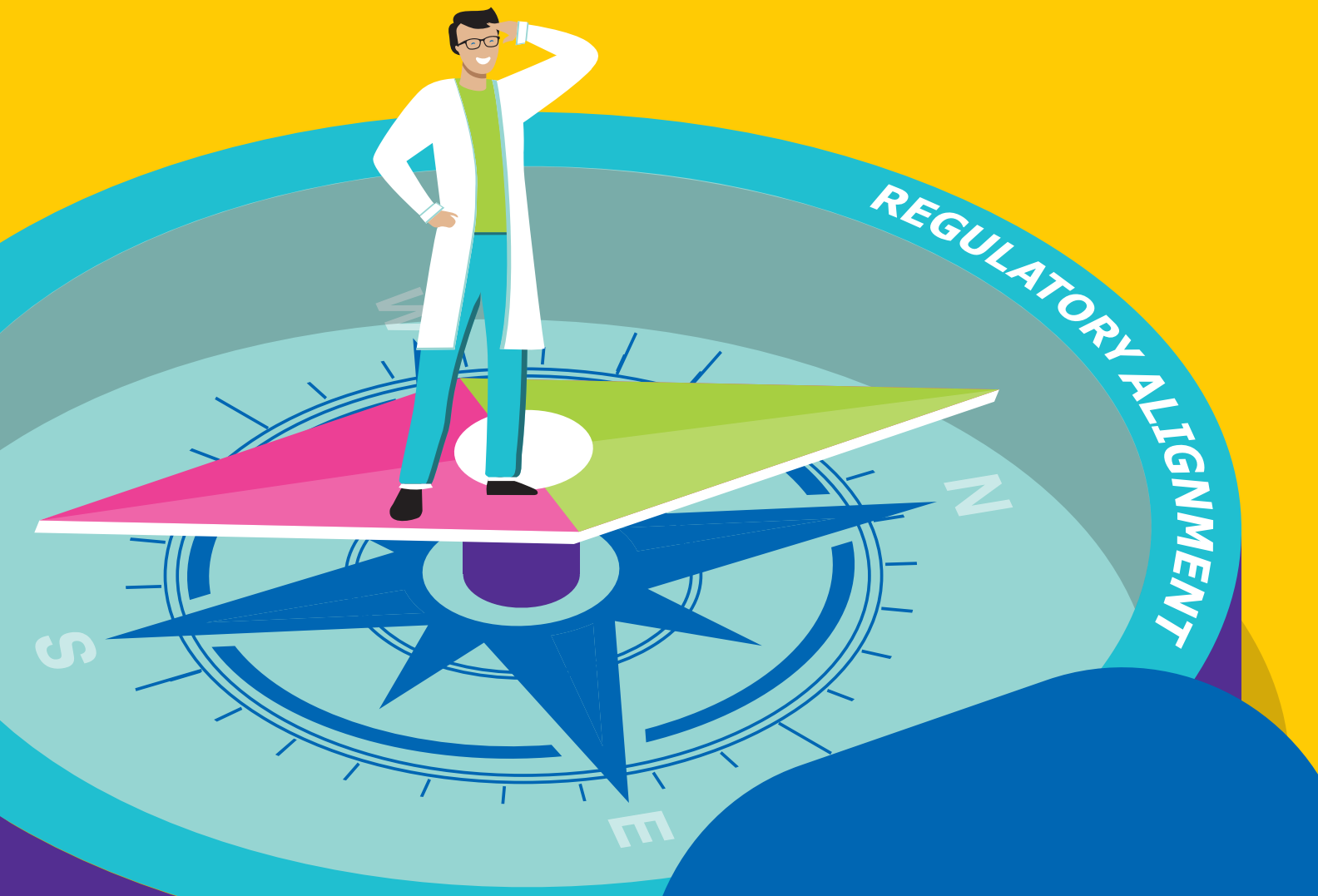
Validation Services: Discover an Easier Way

Align with Regulatory Guidance by Relying on our Expertise and Experience



Millipore®

Preparation, Separation, Filtration & Monitoring Products

Validation Services for You: Manage Process Risks

Regulatory guidance documents provide a framework to manufacturers for the production of drugs that are safe for administration to patients. Drug manufacturers must demonstrate that production equipment is not reactive, additive or absorptive so as to affect the safety, identity, strength, quality or purity of the drug product.

