Biopharmaceutical Filtration Validation

A Perspective on Regulations and Business Risk

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Many aspects of filter validation performed in biopharmaceutical companies are necessary and required by the FDA or other governmental regulatory agencies. However, a survey of current regulations and biopharmaceutical industry practice reveals a sharp distinction between filter validation steps required by regulation and qualification practices that are strongly advisable primarily on the basis of reducing business risk, but not mandated by regulation.

Here we call attention to biopharmaceutical manufacturing stages for which CGMP regulations do and do not apply. We suggest to biopharmaceutical companies that unnecessary filter validation practices can be curtailed at many stages of biopharmaceutical process development. This can benefit a company through savings in cost and time-to-market.

Product Focus: Biopharmaceuticals

Process Focus: Downstream process development

Who Should Read: Process development, QA/QC, and manufacturing/production management

Keywords: CGMP, validation, qualification, filtration, risk management, aseptic and nonaseptic operations

Level: Intermediate

Validation or Qualification?

Many people in the biopharmaceutical industry misunderstand distinctions between the need to validate a filtration process and the need to qualify a process component or raw material. Presently, there is no generally accepted demarcation between what constitutes a "validation" and what constitutes a "qualification."

Validation of a process unit operation or skid generally involves at least four steps: design qualification (DQ), installation qualification (IQ), operation qualification (OQ), and performance qualification (PQ). Validation is of an entire system in which a component or material such as a filter is used and generally includes filters, housing, valves, gauges, plumbing, tanks, and related hardware (Tables 1 and 2).

Validation is generally required for complete systems — often skid-mounted equipment performing a specified unit operation. CGMPs also require process qualification testing on the combined series of process unit operations steps.

Qualification of unit operation components is the foundation of any CGMP-validated unit operation. In filtration unit operations this involves testing and technical evaluation of filters, including performance evaluation of filter elements and materials. Filter performance testing is commonly accomplished by small-scale, fluid-specific, process-specific filterability testing and other tests.

Our focus here is on qualification and/or validation of filters in the biopharmaceutical industry. It emphasizes filter qualification: what it takes to get them qualified for use in a biopharmaceutical filtration process.

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The key findings in our survey of regulations and practices are that

- Many biopharmaceutical companies could reduce business risk by qualifying filters and eliminating needless validations.
- By restricting their filter qualifications to one or two vendors of a given filter, when several vendors are readily available, biopharmaceutical manufacturers unnecessarily restrict their choices and may seriously increase the costs of filtration in a given process.

Filter qualification, in contrast with filter validation, involves basic performance testing, either inline (which may be impractical) or offline

(in small-scale filterability test studies). Such small-scale tests permit comparative testing of multiple vendor offerings of similar types of filter materials, extrapolation to pilot- and production-scale systems, and projections of filtration costs for a given filtration process. Filter qualification testing can be performed during initial process development stages or again during engineering runs at the production-scale manufacturing stage.

Overvalidation

Numerous biopharmaceutical companies are overvalidating processes, applying full validations where in fact they are not required by CGMP or other regulation. In such cases, qualification measures would adequately measure and control business risks associated with a given process filtration step.

Our premise is that biopharmaceutical companies are manufacturers first. As such they should operate their processes as manufacturers, qualifying each component of their biomanufacturing processes — raw materials, components, and unit operations — and then applying CGMP requirements to those processes as necessary.

In observed cases of overvalidation, when manufacturers are uncertain whether or not to validate, they frequently decide to validate rather than to qualify. They do this either out of concern for possible regulatory inspection and compliance issues, or because "legacy validations" have been performed.

The impact of such overvalidation on the industry is considerable. Needless analytical and quality assurance procedures (with related paperwork) generate numerous hours of wasted effort. Time spent by the many people involved in validation could be far better spent on those processes that clearly require CGMP validations. Delays to development and manufacturing operations caused by excessive validations are difficult to measure. But for many companies, delays probably number in the months, with costs running into millions of dollars over the course of product development and manufacturing.

Taking a risk-based approach, in accordance with the growing impact of process analytical technology (PAT), minimizes and can eliminate the tendency to overvalidate. By recognizing the process stages at which CGMPs apply (Table 1) and applying filter qualification procedures where CGMPs are not specifically defined, biopharmaceutical manufacturers are adequately protecting their products, processes, and ultimately the public (patient), while eliminating costs and delays.

