Raw Materials for Biopharmaceutical Manufacturing

SAFC®

Pharma & Biopharma Raw Material Solutions

Introduction

The development and manufacturing of pharma and biopharma products requires high-quality raw materials as well as the expertise on how to use them. The SAFC® portfolio of ready-to-use and customized material solutions were developed to meet the specific needs of pharma and biopharma production and are backed by deep regulatory expertise.

We go beyond just the raw materials as we understand your need for safety, security, scalability, and process efficiency to get health solutions to patients faster.

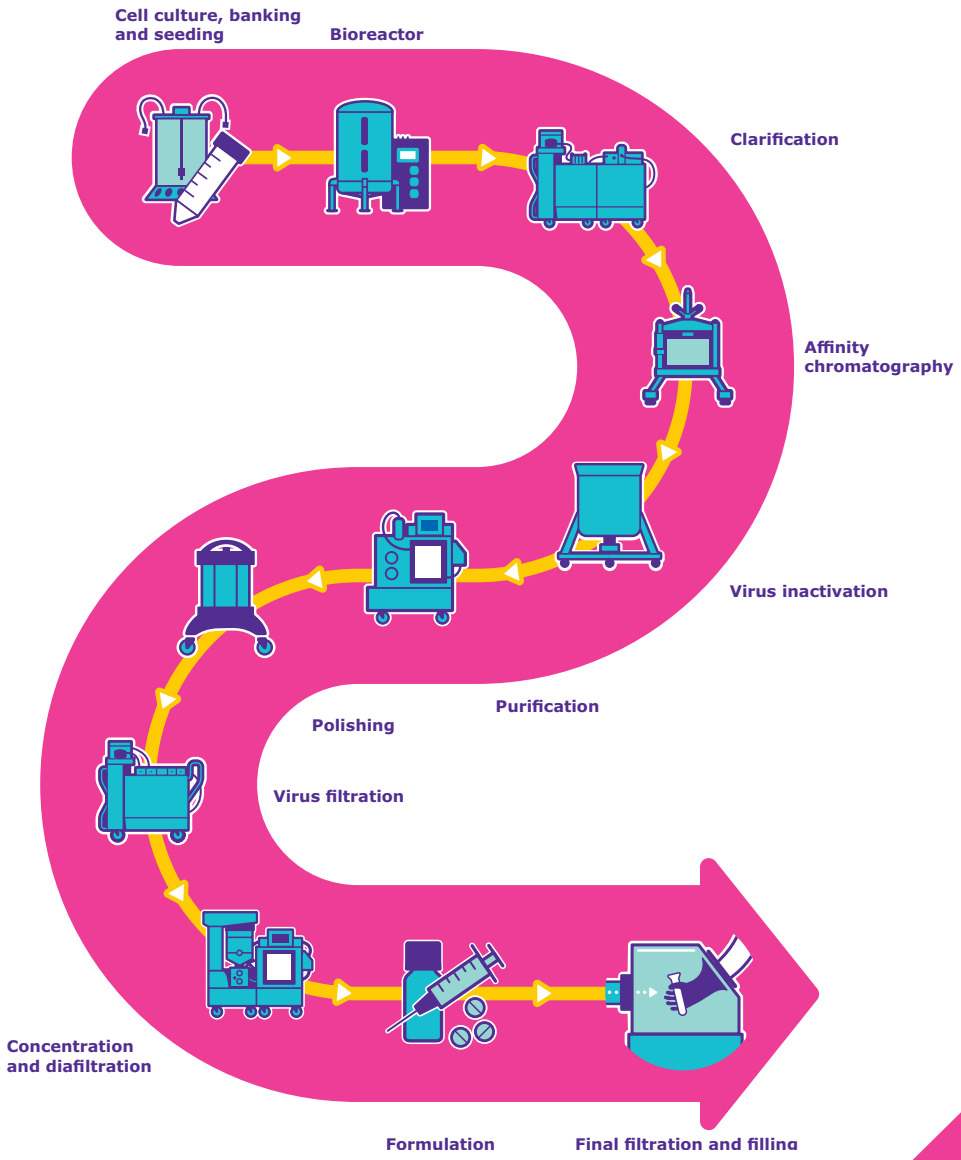
Explore this handbook for a comprehensive overview on our offering of raw materials and excipients for upstream, downstream, and formulation process steps as well as for in-depth information on the regulatory background and our regulatory support.

Contents

The Bioprocess: Our Raw Material Offering for Biopharmaceutical Production

Solutions spanning every step of the process from cell culture to final formulation and everything in between.

Our products meet high quality and purity standards and are supported by extensive documentation and services to help speed up internal qualification procedures and accelerate your drug preparation, tech transfer, manufacturing and regulatory approval process.



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Regulatory

Hot Topics Related to Pharmaceutical Excipients and Process Raw Materials

The regulatory environment is dynamic. We assist our customers in implementing new guidelines and directives.

Risk Assessment and ICH Q3D Guideline for Elemental Impurities

The ICH Q3D Guideline for Elemental Impurities provides a global policy for limiting elemental impurities in final drug products. Proper qualitative and quantitative control of elemental impurities is vital in assessing the contamination risk in the final drug product.

According to ICH Q3D Guideline, a risk assessment for elemental impurities should be performed in any applications for existing or new formulations.

We provide supportive information for our Emprove® Chemicals to facilitate risk assessments of potential elemental impurities.

Chinese Regulation for Excipient Registration

According to the regulation for the registration of an API/excipient in China in order to get the official registration number, not only the API but also the excipient manufacturers need to submit a China Dossier to NMPA. We are supporting the customer's drug application using our APIs/excipients to meet the Chinese regulatory requirements.

Based on the official regulation and requirement, the quality of an API/excipient should meet the specifications in the current Chinese pharmacopoeia. We ensure our registered products in China meet the ChP requirements as well.

Declarations for Pharmaceutical Raw Materials to Support Nitrosamine Risk Assessment

Nitrosamines emerged as a public health concern in relation to pharmaceuticals in 2018 when N-nitrosodimethylamine (NDMA) was found in products containing valsartan, an angiotensin II receptor blocker.[i] NDMA is a genotoxic and carcinogenic agent in animals and is classified as probably carcinogenic to humans by the International Agency for Research of Cancer.[ii]

In response to these findings, regulatory authorities published guidance requiring pharmaceutical manufacturers to assess both chemical and biological products for the possible presence of nitrosamines and, if needed, define appropriate mitigation actions.

Based on product specific evaluation of the potential risk on nitrosamine formation or cross-contamination, nitrosamine declarations are available for the relevant pharmaceutical substances of our product portfolio (i.e. Emprove® API active pharmaceutical ingredients, Emprove® Expert and Emprove® Essential excipients, and Emprove® Evolve products).

[i] Nudelman R, et al. The Nitrosamine "Saga": Lessons Learned from Five Years of Scrutiny. Organic Process Research & Development 2023 27 (10), 1719-1735. DOI: 10.1021/acs.oprd.3c00100

[ii] Li K, et al. Estimated Cancer Risks Associated with Nitrosamine Contamination in Commonly Used Medications. Int J Environ Res Public Health. 2021. Sep 8;18(18):9465. doi: 10.3390/ijerph18189465

Information about Nitrite Concentration Level in Pharmaceutical Excipients

A comprehensive assessment on nitrosamine risks of formulated drug products revealed the presence of nitrosamine drug-substance-related impurities (NDSRIs). Formation of NDSRIs may result from the presence of potentially nitrosatable secondary or tertiary amine moieties in APIs or API impurities and nitrosating agents formed from low levels of nitrite present in excipients as impurities.

The presence of nitrites in excipients poses the risk of nitrosamine formation in drug products. Under suitable conditions, NDSRIs can form during drug product formulation or during storage. Information about the nitrite level in excipients is an important tool to assess and mitigate the risk of NDSRI or other nitrosamine formation.

Consequently, we provide information about detected quantities of nitrites for our comprehensive Emprove® Expert and Emprove® Essential portfolio of excipients to support your risk assessment efforts.

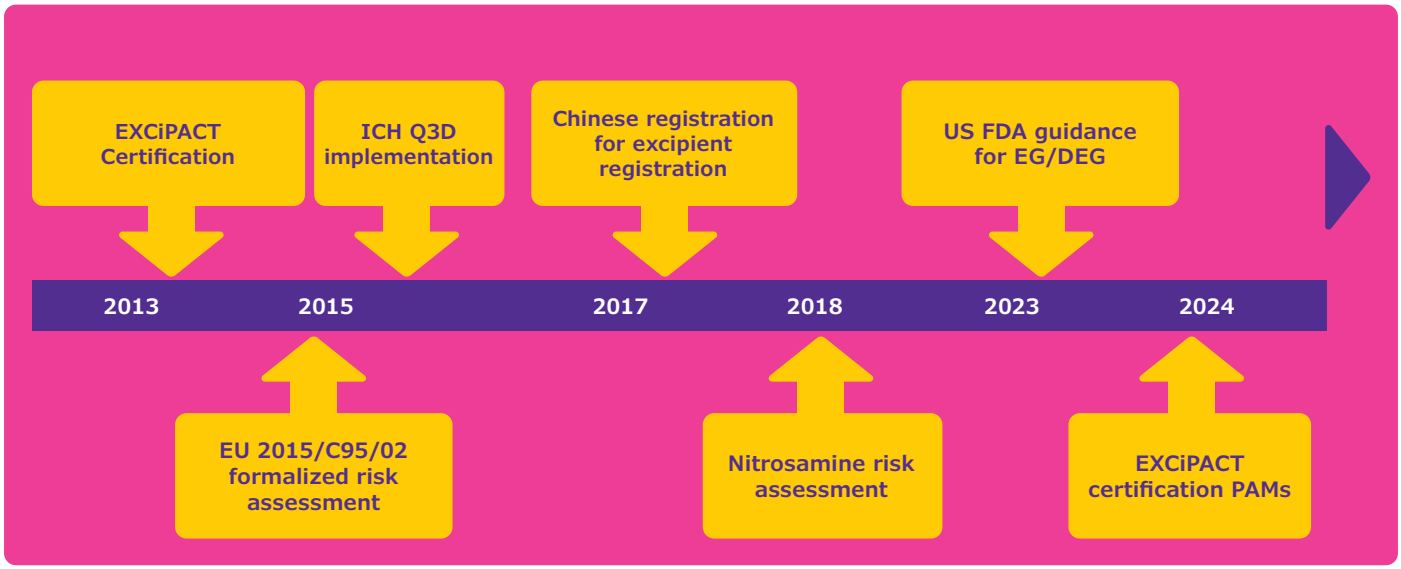
FDA Guidance for Testing of Ethylene Glycol and Diethylene Glycol

In 2022 and 2023, numerous countries reported incidents of oral liquid drug products, contaminated with high levels of ethylene glycol and diethylene glycol, which led to more than 300 fatalities - mostly children under the age of 5.[iii]

Following these incidents and investigations, US FDA issued a guidance on May 2023, for immediate implementation, to alert pharmaceutical manufacturers, compounders, repackagers, and suppliers to the potential public health hazard of glycerin and other high-risk drug components contaminated with diethylene glycol (DEG) or ethylene glycol (EG).

In response to these developments, we have screened all potential high-risk components and performed a risk assessment.
The declaration about EG/DEG content for our APIs and excipients is available in the Emprove® Dossier since 2024.

Development of Regulatory Requirements Since 2013: Pharmaceutical Excipients and Process Raw Materials



Following 2015/C95/02, the manufacturing authorization holder is required to ensure that the excipients used in their process are suitable for use in medicinal products. The effect of these on the quality and safety of the drug must be evaluated by formalized risk assessments. In addition, excipients must be selected from appropriate suppliers who are able to meet these requirements and assessments should be performed to address the identified risks.

Raw materials used in downstream processing of biopharmaceutical APIs may be considered higher risk materials by a drug manufacturer. However, if these buffers or other raw materials are not contained in the final formulation of the drug product, they will be outside the scope of the formalized risk assessment.

[iii] World Health Organization (WHO) Medical Product Alert N°6/2022: Substandard (contaminated) paediatric medicines. 2022 [Internet]. Available from: https://www.who.int/news/item/05-10-2022-medical-product-alert-n-6-2022-substandard-(contaminated)-paediatric-medicines; Food and Drug Administration (FDA) Guidance Document Testing of Glycerin, Propylene Glycol, Maltitol Solution, Hydrogenated Starch Hydrolysate, Sorbitol Solution, and Other High-Risk Drug Components for Diethylene Glycol and Ethylene Glycol: FDA-2023-D-1573. May 2023 [Internet]. Available from: https://www.fda.gov/regulatory-information/search-fda-guidance-documents/testing-glycerin-propylene-glycol-maltitol-solution-hydrogenated-starch-hydrolysate-sorbitol

Pharmaceutical Manufacturer:

Identification and evaluation of risk profile for individual excipients

Risks related to the manufacture and supply of excipients

- Quality management system of the supplier
- Probability of contamination
  - Impurities
  - TSE and viruses
  - Microorganisms/endotoxin
- Manufacturing equipment and facilities
- Environmental management and storage conditions
- Supply chain information

Risks for the applications using the excipients

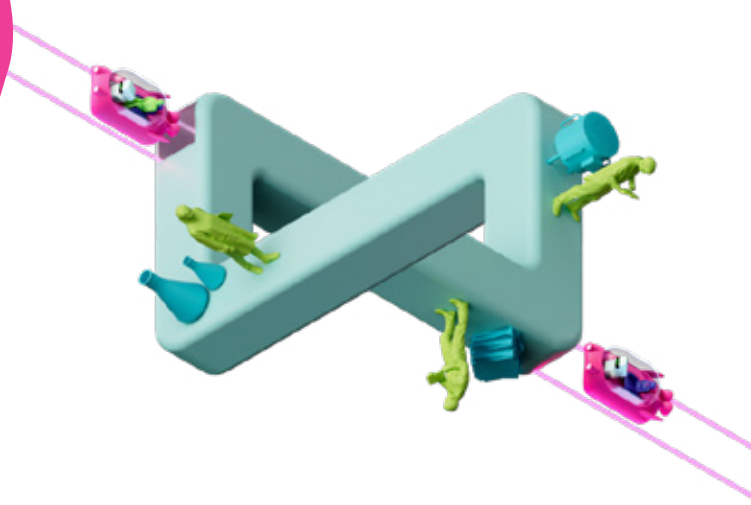
- Dosage form/route of administration
- Functions of the excipients
- Potential impact on critical quality characteristics
- Daily intake/dose

Excipients Used in the Manufacturing Process and Final Formulation of a Biopharmaceutical Product

Risk assessments should consider the following:

- **Bioburden Standards (Microbial Limit, Endotoxins)**
- **Supplier's GMP Management, Quality Control System Change Management Systems**
- **Availability of ICH Q3D Elemental Impurities Data**
- **Supply Chain for Raw Materials, Supply Chain Transparency and Change Control**
- **Stability Test Data (Referring to ICH Q1A)**
- **Acceptability of Production Site Audit**
- **Nitrosamine Declaration and Information on Nitrite Levels**
- **Declaration for Ethylene Glycol/ Diethylene Glycol (EG/DEG)**
- **Animal Component Free (ACF) Facilities and Raw Materials**
- **REACH Compliance**

Regulatory Support for Biopharmaceutical Raw Materials



The Emprove® Program. Over Two Decades of Easing Risk Management.

