

Validation Center

Version 7.1



Liquid & Gas Filtration

For Microelectronics, Pharmaceutical, Fine chemical,
Food and Beverage Industries

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Validation Center

Cobetter Validation Center is committed to providing customers with complete solutions to their various filtration problems. Our Validation Center is divided into: Biopharmaceutical Validation Laboratory and Industrial Laboratory.

The Validation Center with more than 8 Japanese experts and 30 engineers, provides more than 1200 process validation reports for pharmaceutical companies and 1300 technical reports for life science customers annually.



Validation Services

- Microbiological Challenge
- Extractables and Leachables
- Chemical Compatibility
- Product-wetted Integrity Test
- Customized Filtration Solutions
- Filtration Process Optimization
- Ultra-filtration Applications and Filtration Parameters Optimization
- Particle Distribution And Efficiency Testing
- Pollutant Analysis

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Filter Validation Guide

Critical Sterilizing- Grade Filters Validation is as recommended by:

Parenteral Drug Association (PDA) Technical Report 26(2).

Revised 2008/2013: Sterilizing Filtration of Liquids, Supplement to the PDA Journal of Pharmaceutical Science and Technology, Vol 62, No. S-5, Parenteral Drug Association, Bethesda, MD 2008.

See detail below table;

Sterile filter for	Item	Products which can not be sterilized in final container	Sterile filter for terminally sterilized products
Sterilizing Filter selection for each type (Filter manufacturer)	Bacteria retention in water or saline lactose broth (SLB) with integrity test correlation in water or solvent	Recommended	Recommended
	Extractables Analysis	Recommended	Recommended
	Raw Materials Biosafety	Recommended	Recommended
Sterilizing Filter selection for each lot (Filter manufacturer)	Bacteria retention in water or saline lactose broth (SLB) with integrity test correlation in water or solvent	Recommended	Recommended
	Integrity test	Recommended	Recommended
	Sample Inspection e.g. pH ,Bacterial Endotoxin , TOC and Cleanliness	Recommended	Recommended
	Thermal Resistance Test	Recommended	Recommended
Process Validation	Bacterial Retention	Required	Optional
	Extractables	Required	Required
	Chemical Compatibility	Required	Optional
	Integrity Test	Optional	Optional
	Absorption	Evaluate	Evaluate

From new Drugs GMP Guidelines

[Sterilizing-Grade Filters Technology and Application Guide]

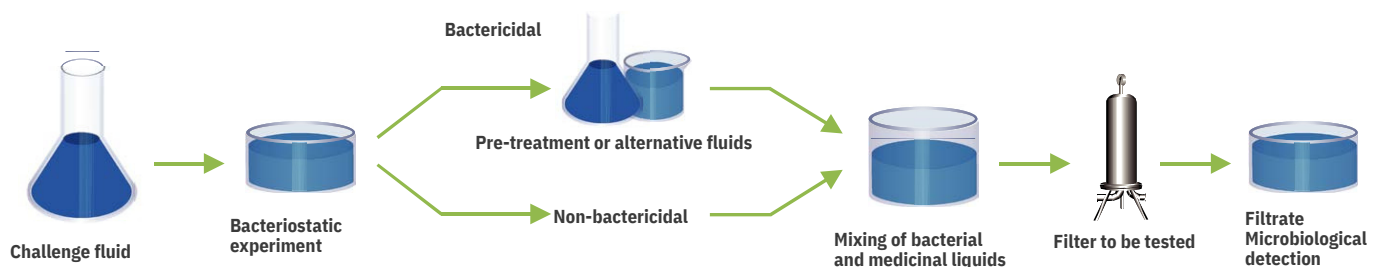
Remarks: Liquid sterilizing-grade filters should be discarded after each lot. The same filter should not be used for more than one working day unless it has been validated

Microbiological Challenge

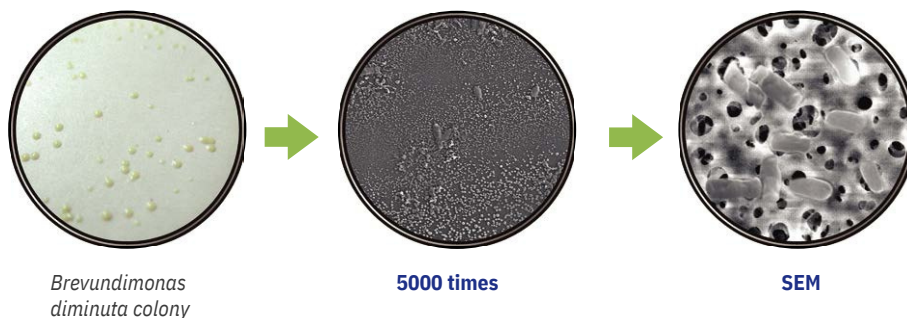
- A sterilizing-grade filter is a filter capable of retaining 107 CFU/cm2 of *Brevundimonas diminuta* (*Brevundimonas diminuta* ATCC 19146) of the effective filtration area under the process conditions
- Microbiological challenge is the only way to confirm if the filter is sterilizing grade



