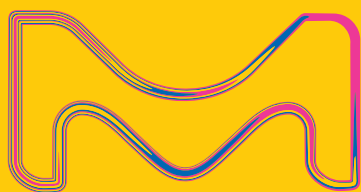
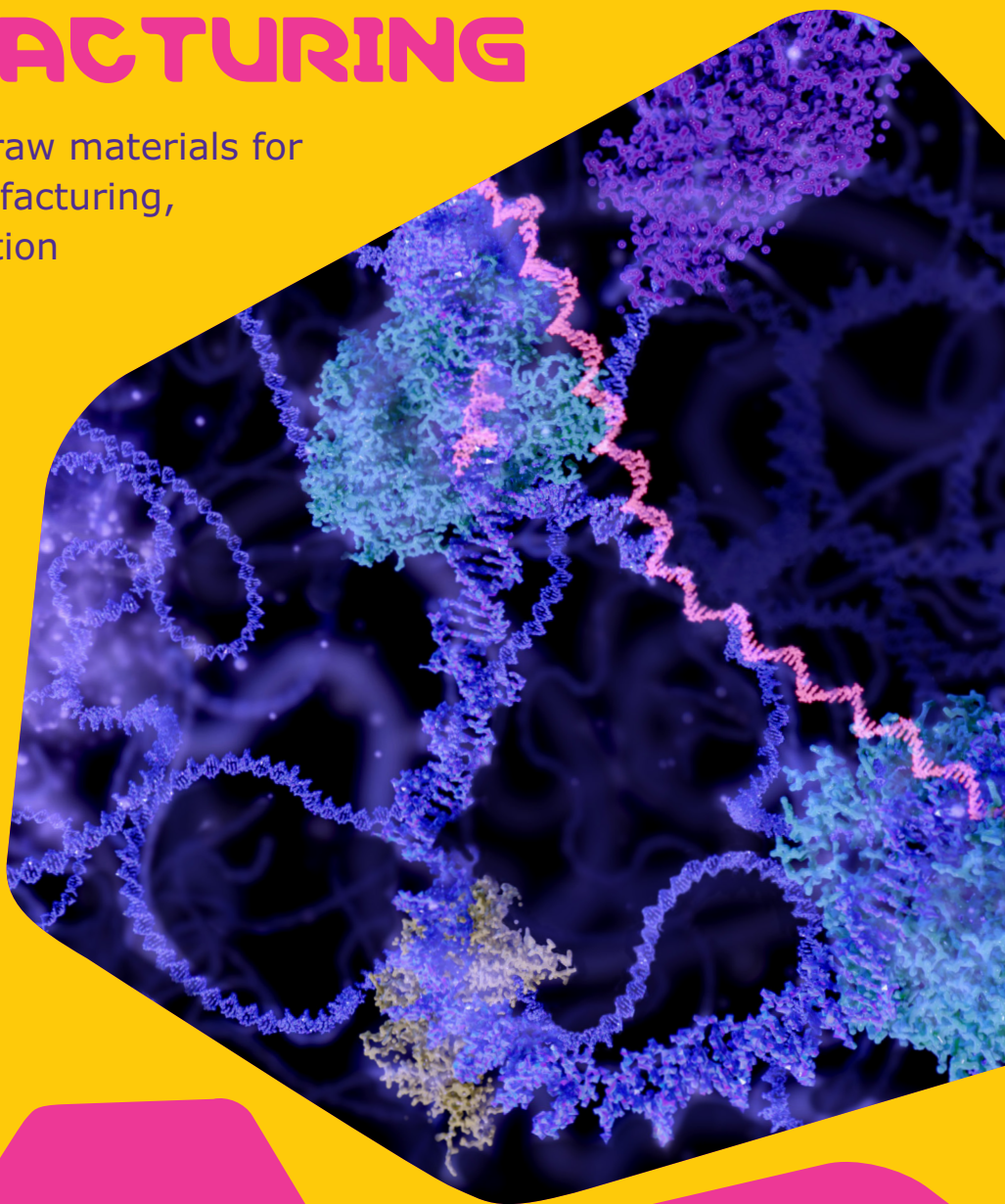


# CHEMICALS FOR MRNA DRUG MANUFACTURING

Providing high-quality raw materials for  
pDNA and mRNA manufacturing,  
as well as LNP formulation



MilliporeSigma is the U.S.  
and Canada Life Science  
business of Merck KGaA,  
Darmstadt, Germany.