For drug manufacturers striving to simplify raw material selection while satisfying regulatory requirements, our Emprove® Chemicals portfolio contains over 400 pharmaceutical raw materials organized by different levels of risk. All raw and starting materials are organized into categories to streamline selection, with each product offering the comprehensive, up-to-date documentation you need to navigate regulatory challenges, manage risks, and improve processes. The portfolio is divided into four categories:

- Emprove® Evolve
- Emprove® Essential
- Emprove® Expert
- Emprove® API

Emprove® Chemicals Portfolio: Raw and Starting Materials

Emprove® Evolve

For Early Stages of Biopharmaceutical Manufacturing

Bridges the gap between lab-grade and GMP compliant raw and starting materials while providing transparent supply chain information and documentation.

Emprove® Essential

For Moderate Risk Applications

Designed for moderate risk applications, Emprove® Essential products offer compliance to the IPEC-PQG GMP Guide and/ or EXCiPACT Certification Standard, supply chain transparency and regulatory support designed to assist drug manufacturers' formalized risk assessments.

Emprove® Expert

For High Risk Applications

Addresses higher risk applications where the lowest microbiological and endotoxin levels are of utmost importance.

Along with the risk management features of Emprove® Essential, the Emprove® Expert line yields products with specified low microbiological and endotoxin levels, supporting the overall risk mitigation strategy.

Emprove® API

For Final Drug Product Compliance with International Standards

Meet the quality and regulatory requirements of active pharmaceutical ingredients, according to ICH Q7 GMP. In order to support final drug product compliance with international standards, our Regulatory Management team offers dedicated support for qualification via Emprove® API information package and regulatory filing of DMFs, CEP and ASMF if applicable.

Emprove® Chemical Dossiers

Our Emprove® Chemicals portfolio is supported by Emprove® Dossiers. This comprehensive documentation facilitates your qualification, risk assessment and process optimization efforts.

	Material Qualification	Quality Management	Operational Excellence	DMF, ASMF, CEP
Emprove® Evolve	•	•	•	
Emprove® Essential	•	•	•	
Emprove® Expert	•	•	•	
Emprove® API				•

The dossiers can be accessed online in our new Emprove® Suite, our information-as-a-service digital platform. A subscription can help you stay current: In addition to viewing and downloading dossiers, you can also receive notification updates to changes to documents, as well as generate metrics and reports.

For more information, please visit: https://sigmaaldrich.com/emprove-chemicals

The M-Clarity™ Program: Your Guide for Quality and Portfolio Transparency

The M-Clarity™ Program includes the majority of our Life Science products. Chemicals and consumables are classified into 6 quality segments (MQ100–MQ600).

- Each segment provides specific documentation and services
- The segments have increasing attributes to meet your application and regulatory requirements
- Transparency allows you to select the right product for your needs

Chemicals and Consumables

MQ100	MQ200	MQ300	MQ400	MQ500	MQ600
For non-regulated laboratory applications, with no change notification requirements	For research and non-regulated industrial applications, with limited change notification requirements	For products used in applications requiring enhanced change control and quality agreement	For critical products and applications driven by high expectations for manufacturing control and requiring verified control or manufacturing control	For highly regulated applications requiring a validated process control	For highly regulated applications under regulatory surveillance
6 attributes	9 attributes	12 attributes	21 attributes	25 attributes	27 attributes
	CNC*	CNC*	CNC*	CNC*	CNC*
		Quality Agreement	Quality Agreement	Quality Agreement	Quality Agreement
			Quality Declarations	Quality Declarations	Quality Declarations

*CNC Change Notification Commitment

Upstream Application

BioPharm Raw Materials Upstream and Cell Culture

In the rapidly evolving biopharmaceutical landscape, manufacturers face increasing pressure to accelerate development timelines while navigating complex regulatory environments.

To meet these challenges, reliable access to high-quality raw materials is essential for supporting both classical and innovative therapies. Our comprehensive portfolio of upstream process chemicals includes raw materials and components for cell culture media formulations and other upstream applications, empowering manufacturers to streamline processes and enhance product quality. Delve into our extensive selection of amino acids and buffers, and discover key products such as cell culture optimized Poloxamer 188 Emprove® Expert, EX-CELL® Antifoam, and CellPrime® rLR3 Recombinant Insulin-like Growth Factor.

Amino Acids

Product	Catalog No.	Product Name	CAS No.	MQ Level
L-Alanine	101700	L-Alanine Emprove® Expert Ph Eur, JP, USP	56-41-7	**500**
L-Arginine	A4474	L-Arginine	74-79-3	**400**
L-Arginine	101587	L-Arginine Emprove® Expert Ph Eur, ChP, JP, USP	74-79-3	**500**
L-Arginine monohydrochloride	A4599	L-Arginine monohydrochloride	1119-34-2	**400**
L-Arginine monohydrochloride	101544	L-Arginine monohydrochloride Emprove® Expert Ph Eur, BP, ChP, JP, USP	1119-34-2	**500**
L-Asparagine monohydrate	101565	L-Asparagine monohydrate Emprove® Expert Ph Eur, ChP, NF	5794-13-8	**500**
L-Asparagine monohydrate	137251	L-Asparagine monohydrate Emprove® Evolve	5794-13-8	**400**
L-Aspartic acid	100129	L-Aspartic acid Emprove® Expert Ph Eur, BP, ChP, JP,USP	56-84-8	**500**
L-Cysteine	C5360	L-Cysteine	52-90-4	**400**
L-Cysteine hydrochloride monohydrate	102735	L-Cysteine hydrochloride monohydrate Emprove® Expert Ph Eur, JP, USP	1880366	**500**
L-Cystine dihydrochloride	137253	L-Cystine dihydrochloride Emprove® Evolve	30925-07-6	**400**
L-Glutamic acid	101791	L-Glutamic acid Emprove® Expert Ph Eur, JP, USP	56-86-0	**500**
L-Glutamine	100286	L-Glutamine Emprove® Expert DAB, JP, USP	56-85-9	**500**
L-Glutamine	G5792	L-Glutamine	56-85-9	**400**
Glycine	G5417	Glycine	56-40-6	**400**
Glycine	100590	Glycine cryst. Emprove® Expert Ph Eur, BP, ChP, JP, USP	56-40-6	**500**
GlycylGlycine	G0674	GlycylGlycine	556-50-3	**500**
L-Histidine	H3911	L-Histidine	71-00-1	**400**
L-Histidine	104352	L-Histidine Emprove® Expert Ph Eur, ChP, JP, USP	71-00-1	**500**
L-Histidine monohydrochloride monohydrate	H4036	L-Histidine monohydrochloride monohydrate	5934-29-2	**400**
L-Histidine monohydrochloride monohydrate	104354	L-Histidine monohydrochloride monohydrate Emprove® Expert Ph Eur, BP, ChP, JP	5934-29-2	**500**
L-Isoleucine	105357	L-Isoleucine Emprove® Expert Ph Eur, USP	73-32-5	**500**
L-Isoleucine	I5281	L-Isoleucine	73-32-5	**400**
L-Leucine	105020	L-Leucine Emprove® Expert Ph Eur, ChP, JP, USP	61-90-5	**500**
L-Lysine monohydrochloride	105701	L-Lysine monohydrochloride Emprove® Expert Ph Eur, BP, JP, USP	657-27-2	**500**
L-Methionine	137250	L-Methionine Emprove® Expert USP, Ph Eur, JP	63-68-3	**500**
L-Phenylalanine	107267	L-Phenylalanine Emprove® Expert Ph Eur, JP, USP	63-91-2	**500**
L-Proline	107430	L-Proline Emprove® Expert Ph Eur, JP, USP	147-85-3	**500**
L-Proline	P8865	L-Proline	147-85-3	**400**
L-Threonine	T4071	L-Threonine	72-19-5	**400**
L-Tryptophan	108396	L-Tryptophan Emprove® Expert Ph Eur, BP, USP	73-22-3	**500**
L-Tyrosine	108378	L-Tyrosine Emprove® Expert Ph Eur, ChP, JP, USP	60-18-4	**500**
L-Tyrosine	T4321	L-Tyrosine	60-18-4	**400**
L-Tyrosine disodium dihydrate	137254	L-Tyrosine disodium salt dihydrate Emprove® Evolve	122666-87-9	**400**
L-Valine	V4638	L-Valine	72-18-4	**400**

Modified Amino Acids

Product	Catalog No.	Product Name	CAS No.	MQ Level
phospho-L-Tyrosine disodium salt	137219	phospho-L-Tyrosine disodium salt Emprove® Evolve	1610350-91-8	**400**
L-Cysteine-S-sulfate sodium salt sesquihydrate	137116	L-Cysteine-S-sulfate sodium salt sesquihydrate Emprove® Expert	150465-29-5	**500**

Carbohydrates

Product	Catalog No.	Product Name	CAS No.	MQ Level
D-(+)-Glucose	137048	D-(+)-Glucose anhydrous Emprove® Expert Ph Eur, BP, USP, ACS	50-99-7	**500**
D(+)-Galactose	137129	D(+)-Galactose, Plant-Derived Emprove® Expert Ph Eur, NF	59-23-4	**500**
N-Acetyl-D-mannosamine	PHG0017	N-Acetyl-D-Mannosamine	7772-94-3	**400**
D-(+)-Glucose HTST	58955C-1BC	50% Glucose (w/v) - HTST treated		**500**
D-(+)-Glucose HTST	58955C-20BC	50% Glucose (w/v) - HTST treated		**500**

Buffers

Product	Catalog No.	Product Name	CAS No.	MQ Level
HEPES	110110	2-[4-(2-Hydroxyethyl)-1-piperazinyl]-ethanesulfonic acid Buffer substance HEPES Emprove® Expert	7365-45-9	**500**
HEPES	137270	2-[4-(2-Hydroxyethyl)-1-piperazinyl]-ethanesulfonic acid Buffer substance HEPES Emprove® Evolve	7365-45-9	**400**
HEPES sodium	137265	2-[4-(2-Hydroxyethyl)-1-piperazinyl]-ethanesulfonic acid Buffer substance HEPES sodium salt Emprove® Evolve	75227-39-3	**400**
Sodium carbonate	137014	Sodium carbonate anhydrous Emprove® Expert Ph Eur, BP, JP, NF	497-19-8	**500**
Sodium hydrogen carbonate	137013	Sodium hydrogen carbonate Emprove® Expert Ph Eur, BP, ChP, USP, JP	144-55-8	**500**

Lipids and Derivatives

Product	Catalog No.	Product Name	CAS No.	MQ Level
Linoleic acid	39269	Linoleic acid	60-33-3	**400**
Oleic acid	104415	Oleic acid Emprove® Evolve	112-80-1	**400**
Sodium butyrate	137127	Sodium butyrate Emprove® Expert	156-54-7	**500**
Sodium cholate	S1702	Sodium cholate hydrate	206986-87-0	**400**
Sodium deoxycholate	S1827	Sodium deoxycholate	302-95-4	**400**
SyntheChol® synthetic cholesterol	137672	SyntheChol® synthetic cholesterol for cell culture Emprove® Expert	57-88-5	**500**
SyntheChol® plant-derived cholesterol	137132	SyntheChol® plant-derived cholesterol for cell culture Emprove® Expert	57-88-5	**500**

Specialty Components

Product	Catalog No.	Product Name	CAS No.	MQ Level
Antifoam / Simethicone	59920C	EX-CELL® Antifoam		**500**
Biotin	RES1052B-B7	Biotin	58-85-5	**400**
Cystamine dihydrochloride	108318	Cystamine dihydrochloride Emprove® Essential	56-17-7	**500**
Cysteamine hydrochloride	137139	Cysteamine hydrochloride Emprove® Essential	156-57-0	**500**
Dextran sulfate sodium salt	RES2029D-A7	Dextran sulfate sodium salt	9011-18-1	**300**
Ferric ammonium citrate	RES20400-A7	Ferric ammonium citrate	1185-57-5	**400**
Ferric citrate	RES4055F-A7	Ferric citrate	2338-05-08	**400**
Hypoxanthine sodium salt	RES6104H-A7	Hypoxanthine sodium salt	45738-97-4	**400**
L-Methionine sulfoximine	104309	L-Methionine sulfoximine Emprove® Essential	15985-39-4	**500**
Methotrexate	M7824	Methotrexate	59-05-2	**400**
Poloxamer 188	137097	Poloxamer 188 Emprove® Expert cell culture optimized	9003-11-6	**500**
Poloxamer 188	137197	Poloxamer 188 Emprove® Expert compendial cell culture grade	9003-11-6	**500**
Sodium pyruvate	105477	Sodium pyruvate Emprove® Essential	113-24-6	**500**
Spermine tetrahydrochloride	137141	Spermine tetrahydrochloride	306-67-2	**400**
Taurine	T4571	Taurine	107-35-7	**400**
Tropolone	108637	Tropolone Emprove® Evolve	533-75-5	**400**
Uridine	137607	Uridine Emprove® Evolve	58-96-9	**400**

CellPrime® Recombinant Growth Factors

Product	Catalog No.	Product Name	CAS No.	MQ Level
rInsulin	4512	CellPrime® rInsulin, recombinant human insulin	11061-68-0	**300**
rAlbumin	106331	CellPrime® rAlbumin, recombinant human albumin	70024-90-7	**400**
rTransferrin	106313	CellPrime® rTransferrin, recombinant, expressed in yeast, from synthetic	11096-37-0	**500**
rTrypsin	106302	CellPrime® rTrypsin (porcine) liquid	9002-07-7	**500**
rTrypsin	106301	CellPrime® rTrypsin (porcine) powder	9002-07-7	**500**
rLR3	106332	CellPrime® rLR3 IGF (liquid)	143045-27-6	**500**
rLR3	106333	CellPrime® rLR3 IGF (powder)	143045-27-6	**500**

Find out more about the products on our webpage:

Bioprocessing cell culture – recombinant supplements

Bioprocessing formulation raw materials – liquid cell culture media buffers

Cell Culture Optimized Poloxamer 188

Poloxamer 188 is a surface-active nonionic polymer used in cell culture media as shear protectant. Recognized as a standard ingredient in cell culture media for commercial production processes, it has been shown to increase the robustness of mammalian cells to shear from sparging, which is one of the strongest contributors to the hydrodynamic stress in bioreactors.

