

## A PROSPECTIVE, OPEN-LABELLED, NON-CONTROLLED OBSERVATIONAL STUDY TO ASSESS DOCTOR PREFERENCE ON FLEXPEN™ FOR TREATMENT OF DIABETES MELLITUS

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in behalf of the FACT Study Group

### ABSTRACT

**Background:** The accuracy and convenience of pen devices for insulin injection have improved quality of life for patients with insulin-treated diabetes mellitus (DM). Prefilled, disposable pens have the advantage of simplicity, with minimal training and attention required and these offer improvements in compliance, freedom and flexibility.

**Objective:** The survey assessed doctor preference in prescribing insulin in a FlexPen™ in diabetes patients in the Philippines under normal clinical practice conditions. The data was based from observations on the use of NovoMix® 30 FlexPen™ (Biphasic Insulin Aspart 30). Data was collected from 256 doctors who were specialised in treating patients with diabetes and had their clinics in the Philippines. A Doctor Preference Questionnaire was developed to assess doctor preference in specific terms of ease of learning and teaching use of FlexPen™, time spent for patient training in use of FlexPen™, ease of setting up the required dose of FlexPen™, Doctor's satisfaction of shifting from any other device to FlexPen™, confidence that the correct amount of insulin will be injected, feedback about the NovoFine® 30G needles, overall experience with FlexPen™.

**Results:** In total, 256 doctors participated and completed the doctor satisfaction questionnaires. Majority of doctors 62.1% felt learning/ teaching the use of FlexPen™ to the patients was "very easy"; and

66.8% healthcare professionals (doctor or their staff) spent less than 10 minutes to train the patients on how to use FlexPen™. About 96% doctors responded that it is very easy or easy to set up the required dose and dose correction using FlexPen™. About (98.8%) doctors were confident or very confident that their patients will inject the correct dosage of insulin using FlexPen™. Almost all doctors (98.4%) satisfied or very satisfied about the patient shifting from other insulin devices to FlexPen™; 39.5% doctors rated the design of FlexPen™ as excellent; 55.5% rated it as good; while 74.6% doctors rated the overall experience of FlexPen™ as excellent.

**Conclusion:** The participating doctors showed high degree of acceptance of Flexpen™. The overall experience of Flexpen™ was excellent.

**Keywords:** Diabetes, pre-filled insulin pen, Flexpen™.

### INTRODUCTION

It is well established that improvements in long-term glycemic control can reduce the incidence and delay the progression of diabetic complications. Patients with type 1 diabetes require insulin from diagnosis. Patients with type 2 diabetes initially benefit from lifestyle intervention programs, for example diet and exercise, but oral antidiabetic agents (OADs) and insulin therapy are usually required over time.<sup>1</sup>

The UKPDS exposed the need for Insulin therapy to arrest the inexorable decline in beta-cell function and concluded that insulin seems to be the natural replacement therapy to offset the progressive loss of beta-cell function seen in type 2 diabetes.<sup>2</sup> However, consensus opinion on how or when or an agreed optimal mode of initiating insulin treatment in type 2 diabetes patients is lacking, and treatment regimens are known to vary between countries.<sup>3,4</sup>

In the treatment of type 2 diabetes with insulin and despite the benefits of tight glycemic control, there is reluctance on the part of physicians and patients to initiate insulin therapy.<sup>5,6</sup> Insulin initiation presents a number of challenges both to the patient and the care-giver, including anxiety

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about injections, the perceived complexity of insulin regimens, inconvenience of a vial and syringe, social acceptability, fear of hypoglycaemia, weight gain and the potential adverse impact of insulin therapy on lifestyle.<sup>7</sup> Thus, insulin therapy is often withheld until late in the disease process for patients with type 2 diabetes mellitus. This results in an enormous burden of disease for patients. Insulin therapy is beneficial in obtaining glycemic control and may attenuate the complications associated with diabetes.<sup>8</sup>

It is in this context that insulin pens have the potential to become a major asset for breaking barriers to early initiation of insulin by improving compliance among diabetic patients. These devices offer substantial improvements in convenience, freedom, and flexibility for all insulin-using patients. In addition, use of pens may also be associated with reduced therapy costs. Furthermore, physicians can also find that their efforts are more rewarded as the better compliance and also the more accurate dosing associated with use of the pen may hold the key to better long-term outcomes.