**SAFC**<sup>®</sup>

Pharma & Biopharma Raw  
Material Solutions

# EMPOWERING MRNA INNOVATION

mRNA technology has emerged as a powerful tool in combating infectious diseases, demonstrating its value in vaccine development. Moreover, it holds remarkable promise as a novel therapeutic approach for unmet medical needs, including the treatment of cancer, genetic disorders, and autoimmune diseases. With an excellent safety profile and high versatility, mRNA technology benefits from a templated manufacturing process that enhances efficiency and accelerates the journey from development to clinical application.

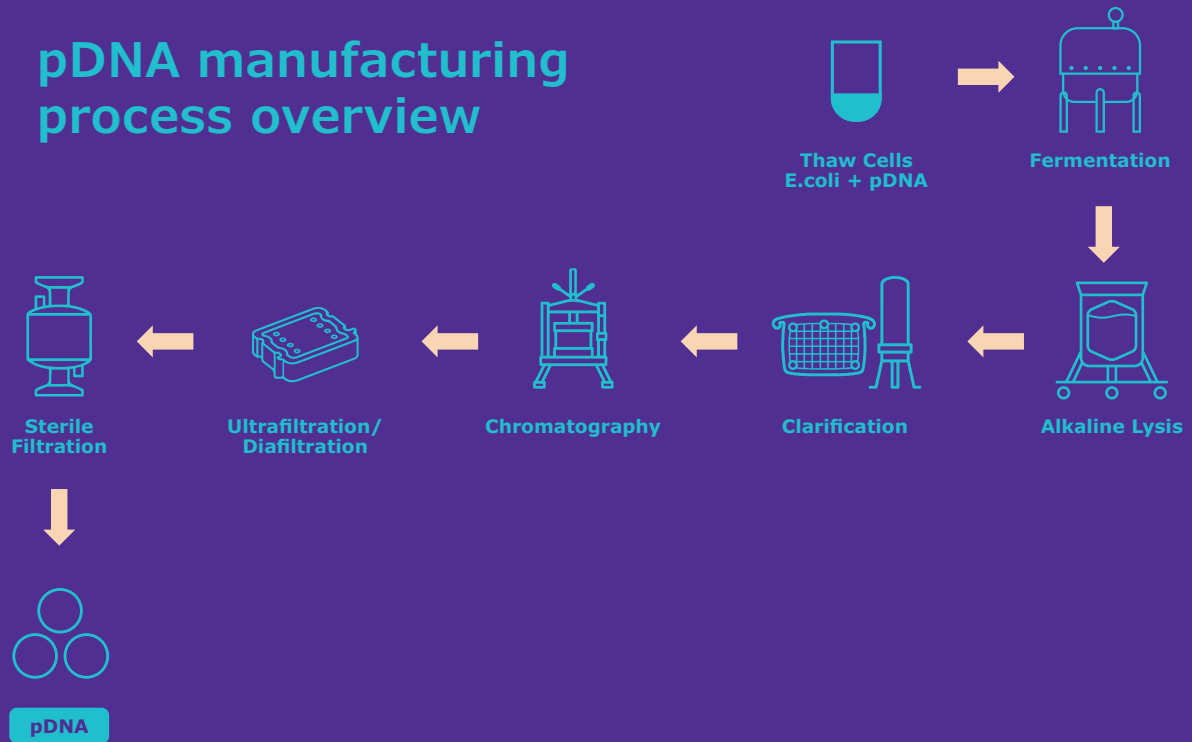
We provide a comprehensive chemical portfolio and custom manufacturing capabilities for the entire mRNA manufacturing process. Leverage our integrated offering for mRNA manufacturing, which includes raw materials for all process steps—from plasmid DNA (pDNA) to mRNA synthesis and final formulation—empowering you to make informed decisions at every stage.



