Developing Preservative-Free Ophthalmics

Manufacturing Strategies for Sterile, Unit-Dose Products Using BFS Technology

The global ophthalmic market is shifting toward preservative-free formulations, driven by increased focus on patient safety, regulatory expectations, and the rising prevalence of chronic eye conditions. Whilst preservatives have traditionally enabled multi-dose products, their long-term use is increasingly associated with ocular irritation and reduced patient adherence, especially in patients requiring long-term therapies such as those with glaucoma or dry eye disease. As a result, pharmaceutical companies are accelerating the development of preservative-free alternatives.

However, removing preservatives introduces significant manufacturing and regulatory challenges—particularly in maintaining sterility throughout the product lifecycle.

In this context, unit-dose packaging and aseptic manufacturing technologies such as Blow-Fill-Seal (BFS) have emerged as critical enablers. BFS offers an integrated, closed-system approach that minimises contamination risk and supports scalable production of sterile preservative-free ophthalmic products.

This paper outlines the key market drivers of preservative-free formulations, technical challenges, and manufacturing strategies shaping the future of ophthalmics, and highlights how BFS technology can support successful ophthalmic product development and commercialisation.

> **“Removing preservatives introduces significant manufacturing challenges, particularly around maintaining sterility throughout the product lifecycle.”**

About The Author

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Market Drivers in Ophthalmics

The ophthalmic pharmaceutical sector is undergoing significant transformation, driven by changing patient needs, demographic trends, and increasing expectations around product safety and tolerability. As chronic eye conditions become more prevalent and treatment durations extend over many years, pharmaceutical companies are placing greater focus on formulations that support long-term patient comfort and adherence. These market dynamics are accelerating interest in preservative-free ophthalmic products and reshaping manufacturing strategies across the industry.

This Global shift is largely driven by the increasing prevalence of chronic ophthalmic disease, particularly conditions such as dry eye disease, glaucoma, and age-related ocular disorders. Many of these conditions require frequent or lifelong administration of topical therapies, creating sustained demand for products that are both effective and well tolerated. As treatment frequency increases, so does awareness of the cumulative impact that certain formulation components may have on the ocular surface over time.

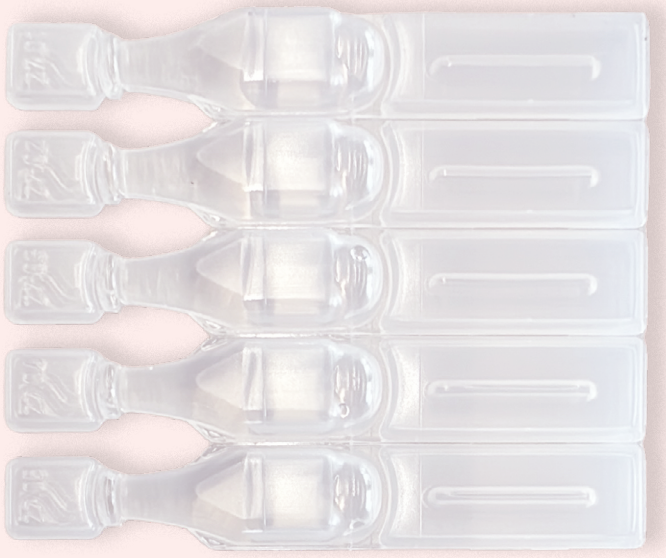
Demographic changes are also contributing to long-term growth in the ophthalmics market. Aging populations in Europe, North America, and other developed regions are associated with higher rates of vision-related disorders and increased demand for ongoing ophthalmic treatment. Older patients often require multiple therapies over extended periods, placing greater importance on product tolerability, ease of administration, and overall patient experience.