Filtration of various types (microfiltration, ultrafiltration, nano or virus filtration) is ubiquitous in biopharmaceutical manufacturing. Many aseptic processes require qualification of a filter as well as validation of the filtration system. However, many nonaseptic filtration processes do not require validation, yet they are being validated by numerous biopharmaceutical manufacturers.

Qualification and Validation Requirements

Tables 1 and 2 summarize filter qualification and validation requirements in the biopharmaceutical industry for aseptic and nonaseptic operations. Typical aseptic operations are WFI storage tank vent filters and formulation and fill/finish filters. Typical nonaseptic operations are downstream purification and viral filters. To manage, control and minimize business risk, it is important to differentiate between processes and systems, which must be validated according to CGMPs, and components, which should be qualified.

All biopharmaceutical manufacturing processes require careful attention, good technique, and judgment. But a heightened awareness of the need to qualify (rather than validate) filters will increase opportunities for managing business risk and open the door wider to better cost control while meeting a manufacturer's responsibility for business risk-management.

Multisource Filter Qualification

Basic flow decay studies (filter-plugging on a small scale, used for extrapolation to pilot or production scale filter systems) can predict process filtration specifications, performance, and economics with a given biopharmaceutical fluid.

Based on its filterability test performance, filter material providing the lowest cost per liter should be selected, provided that other important parameters are met. They include absolute retention, low extractables, low protein-binding, and chemical and thermal compatibility with the product and process.

Sizing of production-scale filters is based on filterability testing using the biofluid involved and calculations of filtrate normalized to filter surface area (e.g., L/m^2).

When qualifying filters, it is best to qualify a minimum of four or five at once for a given application, provided that the filters are constructed of the same materials. Filtration costs are increasingly scrutinized in the industry, and two important issues have arisen.

Flexibility and Vendor Selection: By qualifying only one or two vendors, biopharmaceutical manufacturing operations unwisely restrict their consideration of available technologies. Specifying filtration processes around the products of only one or two vendors can lock end users into a limited choice

Table 1: Qualification requ irements for aseptic and nonaseptic filters

Filtration Types	Nonaseptic Filters			Aseptic Filters		
Process Stage	Animal Toxicity Studies	Phase 1/2	Phase 3/ Commercial	Animal Toxicity Studies	Phase 1/2	Phase 3/ Commercial
Step 1 Engineering Qualification						
Small-scale sizing/ performance	NR/BR[1,2]	NR/BR	NR/BR	NR/BR	NR/BR	RR
(For viral filtration only)	NR/BR	RR[3]	RR	—	—	—
Compatibility testing of filtrate and membrane	NR/BR	NR/BR	NR/BR	NR/BR	NR/BR	RR
(For viral filtration only)	NR/BR	RR	RR	—	—	—
Step 2 GMP Requirements						
QC visual inspection (company material specification)	NR	RR	RR	NR	RR	RR
Lot certified, traceability	NR	RR	RR	NR	RR	RR
Integrity testing	NR	NR	NR	NR	RR	RR
Filtrate bubble point ratio	NR	NR	NR	NR	RR	RR
Sterilization validation	NR	NR	NR	NR	RR	RR
Step 3 Membrane Qualification						
Bacterial retention	NR	VL[4]	VL	NR	VL	RR
Endotoxins	NR	VL	VL	NR	VL	RR
Protein binding	NR	VL	VL	NR	VL	RR
Extractables	NR	VL	VL	NR	VL	RR
Oxidizables	NR	VL	VL	NR	VL	RR
Bacteriostasis/fungistasis testing	NR	VL	VL	NR	VL	RR
Toxicity/biosafety	NR	VL	VL	NR	VL	VL
Non–fiber-releasing	NR	VL	VL	NR	VL	VL

[1] NR = No regulation
[2] BR = Business/processing risk recommended
[3] RR = Qualification required by regulations
[4] VL = Vendor's testing support data and literature

of filters and may not enable selection of the best-performing or most cost-effective products from those on the market. This unnecessary limitation of choices can present a significant business risk in terms of operating costs and availability of materials, regardless of supplier. In the event of a supply problem, an approved alternative vendor or two can guarantee uninterrupted supply of qualified filters.

