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# The redesigned follitropin alfa pen injector: results of the patient and nurse human factors usability testing

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***Objectives:*** A redesigned pen injector for administration of follitropin alfa (follitropin α) has been developed for use in fertility treatment cycles. Pre-summative and summative usability testing was undertaken to assess the risk of dosing errors compared with the existing follitropin α pen. The study also assessed proper use of and dose selection with the redesigned pen.
***Methods:*** Infertile women who were trying to conceive and specialist nurses were recruited from four cities in Germany. Usability goals relating to proper use of the pen device were defined from a risk assessment and further categorized as critical and functional operational goals. Individual, non-interventional, standardized, usability tests were performed with patients and nurses by four experienced research professionals using questionnaires that also included ease-of-use ratings. A non-standardized qualitative analysis of nurse–patient training sessions was performed in the presence of a research professional; reasons for confidence, safety, possible misunderstandings and risks when handling the pen were noted.
***Results:*** The overall risk of dosing errors with the redesigned pen was not higher than with the existing pen. No unexpected operational risks and no major concerns regarding the risk of misuse or dosing errors were identified.
***Conclusions:*** The study provides useful practical information on the redesigned pen from both patient and nurse perspectives.

**Keywords**: follitropin α, human factors, *in vitro* fertilization, infertility, injection device, pen injector, recombinant human follicle-stimulating hormone, usability testing

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## 1. Introduction

Infertility treatment cycles involve the use of a variety of therapies and complex dosing schedules [1]. Gonadotropin treatment is administered to stimulate follicular growth and development in both ovulation induction and assisted reproductive technologies. Follicle-stimulating hormone, luteinizing hormone and human menopausal gonadotropin may be used. The ovarian response is monitored by ultrasound (to identify follicle number and size) and serum estrogen levels, and treatment is tailored accordingly. Final follicular maturation (and ovulation) is triggered using a single dose of human chorionic gonadotropin.

Gonadotropins are often self-injected daily and treatment may last for several weeks [2]. Women may use a number of different injection devices during the course of infertility treatment, including vials and syringes, re-usable pens with cartridges, disposable prefilled pens and syringes [3-6]. Different training is required for the administration of each product and the use of each device. Self-injection of treatment can cause anxiety among patients about whether each dose has been

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administered correctly [3]. In fact, a large proportion of consultation time is occupied by patients' questions about injection technique [3]. Thus, it is important that gonadotropin administration devices are convenient, easy to use and patients feel confident that the correct dose has been injected.

Recombinant human follicle-stimulating hormone [r-hFSH, follitropin alfa (follitropin α)] has been available for self-injection for more than a decade. Although a pen-injection device was introduced in more recent years, follitropin α was originally supplied as a lyophilized formulation for reconstitution before injection using a syringe and needle. With the availability of gonadotropin formulations that can be administered subcutaneously, most patients are now able to perform their own injections after training by their healthcare provider. Several publications report that infertile patients find pen injectors simpler and easier to use than other administration methods [3,7-9].

The first two pen injectors for administration of follitropin α were approved in the USA in 2004 and 2007, respectively [10]. The redesigned follitropin α pen injector is a multi-dose, ready-to-use, prefilled device, which includes a number of new features (**Figure 1A**) [11]. These include: a fully transparent cartridge reservoir with graded markings; a magnifying window that enlarges the dosing number; and a dose display that shows the selected dose, and then either returns to zero after complete injection of the prescribed dose or shows the remaining dose required to be administered by a second pen (if an incomplete dose has been delivered by the first pen) [11].

The redesigned follitropin α pen injector is intended for subcutaneous self-injection and is available in three dosing presentations: 300, 450 and 900 IU. The dose accuracy of the redesigned pen has been demonstrated in accordance with international standards (EN ISO 11608-1:2000) [11-13]. Furthermore, the ease of teaching and learning use of the redesigned follitropin α pen injector has also been demonstrated [14].

