Expert Opinion

informa
healthcare

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

Alastair Clarke† & Geralyn Spollett
†*Site Frankfurt Devices/Device Design & Industrialisation, Sanofi-Aventis Deutschland GmbH, Frankfurt am Main, Industriepark Hoechst, Building K607, D-65926 Frankfurt am Main, Germany*

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

Expert Opin. Drug Deliv. (2007) 4(2):165-174

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

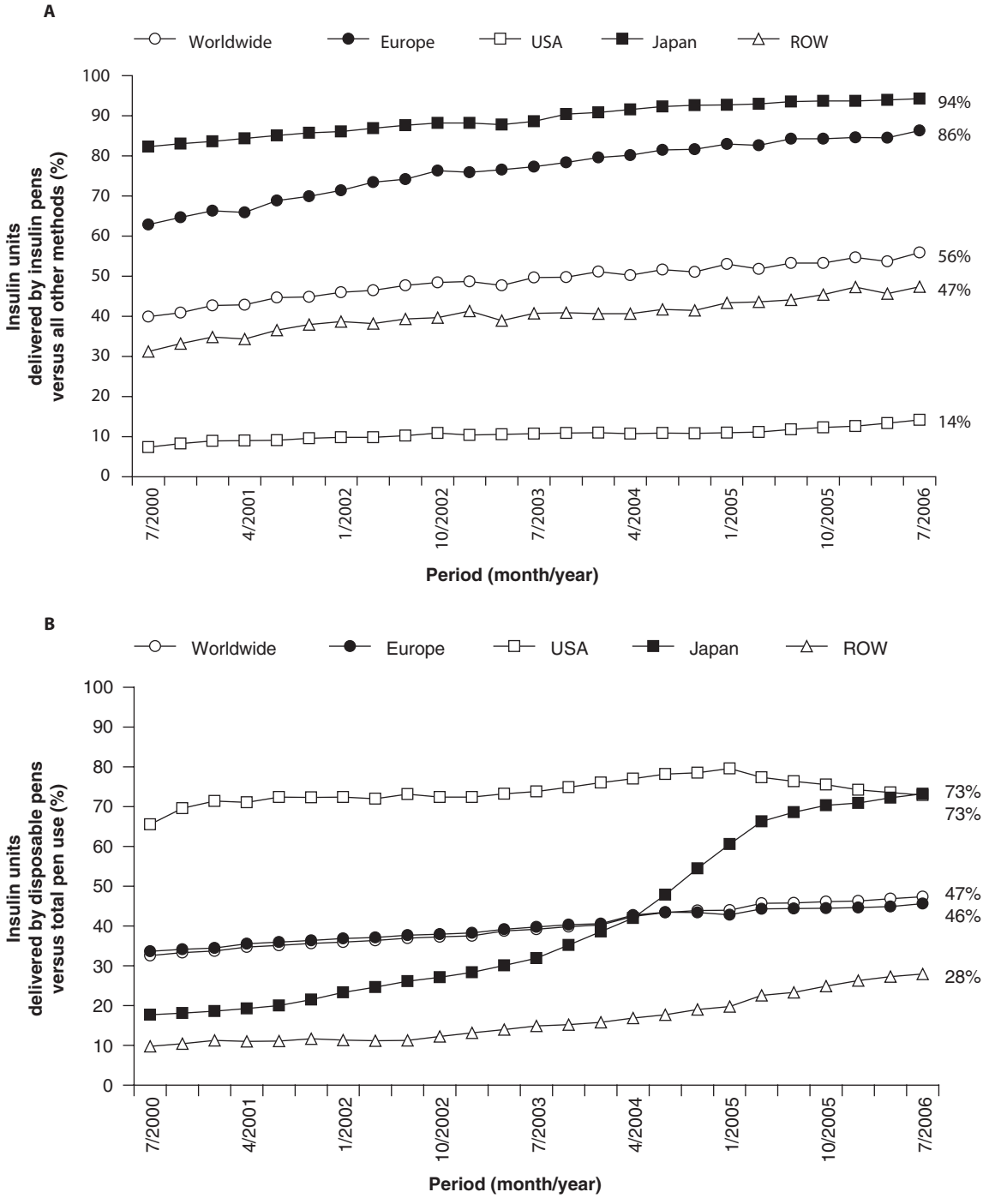

Figure 1. The increasing use of insulin pen devices to administer insulin worldwide and in selected regions (Europe, USA, Japan and rest of the world), between July 2000 and July 2006. A. Insulin units delivered using insulin pen devices as a percentage of total insulin use. **B.** Insulin units delivered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