Physicochemical Information	
CAS Number	9003-11-6
Chemical Formula	$HO(C_2H_4O)n(C_3H_6O)m(C_2H_4O)nH$
HS Code	3402 13 00
Density	1.06 g/cm³ (70 °C)
Flash Point	260 °C
Melting Point	52 °C
pH Value	5.0–7.5 (25 g/L, H_2O)
Bulk Density	1050 kg/m³
Solubility	>100 g/L

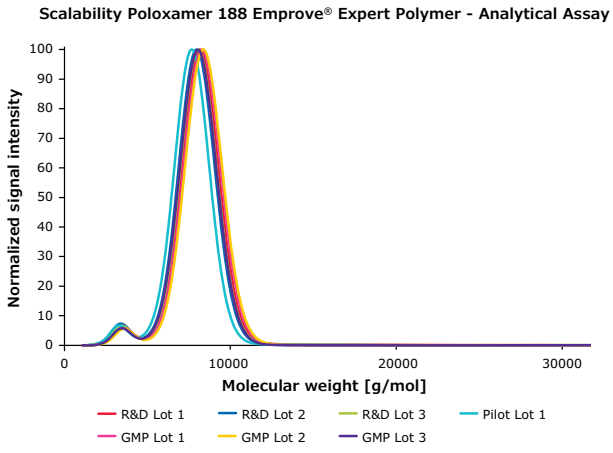
Predictable Protection and Performance

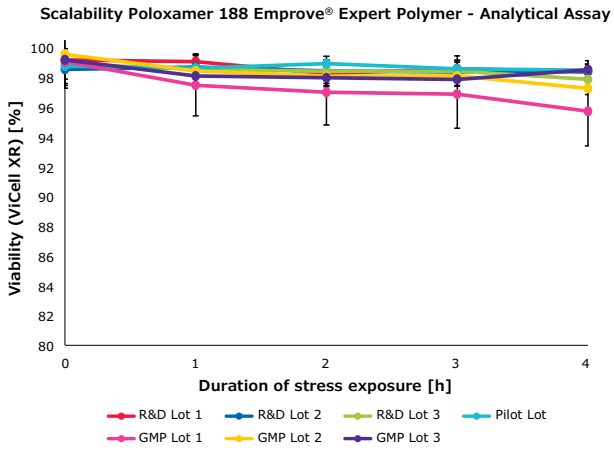
With process intensification through increasing cell densities and production in fed-batch and perfusion, issues such as unexpected loss of cell density and viability in manufacturing operations began to increase. They were correlated to lot-to-lot variation in poloxamer 188 polymer.

Identification of critical parameters for poloxamer 188 polymer was determined by extensive investigation into the sources of lot-to-lot variability, development and validation of proprietary analytical and biological tests, and creation of a reference library consisting of 100+ customer and supplier samples.

Our Poloxamer 188 Emprove® Expert grades have has been developed for reliable quality and consistency and to provide shear stress protection for large-scale cell culture processes.

Our two Poloxamer 188 Emprove® Expert grades are tailored to biopharmaceutical manufacturer's needs, depending on the compendial requirements. For the best shear protection functionality in the bioreactor, the cell culture optimized version (#137097) is recommended, if no compendial requirement is present. If a compendial product is needed, the compendial cell culture grade (#137197) provides a thoroughly tested alternative to assure performance of the cells in the bioreactor. Both of these poloxamer 188 grades have been developed for reliable quality and consistency and to provide shear stress protection for large-scale cell culture processes.





Benefits

- **Consistent quality**
  With methods developed in-house, we are able to predict the performance and ensure lot-to-lot consistency.
- **Proven functionality**
  We test and certify shear protection on the Certificate of Analysis.
- **Superior performance**
  Our products perform superior to lots across different suppliers, batches and quality grades.
- **Reliable supply**
  Large manufacturing capacities ensure reliable supply for our customers.
- **Quality and regulatory insights**
  We provide quality and regulatory documentation with our Emprove® Dossiers.

Our primary recommendation: Poloxamer 188 Emprove® Expert cell culture optimized

Catalog No.	Product Name	CAS No.	MQ Level	Pack Size [kg]
1.37097.0003	Poloxamer 188 Emprove® Expert cell culture optimized	9003-11-6	**500**	3 x 1 (Sample Kit)
1.37097.1000				1
1.37097.9010				10
1.37097.9025				25

Our compendial alternative: Poloxamer 188 Emprove® Expert compendial cell culture grade Ph Eur, NF

Catalog No.	Product Name	CAS No.	MQ Level	Pack Size [kg]
1.37197.0003	Poloxamer 188 Emprove® Expert compendial cell culture grade Ph Eur, NF	9003-11-6	**500**	1
1.37197.1000				1
1.37197.9010				10
1.37197.9025				25

EX-CELL® Antifoam

EX-CELL® Antifoam is a gamma-irradiated simethicone-based solution available in single-use bags. It is formulated from a non-ionic, 30% simethicone emulsion designed for:

- The pharmaceutical and veterinary biological industries.
- Direct supplementation into your culture systems in bioreactors to prevent foaming (foam suppressant) or eliminate foaming (foam dispersant) caused by mixing and shear forces within the cell culture systems, especially industrial bioreactors.
- The product can be aseptically connected to your cell culture system as it is conveniently packaged in ready-to-use single-use bags.

Physicochemical Information	
Chemical information	Simethicone Simethicone Emulsion Polydimethylsiloxane (PDMS)
Chemical name	A-(Trimethylsilyl)-ω-methylpoly[oxy(dimethylsilylene)], mixture with silicon dioxide
Chemical formula	[-(CH3)2SiO-]n
Final Product Testing	**Specification**
Appearance (Color)	White to off-white
Appearance (Form)	Liquid
Endotoxin Level (post-irradiation)	Report Result
Simethicone Emulsion	0.7–1.5%
Defoaming Activity (USP)	≤ 15 s
Irradiation Dosage Range (min.)	≥ 25 kG
Irradiation Dosage Range (max.)	≤ 40 kGy
Irradiation Certificate	Conforms

Application

Our EX-CELL® Antifoam product is an effective antifoam product designed to control foaming typically associated with the use of cell culture media in bioreactors. This product exists as an emulsion, and therefore requires moderate agitation or orbital/reciprocal mixing prior to use. Such mixing manifests a more homogeneous suspension that ensures consistent defoaming activity during use. This product has been shown to be safe for use with both eucaryotic and procaryotic cell culture systems; however, volumes added and dosing regimens should be optimized by each customer to fit their specific cell lines and bioreactor systems.

Through meticulous formulation optimization, quantitative assay techniques, and an understanding of simethicone's binding properties, we provide the precise simethicone concentration of this gamma-irradiated product for each lot produced, which is reported on its Certificate of Analysis. As a result, our EX-CELL® Antifoam represents an optimized formulation, providing consistent simethicone concentration leading to superior product performance.

Benefits

- **Effective foam control**
  Reduces foaming in bioreactors, enhancing process efficiency and product yield.
- **Optimized and Consistent Formulation**
  Precise simethicone concentration ensures reliable performance across batches.
- **Versatile application**
  Demonstrated suitability and safety for both eukaryotic and prokaryotic cell cultures.
- **Risk mitigation and safety**
  Convenient single-use bags allow for aseptic connection, minimizing contamination risk.
- **Regulatory compliance**
  Manufactured in accordance with stringent quality standards.
- **Ready to Use Solution**
  Eliminates the need to manufacture in-house

Ordering Information

Available to supply globally:

Catalog No.	Product Name	MQ Level	Pack Size [L]
59920C-1B	EX-CELL® Antifoam, gamma irradiated	**500**	1
59920C-5B			5

Customized versions of 59920C are also available.

CellPrime® rLR3 IGF Recombinant Insulin-like Growth Factor

CellPrime® rLR3 IGF is a non-animal origin (NAO) recombinant equivalent insulin-like growth factor expressed in *E. coli*. CellPrime® rLR3 IGF has a 13 amino acid N-terminal extension and position 3 substitution of glutamic acid to arginine which contributes to increased stability and robustness in media formulations.

This growth factor has been developed to specifically meet the demands of the life science and biopharmaceutical industries, and thus does not contain components of animal or human origin. The elimination of animal-derived components reduces the incidence of performance variability in the medium and eliminates safety risks due to adventitious agents associated with these components.

CellPrime® rLR3 IGF is used as a growth promoter for a variety of cell culture applications including CHO based processes for the manufacturing of therapeutic proteins such as monoclonal antibodies.

CellPrime® rLR3 IGF is our alternative offer to our formerly offered products LONG®R3 IGF-I Cat. No. 91590C; 85580C
(LONG®R3 IGF-I is a registered trademark of Repligen Corporation)

Features/Application	Former Product	Cellprime® rLR3 IGF
CAS Number	143045-27-6	143045-27-6
Identity – Mass Spectrometry RP HPLC	9108–9112 Da Major peak >60% total peak area	9108–9112 Da Major peak >60% total peak area
Purity SDS PAGE	Single band >95% with same electrophoretic mobility as previous lot	Single band >95% with same electrophoretic mobility as previous lot
Protein by RP HPLC (for Liquid)	0.9–1.1 mg/mL	0.9–1.1 mg/mL
Cell Assays – EC<50 Rat L6 Myoblast Cell Line	EC<50, equal product concentration results in similar viability enhancement	EC<50, equal product concentration results in similar viability enhancement
Cell Assays – Cell Performance CHO Cell Line	NOT TESTED	Product tested for consistent cell performance on viability, growth and production
Endotoxin	≤0.1 EU/µg of protein	≤100 I.U./mL (corresponds to ≤0.1 I.U./µg of protein)
Microbial Tests – TVAC/TAMC	<100 CFU/mL	≤10 CFU/mL
Pathogens	Absent	Absent

Application

CellPrime® rLR3 IGF is used to optimize cell culture formulations to increase cell proliferation, productivity, and viability. With an exact match for the Type I IGF receptor and a lower affinity for IGF binding proteins, CellPrime® rLR3 IGF has increased effectiveness in serum-free cell culture media. Concentrations required to enhance performance is unique to each cell line and may be optimized by using in combination with CellPrime® rInsulin.

Benefits

- **Alternative source** for a pivotal cell culture growth factor
- **High quality**
- **CHO cell culture** tested
- **NAO growth factor** meets chemically defined media
- **CellPrime® dossier** support

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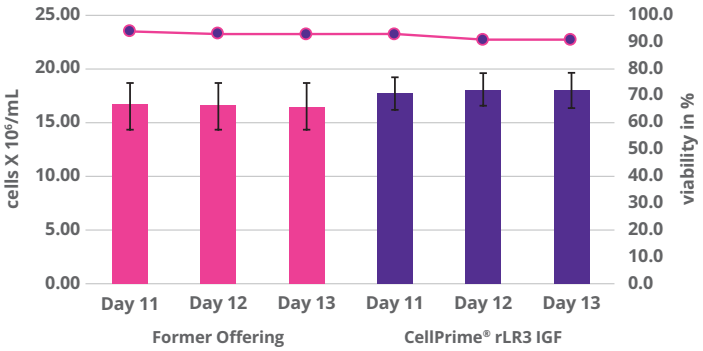
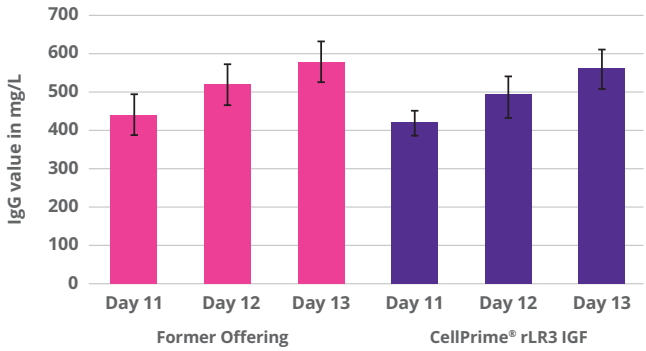
Comparability Data

Both products, the formerly offered component as well as CellPrime® rLR3 IGF deliver comparable performance results be it in enhancing the viability of Rat L6 Myoblast (data not shown) or even more important in CHO cell culture. Viability, growth, and productivity of our reference CHO cell line show good comparability (see graph below). To provide you with this proof we have added our proprietary CHO fed batch test to our release criteria, ensuring that the product will work in your process application.

LR3 Fed-Batch Assay
Proliferation and Viability



LR3 Fed-Batch Assay
Productivity



Ordering Information

CellPrime® rLR3 IGF is available in different pack sizes to support different applications from R&D over process development up to production scale operations.

Catalog No.	Product Name	CAS No.	MQ Level	Pack Size [mL]
1.06332.0005	CellPrime® r LR3 IGF liquid	143045-27-6	**500**	5
1.06332.0100				100
1.06332.0250				250
1.06332.0500				500
1.06332.1000				1000

Catalog No.	Product Name	CAS No.	MQ Level	Pack Size [mL]
1.06333.0005	CellPrime® r LR3 IGF powder	143045-27-6	**500**	5
1.06333.0050				50
1.06333.0250				250
1.06333.0500				500

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Downstream and Formulation Application

Buffer and Bioprocess Chemicals for Downstream and Formulation

In downstream processing, buffer components and additives ensure the required environment for optimal purification and stability of the protein of interest.

We offer a broad portfolio of solid and liquid buffer components, additives as well as bioprocess chemicals and cleaning-in-place solutions. Explore the product lists on the following pages for a comprehensive overview. Choose the delivery format that fits your manufacturing set-up and preferences.