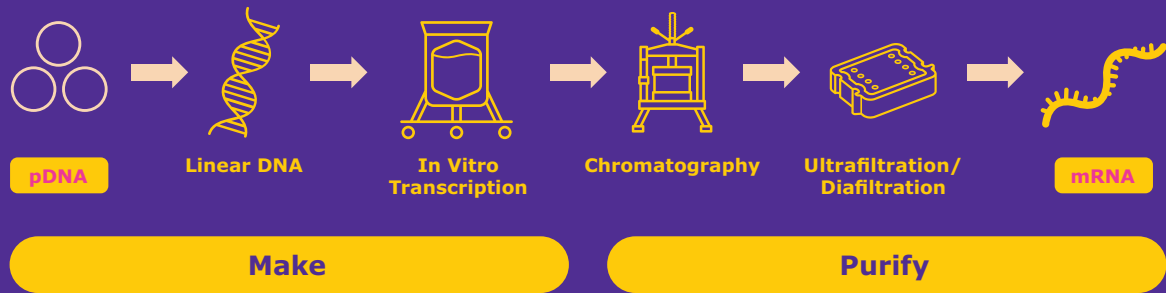
## Main benefits and features

- Comprehensive offering of chemicals for the entire mRNA manufacturing process
- CDMO partner for high-quality custom and off-the-shelf lipids
- Products tested for the absence of endonuclease activity

# pDNA manufacturing process overview



# mRNA manufacturing process overview



# Protect your pDNA and mRNA with our high-quality chemicals

In the complex landscape of pDNA and mRNA manufacturing, ensuring a stable production process that yields a safe product is paramount. Selecting high-quality chemicals is crucial at every step, whether you're focusing on pDNA manufacturing or mRNA manufacturing and formulation.

To minimize the risk of enzymatic degradation during critical phases, such as *in vitro* transcription and downstream purification, it's essential to utilize products **tested for the absence of endonuclease activity**. Additionally, bioburden control throughout the process is vital. To control the risk of microbial and endotoxin contaminations, our product portfolio includes Emprove® Expert products with **specified low microbial and endotoxin levels**.

Relying on our expertise and resources, you can navigate the pDNA and mRNA manufacturing process with confidence.

## Our raw materials for pDNA and mRNA manufacturing



Plasmid Production in E.coli DH5α



Alkaline Lysis

CAS No.	Product No.	Product Name
599920C	59920C	<a href="#">EX-CELL® Antifoam, Gamma Irradiated</a>
50-99-7	137048	<a href="#">D(+)-Glucose anhydrous EMPROVE® EXPERT Ph Eur, BP, USP, ACS</a>
367-93-1	137064	<a href="#">IPTG (Isopropyl-β-D-thiogalactopyranoside) EMPROVE® EXPERT</a>
For our comprehensive portfolio of upstream chemicals, such as amino acids, vitamins, carbohydrates, and buffers please visit: <a href="http://sigmaaldrich.com/upstreamchemicals">sigmaaldrich.com/upstreamchemicals</a>		
64-19-7	137000	<a href="#">Acetic acid (glacial) 100% EMPROVE® EXPERT Ph Eur, BP, JP, USP</a>
10035-04-8	137101	<a href="#">Calcium chloride dihydrate EMPROVE® EXPERT Ph Eur, BP, JP, USP</a>
9001-63-2	5501	<a href="#">CellPrime® rLysozyme recombinant human lysozyme</a>
127-08-2	104820	<a href="#">Potassium acetate EMPROVE® ESSENTIAL Ph Eur, BP, JPE, E 261</a>
6131-90-4	128205	<a href="#">Sodium acetate trihydrate EMPROVE® EXPERT Ph Eur, BP, ChP, JP, USP</a>
151-21-3	817034	<a href="#">Sodium dodecyl sulfate EMPROVE® ESSENTIAL Ph Eur</a>
1310-73-2	137020	<a href="#">Sodium hydroxide pellets EMPROVE® EXPERT Ph Eur, BP, ChP, JP, NF</a>
6381-92-6	137004	<a href="#">Titriplex® III (ethylene dinitrilo tetraacetic acid disodium salt dihydrate) EMPROVE® EXPERT Ph Eur, BP, ChP, JP, USP<sup>1</sup></a>

