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ASSESSING THE IMPACT ON DRUG DOSE DELIVERY OF PASSIVE SAFETY DEVICES

In this article, Adrien Tisserand, Category Manager, Parenteral, at Nemera, reports findings from a comparative study on drug dose delivery of the company's passive needle-safety platform, Safe'n'Sound® and describes how the device's performance in terms of variability of residual volume, together with various other factors, differentiate it from other needle-safety devices.

Historically, injectable drugs were contained in vials and administered in health-care facilities by professionals. But with an increasing trend towards self-administration and at-home administration, prefilled syringes (PFS) emerged in the early 2000s. The growing popularity of the PFS is due to its ease of use, facilitating the injection process and reducing the total injection steps, but also the improved user safety and the reduction of dosage errors. It is also linked to their cost efficiency, not requiring drug as much drug overfilling as vials, which require overfill of up to 25%.

"The comparative residual volumes study highlights how Safe'n'Sound® optimises drug dose delivery, minimising the non-injected volume compared with other commercially available passive safety devices."

In the parenteral industry, needlestick injuries remain a global concern. According to the WHO, more than three million exposures to blood occur every year, resulting in health, psychological and cost issues. Safety devices for PFS have been developed to aid in the protection of users from needlestick injuries. Safety devices are classified in two categories: "passive" if the safety feature automatically activates at the end of the

injection without any additional gesture from the user; or "active" if the user needs to perform an additional gesture to trigger the safety feature once the injection completed.

Nemera has developed Safe'n'Sound® (see Figure 1), a passive safety device platform for PFS, which not only responds to the recommendations of the EU Council Directive 2010/32/EU and US Federal Needle stick Prevention Act, 2000 and aids in the protection from accidental needlestick injuries, but has also been designed to optimise drug dose delivery (consistency of drug dosing) thanks to a patented mechanism. Design optimisation of these output parameters is key for pharmaceutical companies as they could impact treatment efficiency and drug overfilling.

Safe'n'Sound® is an open platform of passive safety devices for prefilled syringes. It is an add-on to the PFS whereby the PFS is snapped in to the safety device. Assembly with the PFS is carried out at the pharma company or CMO facility and, thus, end-users (patients and healthcare professionals) always receive the product assembled.

Safe'n'Sound® 1 mL is on the market in both staked and Luer versions. Nemera has industrial capacity of more than 25 million units per year. Nemera has also developed a version compatible with 2.25 mL staked syringes.



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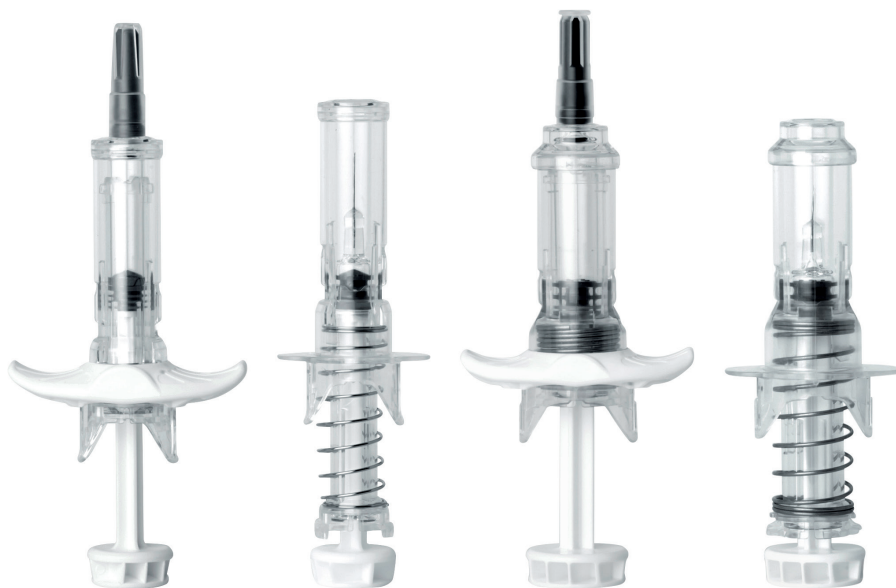


Figure 1: The Safe'n'Sound® platform, for 1 mL and 2.25 mL prefilled syringes.

DRUG-DOSE DELIVERY STUDY

Marketed passive safety devices have based their safety feature mechanism on the same kind of concept: when the head of the plunger rod reaches the position corresponding to the theoretical end of the injection, a spring is released covering the needle with a sheath. In reality, safety feature activation is designed to be triggered just before the theoretical end of the injection to ensure activation. The main advantage of passive safety devices is the limited control the user has on the activation. However, if the activation trigger is not well adjusted, a limited volume of drug may not be injected.

Nemera conducted a study to compare the non-injected volume between three marketed passive safety devices for 1 mL PFS after simulated injection performed by non-healthcare and healthcare professionals.

