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Dose accuracy and injection force dynamics of a novel disposable insulin pen

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SoloStar[®] (sanofi-aventis) is a new, disposable insulin pen for the administration of insulin glargine (Lantus[®], sanofi-aventis) or insulin glulisine (Apidra[®], sanofi-aventis). SoloStar was developed to address a wide range of patient needs and demonstrates advancement over previous devices, owing to its appropriate combination of ergonomically-tested and mechanically improved features. The authors report the results of key investigations carried out by sanofi-aventis as part of the SoloStar development plan, including dose accuracy and injection force testing. Comparisons between SoloStar and two commonly used pens, FlexPen[®] (Novo Nordisk) and the Humulin[®]/Humalog[®] pen (Eli Lilly) establish SoloStar as a state of the art pen that is suitable for most patients with diabetes.

Keywords: delivery device, FlexPen[®], insulin, insulin delivery, insulin pen, Lilly Humulin[®]/Humalog[®] pen, medical device, SoloStar[®], Type 1 diabetes, Type 2 diabetes

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1. Introduction

In the 60 years following the introduction of insulin for diabetes (in approximately 1922), the mainstay of insulin administration was the vial and syringe. The first insulin pumps appeared in the mid-1970s, and pump use today is a small, but important segment of diabetes care. The first insulin pen (NovoPen[®], Novo Nordisk) was launched in 1985. Over 20 years later, insulin pens now account for just over 50% of insulin use worldwide [1]. Figure 1A shows that insulin pens are now the predominant form of insulin delivery in many countries, with the notable exception of the US, where the vial and syringe is most commonly used by people with diabetes. Also noteworthy, Figure 1B shows that the use of disposable pens is increasing, driven by the simplicity and ease of use of these devices. Interestingly, although the use of insulin pens is relatively low in the US, the vast majority of the pens that are used in the US are disposable.

A study of US patient records has demonstrated that converting from the vial and syringe method to insulin pens is associated with improved medication adherence and a reduced likelihood of experiencing a hypoglycemic event (odds ratio = 0.50; 95% CI = 0.37 – 0.68; $p < 0.05$) [2]. Furthermore, all-cause annual treatment costs were reduced by \$1590 per patient (from \$16,359 to \$14,769; $p < 0.01$). Therefore, the use of insulin pens will not only benefit the patient in terms of health and lifestyle, but also the healthcare provider by reducing overall costs per patient [2].

SoloStar[®] (sanofi-aventis) is a new disposable insulin pen. The presently available disposable pens, while addressing many user needs, still leave certain needs unmet. With this in mind, sanofi-aventis has developed a new insulin pen device that will retain the best features of previous pen devices, and improve or incorporate new features in order to meet the needs of a larger audience of pen users. SoloStar addresses a wider combination of user needs than previous individual devices, including the simplicity of use, the force required to deliver the injection, the length to which the pen extends when the dose has been dialed (dial extension), the

