INTERVIEW

In this interview, Natalia Servol speaks about Unither Pharmaceuticals' equipment for compounding and fill-finish of preservative-free products into multidose bottles, part of Unither's unique and innovative preservative-free multidose offering for partners.

NATALIA SERVOL, HEAD OF OPHTHALMIC BUSINESS, UNITHER

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Natalia Servol holds a double master's degree in international business and education, and has more than 10 years' experience in the health industry. Her experience with brands such as Babymoov (Clermont-Ferrand, France) and Laboratoire TVM (part of Dômes Pharma Group, Pont-du-Château, France) gives her a 360-degree understanding of the health and care sector in her role as Head of Ophthalmic Business at Unither Pharmaceuticals.

Here, Ms Servol speaks about the company's equipment for compounding and fill-finish of preservative-free products into multidose bottles, part of Unither's unique and innovative preservative-free multidose offering for partners.

Q What equipment do you currently use for ophthalmic products?

A We have a considerable inventory of manufacturing equipment and versatile tank systems allowing us to work on industrial machines, under GMP conditions, with batch sizes from 3 L to 2,000 L. We additionally offer a variety of ophthalmic moulds going from 0.25 mL to 1.0 mL. We can compound and fill various types of formulation, including solutions, emulsions and gels.

Q How do you answer to your customers' needs such as regulatory and manufacturing requirements?

A I believe that the key to successfully creating relevant ophthalmological products lies in sharing ideas with partners.

Every Unither manufacturing plant has a dedicated R&D team and pilot workshop for the internal development of customer projects. If required, some works can be provided by or executed with the participation of our innovation and development centre in Bordeaux, France, or the back-up manufacturing plant. Our customers benefit from our international R&D and industrialisation footprint end to end, from early-stage work to commercial manufacturing.

"The key to successfully creating relevant ophthalmological products lies in sharing ideas with partners."

Unither has extensive experience of working in a truly international environment, both for project management with partners, and commercial supply. We meet international quality and regulatory standards and are approved by the EU EMA, the US FDA, Brazil's ANVISA, the Korean MFDS, China's MoH and many others.

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Q What ophthalmic technologies does Unither offer?

A Unither's industrial engineering offering comprises three main technologies for sterile manufacturing of ophthalmic products: blow-fill-seal (BFS) in single-unit vials, preservative-free multidose (PFMD), and common multidose (MD) for products with preservatives.

We are always innovating solutions to meet our customers' requirements and we're always aware that ultimately this equates to meeting patients' needs. By building the industrial synergy between two main technologies for preservative-free ophthalmic products, BFS and PFMD, we believe we're truly providing our customers with tailored, sustainable solutions, and patients with products that will enhance their quality of life.

This has been the driving force for our creation and realisation of an innovative PFMD manufacturing line.

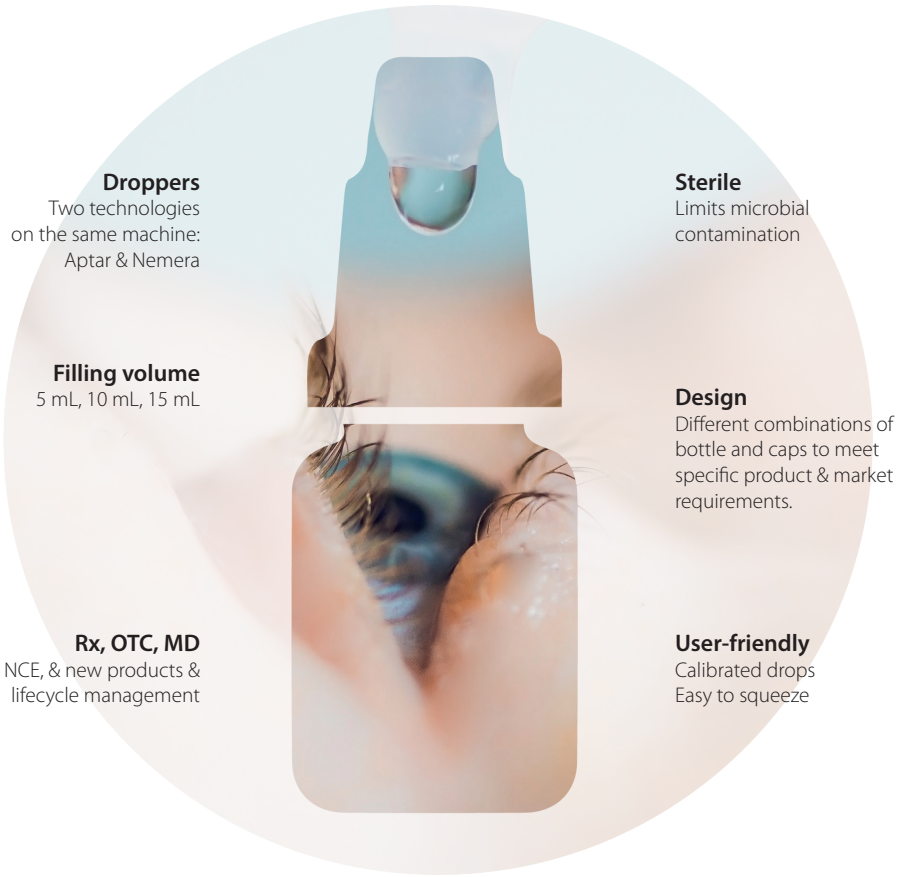

Figure 1: Unither's innovative PFMD manufacturing line is the embodiment of 25 years of know-how.

