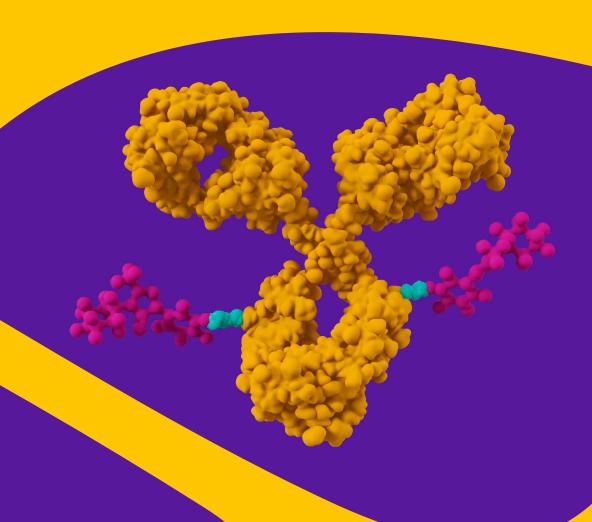


antibody prug conjugates

Products. Services. Expertise.



Millipore ®

Millipore®

Preparation, Separation, Filtration & Monitoring Products

SAFC®

Pharma & Biopharma Raw Material Solutions

BioReliance®

Pharma & Biopharma Contract Testing Services



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

Advanced ADC Solutions

The development journey of an Antibody Drug Conjugate (ADC) is complex and remarkably challenging: it requires linking a unique, tumor targeted monoclonal antibody (mAb) to a potent, cell killing cytotoxic small molecule drug. This requires expertise in small and large molecule development, manufacturing, formulation and testing. Choosing an experienced partner with these skills and the required containment facilities can help advance your ADC to market. Whether you are seeking to build your process based on our tailored technology platforms, a service provider – or a combination of both, we can collaborate with you.

Our ADC Services – integrated from gene sequence to liquid bulk

Complex supply chains with multiple vendors can impede clinical development, lengthening timelines. We offer a seamless supply chain from gene sequence to stability testing of final drug product that minimizes development and manufacturing complexity, reducing time to market. Our team offers:

- Development and manufacturing of monoclonal antibodies, high potency payload molecules, linkers and conjugation services.
- More than 30 years of expertise in process development of more than 270 biologics and in conjugation of more than 85 different constructs.
- Passionate teams with comprehensive experience and a track record of successful execution of customer projects.

Our ADC product offering – Take advantage of our dedicated technological innovations

ADCs are challenging molecules requiring advanced manufacturing suites and dedicated equipment to characterize the molecule and demonstrate its purity, homogeneity and stability. Optimized and robust purification steps using chromatography (hydrophobic interaction or ion exchange) or tangential flow filtration (TFF) are essential to remove process related contamination as well as residuals of linkers and cytotoxic agent, and to concentrate the active pharmaceutical ingredient (API) and stabilize the final bulk substance. ADCs also require an extended containment strategy to protect operators while avoiding the bulk product and the environment from any contamination. We offer a comprehensive portfolio of products from Cell Culture Media to TFF, from buffers to stabilizers to fit your ADC manufacturing needs.

Rely on our expertise to develop the right process, the right systems and the right solutions to empower your ADC to success.



Antibody drug conjugates PPOCESS FLOW

Prefiltration

 Milligard® PES filters and sanitary cartridge housings

- Millipore Express® SHC and SHR hydrophilic filters

Bioreactor

- Sterilizing-grade Aervent® filters
- Mobius[®] single-use bioreactors
- Mobius® commitment services
- NovaSeptum® GO sterile sampling systems
- Cellicon[™] perfusion filter and controller
- ProCellics™ Raman Analyzer with Bio4C™ PAT Raman
- mAbs CTDMO Services biologic process development

Primary clarification

- Millistak+® Pod disposable depth filters, COHC or DOHC media
- Clarisolve® depth filters
- Mobius® FlexReady solution for clarification
- pDADMAC 10% solution flocculation reagent
- Millipore Express[®] PHF filters
- Emprove® buffers, salts and stabilizers

- hydrophilic filters

problem, you can benefit from our expert products and services.

brands, so whatever your life science





Pharma & Biopharma Raw Pharma & Biopharma Filtration & Monitoring Products Material Solutions

- and clinical to commercial cGMP manufacturing

Bioburden reduction

- Milligard® filters
- Durapore® hydrophilic filters
- Millipore Express[®]

Virus inactivation

- Products for solvent/detergent
- Reagents for low pH treatment

MilliporeSigma has brought together the world's leading Life Science

- Mobius® single-use mixing solution
- NovaSeptum® GO sterile sampling system NovAseptic[®] mixers
- BioReliance® Services viral clearance
- Millistak+® Pod disposable depth filters
- Durapore® hydrophilic filters