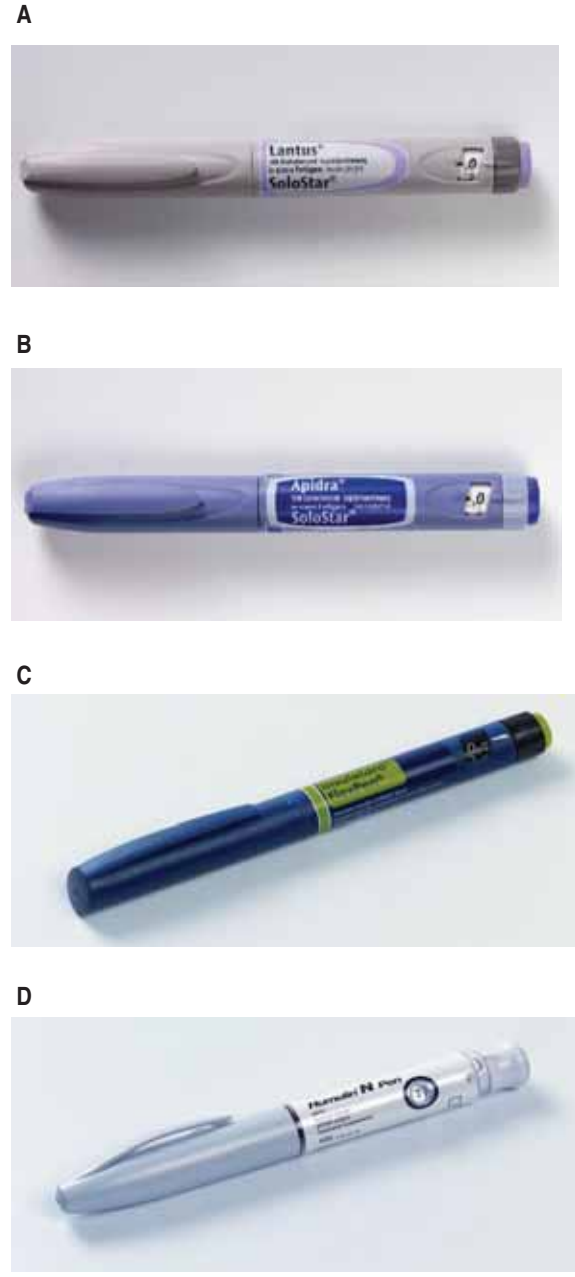

Figure 2. Photographs of SoloStar (A. insulin glargine, B. insulin glulisine), C. FlexPen and D. Lilly Pen.

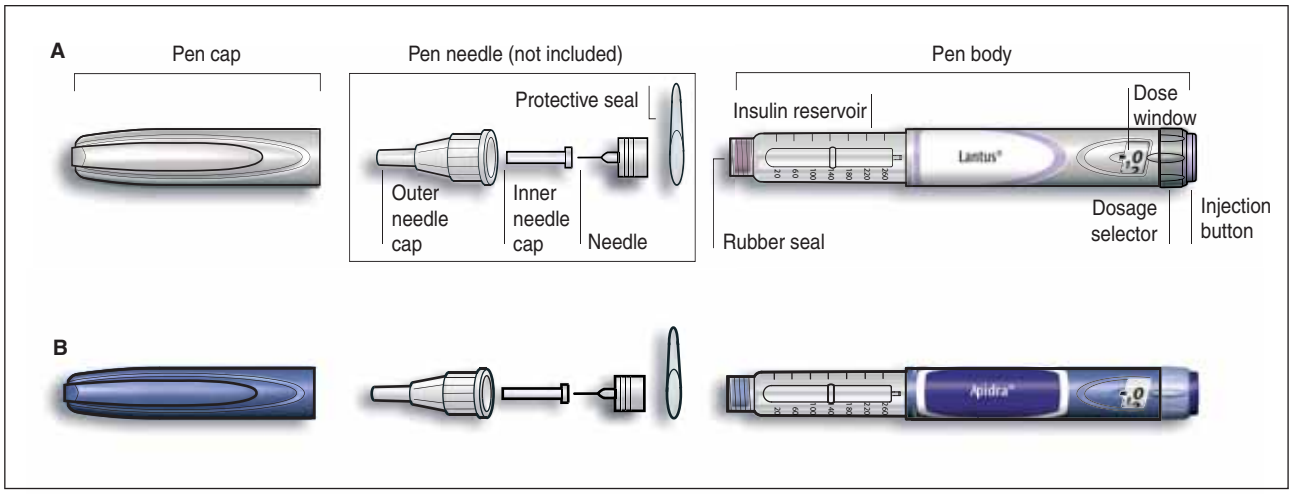

Figure 3. The SoloStar pen device showing key components of the pen and needles, and the color schemes used to help differentiate between insulin formulations to avoid medication errors.

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.

Table 1. The maximum dose, dose increments and dial extension (at 60 units) of SoloStar, FlexPen and Lilly Pen.

