

# Patient and Healthcare Provider Satisfaction with a Pen Device for the Self-administration of Follitropin Beta

a report by

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Once gonadotropins of sufficient purity became available and were shown to be suitable for subcutaneous administration,<sup>1</sup> women undergoing infertility treatment could more easily self-administer gonadotropins than was previously possible when drugs had to be given via the intramuscular route.<sup>2</sup> This development has cleared the way for products and protocols that are more 'patient-friendly,' i.e. those that are discreet and reduce the anxiety associated with the mixing, reconstitution, and self-administration of these drugs. One such advance is the development of the recombinant follicle-stimulating hormone (rFSH) follitropin beta in solution in a pre-filled cartridge form that can be administered using a pen injection device.<sup>3</sup> This delivery system was introduced to the US in 2004 and is marketed as Follistim Pen® (Pen) for use only with the Follistim® AQ Cartridge (follitropin beta). The Pen has been available in Europe since 2000.

Pen injection devices for administering insulin were adopted for the treatment of diabetes some years ago. There is a substantial body of literature accumulated over the past 20 years that attests to the patient-related benefits of the pen injection devices.<sup>4</sup> The use of a pen injection device to administer insulin is well accepted by diabetic patients and their physicians because it is accurate, more convenient, easier to use, and more comfortable than the syringe and needle method of insulin administration.<sup>5-8</sup>

In women undergoing infertility treatment, the Pen enables precise and individualized dosing of follitropin beta from 50 up to 450IU, in increments of 25IU.<sup>3,9,10</sup> The Pen is used in conjunction with the Follistim AQ Cartridge (follitropin beta), which is available in 300, 600, and 900IU sizes. Because the Pen delivers a small injection volume—as small as 30µL, which equals 25IU—through a micro-fine needle (0.33x12.7mm), injections of follitropin beta from the Pen are less painful than injections of rFSH from a conventional syringe and needle. In a study of 60 healthy

volunteers, 70% experienced severe to moderate pain when injected with a conventional syringe and needle compared with only 21.7% when injected with the Pen (p<0.001).<sup>11</sup>

Two open-label, multicenter studies evaluated the ease of use, safety, and efficacy of the Pen in women undergoing ovarian stimulation for *in vitro* fertilization (IVF)<sup>9</sup> and in clomiphene citrate-resistant women undergoing ovulation induction (OI).<sup>10</sup> To determine whether the Pen was easy to use and well understood by subjects, both studies utilized a subject comprehension test conducted by healthcare providers (HCPs), as well as an ease-of-use questionnaire completed by subjects. The investigators concluded that subjects understood how to use the Pen and that follitropin beta administered with the Pen was safe, effective, and well tolerated.

This article presents the results of the Follistim Pen Pal Program, a survey designed to evaluate patient and HCP satisfaction when using the Pen to self-administer follitropin beta. While the two studies described above reported on patient comprehension and ease of use during two clinical trials, the objective of the survey was to assess these parameters in everyday clinical practice. Since patients who self-inject medication require training from HCPs in the proper use of the drug-delivery method, this study also assessed HCP evaluation of patient understanding of the Pen and its use.

## Methods

The program survey was adapted from surveys previously developed and published to assess patient and HCP (physician) satisfaction with a pen for insulin delivery in patients with type 1 or type 2 diabetes.<sup>6</sup> The surveys to evaluate the Pen were administered by 74 fertility clinics throughout the US during 2004 and 2005.

## Patient Surveys

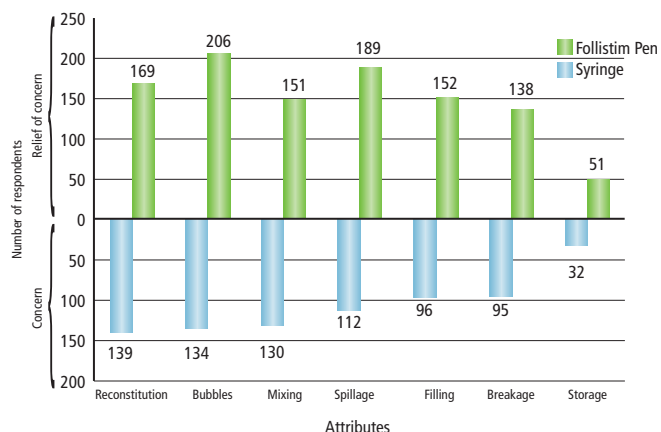
Each clinic was to enroll up to 10 patients willing to complete two surveys: one at baseline (Survey I) and another after self-injecting with the Pen on day five of the treatment cycle (Survey II). Participating patients were expected to exhibit normal response to gonadotropin stimulation in controlled ovarian stimulation (COS) for IVF, as determined by the criteria of the physician. Patients both with and without previous experience of self-administering fertility medications using the syringe method were included. Each patient signed a patient release form indicating her willingness to participate in the survey, and the form was filed in her chart. Patients received training in the preparation, use, and storage of the cartridge and Pen delivery system by the clinic HCPs, who



