Filter Qualification in your Process
Remove the barriers to successful validation
Step by Step Support to Process Improvement

Qualification of Parker domnick hunter filters within your process can be carried out to meet both regulatory and customer requirements in eight simple stages.

Through our dedicated team of professionals we aim to understand the challenges and opportunities you face in meeting current and future performance goals and work with you to find solutions that will add value to your manufacturing process.
Remove the Barriers to Successful Validation

Matching resource to your requirements

Supported by state-of-the-art technical facilities and a specialised international team of dedicated engineers and scientists, Parker domnick hunter is committed to supporting your validation process.
Developing partnerships
We work with you to establish the most effective filtration solution for your process based on your goals and desired process improvements including:

- Minimising product loss
- Reducing downtime
- Increased yields
- Reduce over processing
- Guarantee sterility
- Minimising risk to your process
- Extending service time
- Promoting best practice

Once the correct filters have been chosen, Parker domnick hunter work closely with you to qualify the use of our products within your process.

Development of an application specific strategy
Our Technical Group use your identified parameters to determine the whole qualification package required. This demonstrates that our filters are capable of meeting the performance goals required of your process.

By following simple step by step guidelines outlined by PDA Technical Report No. 26 [Sterilising Filtration of Liquids], we can eliminate any disruption to your business whilst achieving your long term process improvements.

Test work is carried out by our experienced team of scientists and engineers at our excellent test facilities where we are committed to conducting qualification test work on your behalf.

Meeting the standards
Global investment programmes have created first class R&D, manufacturing and support facilities across the world. We are committed to industry standards including:

- PS 9100:2002 - Pharmaceutical Excipients
- ISO 14001:2004 - Environmental Management
Qualification Process
Taking the right steps

Parker domnick hunter follow established scientific recommendations and guidelines recognised as being best practice for sound filter qualification protocol*.

A structured approach to filter qualification

The qualification process can be separated into 8 simple steps which allow confidence in the necessary filter performance. These are applicable, but not limited to, cell culture media, buffers, intermediate aseptic processes and bulk and final sterile filtration.

- Filter selection and sizing
- Development of specific validation strategy and protocols
- Challenge organism viability assessment
- Determination of product wet integrity test values
- Filter conditioning and compatibility testing
- Bacterial challenge in product or surrogate fluid
- Analysis of filter extractables
- Final documentation
Making the Right Choice
Filter selection and sizing

To meet your current and future expectations, we work with you to define your process requirements and select the appropriate membrane materials and system size.
Assess / Review current manufacturing process
We will conduct an on-site consultation of your current filtration train and review any other factors that may have an adverse effect on filter performance. This helps us to identify areas for further improvement and allows us to make best practice recommendations in terms of maintaining product quality, installation operation with appropriate levels of monitoring and control.

Identify future performance targets
Our experience can help to identify key operational areas where there is scope for improvement. We focus on the specific goals that your organisation has identified as key to current and future process development, including:

- Regulatory changes
- Capacity changes
- Product loss
- New product and packaging developments
- Quality requirements
- Financial goals
- Move towards disposable manufacturing
- Faster processing time

Match products to performance criteria
When selecting the appropriate filter system or membrane it is important to consider the following to ensure optimal performance;

- Bacterial retention/ retention efficiency
- Required flow rate
- System size
- Ability to be sterilised
- Disposable manufacturing
- Cleaning / reuse requirements
- Physiochemical interactions of the filter in the product
  - Adsorption
  - Compatibility
  - Potential leachables / extractables safety
- Batch volume
- Product loss
- Operational ranges
- Regulatory compliance

Live on-site testing or small scale process simulation
Testing can be carried out on-site or at our dedicated laboratory facility where small scale process simulation such as Vmax, scale-up, binding studies, dimensional stability and integrity testing, can be carried out directly on your product by our dedicated team of scientists.
Developing a Qualification Strategy
Made to match your process

We tailor strategy and protocols directly to your application, which enables us to seamlessly incorporate our products into your process.
Developing an agreed strategy
Consultation is carried out between our process specialists and your quality and production teams to assess the outer limits of your process. This is carried out through a series of interviews and questionnaires which define your qualification requirements.

At this stage we will agree the component parts within your filter validation strategy including:

- Ownership
- Time-scales
- Volumes of product required
- Worst-case conditions
- Simulation scale
- Scope and extent of testing

Our experience within this field allows us to develop protocols based on previous qualification work undertaken with fluids of a similar make-up, which have been accepted within the industry. This allows us to reduce and simplify the qualification process for your application whilst identifying and removing potential problems before they arise.
Challenge Organism Viability Assessment

Matching the bacterium to your application

Simulating real life risks to your product allows us to establish genuine threats faced and the ability of the filter to confidently remove them.
Challenge organism selection criteria
Historically *Brevundimonas diminuta* has been used to rate sterilising grade filters at a concentration in excess of $10^7$ organisms per cm$^2$ of Effective Filter Area (EFA) with testing carried out following ASTM F838-05 test methodology.

It is important to determine if the standard challenge organism is viable in the process fluid for the exposure time required, simulating the expected period of filter use.