Oversizing of Filtration Systems: To ensure continuity of batch processing, filter manufacturers tend to oversize filter systems. They do this partly out of conservatism, to prevent premature plugging, and possibly also out of a desire to maximize revenue. The cost of oversizing process filters can run to thousands of extra dollars per batch. This excess cost factor is generally recognized only on those rare occasions when a biopharmaceutical company changes vendors at production scale, and the new vendor provides a less costly, yet fully effective and regulatory compliant, filtration system.

Regulatory Guidance

Regulatory guidelines distinguish between *nonaseptic* and *aseptic* filtration. Although minimal regulatory guidance is offered for nonaseptic filtration in biopharmaceutical applications, good business practices should be applied. Regulations do state that a process must not introduce additional bioburden or virus. To fill this regulatory void, manufacturers conservatively apply well-documented aseptic processing guidelines. Unfortunately, this adds major costs without reducing business risk.

On the other hand, many guidelines exist for filtration and filter validation for aseptic processes. Refer to Table 3 for a comparison of the two types.

Nonaseptic Filtration

Filtration steps can be divided into three main objectives and purposes.

Reduction of Viable and Nonviable Particles: There is an important distinction between reduction and removal of viable and nonviable particles. For nonaseptic filtration steps, the key is particulate reduction, with no claim of sterility nor any claim of absolute removal of particles.

Bioburden/Virus Reduction: Bioburden reduction refers to reducing the level of viable particulates such as bacteria and other microorganisms. For this type of filtration operation, regulations may require the quantity of such undefined microorganisms to be reduced by several logs.

For example, virus retentive filters must be qualified by determining their log reduction of viral organisms in the biopharmaceutical fluid. Smaller viruses may penetrate virus filters, depending on the viral challenge level. There is an important distinction between absolute and nominal retention of virus by these filters. A four- to six-log reduction of virus particles can be achieved by virus filtration. However, the production capacity of these membranes is very limited because of their extreme tightness, low dirt-holding capacity, and low flow per unit surface area.

Nonviable Particulate Clarification and Reduction: For this application, as with bioburden/virus reduction, it is unnecessary to use absolute-rated filters. The bioprocessor makes no claim of sterility or complete removal of particles. No integrity test is required. From a business risk perspective, there is no need for integrity testing, and no justification for a more expensive sterilizing grade filter. The manufacturer needs only to reduce the risk from particles at this nonaseptic process step.

Nonaseptic Unit Operations

Downstream purification steps require many filters of different types. Filtration in downstream purification includes reducing viable and nonviable

particulates. One example is to reduce protein aggregates to prevent the plugging of chromatography resins, thereby protecting their effectiveness and service life.

Reducing viable particles reduces business risk. Microbial levels are controlled so that they are not carried into downstream process steps.

Tank Venting: Tank-venting filtration in nonaseptic operations is installed to prevent viable and nonviable particulate from contaminating product fluids. Filters rated 0.2 µm are generally installed. Frequently, quality assurance departments mandate an integrity test at various intervals, such as one, three, or six months. However, in this nonaseptic application, there is no FDA guidance or good business reason to perform an integrity test on the vent filter.

Buffers: If buffers are stored for extended periods, it is important to reduce their level of particulate matter. For example, sodium hydroxide should contain only very low levels of microbes, but it often contains high levels of particulates. The only requirement here is to reach a low level of particulate matter, not sterility. A nominally rated filter can suffice to meet this requirement. Some companies require buffers in nonaseptic processes to be sterile filtered before use, but that is unnecessary because a nominally rated filter can reduce the level of viable and nonviable particulates.

Virus Filtration: Virus filtration is a nonaseptic unit operation. However, the FDA and other regulatory agencies continually advance qualification requirements to ensure effective virus reduction. Virus removal filtration is a size-exclusion and/or classification removal unit operation. The key qualification requirement is that a processor claims virus reduction only, not complete removal.