Usability testing aims to ensure that medical devices reflect good human factors' engineering practices and thus reduce any potential risk to operators [15]. Indeed, manufacturers are required to provide to regulatory agencies validation of the suitability of new devices for their intended use [15]. Summative usability testing is used towards the end of the development process to reveal whether a manufacturer has effectively addressed users' needs and thus to validate the design [15]. As part of the human factors evaluation of the redesigned pen, pre-summative (pilot) and summative usability testing was undertaken to assess the function, handling and risk of dosing errors of the redesigned follitropin α pen injector when used by patients and nurses.

## 2. Methods

### 2.1 Objectives

The primary objective of the study was to show that the risk of dosing errors in the primary user group (patients) was not higher with the redesigned follitropin α pen injector [the GONAL-f®/GONAL-f® RFF (Revised Formulation Female) Prefilled Pen (Merck Serono S.A., Geneva, Switzerland, an affiliate of Merck KGaA, Darmstadt, Germany)] than with the existing pen. The overall objectives included evaluation of the impact of human factors on the use of the redesigned follitropin α pen injector with particular focus on the risks of misuse and dosing errors by infertile women and specialist infertility nurses under simulated use conditions.

### 2.2 Participants

There are two distinct groups of intended users of the follitropin α pen injector. The first group comprises infertile patients who are considered by prescribing healthcare professionals to be capable of safely and effectively performing a self-injection. The second group comprises primarily nurses who train and supervise patients on the proper use of the pen. Both user groups were represented in this usability testing.

Infertile women from a wide range of educational backgrounds (including low educational levels) who were currently undergoing, or about to undergo, fertility treatment to conceive and infertility nurses were recruited via infertility clinics and independent databases. The selection of patients who fulfilled the criteria for fertility treatment ensured that they were well motivated, adequately trained and had access to expert advice (as per prescribing requirements) [16]. All participants provided written, informed consent. The evaluation was non-interventional (as no actual patient injections were performed), and ethics approval was not required in Germany to perform the usability testing.

Key inclusion criteria for patients were an age of 18 – 45 years and being willing to receive hormonal treatment to become pregnant. Patients with needle phobia, as rated by a score of 6 or higher on a scale of 1 – 10, with 1 being 'I am not afraid of syringes' and 10 being 'I am extremely afraid of syringes and I try to avoid any kind of injection', were excluded. The rationale for this approach is that patients with a deep-seated fear of needles would be resistant to any type of injectable therapy and could potentially bias the outcomes. Key inclusion criteria for nurses were having practiced as a qualified nurse for 3 – 25 years, currently working at a specialist infertility centre, and training at least 20 patients per month on the use of a self-injection device for hormonal infertility treatment. Nurses who were aged over 55 years or had participated in any group discussions or interviews for any research studies in the previous month were to be excluded. Neither patients nor nurses with family members employed in the pharmaceutical industry, marketing, research or advertising were permitted to participate. Any participant who used vision-correcting lenses was instructed to wear these during the tests.

Participants were recruited from 15 fertility centres in four German cities: four in Berlin, three in Cologne, three in Frankfurt and five in Hamburg. An equal split of patients (n = 18) and nurses (n = 18) was planned for testing across

