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Development of the SoloSTAR® insulin pen device: design verification and validation

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Background: SoloSTAR® (SOL; sanofi-aventis, Deutschland, GmbH) is a new, disposable insulin injection pen device for use by people with type 1 or type 2 diabetes to administer long- or short-acting insulin. *Objectives*: To discuss factors that have underlined the design process of the SOL device. In addition, to highlight the studies that shaped the direction of its development, such as addressing the unmet needs of people with diabetes, which included a need for better differentiation features and a lower injection force compared with existing prefilled disposable pen devices. *Results*: The development of the SOL pen device was an iterative process involving both patients and the design team, which has lead to a manufacturable, tailor-made pen device. Patients' needs have been taken into account in the pen design; there are numerous differentiators on the device, which avoids confusion between insulin types. Furthermore, the SOL device has a lower injection force compared with other marketed pen devices. Finally, studies have shown that the SOL device is more accurate, easier to use and is preferred by patients over other pens on the market. *Conclusions*: The SOL device has undergone rigorous user and laboratory testing, which has captured evolving improvements to better meet the needs of people with diabetes.

Keywords: design, development, device validation, device verification, diabetes mellitus, engineering, insulin pen device, long-acting insulin, short-acting insulin

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1. Introduction

SoloSTAR® (SOL; sanofi-aventis, Deutschland, GmbH) was developed for use by people with type 1 or type 2 diabetes for the administration of long- or short-acting insulin. Both SOL devices were approved in Europe in 2006 and for the long-acting insulin pen, approval was given in the United States in 2007. SOL is a disposable insulin pen device with a 3 ml capacity (300 units of insulin) designed for use once or several times a day (**Figure 1**). Studies have found that these products are easy to use [1-3], easy to teach [4], they dose accurately and have a lower injection force than both the FlexPen® (FP; Novo Nordisk, Bagsvaerd, Denmark) and the Lilly disposable pen device (LP; Humalog®/Humulin® pen; Eli Lilly and Company, Indianapolis, United States) [5,6].

The SOL pen device was effectively developed from the ground up and the development process took into consideration not only laboratory testing (design verification) and user testing (design validation), but also extensive human and ergonomic factors, which will be discussed here using two case studies to illustrate the stages in the process. Design verification and validation were fed into an iterative design process at every stage of development from initial concept design through proof of principle and proof of concept. As a result, the SOL pen device is an intuitive, easy to use device [1] with a similar user interface (i.e., common mode of operation) as other pen devices, but also fulfils patients' needs to a degree that

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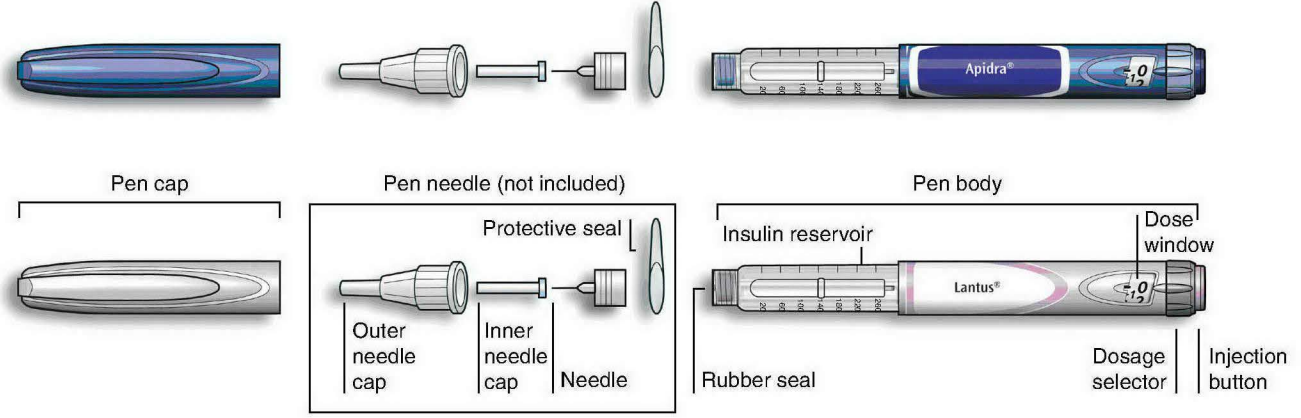

Figure 1. Schematic diagram of the Lantus® SOL (insulin glargine) and Apidra® SOL (insulin glulisine) products.

advances SOL close to the ideal mechanical disposable device. Indeed, some of the features such as addressing the unmet needs of the patient, which included better differentiation features and a lower injection force compared with existing devices that will be discussed, were identified during the development programme in user testing and subsequently incorporated into the end product.

