



DOES THE USE OF INFUSION BAGS PLAY A ROLE IN COMPLIANCE AND OVERALL SAFETY?

Here, **Danielle Labreche**, Head of Business Development & Innovation at Laboratoire Aguettant, asks some searching questions about the performance, safety and efficacy of conventional infusion bags as major injectable delivery systems, and proposes an innovation to improve compliance and security for patients and medical staff.

The delivery of injectable drugs by gravity in plastic infusion bag has been widely used in hospitals for decades and increasingly for the home care market. While hospitals must now contend with several issues that involve quality of patient care, medical staff safety, organisational efficiency, evolving treatment protocols, costs curtailment driving allocation of resources, and environmental issues with managing dangerous waste, we can ask a simple question: **“Is there a link between these concerns and the mode of delivery procured by infusion by gravity?”**

Does it have an impact on any of those critical concerns the first one being treatment compliance? Does it contribute to the risk of exposure to potentially dangerous drugs? What about the risk of nosocomial infections for the patient and creating waste that is damaging to our environment?

The pharmaceutical industry has used this mode of delivery as an inevitable constraint to infuse drugs to patients. Over the past decade, we have seen improvement initiatives in the connectivity area, and manufacturing processes to drive cost down such as blow-fill-seal (B/F/S) technology; but very little to improve efficiency.

This article aims to raise awareness about existing critical issues and the availability of alternatives that provide improved compliance and safety when treating patients with medicines delivered by infusion. First let us look at some facts.

ABOUT INFUSION PERFORMANCE

There are only a few publications on the matter, but it seems to be a well known fact that dead volume is introduced by the use of infusion bags and this prevents the complete dose being delivered to the patient.

A 2008 study conducted at the University Edouard-Herriot (Lyon, France) revealed that for infusion bags of 50-100ml, about **20% of the active product is not infused to the patient**, being trapped either in the infusion bag, the drip chamber or the tubing, when a manual flushing is not performed.¹

Similar results have been found more recently in a Swiss study in 50-100 ml glass vials, Miniflac bottles and Ecobag infusion bags. In fact, it was found that the dead volume varied between **24-47%** when the drip chamber was filled to the mark and **15-32%** when the drip chamber was empty.²

A third study, performed in Brussels in 2010 investigating betalactam (antibiotic) serum concentration indicated that delivering the right dose into the blood is critical for reaching the efficacy level when treating patients.³

These results raise other important questions.

ABOUT UNDER-DOSING AND EFFICACY OF TREATMENT

What exactly is the proportion of adverse effects events that can be attributable to under-dosing from the infusion bag? Can this “non-



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compliance to treatment” induce inefficiencies in cancer or antibiotic treatment, for example?

ABOUT WASTE: FINANCIAL IMPACT

What is the cost impact on the industry and national health systems when as much as 20% of expensive drugs such as cytostatics, monoclonal antibodies, stem cells and blood derivatives are potentially wasted?

To overcome the drug loss, the advice of the authors of the French 2008 study¹ is as follows:

- 1) Inform medical staff and patients of the inherent risk of under-dosing.
- 2) Use a syringe pump.
- 3) Flush the syringe or bag using sodium chloride.

ABOUT NOSOCOMIAL RISK & PREPARATION TIME

Let us assume for a moment that the most cost effective and pragmatic way to overcome under-dosing is to flush manually with a saline diluent directly into the tubing or bag.

Here are two new questions on manual flushing. Firstly, does manual rinsing increase

risk of contamination for the patient as it adds steps to the connection/disconnection protocol? Secondly, does manual flushing increase staff preparation time and create additional waste of supplies? We could probably all agree that the answer is yes to both.

Nevertheless, a systematic flushing between drugs must be performed to maintain the catheter functions and whenever there is a risk of drug incompatibilities or precipitation, creation of biofilm and risk of infections. In the case of molecules with a narrow therapeutic window, the criticalness of compliance with the prescription means that flushing is imposed in the routine treatment protocol.

So, saline flushing is currently performed in hospitals, but at what cost and to what extent, it is not precisely known.

