

## FlexTouch: A Prefilled Insulin Pen with a Novel Injection Mechanism with Consistent High Accuracy at Low- (1 U), Medium- (40 U), and High- (80 U) Dose Settings

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### Abstract

#### Background:

FlexTouch<sup>®</sup> is the only prefilled insulin pen that utilizes an easy touch button that does not extend at any dose in place of a push-button extension. Rigorous testing has shown that the new FlexTouch pen accurately and consistently delivers insulin doses.

#### Methods:

This study assessed dose accuracy of FlexTouch, KwikPen<sup>®</sup>, and SoloSTAR<sup>®</sup>. Dose accuracy for minimum, medium, and maximum doses of each pen type (1, 40, and 80 U for FlexTouch and SoloSTAR and 1, 30, and 60 U for KwikPen) was assessed.

#### Results:

FlexTouch delivered all doses consistently, as demonstrated by low standard deviations. FlexTouch showed similar accuracy to KwikPen at 1 U and to SoloSTAR at 40 and 80 U. However, FlexTouch was significantly more accurate at delivering 1 U of insulin than SoloSTAR ( $p < .0001$ ).

#### Conclusions:

This study demonstrates that FlexTouch, a new prefilled pen, delivers insulin accurately and consistently at low, medium, and high doses. In addition, FlexTouch is currently the only prefilled pen that has a push button that does not extend at any dose, making FlexTouch easier to use than other pens.

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### Introduction

Before the introduction of insulin injection pens, patients with type 1 or 2 diabetes routinely depended on vials of insulin and insulin syringes to deliver their medication

via injection.<sup>1,2</sup> However, use of vials and syringes can be inconvenient and difficult and is often associated with needle anxiety, fear of injection pain, and social awkward-

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**Abbreviations:** (ISO) International Organization for Standardization

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ness.<sup>3-8</sup> Insulin pens, either prefilled or durable, simplify the injection process and are now the main devices used for insulin delivery, especially in Europe, China, and Japan, but less so in the United States.

Importantly, pens have been proven to deliver more accurate and consistent doses of insulin than vials and syringes, particularly at low doses (<5 U), and, as such, potentially contribute to controlling glucose levels more effectively.<sup>9-11</sup> Use of vials and syringes can produce errors of more than 20% at lower doses, and they are usually associated with overdosing, which may contribute to glycemic variation in the patient.<sup>12</sup> Accuracy in delivering the correct insulin dose is the first step to ensuring precise insulin dosing and should help reduce glycemic variations,<sup>13-15</sup> consistent delivery of an accurate dose is likely to increase patient trust in a pen device. Any technical improvement in insulin pens that can reduce variability during insulin injection could further aid the control of glucose levels.<sup>13</sup>

Modern prefilled pens are simple to use and have proven dosing accuracy at low, medium, and high doses.<sup>13-18</sup> FlexTouch<sup>®</sup> (Novo Nordisk A/S, Bagsværd, Denmark) is the only prefilled insulin pen utilizing an easy touch button that does not extend at any dose, instead of a push-button extension during the setting and delivery of insulin doses; this feature was developed to improve the ease of use and handling for patients during insulin injection. Furthermore, the pen features a unique internal spring mechanism that drives the delivery of the insulin dose. Consequently, the activation force is determined by this push-button spring instead of the thumb pressure of the user. FlexTouch has incorporated other features to improve patient satisfaction, including an end-of-dose click for patient convenience, clear dose display, maximum 80 U dose, colored cartridge holder, and NovoTwist<sup>®</sup> needle interface.

This study was designed to investigate the accuracy and consistency of dosing of FlexTouch at minimum, medium, and maximum doses and to compare these with SoloSTAR<sup>®</sup> (sanofi-aventis, Paris, France) and KwikPen<sup>®</sup> (Eli Lilly & Co, Indianapolis, IN) in a controlled laboratory setting.