	SoloStar	FlexPen	Lilly Pen
Maximum dose (units)	80	60	60
Dose increments (units)	1	1	1
Dial extension at 60 units (mm)	25.5	33	11.2

4. Technical testing of the SoloStar pen

4.1 Applicable design standards

Like all insulin pens, SoloStar must meet a number of criteria specified by the International Organization for Standardization (ISO) and, in particular, ISO standards 11608-1, 11608-2 and 11608-3 for insulin pen devices, needles and cartridge systems, respectively. Compliance with these standards is required by the relevant medical devices authorities before the pen and associated accessories can be brought to the market. These standards serve to reassure both people with diabetes and clinicians that the insulin devices they use are of high quality and efficient. For example, when developing an insulin device, key features are regulated, including the presence of a scale on the cartridge holder and the ability of the device to use standard needles. In order to meet the ISO standards, the pens must undergo rigorous testing procedures; the dose accuracy test is a key ISO test and this is described below.

4.2 Dose accuracy testing

Dose accuracy is a core aspect of a pen's function. Consistent dose accuracy reassures patients that their pen, when used properly, will repeatedly deliver the dialed dose, facilitating the correct titration of insulin dose without increased risk of hypo- or hyperglycemia. A more detailed description of the methods used for dose accuracy testing is provided elsewhere [18]. In brief, SoloStar dose accuracy was tested across a range of temperatures (5°C, ambient temperature [18 – 28°C] and 40°C), after hot and cold storage (-40°C, +70°C) and after storage in cyclic, atmospheric conditions.

In accordance with ISO standards, dose accuracy tests were performed with SoloStar pens containing insulin glargine at doses of 1, 40 and 80 units. A total of 30 pens were used for each dose, with two replicates per pen. Pens were also tested after a variety of physical events, including dropping from a height of 1 m at three different orientations and after vibration according to ISO test standards. A different pen (always new and unused) was used for each test.

Table 2 shows results for the dose accuracy of SoloStar pens with insulin glargine at 5°C, ambient temperature (18 – 28°C) and at 40°C, for dialed doses of 1, 40 and 80 units. These results demonstrate that SoloStar is well within the standards for accuracy at each dose (1 unit: 0 – 2 units; 40 units: 38 – 42 units; 80 units: 76 – 84 units). The results of the dose accuracy tests at ambient temperature are illustrated in Figure 4.

Table 2. Dose accuracy of the SoloStar pen device (insulin glargine) at dialed doses of 1, 40 and 80 units at temperatures of 5 °C, ambient temperature (18 – 28 °C) and at 40 °C.

	Insulin dose (insulin glargine) delivered at each dialed dose		
Dialed dose	**1 unit**	**40 units**	**80 units**
Recommended range according to ISO standards	0 – 2	38 – 42	76 – 84
Cool temperature (5 °C)	1.22 ± 0.18	39.85 ± 0.28	79.75 ± 0.29
Ambient temperature (18 – 28 °C)	1.09 ± 0.15	39.92 ± 0.34	79.82 ± 0.28
Hot temperature (40 °C)	1.15 ± 0.11	39.87 ± 0.11	79.73 ± 0.14

Results are means ± standard deviation; 30 pens were used for each dose, with two replicates per pen.
ISO: International Organization for Standardization.

All tests were successfully passed and the results demonstrate that SoloStar pens are very accurate, consistently delivering the dialed doses of insulin well within the specifications of the ISO standard. Therefore, patients using this pen to administer insulin glulisine and/or insulin glargine can be reassured that the dose dialed is the dose that will be administered. Consequently, SoloStar may help to reduce the fear of inaccurate delivery as a contributor to hypoglycemia that is commonly associated with insulin therapy.

4.3 Injection force testing

Injection force testing was performed to measure the force and force characteristics required to dispense a known volume of insulin (40 units) within a fixed time period (4 s). This is not part of ISO standards, but was an additional test carried out to ensure that the performance of the devices meet the needs of the user.

For this test, the following pens were tested:

- SoloStar pens containing insulin glargine or insulin glulisine (20 of each insulin type)
- FlexPens containing insulin detemir (Levemir®, Novo Nordisk), insulin aspart (NovoLog®, Novo Nordisk) or Neutral Protamine Hagedorn (NPH) insulin (Insulatard®, Novo Nordisk) (20 of each insulin type)
- Lilly Pens containing NPH insulin (Humulin N®, Eli Lilly) or insulin lispro (HumaLog®, Eli Lilly) (20 of each insulin type)

For testing, all pens were fitted with Becton Dickinson microfine needles (0.25 mm [31 G] × 8 mm). The same needle

