

## Data Sheet

# Provantage™ Lab Services

## Validation and Qualification of Disposable Assemblies in Bioproduction Processes

The pharmaceutical industry has seen an increased adoption of single-use technologies in a wide array of unit operations. Although the drivers for this adoption are numerous, there are also a few hurdles which need to be overcome to ensure a successful implementation. Among these, Leachables and Extractables concern is cited as the first factor that may restrict the use of disposables in biopharmaceutical manufacturing.

The use of plastic components in direct contact with the drug product batch is perceived as a threat—proven or not—to the process robustness and to the drug product quality. It does not constitute a roadblock and can be overcome by having an appropriate validation and qualification program based on risk assessment and risk management to demonstrate that all potential risks have been identified, taken into account, evaluated for their impact and mitigated or prevented.

**Typically, the risks encountered on a drug manufacturing process can be classified into 3 major areas:**

1. Risks associated to equipment and/or utilities
2. Risks linked to the environment
3. People-related risks

An efficient and optimized process validation strategy needs to cover and look at these 3 sources of risks using guidance, framework provided by regulations and recommendations to see how these could potentially impact the process.

The most common sources of concerns within a given process or potential failures observed are

- Sterilization/decontamination failure
- Cleaning failure
- Storage issue
- Transportation issue
- Mishandling
- Process design issue
- Process performance issue
- Sensitivity to extreme operating parameters

These potential risks have to be assessed during process validation and if needed, appropriate validation and qualification have to be performed to show the risks are being managed.

Since Merck Millipore products are key components of your production processes, their performance related to all mentioned aspects should be demonstrated whenever a risk has been identified.

Provantage™ Lab Services Laboratories can provide you with the expertise, knowledge, methodologies and lab testing capabilities to go through this validation and qualification process.

The strategy for managing a risk involving equipment is specific to a given "process / drug product / equipment" combination. Therefore, the variety of validation and qualification studies is broad and need to be adequately adapted to the risk – nature, occurrence, impact, detectability.



# Some examples of services performed to address our customer's risk include:

## Process design

- Selection and validation of the most appropriate single-use component or assemblies for specific customer process conditions: sterile connectors, sterilizing grade filters, tubing types and materials, disposable bags.
- Determination and validation of the most appropriate single-use assembly design and SOPs to handle specific customer constraints (rinsing efficiency, hold up volumes, etc.)
- Sampling plan design and sampling method qualification (NovaSeptum® Sampling System)

## Process performance

- Consultancy Services
  - Process performance qualification protocol design
  - Extractables and leachables risk assessment
  - Media fill protocol design
- Single-use filter performance
  - Bacterial retention validation for a sterilizing-grade one
  - Bioburden reduction study for others
  - Integrity testing qualification
- Single-use assembly performance
  - Extractables and Leachables study
  - Chemical compatibility study
  - Adsorption/binding study
  - Particle shedding study
- Viral clearance validation services

## Impact of extreme operating parameters — "design space" definition

- Qualification of extreme process parameters conditions (temperature, pressure, chemical compatibility, etc.) on single-use assemblies beyond manufacturer's specifications

## Equipment and process lines sterilization/decontamination

- Custom single-use assemblies sterilization validation
- Impact of customer sterilization/decontamination processes onto single-use assemblies and components (sterilizing grade filters, sterile connectors)

## Equipment and process line cleaning

- Single-use assemblies flushing and rinsing studies
  - Determination of pre-flush volume for extractables elimination
  - Filter post use rinsing volume determination
  - Filter post use integrity testing determination
- Bioburden reduction studies

## Drug product storage

- Single-use assemblies accelerated aging studies in customer storage conditions
- Qualification of sterility hold during process standby in single-use assemblies
- Qualification of in-process container closure integrity (single-use assemblies used as storage containers)
- Qualification of non-permeation to disinfectant applied prior to storage on single-use assemblies
- Single-use assembly performance: Extractables and Leachables study, chemical compatibility study, adsorption/binding study, particle shedding study

## Drug product transportation

- Single-use assemblies shipping studies in customer transportation conditions
- Qualification of drug product/sample transportation conditions in single-use assemblies

## Equipment and drug product handling

- Operator training and certification programs

Current industry and regulatory authorities recommendations advise that any validation or qualification project should start with a risk assessment. We can help you assess the risks to your drug product and production process.

The aim of our services is to demonstrate that our products and technologies that are working with your drug product within your specific process conditions are reliable, robust, efficient and provide the highest performance. Achieving this objective is a joint effort where we work hand in hand with you to exchange information and define most efficient validation strategy.

Our range of validation & qualification expertise and capabilities covers our technologies that are used at different steps of your production process. From

upstream through downstream purification steps to final fill and finish, we can meet your validation and qualification needs that use any of our products and technologies.

We are also able to adapt our Validation and Compliance Services offering to the needs and constraints of your current drug development step. We can guide and advise you on the Validation and Qualification scope to meet regulatory requirements while mitigating your production process risks.

Provantage™ Lab Services network and capabilities allows us to share information and experiences with more than 70 of our experts around the globe and provide consistent and best in class services for global customer projects.



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