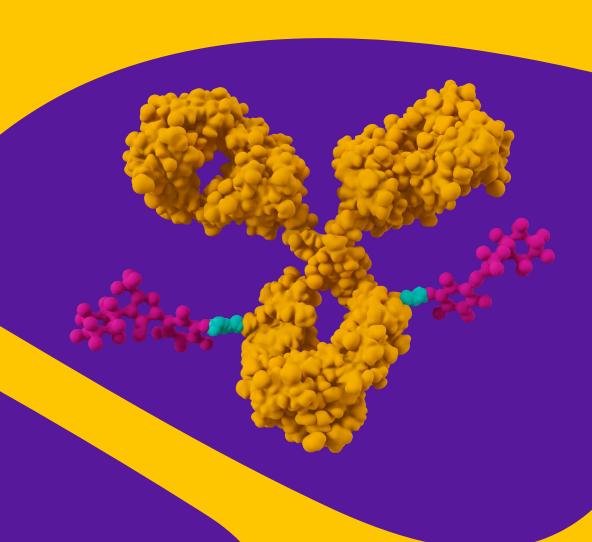


antibody prug conjugates

Products. Services. Expertise.



Millipore ®

Millipore®

Preparation, Separation, Filtration & Monitoring Products

SAFC®

Pharma & Biopharma Raw Material Solutions

BioReliance®

Pharma & Biopharma Contract Testing Services



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

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

Cell culture ingredients and supplements | Media prep | Mixing

 Milligard® PES filters and sanitary cartridge housings

Bioburden reduction

 Millipore Express[®] SHC and SHR hydrophilic filters

• NovaSeptum® GO sterile sampling systems and case

• Sampling system performance validation services

BioReliance® Services – cell bank manufacturing,

cell line characterization, raw material testing

• mAbs CDTMO Services – mammalian cell line development

• Durapore® hydrophilic filters

Bioreactor

- Sterilizing-grade Aervent® filters
- Mobius[®] single-use bioreactors
- Mobius® commitment services
- NovaSeptum® GO sterile sampling systems
- ProCellics™ Raman Analyzer with Bio4C™ PAT Raman
- mAbs CTDMO Services biologic process development
- and clinical to commercial cGMP manufacturing BioReliance® Services – bulk harvest release testing

Primary clarification

- Millistak+® Pod disposable depth filters, COHC or DOHC media
- Clarisolve® depth filters
- Cellicon[™] perfusion filter and controller
 - Millipore Express[®] PHF filters
 - Emprove® buffers, salts and stabilizers
 - Biological buffers
 - Custom clarification systems

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

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



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

Mobius® single-use mixing solution

- NovAseptic[®] mixers
- BioReliance® Services viral clearance and viral safety

Aggregate removal

- Millistak+® Pod disposable depth filters

Protein A affinity chromatography

- Fshmuno® A resin
- ProSep® Ultra Plus resin
- Mobius® FlexReady solution with Smart
- Flexware® assemblies for chromatography
- Mobius® Chrom 20 System

- 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



- QuikScale® and IsoPak® chromatography
- EZ BioPac® and Right Sized Weighing
- Custom chromatography systems and columns

Sterile filtration

• Durapore® 0.22 µm filters

• Liquid and dry powder (customized) cell culture media

• Poloxamer 188 Emprove® Expert cell culture optimized

Cellvento[™] cell culture media

imMEDIAte ADVANTAGE™ custom media

Mobius® single-use mixing solution

• Mobius® powder delivery system

• CellPrime® non-animal origin supplements

• CHOZN® & UCOE® combined cell line development platform

• EX-CELL® Advanced fed-batch system and perfusion medium

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

NovAsentic® mixer

Sterilizing-grade Aervent[®] filters

• Bioprocessing Systems Services

• Cell culture media development services

- Pellicon® Capsules with 30 kD
- Ultracel® Membrane
- Tangential Flow Filtration
- **Ultrafiltration/Diafiltration**
- Lvnx® connectors
- Smart Flexware® assemblies for
- Cogent® Tangential Flow Filtration

Pellicon® 3 cassettes with Ultracel®

- 30kD membranes
- Mobius® FlexReady solution with

services

- TFF cleaning validation services
- Custom Tangential Flow Filtration
- Millipore Express® PHF filters • Emprove® buffers, salts and stabilizers
- GMP manufactured solutions for cleaning in place1
- Ultrafiltration/Diafiltration process development and implementation