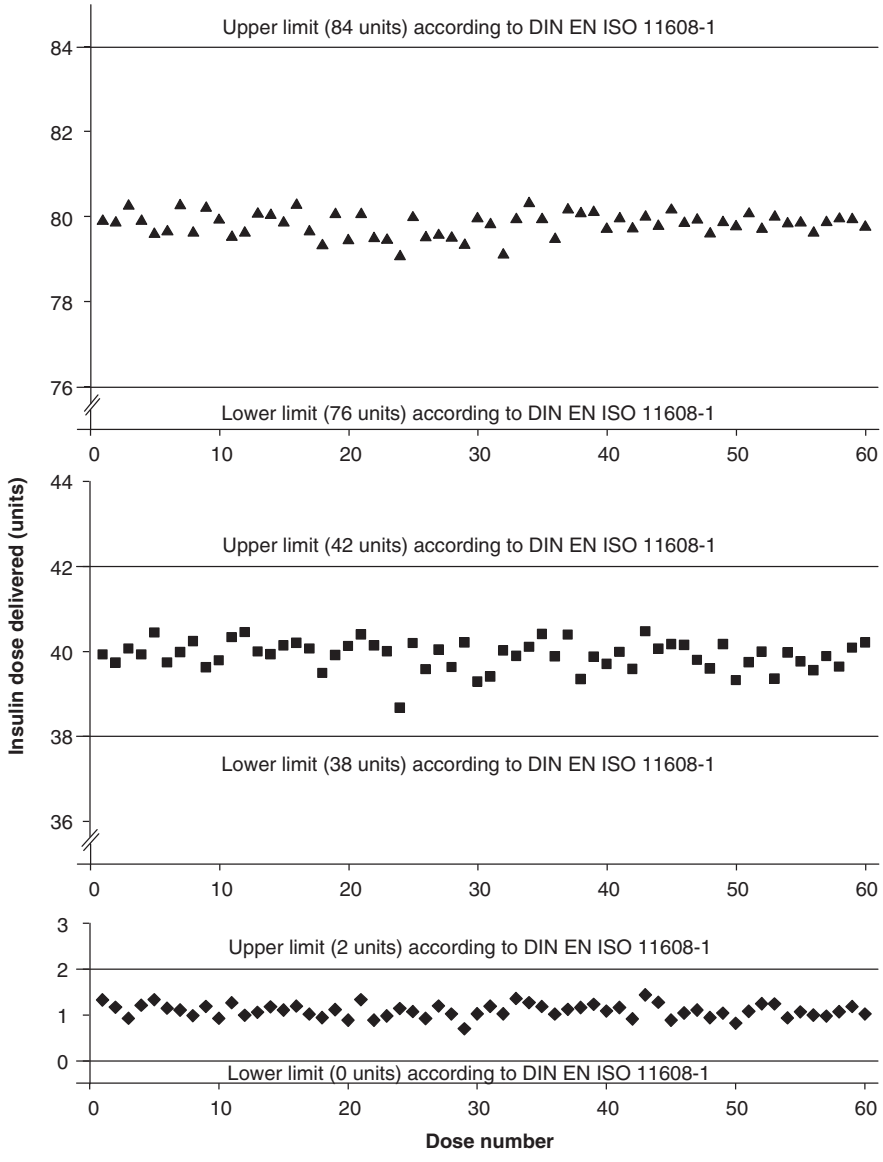

Figure 4. The accuracy of the SoloStar pen at ambient conditions (18 – 28 °C) to deliver fixed doses of 1, 40 and 80 units. The upper and lower limits, as defined by the Deutsche Institut für Normung, English version of the International Organization for Standardization (ISO) standard, 11608-1, are indicated for each dose.
DIN: Deutsche Institut für Normung; EN: English version.

type was used for all pens to ensure a fair comparison. Micro-Fine™ needles are recommended by Becton Dickinson for use with SoloStar, FlexPen and Lilly Pens. Studies with the FlexPen were repeated using NovoFine® (Novo Nordisk) needles (0.25 mm [31 G] × 6 mm). With NovoFine needles, the injection force was consistently greater than with Becton Dickinson needles of the same gauge (31 G) for each insulin type (data not shown). Although Novo Nordisk only recommends Novofine needles for use with the Flexpen, to avoid such a disadvantage for FlexPen, results are reported for all pens using Becton Dickinson needles (0.25 mm [31 G] × 8 mm).

Each pen was inserted into a Zwick Z2.5 force measurement machine with a 250 N load cell, which was programmed to drive in the dispense direction at a velocity that would cause the pen device to dispense 10 units/s. It is common with disposable pens that multiple safety shots are required before insulin appears at the end of the needle. Thus, to ensure that each pen had been fully primed, each new pen was set to deliver a 10-unit priming dose. Each pen was then set to deliver three subsequent doses of 40 units each. The load cell was reset to zero before commencing each test. The force was measured for the duration of each

