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DEVELOPMENT OF PLATFORM INJECTION DEVICES – ADDRESSING HUMAN FACTORS AT AN EARLY STAGE FOR DIFFERENT USER GROUPS

In this article Orfeo Niedermann, Business Development Director, and Jakob Lange, PhD, Account Director, both of Ypsomed Delivery Systems, provide insights into the development of platform products that offer pharma companies low risks and shorter timelines at an attractive cost. The authors then describe how Ypsomed addresses the issue of human factors engineering testing with broad user populations for platform products, using the examples of the YpsoMate autoinjector and UnoPen pen injector platform products.

With the large number of new biologic and biosimilar products launching, the demand for subcutaneous self-injection devices for biopharmaceuticals continues to grow and develop. These devices, including autoinjectors, pen injectors and new large volume patch injectors, are designed for ease of use and improved patient adherence. Timeline and cost pressures are driving both big and small pharmaceutical and biotech companies to source these state of the art devices quickly, and at low risk, for both clinical trials and commercial launch. This has boosted the demand for platform products that can be easily customised to both drug- and marketing-specific requirements, whilst having been thoroughly tested and documented beforehand to minimise project risks and shorten time to market.

PLATFORM PRODUCTS: LOW RISK AND SHORT TIME TO MARKET

Ypsomed has built up a comprehensive offering of platform products that meet key customer needs and are specifically designed to be modified into customer-specific products. The platform products enable flexible customisation, while minimising project risks and shortening time to market. With this approach, described in Figure 1,

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Ypsomed decouples the development of new platform products from the customer project, thereby moving the risks associated with platform development and installation of manufacturing infrastructure in-house. Each customer commercial product is derived from an existing platform product that is based on proven technology.

Driven by patient needs, market intelligence and new technology, the development of novel platform products also requires significant investments in manufacturing capacity. Ypsomed supports its partners not only by customising its injection systems to market demands, dosing needs and the primary container, but also by increasing its installed manufacturing infrastructure to match customer capacity

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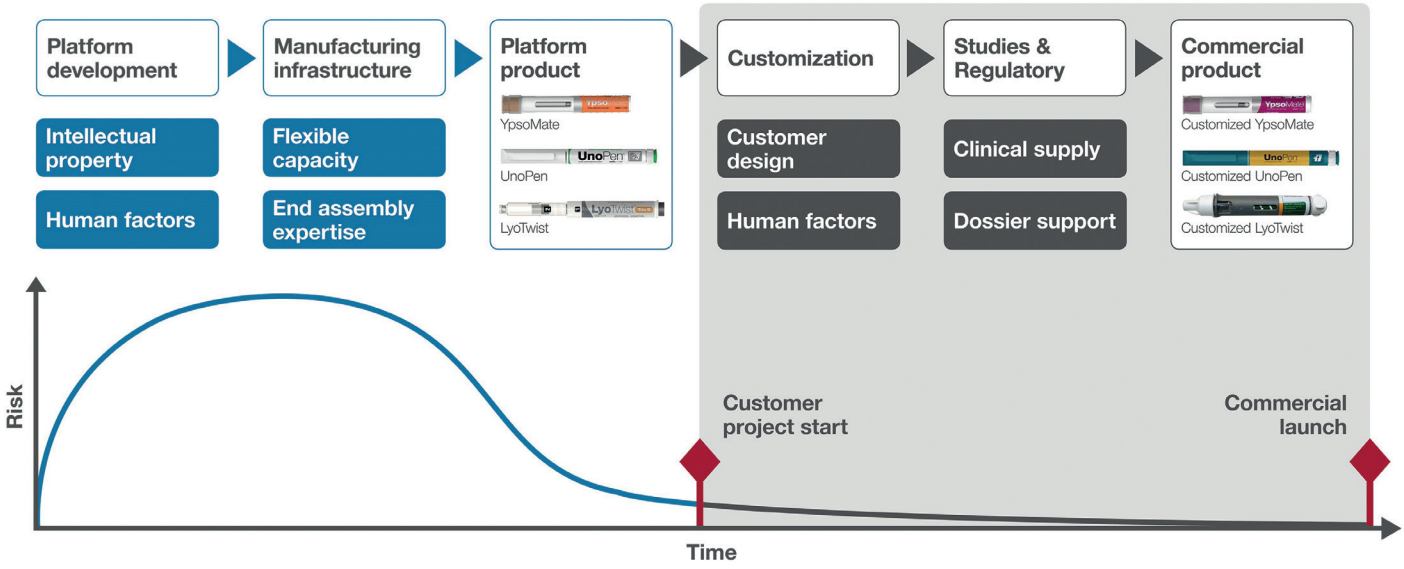