Benefits of powdered raw materials

- **Economize**
  Lowest product and transportation cost compared to other delivery formats
- **Minimize warehouse space**
  Minimal warehouse capacity requirements
- **Own your process**
  Liquid buffer preparation including quality release is in your own hands

Benefits of ready-to-use solutions and concentrates

- **Mitigate risk**
  Reduction of preparation error and contamination risk
- **Reduce process footprint**
  Freeing more manufacturing floorspace
- **Gain efficiency**
  More resources available for value added tasks due to elimination of work associated with liquid preparation including weighing & hydration, filtration and refilling, sample taking and additional quality control testing

Products for Purification Processes

Protein A

At the capture phase of purification, the primary goals are to isolate the target molecule as quickly as possible from the clarified feedstock, reduce the process volume to a manageable scale for subsequent steps, and maximize yield and economy. Affinity chromatography, a method of separating biochemical mixtures based on a highly specific interaction, can effectively achieve these goals. Our range of affinity resins and buffers are designed for high quality and cost effective, high throughput purification of monoclonal, polyclonal and engineered antibodies and are especially suited for large-scale purification of today's and future therapeutic antibodies. Recommended chemicals and buffers suitable for chromatography and purification processes of proteins and other biological products are introduced below.

Protein A Capture

Purpose		Buffers	Buffer pH	CV*	Product	Catalog No.	Category	Compendial
Equilibration		PBS	Same as load sample	5	Sodium dihydrogen phosphate dihydrate	137018	Emprove® Expert	Ph Eur, BP, USP, JPE
					di-Sodium hydrogen phosphate dihydrate	137036	Emprove® Expert	Ph Eur, BP, USP
					Sodium chloride	137017	Emprove® Expert	Ph Eur, BP, ChP, JP, USP
Middle wash No.1 (Choose equilibrium buffer)		PBS	Same as load sample	5	PBS (refer to ingredients above)	--	--	--
Middle wash No.2 (If necessary)	Option 1	Equilibration buffer and ≤ 0.5 M NaCl	Same as harvest sample	5	Sodium chloride	137017	Emprove® Expert	Ph Eur, BP, ChP, JP, USP
					PBS (refer to ingredients above)	--	--	--
	Option 2	Equilibration buffer with pH changed	5.0~6.0	5	Hydrochloric acid fuming 37%	137007	Emprove® Expert	Ph Eur, BP, ChP, JP, NF
					PBS (refer to ingredients above)	--	--	--
	Option 3	Equilibration buffer with 0.1–1.0% polysorbate 80	Same as harvest sample	5	Tween® 80 (Polysorbate)	817061	Emprove® Essential	Ph Eur, JP, NF
					PBS (refer to ingredients above)	--	--	--
Elution	Option 1	0.1 M acetate buffer	3.0–4.0	3	Sodium acetate trihydrate	137012	Emprove® Expert	Ph. Eur., BP, ChP, JP, USP
					Acetic acid (glacial) 100%	137000	Emprove® Expert	Ph Eur, BP, JP, USP
	Option 2	0.1 M citrate buffer	3.0–4.0	3	Citric acid	137002	Emprove® Expert	Ph Eur, BP, ChP, JP, USP, ACS
					tri-Sodium citrate dihydrate	106447	Emprove® Expert	Ph Eur, BP, ChP, JP, USP, ACS, E 331
CIP**	Option 1	150 mM phosphate acid	1.5	3	ortho-Phosphoric acid 85%	100563	Emprove® Expert	Ph Eur, BP, ChP, JP, NF
	Option 2	0.1–0.3 NaOH	13	3(~5)	Sodium hydroxide pellets	137020	Emprove® Expert	Ph Eur, BP, ChP, JP, NF
Column storage		pH 5.2±0.5 sodium acetate buffer with 1% benzyl alcohol	5.2±0.5	3	Sodium acetate trihydrate	128205	Emprove® Expert	Ph. Eur., BP, ChP, JP, USP
					Benzyl alcohol	100987	Emprove® Expert	Ph Eur, BP, JP, NF

* Column Volume

** Either 150 mM phosphate acid or 0.1–0.3N NaOH can be used if they are effective in cleaning; cleaning will be more effective if they are used in combination.

Ethylene Glycol

Ethylene glycol is a widely used solvent in biopharmaceutical processes. Ethylene Glycol Emprove® Evolve meets the increasing quality requirements of the biopharma industry for CIP and chromatography resin storage applications. Its tested application with sodium hydroxide ensures optimal performance, enhances efficiency in cleaning processes, and extends the lifespan of protein A chromatography resins.

Physicochemical Information	
Chemical information	Ethylene glycol
Chemical name	Ethan-1,2-diol
Chemical formula	$HOCH_2CH_2OH$
Final Product Testing	**Specification**
Quality Level	MQ 400
Purity (GC)	≥ 99.5%
Bacterial endotoxins	≤ 10 I.U./mL
Density (d 20 °C/20 °C)	1.113–1.115

Application

Optimizing the CIP process and selecting the appropriate CIP solution can significantly increase the lifetime of chromatography resins.

Adding Ethylene Glycol Emprove® Evolve to a sodium hydroxide solution for cleaning has been shown to extend the lifetime of protein A columns (e.g. Eshmuno® A chromatography resin). Compared to cleaning with NaOH alone, which resulted in a drop in relative antibody yield below the acceptable limit of 80% after 250 cleaning cycles. The combination of Ethylene Glycol Emprove® Evolve and NaOH maintained relative antibody yields above 80% for 600 cleaning cycles (see graph). This clearly demonstrates that the addition of Ethylene Glycol Emprove® Evolve effectively increase the resin lifetime, in this case by 100%.

Consequently, employing Ethylene Glycol Emprove® Evolve to optimize CIP processes in downstream applications supports improved process economics and reduces manufacturing efforts by minimizing the need for new column packing.

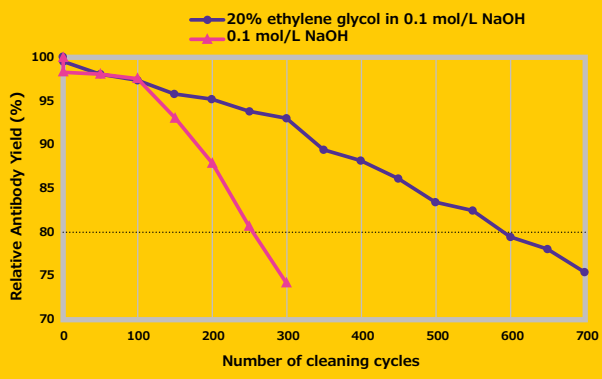


Figure 1: Relative antibody yields over 700 cleaning cycles of Eshmuno® A resin with and without inclusion of 20% ethylene glycol in a 0.1 mol/L NaOH cleaning solution.

Benefits

- Ethylene Glycol Emprove® Evolve cleaning and storage chemical increases the lifetime of Eshmuno® A resin as well as other protein resins.
- The product supports improved process economics and reduces manufacturing efforts by minimizing the need for new column resin packs and packing.
- The inclusion of ethylene glycol in a cleaning solution does not impact re-equilibration time of the protein A column.

Ordering Information

Available to supply globally:

Catalog No.	Product Name	CAS No.	MQ Level	Pack Size [L]
1.37666.1000	Ethylene glycol suitable for cleaning in place Emprove® Evolve	107-21-1	**400**	1
1.37666.9025				25
1.37666.9180				180
1.37666.9950				950

Also available in larger volumes on request (e.g. 16,000 L) in tank containers (ISOtainer).

Cation Exchange/Anion Exchange

Cation exchange capture & elution mode chromatography

Purpose		Buffers	Buffer pH	CV*	Product	Catalog No.	Category	Compendial
Equilibration	Neutral condition	PBS	Same as load sample	5	Sodium dihydrogen phosphate dihydrate	137018	Emprove® Expert	Ph Eur, BP, ChP, USP, JPE
					di-Sodium hydrogen phosphate dihydrate	137036	Emprove® Expert	Ph Eur, BP, USP
					Sodium chloride	137017	Emprove® Expert	Ph Eur, BP, ChP, JP, USP
	Acid area choice 1	25 mM–50 mM acetate buffer	Same as load sample (pH 4.5–5.5)	5	Sodium acetate trihydrate	128205	Emprove® Expert	Ph Eur, BP, ChP, JP, USP
					Acetic acid (glacial) 100%	137000	Emprove® Expert	Ph Eur, BP, JP, USP
	Acid area choice 2	25 mM–50 mM citrate buffer	Same as load sample (pH 4.5–5.5)	5	Citric acid anhydrous powder	137002	Emprove® Expert	Ph Eur, BP, ChP, JP, USP
					tri-Sodium citrate dihydrate	106447	Emprove® Expert	Ph Eur, BP, ChP, JP, SP, ACS, E 331
Middle wash				5	Refer to buffers and ingredients above	--	--	
Elution		Equilibration buffer + 0.5–1 M NaCl	Same as load sample (pH 4.5–5.5)	3	Sodium chloride	137017	Emprove® Expert	Ph Eur, BP, ChP, JP, USP
					Refer to buffers and ingredients above	--	--	
Regeneration		1–2 M NaCl or equilibrium buffer + 1-2 M NaCl		3 (–5)	Sodium chloride	137017	Emprove® Expert	Ph Eur, BP, ChP, JP, USP
CIP		0.5–1.0 N NaOH	13	3 (–5)	Sodium hydroxide	137020	Emprove® Expert	Ph Eur, BP, ChP, JP, NF
Storage		20% ethanol + 150 mM NaCl		5	Ethanol 96%	100967	Emprove® Expert	Ph Eur, JP, USP
					Sodium chloride	137017	Emprove® Expert	Ph Eur, BP, ChP, JP, USP

Anion exchange flow-through mode chromatography

Purpose		Buffers	Buffer pH	CV*	Product	Catalog No.	Category	Compendial
Equilibration	Option 1	PB	Same as load sample	5	Sodium dihydrogen phosphate dihydrate	137018	Emprove® Expert	Ph Eur, BP, ChP, USP, JPE
					di-Sodium hydrogen phosphate dihydrate	137036	Emprove® Expert	Ph Eur, BP, USP
	Option 2	Tris-HCl buffer	Same as load sample	5	Tris(hydroxymethyl) aminomethane (Trometamol) high purity	108307	Emprove® Expert	Ph Eur, BP, ChP, JPC, USP
					Tris(hydroxymethyl) aminomethane hydrochloride	108219	Emprove® Expert	
Loading		Equilibration buffer	Same as load sample	1-2	Refer to buffers and ingredients above	-	-	-
Regeneration		1–2 M NaCl or Equilibration buffer + 1–2 M NaCl	-	3 (-5)	Sodium chloride	137017	Emprove® Expert	Ph Eur, BP, ChP, JP, USP
CIP		0.5–1.0 N NaOH	13	3 (-5)	Sodium hydroxide	137020	Emprove® Expert	Ph Eur, BP, ChP, JP, NF
Column storage		20% ethanol + 150 mM NaCl	-	5	Ethanol 96%	100967	Emprove® Expert	Ph Eur, JP, USP
					Sodium chloride	137017	Emprove® Expert	Ph Eur, BP, ChP, JP, USP

*Column Volume

For a comprehensive overview of buffers, biological buffers, and other salts for downstream applications, please refer to the sections "Solid Buffers and Bioprocess Chemicals" and "Ready-to-use Buffer Solutions and Bioprocess Chemicals (incl. CIP)" in this document.

TFF Concentration/Diafiltration

Purpose	Buffers	Product	Catalog No.	Category	Compendial
Equilibrium/ Diafiltration	Phosphate buffer	Sodium dihydrogen phosphate dihydrate	137018	Emprove® Expert	Ph Eur, BP, ChP, USP, JPE
		di-Sodium hydrogen phosphate dehydrate	137036	Emprove® Expert	Ph Eur, BP, USP
	Acetate buffer	Sodium acetate trihydrate	128205	Emprove® Expert	Ph Eur, BP, ChP, JP, USP
		Acetic acid 30%	137047	Emprove® Expert	Ph Helv
		Sodium chloride	137017	Emprove® Expert	Ph Eur, BP, ChP, JP, USP
	Citrate buffer	Citric acid anhydrous powder	137002	Emprove® Expert	Ph Eur, BP, ChP, JP, USP
		tri-Sodium citrate dihydrate	106447	Emprove® Expert	Ph Eur, BP, ChP, JP, USP, ACS, E 331
		Sodium chloride	137017	Emprove® Expert	Ph Eur, BP, ChP, JP, USP
Formulation	Histidine	L-Histidine monohydrochloride monohydrate	104352	Emprove® Expert	Ph Eur, BP, ChP, JP
	Sucrose	Sucrose	103789	Emprove® Expert	Ph Eur, ChP, JP, NF
	Trehalose dihydrate	Trehalose dihydrate	102776	Emprove® Expert	Ph Eur, ChP, NF, JP
	Sorbitol	Parteck® SI 400 LEX (Sorbitol)	111597	Emprove® Expert	Ph Eur, BP, NF, JP
	Mannitol	D(-)-Mannitol	137096	Emprove® Expert	Ph, Eur, BP, ChP, USP, JP
CIP	0.5 N NaOH	Sodium hydroxide pellets	137020	Emprove® Expert	Ph, Eur, BP, ChP, JP, NF
Storage	0.1 N NaOH	Sodium hydroxide pellets	137020	Emprove® Expert	Ph, Eur, BP, ChP, JP, NF

Solid Buffers and Bioprocess Chemicals

Custom and Catalog Offering for Solid Buffer and Bioprocess Chemicals

Our benefits:

- **High product consistency**
  Our comprehensive global Quality Management System ensures a robust process control designed to yield high-purity raw materials for reproducible processing.
- **Comprehensive buffer offering**
  Broadest buffer portfolio for the pharmaceutical industry with a global manufacturing network at different quality levels to fit your needs from early upstream non-GMP to high risk excipient applications.
- **Risk mitigation**
  Our Emprove® Program provides comprehensive documentation, process control, and supply chain transparency that goes beyond today's regulatory standards – helping you to navigate regulatory challenges, manage risk and improve your manufacturing processes.
- **Process efficiency:**
  - Whatever your requirements are, we are your partner, supporting you with standard and tailored solutions such as powder blending, quality support, dedicated testing protocols or specific packaging options such as direct dispense and **DRYPOUR™ packaging system**.
  - A portfolio of **granulated materials** with reduced caking behavior and right size weighed products in bags, specifically developed to increase process efficiency, support operator safety, and speed up manufacturing processes.