Table 2: Summary of qualifications and requirements

Filtration Type and Stages	Steps
Nonaseptic	
Animal Toxicity Testing	1: Engineering qualifications recommended
Phase 1 through Commercial	1: Engineering qualifications recommended 2: GMP requirements, establish QC inspection and traceability 3: Review of vendor literature recommended
Nonaseptic Viral	
Animal Toxicity Testing	1: Engineering qualifications recommended
Phase 1 through Commercial	1: Engineering qualifications recommended 2: GMP requirements, establish QC inspection and traceability 2: GMP requirements, integrity test 3: Review of vendor literature recommended
Aseptic	
Animal Toxicity Testing	1: Engineering qualifications recommended
Phases 1/2	1: Engineering qualifications required 2: GMP requirements, establish QC inspection and traceability 2: GMP requirements, integrity test and filtrate BPR 2: GMP requirements, validate sterilization 3: Review of vendor literature recommended
Phases 3/Commercial	1: Engineering qualifications required 2: GMP requirements, establish QC inspection and traceability 2: GMP requirements, integrity test and filtrate BPR 2: GMP requirements, validate sterilization 3: Review and confirm vendor literature, required 3: Test bacterial retention, endotoxins, protein bidding 3: Test oxidizables, bacteriostasis/fungistasis

Table 3: Key regulations and guidelines for aseptic and nonaseptic filtration

Filtration Types	Nonaseptic Filters	Aseptic Filters[a]
Regulatory Guidelines and References	21 CFR parts 210 and 211, 600 through 680 FDA Guideline on *General Principles of Process Validation* ICH Q5A, *Viral Filtration* PDA Tech Report No. 41	21 CFR parts 210 and 211, 600 through 680 FDA Guideline, *General Principles of Process Validation* FDA Guidance for Industry. *Sterile Drug Products Produced by Aseptic Processing: CGMP* FDA Guidance, *Sterile Drug Products Produced by Aseptic Processing* PDA Tech Report No. 40 PDA Tech Report No. 26
Purpose and Objectives	Reduction of viable and nonviable particles (bioburden/virus reduction; particulate clarification/ reduction)	Removal of viable and nonviable particles (bioburden and particulates; make/keep process sterile)
Examples of Unit Operations	Purification/downstream Tank-vent filters (nonsterile) Nonsterile buffers Viral filtration	Media Bioreactor/Upstream Tank vent filters (sterile) Buffers (long-term storage) Formulation Fill/finish
Membrane Rated Porosity	> 0.2 micron and nanoviral filtration	> 0.1 µm and < 0.2 µm

[a] Complete references can be found under "For Further Reading"

Aseptic Filtration Operations

Aseptic filtration necessitates inline steam sterilization or autoclaving, aseptic connections, and processing in a laminar airflow environment.

If a manufacturer claims sterility for a fluid or product, it must demonstrate particulate and bioburden removal per CGMPs. The key is the manufacturer's claim. If it claims bioburden removal, not reduction, it must show that the filter was appropriately challenged with a suitable bacterial challenge to provide a minimum LRV (log reduction value) of >7 for the test organism; that extractables testing was performed to industry and company standards; and that a bubble point or diffusion–forward flow test value was established for the filter installation.

Sterilizing-grade filters are qualified by their manufacturers to be microbially retentive. They are provided to end users with considerable validation data

Key Questions and Issues for Assessing Business Risk

Overview of Filtration Step

- Nonaseptic or aseptic filtration?
- Regulation guidelines and requirements
- Validation or qualification?

Decision Process: Only Two Questions

#1: Are you claiming a sterile filtrate?

Yes — go to aseptic filtration
No — go to nonaseptic filtration

Aseptic Filtration

#2: What process stage "phase" are you in?

Animal Toxicity Testing?
Recommend execution of "engineering qualifications" to qualify filters

Phase 1 Through Phase 2?
Recommend execution of "engineering qualifications" to qualify filters

Establish QC visual inspection and lot certified/traceability processes, integrity test procedures, and sterility validation for "GMP requirements" to confirm qualified filters and their sterility

Review vendor literature for "membrane qualifications" to qualify filters

Phase 3 Through Commercial?
Execution of "engineering qualifications" to qualify filters

Establish QC visual inspection and lot certified/traceability processes, integrity test procedures and execute sterility validation for "GMP requirements" to confirm qualified filters and their sterility

Review vendor literature and confirm through testing of "membrane qualifications" to qualify filters

Nonaseptic Filtration

#2: What process stage "phase" are you in?

Animal Toxicity Testing?
Recommend execution of "engineering qualifications" to qualify filters

Phase 1 Through Commercial?
Recommend execution of "engineering qualifications" (required for viral filtrations) to qualify filters

Establish QC visual inspection and lot certified/traceability processes for "GMP requirements" to confirm qualified filters

Review vendor literature for "membrane qualifications" to qualify filters

and manufacturing and quality information for traceability and quality assurance.