■ Microbiological Challenge Basic Process



■ Microbiological Challenge Process Analysis



We will evaluate the impact of your products and processes on the challenged bacteria and provide customized solutions where applicable

Extractables Overview

OVERVIEW

■ Extractables

Refers to chemicals that migrate from any product contact material in an appropriate solvent at a time and temperature exceeding the worst process conditions

■ Leachables

Refers to chemicals that migrate from any product contact material to the product under actual process conditions
Leachables are present in final drug, usually a subset of the extractables

■ Leachables Evaluation Process



■ Leachables Analysis Method

Non-specific Analysis	TOC	Specific Analysis	HPLC	FTIR	GC
	NVR		GC-MS	LC-MS-HPLC	

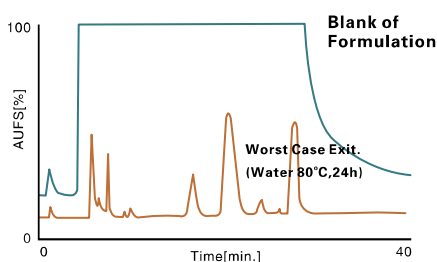
Leachables Experiment Case

Extractables /Leachables analysis of the filter element when there are obstructive substances in pharmaceutical solutions

■ Reagent: 95% ethanol 5% polystyrene

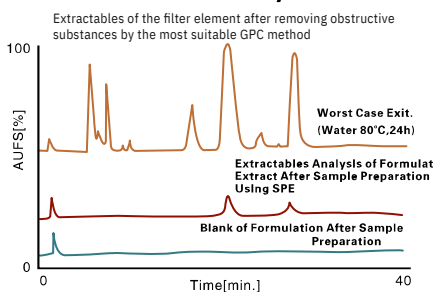
■ Process Conditions: 50°C, 60H Oscillating dissolution

RP-HPLC Analysis



- Polystyrene overlaps with all normal Extractables
- Result: Extractables cannot be analyzed at this point

RP-HPLC Analysis



- Sample Pre-treatment: Remove polymer polystyrene by GPC
- Result: Two types of Extractables were detected in the leaching substance of filter core



We use your liquids and process conditions to analyze leachables

Chemical Compatibility Analysis

In the filter selection stage, we need to verify that the filter is compatible with product being filtered



The chemical compatibility can be quantified and visualized by testing the performance parameters and microstructures, which makes the selection of filter element easy and effective

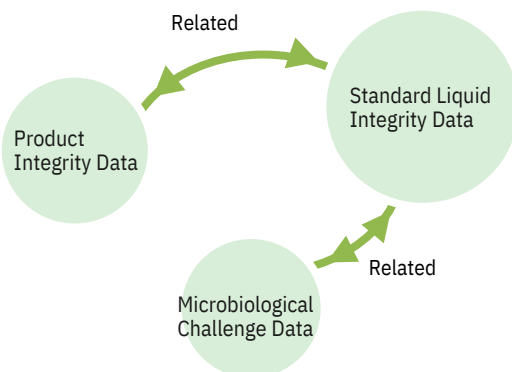
Chemical Compatibility

Filter	Membrane	Support	O-ring	Liquid Medicine
				
Appearance	Appearance	Appearance	Appearance	Appearance
Bubble Point	Tensile Strength		Size	
Diffusion Flow	Flow rate		Weight	
Flow RateSEM	Thickness			

Chemical Compatibility is the basis for all validations; Chemical Compatibility requires a comprehensive evaluation method

Product Integrity Data

In general, product integrity testing can simplify our operations

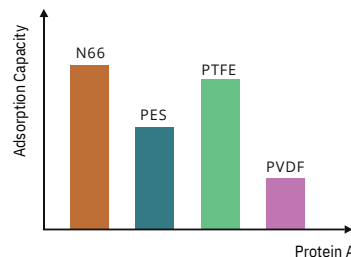


Only by establishing the correlation between integrity and microbiological challenge, you can monitor the filter's sterilization performance by monitoring the integrity of the filter, and your integrity test becomes meaningful.

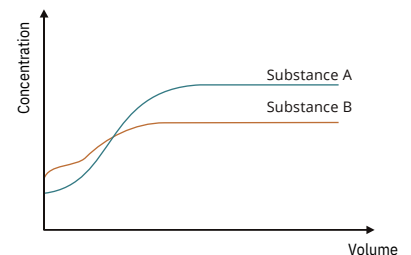
Product Adsorption Analysis

In the production of the product, we need to know whether the product adsorption has an impact on our finished products

Membrane Adsorption Comparison Values



Filtrate Concentration Curve



Provides an accurate adsorption analysis to help minimize the loss of active ingredients