Figure 1: Ypsomed's platform-based product strategy lowers risk and shortens timelines during customer projects.

requirements. Today, Ypsomed offers one of the broadest ranges of self-injection platforms and supports its customers in selecting the ideal device for their specific application.

PERFORMING USABILITY STUDIES WITH PLATFORM PRODUCTS

Successful development of safe and reliable medical devices requires the application of usability evaluation throughout the design cycle, and documented usability testing is an important part of the information required by regulatory authorities in order to grant marketing authorisation. Usability evaluation during device development is typically divided into three parts:

- **Early formative testing:** Conducted in the early development stages to collect feedback from users at various stages of the design process in order to iteratively refine the design, the packaging and its instructions for use (IFU).
- **Late stage formative testing:** Carried out to gain certainty that the device is suitable, and therefore likely to successfully pass design validation.
- **Summative testing:** Performed at the end of development in order to provide objective evidence that the intended use has been met and that the device can be safely and reliably used by the intended patient population.

With the move from development of customer- and indication-specific devices to device platform products used across a wide range of therapies and indications, a new approach to formative usability work, involving user groups with a broad range of user requirements, is necessitated. This raises the question of how to set up a usability engineering programme in line with regulator expectations, without a known specific user population. Ypsomed adopts a two-tiered approach:

- First, the platform device undergoes formative testing with a broad user population, recruited to reflect more general user backgrounds and abilities rather than those of a specific indication.
- Second, the device is customised for a given application and subjected to further formative testing, followed by design validation with the corresponding specific user population.

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Figure 2: UnoPen™ and YspoMate® product platforms. Use steps summarised in Box 1.

UNOPEN AND YPSOMATE LATE STAGE FORMATIVE STUDIES

To illustrate Ypsomed's approach to platform usability, two late-stage formative studies of the UnoPen pen injector and the YpsoMate autoinjector platform devices

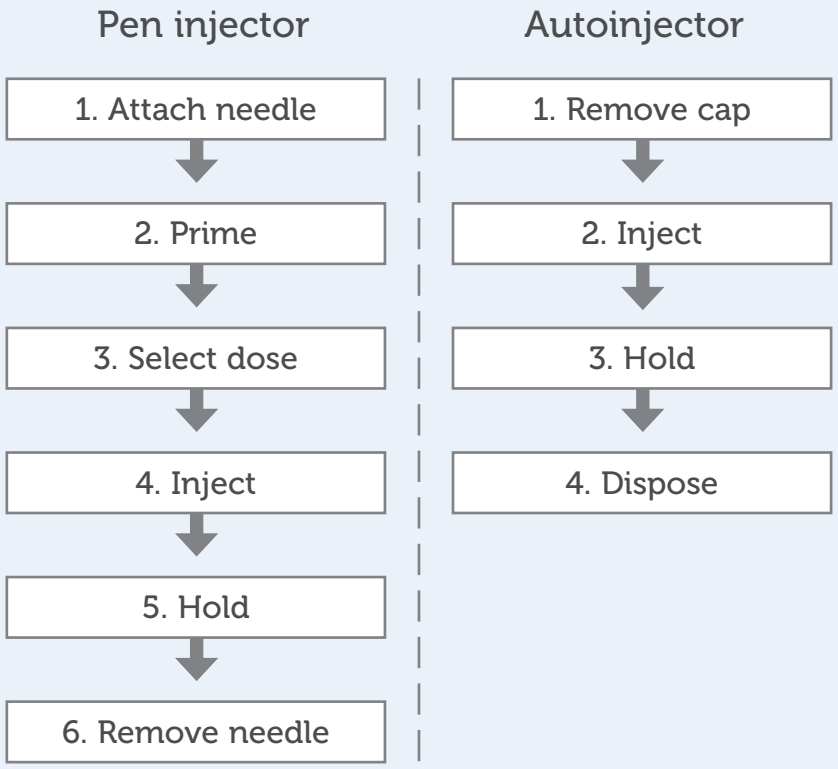
Figure 3: User with impaired dexterity with YpsoMate® autoinjector in formative study.