Aggregate removal

Millipore Express® SHC hydrophilic filters



Cell culture ingredients and supplements | Media prep | Mixing

- Liquid and dry powder (customized) cell culture media
- CHOZN® & UCOE® combined cell line development platform Cellvento[™] cell culture media
- EX-CELL® Advanced fed-batch system and perfusion medium
- imMEDIAte ADVANTAGE™ custom media
- CellPrime® non-animal origin supplements • Poloxamer 188 Emprove® Expert cell culture optimized
- Mobius[®] single-use mixing solution
- Mobius® powder delivery system

- NovaSeptum® GO sterile sampling systems and case
- NovAsentic® mixer
- Sampling system performance validation services
- Sterilizing-grade Aervent[®] filters
- Bioprocessing Systems Services
- Cell culture media development services
- BioReliance® Services cell bank manufacturing,
- cell line characterization, raw material testing • mAbs CDTMO Services – mammalian cell line development

Viral clearance

- Viresolve® Pro solutions
- Mobius[®] FlexReady solution for virus filtration
- BioReliance® Services viral clearance and viral safety testing

Secondary clarification

- system and Millistak+® HC Pro
- clarification
- Millipore Express® PHF filters
- Emprove® buffers, salts and stabilizers
- GMP manufactured solutions for
- EZ BioPac® and Right Sized Weighing

Protein A affinity chromatography

- Fshmuno® A resin
- Mobius® FlexReady solution with Smart Flexware® assemblies for chromatography
- Mobius® Chrom 20 System
- QuikScale® and IsoPak® chromatography
- EZ BioPac® and Right Sized Weighing
- Chromatography column packing services
- Millipore Express® PHF filters • Emprove® buffers, salts and stabilizers
- Biological buffers
- GMP manufactured PAB solution for cleaning in place and storage1
- BioReliance® Services viral clearance and viral safety testing



- Durapore® 0.22 µm filters
- Millipore Express® SHC hydrophilic filters Mobius® 2D and 3D assemblies and storage
- Lvnx® connectors
- NovaSeptum® GO sterile sampling systems
- Custom filtration skids
- Hydrophilic multilayer Durapore® filters
- Integritest® 5 systems • Series 4000™ Single-Round Housings

30kD membranes

- Tangential Flow Filtration
- Ultracel® Membrane Lvnx® connectors
- Mobius® FlexReady solution with Smart Flexware® assemblies for
- Cogent® Tangential Flow Filtration

Ultrafiltration/Diafiltration Pellicon® 3 cassettes with Ultracel®

- Pellicon® Capsules with 30 kD Millipore Express® PHF filters • Emprove® buffers, salts and stabilizers
 - GMP manufactured solutions for cleaning in place1

services

• TFF cleaning validation services • Ultrafiltration/Diafiltration process

• Custom Tangential Flow Filtration

development and implementation

cleaning in place1

Anion-exchange chromatography

- Eshmuno® Q resin
- Fractogel® EMD TMAE Hicap resins
- Mobius® FlexReady solution with Smart Flexware® assemblies for chromatography Mobius® Chrom 20 System
- Natrix® Q Chromatography Membrane Millipore Express® PHF filters

Emprove® buffers, salts and stabilizers

- Biological buffers GMP manufactured solutions for cleaning
- in place¹ • Bioprocessing Systems Services
- Milligard® PES filters
- EZ BioPac® and Right Sized Weighing • BioReliance® Services – viral clearance and viral safety testing

Cation-exchange chromatography

- Fractogel® EMD SO₃, EMD SE Hicap, and EMD COO- resins
- assemblies for chromatography
- EZ BioPac® and Right Sized Weighing

Millipore Express® PHF filters

- Emprove® buffers, salts and stabilizers Biological buffers
- Chromatography column packing services

viral safety testing

• Bioprocessing Systems Services • BioReliance® Services – viral clearance and

• GMP manufactured solutions for cleaning in

Pellicon® 3 cassettes with Ultracel®

- Pellicon® Capsules with 30 kD Ultracel® Membrane
- EZ BioPac® and Right Sized Weighing
- Biological buffers
- cleaning in place1

Raman Software Agents, solvents and linkers

rapid candidate selection

for Antibody Drug Conjugates ADC/bioconjugation and drug-linker CDMO services

Membrane

- Ultracel® 30kD membranes
- Flow Filtration Milligard® PES filters
- Cogent® Tangential Flow Filtration systems

Removal of residual linker UF/DF

- stabilizers • GMP manufactured solutions for cleaning in place1
- Ultrafiltration/Diafiltration process development and implementation services

- Raman Software Emprove® raw materials
- ADCore payload intermediate portfolio

- NovaSeptum® GO sterile sampling systems ProCellics[™] Raman Analyzer with Bio4C[™] PAT
- Bifunctional PEGs

Aggregate removal by chromatography (optional) • Eshmuno® CPX and CMX resins • Emprove® buffers, salts and