Biological Buffers*

Product	Catalog No.	Product Name	CAS No.	MQ Level
Tris				
Tris	108386	Tris(hydroxymethyl)aminomethane (Trometamol) Emprove® Expert Ph Eur, BP, ChP, JPC, USP	77-86-1	**500**
Tris	108307	Tris(hydroxymethyl)aminomethane (Trometamol) high purity Emprove® Expert Ph Eur, BP, ChP, JPC, USP	77-86-1	**500**
Tris	137263	Tris(hydroxymethyl)aminomethane Emprove® Evolve	77-86-1	**400**
Tris HCI	108219	Tris(hydroxymethyl)aminomethane hydrochloride high purity Emprove® Expert	1185-53-1	**500**
Tris HCI	108319	TRIS hydrochloride Emprove® Evolve	1185-53-1	**400**
Tricine	137262	N-[Tris(hydroxymethyl)methyl]glycine Emprove® Evolve	1389475	**400**
Bis Tris				
Bis Tris HCl	137252	2,2-Bis(hydroxymethyl)-2,2′,2″-nitrilotriethanol hydrochloride Emprove® Evolve	124763-51-5	**400**
Bis Tris	137276	2,2-Bis(hydroxymethyl)-2,2′,2″-nitrilotriethanol Emprove® Evolve	6976-37-0	**400**
Bis Tris propane	137269	1,3-Bis[tris(hydroxymethyl)methylamino]propane Emprove® Evolve	64431-96-5	**400**
HEPES				
HEPES	110110	2-[4-(2-Hydroxyethyl)-1-piperazinyl]-ethanesulfonic acid buffer substance HEPES Emprove® Expert	7365-45-9	**500**
HEPES	137270	2-[4-(2-Hydroxyethyl)-1-piperazinyl]-ethanesulfonic acid buffer substance HEPES Emprove® Evolve	7365-45-9	**400**
HEPES sodium	137265	2-[4-(2-Hydroxyethyl)-1-piperazinyl]-ethanesulfonic acid buffer substance HEPES sodium salt Emprove® Evolve	75227-39-3	**400**
MES				
MES	137256	4-Morpholineethanesulfonic acid monohydrate Emprove® Evolve	145224-94-8	**400**
MES	137271	4-Morpholineethanesulfonic acid hydrate Emprove® Evolve	1266615-59-1	**400**
MES sodium salt	137274	4-Morpholineethanesulfonic acid sodium salt Emprove® Evolve	71119-23-8	**400**
MES Hydrate	137271	MES hydrate	1266615-59-1	**400**
MOPS				
MOPS	137273	4-Morpholinepropanesulfonic acid Emprove® Evolve	1132-61-2	**400**
MOPS sodium salt	137258	4-Morpholinepropanesulfonic acid sodium salt Emprove® Evolve	71119-22-7	**400**
PIPES				
PIPES Disodium salt	137259	1,4-Piperazinediethanesulfonic acid disodium salt Emprove® Evolve	76836-02-7	**400**
Others				
Triethanolamine	137148	Triethanolamine (Trolamine) Emprove® Expert Ph Eur, JPE, NF	102-71-6	**500**
Ethanolamine	137044	Ethanolamine Emprove® Expert Ph Eur, BP, NF	141-43-5	**500**

*Pack sizes range from 1 kg up to 500 kg. For more details check out our website: Buffers & pH Adjusters (sigmaaldrich.com)

Buffers*

Product	Catalog No.	Product Name	CAS No.	MQ Level
Carbonate				
Potassium carbonate	104924	Potassium carbonate anhydrous Emprove® Essential Ph Eur, USP, E 501	584-08-7	**500**
Sodium carbonate decahydrate	106384	Sodium carbonate decahydrate Emprove® Essential Ph Eur, BP, E 500	1545739	**500**
Sodium carbonate monohydrate	106386	Sodium carbonate monohydrate Emprove® Essential Ph Eur, BP, NF, E 500	1486118	**500**
Sodium carbonate	106398	Sodium carbonate anhydrous Emprove® Essential Ph Eur, BP, ChP, JP, NF	497-19-8	**500**
Sodium hydrogen carbonate	137013	Sodium hydrogen carbonate Emprove® Expert Ph Eur, BP, ChP, USP, JP	144-55-8	**500**
Sodium carbonate anhydrous	137014	Sodium carbonate anhydrous Emprove® Expert Ph Eur, BP, JP, NF	497-19-8	**500**
Phosphate				
Sodium dihydrogen phosphate dihydrate	137018	Sodium dihydrogen phosphate dihydrate Emprove® Expert Ph Eur, BP, ChP, USP, JPE	13472-35-0	**500**
Sodium dihydrogen phosphate dihydrate granulated	147345	Sodium dihydrogen phosphate dihydrate granulated Emprove® Expert Ph Eur,JPE,USP,BP,ChP	13472-35-0	**500**
Disodium hydrogen phosphate dihydrate	137036	di-Sodium hydrogen phosphate dihydrate Emprove® Expert Ph Eur, BP, USP	10028-24-7	**500**
Potassium dihydrogen phosphate	137039	Potassium dihydrogen phosphate cryst. Emprove® Expert Ph Eur, BP, JPC, NF	7778-77-0	**500**
Dipotassium hydrogen phosphate	137010	di-Potassium hydrogen phosphate anhydrous Emprove® Expert Ph Eur, BP, USP	2139535	**500**
Disodium hydrogen phosphate heptahydrate	137092	di-Sodium hydrogen phosphate heptahydrate Emprove® Expert DAC, USP	7782-85-6	**500**
Disodium hydrogen phosphate heptahydrate granulated	147574	di-Sodium hydrogen phosphate heptahydrate granulated Emprove® Expert USP,DAC	7782-85-6	**500**
Sodium dihydrogen phosphate monohydrate	137093	Sodium dihydrogen phosphate monohydrate Emprove® Expert BP, ChP, USP	10049-21-5	**500**
Acetate				
Sodium acetate trihydrate	128205	Sodium acetate trihydrate Emprove® Expert Ph Eur, BP, ChP, JP, USP	6131-90-4	**500**
Sodium acetate trihydrate granulated	104162	Sodium acetate trihydrate granulated Emprove® Expert Ph Eur, BP, ChP, JP, USP	6131-90-4	**500**
Sodium acetate anhydrous	128202	Sodium acetate anhydrous Emprove® Expert ChP, USP	127-09-3	**500**
Citric Acid and Citrate				
Citric acid anhydrous	137002	Citric acid anhydrous powder Emprove® Expert Ph Eur, BP, ChP, JP, USP	77-92-9	**500**
Citric acid monohydrate	137003	Citric acid monohydrate cryst. Emprove® Expert Ph Eur, BP, ChP, JP, USP	5949-29-1	**500**
tri-Sodium citrate dihydrate	106447	tri-Sodium citrate dihydrate Emprove® Expert Ph Eur, BP, ChP, JP, USP, ACS, E 331	1545801	**500**
Histidine				
L-Histidine	104352	L-Histidine Emprove® Expert Ph Eur, ChP, JP, USP	71-00-1	**500**
L-Histidine HCl H_2O	104354	L-Histidine monohydrochloride monohydrate Emprove® Expert Ph Eur, BP, ChP, JP	5934-29-2	**500**

*Pack sizes range from 1 kg up to 500 kg. For more details check out our website: Buffers & pH Adjusters (sigmaaldrich.com)

Caustics*

Product	Catalog No.	Product Name	CAS No.	MQ Level
Sodium hydroxide	137020	Sodium hydroxide, pellets Emprove® Expert Ph Eur, BP, ChP, JP, NF	1310-73-2	**500**
Potassium hydroxide	105032	Potassium hydroxide, pellets Emprove® Essential Ph Eur, BP, JP, NF, FCC, E 525	1310-58-3	**500**

*Pack sizes range from 1 kg up to 500 kg. For more details check out our website: Buffers & pH Adjusters (sigmaaldrich.com)

Other Salts*

Product	Catalog No.	Product Name	CAS No.	MQ Level
Chlorides				
Calcium chloride dihydrate	142002	Calcium chloride dihydrate Emprove® Expert Ph Eur, BP, ChP, JP, USP, FCC, E 509	10035-04-8	**500**
Magnesium chloride hexahydrate	105832	Magnesium chloride hexahydrate cryst. Emprove® Expert Ph Eur, BP, USP, JPC, FCC, E 511	7791-18-6	**500**
Potassium chloride	137009	Potassium chloride Emprove® Expert Ph Eur, BP, USP, JP	7447-40-7	**500**
Potassium chloride granulated	104165	Potassium chloride granulated Emprove® Expert Ph Eur, BP, JP, USP	7447-40-7	**500**
Sodium chloride	137017	Sodium chloride Emprove® Expert Ph Eur, BP, ChP, JP, USP	7647-14-5	**500**
Sodium chloride granulated	104163	Sodium chloride granulated Emprove® Expert Ph Eur, BP, ChP, JP, USP	7647-14-5	**500**
Sulfates				
Ammonium sulfate (Not for US and Canada)	128218	Ammonium sulfate Emprove® Expert ChP, NF, ACS	7783-20-2	**500**
Ammonium sulfate (US and Canada only)	101816	Ammonium sulfate Emprove® Expert ACS, NF	7783-20-2	**500**
Ammonium sulfate granulated	104161	Ammonium sulfate granulated Emprove® Expert ACS, ChP, NF	7783-20-2	**500**
Sodium sulfate anhydrous	128225	Sodium sulfate anhydrous Emprove® Expert Ph Eur, BP, ChP, USP	7757-82-6	**500**

*Pack sizes range from 1 kg up to 500 kg. For more details check out our website: Buffers & pH Adjusters (sigmaaldrich.com)

Surfactants, Detergents & Stabilizers

Product	Catalog No.	Product Name	CAS No.	MQ Level
N-Acetyl-DL-tryptophan	118488	N-Acetyl-DL-tryptophan Emprove® Expert, Ph. Eur., BP	87-32-1	**500**
L-Arginine	101587	L-Arginine Emprove® Expert Ph Eur, ChP, JP, USP	74-79-3	**500**
L-Arginine monohydrochloride	101544	L-Arginine monohydrochloride Emprove® Expert Ph Eur,BP,ChP,JP,USP	1119-34-2	**500**
Cyclodextrin HPB	142020	Cyclodextrin HPB Emprove® Expert Ph.Eur.,NF	128446-35-5	**500**
Deviron® C16	108693	Deviron® C16 Detergent 30% solution Emprove® Evolve	3332-27-2	**400**
Deviron® 13-S9	108694	Deviron® 13-S9 Detergent Emprove® Expert	68131-40-8	**500**
Glycine crystalline	100590	Glycine cryst. Emprove® Expert Ph Eur,BP,ChP,JP,USP	56-40-6	**500**
Glycine granulated	103669	Glycine granulated Emprove® Expert Ph Eur,BP,ChP,JP,USP	56-40-6	**500**
Hexadecyltrimethylammonium bromide	137142	Hexadecyltrimethylammonium bromide Emprove® Essential meets NF	57-09-0	**500**
myo-Inositol	104731	myo-Inositol Emprove® Expert Ph Eur,FCC,NF	87-89-8	**500**
D(-)-Mannitol	137162	D(-)-Mannitol Emprove® Expert Ph Eur,BP,ChP,JP,USP	69-65-8	**500**
Parteck® SI LEX (Sorbitol)	111597	Parteck® SI 400 LEX (Sorbitol) Emprove® Expert Ph Eur,BP,NF,JP	50-70-4	**500**
Poloxamer 188	137112	Poloxamer 188 Emprove® Expert (stabilized with 70ppm BHT) Ph. Eur., NF	2594628	**500**
Polysorbate 20	817072	Polysorbate 20 Tween® 20 Emprove® Essential Ph Eur, JPE, NF	9005-64-5	**500**
Polysorbate 20	137172	Polysorbate 20 high purity Emprove® Expert Ph Eur, ChP, JPE, NF	9005-64-5	**500**
Polysorbate 80	137009	Tween® 80 (Polysorbate) Emprove® Essential Ph Eur, JP, NF	9005-65-6	**500**
Polysorbate 80	137171	Polysorbate 80 high purity Emprove® Expert Ph Eur, ChP, JPE, NF	9005-65-6	**500**
Sucrose	103789	Sucrose Emprove® Expert Ph Eur,ChP,JP,NF	57-50-1	**500**
Sulfobutylether-β-cyclodextrin	142022	Sulfobutylether-β-cyclodextrin sodium salt Emprove® Expert, Ph. Eur., NF	182410-00-0	**500**
Trehalose dihydrate	102776	Trehalose dihydrate Emprove® Expert Ph Eur,ChP,NF,JP	6138-23-4	**500**

Other Downstream Chemicals

Product	Catalog No.	Product Name	CAS No.	MQ Level
Tri-n-butyl phosphate	100002	Tri-n-butyl phosphate Emprove® Expert Ph Eur	126-73-8	**500**
Caprylic acid (Octanoic acid)	100193	Caprylic acid (Octanoic acid) Emprove® Expert Ph Eur,NF	124-07-2	**500**
CDAP	RES1458C	1-Cyano-4-dimethylaminopyridinium tetrafluoroborate	59016-56-7	**300**
DL-Dithiothreitol	137159	DL-Dithiothreitol Emprove® Essential	3483-12-3	**500**
Glutathione (reduced)	104090	Glutathione (reduced) Emprove® Expert Ph Eur	70-18-8	**500**
L-Glutathione oxidized	G2299	L-Glutathione oxidized	27025-41-8	**400**
Guanidine hydrochloride	137272	Guanidine hydrochloride Emprove® Evolve	54789	**400**
Guanidinium chloride	137037	Guanidinium chloride Emprove® Expert	54789	**500**
2-Mercaptoethanol	137151	2-Mercaptoethanol Emprove® Evolve	60-24-2	**400**
Sodium caprylate	817081	Sodium caprylate Emprove® Expert Ph Eur,ChP,NF	6/1/84	**500**
Urea	137030	Urea cryst. Emprove® Expert Ph Eur, BP, ChP, JP, USP, ACS	57-13-6	**500**
Urea	104166	Urea granulated Emprove® Expert Ph Eur, BP, ChP, JP, USP, ACS	57-13-6	**500**

Custom and Catalog Offering for Solid Buffer and Bioprocess Chemicals

Customization Options

We offer custom solid raw materials used for the manufacture of biopharmaceuticals

- Pre-mix powders
- Customized packaging including right-sized weighing and DRYPOUR™ packaging system
- Granulation
- Customized product specification

Our Solid Buffer Manufacturing Sites

Powder Blends and Packaging Options

Our custom capabilities include blends of powdered raw materials according to your formulation needs.