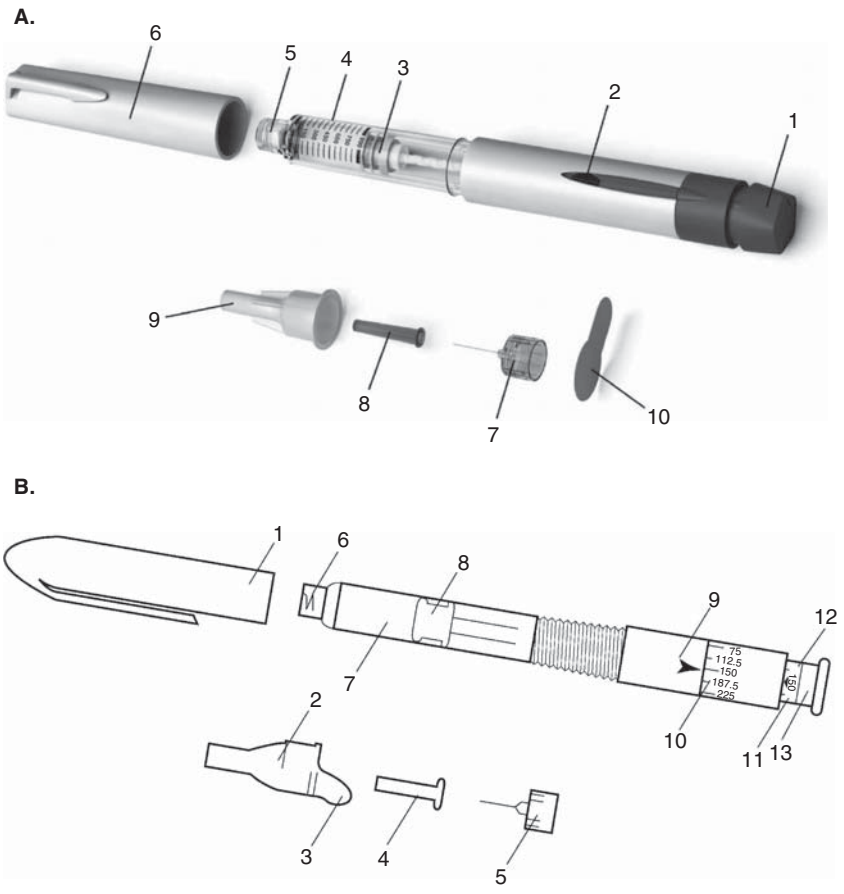


**Figure 1. (A)** The redesigned follitropin α pen injector [6] and **(B)** the existing follitropin α pen. The components of the redesigned follitropin α pen injector: 1, dose-setting knob; 2, dose display; 3, plunger piston; 4, graduated reservoir holder; 5, threaded needle connector; 6, pen cap; 7, removable needle; 8, inner needle shield; 9, outer needle cap; 10, peel-off seal tab. The pen barrel and cartridge comprise Sections 1 – 5. The components of the existing follitropin α pen injector: 1, pen cap; 2, outer needle cap; 3, peel-off seal; 4, inner needle cap; 5, removable needle; 6, threaded tip; 7, liquid holder; 8, plunger piston; 9, dose arrow; 10, black dose selection dial (in IU follicle-stimulating hormone); 11, red dose control scale; 12, grey marker of complete dose delivery; 13, injection button.

This figure is reproduced with permission from (**A**) Merck Serono S.A., Geneva, Switzerland (an affiliate of Merck KGaA, Darmstadt, Germany), who own the copyright of the image. (**B**) The instructions for use of the existing follitropin α pen injector.

the four locations. No more than three nurses were to be recruited from each fertility centre. A screening questionnaire for each user group was used to ensure that all participants met the exclusion and inclusion criteria. Screeners were specifically instructed not to reveal the manufacturer or product to be evaluated. Screeners were also instructed to recruit a balanced mix of educational levels and gonadotropin-injection-naïve (n = 9) versus -experienced (n = 9) patients.

### 2.3 Usability risk assessment

The instructions for use (IFU) included in the packaging of the redesigned follitropin α pen injector provides step-by-step directions for proper use of the prescribed device. During the development process of the redesigned follitropin α pen injector, Merck Serono S.A. used the IFU to identify and analyse potential causes of failure associated with patients' use of the device. This risk assessment was undertaken in compliance with ISO 14971 Standard, *Medical devices – application of risk management to medical devices* [17]. Risks that may result in mistakes were identified; these were related to erroneous dose presetting, mishandling of air bubble removal and mishandling if an incomplete dose is delivered.

### 2.4 Usability goals

Data from the risk assessment were used to assign 'usability goals' for the redesigned follitropin α pen injector (**Figure 1A**) and existing follitropin α pen (**Figure 1B**). The usability goals were then further elaborated as operations and sub-operations. For example, putting on a needle was an operation comprising the following sub-operations: controlling closure integrity of the outer needle cap; removing the peel tab; attaching the needle; and removing the outer needle cap.

Each goal was assigned as a 'critical operational' or 'primary functional' goal. Critical operational goals related to operations that could potentially lead to dosing errors were designated as: removing a large air bubble; checking availability of the full dose; presetting the prescribed dose; and managing an incomplete last dose. Primary functional goals related to correct functioning of the redesigned pen were identified as: attaching a needle; checking for presence of a large air bubble; checking availability of the full dose; presetting the prescribed dose; required steps before injection; required steps for injection; checking the dose delivered; and removing the needle from the pen.

