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A NEW VALUE PROPOSITION OF SMART DEVICES: ADVANCED MEDICATION ADHERENCE MONITORING IN CLINICAL TRIALS

Andreas Schneider, PhD, Business Development Manager, Ypsomed AG, explores a new value proposition of smart injection systems that has received little attention so far: remote monitoring of medication adherence during large multi-centre clinical trials. Introducing how advanced adherence monitoring services resolve some of the key challenges of clinical research practice regarding costs, adherence, data quality and integrity, Dr Schneider explains which technical features are needed for smart devices to provide value-adding adherence monitoring services. The article concludes with a case study describing how such advanced adherence monitoring services are realised with SmartPilot for YpsoMate, a reusable smart add-on that transforms the proven auto-injector platform into a fully connected system.

HOW TO MAXIMISE THE VALUE CREATION OF SMART DEVICES

Healthcare is one of many industries being transformed by innovative digital products and services. Although healthcare may seem to lag behind others in unleashing the full potential of smart connected technologies, pharmaceutical companies and device manufacturers are vigorously pursuing joint R&D programmes to develop novel digital solutions. For example, with the ever-growing global diabetes pandemic, particular efforts are being made to lower the cognitive and emotional burden of insulin therapy with the help of smart devices and digital health platforms. Other therapeutic areas that require repeated self-administration will also benefit, such as hypercholesterolaemia, asthma or rheumatoid arthritis.

Although emerging trends toward outcome-based payment systems, real-time therapy monitoring and patient convenience are driving innovators to develop digital solutions that accelerate drug product market uptake, value propositions may remain vague for patients, healthcare professionals and payers. Tracking medication events and wirelessly transmitting such data to health platforms reflects a necessary, yet insufficient, condition to trigger behavioural change and in turn improve therapy outcomes. It is thus important to shed more light on the value proposition of smart devices for adherence monitoring in clinical trials. In fact, some of the most pronounced challenges investigators and participants are confronted with in large multi-centre trials relate to the absence of advanced adherence monitoring services.

> "Correct dose administration according to the study protocol is at the heart of assessing safety and efficacy endpoints for new investigational drugs."

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"The burden of extensive paperwork for patients ...continues throughout the trial."

CHALLENGES IN CLINICAL RESEARCH PRACTICE TODAY

Investigators face many obstacles that, in sum, reduce the motivation to participate in clinical research. These hurdles start with the recruitment of suitable patients but more significantly relate to the administrative burden of conducting and documenting clinical research. Due to busy patient practices, investigators typically devote little time to actual research. They need to complete large amounts of paperwork, prepare for regular audits and reviews, or are confronted with the ever-increasing complexity of visit schedules and assessments. Efforts are made to understand whether patients' routine administration of the investigational drug is in line with the study protocol.

Current practices advise investigators and study personnel at each site to assess adherence using dosage counts or data patients have captured manually, which are then transferred to the source document after each visit. Phone calls are required to remind patients to take the investigational drug according to the injection schedule or clarify questions. There are also key challenges in tracking whether the correct presentation of the investigational drug was allocated to the assigned treatment arm and recorded in the source document accordingly. For instance, investigators have to detach part of the product label manually and affix it to the patient's unique number in the corresponding source document before dispensing the packaging to the patient.

Similarly, patients value participation in clinical trials based on their perceived individual cost-benefit ratio. Despite today's multi-centre set-up of clinical trials, travelling to the nearest study site may still take up significant time and impose costs. This is particularly relevant if such visits relate to simply monitoring health status, filling in questionnaires or performing dose administration. Furthermore, there is the latent risk of missing doses and hampering the validity of the study. In fact, patients are typically asked to record medication intake manually and inform about dose schedule adjustments or interruptions during the study. As such, the burden of extensive paperwork for patients is not limited to the informed consent process but continues throughout the trial.

Also, there is an overall trend to reduce the injection frequency of novel second-generation biological drugs. Although the added convenience compared with first-generation medications is obvious, investigators are confronted with patients forgetting how to perform the procedure between injections. This may provoke handling errors, trigger additional interactions with trials centres and further diminish overall adherence.