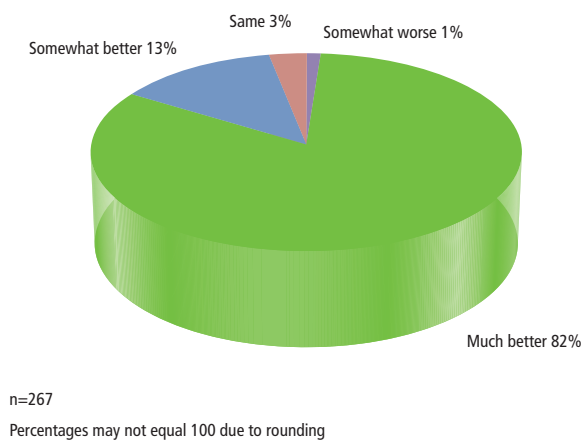
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**Figure 1: Patients’ Concerns about Preparing Fertility Medications Administered with a Conventional Syringe/Needle and Relief of Those Concerns Using the Follistim Pen to Self-administer Follistim AQ Cartridge (follitropin beta)**



**Figure 2: Patients’ Overall Satisfaction with the Follistim Pen to Self-administer Follistim AQ Cartridge (follitropin beta) Compared with the Conventional Syringe/Needle Method**



used standard training materials provided by the sponsor. These materials included written instructions and a video presentation showing a woman giving herself an injection.

Prior to the training patients completed Survey I, which included questions regarding previous self-administration of fertility medications, if applicable. In Survey II, patients were asked to respond to questions relating to their confidence in comprehending how to self-administer their fertility medication and their satisfaction with the Pen. Questions relating to preferences were structured using a five-point Likert scale.

### Healthcare Provider (HCP) Surveys

After patient enrollment and training at each clinic, a designated HCP at the clinic was to complete the HCP survey. This 11-question survey was designed to assess the ease/difficulty of educating patients on self-administration with the Pen, including responding to patient calls to the clinic for additional assistance. The HCPs were asked to compare the effectiveness of current training materials for the Pen with those for the

**Table 1: Patient Responses**

Attribute	Most Frequent Response	
	Survey I—Syringe Method Users number (%)	Survey II—Pen Users number (%)
Number of daily injections	Once per day: 188 (70)	Once per day: 322 (70)
Medication preparation concerns using the syringe method	Presence of bubbles in the medication after mixing: 129 (48)	N/A
Medication preparation; relief of concerns using the Pen method	N/A	Mixing and reconstituting your medication: 325 (70)
Confidence in the accuracy of the dose	Somewhat agree: 121 (45)	Strongly agree: 310 (67)
Comfort with performing injections away from home	Strongly disagree: 85 (32)	Strongly agree: 242 (53)
Convenient to use	Somewhat disagree: 103 (38)	Strongly agree: 397 (86)
Simple and easy to use	Somewhat disagree: 114 (42)	Strongly agree: 392 (85)
Able to perform daily activities	Good: 80 (30)	Excellent: 311 (67)
Overall satisfaction with method	Somewhat satisfied: 97 (36)	Extremely satisfied: 371 (80)
Adequate education	Strongly agree: 178 (66)	Strongly agree: 423 (92)

conventional syringe method. The HCPs were also asked to rate those attributes that would lead them to recommend the Pen over the syringe method. The attributes were rated using an eight-point scale in which one was the most important and eight the least important. Once completed, both the patient and HCP surveys were collected through a co-ordinating center via pre-addressed, postage-paid envelopes.