### 2.5 Pre-summative and summative usability testing

The pre-summative and summative usability testing was performed by Point-Blank International (Berlin, Germany) on behalf of Merck Serono S.A.

Standardized patient and nurse questionnaires were developed based on the critical operational and primary functional goals with the aim of collecting and documenting all possible weaknesses or risks associated with the redesigned and existing follitropin α pen injectors that could affect safe handling.

Items used in the tests included: follitropin α 900 IU pen injectors (both redesigned and existing) containing placebo solution with needles for injection, both labelled as 'demo pen, not for injection', pre-packaged in unlabelled cardboard boxes; an injection sponge; IFU as appropriate for each pen; and a sharps container. All training, questionnaires, ease-of-use assessments and interviews were performed in German.

#### 2.5.1 *Handling tests*

The individual, non-interventional, standardized, usability tests focused on observation of pen handling to show how the patient or nurse used the pens and where major or minor risks may have occurred. Four experienced and appropriately trained research professionals performed the interviews. The research professional rotated the sequences of testing, starting with the redesigned pen with 50% of patients and nurses, and the existing pen with the remaining 50% of participants. Questionnaires were completed by the research professional during the assessment.

Use of the redesigned follitropin α pen injector and existing pen was demonstrated individually to patients and nurses. Patients and nurses were asked to mimic use of the pens (as if they were using them at home or in a healthcare setting) and to talk through their actions so that the research professional could accurately assess each user's actions. Injections were performed into a sponge using a pen that contained a placebo solution, and the research professional recorded each step, including patient comments. Particular attention was paid to use of the pens and dosing errors, and to identifying any problems of misuse. The research professional provided the minimum amount of assistance deemed necessary to allow task progression, and the type of assistance was recorded on a data entry sheet.

Following the handling test, patients and nurses were asked a series of questions to assess ease of use of the pen (with reference to a printed rating scale from 1 to 5). Participants were asked to rate the overall handling of the pen, the ease of removing an air bubble, the ease of injecting the dose, understanding that (if the dose was incomplete) a second pen would be needed to complete the prescribed dose and the ease of setting the remaining dose in the second pen.

The handling tests were conducted in a controlled environment at the following research facilities: Items Test Studio (Berlin), Quotapoint (Cologne), Intrateam (Frankfurt/Main) and Dose Marktforschungsstudio (Hamburg). The research professional sat at a table with the test participant and was able to observe tasks closely without interference. No distractions occurred during the usability tests. The research professional observed and interviewed participants and documented data simultaneously. The tests were recorded using a digital video camera and a microphone. Ample lighting, temperature and seating were provided to effectively and comfortably carry out the interview. Handling tests lasted 45 min with patients and 30 min with nurses.

#### 2.5.2 *Nurse–patient training observations*

A non-standardized qualitative analysis was also conducted to provide in-depth understanding of the reasons for the perceived benefits, or weaknesses, of use of the redesigned follitropin α pen injector. Pen handling was first explained to nurses. 'Real-life' nurse–patient training sessions were then performed in the presence of a research professional who recorded the observations. The research professional then discussed with the patient and nurse reasons for possible risks and misunderstandings when handling the pen. The discussions were transcribed and reviewed to provide additional insights.

#### 2.5.3 *Pre-summative test*

A pre-summative test was conducted to practice and fine-tune the handling test questionnaires and qualitative interviews. The test consisted of 45- to 60-min interviews with two patients and a 90-min interview with one nurse. Additionally, one 90-min non-participant observation of a nurse–patient training session was conducted.

Fine tuning of the wording of questions in the patient and nurse individual handling tests was performed following the pre-summative test, to clarify the ease of setting the remaining dose in the second pen. In addition, a request was made for patients to complete a treatment diary to record the daily dose administered and to help calculate the remaining amount of follitropin α in the pen.