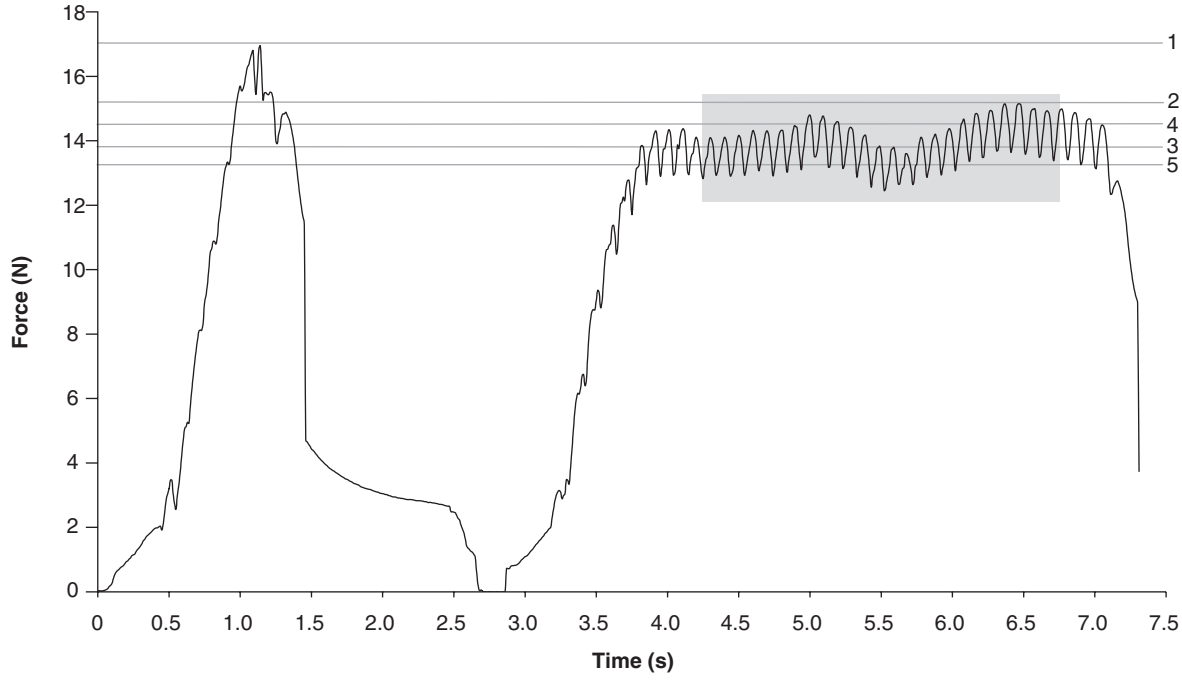

Figure 5. A typical force plot showing the force (N) required for one priming dose (10 units) and one 40-unit dose. The force characteristics are represented as horizontal lines. **1.** Peak priming force (maximum force measured during the priming dose). **2.** Peak dose force (maximum force measured during any of the three 40-unit doses). **3.** Mean plateau dose force (mean force measured during the 2.5 s plateau period of each of the three 40 unit doses). **4.** Mean peak plateau dose force (mean of the peak dose force measured during the plateau period). **5.** Mean dose force for the total dose (mean dose force taken for all three 40 unit doses).
The grey shaded box shows the 2.5-s sample that was used for the calculation of the plateau forces for each pen, to eliminate any biasing from the acceleration and/or deceleration of the force machine.

dispense; the force characteristics were calculated as demonstrated in Figure 5.

Table 3 shows a comparison of injection forces for SoloStar, FlexPen and Lilly Pen. SoloStar with insulin glulisine has a mean total injection force that is > 40% lower than FlexPen with insulin aspart, while SoloStar with insulin glargine has a mean total injection force that is > 30% lower with FlexPen containing insulin detemir. Furthermore, SoloStar with either insulin glulisine or insulin glargine has a mean injection force that is less than half that of the Lilly Pen containing either insulin lispro or NPH insulin.

Figure 6 shows the force profile for a single dose of 40 units delivered in 4 s for SoloStar with insulin glulisine, FlexPen with insulin aspart and Lilly Pen with insulin lispro. The force profiles shown are representative of each set of results. The graph shows that the injection force with SoloStar is the lowest of the three pens tested.

Figure 6 also shows that SoloStar has the smoothest injection force profile (the smallest force difference between peaks and troughs during the injection), especially when compared with FlexPen, which has the highest peak-to-trough variation (one peak per unit delivered), with the result that the injection with SoloStar will feel more soft and gentle, as well as easier to use. The smoother injection force with SoloStar is primarily due to the smaller force difference between the peaks and troughs during injection. Of note is the finding that the injection force was low, despite testing with a very fine needle gauge; the smaller the pen needle gauge, the greater the force needed to complete the injection.

These results show that SoloStar requires low forces in order to inject a dose of insulin. Therefore, patients will find it easy to inject insulin with SoloStar.

5. Conclusions

From a patients' perspective, the simplicity of use of a specific device is an important factor when deciding on which pen to use on a day-to-day basis; SoloStar was designed with this factor at the forefront of the design process. From a clinical perspective, the accuracy of the dose delivered is a key factor when selecting an insulin delivery system. Lack of accuracy may increase risk of hypo- or hyperglycemia. The results presented here for SoloStar demonstrate that, used correctly, SoloStar will accurately administer the dialed dose of insulin,

Table 3. A comparison of injection forces between SoloStar, FlexPen and Lilly Pen.