(Figures 2 and 3) have been performed and published.[1,2] Both studies were conducted with broad user populations, defined to represent user requirements across a range of indications. Specifically, the studies were designed and carried out with the goal of understanding whether the platform device and its IFU were suitable for users in all intended applications, and whether the device would be likely to pass summative usability tests for specific indications.

UnoPen is a disposable, multiple variable dose pen injector holding a 3 mL cartridge. The device is fully manual and similar in design to insulin pen injectors currently on the market. The UnoPen operates according to the principles of "dial-to-dose" and "push-to-inject". It is designed for ease of use, with a geared dosing mechanism to provide reduced injection force and a dose scale with large, easy to read numbering.

YpsoMate is a single dose, single use two-step autoinjector intended for the subcutaneous self-injection of drugs in the context of various treatments requiring relatively infrequent (weekly, bi-weekly or monthly) injections of a single fixed dose. The device contains a 1 mL long prefilled syringe and features automated delivery of the drug into the subcutaneous tissue once triggered by pushing the device onto the skin. The handling steps for each device are summarised in Box 1.

BOX 1: HANDLING STEPS FOR THE UNOPEN™ PEN INJECTOR AND YPSOMATE® AUTOINJECTOR.



Participants and Procedures

As both device platforms are used across different medical indications and patient groups, no specific indication was used to define the user groups to participate in the studies. Rather, relevant user requirements were selected which can reasonably be expected to be found in a wide range of applications. Ideally, any user population for subsequent products would be a subset of the user properties thus defined. Table 1 presents the different defined user groups for the two studies. The different user groups reflect differences in the abilities of potential end users.

For both studies, participants were recruited through market research agencies and scheduled to attend individual sessions. As part of each session, the participants provided personal information, studied the IFU and performed simulated injections into an injection pad. For the pen study, no training was provided and the participants performed a distraction task between the two injections. In the autoinjector study, in addition to the self-study of the IFU, the device was demonstrated to the participants

Definition (abbreviation)	Characteristics
Healthcare professionals (HCP)	Healthy qualified user
Caregivers (CG)	Healthy lay user
Diabetics with retinopathy (DR)	Impaired vision
Diabetics with neuropathy (DN)	Impaired tactile perception
Patients with arthritis (AR)	Impaired dexterity
Adolescents (AD)*	Lay user of 12-18 years of age

Table 1: User groups as defined for the two studies. *Only included in the pen study

> "Both devices could be safely and efficiently used by all user groups, with overall success rates in performing injections above 95%, and high reported degrees of confidence and comfort in using the devices across all user groups."

followed by a distraction task directly after which the two injections were performed. These differences in procedure correspond to the expected use scenarios for the two device types.

In both studies, the outcome was recorded as:

1. Injection success rate.
2. Participant feedback on device handling.
3. Observed deviations from IFU procedure and user errors.

Results and Conclusions

The injection success rates for both devices/studies are summarised in Figure 4, while the self-reported data on confidence and comfort is presented in Figure 5.

Both devices could be safely and efficiently used by all user groups, with overall success rates in performing injections above 95%, and high reported degrees of confidence and comfort in using the devices across all user groups. The number of user errors observed for the pen was in line with previous studies, and higher than for the autoinjector, reflecting the differences in handling complexity between the devices. For the pen, experienced users sticking to their habits rather than not understanding or misinterpreting the IFU was the main reason for user errors. For the autoinjector, virtually all observed use errors concerned the holding time after injection, with users typically making the error of holding for less than the required time.

The observation that both devices could be safely and efficiently used by all tested user groups provides confidence that the device and IFU will pass future summative testing in specific applications, which has since been corroborated by a significant number of customers for both YpsoMate and UnoPen.