### 2.6 Data analysis

The sample size for the summative testing was based on Health Authority requirements, which stipulate that a

**Table 1. Demographic characteristics of patients (n = 18) participating in the individual handling test.**

| Characteristic | |
|---|---|
| *Age, years* | |
| Mean (SD) | 34.2 (5.6) |
| Median (range) | 33.5 (26 – 46) |
| *Education, n (%)* | |
| GCSE | 7 (38.9) |
| High school | 9 (50.0) |
| University | 2 (11.1) |
| *Previous treatment, n (%)* | |
| Yes | 9 (50.0) |
| No | 9 (50.0) |

'GCSE' (General Certificate of Secondary Education) level indicates schooling up to 16 years of age.
'High school' level indicates schooling up to 18 years of age.

**Table 2. Demographic characteristics of nurses (n = 18) participating in the individual handling test.**

| Characteristic | |
|---|---|
| *Age, years* | |
| Mean (SD) | 37.7 (10.5) |
| Median (range) | 32.0 (24 – 61) |
| *Experience, years* | |
| Mean (SD) | 14.2 (8.7) |
| Median (range) | 12.0 (4 – 33) |
| *Education, n (%)* | |
| GCSE | 16 (88.9) |
| High school | 2 (11.1) |

'GCSE' (General Certificate of Secondary Education) level indicates schooling up to 16 years of age.
'High school' level indicates schooling up to 18 years of age.
Nurses were not asked to report on university education.

minimum of 15 individuals from each distinct user group (patients and nurses) should participate in a usability test [13,18].

Possible user scores for each operation (and sub-operation) were: 0 – operation missed; 1 – operation performed with help; 2 – operation performed without help. As per the EU Summary of Product Characteristics, the first injection using the pen should be performed under direct medical supervision [2]. Therefore, user scores of '2' and '1' were considered a handling success, whereas a user score of '0' was considered a failure. For some operations, not remembering to complete a particular step was considered a failure.

For critical operations performed by patients, direct comparison of the two pens was conducted (in agreement with the primary objective). Critical operational scores with the redesigned pen were compared with those from the existing pen. For each operation, the test score was calculated as the number of patients having missed the operation divided by the total number of patients who performed the operation. Thus, a lower test score indicated a better outcome than a higher test score.

Ease-of-use assessments were rated on a scale of 1 – 5, where 1 indicated 'it was very difficult' and 5 indicated 'it was very easy'.

Descriptive statistics are presented, including number (n), mean, standard deviation (SD), median, minimum and maximum.

## 3. Results

### 3.1 Handling tests

Eighteen patients and 18 nurses participated in the handling tests. The number of patients and nurses recruited from Berlin was 5 and 10, Cologne 4 and 1, Frankfurt 5 and 3, and Hamburg 4 and 4, respectively. Due to a lack of nurse candidates in Cologne, more were recruited in Berlin to ensure that target participant numbers were met.

#### 3.1.1 *Demographic characteristics*

Patient demographic characteristics are shown in **Table 1**. Mean (SD) patient age was 34.2 (5.6) years. Although one patient (aged 46 years) exceeded the predefined age limit by 1 year, this protocol deviation was not considered a major violation. Nine patients were gonadotropin-injection-naïve and nine were gonadotropin-injection-experienced.

Nurse demographic characteristics are shown in **Table 2**. The mean (SD) age was 37.7 (10.5) years and the median number of years of nursing experience was 12.0. Although one nurse (aged 61 years) exceeded the stated age limit, this event was not considered to be a major protocol deviation.

#### 3.1.2 *Operational and functional goal testing*

Test scores for the critical operations' assessments for the redesigned and existing pens are shown in **Table 3**. For three of the four critical operations, the test scores for the redesigned pen were better than or equal to the scores of the existing pen, thereby showing that the overall risk of dosing errors with the redesigned pen is not higher than with the existing pen.

For one critical operation, checking availability of the full dose, the redesigned pen had a poorer score than did the existing pen. Failure of one of the two sub-operations (check the content of the pen reservoir) decreased in frequency each time the procedure was performed by patients using the redesigned pen (three times with three different doses; n = 13, n = 10, n = 8; **Table 4**). It is not clear why the frequency of failure did not decline in the nurse group.

