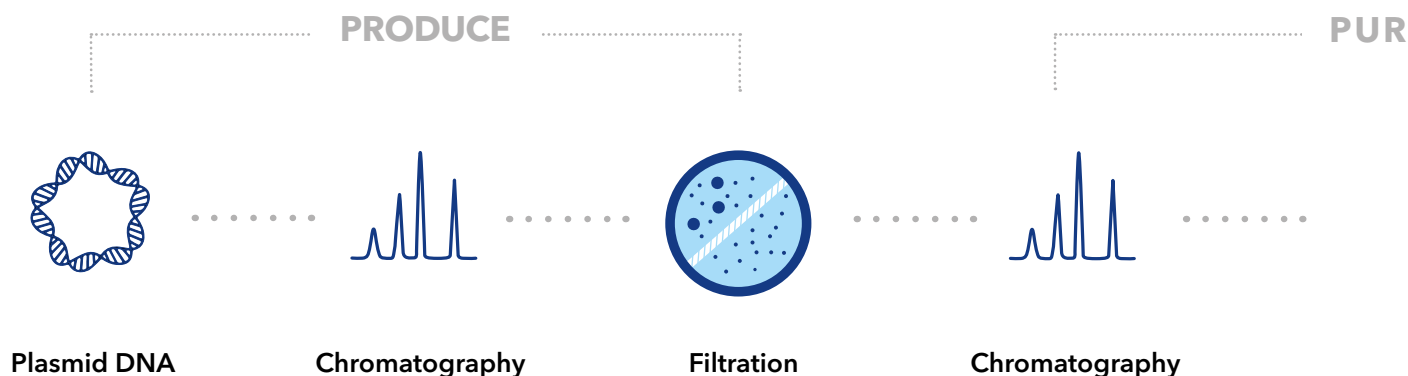
This print product is awarded with the Blue Angel.

www.blauer-engel.de/uz195

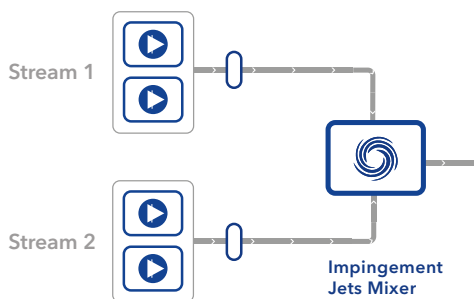


UF6

PROCESS OVERVIEW



IJM Skid for lipid nanoparticle production



Flow scheme for example for mixing of lipids and API

SKIDS - FROM R&D TO MANUFACTURING

The number of parallel units depends on the application. Also, the number of pumps, flow meters, jet mixers and pipes can be adapted to the required conditions and scale. All skids are built in a stainless steel frame on casters and are suitable for CIP cleaning procedures in pharmaceutical production. The Small Production Scale Unit IJM Skid contains two parallel mixing units. Each unit contains four pumps. Concentrated Active Pharmaceutical Ingredient (API) solution is diluted first and then mixed with the organic phase. Finally, the mixture is quenched in a third mixer. Both units can be operated independently. The Large Production Scale Units can be configured with up to eight parallel mixing units depending on the customer requirements. Each unit consists of two pumps to deliver lipid and API streams, two flow meters for flow control and one jet mixer. Depending on the configuration, the predilution of the API and quenching can be performed for the combined flow of all units in one process step outside the Impingement Jets Mixing (IJM) Skid.

LOOKING FOR LIQUID CHROMATOGRAPHY?



As experts in liquid chromatography KNAUER offers a large variety of systems, solutions and applications for **analytical HPLC**, **preparative HPLC** and **FPLC**.

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IFY

FORMULATE AND FILL



Sterile filtration



Formulation with
Impingement Jets
Mixing Technology



Drug product
(e.g. lipid nanoparticles
carrying API)

THE TECHNOLOGY

Impingement jets mixing technology (IJM) enables the formulation and production of high-quality lipid nanoparticles carrying API (e.g. for **mRNA vaccines**). The encapsulation process of active pharmaceutical ingredients with lipids is based on impingement jets mixing technology, where two streams collide at high velocity in a jet mixing chamber. One of the streams contains the lipids in organic solvents and the other stream the API in water.

The mixing at high velocity reduces the solubility of the lipids so that homogenous nanoparticles are formed. The quality of nanoparticles depends on the streams' flow stability, the mixer geometry and the fluid velocities. As a final step, the mixture is quenched to stop particle growth.