You can benefit from our deep product and process knowledge, proven methods and established protocols to develop robust scale-down models that can be tested under your worst-case process conditions.

Our Validation Services team provides project management support and access to a team of experts, dedicated to ensuring reliability, who can help you throughout the validation process.

Whether your focus is alignment with global guidelines or you need consultative expertise to implement compliant, robust and effective validation strategies, partner with us for:

- Understanding of the most recent quality and regulatory standards
- Technology leadership with almost 50 years of experience in pharma/biopharma filtration
- Industry recognition as a pioneer in the validation of critical sterile filtration systems

Our Comprehensive Validation Offering Guarantees You an Easy Path Forward

As the validation pioneer, we have the expertise to develop your critical validation studies:

1987
First filter supplier to deliver validation service

5
labs around the globe

800+
bacterial retention tests per year

1,000+
E&L evaluations per year

Our streamlined process and simplified price structure make it easy to find the services and level of support you're looking for including:

- Extractables & Leachables Safety Evaluation
- Bacterial Retention Testing
- Filter Integrity Testing
- Chemical Compatibility Study
- Consultancy

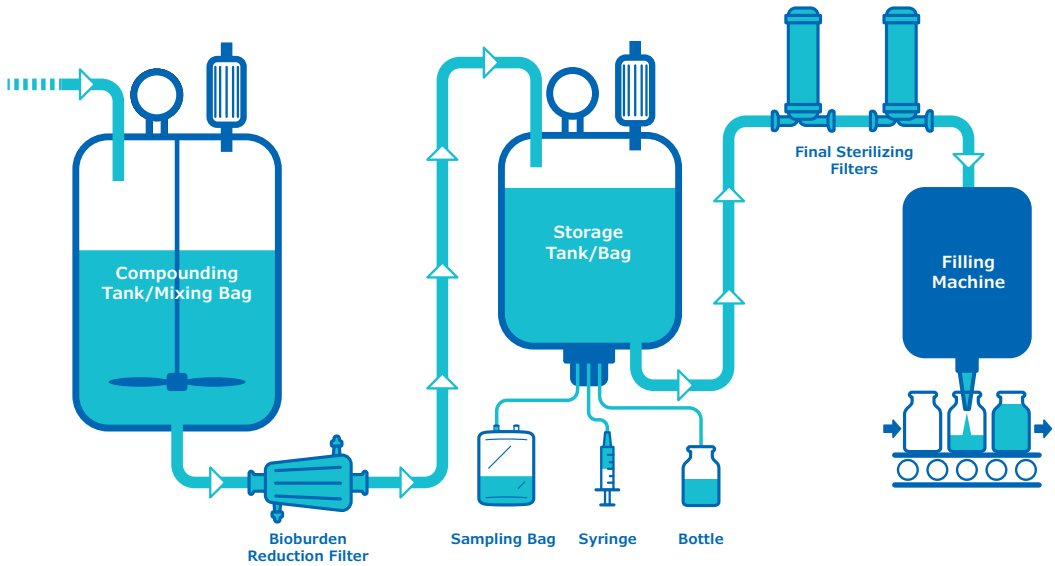
You select your path: simplicity and convenience, or flexible optionality. Either way, you'll feel confident throughout your process validation.

Discover an Easier Way to Choose the Right Validation Services

Upstream to the Compounding Tank/Mixing Bag
- Chemical compatibility
- Extractables/patient safety

Final Storage Single-Use Assembly
- Chemical compatibility
- Extractables/patient safety/leachables
- Non-permeation test

Final Sterilizing Filters and/or Single-Use Assembly
- Bacterial retention validation
- Bubble point/diffusion determination
- Chemical compatibility
- Extractables/patient safety/leachables
- Binding study
- Particle shedding study
- Vmax™ confirmation i.e. filter fouling evaluation



Bioburden Reduction Filter
- Chemical compatibility
- Extractables/patient safety
- Bubble point/diffusion determination

Sampling System
- Chemical compatibility
- Functionality test
- Non-permeation test

Regulatory Guidance
Recommendation, based on the pharmaceutical application and risk assessment

We partner with you to implement a compliant, robust and effective validation strategy.

Extractables & Leachables

Discover an Easier Way to Show That Plastic-Product-Contact Materials Do Not Adversely Affect Patient Safety

As single-use technology is increasingly used in drug production, industry associations have developed standard test protocols for assessing extractable and leachable (E & L) compounds from contact surface materials in drug product manufacturing.