Both patients and nurses achieved most of the primary functional goals of the redesigned follitropin α pen injector (**Table 4**). Failure rates were the highest for: checking the content of the pen reservoir; checking the preset dose; and putting back the outer needle cap. Nine patients and nine nurses forgot to check the preset dose before injecting. No additional risks related to the use of the redesigned follitropin α pen

**Table 3. Results of the critical operation goal testing in patients (n = 18).**

| Critical operation/sub-operation | Test score per operation* | |
|---|---|---|
| | Redesigned pen | Existing pen |
| Remove large air bubble | 0.056 | 0.167 |
| Check presence of large air bubble | | |
| Remove inner needle and shield | | |
| Remove large air bubble | | |
| Check over availability of the full dose | 0.574 | 0.056 |
| Check and remember dose prescription | | |
| Check content of pen reservoir | | |
| Preset the prescribed dose | 0.000 | 0.000 |
| Turn dose setting knob | | |
| Read prescribed dose figure | | |
| Handle an incomplete dose | 0.000 | 0.000 |
| Prepare a new pen for completing the dose | | |
| Preset the missing amount of dose | | |

*Test score = number of patients having failed the operation/total number of patients who performed the operation. Lower scores indicate better outcomes.



injector were identified during the test, and no major concerns regarding the risk of misuse and dosing errors were observed.

Following the pre-summative test, almost all participants filled in the treatment diary correctly after the administration of three different doses (patients, 16/16; nurses, 16/17).

#### 3.1.3 *Ease of use ratings*

The ease of use of the redesigned follitropin α pen injector was rated favourably. **Table 5** includes the results of each of the questions per group of participants (maximum possible score = 5). For the five questions on ease of use, scores ranged from 4.44 to 4.83 for patients and from 4.18 to 4.94 for nurses. Both patients and nurses rated the overall handling of the redesigned follitropin α pen injector highly, with a mean (SD) score of 4.61 (0.61) by patients and 4.50 (0.52) by nurses.

### 3.2 Nurse–patient training observations

Four patients and four nurses participated in the qualitative nurse–patient training sessions for the redesigned follitropin α pen injector. Two nurse–patient training sessions were performed in Berlin, one in Frankfurt and one in Hamburg; one was scheduled in Cologne, but participants did not present for the appointment. The information below is based on the transcriptions of the nurse–patient training sessions.

Most participants reported that the removal of a large air bubble from the redesigned follitropin α pen injector was uncomplicated and easy to do. Patients noted that they were able to estimate whether the next dose could be fully delivered by looking at the pen reservoir. Patients and nurses stated that setting the dose was uncomplicated and easy: the display clearly indicates the units and a dose correction is possible at any point.

All participants considered injection of the required dose using the redesigned follitropin α pen injector to be uncomplicated and easy to handle. Patients and nurses commented that the redesigned pen clearly indicates in the display whether the dose has been completely delivered. Users reported that the redesigned pen engenders confidence in setting the correct dose and for ease of identifying a missing dose amount. Identification of an incomplete dose and the exact number of missing units was reported to be easy. Indeed, the indication on the dose display of the exact number of units that need to be injected with a second pen was found to be one of the main advantages of the redesigned pen.

## 4. Discussion

In the current pre-summative and summative usability testing, the redesigned follitropin α pen injector was not associated with an overall increase in risk of dosing errors versus the existing pen. There were no unexpected operational risks or major concerns regarding the risk of misuse or dosing errors identified in this study.

The redesigned follitropin α pen had poorer scores than the existing pen only for 'checking availability of the full dose', which reflects the different functioning of the two pens. Checking of the dose control scale to confirm whether the selected dose is available for injection is a mandatory step with the existing pen. If this operation is missed, a patient would not know whether a complete dose had been delivered. With the redesigned pen, however, this operation is simply for visual reference purposes and is not required to set the dose. Thus, failure to perform this operation did not lead to a higher risk of dosing errors with the redesigned pen, as demonstrated in the results of the two critical operations 'presetting the prescribed dose' and 'handling an incomplete dose'. Furthermore, the frequency of failure of this critical