At the same time, patient expectations and regulatory agencies are playing an increasingly important role in ophthalmic product development. Healthcare providers and pharmaceutical companies are placing greater emphasis on comfort, convenience, and long-term usability, particularly for therapies intended for chronic use, while regulators are encouraging greater focus on excipient safety and product tolerability. As a result, preservative-free formulations are increasingly viewed as more suitable for sensitive or frequently treated eyes, supporting broader efforts to improve patient comfort, adherence, and overall treatment experience.

Together, these trends are reshaping ophthalmic development strategies and driving increased investment in preservative-free formulations and advanced sterile manufacturing approaches.

Limitations of Preservatives in Ophthalmic Products

Preservatives have historically been essential in maintaining sterility in multi-dose formulations. The role of preservatives has evolved from being a purely protective formulation component to a potential contributor to disease pathology, particularly in long-term treatment settings.



However, their limitations are becoming more apparent.

Clinical Considerations

Repeated exposure to preservatives—particularly benzalkonium chloride (BAK)—has been associated with::

- Ocular surface irritation
- Inflammation
- Disruption of tear film stability

Impact on Patient Adherence

Discomfort associated with preserved formulations can reduce adherence, particularly in patients requiring long-term treatment.

Regulatory and Market Pressure

There is growing preference among regulators and clinicians for preservative-free formulations, especially in chronic indications.

As a result, pharmaceutical companies are increasingly prioritizing preservative-free development strategies.

Manufacturing Challenges of Preservative-Free Ophthalmics

In preservative-free systems, sterility is no longer a formulation attribute—it is entirely a manufacturing outcome. Without antimicrobial protection built into the formulation, manufacturers must rely entirely on process control, packaging integrity, and contamination prevention to maintain product safety.

The implications for **sterility assurance** are significant; in preserved products, preservatives provide an additional safeguard against microbial contamination during storage and use, but in preservative-free formulations that safety margin no longer exists. Sterility must therefore be maintained consistently throughout manufacturing, filling, packaging, distribution, and administration, with even minor contamination risks carrying serious implications for patient safety.

These demands extend to **packaging constraints**, where conventional multi-dose bottles may increase contamination risk once opened, making them less suitable for preservative-free applications. This has accelerated the industry shift toward unit-dose formats and advanced container systems designed to reduce microbial ingress. The removal of preservatives also adds considerable **process complexity**, requiring tighter contamination control (container closure integrity), more rigorous aseptic practices, and careful management of interactions between formulation, packaging materials, and filling processes to ensure long-term stability and sterility.

Container systems must prevent microbial ingress while maintaining compatibility with the formulation. Extractables and leachables represent an additional concern, particularly in polymer-based systems.

Underpinning all of this are **regulatory expectations** that are significantly higher than for conventional preserved products. Agencies apply heightened scrutiny because sterility assurance depends entirely on manufacturing and packaging performance. Regulatory agencies require robust contamination control strategies, validated aseptic processes, environmental monitoring, and sterility testing to ensure product safety and consistent product quality throughout the product lifecycle. Together, these challenges are driving increased adoption of advanced sterile manufacturing technologies and unit-dose delivery approaches across the ophthalmic sector.

Unit-Dose Formats as a Strategic Approach

Unit-dose (single-use) packaging has emerged as a preferred solution for preservative-free ophthalmics products

Key Advantages

- Eliminates need for preservatives
- Reduces risk of contamination
- Simplifies patient use
- Supports regulatory acceptance

Growing Adoption

Unit-dose formats are increasingly used across:

- Artificial tears
- Anti-glaucoma treatments
- Post-surgical therapies

For pharmaceutical companies, unit-dose strategies offer a clear pathway to safer and more patient-friendly products.

Blow-Fill-Seal (BFS) Technology

Blow-Fill-Seal technology is a well-established aseptic manufacturing process in which plastic containers are formed, filled, and sealed in a continuous, enclosed system.

Polymer is extruded to form a container

The container is filled with sterile product

The container is hermetically sealed

All steps occur in a controlled environment with minimal human intervention.