Two types of insulin pens are available today: prefilled and reusable. Prefilled pens are simply discarded when the insulin cartridge is spent, whereas reusable pens contain a replaceable insulin cartridge that is loaded into and removed from the pen by the patient. Most pens function on simple mechanical principles and are durable. The technique for insulin delivery is similar for both prefilled and reusable pens. Prefilled, disposable pens have the advantage of simplicity, with minimal training required, as patients are not required to install a new cartridge when the pen is empty. In many patients, these devices have been demonstrated to improve accuracy of insulin administration and/or adherence.<sup>9</sup>

In a study done by Rubin and Peyrot (2004), it was noted that interest in intensified insulin therapy has contributed to the increased popularity of alternative insulin delivery systems, including insulin pen delivery devices.<sup>10</sup> Patients had a marked preference for premixed insulins delivered in a pen-type syringe over conventional insulin therapy. Premixed insulin delivered by a pen-type syringe promises to ease the burden of daily injections for many diabetic patients.<sup>11</sup>

NovoMix® 30 Flexpen™ (Biphasic Insulin Aspart 30) is a prefilled insulin pen device that deliver a 30/70 mixture of rapid-acting and intermediate-acting analogue insulin (a suspension of soluble insulin aspart and protamine-crystallized insulin aspart).<sup>10</sup>

This paper presents the results of assessment of physician preference using physician questionnaire in prescribing Insulin in FlexPen™ in diabetes patients in Philippines. The objective of this survey was to determine doctor preference in prescribing insulin in a Flexpen™ for treatment of diabetes mellitus patients in Philippines.

## MATERIALS AND METHODS

### *Design of the survey*

The survey was conducted to assess doctor preference in prescribing insulin in a FlexPen™ in diabetes patients in the Philippines under normal clinical practice conditions. The data was based from observations on the use of NovoMix® 30 FlexPen™ (Biphasic Insulin Aspart 30). No patient was assigned to any particular treatment group and there was no study-specific procedure apart from data collection with physicians. Data was collected from 256 doctors who were specialised in treating patients with diabetes and had their clinics in the Philippines.

### *Assessment of Doctor Satisfaction*

A questionnaire (Doctor Preference Questionnaire; Appendix) was developed to assess doctor preference in specific terms of ease of learning and teaching use of FlexPen™, time spent for patient training in use of FlexPen™, ease of setting up the required dose of FlexPen™, Doctor's satisfaction of shifting from any other device to FlexPen™, confidence that the correct amount of insulin will be injected, feedback about the NovoFine® 30G needles, overall experience with FlexPen™.

### *Statistical analysis*

Discrete variables were displayed in frequency tables (N, %) and in the form of graphical representation.

## RESULTS

A total of 256 doctors participated in the study and completed the doctor satisfaction questionnaire. Among 256 doctors who participated in the study, there were 78 endocrinologists, 129 diabetologists and 49 physicians of varied specialties (Internal medicine, general practitioners, cardiologists, etc).

One hundred fifty nine (62.1%) doctors felt learning and teaching the use of FlexPen™ to the patients was “very easy” whereas 94 (36.7%) perceived it as “easy” (Figure 1).

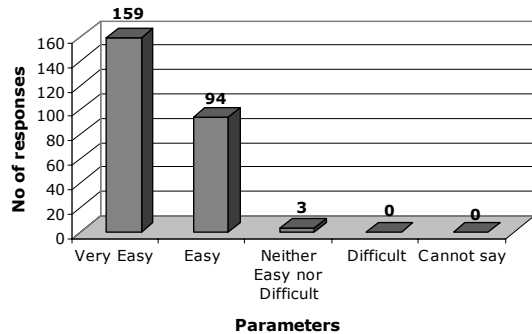


Fig. 1. Ease to Learn/ Teach How To Use FlexPen™

Seventy two (28.1%) doctors (or their staff) spent less than 5 minutes whereas 99 (38.7%) doctors (or their staff) spent 6 to 9 minutes for training the patient in using the FlexPen™ (Figure 2).