<sup>1</sup>Endonuclease activity free

During *in vitro* transcription, the pDNA template is transcribed into mRNA through an enzymatic reaction involving critical components such as RNA polymerase, nucleoside triphosphates (NTPs), inorganic pyrophosphatase (IPP), and RNase inhibitors. Our IPEC-PQG GMP-quality dithiothreitol (DTT) and spermidine enhance this process by reducing RNase activity and improving transcription efficiency and nucleic acid stability. Count on our high-quality products to support your mRNA production effectively.

## Our raw materials for mRNA manufacturing, continued



### pDNA Linearization and In Vitro Transcription

CAS No.	Product No.	Product Name
56-65-5	137201	Adenosine 5'-triphosphate (ATP), 100 mM Sodium Solution, EMPROVE® EXPERT
86-01-1	137203	Cytidine 5'-triphosphate (CTP), 100 mM Sodium Solution, EMPROVE® EXPERT
65-47-4	137202	Guanosine-5'-triphosphate (GTP), 100 mM Sodium Solution, EMPROVE® EXPERT
63-39-8	137204	Uridine 5'-triphosphate (UTP), 100 mM Sodium Solution, EMPROVE® EXPERT
1428903-59-6	137206	N1-Methyl-pseudouridine 5'-triphosphate (N1-Me-UTP), 100 mM Sodium Solution, EMPROVE® EXPERT †
3483-12-3	137159	DL-Dithiothreitol (DTT) EMPROVE® ESSENTIAL <sup>1</sup>
7791-18-6	105832	Magnesium chloride hexahydrate cryst. EMPROVE® EXPERT Ph Eur, BP, USP, JPC, FCC, E 511 <sup>1</sup>
124-20-9	137165	Spermidine EMPROVE® EXPERT <sup>1</sup>
6381-92-6	137004	Titriplex® III (ethylene dinitrilo tetraacetic acid disodium salt dihydrate) EMPROVE® EXPERT Ph Eur, BP, ChP, JP, USP <sup>1</sup>
1185-53-1	108219	Tris(hydroxymethyl)aminomethane hydrochloride EMPROVE® EXPERT <sup>1</sup>
77-86-1	108307	Tris(hydroxymethyl)aminomethane (Trometamol) high purity EMPROVE® EXPERT Ph Eur, BP, ChP, JPC, USP <sup>1</sup>



