



# ADVANCED INNOVATIONS ON A NEW GENERATION OF PLASTIC PREFILLED SYRINGES

Aguettant has developed and launched a new polypropylene prefilled syringe designed to improve safety and quality of care whilst maintaining acceptable cost levels. Danielle Labreche, Director, Business Development & Innovation at Aguettant, and Guillaume Bonnefond, Plastic Engineer & PFS Project Manager, explain the benefits of the new syringe and provide details of its patented design features.

To date prefilled syringes have been designed and commercialised globally on the market, in various shapes, sizes and materials.

Plastic syringes bring a true benefit over glass. Plastic provides improved robustness against breakability and better ergonomics (lightweight), while delivering for many products an adequate stability performance level regarding water/gas permeability as well as extractibles/leachables.

**“NESTED PREFILLABLE SYRINGES, AND THE ASSOCIATED MANUFACTURING EQUIPMENT, STILL REMAIN COST PROHIBITIVE FOR MOST INEXPENSIVE EMERGENCY AND CRITICAL DRUGS”**

In the industry, standard empty plastic syringes (made of cyclo-olefin polymer (COP) or cyclo-olefin co-polymer (COC)) are available in a ready-to-fill format, arranged in nests, pre-siliconised and pre-sterilised. Glass, sterile, ready-to-fill syringes are also available in the same nest format.

It is true that the main advantage of the “nest” manufacturing process over the “bulk” process rests in its flexibility for development or multiple format productions, independently of the volumes produced. However, these nested prefillable syringes (glass and plastic), and the associated manufacturing equipment, still remain cost prohibitive for most inexpensive emergency and critical drugs. At the same time though,

prefilled syringes are highly anticipated by healthcare professionals in the hospital and homecare markets.

Having this in mind, Aguettant took the challenge to design a new generation of polypropylene prefilled syringes, intending to improve safety and quality of care at an acceptable cost for the market.

It took five years of product and industrial development and more than €5 million invested to bring this new syringe to life. Aguettant PFS (see Figure 1) was finally launched at the international fair for Anaesthesia and Critical Care (SFAR) held on September 28, 2009 in Paris.

Aguettant PFS is produced bulk-wise, it is terminally sterilised with steam in a peelable blister pack. This syringe delivers true design innovations of which two are patented worldwide:

- 1 A SIMPLE AND SECURE OPENING SYSTEM**
- 2 IMPROVEMENT OF THE STOPPER STERILISATION EFFICIENCY**

## **A SIMPLE AND SECURE OPENING SYSTEM**

The syringe is sealed at its end by a frangible obturator which is injection molded in one embodiment with the barrel of the syringe (see Figure 2a). The frangible obturator itself is covered by a protective cap (Figure 2b).



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A simple rotation of the protective cap breaks the frangible obturator and opens the tip of the syringe. After opening and removal of the protective cap (see Figure 3 on page 10), the Luer Lock male connector at the end of the syringe allows a secured connection with any transfer set, catheter or any other compatible female port for needle-free administration or reconstitution.

**This concept offers several advantages:**

- **Closure integrity:** the integrity of the syringe at the tip end is guaranteed by design since the obturator is molded in one embodiment with the barrel.
- **Reduction of leachables:** the plunger stopper and the barrel of the syringe are the only two components in contact with the product; the protective cap is not. The risk of interactions between the container and the solution is therefore reduced.
- **Sterility of the connector:** as for the sterility of the solution, the sterility of the external surface of the syringe is guaranteed through terminal sterilisation process. The Luer connector is not in contact with the cap and the sterilisation efficiency is therefore enhanced (the sterilisation agent can easily pass through large openings in the cap frame and circulate in the critical Luer Lock area)
- **Convenience and security of use:** the opening system is simple and fast without any risk of manual contact with the Luer Lock connector thus precluding risk of user contamination of this critical area. These points have a special importance in emergency situations. A tamper evident system is also provided by this opening system.



**Figure 1: The recently launched Aguettant PFS**

**IMPROVEMENT OF THE STOPPER STERILISATION EFFICIENCY**

The second innovative concept relating to its prefilled syringe that Aguettant has patented improves the sterilisation efficiency by moist heat of a specific area of the syringe: the annular chambers created between the barrel and the stopper sealing lips that ensures closure integrity at the plunger end (see Figure 4 on page 10).