Pen	Insulin	Mean force for total dose (N)	Mean plateau dose force (N)	Peak dose force (N)	Mean peak plateau dose force (N)	Peak priming force (N)
SoloStar	Insulin glulisine	10.3	12.0	14.2	12.6	18.7
	Insulin glargine	11.3	13.4	15.2	13.9	17.4
FlexPen	Insulin detemir	16.3	18.3	23.9	21.2	22.6
	Insulin aspart	17.2	19.2	25.5	22.7	23.8
	NPH insulin	17.7	19.9	25.5	22.8	21.7
Lilly Pen	NPH insulin	24.4	28.0	30.7	28.3	24.4
	Insulin lispro	25.3	28.8	32.9	29.2	26.6

Each pen was set to deliver one 10-unit dose to prime the pen, and then to deliver three subsequent doses of 40 units each. The force characteristics were calculated as shown in Figure 5.

allowing reliable dose adjustment and minimizing the risk of hypo- or hyperglycemia arising from inaccuracies in dose delivery. This may enhance patient adherence to insulin therapy and reduce diabetes-related treatment costs, as demonstrated with other pen devices [2].

The injection force and profile data presented show that SoloStar has significantly improved injection force characteristics compared with FlexPen and Lilly Pen. This lower injection force, smoother injection profile and shorter dial extension, compared with FlexPen, mean that patients can inject their insulin more easily. Such mechanical characteristics are of significant clinical benefit for the large number of people who have diabetes with impaired hand function [13-16], who may otherwise have limited ability to inject insulin themselves.

An ideal pen needs to offer an appropriate combination of achievement against multiple features. For example, despite the shorter dial extension with the Lilly Pen, the force required to inject a dose of insulin is greater. With SoloStar, the achievements on injection force and dial extension are coupled with many other needed features, including simplicity of operation, a higher maximum dose (80 units) and different colors for basal and meal time insulin (a first for a disposable pen). This combination of design features means that the SoloStar pen is suitable for use by most people with Type 1 or Type 2 diabetes.

6. Expert opinion

According to the consensus statement from the American Diabetes Association and the European Association for the Study of Diabetes on management of hyperglycemia in Type 2 diabetes, a haemoglobin A_{1c} level $\geq 7\%$ should serve as a call to initiate or change therapy. As diabetes progresses, it becomes necessary to introduce insulin therapy to achieve or maintain adequate diabetes control.

As the transition to insulin from oral therapy requires intensifying self-care management, it is often a time of stress for the patient. Not only does the patient need to consider how insulin use will affect lifestyle therapies, such as nutrition and physical activity, the patient also needs to learn how to successfully incorporate a therapy that must be self-injected. Pen devices have reduced some of the anxiety associated with initiating insulin therapy for many patients, due to their ease of use and the fact that they complement the flexibility of modern lifestyles by being much more portable than a vial and syringe. In most circumstances, patients prefer pen devices for the delivery of insulin, and many diabetes patients who have been using vial and syringes will request that insulin be prescribed in pens, citing simplicity, accuracy and flexibility as the key reasons for the request. If patients feel that the pen is easier to use and more socially acceptable, the likelihood of adherence to insulin therapy is increased.

Patients starting on insulin, such as Type 2 diabetes patients who are prescribed oral agents and one injection of basal insulin per day, find that the pen device can be more easily incorporated into their daily routine. The improvements made in the SoloStar device – simplicity of use, reduced injection force and high dose capability – make this a desirable device for first-time insulin users.

For patients with Type 1 diabetes or for those with Type 2 diabetes with significant β-cell deficit, the present trend is for intensive insulin management with a basal insulin, such as insulin glargine, plus premeal rapid-acting insulin. This system of subcutaneous insulin replacement mimics the body's physiologic insulin secretory pattern and results in better glucose control. However, in order to successfully adopt this insulin regimen, the patient must be willing to give insulin prior to the ingestion of any carbohydrate-containing meal or snack. Many patients will need to inject insulin 5- to 7-times per day; for these patients, insulin pens make intensive therapy 'liveable'. SoloStar is available in two distinct color schemes for patients who use both basal and rapid-acting, bolus insulin (Figure 3), to help prevent confusing the pens containing the different insulins.

