Vaccine process. Recombinant antigen expressed in bacteria. Products. Services. Expertise.

Most of the modern vaccine pipeline is based on bacterial expression, due to the ease of production and low manufacturing costs.

Bacterial production of vaccines does present challenges. While bacterial platforms are generally regarded as safe, there are process-related challenges with endotoxin removal and, as with any process, the goal of optimizing recovery and yield. With bacterial-produced proteins of all varieties, there is the additional challenge of assuring proper refolding of the protein following purification. Such challenges must be overcome during process development and implementation in order to assure high-quality product.

Given the challenges associated with bacterial expression of vaccine, it is critical to choose a partner with experience meeting and overcoming these types of issues. Merck Millipore's regulatory knowledge, integrated portfolio, and applications expertise can help you overcome your bacterial vaccine process challenges.

No guide will replace the need to conduct process development and optimization experiments. The unique nature of every process stream combined with application and regulatory requirements play a part in determining the optimum process solutions. Use this selection guide as a starting point for selecting and sizing the most appropriate Merck Millipore solutions.

Merck Millipore is a division of MERCK

Vaccine process. Recombinant antigen expressed in bacteria. Products. Services. Expertise.

Fermentation

- Liquid and dry powder (customized) cell culture media
- Poloxamer 188 suitable for biopharmaceutical production Ph.Eur.,NF
- IPTG
- Sterilizing-grade Aervent® filters
- NovaSeptum® sampling systems
- Lynx® connectors
- NovAseptic® mixer
- EMPROVE® bio carbohydrates, glycerol, vitamins, and minerals
- NaOH solutions for CIP or fermenters

Cell culture media filtration:

- Polysep™ filters
- Durapore® hydrophilic filters
- Millipore Express® hydrophilic filters

Cell harvest

- EMPROVE® bio buffers
- GMP manufactured solutions for cleaning in place and storage[1]

Cell disruption

- CellPrime® rLysozyme
- Mobius® single-use mixing solution
- NovAseptic® mixer

Inclusion bodies harvest

- Benzonase® endonuclease and Benzonase® ELISA kit II
- Magnesium chloride hexahydrate cryst. EMPROVE® Ph Eur, BP, USP, JPC, FCC, E 511
- Prostak™ micro filtration modules with Durapore® membrane
- EMPROVE® bio buffers
- GMP manufactured solutions for cleaning in place and storage[1]

Inclusion bodies solubilization

- Guanidine HCL
- Mobius® single-use mixing solution
- NovAseptic® mixer

Clarification

- Millistak+® HC filter
- Millistak+® Pod disposable depth filter system and HC housings
- Pellicon® 2 cassettes with Biomax® 100 or 300 kD membrane
- Cogent® Tangential Flow Filtration systems
- Custom Tangential Flow Filtration systems
- EMPROVE® bio buffers
- GMP manufactured solutions for cleaning in place and storage[1]

Protein refolding

- L-Arginine / L-Arginine-HCl
- L-Cystin / L-Cysteine Glutathione, reduced
- Triton X-100 suitable for biopharmaceutical production EMPROVE® Bio Ph Eur, NF
- EMPROVE® bio buffers
- Mobius® single-use mixing solution
- NovAseptic® mixer

Secondary clarification

- Millistak+® HC filter
- Millistak+® Pod disposable depth filter system and HC housings
- EMPROVE® bio buffers
- GMP manufactured solutions for cleaning in place and storage[1]

Prefiltration and bioburden reduction

- Milligard® filters
- Hydrophilic multilayer Durapore® filters
- Millipore Express® SHC hydrophilic filters

First chromatography

- Eshmuno® S and Q resins
- Fractogel® EMD TMAE, EMD TMAE Hicap, EMD DEAE, EMD DMAE, EMD SO3, EMD SE Hicap and EMD COO
- Chromabolt™ prepacked chromatography columns
- Mobius® FlexReady solution with Smart Flexware® assemblies for chromatography
- Mobius® 2D and 3D assemblies and storage systems
- QuikScale® and IsoPak® chromatography columns
- K-Prime® chromatography systems
- Custom chromatography systems and columns
- EMPROVE® bio buffers
- GMP manufactured solutions for cleaning in place and storage[1]
- Chromatography column packing services
- Implementation services for Mobius® FlexReady solution

pH adjustment

- Mobius® single-use mixing solution
- NovaSeptum® sampling systems
- NovAseptic® mixer
- EMPROVE® bio buffers