## Methods

Pens tested were

- FlexTouch filled with 3 ml Levemir<sup>®</sup> (insulin detemir; Novo Nordisk A/S, Bagsværd, Denmark; lot numbers XL700018 and YP51685);

- FlexTouch filled with 3 ml NovoRapid<sup>®</sup> (insulin aspart; Novo Nordisk A/S, Bagsværd, Denmark; lot numbers XL700014 and XL700015);
- SoloSTAR filled with 3 ml Lantus<sup>®</sup> (insulin glargine; sanofi-aventis, Paris, France; lot numbers 40C531 and 40C659); and
- KwikPen filled with 3 ml Humalog<sup>®</sup> (insulin lispro; Eli Lilly & Co, Indianapolis, IN; lot numbers A656889F and A638534F).

In this study, pens were as follows: 30 pens from two different production lots (15 each) for FlexTouch with Levemir, FlexTouch with NovoRapid, SoloSTAR with Lantus, and KwikPen with Humalog. Each of the 30 pens was used to deliver each dose twice (60 measurements of each dose level with each pen type were performed) as described in International Organization for Standardization (ISO) 11608-1:2000.<sup>19</sup> Dose accuracy was measured in standard conditions: pens were exposed to 20 °C ( $\pm 2$  °C) and relative humidity 45% ( $\pm 7.5\%$ ) for at least 4 h before measuring dose accuracy. Dosing accuracy for minimum, medium, and maximum doses of each pen type (1, 40, and 80 U for FlexTouch and SoloSTAR and 1, 30, and 60 U for KwikPen) was tested.

The manufacturers' recommended needle was attached to each pen (NovoFine<sup>®</sup> 31 G 6 mm needles for FlexTouch and BD Micro-Fine<sup>™</sup> 31 G 5 mm needles for SoloSTAR and KwikPen). Air was expelled according to manufacturers' protocol by performing air shots until liquid appeared at the tip of the needle. After the pen was held in place, the appropriate dose was discharged and weighed (5 s for KwikPen, 10 s for SoloSTAR, and 6 s for FlexTouch according to instructions for use of each pen), using a sensitive pharmaceutical balance (Mettler AX1, Mettler Toledo, Glostrup, Denmark). Results were corrected for the specific density of the insulin formulations using the following conversion factors: FlexTouch (NovoRapid 1.005; Levemir 1.008), KwikPen (Humalog 1.004), and SoloSTAR (Lantus 1.003). The conversion factor was used to calculate relative difference from target and unit values. FlexTouch was tested with both basal and rapid-acting insulin analogs, and results for FlexTouch NovoRapid and FlexTouch Levemir were pooled. As accuracy is determined by the pen and not the insulin, the mean value and standard deviation (SD) were calculated. Outcome measures were accuracy and consistency of the dose delivered from the pens compared with the specified dose. Results were compared with the acceptable range, as defined in

ISO regulations (ISO 11608-1:2000): 0–2 U for 1 U dose, 28.5–31.5 U for 30 U, 38–42 U for 40 U, 57–63 U for 60 U, and 76–84 U for 80 U.

The statistical software package JMP 8.02 was used for all calculations. Pairwise comparisons were made in analysis of variance (fit model) and using Tukey’s honestly significant difference or pairwise comparisons if only two comparisons were made.

## Results

All doses delivered from FlexTouch were within ISO limits (ISO 11608-1:2000). FlexTouch was accurate in the delivery of 1 U (mean ± SD, 0.98 ± 0.07 U, range 0.72–1.18 U), 40 U (39.86 ± 0.33 U, range 38.90–40.63 U), and 80 U (79.76 ± 0.64 U, range 78.49–81.39 U), with a very low deviation from the target dose (Figure 1). FlexTouch had consistent accuracy when delivering 1, 40, and 80 U as demonstrated through the repetitive test results (as shown in Figures 2–4) and demonstrated by relatively low SDs.

