UNITHER PHARMACEUTICALS' INNOVATIVE APPROACH TO OPHTHALMIC MANUFACTURING

In this interview, Natalia Servol shares insights into Unither Pharmaceutical's preservative-free multidose technology. With a focus on addressing patient needs and meeting industry demands, Unither Pharmaceuticals offers a distinctive approach to sterile manufacturing in the ophthalmic sector.

NATALIA SERVOL, UNITHER PHARMACEUTICALS

Natalia Servol holds a double master's degree in international business and education, and has more than 12 years' experience in the health industry. Her experience with brands such as Babymoov (Clermont-Ferrand, France) and Laboratoire TVM (part of the 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 technologies does Unither offer for ophthalmic products?

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

We are always looking for innovative solutions to meet our customers' requirements and we're always aware that, ultimately, this equates to meeting patients' needs. By building industrial synergy between the 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 behind the creation and realisation of an innovative PFMD manufacturing line.

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

Q Can you tell us more about the PFMD line?

A We are proud and delighted with our cutting-edge PFMD line, which is an embodiment of more than 30 years of sterile know-how. It represents uncountable hours of teamwork with external suppliers and customers (Figure 1).

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

The PFMD product is manufactured by aseptic processing. Aseptic manufacturing and the sterile fill-finish process, in which the drug product, container and closure/cap are first subjected to separate sterilisation methods – appropriate to each component and its requirements – and then brought together by the isolator machine.

Q How did you develop this process?

A The PFMD line at Unither is the result of an idea, customer feedback and demands to meet patient needs. As of today, we work with technologies from two major companies in the ophthalmic industry: Aptar Pharma (Crystal Lake, IL, US) and Nemera (Lyon, France). However, our patient-oriented philosophy means that new tailored solutions will be added to our offering in the near future.

Q How do you respond to customers' needs?

A Every one of our manufacturing plants (in France, the US, Brazil and China) has a dedicated R&D team and pilot workshop for internal development and 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 the R&D and international industrial footprint of Unither, from early-stage work to commercial manufacturing.

We answer and meet all relevant international quality and regulatory

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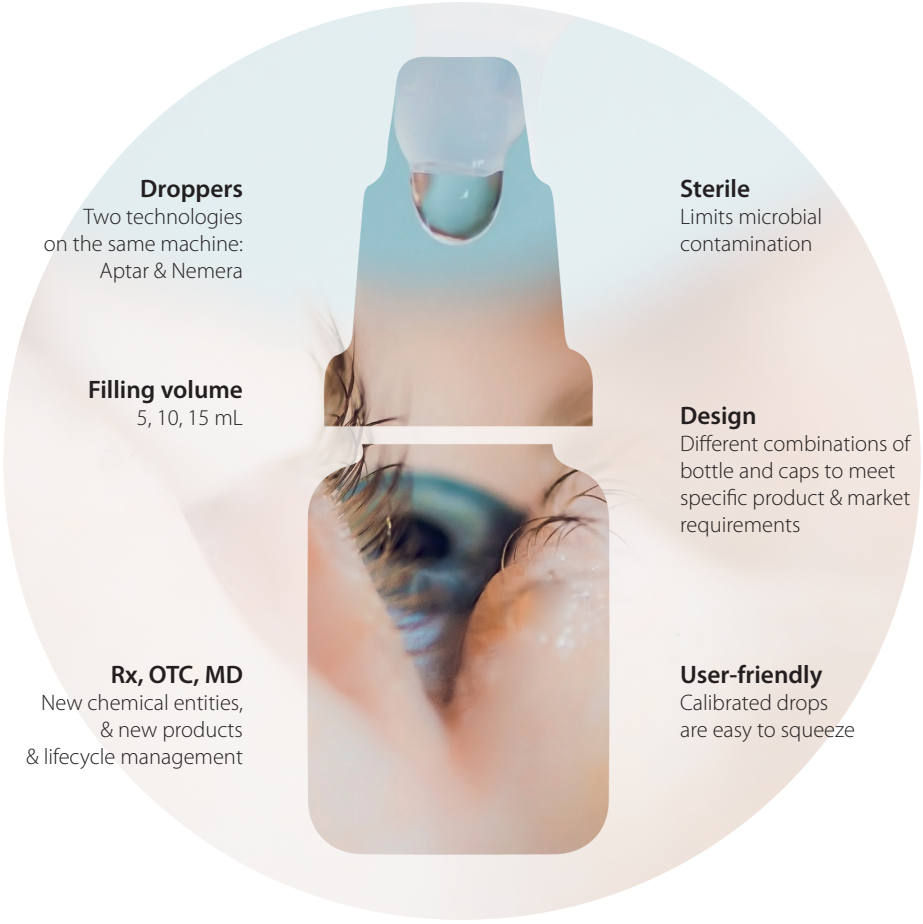