### Chromatography

64-19-7	137000	Acetic acid (glacial) 100% EMPROVE® EXPERT Ph Eur, BP, JP, USP
75-05-8	137134	Acetonitrile EMPROVE® ESSENTIAL
7783-20-2	128218	Ammonium sulfate EMPROVE® EXPERT ChP, NF, ACS
100-51-6	100987	Benzyl alcohol EMPROVE® EXPERT Ph Eur, BP, JP, NF
7647-01-0	137007	Hydrochloric acid fuming 37% EMPROVE® EXPERT Ph Eur, BP, ChP, JP, NF
127-08-2	104820	Potassium acetate EMPROVE® ESSENTIAL Ph Eur, BP, JPE, E 261
7447-40-7	137009	Potassium chloride EMPROVE® EXPERT Ph Eur, BP, USP, JP <sup>1</sup>
7778-77-0	137039	Potassium dihydrogen phosphate cryst. EMPROVE® EXPERT Ph Eur, BP, JPC, NF <sup>1</sup>
6121-90-4	128205	Sodium acetate trihydrate EMPROVE® EXPERT Ph Eur, BP, ChP, JP, USP
7647-14-5	137017	Sodium chloride EMPROVE® EXPERT Ph Eur, BP, ChP, JP, USP <sup>1</sup>
13472-35-0	137018	Sodium dihydrogen phosphate dihydrate EMPROVE® EXPERT Ph Eur, BP, ChP, USP, JPE <sup>1</sup>
10028-24-7	137036	di-Sodium hydrogen phosphate dihydrate EMPROVE® EXPERT Ph Eur, BP, USP <sup>1</sup>
7782-85-6	137092	di-Sodium hydrogen phosphate heptahydrate EMPROVE® EXPERT DAC, USP <sup>1</sup>
6381-92-6	137004	Titriplex® III (ethylene dinitrilo tetraacetic acid disodium salt dihydrate) EMPROVE® EXPERT Ph Eur, BP, ChP, JP, USP <sup>1</sup>
1185-53-1	108219	Tris(hydroxymethyl)aminomethane hydrochloride EMPROVE® EXPERT <sup>1</sup>
77-86-1	108307	Tris(hydroxymethyl)aminomethane (Trometamol) high purity EMPROVE® EXPERT Ph Eur, BP, ChP, JPC, USP <sup>1</sup>