Diafiltration

- Pellicon® cassettes
- Mobius® FlexReady solution with Smart Flexware® assemblies for Tangential Flow Filtration
- Cogent® Tangential Flow Filtration systems
- Custom Tangential Flow Filtration systems
- EMPROVE® bio buffers
- GMP manufactured solutions for cleaning in place and storage[1]
- TFF cleaning validation services
- Implementation services for Mobius® FlexReady solution

Intermediate chromatography

- Eshmuno® CPX resin
- Fractogel® EMD TMAE, EMD TMAE Hicap, EMD DEAE, EMD DMAE, EMD SO3, EMD SE Hicap and EMD COO
- Fractogel® EMD Phenyl (S) resin
- Chromabolt™ prepacked chromatography columns
- Mobius® FlexReady solution with Smart Flexware® assemblies for chromatography
- Mobius® 2D and 3D assemblies and storage systems
- QuikScale® and IsoPak® chromatography columns
- K-Prime® chromatography systems
- Custom chromatography systems and columns
- EMPROVE® bio buffers
- GMP manufactured solutions for cleaning in place and storage[1]
- Chromatography column packing services
- Implementation services for Mobius® FlexReady solution

Polishing chromatography

- Eshmuno® Q and CPX resins
- Fractogel® EMD TMAE, EMD SO3 and EMD BioSEC
- Chromabolt™ prepacked chromatography columns
- Durapore® hydrophilic filters
- Mobius® FlexReady solution with Smart Flexware® assemblies for chromatography
- Mobius® 2D and 3D assemblies and storage systems
- QuikScale® and IsoPak® chromatography columns
- K-Prime® chromatography systems
- Custom chromatography systems and columns
- EMPROVE® bio buffers
- GMP manufactured solutions for cleaning in place and storage[1]
- Chromatography column packing services
- Implementation services for Mobius® FlexReady solution

Ultrafiltration/ Diafiltration

- Pellicon® cassettes
- Mobius® FlexReady solution with Smart Flexware® assemblies for Tangential Flow Filtration
- Cogent® Tangential Flow Filtration systems
- Custom Tangential Flow Filtration systems
- EMPROVE® bio buffers
- GMP manufactured solutions for cleaning in place and storage[1]
- TFF cleaning validation services
- Implementation services for Mobius® FlexReady solution

Lynx® connectors

Final formulation

- Mobius® single-use mixing solution
- NovaSeptum® sampling systems
- Mobius® 2D and 3D assemblies and storage systems
- NovAseptic® mixer
- EMPROVE® buffers, salts, stabilizers, and pH adjustment solutions

Lynx® connectors

Sterile filtration

- Durapore® hydrophilic filters
- Millipore Express® hydrophilic filters
- Mobius® 2D and 3D assemblies and storage systems
- NovaSeptum® sampling systems
- Custom filtration skids
- Integritest® 4 Series automated filter integrity test instrument

Lynx® connectors

Final fill

- Mobius® single-use fill finish assemblies
- Mobius® 2D and 3D assemblies and storage systems
- Particle shedding validation services

Provantage® services include process development, process validation, equipment qualification, and GMP drug production | Merck Millipore biopharmaceutical courses

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.

To place an order or receive technical assistance

In Europe, please call Customer Service:

France: 0825 045 645
Germany: 01805 045 645
Italy: 848 845 645
Spain: 901 516 645 Option 1
Switzerland: 0848 645 645
United Kingdom: 0870 900 4645

For other countries across Europe,
please call: +44 (0) 115 943 0840

Or visit **www.merckmillipore.com/offices**

For Technical Service visit: **www.merckmillipore.com/techservice**

MERCK MILLIPORE

www.merckmillipore.com

[1] based on IPEC - PQG GMP guide for pharmaceutical excipients 2006.