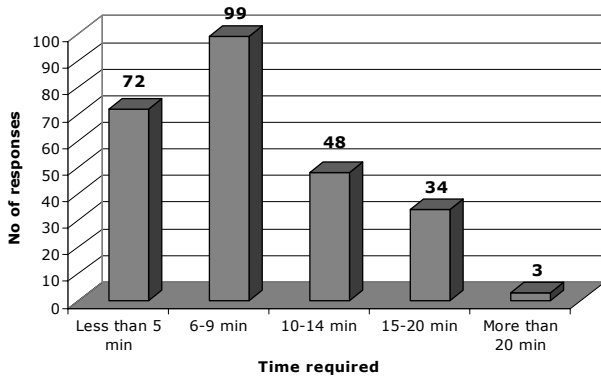


Fig. 2. Time Required To Train How To Use FlexPen™

For the question “How easy/ difficult is it to set up the required dose and do even dose correction using FlexPen™”, 139 (54.3%) doctors responded “very easy”, 107 (41.8%) responded as “easy” and 10 (3.9%) as “neither easy nor difficult” (Figure 3).

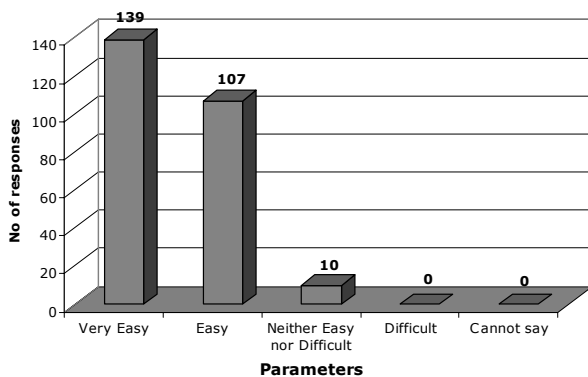


Fig. 3. Ease of Setting Up the Required Dose and Dose Correction Using FlexPen™

One hundred forty five (56.6%) doctors were “very confident” and 108 (42.2%) were “confident” that their patients will inject the correct dosage of insulin using FlexPen™ (Figure 4).

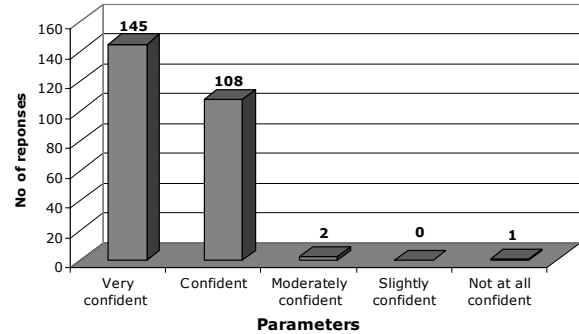


Fig. 4. Doctors' Confidence in Injecting Correct Dose Using FlexPen™ by Patients

One hundred forty five (56.6%) doctors were “very satisfied” and 107 (41.8%) doctors were “satisfied” about the patient shifting from other insulin devices to FlexPen™ (Figure 5). No doctor was dissatisfied about the patient shifting from other devices to FlexPen™.

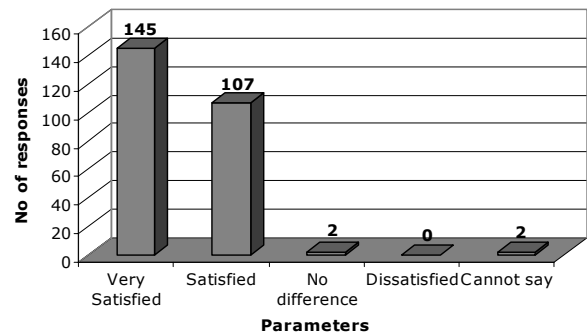


Fig. 5. Satisfaction Level of Physicians Shifting Patients from Other Insulin Devices to FlexPen™

The design of the FlexPen™ has been rated as “excellent” by 101 (39.5%), very good by 142 (55.5%), good by 12 (4.7%) and satisfactory by only 1 (0.4%) doctors. No doctor reported the design liking as “bad” (Figure 6).

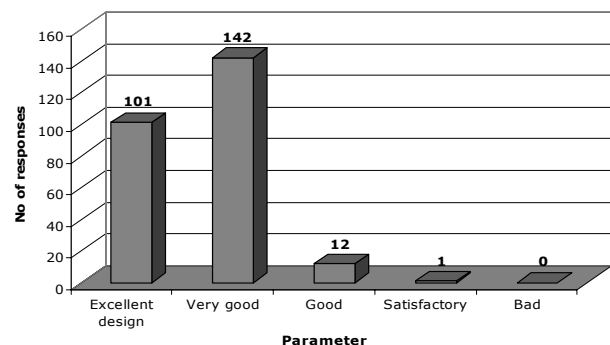


Fig. 6. Doctors' Liking for Design of the FlexPen™

One hundred forty seven (57.4%) of the doctors had perceived NovoFine® 30G needles as very painful and 100 doctors (39.1%) have found it as slightly painful (Figure 7).