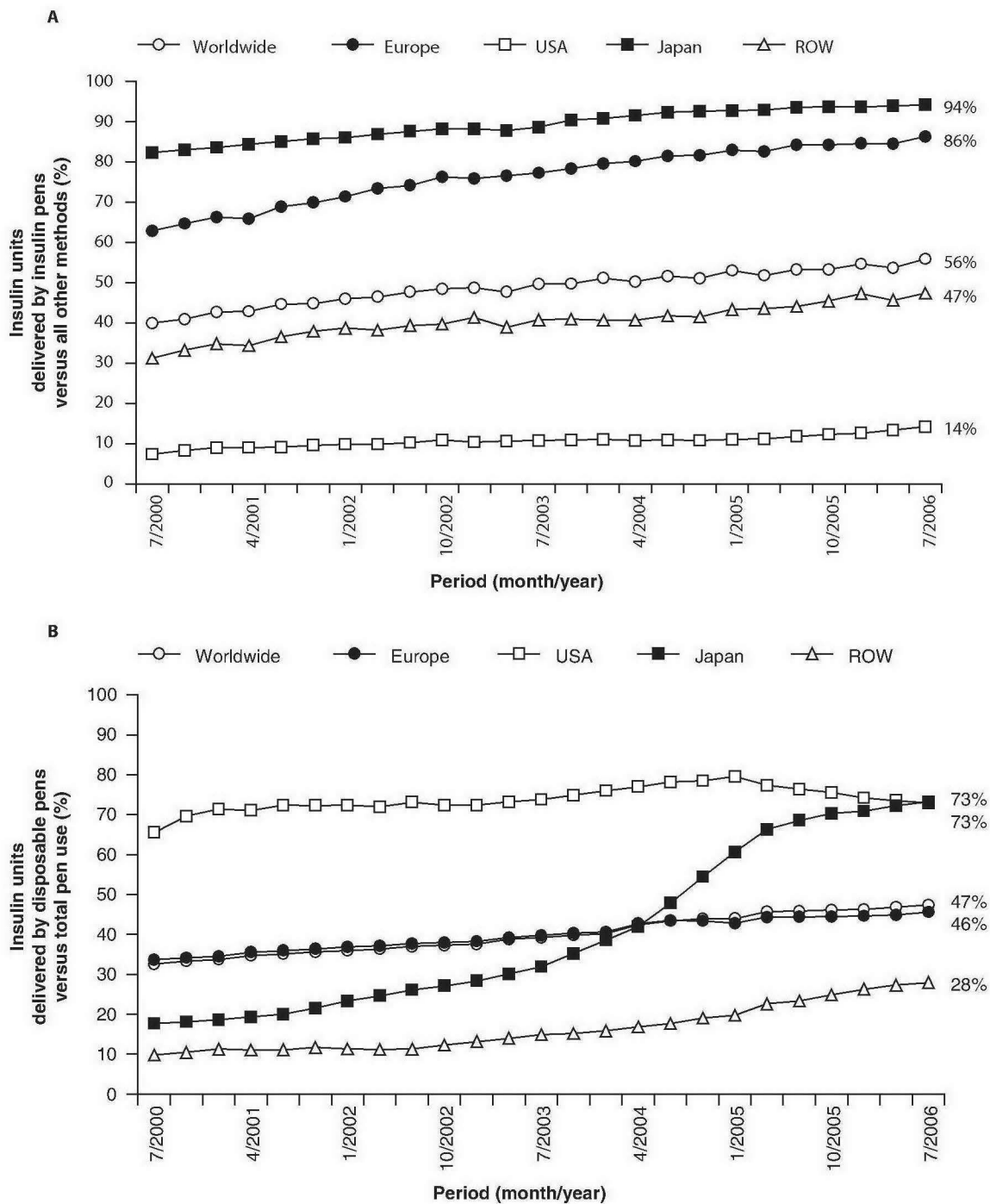


Figure 1. The increasing use of insulin pen devices to administer insulin worldwide and in selected regions (Europe, USA, Japan and rest of the world), between July 2000 and July 2006. A. Insulin units delivered using insulin pen devices as a percentage of total insulin use. **B.** Insulin units delivered using disposable pens as a percentage of total use of insulin pens.

ROW: Rest of world.
Data from [1].

strength and robustness of the pen, the maximum dose of insulin deliverable in one injection, the ease of reading the dose display, and the identification of different insulins when used in the same type of pen.

This paper provides an overview of the evolution of pen technology, leading to a detailed description of the new SoloStar pen. Key tests carried out as part of the sanofi-aventis development program are reported, and the relevance of these results to patients and healthcare professionals is also discussed.

2. The evolution of insulin pens

The vial and syringe was the predominant route of insulin administration for patients with diabetes for over 60 years, although in some regions (e.g. the US), the vial and syringe is still most commonly used (Figure 1). However, this method of administration is associated with numerous disadvantages, including fear of injections [3,4], inconvenience, poor dose accuracy [5], the lack of social acceptance [6] and inaccuracy when self-mixing insulin [7]. These limitations manifest in a profound psychological resistance to insulin in both diabetes patients and healthcare providers [8,9].

The advent of insulin pens has gone some way to address the unmet needs associated with the vial and syringe method. The first pen device, NovoPen, was launched in 1985. It was a very simple pen, with a cartridge containing 150 units of 100 unit/ml short-acting insulin and used a 27-gauge needle. The pen delivered 2 units of insulin after a push on the button at the top [10]. Since then, insulin pens have continued to evolve, becoming increasingly sophisticated devices designed to meet more of the needs of the diverse and growing diabetes population. The features now offered include easy dose dialing and dose correction, large dose displays (mechanical and electronic), low injection force, small, slim and easily portable size, click-in/click-out cartridge change, dose confirmation at the end of injection, higher maximum doses, larger cartridge capacity, 1 and ½ unit dial increments, and visual and tactile differentiation of pens with different insulin.

In present practice, the Humulin®/Humalog® pen (Eli Lilly), hereafter referred to as Lilly Pen, and the FlexPen® (Novo Nordisk), are both well accepted and widely used disposable insulin devices; however, as discussed above, devices are continually evolving. The SoloStar pen builds upon the strengths of existing devices and combines these with additional features, as outlined below. Figure 2 shows a photograph of the three pen devices.

3. SoloStar pen

The SoloStar pen is a new medical device for the administration of insulin. SoloStar was approved in the EU in 2006. It is a disposable insulin pen device, designed for use once or several times a day, with a capacity of 300 units (3 ml) of insulin, and is available for administration of the basal insulin, insulin glargine



Figure 2. Photographs of SoloStar (A. insulin glargine, B. insulin glulisine), C. FlexPen and D. Lilly Pen.

(Lantus®, sanofi-aventis) and the prandial insulin, insulin glulisine (Apidra®, sanofi-aventis), for patients with either Type 1 or Type 2 diabetes (Figure 3).

The SoloStar device was effectively developed 'from the ground up', taking into consideration human and ergonomic factors and limitations, as well as advancements in technology. As a result, SoloStar is an intuitive, easy to use device with the same common mode of operation as other pens, as well as a number of improved features.