FlexTouch was significantly more accurate for the delivery of 1 U versus SoloSTAR (1.14 ± 0.22 U, range 0.49–1.39 U,  $p < .0001$ ). No significant differences were detected in accuracy of delivery of 40 U ( $p = .155$ ) or 80 U ( $p = .071$ ) between FlexTouch and SoloSTAR. FlexTouch was slightly (nonsignificantly) more accurate for delivery of 1 U than KwikPen (1.03 ± 0.1 U, range 0.8–1.3 U,  $p < .159$ ). Overall, the calculated minimum, mean ± SD, and maximum delivered doses of all pens were within ISO limits at all dose levels tested. The range of delivered doses for all pens at minimum, medium, and maximum U doses are

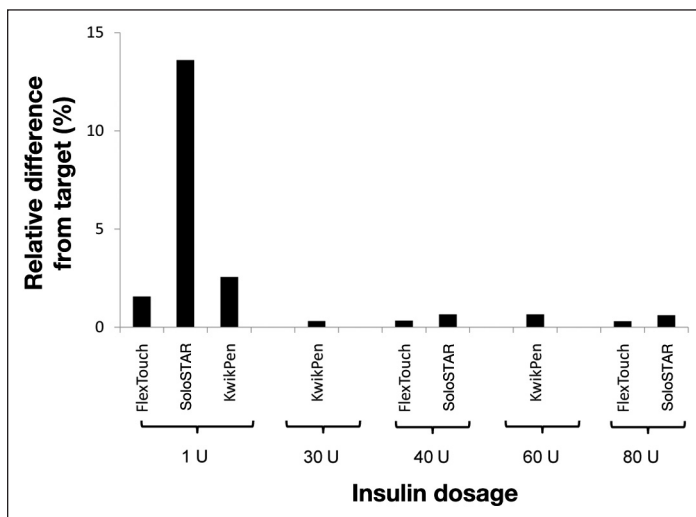


Figure 1. Mean relative percentage difference from target dose for FlexTouch, SoloSTAR, and KwikPen.

shown in Figures 2–4. Variability was more marked with SoloSTAR at the minimum dose than with other pens (Figure 2).

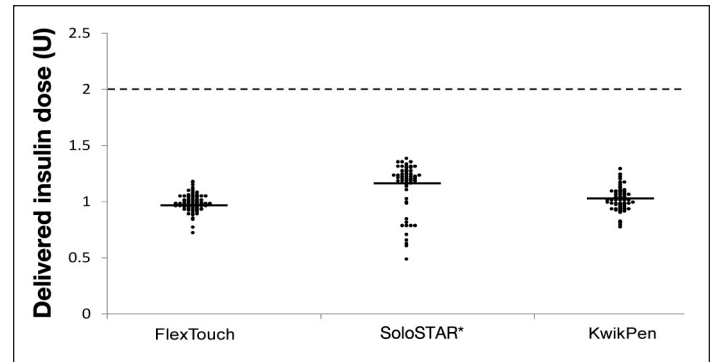


Figure 2. Dose accuracy of the three insulin pens, FlexTouch, SoloSTAR, and KwikPen, at 1 U. The solid line indicates mean value, and the dashed line represents the limit of the ISO acceptance range. The asterisk represents  $p < .0001$  FlexTouch versus SoloSTAR and KwikPen versus SoloSTAR.

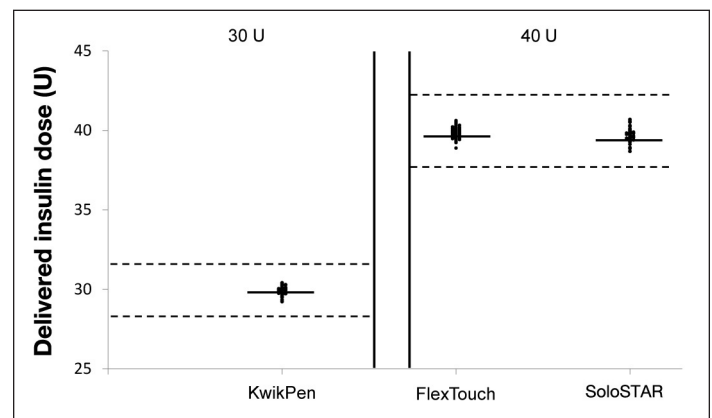


Figure 3. Dose accuracy of KwikPen at 30 U and FlexTouch and SoloSTAR at 40 U. The solid line indicates mean value, and the dashed lines represent the limits of the ISO acceptance range.