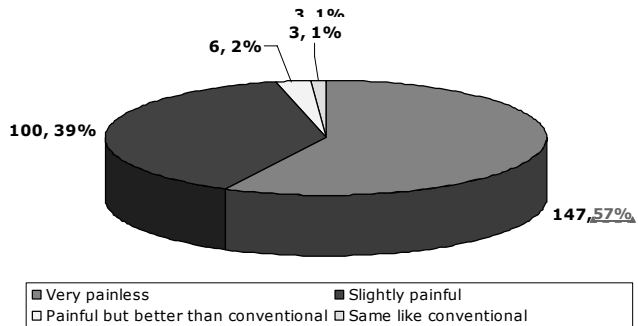


Fig. 7. Feedback on NovoFine® 30G Needles

The most common reason for doctor’s preference towards prefilled/ disposable insulin delivery system was it is “simpler and more convenient”. The other reasons were it is “modern/ innovative”, it “helps in convincing patients” and “it comes from Novo Nordisk” (Figure 8).

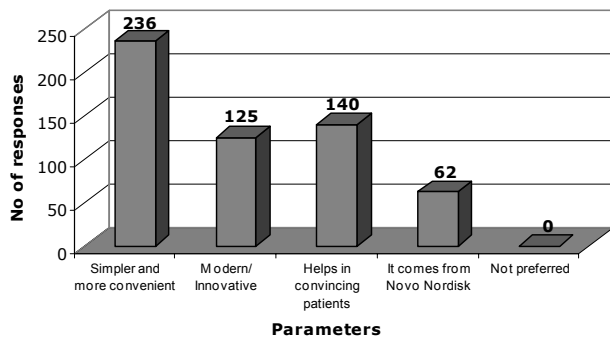


Fig. 8. Reasons for Doctors’ Preference Towards Pre-Filled/ Disposable Insulin Delivery Systems

Two hundred six (80.5%) doctors responded as “yes” and 23 (9%) as “slightly” when asked about their confidence towards prescribing insulin increase knowing that the insulin, needle and injector come from the same company (Figure 9).

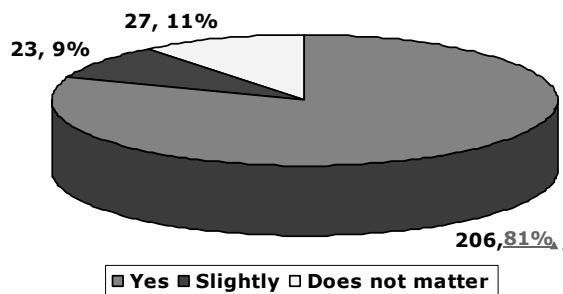


Fig. 9. Confidence Towards Prescribing Insulin Increase Knowing That The Insulin, Needle and Injector Come From the Same Company

Two hundred fifty six (99.6%) doctors responded that they would recommend the use of FlexPen™ to other doctors and all the doctors (100%) responded that they would continue prescribing FlexPen™ to patients in managing diabetes.

Overall experience

One hundred ninety one (74.6%) doctors rated the overall experience of FlexPen™ as excellent (Figure 10).

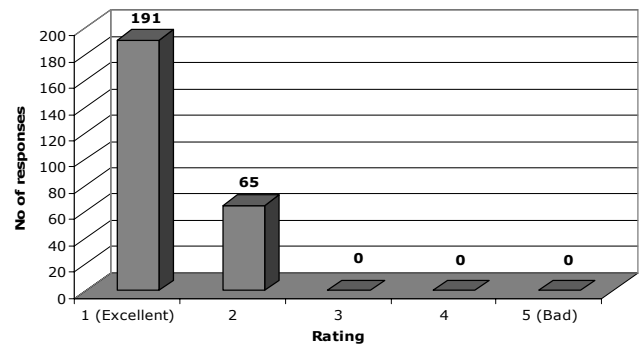


Fig. 10. Overall Experience with FlexPen™

DISCUSSION

The data from the survey indicate that FlexPen™ has been accepted by the doctors and rated the overall experience as 1 or 2 (on a scale of 1 to 5; 1 being excellent).