**Table 4. Overall results of the critical operational* and primary functional goal testing of the redesigned follitropin α pen in patients (n = 18) and nurses (n = 18).**

| Critical operational* or primary functional goal | Number of failures (score '0') | |
|---|---|---|
| | Patients | Nurses |
| *Put on needle* | | |
| Control closure integrity outer needle cap | 2 | 1 |
| Remove peel-off tab | 0 | 0 |
| Attach needle | 1 | 0 |
| Remove outer needle cap | 1 | 0 |
| *Remove large air bubble* | | |
| Check presence of large air bubble | 2* | 0 |
| Remove inner needle and shield | 0* | 0 |
| Remove large air bubble | 1* | 0 |
| *Check availability of full dose* | | |
| *[assessed three times with three different dose settings (75, 150 and 187.5 IU)]* | | |
| Check and remember dose prescription‡ | 1 | 1 |
| | 0 | 0 |
| | 0 | 0 |
| Check content of pen reservoir‡ | 13* | 11 |
| | 10* | 12 |
| | 8* | 10 |
| *Preset prescribed dose* | | |
| Turn dose setting knob | 0* | 0 |
| Read prescribed dose figure | 0* | 0 |
| *Before injecting* | | |
| Check preset dose | 9 | 9 |
| Correct preset dose (if incorrect) | 0 | 0 |
| Remove inner needle shield | 0 | 0 |
| *Injecting* | | |
| *[assessed three times with three different dose settings (75, 150 and 187.5 IU)]* | | |
| Inject‡ | 0 | 0 |
| | 0 | 0 |
| | 0 | 0 |
| Insert needle into skin‡,§ | 0 | 0 |
| | 0 | 0 |
| | 0 | 0 |
| Press dose-setting knob as far as it goes‡,§ | 0 | 0 |
| | 1 | 0 |
| | 0 | 0 |
| Keep pressing with the needle in the skin‡,§ | 1 | 0 |
| | 1 | 1 |
| | 0 | 1 |
| Remove needle from skin‡,§ | 2 | 0 |
| | 0 | 2 |
| | 0 | 1 |
| *Control dose delivered* | | |
| *[assessed three times with three different dose settings (75, 150 and 187.5 IU)]* | | |
| Read number in dose display‡ | 0 | 1 |
| | 1 | 1 |
| | 0 | 0 |
| *If dose delivered is incomplete* | | |
| Prepare a new pen for completing the dose | 0* | 0 |
| Preset the missing amount of dose | 0* | 0 |
| *Taking off the needle* | | |
| Put back the outer needle cap | 5 | 0 |
| Grip outer needle cap and unscrew the needle | 3 | 0 |
| Dispose of safely | 1 | 0 |
| Put on pen cap | 0 | 0 |

*Critical operational data were collected only from patients. Nurses also completed these functions as primary functional goals.

‡Functions were performed on more than one occasion and results are listed in order of occurrence.

§The term 'skin' is used to indicate the sponge provided for simulation testing.

**Table 5. Ease-of-use ratings for the redesigned follitropin α pen injector by patients and nurses.**

| Assessment | Patients | Nurses |
|---|---|---|
| *Overall handling* | | |
| n | 18 | 18 |
| Mean (SD) | 4.61 (0.61) | 4.50 (0.52) |
| Range | 3 – 5 | 4 – 5 |
| *Removing an air bubble* | | |
| n | 18 | 17 |
| Mean (SD) | 4.44 (0.70) | 4.18 (1.18) |
| Range | 3 – 5 | 2 – 5 |
| *Injecting the dose* | | |
| n | 18 | 18 |
| Mean (SD) | 4.78 (0.55) | 4.83 (0.51) |
| Range | 3 – 5 | 3 – 5 |
| *Understanding that a second pen may be needed to complete the prescribed dose* | | |
| n | 16 | 18 |
| Mean (SD) | 4.81 (0.4) | 4.94 (0.24) |
| Range | 4 – 5 | 4 – 5 |
| *Setting the remaining dose in the second pen* | | |
| n | 18 | 18 |
| Mean (SD) | 4.83 (0.51) | 4.94 (0.24) |
| Range | 3 – 5 | 4 – 5 |

Ratings were on a scale of 1 – 5 (1 = 'it was very difficult', 5 = 'it was very easy').
SD: Standard deviation.

operation decreased each time the procedure was performed by patients with the redesigned pen.