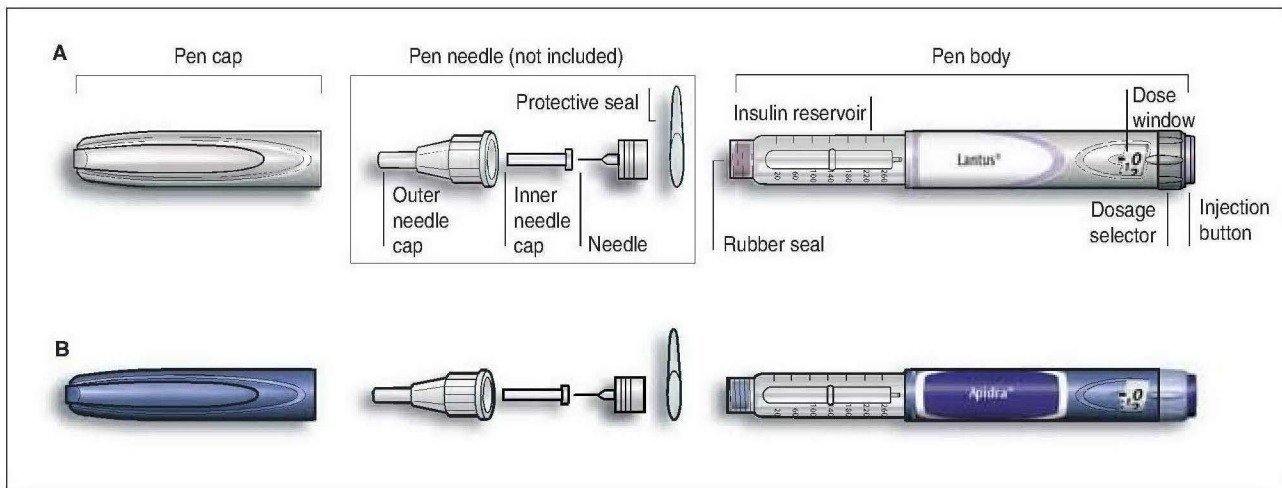


Figure 3. The SoloStar pen device showing key components of the pen and needles, and the color schemes used to help differentiate between insulin formulations to avoid medication errors.

Human factor input was key in the development of SoloStar. Ergonomic tests were carried out to establish what features would improve the usability of the device. These tests included gathering anthropometric data on the intended user populations in order to be able to recommend the most suitable basic dimensions of the pen, establishing relevant human strength data to identify the maximum operating force that is required to push the injection button, and gathering information on the optimal dosage display window so that the needs of visually impaired users are taken into account.

These ergonomic findings fed into the development of the strength and robustness of SoloStar. In particular, the device is strong enough to prevent users from breaking it if they try to dial beyond 80 units or selecting more units than that which are left in the pen. The findings also influenced the desired injection force of SoloStar; due to its highly efficient drive mechanism, SoloStar has a significantly lower injection force than the FlexPen and the Lilly Pen. Lower injection force means that the user can steadily apply pressure to the end of the pen, without experiencing hand fatigue or diminished grip strength. This is a key feature for users, helping them to feel comfortable while delivering their injection and confident knowing that it was successfully completed. Human factors were also considered when developing the dial extension. The dial extension of SoloStar has been designed to enable patients to administer even the maximum insulin dose with ease. Limited joint mobility of the hand, also referred to as cheiroarthropathy, is a significant problem for patients with diabetes and may affect daily life [11]. It has been estimated that up to 58% of patients with diabetes have limited joint mobility of the hand [12] and significantly lower grip strength compared with healthy controls [13]. Such impairments are commonly the result of connective tissue disorders [14] or diabetic neuropathy [15,16].

To overcome such dexterity problems, a short dial extension will facilitate easier grip during injection and easier depression of the injection button.

Table 1 compares key features of SoloStar, FlexPen and Lilly Pen. Lilly Pen has the shortest dial extension for a given dose; however, as shown in results in the next section, the Lilly pen has a significantly higher injection force. When dialing a dose of 60 units, dial extension is 23% lower with SoloStar than with FlexPen, and SoloStar requires a lower injection force than FlexPen. The maximum dose of SoloStar is 80 units, which exceeds the maximum dose of most other devices, including FlexPen (60 units) and Lilly Pen (60 units).

In order to differentiate the insulin glargine pen from the insulin glulisine pen, SoloStar is manufactured in two different exterior colors: grey for insulin glargine and blue for insulin glulisine. This is the first time a disposable insulin pen has differentiated the type of insulin contained in the pen using a different color pen body. Other disposable devices that are used to administer more than one type of insulin have the same pen body color, and are differentiated only by the label on the pen or by small color details, such as those found on the injection button. Human factors and healthcare professional input were taken into account when developing the SoloStar. It was suggested that a completely separate color would provide additional means of differentiating the two insulins and, thus, further minimize any potential to confuse the two devices. However, errors in dosing are less likely with insulin pens than with the vial and syringe [17,101]. In addition, the insulin glulisine pen has a differentiating tactile feature on the injection button to prevent confusion between the pens for patients with visual impairments.

The injection force and dose accuracy of SoloStar are discussed in detail below.

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