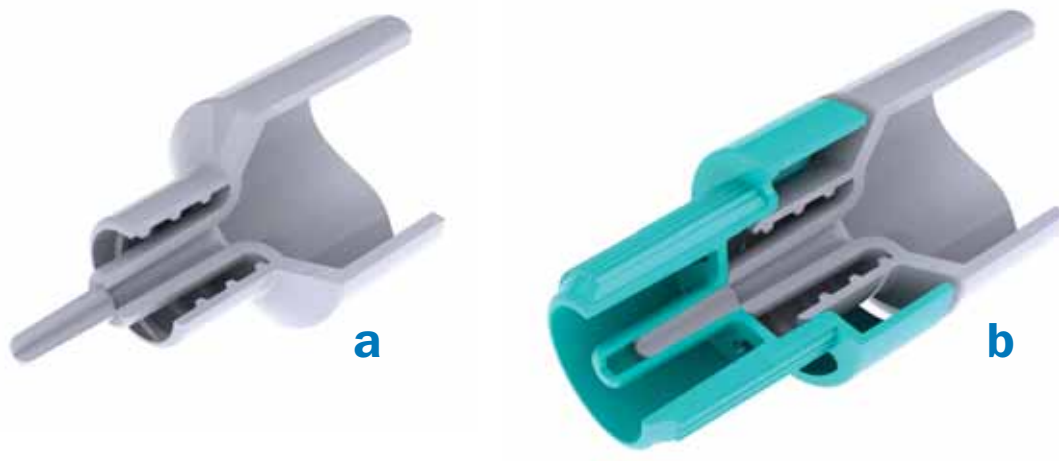
The plastic barrel of the syringe, which is injection molded, is provided with two channels leading to the open end of the syringe. When the stopper is inserted into the

syringe after filling, it is placed below these two channels (Figure 4a)

During the sterilisation process, the plunger is pushed back as the temperature and pressure increases, until a backstop annular bead that prevents the plunger from being ejected of the syringe (Figure 4b).

At this step the channels in the syringe barrel create a passage for the vapour penetration between the lips of the stopper (Figure 4c).

During cooling as the temperature and pressure decrease in the syringe, the stopper goes back below the channels ensuring a perfect sterile barrier (Figure 4d).



**Figure 2: a) Molded tip with frangible obturator; b) with protective cap (shown in blue) fitted**

“EPHEDRINE IS THE FIRST OF MANY MOLECULES EXPECTED TO BE MARKETED BY AGUETTANT, IN THIS MOST COST-EFFECTIVE READY-TO-USE PREFILLED SYRINGE.”

This concept improves sterilisation efficiency in a critical area which may be important for heat-sensitive drug products for which the stability would detrimentally be affected by an excessive sterilisation time.

### LOOKING AHEAD

Since 1903, Aguettant’s main challenge has been to make it easier and safer for healthcare professionals to attend their patients and provide comfort, confidence and better quality of care. Motivated by this responsibility, Aguettant developed this new generation of plastic prefilled syringes.

Ephedrine is the first of many molecules expected to be marketed by Aguettant, in this most cost-effective ready-to-use prefilled syringe.

To date, Laboratoire Aguettant has to its credit 14 patents on innovative delivery system devices. At Pharmapack 2010 in Paris on February 1, the company launches a range of delivery systems under a new brand: “AGUETTANT SYSTEM”.