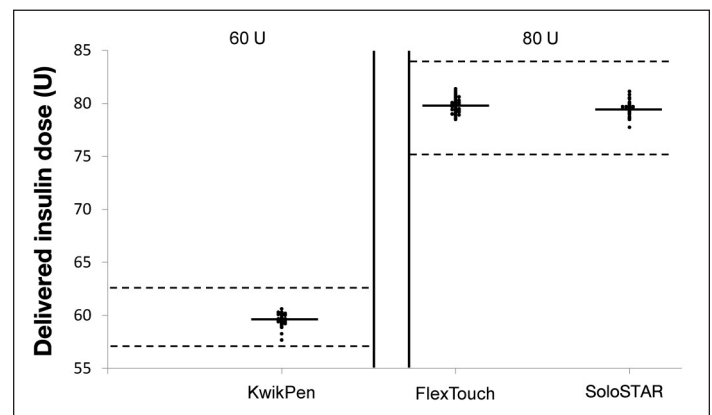


Figure 4. Dose accuracy of the three insulin pens, KwikPen at 60 U and FlexTouch and SoloSTAR at 80 U. The solid line indicates mean value, and the dashed lines represent the limits of the ISO acceptance range.

## Discussion

Overall, the findings from this study demonstrate that the new prefilled FlexTouch pen delivers insulin accurately and consistently at low, medium, and high doses. This is demonstrated by the accurate mean dose delivered and the small SDs. FlexTouch was significantly more accurate than SoloSTAR at the 1 U dose and had similar accuracy to KwikPen. Accuracy at all doses was within the acceptable limits of ISO 11608-1:2000 for all pens tested.

As well as the accuracy for delivering insulin, the consistency of insulin delivery is an important aspect of insulin delivery devices.<sup>20</sup> Consistency is a measure of the variability of delivered doses with a given device. Minimizing variability in the delivered dose, that is, ensuring that an accurate dose is delivered consistently, thus maximizing or enhancing optimal diabetes management, is an important factor in generating trust in the pen. Low SDs observed with FlexTouch showed the consistency of insulin delivery with this pen.

These tests were conducted using the manufacturers' recommended needle for each pen type to ensure that the pens were used according to the manufacturers' instructions.

Insulin pens with high dosing accuracy are important tools that aid in improving treatment adherence<sup>5,21</sup> and, therefore, may potentially help control glucose levels and reduce the long-term complications of hyperglycemia. The innovative design of FlexTouch, with its easy touch button, end-of-dose click, accurate dosing from 1–80 U, and unique spring-loaded mechanism for easy dose delivery will help to simplify insulin regimens for people with diabetes and health care professionals. Patients with decreased manual dexterity or arthritis may especially benefit from use of this pen, and the accuracy results presented here imply that FlexTouch offers an improvement for accurate insulin injection in a wide range of patients.

This test was set up in alignment with the ISO regulations (ISO 11608-1:2000) to ensure sufficient powering and validity of the results. ISO 11608-1:2000 is a technical specification designed to ensure that insulin pens perform within a predefined level of accuracy. The ISO standard is not a guideline to competitively measure and compare accuracy between different pen types. Measurement of consistent and accurate dosing of insulin pens is very relevant to diabetes treatment, particularly at lower doses where accuracy is linked to a significant decrease in fasting

glucose treatment outcome and improved quality of life.<sup>22</sup> Delivery of an accurate minimal dose is specifically important for people with diabetes requiring small doses, such as children and patients with type 1 diabetes.<sup>11</sup> Therefore, while we have used ISO limits to define accuracy in this study, these are not necessarily clinically relevant. Instead, it may be best to simply consider the most suitable pen to be that which consistently delivers insulin as close as possible to the intended dose.

## Conclusion

Insulin pens with good accuracy help facilitate optimal insulin delivery for people with diabetes. Once it becomes established that a pen device will deliver accurately and reliably, thus improving adherence, these factors may assist in the control of glucose levels and reduce long-term hyperglycemia. This study demonstrates that FlexTouch, the only prefilled pen with no push-button extension, delivers insulin accurately and consistently at low, medium, and high doses. The features of this pen, including the easy touch button, will be of benefit to all insulin users but may be particularly beneficial to those with impaired manual dexterity.

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### Disclosures:

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