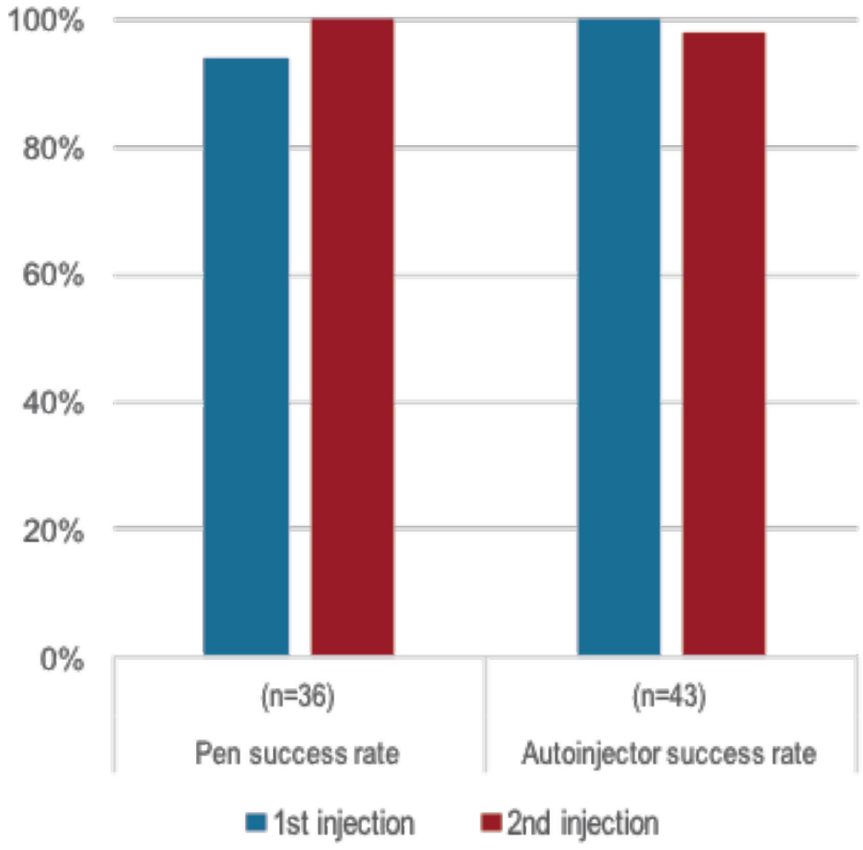


Figure 4: Injection success rates for the two devices from each study.