Aligned with these industry best practices we can help you adopt a risk-based approach to assess E & L:

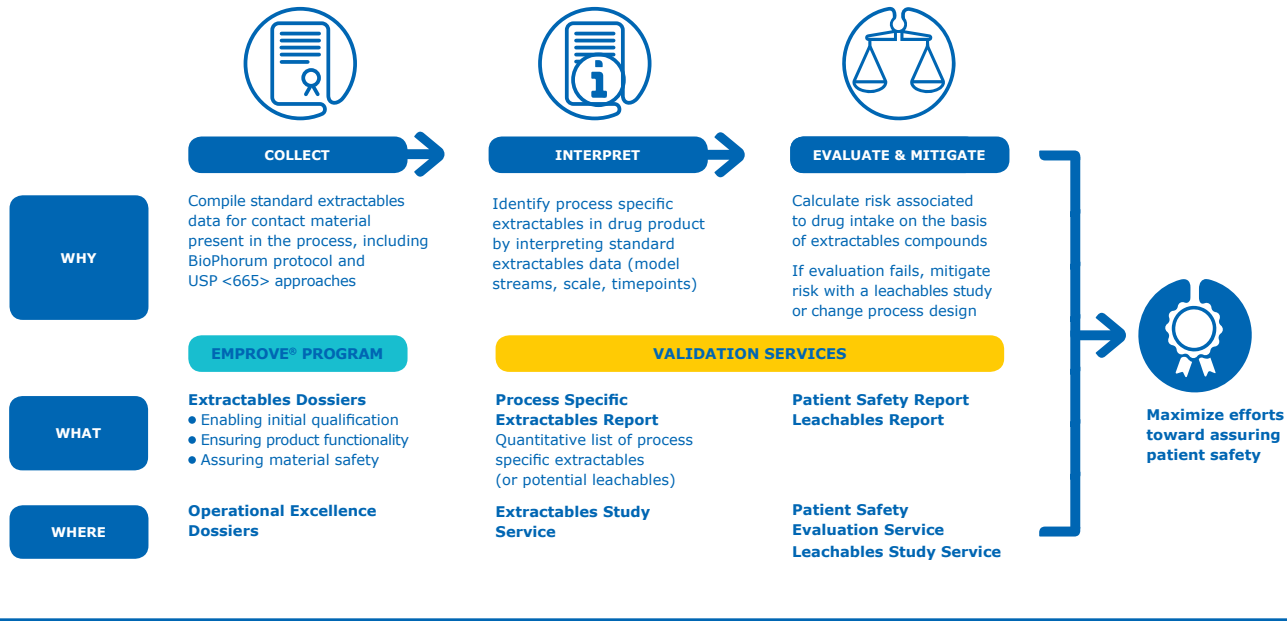
1. First, we perform a safety evaluation based on worst-case conditions:
   - We provide standard extractables data: We have developed an extensive library of standard extractables data, available on request
   - OR, if necessary, we perform studies designed for your process and system (e.g., lipid formulation, high organic concentration)
2. If there may be some risk, we perform a second safety evaluation on the basis of leachables — this second step considers actual process conditions

Discover an Easier Way to Access Standard Extractables Data: Emprove® Dossiers

The Emprove® Program contains over 400 raw and starting materials, and approximately 50 product families covering filters, single-use components, and chromatography resins. Each product portfolio is supported with Emprove® Dossiers which provide comprehensive, up-to-date documentation to help you navigate regulatory challenges, manage risk and improve your manufacturing processes.

The Emprove® Operational Excellence Dossiers for filters and single-use systems provide standard extractables data that align with industry standards such as the relevant BioPhorum protocols and USP general chapter.

An Easier Way to Achieve a Seamless and Robust E&L Assessment



Bacterial Retention Testing

Discover an Easier Way to Test Filter Performance

Confirming the bacterial retention capabilities of sterilizing-grade filters is a critical element of filter validation, and is outlined in global regulatory guidance documents for aseptic drug manufacturing.

We perform bacterial retention testing with a scale-down model under worst-case process conditions using at least one membrane at or near the minimum integrity specification.

Brevundimonas diminuta (*B.diminuta*) is the standard test microorganism, although we can evaluate other strains on request. Complete retention of the test organism confirms sterilizing-grade performance of your filter.