## Results

### Patient Surveys

A total of 611 patients were enrolled to participate in the survey. Of these, 466 patients (76%) returned both surveys. Two hundred and seventy respondents (58%) had previously self-administered fertility medication injections with a conventional syringe, and 196 (42%) had not previously self-administered fertility medications. The most frequent responses of patients to matched pairs of questions in both surveys are summarized in *Table 1*. Overall, 80% of patients were “extremely satisfied” with the Pen, while 36% of syringe users were “somewhat satisfied” (most frequent response for each).

Patients who had previously self-administered fertility medications reported concerns about the attributes of preparing their medication and relief of those medication preparation concerns when using the Pen (see *Figure 1*).

The majority of patients who had previous experience of self-administering fertility medications preferred the Pen over the syringe method, with 82% responding that the Pen was “much better” and 13% responding that the Pen was “somewhat better” than a syringe (see *Figure 2*).

### Healthcare Provider (HCP) Surveys

A total of 45 HCPs (61%) from the 74 clinics responded to the HCP survey. Ninety-eight percent rated the Pen as “much better” or

**Table 2: Relative Importance to Healthcare Providers of Various Attributes for Recommending the Pen versus the Syringe Method**

Attribute	Percentage of Respondents Who Gave a High (1, 2, or 3) Rating* to Each Attribute
Ease of use	91.1
Accurate dosing	90.9
Convenience	88.9
Relief of stress	88.9
Multidose cartridge	88.6
Patient compliance	86.7
Fine-tuning in 25IU increments	82.2
Excellent tolerability	82.2
Storage flexibility	73.3
Discreet use	73.3
Less training time	70.5

\*Healthcare providers were asked to rate each attribute according to an eight-point scale, with one being the most important and eight being the least important.

“somewhat better” overall than the syringe method. Eighty-two percent of respondents “agreed strongly” or “somewhat agreed” that it took less time to train patients to use the Pen versus a syringe. All HCPs responded (strongly agreed or somewhat agreed) that the Pen was less intimidating for patients, while 93% responded that they felt confident in the ability of their patients to accurately deliver the correct dose of follitropin beta with the Pen (see *Figure 3*). Approximately 98% “agreed strongly” or “somewhat agreed” that they had received all the necessary educational materials to train patients to use the Pen correctly.

The anticipated time required for training patients with the Pen compared with the syringe method is shown in *Figure 4*. The majority of HCPs (78%) reported that it took between five and 15 minutes to train patients to use the Pen, whereas most (76%) reported it took between 10 and 30 minutes to train patients to use the syringe method. When asked about the number of callbacks from patients using the syringe method, 12 (27%) reported three phone calls per patient and 10 (22%) reported one phone call per patient. For the Pen, 21 (54%) reported one phone call per patient and seven (16%) reported three phone calls per patient.

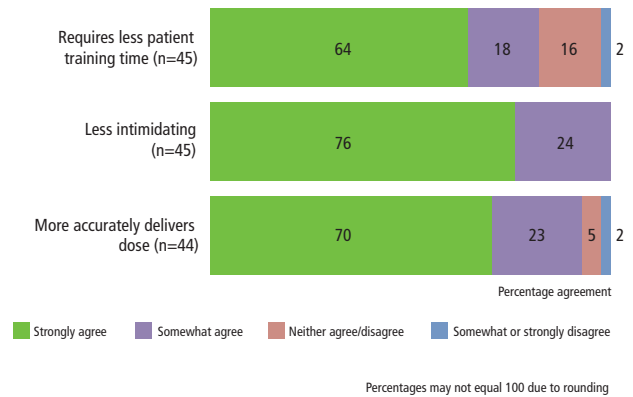
When asked to rate attributes that would lead them to recommend the Pen over the syringe method, the HCPs provided the responses shown in *Table 2*. The HCPs ranked ease of use as the most important attribute. On average, 91% of HCPs said they would “definitely” or “probably” recommend the Pen for all types of infertility patients, while 93% would “definitely” or “probably” recommend the Pen to their colleagues.