Where organisms are non-viable, alternative organisms or surrogate process fluids may be recommended. We have developed a risk based approach to organism selection based on the natural bioburden contained within your process fluid to make testing with standard organisms relevant to your process. In bactericidal fluids, active ingredients may be removed to simulate process conditions or an inert carrier can be substituted.

Testing is carried out by our Laboratory Support Group in our dedicated bio-containment facility. We inoculate your product and assess challenge organism viability over a designated time period. Naturally occurring bioburden can also be isolated and identified at this stage.
Minimise the Steps
Process preparation and integrity testing

Providing test parameters will give you Pass / Fail criteria unique to your product minimising the amount of disruption and product loss, providing greater control and accuracy.
Parker domnick hunter can correlate our integrity test parameters to supply you with test conditions providing ease of use and validated parameters for your product. This testing will enable you to minimise the number of steps in your production process including:

- Water wetting of the filter
- Solvent flushing
- Drying / water removal or purging
- Validation of the above stages on active ingredients

The process
Parker domnick hunter take filters from separate manufacturing batches for analysis during this test. The filters selected represent operating specification extremes to provide worst case performance scenarios.

The test filters undergo a series of stages to determine their mean diffusional flow and bubble point values when wet in water. The product performance is then assessed with the test filters wet in your product providing accurate assessment of the effects of changing surface tension and diffusion constants. Establishing the ratio between water wet testing and product wet testing determines new values for integrity test pressure, diffusional flow and bubble point.
Filter Conditioning
Simulating your process

Small to full scale simulation of your process recreated for true and accurate assessment of our filters to give you complete confidence in performance.
Parker domnick hunter’s team has access to specially designed simulation test rigs and analytical equipment to provide an accurate simile of your process under laboratory conditions. This provides an accurate measurement of how our filters will perform under extreme process variables giving you complete confidence in how Parker domnick hunter’s filters will work with your product and the performance benefits they may bring.

Our Process Simulation Test Rigs (PSTR) conduct a range of tests including:

- Long term contact studies
- Cyclical steam testing
- High pressure pulsing
- Forward and reverse collapse or burst pressure
  - CIP Chemical cleaning simulation
  - Extreme temperature exposures
  - Retention efficiency studies
- Flow rate performance
- Filter lifetime
- Pressure drop
Bacterial Retention
How will the filter perform with your product

We recognise that each customer has a unique product which has the potential to react differently with the challenge organism or selected filter. Bacterial challenge testing allows us to provide a unique qualification to be tailored to you.
Bacterial retention studies in product or surrogate fluid gives us accurate analysis of how a diminutive organism will respond in a given fluid which may have a direct impact on cell size and therefore, the filter’s retention capability. Typical change factors may include:

- Osmolarity
- pH levels
- Growth factors
- Antimicrobial effects
- Temperature
- Ionic strength

The filter may also be influenced by its interaction with the product, for example by surface tension altering from standard test fluids. These studies allow us to assess any impact on the process through a possible change in retention and efficiency. Typical factors may include:

- Time in service
- Clean-In-Place (CIP)
- Steam-In-Place (SIP)
- Batch size
- Viscosity
- Flow rate
- Operating pressures
- Pre-filtration stages
- Surface tension
- Presence of surfactants
- Natural bioburden

When carrying out a bacterial challenge test to rate our 0.2 micron sterilising grade filters, Parker domnick hunter follow strict guidelines laid out in ASTM F838-05.

PDA technical report No. 26, Sterilising Filtration of Liquids recognises that the ASTM standard represent worst case scenario, however, it can not re-create process conditions which is why Parker domnick hunter carry out extensive process testing that may include:

- Continuous process simulation with live challenging which can range from 24 hours to several months
- Pre-conditioning of cartridges
- Challenges in surrogate fluids (with active ingredients or bactericidal components removed)
- Extreme pressure, pulsing simulating blockage
- Extended contact
Analysis of Filter Extractables and Leachables

Policing undesirable content

It is a pharmaceutical regulatory expectation that filter users investigate, minimise and remove (where possible) the level of extractables (soluble material) within the manufacturing process.
Ensuring product safety

Parker domnick hunter meets strict industry guidelines for ensuring toxicity, animal derived materials and bio-compatibility of our products, however, we also take several samples of product which we expose to the chosen filters. The initial filtrates are then captured for analysis using a range of analytical techniques to match your requirements.

An extractable is a chemical removed from the material by an artificial or exaggerated force e.g. solvent, temperature or time.

A leachable migrates from the contact surface into the process fluid during normal use. Parker domnick hunter carry out several procedures to ensure product safety at all times.

Our standard testing includes Attenuated Total Reflection – Fourier Transform Infrared (ATR-FTIR). Testing is performed to ensure that the extractable materials from the filter are within acceptable limits when subject to worse case operational conditions.

Analysis of active ingredient

Samples of product can be returned for analysis using your standard QC methodologies to ensure conformance to your specification when tested to your protocols.

More advanced techniques

Once filter extracts are retrieved the total amount and identity of the filter derived materials can be determined through analytical methods. These include:

- Reverse phase high performance liquid chromatography (RP-HPLC)
- Liquid chromatography with mass spectroscopy (LC-MS)
- Gas chromatography with mass spectroscopy (GC-MS)