- Mobius® FlexReady solution with SmartFlexware®
- Custom chromatography systems and columns
- stabilizers
- assemblies for chromatography GMP manufactured solutions for QuikScale® chromatography cleaning in place1 Chromatography column

- 30kD membranes
- Filtration packing services

Removal of residual cytotoxic | Final formulation by UF/DF Pellicon® Capsules with 30 kD

- Ultracel® Membrane Pellicon® 3 cassettes with Ultracel®
- Mobius® FlexReady solution with Smart Flexware® assemblies for Tangential Flow
- Custom Tangential Flow Filtration systems

• Millipore Express® PHF filters

- GMP manufactured solutions for cleaning in place1
- Ultrafiltration/Diafiltration process development and implementation services

Sterile filtration

- Durapore® 0.22 μm filters
- Hydrophilic multilayer Durapore® filters
- Millipore Express® SHC hydrophilic filters Mobius® 2D and 3D assemblies and
- NovaSeptum® GO sterile sampling
- Custom filtration skids • Integritest® 5 system

storage systems

Diafiltration

- 30 kD membrane
- Millipore Express® PHF filters
- Emprove® buffers, salts and stabilizers
- GMP manufactured solutions for



Final fill

- Mobius® single-use fill finish assemblies
- Mobius® 2D and 3D assemblies and storage systems
- BioReliance® Services bulk lot release testing and final product release testing



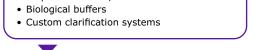




Bioburden reduction

- Durapore® hydrophilic filters

- BioReliance® Services bulk harvest release testing



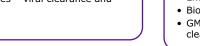
- Millistak+® Pod disposable depth filter
- Mobius® FlexReady solution for
- · Biological buffers

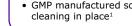
Custom chromatography systems and columns

- Eshmuno® CPX, CMX and CP-FT resin
- Mobius® FlexReady solution with SmartFlexware®
- Mobius® Chrom 20 System

Custom chromatography systems and columns

place¹







Mobius® single-use mixing solution

Conjugation with linker molecule

- Lynx® connectors
- Mobius® FlexReady solution with Smart Flexware® assemblies for Tangential
- Emprove® buffers, salts and

Conjugation with cytotoxic molecule

- Mobius[®] single-use mixing solution
- Biological buffers
 - Bioprocessing Systems Services

- Biological buffers
- Milligard® PES filters







Sterile filtration

systems

ANTIBODY **MODIFICATION**

- ProCellics™ Raman Analyzer with Bio4C™ PAT
- BioReliance® Services Product Characterization

ChetoSensar[™] solubility enhancing technology

• ADC Express[™] non GMP conjugation services for

Linear bifunctional PEGs

Pellicon® Capsules with 30 kD Ultracel®

- EZ BioPac® and Right Sized Weighing
- Pellicon® 3 cassettes with Biomax® or
- Millipore Express® PHF filters
- Custom Tangential Flow Filtration
- TFF cleaning validation services

Millipore Express® high area hydrophilic filters

- - Millipore Express® PHF filters
- Cogent® Tangential Flow Filtration systems
- Emprove® buffers, salts and stabilizers

We provide information and advice to our customers on application technologies and regulatory matters to the best of our knowledge and ability, but without obligation or liability. Existing laws and regulations are to be observed in all cases by our customers. This also applies in respect to any rights of third parties. Our information and advice do not relieve our customers of their own responsibility for checking the suitability of our products for the envisaged purpose.

The holder of the manufacturing authorization shall ensure that the excipients are suitable for use in medicinal products by ascertaining the appropriate good manufacturing practice.

This is particularly true if the material in a certain application is regarded as high risk excipient, for example in parenteral dosage forms.

Millipore®

The Millipore portfolio of MilliporeSigma offers an ecosystem of industry-leading products and services, spanning preparation, separation, filtration and monitoring, as well as clinical and commercial biomanufacturing CTDMO services – all of which are deeply rooted in quality, reliability and time-tested processes. Our proven products, expert services and regulatory and application expertise are a strong foundation you can rely on to consistently perform at the highest level.

SAFC®

The SAFC portfolio of MilliporeSigma offers customized and ready-touse raw material solutions, backed by deep regulatory expertise. Our high-quality products and services are supported by an experienced and responsive team of raw material and regulatory experts who are committed to understand your requirements and provide tailored solutions that meet your exact needs.

BioReliance®

The BioReliance portfolio of MilliporeSigma encompasses biopharmaceutical characterization, and biosafety testing services. Our experienced teams and operational expertise make us the partner who supports you all the way and always has your vital goal in mind.

Click. Explore. Learn more.

WEB PAGE ADC MANUFACTURING Sigma-Aldrich.com/adc-manufacturing

PROCESSING APPLICATION GUIDE

Identify the relevant products for your process: MilliporeSigma.com/BAG