**Discussion**

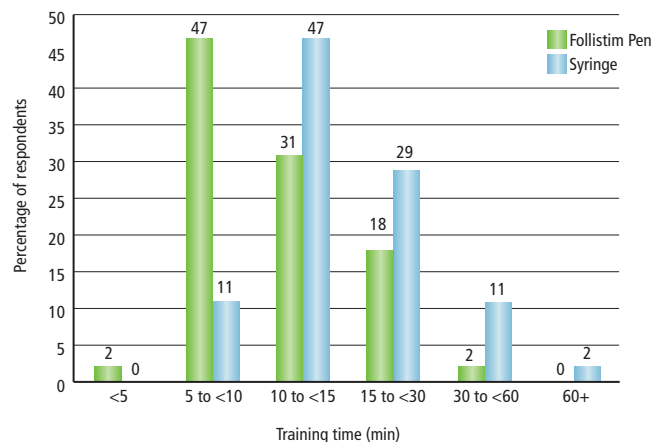
Diabetic patients have benefited from the iterative technical improvements in insulin delivery systems over the past 20 years.<sup>4</sup> While infertility treatment should be made as effective as possible, it should also be as simple and patient-friendly as possible.

Ovarian stimulation protocols can be made more patient-friendly through the use of innovative products that do not require reconstitution and that can be self-administered with ease and confidence. Previous studies have shown that patients understand how to use the Pen to correctly administer the desired dose of follitropin beta in both the OI with intrauterine

**Figure 3: Agreement of Healthcare Providers with Statements Regarding the Follistim Pen**



**Figure 4: Healthcare Providers’ Anticipated Patient Training Time for the Follistim Pen versus the Conventional Syringe/ Needle Method**



insemination (OI/UI)<sup>10</sup> and the IVF settings.<sup>9</sup> For the treating physician, knowing that it is easier for the patient to administer the prescribed amount each time translates into more confidence that the predicted response will be achieved.

In this study, 466 out of 611 patients (76%) who received the surveys responded, and 45 out of 74 HCPs (61%) responded. Responses to some questions on either Survey I or Survey II could not be matched; therefore, they were not included in the comparison of the two methods. It is also important to note that survey takers did not respond to every question on the surveys; thus, the number of respondents for individual questions varies. Nonetheless, 82% of patients reported that the use of the Pen was much (and 13%, somewhat) better than their previous experience with the syringe and needle method. The majority of HCPs strongly agreed that the Pen required less patient training time, was less intimidating, and more accurately delivered the correct dose.

These two findings suggest that both the patients and the assisted reproductive technology (ART) staff understand the benefits of this delivery system for administering gonadotropins.

Unfortunately, most cycles of ART do not result in the successful establishment of a viable pregnancy. For the couple seeking a child, this translates into the need to accept that they may have to come back and try again. However, even in a situation where the IVF treatments were offered at no cost to patients, a relatively high percentage of couples discontinued treatment before completing the three cycles that were offered.<sup>12</sup> Most of those discontinuing treatment did so because of psychological stress. Evidence is emerging of an association between the stress of infertility treatment and patient drop-out and pregnancy rates.<sup>13</sup> Improvements in the treatment process that make the overall experience less stressful and intrusive will help to ensure that the couple does come back for additional cycles in order to achieve a successful pregnancy. Results from the current study suggest that the Pen is a more user-friendly drug-delivery device for COS and provides patients with a less stressful and intrusive experience than the conventional syringe method.

The vast majority of women with fertility problems who seek treatment receive non-invasive treatments that could be considered 'low-technology' interventions.<sup>14</sup> However, the prospect of infertility treatment remains intimidating, and barriers exist for patients that sometimes prevent them from seeking the services that could help them become pregnant.<sup>15</sup> Simplification of infertility treatment processes through the use of technological innovations such as the Pen should improve the experience of patients with infertility treatments and therefore also improve their chances of achieving a successful pregnancy. Based upon the responses received from both patients and HCPs, the

### SAFETY INFORMATION on Follistim® AQ Cartridge and Follistim® AQ Vial

- Follistim® AQ Cartridge/Vial, like all gonadotropins, is a potent substance capable of causing mild to severe side effects including ovarian hyperstimulation syndrome (OHSS), with or without pulmonary or vascular complications.
- Follistim® AQ Cartridge/Vial should be prescribed only by physicians who are experienced in infertility treatment, who should advise their patients of treatment risks, including OHSS and multiple births.

### SAFETY INFORMATION on Follistim® AQ Cartridge

- Follistim® AQ Cartridge administered with Follistim Pen® delivers on average 18% more follitropin beta compared with lyophilized preparations administered with a conventional syringe and needle. A lower dose should be considered when using Follistim® AQ Cartridge.

Follistim Pen offers a more convenient, easier, safer, and more accurate method of self-administering follitropin beta than the conventional syringe method. ■

### Acknowledgments

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