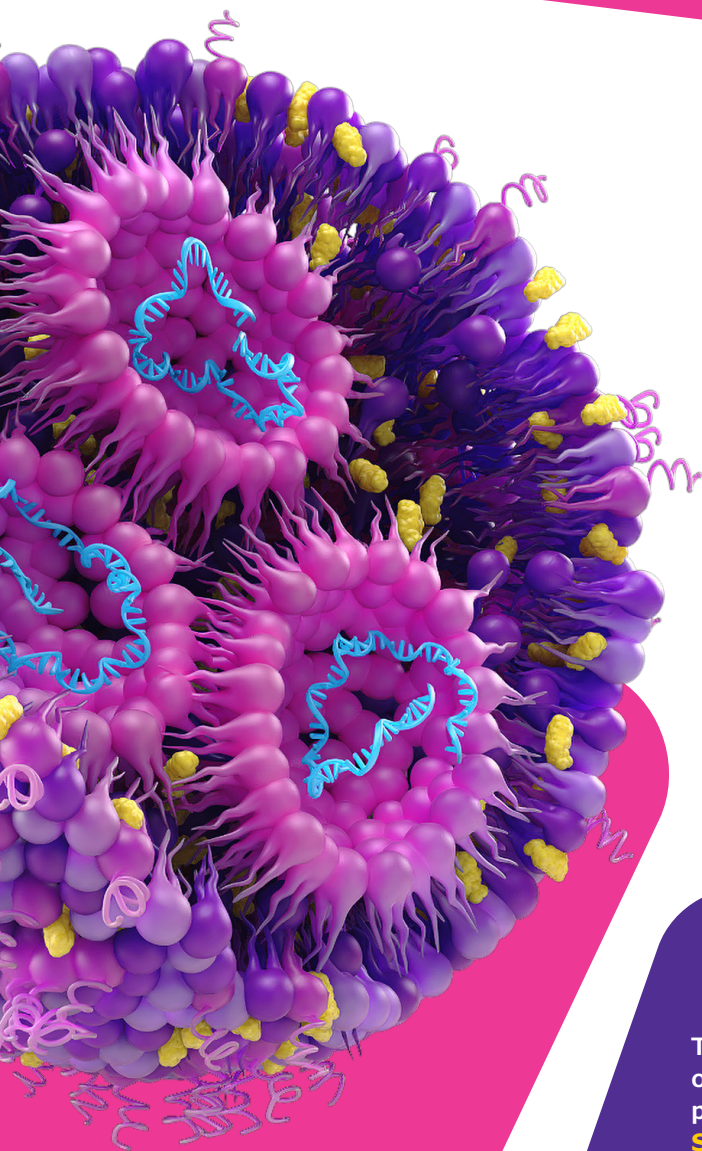
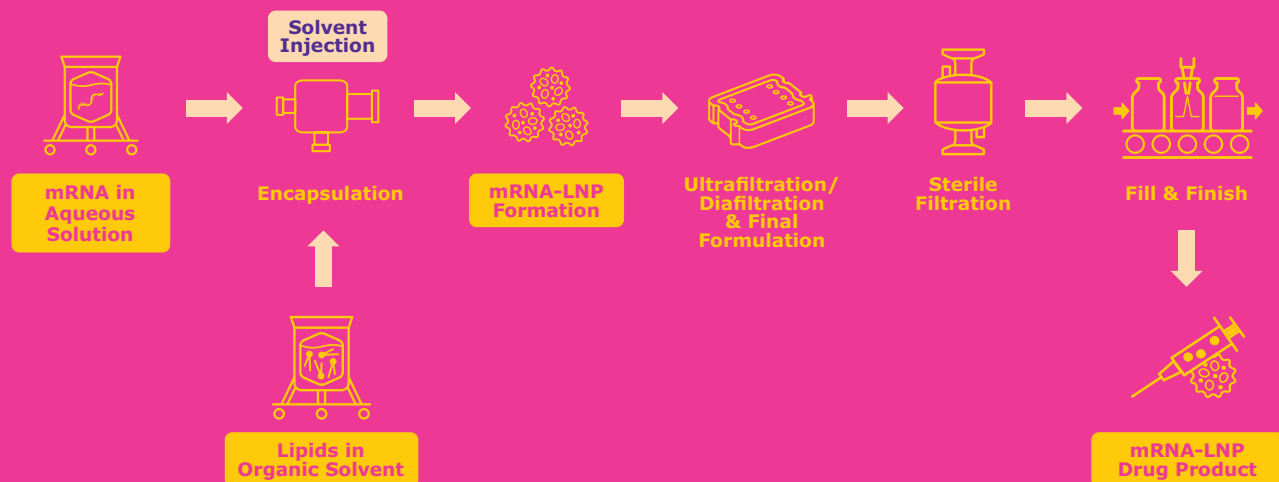
### Ultrafiltration / Diafiltration

7447-40-7	137009	Potassium chloride EMPROVE® EXPERT Ph Eur, BP, USP, JP <sup>1</sup>
7778-77-0	137039	Potassium dihydrogen phosphate cryst. EMPROVE® EXPERT Ph Eur, BP, JPC, NF <sup>1</sup>
7647-14-5	137017	Sodium chloride EMPROVE® EXPERT Ph Eur, BP, ChP, JP, USP <sup>1</sup>
13472-35-0	137018	Sodium dihydrogen phosphate dihydrate EMPROVE® EXPERT Ph Eur, BP, ChP, USP, JPE <sup>1</sup>
1310-73-2	137020	Sodium hydroxide pellets EMPROVE® EXPERT Ph Eur, BP, ChP, JP, NF
10028-24-7	137036	di-Sodium hydrogen phosphate dihydrate EMPROVE® EXPERT Ph Eur, BP, USP <sup>1</sup>
7782-85-6	137092	di-Sodium hydrogen phosphate heptahydrate EMPROVE® EXPERT DAC, USP <sup>1</sup>
6381-92-6	137004	Titriplex® III (ethylene dinitrilo tetraacetic acid disodium salt dihydrate) EMPROVE® EXPERT Ph Eur, BP, ChP, JP, USP <sup>1</sup>
1185-53-1	108219	Tris(hydroxymethyl)aminomethane hydrochloride EMPROVE® EXPERT <sup>1</sup>
77-86-1	108307	Tris(hydroxymethyl)aminomethane (Trometamol) high purity EMPROVE® EXPERT Ph Eur, BP, ChP, JPC, USP <sup>1</sup>

#### <sup>1</sup>Endonuclease activity free

† Customer shall at all times be solely responsible for obtaining all necessary licenses and rights to use this product for its intended application and any compliance with existing laws and regulations. Customer understands that the seller is not liable for any patent infringement claims related to Purchaser's use of this product.