1.1 What are design verification and validation?

The core of design verification and validation is best described by two simple questions: 'Did I design the product right?' must be answered positively to pass design verification; 'Did I design the right product?' needs to be evaluated in design validation. Design verification is a laboratory-based exercise and involves the assessment of device function, including individual components, from a technical perspective. International standards have to be fulfilled and compliance proven. In addition to parameters set by the International Organization for Standardization (ISO), other parameters are defined as part of the design brief and, therefore, are implicit in the verification process. One such factor is the injection force of the device. Testing operating forces and torques has become state of the art and has been included to verify the end product against the design brief. The aim of design verification is to quantitatively ensure the individual components and the device fulfils the technical requirements.

For design validation it has to be demonstrated that the user can operate the device and that it answers their needs, and that the collection of objectives (i.e., design brief) is achieved. There are many ways to understand the degree of overlap of user requirements and device functionality. Ergonomics and human factors specialists can be consulted, as well as medical advisors who oversee large numbers of patients. However, to best validate a product, it has to be bought to the user. User surveys and studies in clinical settings, which were performed continuously during the development, are appropriate means to get direct feedback and understand the degree of overlap, and demonstrate that the end product fulfils the needs of the users as reflected in the design brief.

1.2 Why was a new insulin pen device needed?

The use of the vial and syringe is still relatively common in some regions, particularly in the US. It had been estimated that in the US, only 14% of patients using insulin were using insulin pen devices (prefilled pens or cartridges) as a percentage of total insulin use, whereas in Europe, 92% of patients were using insulin pen devices [7]. However, it has been demonstrated that switching from the vial and syringe to insulin pens results in increased medication adherence and reduced treatment costs [8]. There are several prefilled and reusable insulin pen devices now on the market, although availability may vary in some regions/countries. Each device offers the patient specific advantages compared with the other pen devices. However, despite the multitude of pens available, there remains scope for further development of insulin pen devices in response to unmet patient needs. Some of these unmet needs will be discussed here, in relation to the development of the SOL pen device.

1.3 Original development requirements/design brief

The original design specification of the SOL pen device was based on the feedback from users with respect to existing devices plus research to understand the basic needs of customers (2001/2002). Here, users are considered to be patients as they inject insulin using the pen, as well as doctors, nurses and pharmacists as they prescribe, train and/or advise the patients on the pen. In addition, human factors analysis by means of a literature search provided basic requirements. The intent was to provide a pen device with better characteristics than the FP and the LP, as those were the most commonly used prefilled pen devices on the market at the time. Factors such as maximum length, diameter and injection force provided an integral part of the initial specification. Refinement of the requirements was done on the basis of human factor and ergonomic analyses.

1.4 Guidelines and standards for insulin pen devices

Insulin pen devices are subject to several regulatory guidelines developed by the national/international medical regulatory bodies, for example, FDA and the European Agency for the Evaluation of Medicinal Products (EMEA). Before approval from the FDA and EMEA can be sought, pen devices and related materials must also meet several criteria specified by ISO, in particular, ISO 11608-1 for insulin pen devices [9].

The guidelines for insulin pen devices cover not only specific aspects of device use, such as dose accuracy or visibility of the selected dose, but also that the pen device doses correctly after storage in a range of environmental conditions (e.g., temperature and humidity), functions properly after being dropped from a height of 1 m at various orientations and that labels or other distinguishing marks are durable during use. However, factors such as injection force and design features such as colour and size are not covered by the ISO standards. Thus, for the design verification and validation of the SOL pen device, tests were performed to ensure it met the ISO guidelines and that it met the more stringent targets that were set internally. Furthermore, user testing was carried out to ensure that the SOL pen device was intuitive to use by the intended population.

1.4.1 *Unmet needs*

1.4.1.1 *Insulin dose*

Increasing doses of insulin are required over time to overcome the insulin resistance and relative insulin deficiency. Indeed, many patients need to administer individual doses of insulin > 60 units, the maximum dose of many insulin pen devices, thus necessitating several injections. As a result, the design brief of the SOL pen device included the recommendation of a maximum dose of 80 units.