MATERIALS & METHOD

Three registered nurses and seven non-healthcare professionals were involved in the study. Each user performed six injections on a silicone pad (Figure 2) with each of the three passive safety devices. Safety devices were equipped with 1 mL PFS and stopper from the same batch, and filled with 0.5 mL of distilled water. To reach those



Figure 2: In the study, each user performed six injections on a silicone pad. (Safe'n'Sound® device shown here post-injection, i.e. in the safety-activated state).

conditions, marketed safety devices were disassembled from the syringes containing the marketed drug, and mounted with the new syringe and stopper mentioned previously. The specific plunger rod of each device was screwed back in the new stopper. As a result, the only difference between the three systems including the syringe, the stopper, the distilled water and the safety device was the safety device. As syringes, stopper and liquid used were the same, injection force was similar between the systems. Safe'n'Sound® device is referenced as Safe'n'Sound® System. The two other marketed devices A and B are respectively referenced as System A and System B.

The tests were performed according to Nemera internal protocol P084-02.¹ The main steps were:

1. Assembly of the empty syringe with the device
2. Stopper screwing on the device specific plunger rod
3. Plunger rod insertion (syringe temporarily uncapped)
4. System weighting without syringe needle shield (mass1)
5. Syringe filling with 0.5ml of distilled water by suction
6. System weighting (mass2).

The non-injected volume was defined as the difference between the weight after injection and the weight of the empty system (mass2 - mass1).

As shown in Figure 3, average and variability of the non-injected volume

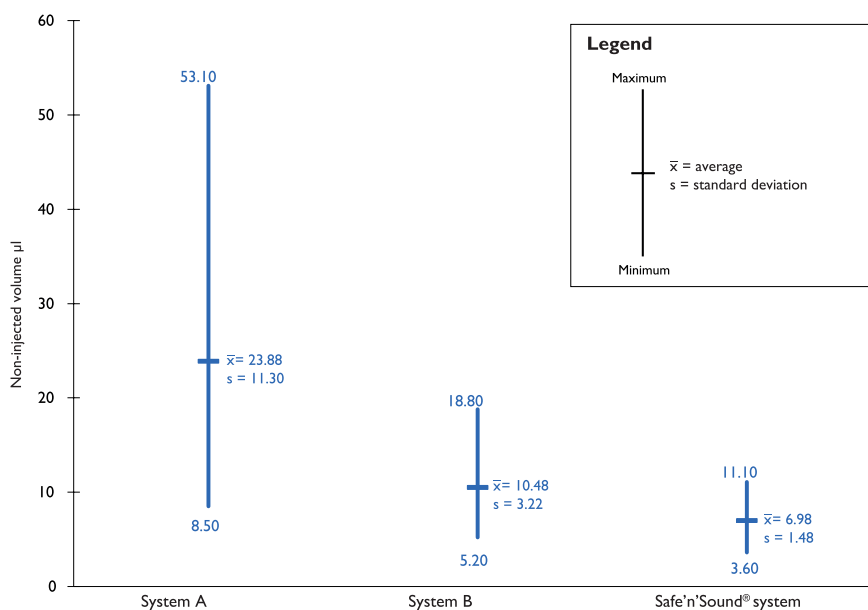


Figure 3: Results showing the measured non-injected volume with three different needle-safety systems.

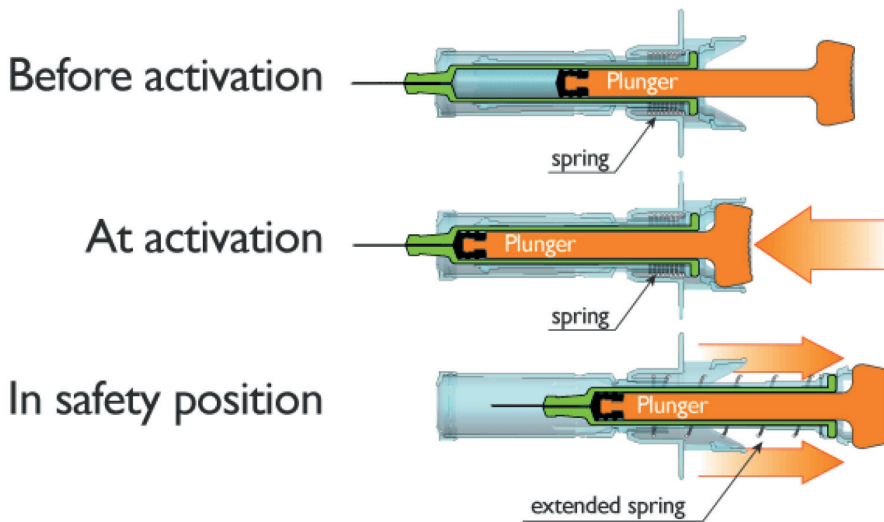


Figure 4: The Safe'n'Sound® mechanism helps syringe emptying, thanks to the two opposites forces applied by the user and the spring during injection.

were very different between the systems. Safe'n'Sound® demonstrated better results than the two comparators, with significantly lower values for both parameters. The average non-injected volume of system A and B were respectively 3 and 1.5 times higher than the non-injected volume from Safe'n'Sound®. Moreover, three residual volume values out of the 60 for System A were larger than 50 µL, representing 10% of the filled volume.