**AGUETTANT SYSTEM** represents a guarantee of quality design and innovative technology by Aguettant.

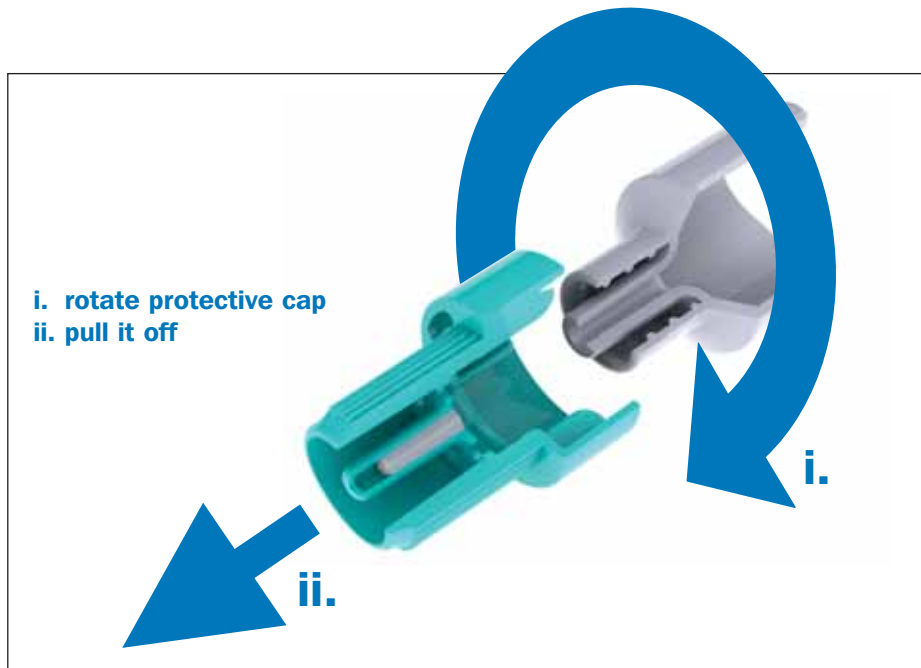


Figure 3: Opening the syringe

#### This new brand is comprised of:

- the recently launched ready-to-use Aguettant PFS
- the multidose self-injector pen
- the self-flushing perfusion bag
- the Mapset®, a reconstitution device for powder drugs

- €81 million turnover for 2009 in 70 countries
- 400 products registered
- 14 patents on innovative delivery system devices for injectables
- 5% of turnover dedicated to R&D

### ABOUT AGUETTANT

As an independent laboratory, Aguettant has the flexibility and reactivity that are critical to seize opportunities for alliances, partnerships and licensing of its patents and technologies.

#### The company has:

- 550 employees worldwide

#### In France Aguettant is:

- a partner to 3000 clinics and hospitals and 1200 professionals outside of hospitals.
- third-ranked supplier (in units) of hospitals and clinics.
- leader\* in the sectors of :
  - anaesthesia/ intensive care
  - injectable morphine
  - irrigation and rinsing
  - small-volume infusion
  - injectable trace elements

\* in number of units sold. Source: IMS 2008

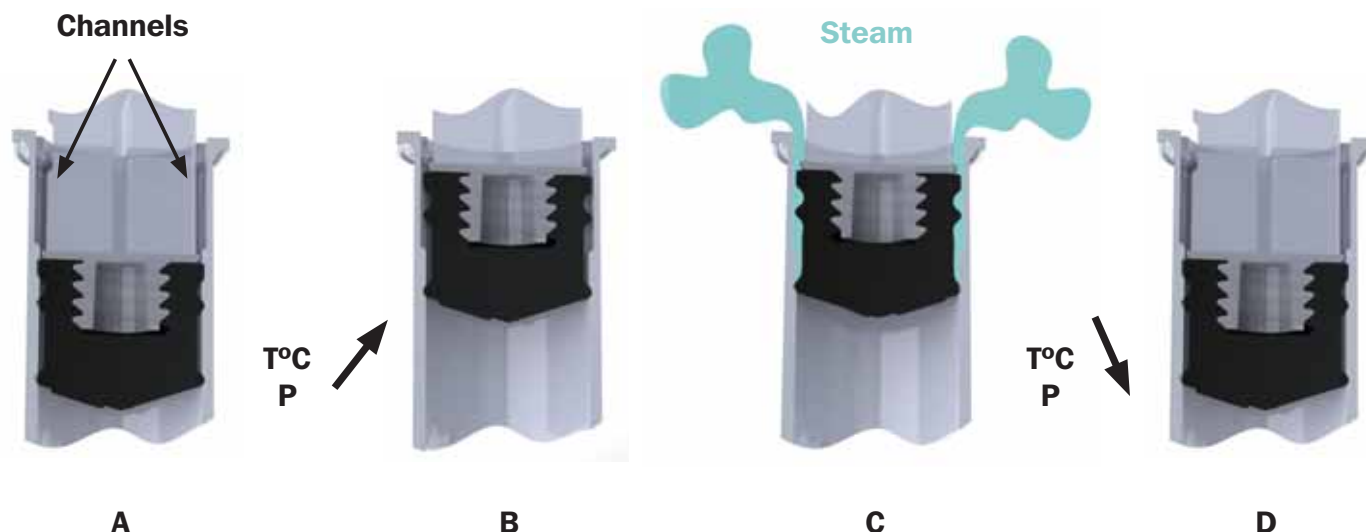


Figure 4: Process of stopper terminal sterilisation by moist heat