IDENTIV WHITE PAPER

Improving Medication Adherence:

Scaling Cost-Effective Digital Technologies

Incorporating connectivity solutions has the potential to improve compliance and deliver desired clinical outcomes.

Jelson Mateus [1], Louis Somlai [2], Deepak Prakash [1]

1. Identiv, USA 2. Eli Lilly and Company, USA

BACKGROUND

Solving the problem of medication adherence has been a major area of focus for pharmaceutical and healthcare organizations[1]. The costs of poor compliance are staggering and estimated in excess of $250 billion dollars, impacting nearly 125,000 patients in the U.S. annually. The Internet of Medical Things, a sub-segment of the Internet of Things, encompassing connected technologies, data and analytics, has the potential to address the problem of poor medication adherence and improve patient outcomes.

Connected devices, when deployed at scale, can help enhance traditional adherence protocols through automated monitoring, usage reminders and intervention alerts. The rest of this whitepaper presents an example of connected technologies reduced to practice as part of an innovative drug delivery system.

Autoinjectors have been a critical part of the pharmaceutical industry's drug delivery system offerings to facilitate self-administration of injectable medications. It is a fast-growing category of products with an estimated market size of $1.4 Billion in 2024[2]. This family of devices is an essential part of delivering enhanced patient experience and improved clinical outcomes.

Autoinjectors have now integrated connected and digital technologies to further expand their capabilities around data collection and transmission, and can be an important tool in monitoring adherence, including clinical trials[3]. Important parameters such as date and time of injection as well as the status of the injector device (also referred to as an "injection pen") can be seamlessly collected and integrated.

Design For Purpose:
Connected “Smart” Labels

A practical and cost-effective way of providing the aforementioned information is through the use of a connected label that can be applied to the external surface of the injector device. A connected label uses short-range wireless technology, such as RFID, that allows for data exchange as part of an integrated data intelligence system.

The functionality of such labels can be further enhanced through the addition of sensing critical parameters such as temperature. Monitoring the temperature ensures safety of the injectable drug throughout its value chain.

Given the importance of autoinjectors from a patient experience and safety standpoints, can there be a practical and cost-effective way to deliver the promise of connected labels for pharmaceutical companies? Could a single label balance form-factor simplicity, manufacturability and be sufficiently low profile to deliver an unobtrusive patient experience?

Technology Basics:
NFC & Capacitive Sensing

For the connected label that could be applied externally to the existing autoinjector housing with the requisite functionality, Near Field Communication (NFC) technology was the logical choice. The NFC platform, commonly available in smartphones, incorporates a low-cost, battery-free addition for identification, authentication, and can integrate sensing functionality into secondary packaging such as the proposed label.

One of the critical elements that drives the NFC technology is the selection of the chip. The latest generation of these fully programmable controllers with an NFC interface can integrate sensors, for example temperature, in them. Furthermore, the functionality of these chips can be significantly enhanced to include a capacitive sensor interface that can provide reliable status detection of the injector pen.

Capacitive sensing detects changes in capacitance between two conductive surfaces. To reliably detect the status of the injector, the label (Fig. 1) incorporated two capacitive sensing plates covering the length of the spring in the injection pen (FIG 2).

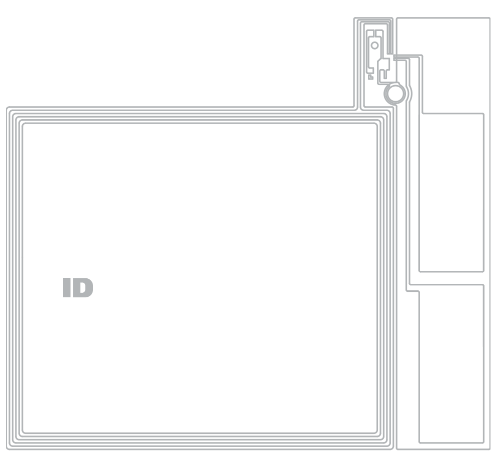

Fig. 1. Capacitive sensing design

Fig. 2. Sensing plates on injector body

The trilobular basecap of the injection device is a registered trademark owned or licensed by Eli Lilly and Company, its subsidiaries or affiliates.

The plates measured the difference in electrical capacitance of the metal spring underneath which changes depending on its state; compressed or pre-fired (medication has not been dispensed) vs. decompressed or post-fired (medication has been dispensed). Additionally, since the autoinjector is moved in and out of cold storage with the label attached, it turned out to be necessary to also monitor the temperature of the label in order to set the correct capacitance threshold for determining whether the spring is expanded or compressed (FIG 3).