1.4.1.2 *Hand function and injection force characteristics*

Limited joint mobility of the hand, commonly referred to as cheiroarthropathy, is frequently observed in patients with diabetes, particularly elderly patients, which may occur as a result of connective tissue disorders or diabetic neuropathy, and is characterised by low grip strength and/or limited dexterity [10-15]. As a result, the recommendation in the design brief was for the SOL pen device to have a lower injection force than other prefilled devices available at the time, as well as a short dial extension length to reduce the mechanical strain on the user's thumb. Indeed, one would anticipate that a short dial extension with low force requirements would be easier to use for most of the patients.

1.5 Overview of the SOL pen design verification and validation process

Numerous concepts were initially investigated; all could fulfil the design brief, but used different mechanical principles. Complex designs, such as an odometer mechanism for displaying the dose, were investigated, as well as toothed rod type mechanisms and simple tampo-printed dose scales. Of the proposals mentioned earlier, very few were selected after mechanism concept evaluation, which used quality function deployment techniques (QFD). These techniques ensured end user requirements were the main focus of selection. Extra parameters, such as complexity, technical risk or perceived patent infringement risk, were taken into consideration.

The selected concepts were then progressed through the design verification and validation processes. As described earlier, the verification and validation of the SOL pen device followed an iterative process: at each stage of the process, studies were done to assess technical aspects (i.e., the mechanical/physical properties) and user aspects (i.e., feedback from the intended user population). Additionally, structured risk assessment was done at each stage, with the results used for risk management of the device. Failure mode and effects analysis (FMEA) and user task analyses served as tools for risk assessment and provided an approach from two different directions. The FMEA helped us to understand which component failure or feature malfunction could lead to critical loss in performance and the user task analyses highlighted potential ambiguity leading to reasonably foreseeable misuse.

Studies done at each stage of the process assessed not only the pen device itself (block models, proof of principle rigs, proof of concept prototypes and eventually the industrialised pen), but also individual components and features (including dial display, pen colours, label size and format, dose knob, pen cap and clip, overall dimensions). Results of these studies were fed back into the iterative design process, as summarised in **Figure 2**, to ensure the ongoing developments in pen device design and function continued to meet not only the original design specification, but also subsequent suggestions and recommendations leading to an updated design brief to further meet the patients' needs.

As shown in this figure, there are two key areas that govern the design and development process. On the one hand, it is important to understand the patient's needs through a combination of literature research, ergonomics studies and user testing. On the other, it is important to respond to these needs with rational design and adaptation to ensure a solution is found before the next stage of development can be entered. User testing and laboratory-based testing performed at each stage of the development cycle helps ensure that the design is verified and validated.

1.6 Objectives

The design validation process involved nine user studies, which were done with a total of > 2,300 participants, including health-care professionals (nurses and physicians) and people with diabetes. Moreover, 12 ergonomics analyses were done in addition to numerous meetings with health-care professionals (nurses and physicians), which are part of an advisory board that allows medical experts to provide feedback on most aspects of product development. Technical tests of all products and components were performed in advance of each user/ergonomics study to ensure the product and component

