

A NEW GENERATION OF OPHTHALMIC PRODUCTS WITH PYLOTE ECO-FRIENDLY PROTECTION OFFERS IMPROVED SAFETY AND COMFORT FOR PATIENTS

INTRODUCTION

Like all pharmaceuticals, ophthalmic preparations are subject to microbiological contamination. Both ophthalmic solutions used for diagnostic and therapeutic purposes have been found to be contaminated by pathogenic bacteria with reported rates as high as 70%, associated with severe ocular infections such as keratitis and endophthalmitis.¹

Preservatives are recommended to prevent microbial proliferation both during storage, after opening, and while in use by the patient. However, many clinical studies indicate a direct correlation between the presence of preservatives and the onset of ocular side effects of long-term treatments, ranging from irritation and discomfort to chronic inflammation of variable intensity, and even the progressive development of fibrosis, which may over time bring the visual prognosis into play.² Studies comparing preservative-free and preserved eye dropper treatments clearly show that all recorded symptoms are significantly more frequent in patients taking preserved medications. Moreover, improved results, adherence and quality of life are observed in groups taking preservative-free medications.^{3,4}

Another key point is that in clinical studies indicating a contamination of ophthalmic products, the great majority of contaminants were found in the dropper tips (between 70 and 100% of preparations): the residual contents are thus rarely contaminated.⁵⁻⁷ This is not surprising, as eye droppers are contaminated essentially by the hands when handling the bottle, or by contact of the tip with the eyelids, lashes, conjunctiva or tears. There is also a risk of cross-contamination when the same eye droppers are shared by several patients, especially in a hospital environment or within the same family.

It would therefore appear important to develop preservative-free ophthalmic solutions that guard against in-use contamination. In this context, Pylote has developed and industrialized a 100% mineral antimicrobial technology, a world-first that guarantees safe and comfortable use of ophthalmic solutions throughout their shelf-life, with an entirely eco-friendly approach.

**THE PROTECTION
FOR A BETTER LIFE**
by **pylote** 

eco-friendly protection

EXISTING PRESERVATIVE-FREE OPHTHALMIC SOLUTIONS

The typical approach is based on making radical changes to primary packaging. The first preservative-free eye solution consisted in switching from multi- to unit-dose, with sterile single-dose containers. This initiative is indeed very effective in reducing the risk of in-use and cross-contamination. However, it is best adapted to treatment over a short period of time, and is questionable from an environmental point of view, especially regarding the carbon footprint and the volume of waste generated.

Various multi-dose preservative-free eye droppers have also been developed, using increasingly complex primary packaging with the addition of filters, clip closures or foams, the aim being to protect the residual solution in the vial. This increased complexity is not without consequences on many aspects, including cost, carbon footprint, volume of waste, and ease of use, for example. These systems appear to prevent microbial contamination of the content (behind the additional parts), but offer limited protection against the greater risk of contamination which occurs

on the tip. Taking this into account, some of these mechanical systems have biocidal chemical additives incorporated into the tip, mainly silver (nano)particles. These additives have antimicrobial properties based on the release of molecules/ions from the host material. This implies that they are consumed over time, and cannot be controlled. Consequently, antimicrobial efficiency is reduced or ceases, and the formula in contact with it is polluted. Many studies have also demonstrated their potential toxicity for humans and the environment, in addition to the fact that certain microorganisms are resistant to these (nano)particles,⁸⁻¹⁰ something the World Health Organization considers one of the biggest threats to public health.¹¹

PYLOTE'S BREAKTHROUGH INNOVATION

Pylote is developing, producing and marketing an innovative technology based on an exclusive manufacturing process to create 100% mineral microspheres. This antimicrobial breakthrough solves the preservative-free problem, without the addition of toxic substances and in full compliance with regulatory requirements, and without any modification of packaging design or parameters, the current manufacturing/filling process or the use of the final product by consumers.

- *Microsphere production*

Specific patented ceramic microspheres were synthesized via a one-step green chemistry manufacturing process. They are 100% mineral, COSMOS-approved and in compliance with European, United States, Brazilian and Japanese Pharmacopoeia and Commission Regulation (EU) No 10/2011 on food contact materials. Their composition, size (non-nano), structure and density are perfectly controlled.



- *Primary packaging manufacturing and filling*

Microspheres are directly and homogeneously integrated into the final product materials so no changes are necessary to the industrial manufacturing process and regulatory documentation.¹² Various regulatory and quality controls were performed to demonstrate the worldwide compliance of the Pylote Added (with microspheres) packaging systems and their construction materials with respect to their user safety impact (extractables/leachables, biological reactivity, etc.).¹³ No difference was observed between Pylote Added and standard packaging in terms of weight, thickness, leakage, fitting, drop size, assembly and use. Packaging is then filled under sterile conditions in line with the usual filling process (compliance with Media Fill Test).¹⁴⁻¹⁵