The buffer products are supplied in an array of safe and reliable packaging options. Depending on the quantities needed, products are typically provided in:

- Glass bottles
- Plastic bottles
- Plastic pails (square and round)
- Plastic drums (square and round)
- Fiber drums

Liners used in our bulk products are classified as slip agent-free to reduce the risk of contamination.

DRYPOUR™ Packaging System

DRYPOUR™ packaging consists of a polyethylene (PE) drum with a tamper-evident seal, a PE liner with integrated desiccant bags (non-product contact) and a breathable interior Tyvek® liner. This triple protection delivers two invaluable results: dramatically reduced caking for specific chemicals which reduces the material preparation time and no contamination risk from the desiccant.

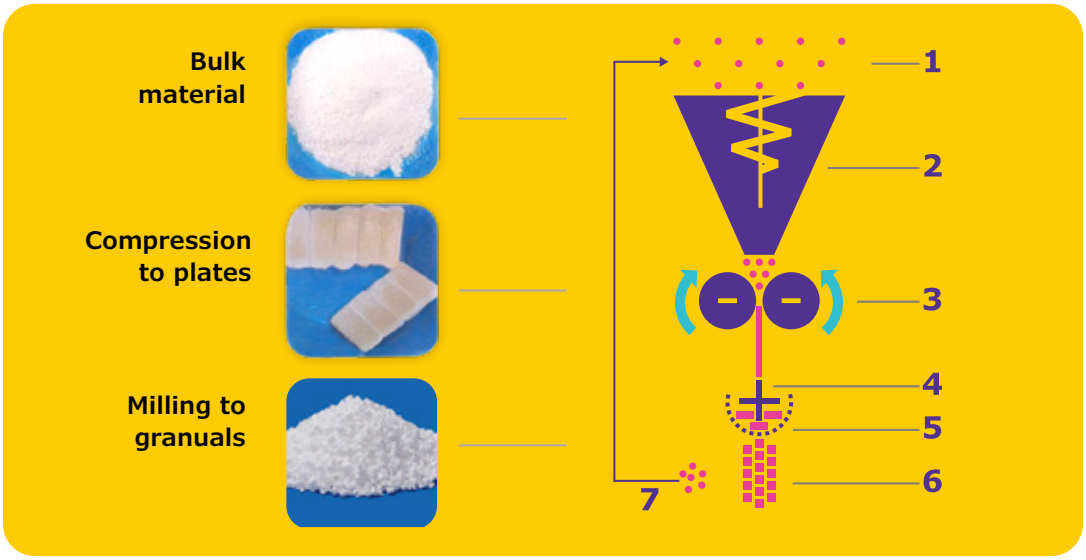
Powder Transfer Bags Using Right Sized Weighing

Our custom capabilities allow us to provide products in different package sizes including right-size weighing to your specific needs. If supplied in powder transfer bags, powdered raw materials can directly be connected to the hydration tank to minimize labor requirements and possible contamination risks as well as increase personnel and facility safety.

Granulation of Powdered Raw Material

Dry granulation offers several advantages for solid buffers and bioprocess chemicals:

- **Enhanced Handling and Processability:**
  Granulated materials are easier to handle and process, streamlining buffer preparation
- **Minimized Dust Formation:**
  Reduces dust exposure, enhancing operator safety and maintaining a cleaner work environment.
- **Reduced Caking:**
  Significantly decreases caking behavior, facilitating smoother manufacturing processes and improving flowability.
- **Stable Homogeneity:**
  Ensures consistent composition throughout the granulated material, improving product reliability.
- **Water and Additive-Free Raw Material Manufacturing Process:**
  Utilizes only compression force, eliminating the need for additional solvents or binders.



Principle of dry granulation by roller compaction. A typical roller compactor setup comprises (1) bulk material, (2) funnel with mixer and tamp auger, (3) hydraulic compression rolls (temperature controlled), (4) rotor sieve mill, (5) vibrating sieve, (6) final granules, (7) fine particles re-circulation.

Ready-to-use Buffer Solutions and Bioprocess Chemicals (incl. CIP)

Ready-to-use Liquids

Although essential, ready-to-use liquid preparation is a non-value-added activity that utilizes a significant amount of time, labor and manufacturing floor space which can turn into a limiting factor for your facility output.

Our benefits:

- **High product reproducibility & performance:** We use only high-quality raw materials including Emprove® Chemicals from a global supply network covered under a comprehensive company-wide Global Quality Management System that ensures a robust process control.
- **Global supply:** Our global supply concept is based on regional production sites in the U.S., Europe and Asia.
- **Comprehensive standard packaging offering:** We offer a fully qualified standard packaging portfolio including shipment tests according to ISTA 3H guidelines to mitigate supply chains risks, speeding up product access and supporting a more sustainable transport management with a returnable outer container program.
- **Customization and tailored support:** We partner with you to meet your specific requirements ranging from specific formulations including liquid concentrates, quality support, dedicated testing protocols to a wide range of fully qualified packaging options and configurations.

Ready-to-use Sterile-filtered Liquid Solutions

Product	Catalog No.	Product Name	CAS No.	MQ Level	Pack Size [L]
PBS					
DPBS	59300C	Dulbecco's Phosphate Buffered Saline (DPBS), with calcium, with magnesium, liquid, sterile-filtered		**500**	1
DPBS	59321C	Dulbecco's Phosphate Buffered Saline (DPBS modified), without calcium, without magnesium, liquid, sterile-filtered		**400**	1
DPBS	59331C	Dulbecco's Phosphate Buffered Saline (DPBS modified), 10X, without calcium, without magnesium, liquid, sterile-filtered		**400**	1
Others					
NaCl	59222C	Sodium chloride solution 5 M, sterile filtered		**300**	1 / 0.5

Liquid Solutions MyWay

Liquid Solutions MyWay (LSMW) are a portfolio of high-quality sterile filtered liquid solutions supplied in ready-to-use standard bags. These products are all manufactured using Emprove® raw materials. The portfolio contains some of the most frequently used liquid buffers which are ready-to-order with pre-defined pricing and shelf life.

Available to supply globally (excluding 20% Ethanol 58340C and 58345C: EMEA only)

Product No.	Product Name	MQ Level	Pack Size [L]
59910C	Packaged Water for Injection	**400**	10, 20, 50, 100, 200
55120C	Phosphate Buffered Saline (PBS)	**500**	20, 50, 100, 200
55220C	Sodium chloride solution 1 M	**400**	20, 50, 100, 200
58300C	Sodium hydroxide solution 0.1 M	**400**	20, 50, 100, 190
58310C	Sodium hydroxide solution 0.5 M	**400**	20, 50, 100, 190
58320C	Sodium hydroxide solution 1 M	**400**	20, 50, 100, 190
58340C	Ethanol solution 20% (v/v) (EMEA only)	**400**	20, 50, 100, 190
58345C	Ethanol 20% (v/v), sodium chloride 150 mM (EMEA only)	**400**	20, 50, 100, 190
58400C	Tris solution 1 M	**400**	20, 50, 100, 200
58410C	Tris concentrate 2.5 M (50 mM Tris, pH 7.5, at 50x dilution)	**400**	20, 50, 100, 200
55256C	Acetic Acid concentrate 5 M (100 mM Acetic Acid, pH 3.2, at 50x dilution)	**400**	20, 50, 100, 190
55258C	Citric Acid concentrate 1.5 M (50 mM Citric Acid, pH 3.2, at 30x dilution)	**400**	20, 50, 100, 190

Please note: 1 L samples can be supplied on request per order.

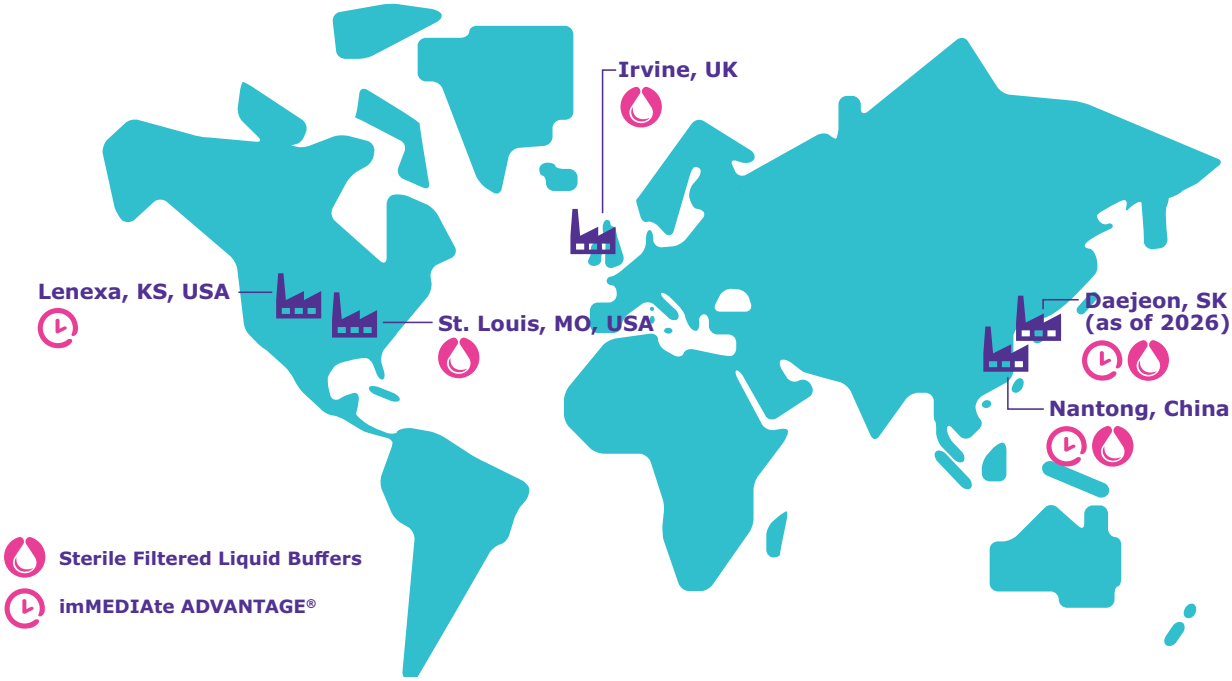
Custom Product Offering for Ready-to-use Solutions

Customization Options

We offer custom-made liquids including sterile filtered buffer components and additives used for the manufacture of biopharmaceuticals

- Custom processing liquid formulations incl. buffer concentrates
- Custom packaging options
- Custom product specifications/testing protocols

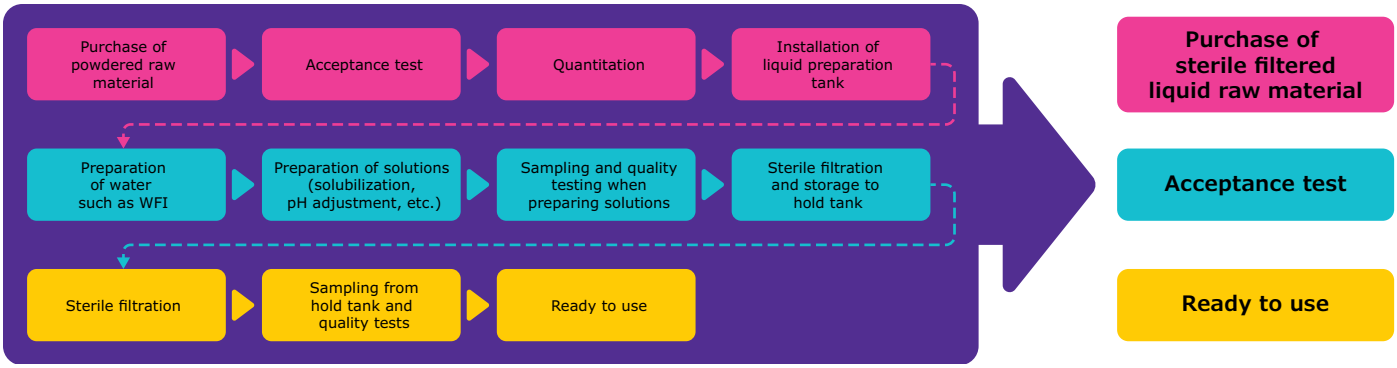
Our Liquid Buffer Manufacturing Sites



Customized Production of Liquid Buffers

In order to meet your specific processing needs, we can customize your liquid buffer formulations using our comprehensive offering of high-quality raw materials. With our experience in buffer concentrates and stock solutions, you can move towards next-generation processing using buffer in-line dilution or buffer stock blending.

We manufacture ready-to-use liquids according to required specifications using dedicated testing protocols and fill them in single-use bags from 1 to 1000 L sizes. The breadth of packaging options includes stocked standard bags or custom configurations depending on your preferences.



Process Liquids – Manufacturing Sites Comparison

Description	St. Louis US	Irvine UK	Daejeon SK (2026)
Animal component-free/non-animal origin manufacture	•	•	•
Batch size capability	50–10,000 L	50–10,000 L	50–10,000 L
Hazardous material handling*	•	•	•
ISO9001:2015 standard EXCiPACT certified	•	•	•
High Temperature Short Time (HTST) capabilities	300–6,000 L	2,000–10,000 L	Not available
PET bottles	10–2,000 mL	10–2,000 mL	10–2,000 mL
2D & 3D Single-use bags**	1–500 & 1,000 L (standard and custom)	1–500 & 1,000 L (standard and custom)	1–500 & 1,000 L (standard and custom)
Fleet management	Acc. to proprietary policy	Acc. to proprietary policy	Acc. to proprietary policy
Comprehensive E+L data pack	•	•	•
ISTA ship testing for bags (totes, drums, flex stations)	•	•	•
Performance testing for bags (Real time stability testing capability)	•	•	•

* Aqueous dilutions, some site-specific and volume dependent limitations
** Mobius® and Meissner primary options, other custom packaging options upon request

HTST: High Temperature, Short Time
E+L: Extractables and Leachables
ISTA: International Safe Transit Association

ImMEDIAte ADVANTAGE® Program – A non-GMP Service for Liquid Buffer Formulations

Our imMEDIAte ADVANTAGE® service for pre-GMP small scale custom buffers provides the quick turn-around you need to complete your development work faster, enabling you to evaluate a pre-GMP sample for suitability and feasibility before scaling up. To support global process developers, all our imMEDIAte ADVANTAGE® centers are aligned with key elements of our GMP Quality Systems, providing flexibility and expedited access to the small-volume, custom products you need to support scale-up from development to commercial production.