ABOUT DRUG EXPOSURE RISK

Finally, one issue not yet discussed here but of the highest importance for infused drugs relates to toxic molecules, such as in cytostatics, and the risk of exposure and contamination for the medical staff. On this topic, in 2007, the French Health Agency (AFSSAPS) published

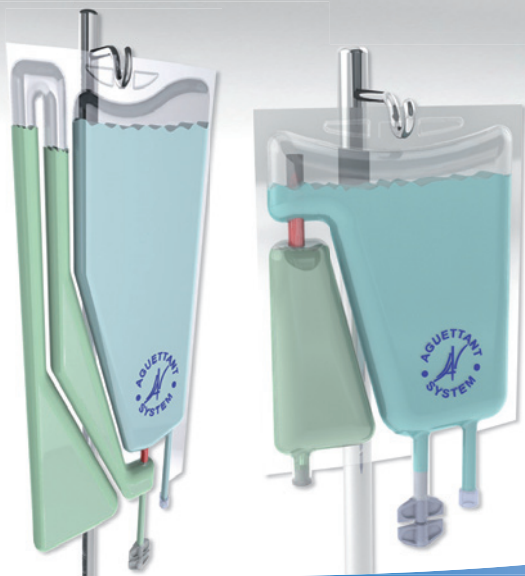
guidelines for Good Preparation Practices for dangerous molecules.

It stipulated: **“If possible, preparations containing dangerous substances are presented ready to use, i.e. including the delivery device connected and purged with diluent, in order for the medical staff to provide care that is free of risks to their health.”**

Hospitals’ centralised reconstitution units have in place high security measures and expensive means to control the risks of drug presence in their environment (on the floor, on the working surfaces such as tables and counters, and on the infusion bag surface) before they are dispensed. Yet despite the good practice recommendations, implementation is not always simple and often risks are present when the final preparations are performed on the wards.

The problem of toxic drug exposure is even more pertinent in the home-care arena where oncology treatment will be increasingly present. Consequently, as a social responsibility, it is important that a fully secured system be designed and becomes soon available to contribute to reducing risks of exposure, providing safe working conditions for carers and medical practitioners.

INTRODUCING A NEW GENERATION OF INFUSION BAG THE AGUETTANT® SELF-FLUSHING INFUSION BAG



AGUETTANT® Self-Flushing Infusion Bag, designed in its offices based in Lyon, France and patented worldwide, aims at securing the injectable drug delivery and improving compliance by performing automatically a flushing of the connecting line without any medical staff intervention.

This infusion bag system can be adapted to fit different drug/flushing volumes requirement and will accept several types of connections, including standard **LUER LOCK** connector which enables a needle-free system.

Two versions of the self-flushing flexible bag are available :

- The dual chamber version enables to perform a **POST** flushing.
- The triple chamber version provides an additional key feature **PRE** and **POST** flushing, which is the **guarantee of protecting the medical staff against exposure risks to hazardous drugs.**

The AGUETTANT® Self-Flushing Infusion Bag is part of AGUETTANT System® portfolio, a new label providing a guarantee of quality design and innovative technology.

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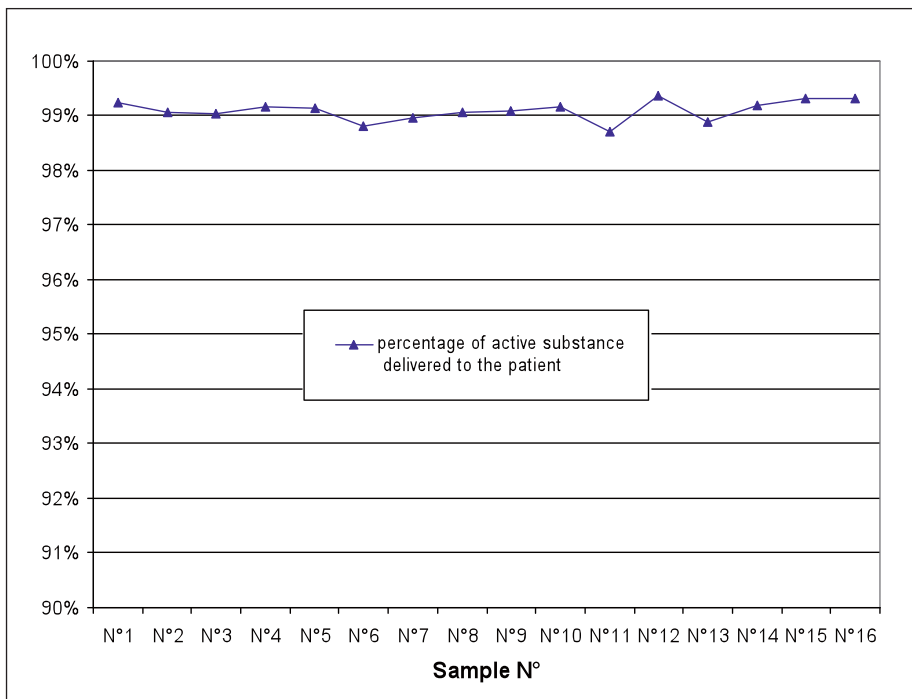


Figure 1: Aguettant's Self Flushing Infusion Bag showing that more than 98.5% of the active ingredient is delivered.