DISCUSSION

The study highlights how safety device design impacts non-injected volume. Improved performances of Safe'n'Sound® system can be explained for the following reasons:

1. Just before the end of injection, an extra force is applied by the user which activates the safety feature. As Safe'n'Sound® is a passive safety device, this extra force is not felt by the user who continues to push on the plunger rod to complete the injection. A spring is then released pulling the syringe back, while the user thumb is still pushing on the plunger rod. These two opposites

forces applied by the user and the spring during the injection process help emptying the syringe (Figure 4).

This patented mechanism compensates the advanced release of the safety feature which happens on the three marketed passive safety device. It is critical not to have an additional force too high (the user must not feel it) as it could give him the false perception that the injection is completed. If so, the user could stop pushing on the plunger, resulting in higher non-injected volume and device non-activation. The adjustment of this additional force being critical for safety devices, it has been validated through simulated user studies for Safe'n'Sound®.²

2. In addition to its mechanism, Safe'n'Sound® has also been designed for ease of use. Through several design features, Safe'n'Sound® improves the ergonomics for the user, allowing them to push smoothly and continuously on the plunger rod until the end of the injection. It results in an improved precision of injection. With Safe'n'Sound®, users can activate the device in a very convenient and repeatable way, making it less user dependent than other marketed safety

device. This advantage is even more critical for non-professional users.

3. Moreover, contrary to other passive safety device, Safe'n'Sound® spring is located at the syringe flange allowing clear visibility of the tip and inspection of the drug prior during and after injection. As a result, if necessary, the user can check that all the drug has been delivered prior removing the pressure on its thumb.

4. Nurses agree that Safe'n'Sound® doesn't modify the standard injection process.²

CONCLUSION

The comparative drug-dose delivery study highlights how Safe'n'Sound® optimises drug dose delivery, minimising the non-injected volume (lower average and variability) compared with other commercially available passive safety devices. This promotes increased treatment compliance and results in cost savings for pharmaceutical companies, reducing the need for overfilling. Other tests³ have further highlighted how Safe'n'Sound® guarantees a non-injected volume comparable with a naked syringe. The performance of Safe'n'Sound® is linked with its function, which reduces human error.

Design optimisation of these output parameters is key for pharmaceutical companies as they have an impact on treatment efficiency and drug overfilling.

In addition to lower variability of residual volume highlighted in the study, Safe'n'Sound® differentiates from other passive safety devices on numerous other points. For example, the platform integrates numerous ergonomic features to facilitate the handling, gripping and comfort for the user: a large thumb pad surface to smooth the injection; large built-in finger flange to facilitate handling; a round shape for easy and comfortable handling; a spring located



Figure 5: An optional ergonomic extended finger flange (available in a variety of colours) overcomes the problematic of dexterity issues and drug viscosity.

at the syringe flange position to provide good visibility of the syringe tip and able inspection of the drug; an optional ergonomic extended finger flange (available in a variety of colours) to overcome the problematic of dexterity issues and drug viscosity (see Figure 5).

Results from Safe'n'Sound® simulated

clinical user study performed with device-naïve patients and healthcare professionals from US and Europe showed how these design features translate into real clinical benefit.

There are numerous advantages for pharma companies too, in addition to those arising from clear clinical and patient ben-

efits. For example, thanks to its specific patented clips design, Safe'n'Sound® requires low force to snap the syringe into the safety device while high force is required to unload the syringe. As a result, the risk of syringe breakage during insertion is reduced and the syringe is held firmly once inserted into Safe'n'Sound®.

Finally, the device is robust against shocks and vibrations allowing safe handling during transport and on assembly lines. Consequently, Safe'n'Sound® can be delivered in trays or bulk, making it a cost-effective solution for pharmaceutical partners.

SAFE'N'SOUND® KEY FEATURES

- Single-use device
- Designed for patients and healthcare professionals
- Suitable for a wide range of patients including children and adults
- Compatible with subcutaneous and intramuscular injections
- Easy to use, convenient and ergonomic system
- Robust, reliable device ensuring safer injection
- Patented product/ 510(k) cleared
- On the market for both staked and Luer versions
- Open platform of add-on safety devices
- Compatible with 1ml & 2.25ml syringes of different:
 - o filling volume
 - o flange type (e.g. cut, round, small round, extra small round etc)
 - o suppliers (ISO standard marketed syringes including from BD, Gerresheimer, Nipro Glass, Ompi, Schott etc)
- Available in bulk or tray
- Optional ergonomic extended finger flange.

REFERENCES

1. *Nemera internal test protocol P084-02 (Safe'n'Sound® 1 ml long staked and Luer lock – n non-injected volume).*
2. *Biomatech Study Report 77291, "Simulated clinical use testing on a passive safety device for prefilled syringes".*
3. *Nemera Internal Test Result Report: TRR_01006-908853.*

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