Advantages of BFS in Ophthalmic Manufacturing

Blow-Fill-Seal (BFS) technology has become an increasingly important manufacturing platform for preservative-free ophthalmic products. By combining container formation, sterile filling, and sealing within a single enclosed process, BFS helps manufacturers address key sterility, efficiency, and scalability challenges associated with ophthalmic production.

Because containers are formed, filled, and sealed in a highly automated system with limited operator intervention, BFS significantly reduces contamination risk compared with traditional filling methods. BFS also supports the Quality by Design (QbD) paradigm by controlling critical process parameters (CPP) and ensuring the reproducibility of sterility assurance levels (SAL). This makes the technology particularly well suited for sterile ophthalmic products where maintaining product integrity is essential.

BFS is also highly effective for unit-dose ophthalmic production, supporting the manufacture of single-use vials without relying on antimicrobial preservatives. These formats are increasingly preferred for preservative-free products, helping reduce contamination risk during patient use while supporting ease of administration.

In addition to supporting sterility assurance, BFS platforms are highly scalable and suitable for both clinical and commercial manufacturing. The integrated nature of the process also reduces manual handling and streamlines production, helping improve operational efficiency and batch consistency.

As a well-established sterile manufacturing technology, BFS is widely accepted by global regulatory authorities and supports compliance with EU GMP and international pharmaceutical standards. Its proven track record continues to make it a strong platform for the development and commercial manufacture of preservative-free ophthalmic products.

Blow-Fill-Seal technology provides a robust and scalable solution.

Key Considerations for Pharma Companies

When developing preservative-free ophthalmics using BFS, several factors must be considered:

Formulation Compatibility

- Stability in plastic containers
- Sensitivity to heat and processing conditions
- Interaction with packaging materials

Process Development

- Optimization of filling parameters
- Validation of aseptic processes
- Scale-up from development to commercial production

Quality and Compliance

- Environmental monitoring
- Media fills and validation
- Inspection readiness

Partner Selection

Choosing an experienced CDMO with BFS expertise is critical to minimizing risk and ensuring successful outcomes.

Typical Development Pathway

A simplified pathway for preservative-free ophthalmic products includes:

1. Formulation development and feasibility assessment
2. Compatibility testing with BFS materials
3. Process development and optimization
4. Clinical manufacturing
5. Scale-up and validation
6. Commercial production and supply

Early alignment between formulation and manufacturing is essential to avoid delays.

Conclusion

The transition toward preservative-free ophthalmics reflects a convergence of clinical evidence, regulatory evolution, and patient-centric design. While this approach introduces manufacturing complexity, technologies such as Blow-Fill-Seal provide a proven and scalable solution.

For pharmaceutical companies, success will depend on selecting the right manufacturing strategy and partner—balancing innovation, compliance, and efficiency.

BFS-enabled unit-dose production offers a clear pathway to meet these demands and support the next generation of ophthalmic products.

Curida supports preservative-free ophthalmic manufacturing through advanced BFS technology, aseptic processing expertise, and GMP-compliant sterile production. The upcoming installation of the first Rommelag 550 BFS machine in Europe will further expand scalable unit-dose manufacturing capacity and strengthen support for clinical and commercial ophthalmic programs for customers across 80 countries worldwide.

Curida's Capabilities in Ophthalmics

Curida provides integrated support for the development and manufacture of preservative-free ophthalmic products using BFS technology.

Core Capabilities

- ✔ BFS manufacturing for sterile, unit-dose ophthalmics
- ✔ Support for preservative-free formulations
- ✔ Scalable production from clinical to commercial volumes
- ✔ GMP-compliant quality systems

Technical Expertise

- ✔ Aseptic processing and validation
- ✔ Environmental monitoring
- ✔ Regulatory compliance and inspection readiness

By combining advanced manufacturing technology with strong quality systems, Curida supports pharmaceutical companies in bringing ophthalmic products to market efficiently and reliably.

Contact us

To learn more about Curida's ophthalmic manufacturing capabilities or discuss your project:

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