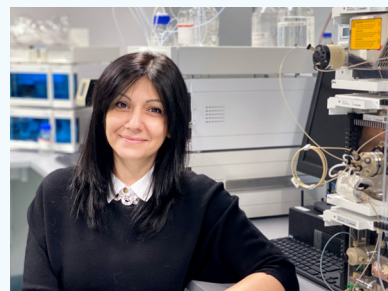
System for LNP formulation consisting of:

- KNAUER high-pressure dosing pumps 80P
- Coriolis flow meters
- KNAUER IJM mixers
- Inlet manifolds for lipid/ethanol mixture and mRNA/buffer mixture
- Outlet manifold for LNP solution
- Back-seal washing system
- Frame (stainless steel system 1.4301)
- Installation & familiarization by KNAUER
- A customized Technical documentation which is order- and article-related
- Customer Service before, during and after the set up
- Capillary customization and labeling
- FAT (Factory Acceptance Test at KNAUER Berlin)
- SAT (Site Acceptance Test at customer site)




WHAT THE EXPERT SAYS

'I am delighted that we have been able to successfully deliver all our systems for vaccine production on time. It makes our team proud that we are helping to combat COVID-19 in this way.'

Lilit Avagyan, Business Development Manager



IMPINGEMENT JETS MIXING SKIDS BY KNAUER

	Pilot Scale Unit	Small Production Scale Unit	(Customized) Large Production Scale Units*
			
Number of impingement jets mixers	1	2	up to 8
Number of pumps	4	8	up to 16
Number of flow meters	4	8	up to 16
Number of valves	1	2	–
Process connection inlet**	1/2" Tri-clamp (4 inlets)	3/8" and 1/4" barbed fitting (6 inlets)	Sanitary Clamp Connector (2 inlets)
Process connection outlet**	1/2" Tri-clamp (1 outlet)	1/4" barbed fitting (2 outlets)	Sanitary Clamp Connector (1 outlet)
Volumetric flow rate	up to 1 l/min	up to 2 l/min	depending on configuration
Volumetric flow rate	up to 60 l/h	up to 120 l/h	depending on configuration
Maximum operating pressure***	100 bar	100 bar	50–70 bar
Liquid temperature range	4–60 °C (39.2–140 °F)	4–60 °C (39.2–140 °F)	4–60 °C (39.2–140 °F)
Wetted materials	stainless steel, PEEK, titanium, FFKM, PTFE (GFP 55), aluminum oxide, ruby, sapphire, EPDM	stainless steel, PEEK, titanium, FFKM, PTFE (GFP 55), aluminum oxide, ruby, sapphire	stainless steel, PEEK, titanium, FFKM, PTFE (GFP 55), aluminum oxide, ruby, sapphire, EPDM
Software	CDS, 21 CFR part 11 compliant	CDS, 21 CFR part 11 compliant	not included, necessary interfaces for the integration into PLC
Interfaces	pump: LAN, RS-232, pin header connectors; flow meter: RS-232 + FLOW-BUSTM; valve drive: LAN	pump: LAN, RS-232, pin header connectors; flow meter: RS-232 + FLOW-BUSTM; valve drive: LAN	pump: LAN, RS-232, pin header connectors; flow meter: RS-232 + industrial interfaces
Power supply	pump: 100–240 V, 50–60 Hz; flow meter: +15...24 V DC, valve drive: 24 V DC	pump: 100–240 V, 50–60 Hz; flow meter: +15...24 V DC, valve drive: 24 V DC	pump: 100–240 V, 50–60 Hz; flow meter: +15...24 V DC
Power consumption (per device)	pump: maximum 320 W; flow meter: 3 W; valve drive: 65 W	pump: maximum 320 W; flow meter: 3 W; valve drive: 65 W	pump: maximum 320 W; flow meter: 3 W
Ambient conditions	temperature range: 4–40 °C; 39.2–104 °F; below 90 % humidity (non-condensing)	temperature range: 4–40 °C; 39.2–104 °F; below 90 % humidity (non-condensing)	temperature range: 4–40 °C; 39.2–104 °F; below 90 % humidity (non-condensing)
Dimensions (W x H x D)	900 x 915 x 700 mm	1000 x 1290 x 700 mm	depending on configuration
Net weight (approx.)	150 kg	250 kg	depending on configuration
API-predilution and quenching	Yes	Yes	depending on configuration
GMP-ready documentation	Yes	Yes	Yes
Factory acceptance test	Yes	Yes	Yes
Site acceptance test	Yes	Yes	Yes
Purchase order lead time	about 3 months	about 3 months	minimum 5 months, depending on customer requirements

*design of the skid on customer requirements **different connections on request ***depends on specific pump configuration and application

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Depending on the process the end user must consider the legal situation of patents and intellectual property. KNAUER is designing the customized hardware solution on customer's request, process and chemistry are not included. Technical information are subject to change.