# mRNA-LNP formulation process overview



Naked mRNA is inherently unstable, making drug delivery systems essential for effective delivery of the mRNA into the human body and into target cells. Encapsulation is a critical step, and selecting high-quality excipients and lipids is vital for success.

Lipid nanoparticles (LNP) are the preferred platform for mRNA delivery, composed of four different lipids that protect the mRNA from degradation. Consistent lipid quality is crucial for stable LNPs and reproducible results.

Our custom and “off-the-shelf” portfolio lipids together with our tailored support and services ensure you meet your specific needs and achieve optimal performance and quality for mRNA vaccines and therapeutics.

To learn more on our integrated CDMO offering for mRNA, Lipids, LNP and Fill & Finish, please visit our website:

[SigmaAldrich.com/CTDMO](https://www.sigmaaldrich.com/CTDMO)

# Our raw materials for mRNA-LNP formulation



mRNA in Aqueous Solution



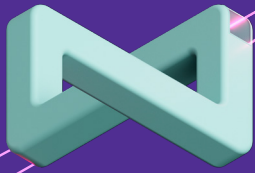
Lipids in Organic Solvent



Ultrafiltration/  
Diafiltration &  
Final Formulation

CAS No.	Product No.	Product Name
64-19-7	137000	<a href="#">Acetic acid (glacial) 100% EMPROVE® EXPERT Ph Eur, BP, JP, USP</a>
77-92-9	137002	<a href="#">Citric acid anhydrous powder EMPROVE® EXPERT Ph Eur, BP, ChP, JP, USP<sup>1</sup></a>
5949-29-1	137003	<a href="#">Citric acid monohydrate cryst. EMPROVE® EXPERT Ph Eur, BP, ChP, JP, USP<sup>1</sup></a>
7647-01-0	137007	<a href="#">Hydrochloric acid fuming 37% EMPROVE® EXPERT Ph Eur, BP, ChP, JP, NF</a>
6121-90-4	128205	<a href="#">Sodium acetate trihydrate EMPROVE® EXPERT Ph Eur, BP, ChP, JP, USP</a>
6132-04-3	106447	<a href="#">tri-Sodium citrate dihydrate EMPROVE® EXPERT Ph Eur, BP, ChP, JP, USP, ACS, E 331<sup>1</sup></a>
1310-73-2	137020	<a href="#">Sodium hydroxide pellets EMPROVE® EXPERT Ph Eur, BP, ChP, JP, NF</a>
7664-93-9	100713	<a href="#">Sulfuric acid 95–98% EMPROVE® ESSENTIAL Ph Eur, BP, JPE, NF</a>
67-64-1	100013	<a href="#">Acetone EMPROVE® ESSENTIAL Ph Eur, BP, JPE, NF</a>
	586054	ALC0159
	586224	ALC0315
	W004591	Cholesterol
	500244	(R)-DODMA
	578632	DMG PEG 2000
	587762	DOPE
	CH2900013	DOPC
	P3726	DPPC
	572495	DSG PEG 2000
	W2660	DSPC
	CH2900029	(R)-DOTAP Cl
	500249	(R)-DOTMA Cl
	589692	(R,S)-DOTAP Cl
	CH2900030	(S)-DOTAP Cl
64-17-05	100967	<a href="#">Ethanol 96% EMPROVE® EXPERT Ph Eur, ChP, JP, USP</a>
64-17-05	100986	<a href="#">Ethanol absolute EMPROVE® EXPERT Ph Eur, BP, ChP, JP, USP</a>
64-17-05	ARK2210	Ethanol API
67-56-1	106008	<a href="#">Methanol EMPROVE® ESSENTIAL Ph Eur, BP, JPE, NF</a>
67-63-0	137040	<a href="#">2-Propanol 70% (v/v) EMPROVE® EXPERT USP</a>
57-88-5	104672	<a href="#">Synthechol® Synthetic Cholesterol EMPROVE® EXPERT Ph Eur, BP, JP, NF</a>
7647-14-5	137017	<a href="#">Sodium chloride EMPROVE® EXPERT Ph Eur, BP, ChP, JP, USP<sup>1</sup></a>