Key benefits include:

- Qualified, same-source raw materials as our large-scale GMP facilities, with the added option of unique, non-qualified raw materials for your development needs
- Scalable systems that ensure reproducible product quality and performance
- Master formulation management, batch management, and controlled process procedures
- Product documentation that includes certificates of analysis and safety data sheets for every individual product
- Standard packaging ensuring quick delivery, product integrity, and compatibility with large-scale manufacturing

Liquid solutions:

- Batch sizes: 1–200 L
- Standard packaging:
  - Gamma irradiated PET bottles (100 mL–2,000 mL)
  - Gamma irradiated bags (1–20 L)

Bioprocess Chemicals (incl. CIP)

Every biomanufacturing process involves cleaning to protect equipment and prevent cross-contamination. Cleaning in place (CIP) solutions are used to clean stainless steel tanks and piping systems, to wash and store chromatography resins, and to regenerate membranes. CIP solutions typically include highly concentrated caustics (e.g., sodium hydroxide), acids (e.g., hydrochloric acid, phosphoric acid) or solvents (e.g., ethanol). As these solutions are considered as dangerous goods, their transport packaging is qualified according to UN rating. Our CIP portfolio contains a lot of catalog products, which are available in bottles, drums, or intermediate bulk containers (IBC). To support large scale manufacturing, our CIP solutions can be also supplied in tank containers up to 18,000 L, with a controlled and trackable fleet management program.

Benefits

In addition to the benefits of our ready-to-use solutions the CIP offering provides the following advantages:

- **Improved operator safety:** Our coded discharge system increases the safety of handling caustics and acids by avoiding operator error, drips, outgassing and damage of product equipment.
- **Fit-for purpose packaging:** Large variety of pack sizes and packaging types available from 1 L bottles to 18,000 L tank containers.
- **Recommended for high-risk applications:** All our MQ 500 GMP (IPEC-PQG/ EXCiPACT) solutions for CIP and buffer preparation are manufactured under excipient GMP conditions and feature low endotoxin and bioburden levels.

1 L → **18,000 L**

Product	Catalog No.	Product Name	MQ Level
Acetic and Citric Acid			
Acetic acid	137035	Acetic acid 1 mol/L Emprove® Expert	**500**
Acetic acid	137094	Acetic acid 25% Emprove® Expert	**500**
Acetic acid	137047	Acetic acid 30% Emprove® Expert Ph Helv	**500**
Acetic acid	137034	Acetic acid 60% Emprove® Expert	**500**
Acetic acid	137011	Acetic acid 75% Emprove® Expert	**500**
Acetic acid	137072	Acetic acid 80% Emprove® Expert	**500**
Acetic acid	137000	Acetic acid 100% Emprove® Expert Ph Eur, BP, JP, USP	**500**
Citric acid	480855	Citric acid 50% Emprove® Expert	**500**
Hydrochloric Acid			
HCl	110165	Hydrochloric acid 1 mol/L Emprove® Expert	**500**
HCl	480934	Hydrochloric acid 2 mol/L Emprove® Expert	**500**
HCl	480592	Hydrochloric acid 10% Emprove® Expert Ph Eur, JP, NF	**500**
HCl	137312	Hydrochloric acid 25% Emprove® Expert Ph Eur, Helv	**500**
HCl	480680	Hydrochloric acid 3 mol/L Emprove® Expert	**500**
HCl	137055	Hydrochloric acid 4 mol/L Emprove® Expert	**500**
HCl	480791	Hydrochloric acid 5 mol/L Emprove® Expert	**500**
HCl	110164	Hydrochloric acid 6 mol/L Emprove® Expert	**500**
HCl	137007	Hydrochloric acid fuming 37% Emprove® Expert Ph Eur, BP, ChP, JP, NF	**500**
Other Acids			
H_3PO_4	480939	Phosphoric acid 1 mol/L Emprove® Expert	**500**
H_3PO_4	100250	Phosphoric acid 75% Emprove® Expert	**500**
H_3PO_4	100563	ortho-Phosphoric acid 85% Emprove® Essential Ph Eur, BP, JPE, NF, E 338	**500**
H_2SO_4	480704	Sulfuric acid 10% Emprove® Expert	**500**
Sodium Hydroxide			
NaOH	137058	Sodium hydroxide solution 0.1 mol/L Emprove® Expert	**500**
NaOH	137084	Sodium hydroxide solution 0.15 mol/L Emprove® Expert	**500**
NaOH	100233	Sodium hydroxide solution 0.25 mol/L Emprove® Expert	**500**
NaOH	137060	Sodium hydroxide solution 0.5 mol/L Emprove® Expert	**500**
NaOH	137031	Sodium hydroxide solution 1 mol/L Emprove® Expert	**500**
NaOH	480512	Sodium hydroxide solution 2 mol/L Emprove® Expert	**500**
NaOH	100232	Sodium hydroxide solution 10% Emprove® Expert	**500**
NaOH	137041	Sodium hydroxide solution 5 mol/L Emprove® Expert	**500**
NaOH	137032	Sodium hydroxide solution 6 mol/L Emprove® Expert	**500**
NaOH	480005	Sodium hydroxide solution 20% low iron Emprove® Expert	**500**
NaOH	480659	Sodium hydroxide solution 25% (w/w) low iron Emprove® Expert	**500**
NaOH	480763	Sodium hydroxide solution 8 mol/L Emprove® Expert	**500**
NaOH	480648	Sodium hydroxide solution 10 mol/L Emprove® Expert	**500**
NaOH	100221	Sodium hydroxide solution 10 mol/L suitable for cleaning in place	**100**
NaOH	137023	Sodium hydroxide solution 32% Emprove® Expert	**500**
NaOH	100238	Sodium hydroxide solution 50% Emprove® Expert	**500**
NaOH	100239	Sodium hydroxide solution 50% suitable for cleaning in place	**200**
Solvents			
Benzyl alcohol	100987	Benzyl alcohol Emprove® Expert Ph Eur, BP, JP, NF	**500**
Ethanol	480910	Ethanol 20% Emprove® Expert	**500**
Ethanol	100967	Ethanol 96% Emprove® Expert Ph Eur, ChP, JP, USP	**500**
Ethanol	100986	Ethanol absolute Emprove® Expert Ph Eur, BP, ChP, JP, USP	**500**
Isopropanol	137040	2-Propanol 70% (v/v) Emprove® Expert USP	**500**
Miscellaneous			
Ethylene glycol	137666	Ethylene glycol Emprove® Evolve	**400**
NaCl	137076	Sodium chloride solution 3 M Emprove® Expert	**500**

For more details check out our website: CIP Cleaning in Place

Removal of Adventitious Agents and Impurities

The Benzonase® Family

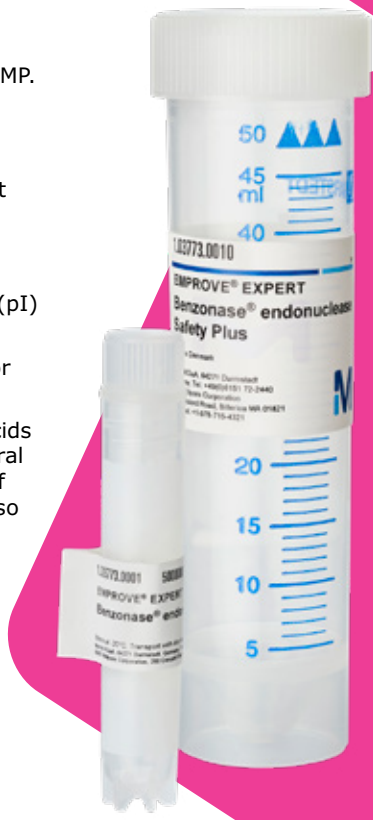
The Benzonase® portfolio—the smart solution for DNA removal in biopharmaceutical production—has proven its value for over 30 years. Balancing efficiency and regulatory compliance by delivering reliability and high-quality due to manufacturing under excipient GMP. Benzonase® endonuclease is originated from bacteria *Serratia marcescens* and expressed in *E.coli* K12. It is nonspecific, making it highly active against all kinds of nucleic acids (DNA, RNA, circular, single or double stranded).

Benzonase® Salt Tolerant endonuclease Emprove® Expert is a newly developed enzyme, that differs in the amino acid sequence from other Benzonase® endonucleases. It was designed with state-of-the-art protein engineering capabilities to ensure the highest activity at high salt concentrations.

The protein is a monomer with a molecular weight of about 27 kDa and an isoelectric point (pI) at pH 9.68.

It is functional between pH 6 and 10 and from 0 °C to 37 °C. Mg^{2+} (1–10 mM) is required for enzyme activity as with other Benzonase® endonucleases.

Benzonase® endonucleases have an exceptionally high level of specific activity for nucleic acids without any detectable proteolytic activity, making it a suitable tool for the purification of viral vaccines, viral vectors for vaccine, cell & gene therapy and oncolytic applications. The use of Benzonase® endonuclease can reduce the levels of DNA by more than 100,000-fold while also decreasing viscosity and protecting downstream equipment from DNA fouling.



Benefits

Benefits of using Benzonase® endonuclease in a viral manufacturing process:

- **Prevents yield loss**
  due to virus-nucleic acid complexes
- **Prevents fouling**
  of downstream equipment
- **Reduces viscosity**
  of process intermediates

Regulatory expectations and documentation for viral vaccines and vectors:

- Residual DNA considered a contaminant requiring removal (size of residual DNA no more than 100–200 bp, less than 10 ng per dose).
- FDA Bulk Biological Master File and Emprove® Dossiers available.

Find here in-depth information on our Benzonase® endonuclease portfolio

Ordering Information

Catalog No.	Product Name	MQ Level	Pack Size
101654.0001	Benzonase® endonuclease, purity grade II (≥90%), for biotechnology	**100**	100,000 U/vial
101656.0001		**200**	500,000 U/vial
101695.0001	Benzonase® endonuclease Emprove® Expert	**500**	100,000 U/vial
101697.0001		**500**	500,000 U/vial
101697.0010		**500**	5,000,000 U/vial
103773.1010	Benzonase® endonuclease Safety Plus Emprove® Expert (≥99.0% purity)	**500**	100,000 U/vial
103773.0001		**500**	500,000 U/vial
103773.0010		**500**	5,000,000 U/vial
104445.1010	Benzonase® Salt Tolerant Endonuclease Emprove® Expert	**500**	80,000 U/vial
104445.0001		**500**	400,000 U/vial
104445.0010		**500**	4,000,000 U/vial
104358	Benzonase® ELISA Kit III		5 x 96 WELLS
EZBNZST-185K	Benzonase® ST ELISA with ZooMAb Antibodies	**300**	1 x 96 or 5 x 96 WELLS

Viral Inactivation

High Quality Chemicals for Virus Inactivation

As a drug manufacturer, you are required to ensure the viral safety of your biological therapeutic products. Chemicals, which are used for virus inactivation (e.g. detergent or low pH treatment), must meet the same high quality standards as other raw materials in your process. Our detergents are manufactured to high-quality standards, ensuring reliability for your processes. Deviron® C16 meets ISO 9001 standards, and Deviron® 13-S9 complies with IPEC-PQG-GMP standards, providing you with consistent and safe performance. They bear the Emprove® trademark and come with comprehensive regulatory documentation that contributes to the quality of your registration dossier. The result: making your work even faster and more cost-efficient.

Viral Inactivation in Biologics Manufacturing

Ensuring viral safety is essential for maintaining the safety profile of drug products for patients. Unlike methods such as chromatographic separation or virus filtration that physically remove viruses, viral inactivation techniques utilize chemicals or low pH conditions to effectively reduce the presence of infectious enveloped viruses.

The specific approach to viral inactivation varies based on the process and the type of molecule involved. However, the fundamental requirement remains consistent: the use of high-quality chemicals that are free from viral contaminants and suitable for biologics manufacturing.

Virus inactivation - S/D treatment

Product	Catalog No.	Product Name	CAS No.	MQ Level
Tri-n-butyl phosphate	100002	Tri-n-butyl phosphate Emprove® Expert Ph Eur	126-73-8	**500**
Deviron® 13-S9 Detergent	108694	Deviron® 13-S9 Detergent Emprove® Expert	68131-40-8	**500**
Deviron® C16 Detergent	108693	Deviron® C16 Detergent 30% solution Emprove® Evolve	3332-27-2	**400**
Tween® 80	817061	Tween® 80 (polysorbate) Emprove® Essential Ph Eur, JP, NF	9005-65-6	**500**

Virus inactivation - low pH treatment

For acids and buffers for low pH treatment, please refer to the sections "Solid Buffers and Bioprocess Chemicals" and "Ready-to-use Buffer Solutions and Bioprocess Chemicals (incl. CIP)" in this document or to our webpage

The Deviron® Detergent Portfolio

Greener Alternatives to Triton™ X-100 for Biopharmaceutical Applications

Several critical steps in biologics production, including viral inactivation and cell lysis are performed with detergents.

Triton™ X-100 detergent (4-tert-octylphenol polyethoxylate) is the primary detergent templated in biomanufacturing processes. As of January 2021, its unauthorized use has been prohibited in the European Union by the European Commission, due to its labelling as a Substance of Very High Concern (SVHC) and its inclusion on the Authorisation List (Annex XIV) of REACH (Registration, Evaluation, Authorisation and Restrictions of Chemicals).

The endocrine disruption and mutagenic effects of Triton™ X-100 degradation product have been pointed out as a potential danger to patients and the environment, leading to strict guidelines regarding its usage.

With a deep knowledge of the detergent field and the need for alternatives to Triton™ X-100, we have screened more than 30 detergent molecules and launched the Deviron® C16 Emprove® Evolve detergent and the Deviron® 13-S9 Emprove® Expert detergent.

Our Deviron® portfolio of detergents is a best-in-class alternative to Triton™ X-100 detergent used for biomanufacturing applications.

Benefits

Environmental Safety

Deviron® detergents do not form harmful degradation products, minimizing disposal risks and ensuring compliance with environmental regulations.

Performance

Deviron® detergents show high efficiency in viral inactivation and cell lysis, comparable or superior to benchmark detergents TritonTM X-100 and Polysorbate 20, respectively.

Compatibility with Bioprocess

Deviron® detergents do not adversely affect the yield, purity or activity of biopharmaceutical products and can be integrated seamlessly into existing workflows.