Medical therapy for diabetes mellitus has changed dramatically since Banting and Best discovered insulin in 1921. Not only have therapies for diabetes advanced significantly, but the technology for the delivery of insulin has also changed. Nonetheless, syringes were the sole method of insulin delivery for decades. The original glass syringes and their large, reusable needles had to be boiled for sterilization.

Although advancements in technology have provided various sizes of syringes and needle systems, the traditional insulin injection process remains time-consuming, cumbersome, inconvenient, and somewhat painful. Furthermore, insulin dosing via syringe is associated with a high risk of dosage errors; as many as 80% of patients carry out some aspect of insulin administration via syringe incorrectly.<sup>12</sup> Now, to allow more flexibility and convenience, patients are seeking options other than the traditional vial-and-syringe delivery method.

Insulin Pens meet this need and also address the issues of convenience, more dose accuracy and social issues.

Pen devices that are easy and efficient to operate correctly with minimal discomfort appear to increase patients' acceptance of, and adherence to, treatment regimens.<sup>1</sup>

Insulin pens have been available for more than a decade all over the world and there are many publications in the literature available for patient preference and patient acceptability of insulin devices. After the pen's introduction in 1985, Jefferson and associates<sup>13</sup> evaluated patient preferences and blood-glucose control indexes in 10 adolescents with diabetes, aged 12 to 17 years. Over a 3-month period, mean HbA<sup>1c</sup> levels decreased from  $13.7 \pm 2.7\%$  to  $11.7 \pm 3.4\%$ . Most patients reported the pen's advantages outweighed the inconvenience of multiple injections. Since that time, pens have undergone many significant improvements.

Plevin and Sadur<sup>14</sup> assessed the acceptance of pen injections among 64 adult patients -- 19 with type 1 and 45 with type 2 diabetes. Most of the patients had been treated with insulin for 6 months to 43 years before the study; 22 of the 64 patients were new insulin users. Patient comments regarding the pen were extremely positive: 98% reported the pen was convenient and easy to use, and 91% wanted to continue its use.

In an Italian study,<sup>12</sup> the safety, efficacy, and acceptability of a prefilled insulin injection pen device was assessed in 60 patients with diabetes who were over 50 years of age and were using conventional insulin syringes. About 90% of patients administered insulin more quickly and easily with the pen than with the conventional syringe. The investigators concluded that the prefilled insulin pen was safe, efficacious, and highly accepted in patients with diabetes over age 50. Ease of accurate dosing is particularly important for older patients, who may have impaired vision, arthritis, or reduced motor coordination.

Two multicenter surveys<sup>15</sup> of 1,310 adult insulin users were conducted to assess the effect of prefilled and reusable pens on compliance with insulin, diet, and exercise regimens and on perceived well-being. Most patients found the pen easy to use (92% when using prefilled pens and 98% when using reusable pens). The survey showed that patients were very positive about the pen devices: 77% of pen users found it easier to comply with the insulin regimen using the pen than with conventional syringes, and 73% of pen users achieved more accurate insulin dosing than when syringes were used. More important, 85% of pen users never missed a scheduled injection, compared with 72% of patients using the vial-and-syringe

method. The investigators reported that patients' attitudes improved regarding insulin therapy; they had greater confidence in managing their disease.

In an 8-center, open, randomised, cross-over study from Morocco, Kadiri and associates<sup>16</sup> compared the acceptance and safety of NovoPen<sup>®</sup> 3 with that of conventional syringes and vials when initiating insulin treatment in 96 type 2 diabetes patients with secondary failure to oral hypoglycaemic agents. Injection pain was significantly lower with NovoPen<sup>®</sup> 3 than with syringes and vials ( $p = 0.0018$ ). Acceptance of insulin injections was significantly higher by patients using NovoPen<sup>®</sup> 3 than by those using syringes and vials ( $p=0.0059$ ). Setting and drawing up the dose of insulin was also easier for patients using NovoPen<sup>®</sup> 3 ( $p=0.0490$ ). At the end of the study, most patients (89.5%) said that they preferred NovoPen<sup>®</sup> 3 to syringes and vials. The authors concluded that use of NovoPen<sup>®</sup> 3 provided better acceptance of insulin injections than use of conventional syringes and vials during initiation of insulin therapy in type 2 diabetes patients with secondary failure to treatment with oral hypoglycaemic agents.