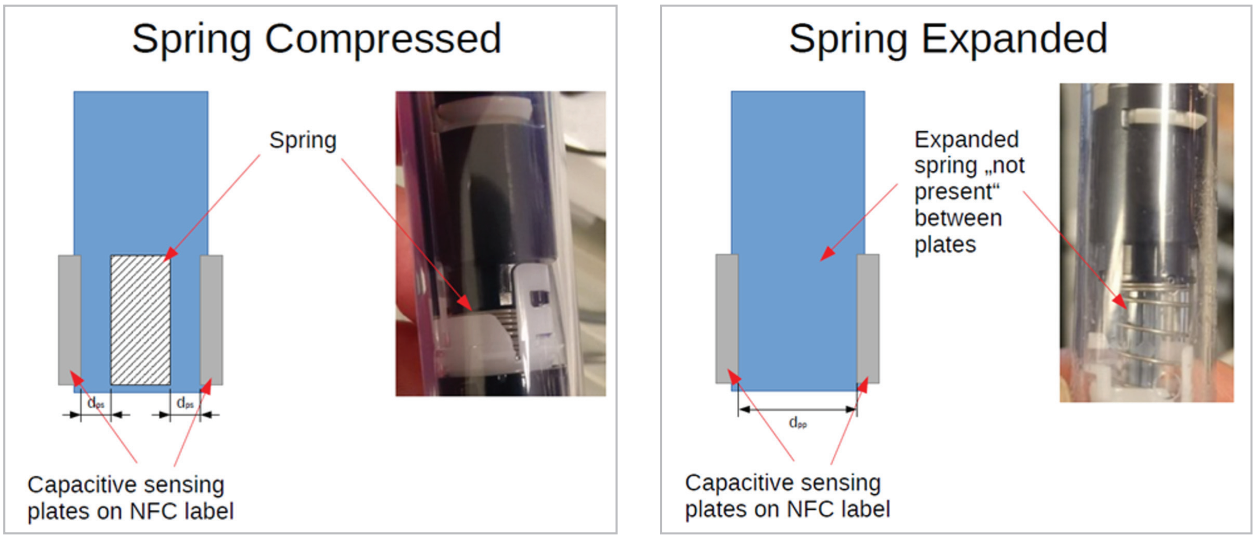

Fig. 3. Capacitive sensing and spring status

Observations

Capacitive Sensing Viability

The initial set of experiments demonstrated that capacitive sensing is a dependable way to discern the status of the autoinjector in both its pre-fired and post-fired conditions. At room temperature (75 to 77 ^{o}F), an average and repeatable differential of approximately 30 fF (femtoFarad, units for capacitance) was observed.

It is worth noting that in order to boost the signal magnitude, addition of copper tape can be helpful to increase the size of the capacitive sensing electrode and have it extend around the circumference of the injector device.

Temperature Dependency

As mentioned previously, the autoinjector device is typically taken in and out of refrigerated conditions. To understand the impact of temperature on capacitance signal, the experiments were repeated at typical refrigeration temperature (approximately 46 ^{o}F).

A wide range of capacitance differential was observed ranging from a low of 30fF to a high of 120 fF. While the results showed that temperature needs to be compensated for, the jump to higher differences (for example, 120 fF) was rather surprising. Upon further analysis, it was found to be an artefact of the chip using an in-built autorange detection algorithm. Our informed opinion is that such jumps can be avoided by disabling such autorange detection algorithms in the firmware in future designs. However, we conclude that temperature compensation in the measurement of capacitive signals is required.

Impact of Electrode Position

In order to understand the impact on the capacitive signal strength, it is first important to understand how it is derived. The signal strength of the capacitive measurement, C_{signal}, is the difference between the total capacitance in the compressed state ($C_{total,comp}$) and the expanded state ($C_{total,exp}$).

$$C_{signal} = C_{total,comp} - C_{total,exp}$$

For maximizing the signal strength of the capacitive measurement, C_{signal}, it is necessary to have a matching overlap of the capacitive sensing electrodes and the compressed spring. However, given the practicalities of manufacturing, variances in placement are to be expected.

In measuring the values in a batch of autoinjectors (N=40), positioning of the electrodes was a trial and error process. One such example (Injector #4) is shown in the chart below (Fig 4), repositioning the electrode allowed for a greater differential in signal strength between the pre-fired and post-fired states.