The questions and potential problems raised here are significant. With these issues in mind, Aguettant has developed and patented worldwide a concept of infusion bag that is bringing, increased quality of patient care and solutions to important hospital and globally social concerns.

The innovation resides in the automatic rinsing of the infusion bag and line. This novel functionality substantially increases compliance with the treatment regimen for both doctors and patients as the **full prescribed active drug**

dose is infused. Equally importantly, the system provides protection against the risk of exposure before, during and after delivery. Furthermore, the flushing is performed in a closed environment and thus contributes to the waste reduction with simple, safe handling procedures.

Aguettant's Self Flushing Infusion Bag outperforms the current gravity infusion systems. As shown in Figure 1, research conducted by Aguettant on its prototypes (100ml / 30ml) demonstrated more than 98.5% of the active

ingredient being delivered to patients (unpublished results).

Two concepts are proposed:

- The Aguettant® Self-Flushing Infusion Bag provides a POST Flushing to address mainly compliance improvement (see Figure 2a).
- The Aguettant® Self-Flushing Infusion Bag PLUS - providing a PRE and POST flushing, so that the medical staff is never in contact with the drug during connection/ disconnection and automatically executes a POST flushing (see Figure 2b).

In summary, a systematic self flushing guarantees to:

- Improve compliance for the patient
- Reduce risks of exposure to toxic drugs for healthcare professionals and carers
- Minimise risks of nosocomial infections for patients (it is a closed system)
- Prevent drug incompatibilities and maintain catheter functions
- Free up healthcare workers' time for attending to patients
- Reduce the need for supplies and drug wastage

Aguettant announced in August 2010 that it has entered into an exclusive licence agreement for the Self-Flushing Infusion Bag patent with Pfizer in Europe for its antifungal portfolio.

AGUETTANT SYSTEM®

The new delivery device described here is part of the AGUETTANT System® range, which includes only patented devices such as its Plastic Prefilled Syringe and its Multi-Dose, Multi-Usage Self-Injector Pen.

It is Aguettant's plan to deploy such novel concepts and products to the pharmaceutical industry so that the hospital and homecare markets can provide improved quality of patient care in a safer environment for all.

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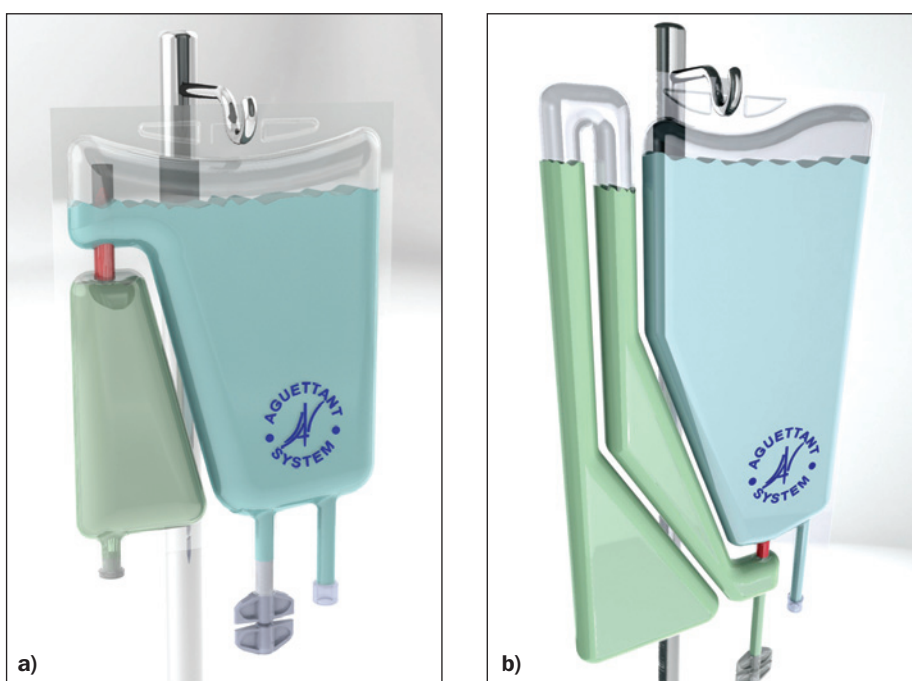


Figure 2: a) the Self Flushing Infusion Bag and b) the Self Flushing Infusion Bag PLUS.

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