CROs are similarly under pressure to reduce costs and optimise logistics for clinical trial monitoring. These activities target supplies strategy and planning, expiry management or return and destruction of investigational drug supplies. Most importantly, complexities also arise with trial site and patient management, such as patient enrolment and visits, treatment allocation, dosing and dispensing.

Currently there is no mechanism available targeting adherence data quality and integrity or data collection mechanisms. This is all the more surprising in that correct dose administration according to the study protocol is at the heart of assessing safety and efficacy endpoints for new investigational drugs.

SMART DEVICE REQUIREMENTS FOR ADHERENCE MONITORING SERVICES

Smart devices must feature certain sensing capabilities in order to be used as effective advanced adherence monitors. Let me illustrate these core requirements with

Figure 1: SmartPilot for YpsoMate (right) is a reusable smart add-on, transforming the two-step auto-injector YpsoMate into a fully connected combination product. Advanced sensing capabilities to track device usage and guide patients through the injection process are at the heart of effective adherence monitoring. Relevant injection data is then transmitted to a gateway, such as a hub or mobile app (left), to be made available to clinical trial sites.

SmartPilot for YpsoMate, a reusable add-on that transforms the proven and unchanged two-step auto-injector platform into a fully connected smart product system (Figure 1).

At its heart, SmartPilot contains a contactless sensor solution that differentiates between various states of the two-step auto-injector platform. In so doing, SmartPilot not only tracks whether an injection event

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has occurred according to the medication schedule but also whether that injection was successfully completed. Additionally, it can guide patients step-by-step through the injection process. Guidance includes direct visual and audible feedback on the SmartPilot add-on itself or the remote real-time display of the instructions for use on a companion mobile app.

SmartPilot adds another dimension to patient guidance: it identifies investigational drugs, tracks medication allocation to treatment arms, and thereby simplifies clinical trial supply monitoring. SmartPilot enables authentication of the combination product at the point-of-use. As such, it may alert users in case a batch of investigational drug has to be corrected or removed from the clinical trial.

Most importantly, SmartPilot enables

SmartPilot Capabilities	Description	Benefits			
		For CROs	For Investigators / Study Site	For Participants / Patients	Pharma Companies
Tracking injection time/date	Advanced sensor to automatically track and wirelessly transmit date/time of injection events	• Remotely monitor adherence to injection schedule as defined in study protocol • Real-time access to usage patterns "outside visits" • Define measures based on detailed insights (e.g. adherence patterns per site) • Reduced efforts in site and patient management • Overview of patient IDs at risk of exclusion due to non-adherence	• Automated data capturing in source document/case report form • Automated patient reminder/notification systems • Remote adjustments to participants' medication schedule • Automated notification services (e.g. in case a patient risks exclusion from study)	• Convenience through automated entries in injection diary • Reminder and notification services • Ensuring medication schedule is up-to-date • Overview of injection history and schedule of future injections	• Automated adherence tracking to improve overall data quality and integrity • Real-time overview of adherence data "outside" visits • Cost efficiencies due to lower administrative overhead/shorter duration of clinical trials • Prevent patient exclusion due to non-adherence (injection schedule)
Step-by-step patient guidance	Guide patients real-time and step-by-step through the instructions for use, advise on critical use steps, and inform about potential handling errors, if any	• Implement specific measures at study site (e.g. device training campaigns due to unusual usage patterns) • Insights into use patterns per treatment arm/study site	• Notification services in case of repeated use errors (i.e. "call to action") • Automated patient interaction on device usage throughout clinical trials	• Further confidence in effectively using devices • Avoid use errors due to forgetting proper procedure between injection events • Less traveling to study site to administer drug	• Complete picture of adherence, including actual device usage • Real-time insights into usage patterns across sites (i.e. differences in geographies/countries) • Prevent patient exclusion due to non-adherence (device usage)
Identification of drug product	Authentication of investigational drug product based on unique identification number	• Track-and-trace of investigational drug to increase transparency of drug supply • Additional efficiencies in trials monitoring	• Confirm correct allocation of investigational drug to treatment arm • Automated database entries to avoid conflicts between various sources of raw data	• Confirmation that correct YpsoMate is at use (e.g. dose strength versus placebo) • Alert users in case certain batches have to be corrected or removed from clinical trial	• Increase patient safety with track-and-trace solutions • Simplify drug allocation to sites and treatment arms
No modification to injection device	Sensor solution does not require any modification to auto-injector mechanics; same configuration used for clinics and commercials	• SmartPilot platform adherence monitoring infrastructure used across customer-specific YpsoMate variants • Proven auto-injector device used in clinical studies	• Known auto-injector platform subjected to advanced adherence tracking services • Injection could be performed at study site without smart connected SmartPilot add-on	• Same handling concept used for clinical studies as for commercial phase • No mechanical interface visible on YpsoMate to avoid patient confusion/ complaints	• No change to auto-injector required when moving from connected clinical to commercial configuration • SmartPilot platform used as adherence monitoring tools across clinical trial programmes