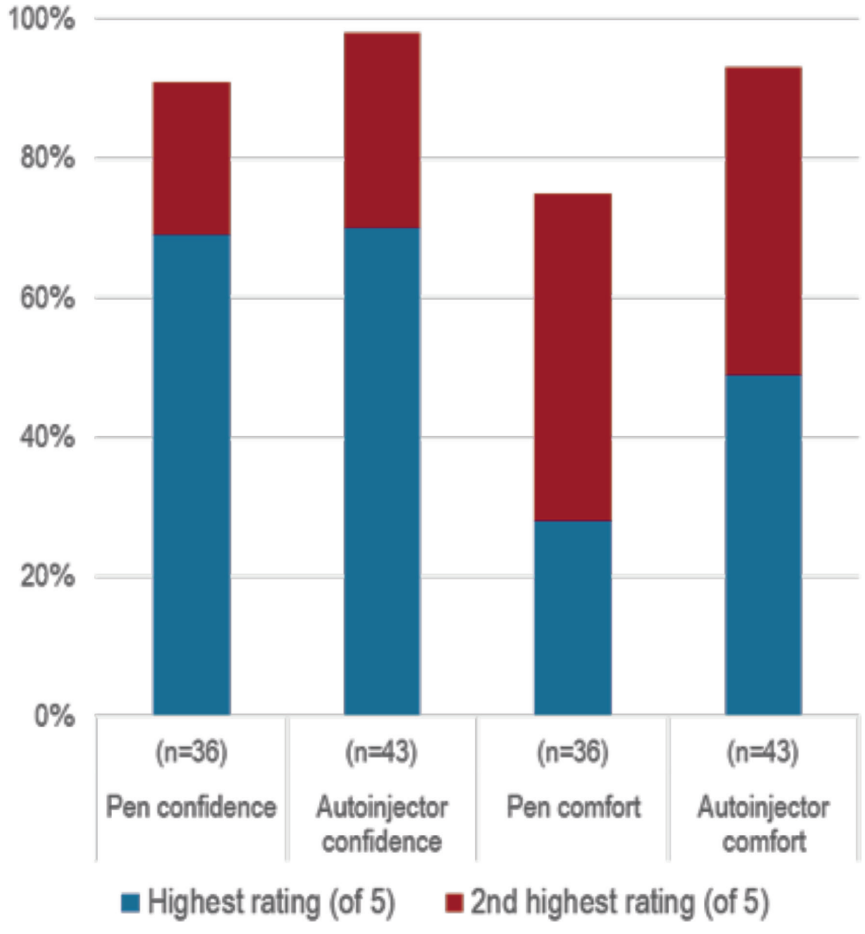


Figure 5: Participant self-reported confidence and comfort in use of the two devices from each study.

REINFORCING THE SUCCESS OF PLATFORM PRODUCTS

The move from long, costly and risky bespoke device development to customisation projects based on established platform products is very well received in the market, providing pharmaceutical and biotech companies with state of the art devices quickly, at low risk for their clinical and market needs. First customer product versions have received approval in regulated markets and initiated commercial marketing.

With Ypsomed's innovative approach to conducting usability work on device platform products, using broad user populations, it becomes possible to build a solid foundation for the usability activities conducted as part of product customisation in customer projects. Although indication-specific summative work will always be required for submission and approval, the basis provided at the platform level reduces the amount of additional work required and significantly de-risks the later stages of the human factors engineering process.

ABOUT THE COMPANY

Ypsomed is the leading independent developer and manufacturer of innovative autoinjector and pen injector systems for self-administration. The customisable platform products cover autoinjectors for prefilled syringes in 1 mL and 2.25 mL format, disposable pens for 3 mL and 1.5 mL cartridges, re-usable pens, ready to use prefilled wearable bolus injectors and injection devices for drugs in dual-chamber cartridges. Unique click-on pen needles and infusion sets complement the broad self-injection systems product portfolio.

As a pioneer with more than 30 years of experience in the development and manufacturing of innovative injection and infusion systems, Ypsomed is strategically developing of a range of smart devices and services, supported by unique in-house capabilities in electronics, software and connectivity. Ypsomed's smart device solutions strive to transform patients' lives by capturing therapy-relevant parameters and processing them to facilitate self-management of diseases.

Ypsomed's platform products are developed and manufactured in Switzerland with strong in-house competencies covering concept and product development, tool-making, injection moulding and automated assembly. Ypsomed is ISO 13485 certified and all processes are run according to design control and cGMP guidelines with operational QA/QC experts on-site at each location. Ypsomed's US FDA registered manufacturing facilities are regularly inspected by both pharma customers and regulatory agencies and supply devices for global markets including US, Europe, Japan, China and India.

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ABOUT THE AUTHORS

Orfeo Niedermann is Business Development Director with Ypsomed Delivery Systems. His responsibilities at Ypsomed include business development activities in the US, Europe, Japan and China as well as product strategy for Ypsomed's range of YpsoMate autoinjector devices. He has spoken at numerous international conferences and authored or co-authored a number of articles.

Mr Niedermann studied mechanical engineering at the Swiss Federal Institute of Technology in Zurich, Switzerland (MSc ETH) and management in Bern (MBA BFH). Before joining Ypsomed in 2005, he was in the packaging machinery industry in various positions including engineering, project management, sales and R&D management.

Jakob Lange is an Engineer and Materials Scientist by training, with an MSc in Chemical Engineering from the Royal Institute of Technology in Stockholm, Sweden and a PhD in Polymer Science from the Swiss Federal Institute of Technology in Lausanne, Switzerland. He has written and published more than 30 peer-reviewed papers on medical devices, packaging materials and polymers and is a regular contributor to technical and scientific conferences.

After previous positions with Nestlé in Lausanne, Switzerland and GE Healthcare Biosciences in Uppsala, Sweden, Jakob joined Ypsomed in 2006, where he has held different positions within Marketing and Sales as well as in R&D Project Management. Currently he has the role of Account Director in M&S Delivery Systems, overseeing a team of Product Managers with focus on managing customer relationships in device development projects, as well as for marketed device products.

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