During the next 5 – 10 years, the use of insulin and pen devices for insulin delivery will continue to increase in settings outside of the diabetes specialty offices. As the number of patients

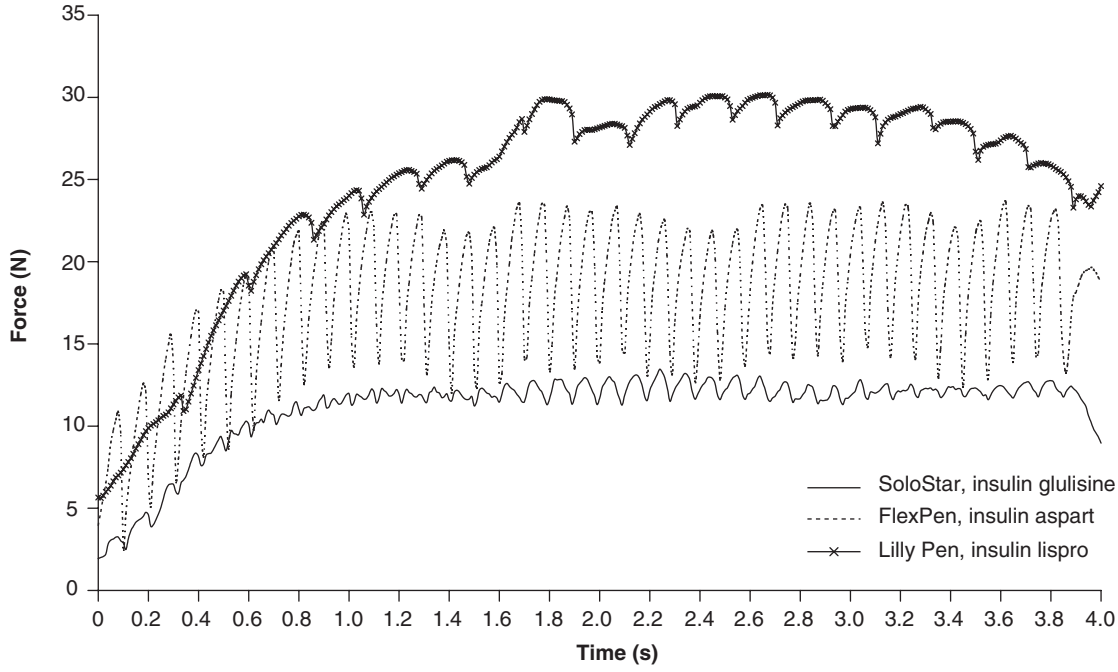

Figure 6. The force required to inject 40 units of insulin to be delivered in 4 s for a representative pen of SoloStar with insulin glulisine, FlexPen with insulin aspart and Lilly Pen with insulin lispro.

treated with insulin in the primary care setting continues to grow, there is a need for simple, effective insulin regimens. The addition of a basal insulin to oral therapy is usually the easiest method to reach and sustain blood glucose targets, while keeping the self-management program as easy for the patients as possible. The time and attention necessary to educate patients in insulin administration will fall to the physician or the office staff. Teaching patients to use a pen device requires much less time than any other insulin delivery method. The ease and simplicity of the insulin pen device helps to instil confidence in the patient that it is a skill that can be learnt without difficulty.

When evaluating the insulin pens presently available for use, each product has certain attributes that address the needs of the insulin user, including a basic need for accuracy. The data presented here show that SoloStar is highly accurate and safe for patients to use.

Specific features of insulin pens are considered more important in certain patient populations. For example, dexterity and visual issues may be the defining characteristics in selecting a pen for a person using insulin for the first time. Having the hand strength necessary to depress the injection button without interruption and without causing movement of the needle at the injection site is a critical component of proper pen use. The SoloStar has reduced the injection force significantly, which, in combination with the shorter dial extension than some other insulin pens, means that patients with varying hand strength or dexterity can use this pen device comfortably.

SoloStar is an intuitive device in that patients who have never seen an insulin pen before can very easily and very quickly learn how to use it. Used with insulin glargine and insulin glulisine, SoloStar will provide a useful tool in both primary and secondary care management of diabetes.

Conflict of interest

A Clarke is an employee of sanofi-aventis. G Spollett serves on advisery boards for sanofi-aventis, Eli Lilly and Amylin Pharmaceuticals. She is also on the speakers bureau for Novo Nordisk and Pfizer.

Bibliography

Papers of special note have been highlighted as either of interest (•) or of considerable interest (••) to readers.

1. IMS HEALTH: IMS Midas(TM) June 2006, Quarterly insulin sales volume in units. (2006)
2. LEE WC, BALU S, COBDEN D, JOSHI AV, PASHOS CL: Medication adherence and the associated health-economic impact among patients with Type 2 diabetes mellitus converting to insulin pen therapy: an analysis of third-party managed care claims data. *Clin. Ther.* (2006) 28(10):1712-1725.

•• This paper demonstrates that switching from the vial and syringe to pen devices is associated with improved medication adherence, fewer claims for hypoglycemic events, and reduced emergency treatment, leading to lower annual treatment costs, despite the higher cost of medication associated with pens versus the vial and syringe.