Specifically, a filter manufacturer usually validates filter microbial retention, extractables, and compatibility. Manufacturers often repeat most or all aspects of aseptic filter validation in their own processes. This work can be minimized when a filter manufacturer supplies an extensive validation report and detailed protocols for installing, sterilizing, and integrity-testing the filters.

Aseptic Unit Operations

Formulation and Fill: For formulated product, sterile filtration validation is required by CGMP regulation. Formulation of a drug substance refers to the last unit operation performed on that drug or biopharmaceutical before it is sent to fill/finish operations to become drug product, or before it leaves a facility to be processed by a contract packager. Some companies do not formulate until their product reaches the fill/finish operations stage. If bioprocessors want to claim sterility, even if their products are held in bulk containers, it makes sense from a business viewpoint and should be claimed and suitably validated.

Media: Sterile media production by filtration is a unit operation that requires validation of sterile filtration. This includes measurement of extractables, correlation of destructive and nondestructive integrity tests, and process- and fluid-specific integrity tests to demonstrate filter integrity before and after each filtration run. Producing sterile media by sterile filtration requires steam-in-place (SIP) or autoclaving, assembly in a sterile environment, and use of aseptic connections.

Most companies do not perform extractables testing on sterile filters used in media operations. Yet in an aseptic process, the FDA requires that all these steps be validated.

The key validation consideration is that although these processes are upstream of final processing steps, if the bioprocessor claims sterility, they must be validated accordingly.

WFI Tank Vent Filters: CGMPs require that a sterile tank vent filter be installed and maintained atop a WFI (water for injection) tank. The filter must be pre- and post-use integrity tested according to FDA regulations. Filters most commonly used are 10-in. or larger PTFE (polytetrafluoroethylene) filters installed in steam-jacketed housings to prevent condensate from accumulating inside the housing and blocking free flow air in both directions through the hydrophobic (non-water-wetting) filter.

Tank-vent filtration in an aseptic filter application is designed to prevent entry of both viable and nonviable particles into the air space above a biopharmaceutical fluid tank. This application requires total removal of particulates, both viable and nonviable. So suitable integrity testing must be performed on the filter, and it must be validated.

Producing Sterile Buffers for Long-Term Storage: If a bioprocessor claims sterility of a buffer for a specified period, such as 25 or 50 days (as is becoming common), the claim must be validated with the appropriate sterilizing-grade filter and biocontainer combination. It must be established by bacterial challenge that the filter will provide a >7 log microorganism reduction in each buffer system filtered and stored by this method.

What is Required and When? The Decision Process

Step 1, Engineering Requirements — Sizing, Performance and Compatibility: As Table 1 indicates, there are no CGMP requirements for nonaseptic unit operations during animal toxicity studies through the phase 3/commercial stages of process development.

The most significant aspect of engineering requirements for aseptic filtration unit operations is that CGMP requirements are mandated only for compatibility testing of a membrane filter against filtered material (filtrate) during phase 3/commercial development.

For all other engineering requirements, small-scale sizing and performance measurement are highly recommended as good business practice, but they are not mandated by regulation. Similarly, compatibility testing of the membrane filter and the filtered liquid is good business practice.

Qualification testing for compatibility of the structural

components of cartridge or capsule filters (usually polypropylene) is also recommended but not required during toxicity studies and phases 1 and 2. This is part of process validation during phase 3/commercial development for both nonaseptic and aseptic operations. For nonaseptic applications and aseptic applications up to phase 1, a filter should be considered a component of the system, and it can be swapped out at any time with a like-for-like filter.

Step 2, CGMP Requirements — Control and Integrity: In nonaseptic operations, GMPs mandate QC visual inspection, assignment of a materials specification tied to a part number, and lot certification and traceability. But again, nonaseptic operations do not require filter integrity testing, determination of filtrate bubble-point ratio, or sterilization validation.

For aseptic operations, CGMP requirements first apply during phase 1 and 2 for QC visual inspection, assignment of a company material specification, lot certification and traceability, integrity testing, and sterilization validation. At these stages, providing a filtrate bubble point ratio [(filtrate bp/water bp) × 100] is still not required.