Figure 1: Unither's innovative PFMD manufacturing line is the embodiment of 30 years of know-how.

standards – are approved by the EMA, US FDA, the ANVISA (Brazil), MFDS (Korea), MoH (China) and many others.

> "Our R&D site in Bordeaux has made a strategic move and the whole team is working hard to turn our Bordeaux site into an R&D Centre of Excellence for Ophthalmology."

We work in an international environment, both for transversal project management and commercial supply.

Q What is next in line for Unither?

A Plenty of exciting projects! Our R&D site in Bordeaux has made a strategic move and the whole team is working hard to turn our Bordeaux site into an R&D Centre of Excellence for Ophthalmology. We keep creating innovative solutions together with our partners. Among many exciting developments, we'd like to mention Curecall (Paris, France), a start-up that specialises in the monitoring of chronic ocular diseases – a user-friendly solution for doctors and patients.

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

We will be delighted to discuss these ideas at the ARVO annual meeting and other specialised events.

ABOUT THE COMPANY

Unither Pharmaceuticals is a pharmaceutical subcontractor specialising in the development and manufacturing of single-dose liquid formulations, including eye drops, saline solutions and asthma medications in BFS single doses and liquid stick-packs, for originator pharmaceutical companies and generics manufacturers. Currently employing more than 2,200 people in eight manufacturing plants in France, the US, Brazil and China, Unither Pharmaceuticals recorded sales of €475 million (£406 million) in 2023.

UNITHER PHARMACEUTICALS

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IN WHICH ISSUES SHOULD YOUR COMPANY APPEAR?

www.ondrugdelivery.com/participate

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Ophthalmic Product Development

by Unither Pharmaceuticals

PREFORMULATION STUDY

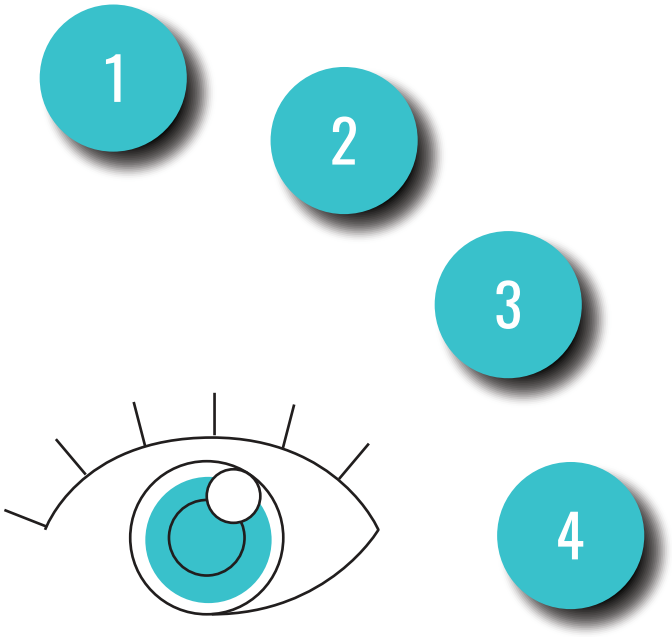
- API characterization: Optical microscopy, assays, DRX, PSD, Log P, Log D, membrane permeability…
- Compatibility study
- Solubility study:
  - Solubility at saturation in different media
  - Solubility improvement: Cyclodextrin complexation, co-solvent, surfactants, micronization…
  - Modelization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

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



DEVELOPMENT CYCLE

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
- Clinical batches manufacturing

INDUSTRIALIZATION

- Small commercial batches
- Process validation
- ICH stability studies and on going stability studies

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