Ease of Removal

Deviron® detergents can be efficiently removed from the product stream by downstream operations. Trace amounts can be determined with a sensitive detection method (e.g. HPLC-CAD).

Reliable supply

Large manufacturing capacities ensure reliable supply to our customers.

Quality and Regulatory Compliance

Deviron® detergents are manufactured to high standards. Deviron® C16 adheres to ISO9001 standards, while Deviron® 13-S9 meets IPEC-PQG-GMP requirements, both supported by Emprove® Dossiers for regulatory support.

Choosing Deviron® detergents allows biopharmaceutical manufacturers to achieve effective viral inactivation and cell lysis in biopharmaceutical applications while meeting environmental and regulatory standards, ensuring product safety and quality. As shown in the following table, our Deviron® detergents, part of the Emprove® Program, uniquely meet the necessary purity, regulatory, and efficacy requirements, offering comparable or superior performance to Triton™ X-100.

Description	Deviron® C16 Detergent 30% solution Emprove® Evolve	Deviron® 13-S9 Detergent Emprove® Expert	Triton™ X-100 Emprove® Expert Ph Eur
Catalog number	108693	108694	108643
Surfactant type	Zwitterionic (pI 8.9)	Non-ionic	Non-ionic
Chemical name	N,N-Dimethyltetradecylamin-N-oxide	Alcohols, C11-15-secondary, ethoxylated	4-(1,1,3,3-tetramethylbutyl) phenol ethoxylated
CAS number	3332-27-2	68131-40-8	9036-19-5
Critical micelle concentration (CMC)	0.002–0.003% wt (24 °C)	0.005% wt (24 °C)	0.013% wt (24 °C)
Biodegradability (readily biodegradable: >60% within 28 days) OECD 301	Readily biodegradable: 88% degradation (OECD 301B)	Readily biodegradable: 74% degradation (OECD 301B)	Substance of Very High Concern as defined by REACH
Virus inactivation efficiency LRV ≥ 4 (@ ≥0.5% wt,15-25 °C)	Better or comparable to benchmark	Better or comparable to benchmark	Benchmark
Cell lysis efficiency for viral vector processing	Better or comparable to benchmark	Better or comparable to benchmark	Benchmark
Endotoxins removal for plasmid manufacturing: Natrix® Q chromatography membrane/ detergents added to wash buffer supplement	99.997% removal	99.969% removal	99.997% removal
Emprove® & M-Clarity™	Emprove® Evolve MQ400, (ISO9001 or equivalent)	Emprove® Expert MQ500, (IPEC-PQG GMP)	Emprove® Expert MQ500, (IPEC-PQG GMP)
Composition	30% aqueous solution	Pure substance (100%)	Pure substance (100%)
Customized certificate of analysis options	Available	Available	Available
Toxicology report	Available	Available	NA

Ordering Information

The Deviron® detergent portfolio exists of two products and is available in different pack sizes to support different applications from R&D over process development up to production scale operations:

Catalog No.	Product Name	CAS No.	MQ Level	Pack Size [L]
108693.1000	Deviron® C16 Detergent 30% solution Emprove® Evolve	3332-27-2	**400**	1
108693.2500				2.5
108693.9025				25
108694.1000	Deviron® 13-S9 Detergent Emprove® Expert	68131-40-8	**500**	1
108694.2500				2.5
108694.9025				25

Viral Clearance

As a drug manufacturer, you are required to ensure the viral safety of your biological therapeutic products. Our Viresolve® Pro Solution portfolio provides a comprehensive, flexible template solution for viral clearance within mAb and recombinant protein bioproduction. This proven viral clearance solution delivers the highest levels of retention assurance and productivity across a broad range of feed stream characteristics. Chemicals and buffers used in conjunction with virus filtration processes must meet the same high quality standard as other raw materials in your process. Our detergents are manufactured to high-quality standards, ensuring reliability for your processes. Deviron® C16 meets ISO 9001 standards, and Deviron® 13-S9 complies with IPEC-PQG-GMP requirements, providing you with consistent and safe performance. They are part of our Emprove® Program and come with comprehensive regulatory documentation that contributes to the quality of your registration dossier. The result: making your work even faster, safer and more cost-efficient.

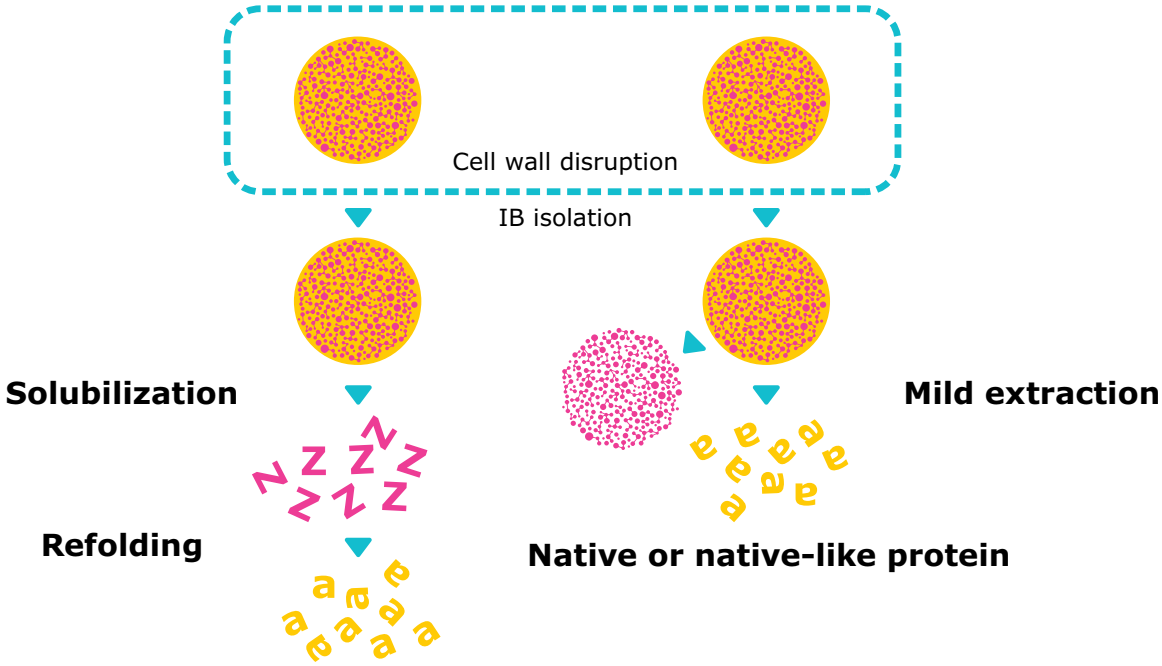
Viral clearance membrane filtration

Purpose	Buffers	Product	Catalog No.	Category	Compendial	MQ Level
Equilibration buffer	Phosphate buffer	Sodium dihydrogen phosphate dihydrate	137018	Emprove® Expert	Ph Eur, BP, ChP, USP, JPE	500
		di-Sodium hydrogen phosphate dihydrate	137036	Emprove® Expert	Ph Eur, BP, USP	500
	Acetate buffer	Sodium acetate trihydrate	128205	Emprove® Expert	Ph Eur, BP, ChP, JP, USP	500
		Acetic acid 30%	137047	Emprove® Expert	Ph Helv	500
		Sodium chloride	137017	Emprove® Expert	Ph Eur, BP, ChP, JP, USP	500
	Tris-HCl buffer	Tris(hydroxymethyl) aminomethane (Trometamol) high purity	108307	Emprove® Expert	Ph Eur, BP, ChP, JPC, USP, ACS	500
		Tris(hydroxymethyl) aminomethane hydrochloride	108219	Emprove® Expert		500
CIP	0.5 N NaOH	Sodium hydroxide	137020	Emprove® Expert	Ph Eur, BP, ChP, NF, JP	500

Chemicals for Recovering Active Proteins from Bacterial Inclusion Bodies

Proteins used to treat diseases, like antibodies or coagulation factors, can be produced as biotherapeutics. While producing biotherapeutics in mammalian cell culture presents challenges due to demanding cultivation conditions and limited yield, it remains the primary method for complex biotherapeutics, as the modification and refolding which is critical for the protein's functionality cannot be artificially replicated.

Bacterial production, such as using *E. coli*, is an alternative, albeit with its own challenges. Typically, proteins are intracellularly expressed, requiring cell lysis (physical or chemical) for product recovery. In some cases, proteins are expressed as inclusion bodies (IBs), necessitating chemical solubilization and post-translational modifications, such as glycosylation and refolding.

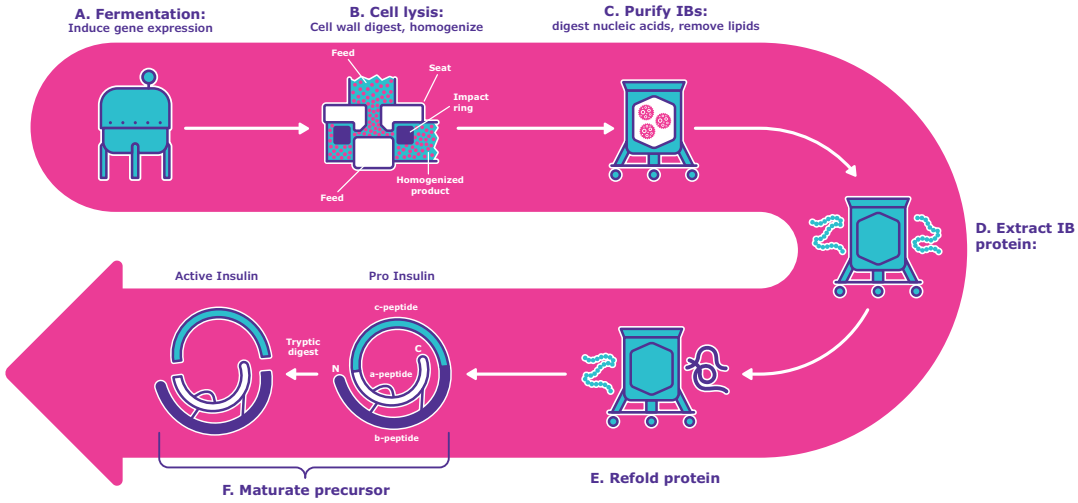


Pink shapes in IBs represent the amyloidal scaffold in which proteins with native-(like) conformational states are embedded (blue). The **Z** symbols represent solubilized unfolded polypeptides whereas **a** symbols represent protein in the native-(like) conformation.

Despite those challenges, the expression of recombinant proteins in bacteria or yeast has two advantages: low requirements on cultivation conditions and potentially factor higher yields, saving space, time, labor and resulting cost. We offer a portfolio, dedicated to support those challenges, enabling manufacturers to take advantage of bacterial fermentation processes.

To demonstrate the whole process of bacterial fermentation, the production process for therapeutic recombinant insulin expressed in *E. coli* is shown. The conventional strategy for this manufacturing process encompasses the following major steps:

- Induction of heterologous expression (A)
- Cell harvest and lysis (B)
- IB purification (C)
- IB protein extraction (D)
- Protein refolding (E)
- r Insulin precursor intermediate maturation (F)
- Various chromatography steps - not covered here



The chemicals and recombinant enzymes that can be used in each step are listed:

Chemicals for Recombinant Protein Expression

Product	Catalog No.	Product Name	MQ Level	Function
Induce gene expression				
A	137064	Isopropyl-β-D-1-thiogalactopyranosid Emprove® Expert (IPTG)	**500**	Induce gene expression
A	PHG0010	Isopropyl-β-D-1-thiogalactopyranosid (IPTG)	**300**	Induce gene expression
Purify IBs				
C	101656	Benzonase® purity grade II (>90%) for biotechnology)	**100**	Digest nucleic acids trapped in IBs
C	103773	Benzonase® endonuclease Safety Plus Emprove® Expert (≥99% purity)	**500**	Digest nucleic acids trapped in IBs
Extract IBs				
D	137159	DL-Dithiothreitol Emprove® Essential	**500**	Reduce intra/intermolecular disulfide bonds
D	137272	Guanidine hydrochloride Emprove® Evolve	**400**	IB dissolution
D	137037	Guanidinium chloride Emprove® Expert NF	**500**	IB dissolution
D	137151	2-Mercaptoethanol Emprove® Evolve	**400**	Reduce intra/intermolecular disulfide bonds
D	137030	Urea cryst. Emprove® Expert Ph Eur, BP, ChP, JP, USP, ACS	**500**	IB dissolution
D	104166	Urea granulated Emprove® Expert Ph Eur, BP, ChP, JP, USP, ACS	**500**	IB dissolution
Protein Refolding				
E	101587	L-Arginine Emprove® Expert Ph Eur, ChP, JP, USP	**500**	Aggregation inhibitor
E	101544	L-Arginine monohydrochloride Emprove® Expert Ph Eur, BP, ChP, JP, USP	**500**	Aggregation inhibitor
E	C5360	L-Cysteine	**400**	Redox reagent
E	102735	L-Cysteine hydrochloride monohydrate Emprove® Expert Ph Eur, JP, USP	**500**	Redox reagent
E	104090	Glutathione (reduced) Emprove® Expert Ph Eur	**500**	Redox reagent
E	G2299	L-Glutathione oxidized	**400**	Redox reagent
E	103789	Sucrose Emprove® Expert Ph Eur, ChP, JP, NF	**500**	Protein stabilizer
E	102776	Trehalose dihydrate Emprove® Expert Ph Eur, ChP, NF, JP	**500**	Protein stabilizer

Other Processing Raw Materials

Catalog No.	Product	MQ Level	Function
128218	Ammonium sulfate Emprove® Expert ChP, NF, ACS	**500**	Precipitation
100201	Phenol Emprove® Essential Ph Eur, ChP, JP, USP	**500**	Preservative
817043	Thimerosal Emprove® Essential Ph Eur, BP	**500**	Preservative
137123	Benzalkonium chloride Emprove® Expert Ph Eur, JP, NF	**500**	Preservative
137124	Benzalkonium chloride (50% aqueous solution) Emprove® Expert Ph Eur, NF	**500**	Preservative

Links to more in-depth information:

Bioprocessing & Formulation Raw Materials

The Emprove® Program – Two Decades of Easing Risk Management

Quality and Regulatory Management

Granulated Raw Materials for Pharmaceuticals

MilliporeSigma
400 Summit Drive
Burlington, MA 01803

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