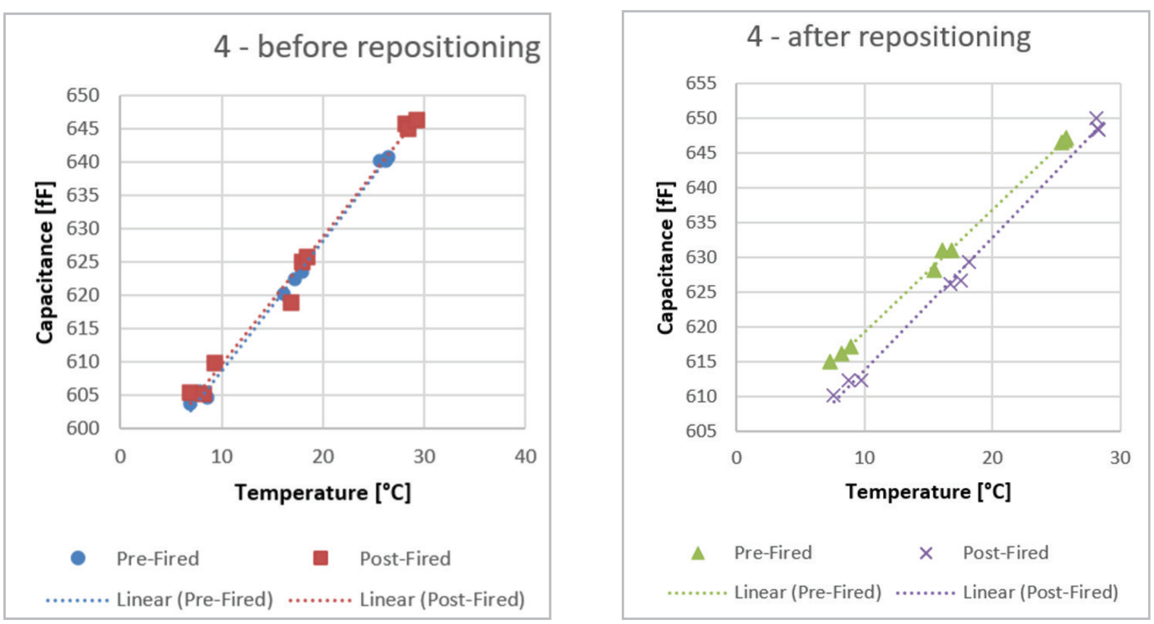

Fig. 4. Temperature profiles and electrode position

From the overall set of values, we can conclude that increasing the height of the electrode can be helpful in improving placement accuracy, and a final validation be performed on the optimal placement based on the manufacturing equipment to account for additional variances.

Impact of Smartphones

As detailed previously, NFC platforms are incorporated in commonly available smartphones. However, the reading of a NFC label is handled very differently between the most widely used operating systems - Apple's iOS and Alphabet's Android.

In iOS devices, the NFC field is generally "off", and smartphone only polls a NFC label at periodic intervals. Whereas in Android devices, the NFC field is generally "on", and the smartphone polls a NFC label at pre-determined intervals. Given this difference, it was essential to understand if a smartphone's NFC field had an impact on the capacitive sensing measurement.

For the purpose of this experiment, iPhone 12 (for iOS) and a Samsung S8 (for Android) were used with each device reading a NFC label 5 times. All measurements were normalized to 32 ^{o}F.

Based on the 5 readings, results showed that there was no meaningful difference in measured capacitance between the two smartphone platforms - Capacitance for Android was an average of 558 +/- 1.8 (fF) while iOS had an average of 556 +/- 0.68 fF.

Conclusions

From the series of experiments, it can be concluded that there is a reliable and effective way to distinguish the status of an autoinjector device thereby enhancing device and patient safety. The use of capacitive sensing electrodes represents a comprehensive and practical way to understand device functionality.

While the final manufacturability was not studied, based on our expertise, a label can be designed with proper materials including a robust carrier (e.g., PET) and adhesive (e.g., high-tack acrylic). Given the curved surface of the autoinjector, it is important to have a non-peeling label to ensure proper functionality.

From a big picture, the use of a connected label -integrating wireless and sensing capabilities- provides a robust and scalable approach to enhance the practical use of appropriate devices in a connected ecosystem. When combined with the power of data and analytics, it provides a promising approach to address continued challenges around medication adherence.

As digital technologies evolve, the adoption of such solutions into healthcare, supported by appropriate regulatory and clinical frameworks, has the potential to improve patient outcomes with continued emphasis on safety and compliance.

This study was sponsored by Eli Lilly and Company as part of a research project.

References

1. https://www.mckinsey.com/industries/life-sciences/our-insights/improving-patient-adherence-through-data-driven-insights
2. https://www.marketsandmarkets.com/ResearchInsight/autoinjector-market.asp
3. https://adheretech.com/the-adherence-crisis-in-clinical-trials/