Viral clearance

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

· Biological buffers GMP manufactured solutions for

cleaning in place1 • EZ BioPac® and Right Sized Weighing

Secondary clarification

system and Millistak+® HC Pro

• Mobius® FlexReady solution for

Millipore Express® PHF filters

clarification

• Millistak+® Pod disposable depth filter

• Emprove® buffers, salts and stabilizers

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

viral safety testing

• Milligard® PES filters • EZ BioPac® and Right Sized Weighing

• Bioprocessing Systems Services

• BioReliance® Services – viral clearance and

Cation-exchange chromatography

- Eshmuno® CPX, CMX and CP-FT resin
- Fractogel® EMD SO₃, EMD SE Hicap, and EMD COO- resins
- Mobius® FlexReady solution with SmartFlexware® assemblies for chromatography
- Mobius® Chrom 20 System

Millipore Express® PHF filters

- EZ BioPac® and Right Sized Weighing
- Custom chromatography systems and columns
- Emprove® buffers, salts and stabilizers Biological buffers

• Bioprocessing Systems Services

viral safety testing

• GMP manufactured solutions for cleaning in place¹

• BioReliance® Services – viral clearance and

- Ultracel® Membrane Millipore Express® PHF filters Chromatography column packing services
 - Emprove® buffers, salts and stabilizers
 - GMP manufactured solutions for

ANTIBODY **MODIFICATION**

Conjugation with linker molecule

 Mobius® single-use mixing solution • ProCellics™ Raman Analyzer with Bio4C™ PAT Raman Software

Agents, solvents and linkers

- Linear bifunctional PEGs • BioReliance® Services – Product Characterization for Antibody Drug Conjugates
- ADC/bioconjugation and drug-linker CDMO services ChetoSensar[™] solubility enhancing technology • ADC Express[™] non GMP conjugation services for rapid candidate selection

Removal of residual linker UF/DF

- Pellicon® Capsules with 30 kD Ultracel® Membrane Lynx® connectors
- EZ BioPac® and Right Sized Weighing • Pellicon® 3 cassettes with Biomax® or Ultracel® 30kD membranes

Mobius® FlexReady solution with Smart

Flexware® assemblies for Tangential

- Flow Filtration Milligard® PES filters
- Cogent® Tangential Flow Filtration systems
- Millipore Express® PHF filters
- GMP manufactured solutions for cleaning in place1

Custom Tangential Flow Filtration

- NovaSeptum® GO sterile sampling systems
 - Emprove® raw materials

Conjugation with cytotoxic molecule

- ProCellics[™] Raman Analyzer with Bio4C[™] PAT Raman Software
- Bifunctional PEGs ADCore payload intermediate portfolio
- Eshmuno® CPX and CMX resins Emprove® buffers, salts and Mobius® FlexReady solution with SmartFlexware®
- Custom chromatography systems and columns

QuikScale® chromatography

Aggregate removal by chromatography (optional)

- Biological buffers assemblies for chromatography
 - packing services

Removal of residual cytotoxic | Final formulation by UF/DF

- Ultracel® Membrane
- 30kD membranes Mobius® FlexReady solution with Smart
- Custom Tangential Flow Filtration systems
- - in place1
 - 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

• BioReliance® Services – bulk lot release testing and final product

implementation services

- Emprove® buffers, salts and stabilizers
- TFF cleaning validation services Ultrafiltration/Diafiltration process development and

Millipore Express® high area hydrophilic filters

- Mobius[®] single-use mixing solution
- Millipore Express® PHF filters

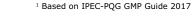
stabilizers

- GMP manufactured solutions for cleaning in place1 Chromatography column
- Bioprocessing Systems Services

Pellicon® Capsules with 30 kD Millipore Express® PHF filters

- Pellicon® 3 cassettes with Ultracel®
- Flexware® assemblies for Tangential Flow Filtration Cogent® Tangential Flow Filtration systems
- Emprove® buffers, salts and stabilizers Biological buffers
- GMP manufactured solutions for cleaning Ultrafiltration/Diafiltration process
 - Milligard® PES filters

- storage systems
- NovaSeptum® GO sterile sampling
- Custom filtration skids • Integritest® 5 system





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

Merck has brought together the

so whatever your life science

world's leading Life Science brands,

- NovaSeptum® GO sterile sampling system
 - Durapore® hydrophilic filters









Diafiltration Pellicon® 3 cassettes with Ultracel®

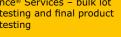
- 30 kD membrane Pellicon® Capsules with 30 kD
- EZ BioPac® and Right Sized Weighing
- Biological buffers
- cleaning in place1

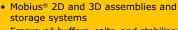


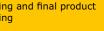


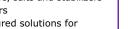
• Emprove® buffers, salts, and stabilizers

release testing











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 Merck 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.

BioReliance®

The BioReliance portfolio of Merck 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.

SAFC®

The SAFC portfolio of Merck offers customized and ready-to-use 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.

Click. Explore. Learn more.

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

PROCESSING APPLICATION GUIDE

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