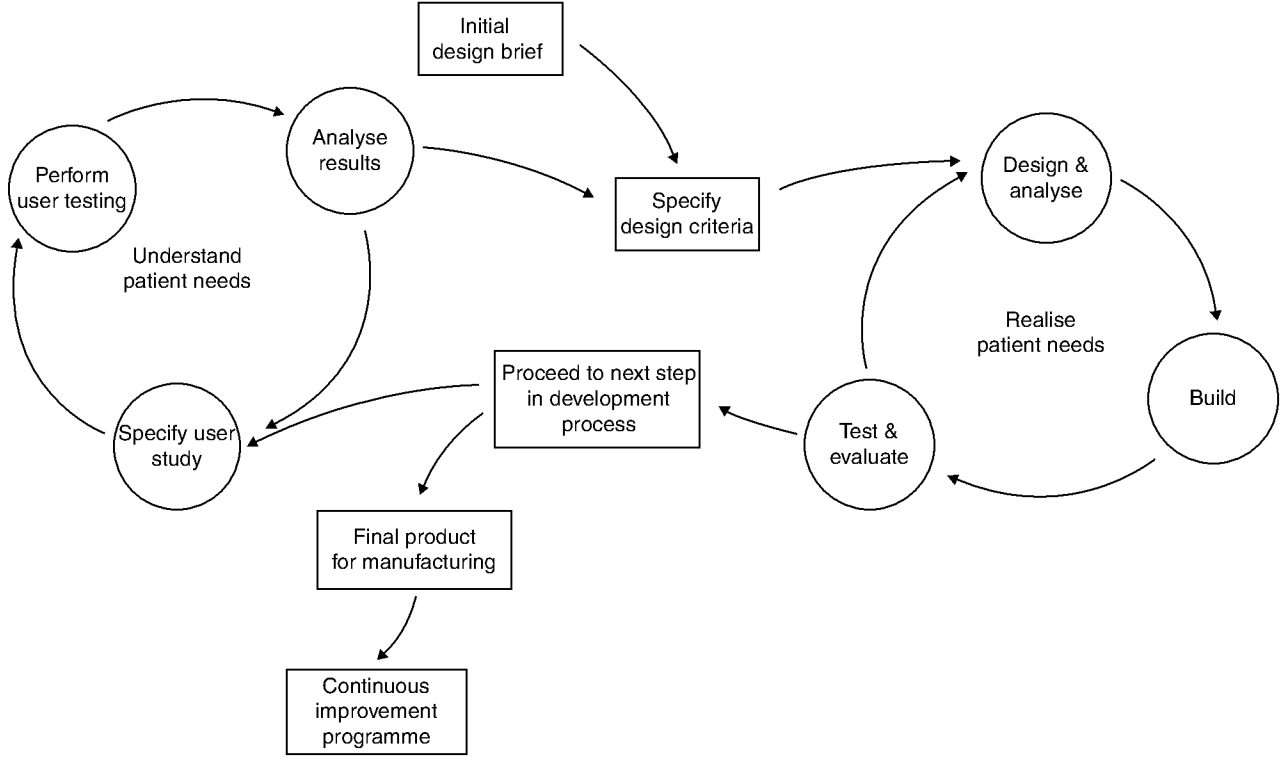

Figure 2. A simplified diagram illustrating the feedback loops for the input of technical testing and user testing results on the design and development of the SOL pen device.

met the design brief and ISO guidelines. It is not the aim of this paper to discuss all details of the extensive test programme (in excess of several 10,000 pen devices and components were tested). Instead, we have focused on two key events that helped shape the development of the SOL pen device; these two events are exemplary for the development process and systems applied for SOL. An overview of the development method is shown in **Figure 3**. In brief, each stage of the development process involved an iterative approach, and the process was guided by user research as well as laboratory testing.

First, we wish to discuss the rationale for developing the SOL pen devices with distinct body colours specific for the delivery of long- or short-acting insulin devices. Second, we wish to discuss the impact of mechanics on the function of the dose dial extension and injection force. For both characteristics, we will present the results of studies in which these characteristics were identified, provide a summary of the impact on the verification process and the final validation testing.

2. Case studies

2.1 Colour differentiation

Problems with visual acuity are relatively common in diabetes, and may be either age related, such as macular degeneration or cataract formation [16,17], or diabetes related, with onset and progression of diabetic retinopathy [18-20]. People with diabetes, particularly those with type 1 diabetes, but also some with type 2, often use more than one type of insulin to manage the basal and prandial insulin requirements, which can be provided by insulin glargine and insulin glulisine, respectively.

Owing to the differences in typical dose and pharmacodynamic characteristics of basal and prandial insulins, it is important that the delivery devices (pen device or vial) are sufficiently differentiated to ensure a low risk for confusing the two insulin formulations and to minimise the risk of hypoglycaemia. Typically, this may involve some colour applied to the label and dose button of the device along with text and potentially tactile features.

2.1.1 *Colour deficiencies*

Colour deficiencies in people with diabetes occur primarily as a result of retinopathy [21], which is associated with altered colour perception owing to a reduction of light falling on the retina and the death of cones where the oxygen supply is restricted, or maculopathy, such as age-related macular degeneration, which is associated with an accumulation of fluid in the cone-rich area of the fovea, leading to distorted vision along with altered colour perception [16]. People with poorly controlled diabetes (type 1 or type 2) are at increased risk of developing retinopathy, whereas risk factors for maculopathy include aging, smoking and poor glycaemia

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