13472-35-0	137018	<a href="#">Sodium dihydrogen phosphate dihydrate EMPROVE® EXPERT Ph Eur, BP, ChP, USP, JPE<sup>1</sup></a>
10049-21-5	137093	<a href="#">Sodium dihydrogen phosphate monohydrate EMPROVE® EXPERT BP, ChP, USP<sup>1</sup></a>
10028-24-7	137036	<a href="#">di-Sodium hydrogen phosphate dihydrate EMPROVE® EXPERT Ph Eur, BP, USP<sup>1</sup></a>
7782-85-6	137092	<a href="#">di-Sodium hydrogen phosphate heptahydrate EMPROVE® EXPERT DAC, USP<sup>1</sup></a>
57-50-1	103789	<a href="#">Sucrose EMPROVE® EXPERT Ph Eur, ChP, JP, NF<sup>1</sup></a>
6138-23-4	102776	<a href="#">Trehalose dihydrate EMPROVE® EXPERT Ph Eur, ChP, NF, JP<sup>1</sup></a>
1185-53-1	108219	<a href="#">Tris(hydroxymethyl)aminomethane hydrochloride EMPROVE® EXPERT<sup>1</sup></a>
77-86-1	108307	<a href="#">Tris(hydroxymethyl)aminomethane (Trometamol) high purity EMPROVE® EXPERT Ph Eur, BP, ChP, JPC, USP<sup>1</sup></a>

<sup>1</sup>Endonuclease activity free



# The Emprove<sup>®</sup> Program

20 years of speeding up your journey,  
and still accelerating.



Maintaining compliance with current Good Manufacturing Practices (cGMPs) at any given time in your drug manufacturing process can be complex and challenging – especially in a global, dynamic environment. As a drug manufacturer, you need to compile a vast amount of information from your suppliers to ensure that the raw materials and components you purchase meet the technical, regulatory and supply needs for their designated application, use and function. This can be resource- and time-intensive, as well as expensive.

20 years ago, we launched the Emprove<sup>®</sup> Program to accelerate your risk assessments and help you maintain compliance. As your processes evolved, so did the Emprove<sup>®</sup> Program, anticipating challenges and keeping you ahead of the curve. With a comprehensive digital platform, the Emprove<sup>®</sup> Program speeds your drug development journey by offering convenient access to reliable

information for a broad portfolio of high-quality products. This way, the Emprove<sup>®</sup> Program enables you to:

- Make more agile, risk-based decisions
- Maintain compliance and
- Demonstrate control – saving you time and money

**DISCOVER THE EMPROVE<sup>®</sup> PROGRAM**

The Emprove<sup>®</sup> Suite is a digital information-as-a-service platform that helps you make informed decisions, ensure compliance, and demonstrate process control.

**SUBSCRIBE TO EMPROVE<sup>®</sup> SUITE**

**For more information visit:**  
[SigmaAldrich.com/integrated-offerings/mrna-development-manufacturing](https://SigmaAldrich.com/integrated-offerings/mrna-development-manufacturing)

The Life Science business of Merck operates as MilliporeSigma in the U.S. and Canada.

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**SAFC<sup>®</sup>**