The US FlexPen<sup>™</sup> study team<sup>17</sup> assessed patient preference, efficacy, and safety profiles of the newest prefilled, disposable pen from Novo Nordisk containing the premix insulin analogue, biphasic insulin aspart (NovoLog<sup>®</sup> Mix 70/30 FlexPen<sup>™</sup>) and conventional vial/syringe injection method for insulin injection therapy among patients with diabetes mellitus. Seventy-four percent of patients indicated a preference for the pen over the vial/syringe method and 74% considered it easier to use overall.

The ORBITER study group<sup>18</sup> assessed the impact on the quality of treatment of replacing traditional syringe insulin injections with NovoLet<sup>®</sup> pre-filled insulin pen. The study enrolled 1,622 insulin-treated diabetic patients from 91 Italian diabetes care centers. The survey was carried out by comparing the outcomes of the widely used Diabetes Treatment Satisfaction Questionnaire (DTSQ), at the time of enrolment and 30 days later. The following items were assessed: knowledge of the pathology, flexibility and ease of treatment, continuation and recommendation, hypoglycaemia/hyperglycaemia status and satisfaction. Replacement of the syringe with the NovoLet<sup>®</sup> device produced a statistically significant improvement in all items assessed by the questionnaire. Scores were particularly relevant for the items "continuation" and "recommendation" and in subjects with an active working and social life. Elderly patients also indicated that the new device

was easier to use and handle, although in a slightly less marked way.

Lawton S and Berg B<sup>19</sup> assessed comparative evaluation of patient and healthcare professionals' acceptance of FlexPen.<sup>TM</sup> The results showed that 94% of the patients were very confident in their ability to use FlexPen.<sup>TM</sup> Similarly, 92% of the healthcare professionals stated that they would be confident in their patients' ability to use FlexPen.<sup>TM</sup> With regard to ease of selecting the required dose, FlexPen<sup>TM</sup> was rated by the healthcare professionals on a scale as 6.38 (7=very easy; 1=very difficult). Similarly, FlexPen<sup>TM</sup> was rated by the healthcare professionals and patients as 6.4 and 5.87 (7=very easy; 1=very difficult). Eighty five percent of the healthcare professionals responded that it would be easy to teach how to use the FlexPen.<sup>TM</sup> Seventy one percent healthcare professionals stated that they would require less time to instruct patients to teach how to use FlexPen.<sup>TM</sup> Also, 74% healthcare professionals believed that FlexPen<sup>TM</sup> would lead to greater compliance with therapy. The results of our study also showed very similar findings as given by Lawton S and Berg B.

The study of Hänel<sup>20</sup> showed that FlexPen<sup>TM</sup> was more accurate in the delivery of 10 U or 30 U of insulin. Eight pens from two different production lots of each type were tested 24 times at 10 U and 9 times at 30 U, and the mean absolute deviation for 10 U and 30 U was 1.64% and 0.83%, respectively, for FlexPen.<sup>TM</sup>

## CONCLUSION

This study was the first attempt to get the Doctors' perceptions about the use of devices in management of diabetes mellitus in Philippines. The participating doctors showed high degree of acceptance of NovoMix<sup>®</sup> 30 Flexpen<sup>TM</sup> (Biphasic Insulin Aspart 30). The overall experience of NovoMix<sup>®</sup> 30 Flexpen<sup>TM</sup> (Biphasic Insulin Aspart 30) was excellent. These results of this survey were in line with the other studies published for the Insulin devices.

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#### *Appendix: Doctor Preference Questionnaire*

1. How easy/ difficult was it for you to learn and teach the use of FlexPen™?
2. How much time did you and your staff spend training the patient in using the NovoMix® 30 FlexPen™ (Biphasic Insulin Aspart 30)?
3. How easy/difficult is it to set up the required dose and do even dose correction using FlexPen™?
4. How confident are you that your patient will inject the correct dosage of insulin using FlexPen™?
5. What is your satisfaction level from shifting a patient from other insulin devices to FlexPen™?
6. How well do you like the design of the FlexPen™?
7. How do you rate NovoFine® 30G needles according to your patients' feedback?
8. What are the reasons for your preference towards pre-filled/ disposable insulin delivery systems?
9. Does your confidence towards prescribing insulin increase knowing that the insulin, needle and injector come from the same company?
10. Would you recommend the use of FlexPen™ to other doctors?
11. Will you continue prescribing FlexPen™ to patients in managing diabetes?
12. On a scale of 1 to 5, how do you rate overall experience with FlexPen™ in comparison to vials and syringes( 1 is excellent and 5 is Bad )