- *Antimicrobial activity of Pylote technology*

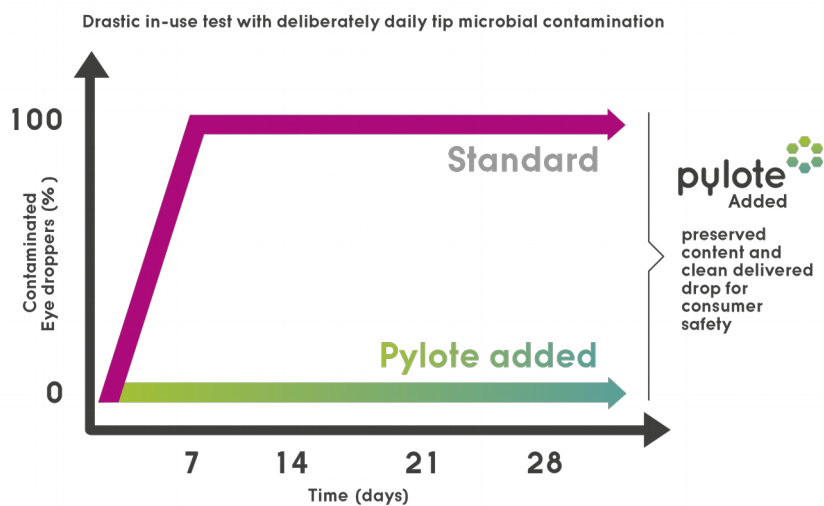
The antimicrobial activity of microspheres is linked to the production of reactive species, mainly hydroxyl radicals, on the particle surface, causing plasmid membrane disorganization by direct contact. Pylote technology has been evaluated by independent certified laboratories using the JIS Z 2801 standard and its counterpart, ISO 22196. The effect is significant on a wide variety of microorganisms, including bacteria expressing acquired antibiotic resistance, and viruses such as a serotype of adenovirus implicated in conjunctivitis. In addition, this antimicrobial activity is fully maintained regardless of storage conditions and for at least four years, demonstrating that the microspheres are not consumed over time.¹⁶

- *Protection from microbial contamination during use*

As previously described, to fully protect patients against the risk of microbial contamination, the ophthalmic product must protect not only the formula inside, but, more importantly, the tip, to deliver a microbiologically clean drop throughout use of the product.

To demonstrate the performance of the Pylote technology incorporated into three-part eye droppers, a specific protocol, simulating more extreme product use than conventional “in-use tests”, was developed by international certified independent laboratories. The tip was deliberately contaminated with the same microbial strains used in antimicrobial-effectiveness testing,¹⁷ on standard eye droppers versus Pylote Added ones, several times a day for at least 28 days. Microbiological examination of the vial contents and of the delivered drop were regularly performed.

Results highlight full control by Pylote Added eye droppers of formulation contamination risks inside the vial and on the delivered doses for all the tested strains. Pylote Added eye droppers were not contaminated throughout the test, whereas all those in standard packaging were fully contaminated from the seventh day.



- *Pylote technology stability and safety*

Once they have been integrated into plastic materials, microspheres do not migrate. Compatibility studies have been carried out by placing Pylote Added eye droppers filled with test or commercial solutions under long-term and accelerated conditions of aging.¹⁸ The amounts of microspheres detected in the formulas are negligible, or even below the quantification thresholds.¹⁹ First, this guarantees the same efficiency of the technology for safety, performance and worldwide compliance, and, second, the same physico-chemical formula over time (no modification of pH, osmolarity, conductivity, etc.). Other studies with very sensitive molecules have also shown that there is neither an impact on the adsorption of the drug on Pylote Added surfaces, nor detection of any oxidized products on formulations.

- *Consumer & environmental final product benefits*

Unlike existing preservative-free solutions, Pylote technology makes it possible to maintain the microbiological cleanliness of simple, multi-dose packaging such as the well-known three-part eye droppers, without adding additional parts or changing the material grade or reference. This has a positive impact on the environment: the packaging remains light, small and compact, therefore reducing the carbon footprint and the volume of waste generated. Moreover, the plastic for Pylote Added packaging is unchanged, maintaining full recyclability.

The technology also provides greater comfort and safety for the patient, for whom the use of the treatment remains easy with precision-control over the delivered dose (ruling out the possibility of overdose), and is adapted to a long treatment period.

CONCLUSION

Pylote has industrialized a unique green innovation that supports preservative-free eye droppers while providing complete protection against the risk of microbial contamination of the formula and the consumer, not only during storage, but, most importantly, throughout the period of use. This technology also ensures the tip is kept clean and limits cross-contamination when the same eye dropper is shared by several patients.

Given that microspheres are 100% mineral, they do not contain any nanoparticles or toxic substances and there is no migration from the host material, Pylote technology is totally safe for consumers and the environment. Since this technology requires no change in packaging design, the actual manufacturing/filling process or the use of the final product, it represents a safe, cost-effective, environmental and worldwide regulatory-compliant solution to the preservative-free problem.

Eye droppers are just one of several applications of this technology, which is highly suitable for other products with a high risk of microbial contamination during use and/or where it is necessary to avoid preservatives, such as nasal sprays, liquid sticks and respiratory masks. This eco-friendly protection technology is also available for other consumer products, such as cosmetics or food.

In accordance with Pylote's policy, all results are obtained by independent, certified laboratories.

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BIO

This publication is provided by the Marketing & Sales Department of Pylote. Created in 2009, Pylote conceives and products innovative unique green mineral microspheres that can be integrated in many pharmaceutical accessories, through an exclusive in-house manufacturing process. Through a complete industrial offer and a licensed commercial model, Pylote brings added value to its clients, who are also present in cosmetic, food or industrial markets, by proposing end consumers with greener, cleaner and safer products.



Company website:

www.pylote.com