Some biopharmaceutical companies have determined to fix a "lock-in phase" for their process, at which stage the process is considered "set." More and more of these lock-in phases are occurring during phase 1. This presents a significant business risk by foreclosing on opportunities to make process changes, including qualifying viable alternative materials such as filters at later phases of process development.

In phase 3/commercial aseptic filtration operations, QC visual inspection/company materials specification, integrity testing, providing and using a bubble point ratio, and sterilization validation are mandated by CGMPs.

Step 3, Membrane Qualification — Component Evaluation and Testing: Our analysis indicates that CGMP mandates for membrane filter tests listed in Table 1 are not in effect until phase 3/commercial production of a sterile biopharmaceutical.

For Further Reading

Current Good Manufacturing Practice for the Manufacture, Processing, Packaging, or Holding of Drugs. *Code of Federal Regulations* Parts 210 and 211, Title 21, Rev. 2005; www.fda.gov/cder/dmpq/cgmpregs.htm.

Current Good Manufacturing Practices for Biologics. *Code of Federal Regulations* Parts 600–680, Title 21; www.gpoaccess.gov/cfr/index.html.

US FDA. *Guideline on General Principles of Process Validation.* May 1987; www.fda.gov/cder/guidance/pv.htm.

US FDA. *Sterile Drug Products Produced by Aseptic Processing – Current Good Manufacturing Practice* (Guidance for Industry) 2004; www.fda.gov/cder/guidance/5882fnl.htm.

ICH (International Conference on Harmonisation)/US FDA. *Q7A Good Manufacturing Practice Guidance for Active Pharmaceutical Ingredients* (Guidance for Industry). August 2001; www.fda.gov/cder/guidance/4286fnl.htm.

US FDA. *Manufacturing, Processing, or Holding Active Pharmaceutical Ingredients* (Guidance for Industry) March 1998; www.fda.gov/cder/guidance/1289dft.pdf.

ICH. *Q5A Viral Safety Evaluation of Biotechnology Products Derived from Cell Lines of Human or Animal Origin* (Guidance for Industry). September 1998; www.fda.gov/cder/guidance/Q5A-fnl.pdf.

Meltzer TH, Jornitz MW. *Filtration in the Biopharmaceutical Industry.* Marcel Dekker, Inc.: New York, NY, 1998.

PDA Technical Reports (available to order at www.pda.org/science/SAB_INFO/miscDocs/PDA_Final_Technical_Report.xls)

17: *Current Practices in the Validation of Aseptic Processing — 1992.* 47(S1) 1993.

23: *Industry Survey on the Current Sterile Filtration Practices* 51(S1) 1997.

24: *Current Practices in the Validation of Aseptic Processing.* 51(S2) 1997.

26: *Sterilizing Filtration of Liquids.* 52(S1) 1998.

40: *Sterilizing Filtration of Gases.* 58(S1) 2005.

41: *Viral Filtration.* 59(S2) 2005

Nonaseptic operations specify no test requirement for bacterial endotoxin, endotoxin, protein binding, extractables, oxidizable substances, toxicity/biosafety, non–fiber-releasing filter properties, and bacterio- or fungistasis. For nonaseptic operations, vendor literature can be relied on for all these aspects, starting with animal toxicity studies and extending through phase 3/commercial production.

Aseptic operations specify no test requirements during animal toxicity studies or phase 1 and 2 product development. Again, vendor testing, support data, and literature can be relied on through phase 1 and 2 development. CGMP requirements for these tests apply only in phase 3/commercial production.

Given the lack of regulatory requirements for membrane qualification before phases 1 and 2 for aseptic filtration unit operations, it is evident that qualifying multiple filter vendors can increase the opportunity for an effective, economic, and reliable supply of filters.

Evaluating New Opportunities

Some biopharmaceutical regulatory departments tend to overvalidate, applying legacy validations to filtration operations when validation is not required. If the full-scale validation process is applied indiscriminately or overapplied, a biopharmaceutical company will incur far more regulatory cost and delay than is required by CGMPs or justified on the basis of controlling business risk.

A better understanding and application of filter qualification and validation can bring significant benefits to biopharmaceutical manufacturers. It can help to streamline activities and save wasted labor. It can also reveal new opportunities to cut operating materials costs through evaluation of competitive filters. We recommend that biopharmaceutical companies explore every such opportunity to streamline their qualification and validation operations while maintaining regulatory compliance.

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