Table 1: SmartPilot's sensing capabilities translate into value-added services for key stakeholders in clinical trials.

"SmartPilot enables advanced adherence tracking services without requiring any physical modification to YpsoMate."

advanced adherence tracking services without requiring any physical modification to YpsoMate. The same auto-injector configuration can be used flexibly with SmartPilot for clinical trials or without for commercial drug product.

SmartPilot sensing capabilities enable a number of value-adding adherence monitoring services during clinical trials. In doing so, SmartPilot sets the foundation for more patient-centric clinical trial design. Advanced notification and reminding services not only reduce the frequency of patient visits but also help to increase patient interest and enrolment in trials. Furthermore, automated adherence data tracking significantly reduces the administrative burden at clinical trial sites. For instance, certain sites may configure an automated alert if a patient repeatedly injects a partial dose only.

Table 1 summarises SmartPilot's core functionalities as related to the various stakeholders' value propositions.

The ability to monitor the progress of clinical trials in real-time is equally important to CROs and pharmaceutical sponsors. Remote trial monitoring dashboards may include insights into detailed patient adherence patterns. Innovative decision-making tools enable CROs to quickly respond to, and take appropriate measures against, emerging peculiarities in adherence patterns during clinical trials (Figure 2). For instance, CROs may think of device training and education seminars at certain clinical sites should handling errors accumulate over time.

Figure 2: The clinical trial adherence monitoring dashboard sheds light on the two critical dimensions of adherence monitoring throughout clinical trials: injection schedule, as per study protocol, and correct dose administration. The summary report enables real-time monitoring of adherence patterns and, for instance, allows swift action to be taken if handling errors accumulate at certain clinical trial sites.

CONCLUSION

The soaring costs in designing, implementing, and monitoring clinical trials point to a clear need for a fresh approach. New designs are required that minimise administrative tasks at trial sites and reduce the burden of participation on patients. Here, I described how such innovative, patient-centric trial designs can be enabled by advanced adherence tracking services, realised through smart devices. These services facilitate safe and effective self-administration of investigational drugs, enable complete remote patient monitoring and improve the quality and integrity of adherence data (Figure 3).

This article illustrates how the integration of smart devices in clinical research practice offers a unique value proposition and addresses some of the greatest challenges in performing large multi-centre clinical trials. It also disentangles what sensing capabilities a smart device must have in order to unleash its full potential as an effective clinical trial monitoring aid.