"Today, we are proud to introduce to you our innovative PFMD line for aseptic manufacturing of ophthalmic products."

Q **Can you tell us more about the PFMD manufacturing line?**

A Today, we are proud to introduce to you our innovative PFMD line for aseptic manufacturing of ophthalmic products (Figure 1).

We are especially proud and delighted with this achievement, a cutting-edge PFMD line that is the embodiment of more than 25 years of sterile know-how. It represents the result of uncountable hours of work by our teams together with external suppliers and customers.

By creating a synergy with unit-dose vials, the PFMD presentation acts as a complement to BFS and gives patients continuous security and product quality throughout their treatment period.

Q **How did you come up with this concept?**

A The new PFMD offering at Unither came about as a result of internally generated innovation and ideas, from our customers' feedback, and from our constant drive towards meeting patient needs.

As of today we work with technologies from two major players in the ophthalmic space: Aptar Pharma and Nemera. Looking to the near future, our patient-oriented philosophy means that we foresee novel tailored solutions being added to our offering in the near future.

Q **What is coming next for Unither?**

A We have plenty of exciting projects underway and on the horizon! We've recently taken a strategic decision to transform our Bordeaux R&D site into a Center of Excellence for Ophthalmology R&D, and the entire team is hard at work on this project.

We continue to create innovative solutions together with our partners. Among many novel initiatives we're supporting, one that I'd like to mention here is CureCall (Paris, France), a start-up specialising in the monitoring of chronic ocular diseases – a user-friendly solution for doctors and patients.

We foresee great challenges in the ophthalmic field and we do believe that vision science can overcome them by collaboration and free sharing of ideas within interdisciplinary teams. Our credo is be open-minded.

Unither will be attending numerous specialised events over the coming months, including the ARVO 2022 Annual Meeting (Denver, CO, US, May 1–4, 2022), and would welcome the opportunity to welcome new contacts to its booth.

ABOUT THE COMPANY

Unither Pharmaceuticals is a global pharmaceutical CDMO specialising in tailored dosage forms designed to simplify the lives of patients. Focused on R&D, key pharmaceuticals, niche product manufacturing and lifecycle management, Unither is best known for offering industrial solutions for the production of sterile and non-sterile liquids. It is a liquid stick-pack pioneer with an annual capacity of 500 million stick-packs, and a BFS leader with a 4 billion capacity for sterile vials.

Unither is a growing company working with an important number of customers whose products are sold in more than 100 counties worldwide. All this is possible due to Unither's industrial footprint on four continents: Europe (France), South America (Brazil), Asia (China) and North America (the US).

UNITHER PHARMACEUTICALS

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Ophthalmic Product Development

by Unither Pharmaceuticals

PREFORMULATION STUDY

- API characterization: Optical microscopy, assays, DRX, PSD, Log P, Log D, membrane permeability…
- Compatibility study
- Solubility study:
  - Solubility at saturation in different media
  - Solubility improvement: Cyclodextrin complexation, co-solvent, surfactants, micronization…
  - Modelization (software)
  - Early conservation study
- Preclinical batches manufacturing

ANALYTICAL METHODS DEVELOPMENT

- API assay
- Impurities assay and forced degradation study
- Preservative and antioxidant assays if necessary
- Sterility and microbiological controls
- Finished Product Photostability study

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DEVELOPMENT CYCLE

FORMULATION STUDY

- Different forms: Solution, Gel, Emulsion, Micellar solution, Micro and nanoemulsion, Nanosuspension
- Formulation development by QBD (risk analysis and DoE on Jmp software)
- Rheology (viscoelastic behavior, gelation assessment, resistance under simulated eye blinking, viscosity behavior after tear contact...)
- Bioadhesion (mucoadhesive force)
- PSD by laser diffraction and DLS, Zeta potential if necessary
- Packaging choice: single or multiple use, glass or plastic
- Finished product characterization: Appearance, pH, Osmolality, Density, Drop size, Viscosity

STERILIZATION STUDY

- Steam sterilization impact
- Filtration study
- Filterability study

CONTAINER/CONTENTS INTERACTIONS

- Stressed studies
- Extractables and leachables (support of packaging supplier)

SCALE-UP STUDY

- Process robustness evaluation by QBD (risk analysis and DoE on Jmp software)
- Preliminary stability study
- Technical batches
- Analytical methods validation
- Cleaning verification (product cleanability) with LOQ method validation and recovery efficiency
- Clinical batches manufacturing

INDUSTRIALIZATION

- Small commercial batches
- Process validation
- Sterilization validation
- ICH stability studies and ongoing stability studies
- ICHQ3D and nitrosamines studies

ARVO2022
May 1 – 4 | Denver
Visit our booth #2019

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