Bacterial Retention Testing by our Validation Services Team Aligns with Worldwide Regulatory Guidance and Industry Standards

- FDA Guidance on Sterile Drug Products Produced by Aseptic Processing
- European Union, Japan and China Good Manufacturing Practices
- Parenteral Drug Association's (PDA) Technical Report 26
- Aseptic Processing of Health Care Products ISO 13408-2

Filter Integrity Testing

Discover an Easier Way to Establish Your Product's Filter Integrity Test Specification

The integrity of your critical sterilizing filter should be tested before and after use.

The Certificate of Quality lists minimum integrity test specifications for the filter wetted with a standard fluid such as water or alcohol. To minimize delays in production, many manufacturers use filter bubble point values specific to the product being processed. We can help determine the minimum integrity test specification for

- filters wetted with your drug product
- filters wetted with your drug product and rinsed with a specific fluid

Chemical Compatibility Testing

Discover an Easier Way to Evaluate the Compatibility of Product Contact Components

Selecting and qualifying a filter or single-use assembly means evaluating the physical compatibility of all components in contact with your drug product including filters and single-use systems. These should not be reactive, additive or absorptive with your drug product. All filters and single-use systems used in your manufacturing process must be shown to be fit for use, compatible with your process and not reactive, additive or absorptive when confronted with your drug product.

In alignment with global GMP guidelines, we assess:

- Filter and single-use assembly materials
- Process fluid composition
- Process conditions
- Regional and intended market regulations

Chemical compatibility studies can range from a compatibility report based on existing data to testing the filter devices and comparing product performance before and after exposure to your product under your processing conditions.

Validation Services Consultancy

Take Advantage of our Global Team of Experts

With Validation Services available through an expansive, global network of laboratories and in-country/in-region experts, you can access rapid-response local assistance wherever you need it.

Our validation experts will develop a comprehensive validation strategy, aligned with the regulatory guidance for the countries in which you manufacture and market your drug product. We will determine:

- The right services needed for your quality risk management
- The right validation plan to optimize studies

We tailor our response, dependent on your needs, supporting all our filtration devices, single use components and assemblies.

Strategically Located, Harmonized Validation Services Provide the Support You Need

Discover an Easier Way to Global Regulatory Alignment

Validation can involve many steps. Selecting the right validation package, aligned with global regulatory guidelines, can be a challenge.

New, Streamlined Ordering and Pricing for Better Value and a Better Experience

Our streamlined process and simplified price structure make it easy to find the services and level of support you're looking for, all with our product management support keeping you informed about lead times and report dates.

You benefit from:

- A simpler way to order the right validation services
- A partner that will ensure the validation services are aligned with the most up-to-date quality and regulatory standards
- The right level of service for your needs, including customized solutions when desired

Choose the Classic or Advanced Package

Our two predefined service levels can help determine the level of service you need. Whichever you choose, Merck validation experts will be with you at every turn.

Classic

Rely on us for guidance. We'll do what's required to get your validation study done — with the highest quality standards.

Advanced

Let's collaborate. We'll discuss your specific requirements and customize a validation plan for more complex studies.

	Classic	Advanced
Satisfies Applicable Global Regulatory Expectations	•	•
Regulatory Query/Inquiry Assistance	•	•
Online Support	•	•
Call-in Support from Project Management Team	•	•
Test Customization[1]	—	•
Bacterial Retention and Compatibility Study Conditions	Process duration 48hr max Cold and room temperature	Maximum process duration Maximum process temperature
Extractables Study Conditions	Standard model streams in accordance with industry guidance	Custom
Integrity Testing	1 product lot	3 product lots
Templated Documentation	•	—
Customized Documentation	—	•
Documentation Revision	1 on specific fields[2]	Up to 3 on full document

1 Classic testing covers a predetermined range of process conditions with defined study parameters. Advanced testing provides a higher level of customization, including process conditions, additional test equipment/resources, and more complex study requirements.

2 Drug product & process information fields

Millipore®

Preparation, Separation,
Filtration & Monitoring Products

Merck KGaA
Frankfurter Strasse 250
64293 Darmstadt, Germany

Request a quote:
SigmaAldrich.com/sufiltervalidation

sigmaaldrich.com/sufiltervalidation

Email: **info-validation@merckgroup.com**

MK_BR7456EN Ver. 4.0
46951
07/2023