ABOUT THE COMPANY

Ypsomed is the leading independent developer and manufacturer of innovative

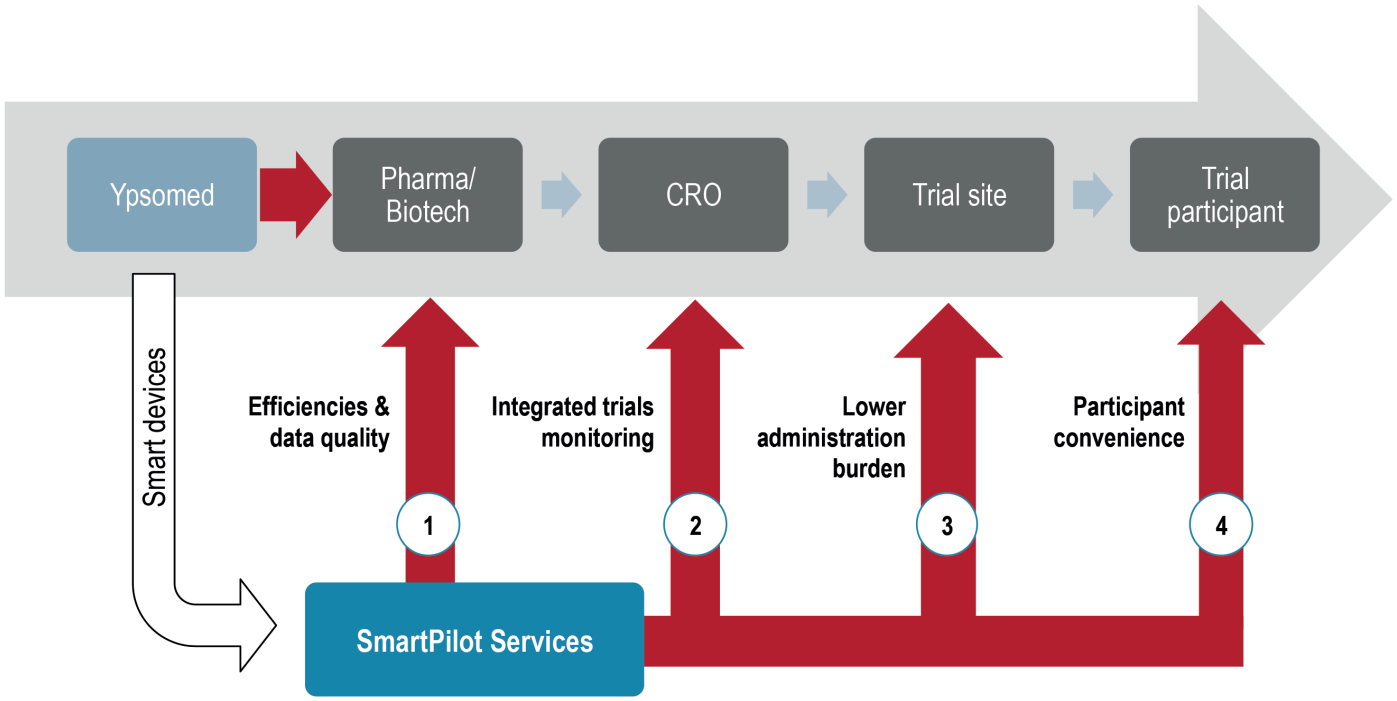

Figure 3: Overview of how SmartPilot clinical trial monitoring services create value for stakeholders. SmartPilot reduces the burden of participation in, and administration of, clinical trials that in turn creates cost efficiencies for pharmaceutical sponsors and improves data quality and integrity.

auto-injector and pen injector systems for self-administration. Their customisable product platforms cover auto-injectors for prefilled syringes in 1 mL and 2.25 mL format, disposable pens for 3 mL and 1.5 mL cartridges, reusable pens, ready-to-use prefilled wearable bolus injectors and injection devices for drugs in dual-chamber cartridges. Unique click-on needles and infusion sets complement their broad self-injection systems product portfolio.

With more than 30 years of experience and pioneering spirit in the development and manufacturing of innovative injection systems Ypsomed is well equipped to tackle digital healthcare challenges and is strategically working on the development of a range of smart devices. Anticipating the future needs of patients, pharmaceutical customers, payers and healthcare professionals Ypsomed moves beyond purely connected entities. Its smart device solutions strive to transform patients' lives by capturing therapy-relevant parameters and processing them to facilitate the self-management of diseases. It leverages unique in-house capabilities in electronics, software and connectivity for the development of new smart products and services.

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.

ABOUT THE AUTHOR

Andreas Schneider is Business Development Manager with Ypsomed Delivery Systems. His responsibilities at Ypsomed include the definition and development of new platform devices with a particular emphasis on connected and smart device systems. As such, he has been actively involved in the design and development of SmartPilot for YpsoMate, a reusable connected add-on that transforms the proven two-step auto-injector into a connected system. Dr Schneider has published various articles and held presentations in the areas of innovation management and drug delivery. He received his PhD in Innovation Management and Organisation Sciences from ETH Zurich, Switzerland.

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