This study was also designed to evaluate the impact of human factors on the use of the redesigned follitropin α pen injector with particular focus on the risks for misuse and dosing errors. Most of the primary functional goals of the redesigned follitropin α pen injector were achieved by both patients and nurses. Failure rates were highest for: checking the content of the pen reservoir (sub-operation of the critical operation checking availability of the full dose as discussed above); checking the preset dose; and putting back the outer needle cap. It must be noted, however, that in some cases 'failure' denoted forgetting to perform a task rather than failure to perform a task correctly. For example, nine patients and nine nurses forgot to check the preset dose before injection.

From the qualitative training session observations, both patients and nurses reported that they were confident about correct dose setting and administration. The ability to readjust a dose after dose setting was considered to be an important feature. When there is insufficient drug for a full dose in the first pen, the indication in the dose display of the amount of drug required for a second dose was also considered a useful feature. When asked about the overall ease of use, both patients and nurses rated the redesigned pen highly.

Nurses are closely involved in the administration and injection training of patients in normal clinical practice, so their input was considered important for addressing the study objectives. Thus, this study provides useful, practical information on the redesigned follitropin α pen injector from a specialist nurse perspective.

Currently, infertility treatment involves the administration of multiple gonadotropins and the use of various administration devices [1]. Thus, patients and nurses have to learn how to use several different devices for the administration of treatment. Several reports indicate that patients undergoing infertility treatment find pen injectors simpler and easier to use than other administration methods [3,7-9,19]. Furthermore, the ease of teaching and learning of the redesigned follitropin α pen injector has previously been assessed in 73 women with infertility and 28 specialist nurses [14]. Most patients (88%) in that study found it easy to learn how to use the pen. All nurses considered the redesigned pen easy to learn and believed it would be easy to teach patients how to use.

The current study has some minor limitations. First, this was a simulation test to evaluate the functioning of the pen and, as such, has limited statistical power to allow conclusions to be made concerning comparison with the existing pen. Data on use of the redesigned follitropin α pen injector in clinical practice would also be valuable. Second, only qualitative information was available from the nurse–patient training observations. Third, as the study design was primarily observational and non-interventional, there was no opportunity to query the patients and nurses regarding certain operational steps, such as 'check the availability of the full dose'. Although forgetting to 'check the availability of the full dose' was not associated with an increase in dosing errors, further insights regarding failure to remember this step would have been helpful.

Overall, the redesigned pen was found by both patients and nurses to be uncomplicated and easy to use.

## 5. Conclusions

The study met its primary objective, which was to show that the risk of dosing errors by patients was not higher with the redesigned follitropin α pen injector than with the existing pen. Test scores for the redesigned follitropin α pen injector were better than or equal to the scores of the existing pen for three of the four critical operations. Thus, the overall risk of dosing errors with the redesigned pen was not higher than with the existing pen, and in some cases, failure of an operation was due to forgetting to perform it.

Both patients and nurses rated highly the ease of use of the redesigned pen. On a scale of 1 – 5, for five different questions relating to ease of use, all scores were above 4 for patients and nurses. The overall handling scores indicated that both patients and nurses found the redesigned pen easy to use.

During qualitative observations of nurse–patient training sessions with the redesigned follitropin α pen injector, all participants considered injection of the required dose to be uncomplicated and easy to handle. One of the main benefits of the redesigned pen was reported to be the indication of the exact number of units of follitropin α that needed to be

injected using a second pen in order to complete the prescribed dose.

In summary, use of the redesigned follitropin α pen injector was not associated with a higher overall risk of dosing errors than the existing pen. No unexpected operational risks or major concerns regarding the risk of misuse or dosing errors were identified in this study. The overall ease of use of the redesigned pen was rated favourably by patients and nurses.

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## Declaration of interest

This study was sponsored by Merck Serono S.A., Geneva, Switzerland (an affiliate of Merck KGaA, Darmstadt, Germany). JC Schertz is an employee of EMD Serono, Inc., and P Arriagada and H Saunders are employees of Merck Serono S.A., Geneva (affiliates of Merck KGaA, Darmstadt, Germany). C Hecker and B Lang are employees of Point-Blank International.



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