3. Fear of the injection must not be an argument. Every second type 2 diabetic patient needs insulin. *MMW Fortschr. Med.* (2002) 144(49):60.
4. WAGNER J, MALCHOFF C, ABBOTT G: Invasiveness as a barrier to self-monitoring of blood glucose in diabetes. *Diabetes Technol. Ther.* (2005) 7(4):612-619.
5. KEITH K, NICHOLSON D, ROGERS D: Accuracy and precision of low-dose insulin administration using syringes, pen injectors, and a pump. *Clin. Pediatr. (Phila)* (2004) 43(1):69-74.
6. SUMMERS KH, SZEINBACH SL, LENOX SM: Preference for insulin delivery systems among current insulin users and nonusers. *Clin. Ther.* (2004) 26(9):1498-1505.
7. BELL DS, CLEMENTS RS, Jr., PERENTESIS G, RODDAM R, WAGENKNECHT L: Dosage accuracy of self-mixed vs premixed insulin. *Arch. Intern Med.* (1991) 151(11):2265-2269.

• This paper demonstrates the perceptions of patients with Type 2 diabetes and their providers to insulin and demonstrate the profound psychological resistance to insulin therapy.

8. POLONSKY WH, FISHER L, GUZMAN S, VILLA-CABALLERO L, EDELMAN SV: Psychological insulin resistance in patients with type 2 diabetes: the scope of the problem. *Diabetes Care* (2005) 28(10):2543-2545.

• This paper demonstrates the perceptions of patients with Type 2 diabetes and their providers to insulin and demonstrate the profound psychological resistance to insulin therapy.

9. PEYROT M, RUBIN RR, LAURITZEN T *et al.*: Resistance to insulin therapy among patients and providers: results of the cross-national Diabetes Attitudes, Wishes, and Needs (DAWN) study. *Diabetes Care* (2005) 28(11):2673-2679.
10. SPIJKER A, HOEKSTRA J, ERKELENS D: The insulin pen: a new device for multiple insulin injections. *Transplantation Proceedings* (1986) 18(6):1689-1690.
11. ALJAHLAN M, LEE KC, TOTH E: Limited joint mobility in diabetes. *Postgrad. Med.* (1999) 105(2):99-101, 105-106.
12. STARKMAN HS, GLEASON RE, RAND LI, MILLER DE, SOELDNER JS: Limited joint mobility (LJM) of the hand in patients with diabetes mellitus: relation to chronic complications. *Ann. Rheum. Dis.* (1986) 45(2):130-135.

• This paper provides a historical perspective of the prevalence and causes of manual dexterity problems in patients with diabetes, and highlights the key unmet needs of insulin administration for patients with diabetes.

13. SAVAS S, KOROGLU BK, KOYUNCUOGLU HR *et al.*: The effects of the diabetes related soft tissue hand lesions and the reduced hand strength on functional disability of hand in type 2 diabetic patients. *Diabetes Res. Clin. Pract.* (2006) [Epub].
14. ROSENBLOOM AL: Limitation of finger joint mobility in diabetes mellitus. *J. Diabet. Complications* (1989) 3(2):77-87.

• This paper provides a historical perspective of the prevalence and causes of manual dexterity problems in patients with diabetes, and highlights the key unmet needs of patients with diabetes for insulin administration.

15. ZIEGLER D, GRIES FA, SPULER M, LESSMANN F: The epidemiology of diabetic neuropathy. DiaCAN Multicenter Study Group. *Diabet. Med.* (1993) 10(Suppl. 2):82S-86S.

• This paper provides a historical perspective of the prevalence and causes of manual dexterity problems in patients with diabetes, and highlights the key unmet needs of patients with diabetes for insulin administration.

16. SCHADY W, ABUAISHA B, BOULTON AJ: Observations on severe ulnar neuropathy in diabetes. *J. Diabetes Complications* (1998) 12(3):128-132.
17. ADLERSBERG MA, FERNANDO S, SPOLLETT GR, INZUCCHI SE: Glargine and lispro: two cases of mistaken identity. *Diabetes Care* (2002) 25(2):404-405.
18. CLARKE A, DAIN MP: Dose accuracy of a reusable insulin pen using a cartridge system with an integrated plunger mechanism. *Expert Opin. Drug Deliv.* (2006) 3(5):677-683.

Website

101. http://www.ismp.org/newsletters/acutecare/articles /20061130.asp INSTITUTE FOR SAFE MEDICATION PRACTICES: Pen injectors: technology is not without impending risks. (Accessed 8th January 2007).

Affiliation

Alastair Clarke†1 & Geralyn Spollett2
†Author for correspondence
1Head of Device Design and Industrialisation, Sanofi-Aventis Deutschland GmbH, Frankfurt am Main, Site Frankfurt Devices/Device Design & Industrialisation, Industriepark Hoechst, Building K607, D-65926 Frankfurt am Main,Germany
Tel: +49 (0) 69 305 40475;
Fax: +49 (0) 69 305 40496;
E-mail: Alastair.Clarke@sanofi-aventis.com
2Nurse Practitioner and Associate Director of the Yale Diabetes Center, Yale University, Section of Endocrinology, New Haven, USA