NORMALISING CONNECTIVITY – COULD UNCONNECTED DEVICES BECOME THE EXCEPTION?

When discussing the future of drug delivery, the rise of connected technology frequently dominates the discourse. Looking at the next generation of technologies in this area, Charlotte Harvey, Consultant Mechanical Engineer, Sagentia, ponders the prospect of connectivity becoming the baseline – at what point will drug delivery devices without connectivity become the exception?

Consider the question: "Why should I add connectivity to my drug delivery device?" As connected technology becomes ever more mainstream across all aspects of modern life, that question is likely to change to "Why should I not?"

Connected devices are a growing trend within the drug delivery space. Not only does connectivity enhance existing devices, advancing technologies give rise to opportunities for new use cases which further the ambition of moving healthcare away from the hospital and into the home. With the increased dominance of connected devices in the consumer sector, users' expectations and behaviours have changed. Emerging technologies promise ubiquitous, reliable and effective connectivity, leading to the conclusion that adding it to drug delivery devices will ultimately become a no-brainer.

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WHY ADD CONNECTIVITY?

Historically, the main drivers for designing a connected drug delivery device have been to:

- Improve patient outcomes
- Reduce healthcare costs
- Improve usability
- Differentiate the product on the market.

The first two of these drivers are addressed by focusing on improving medication adherence, which is therefore becoming

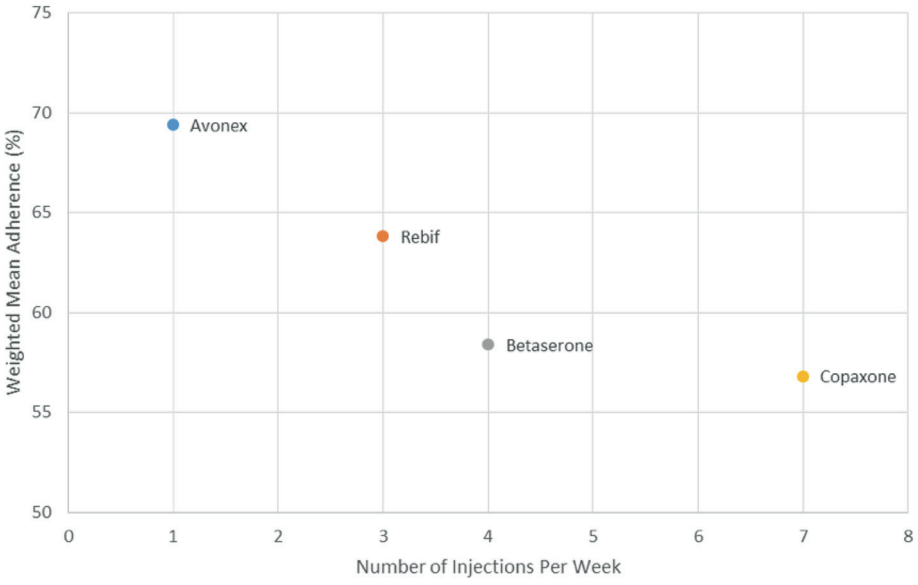

Figure 1: Weighted mean adherence rates plotted against the number of injections per week for four disease modifying drugs for multiple sclerosis.[1] Note that Avonex is an intramuscular injection whereas the rest are subcutaneous.

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an important goal for pharmaceutical companies and healthcare professionals (HCPs). A 2013 literature review[1] (Figure 1) showed how adherence is an issue for some multiple sclerosis (MS) drugs, with weighted mean adherence rates below 70%. Clearly the medical profession wants to see this percentage increase and so improve outcomes for their patients.

Connected devices give HCPs the opportunity to monitor patients more closely in order to make sure that not only are they using their devices, but also that the way they are using them is correct and efficacious. HCPs can then work with patients who are not taking their drugs or who are taking them incorrectly. On a larger scale, this information can be fed back to device manufacturers so they can improve adherence in their redesigns. Any data which can be gathered that explain why the adherence levels are low for certain populations is even better. For instance, the literature review[1] found a correlation between adherence rates and number of injections per week.

From a healthcare perspective, treating patients in hospital increases costs, using up resources such as HCPs and bed space. In parallel, there is also a growing number of patients who would like to see healthcare moving away from the hospital and into the home. For example, a June 2017 industry insight report from Ericsson Consumerlab showed that 39% of chronic patients prefer online consultations to face-to-face meetings.[2] This is because these patients tend to prefer managing their treatment in a familiar environment, without the need to make appointments and travel frequently. Connectivity allows for remote care and reduced physical contact between physicians and patients.

IDENTIFYING BARRIERS TO ADDING CONNECTIVITY

The decision to add connectivity to a device is significant because doing so can be complex. It is not entirely straightforward to add Bluetooth or Wi-Fi features to a device, particularly one which was previously fully mechanical. Additionally, new sensing technologies may need to be added to collect data, for example, injection force, time between drug readiness and injection, and inhalation profile. There are trade-offs between the need for the data and other factors (development time, device size, safety, etc), and so not every reason for a connected device is sufficient to build a compelling business case.

When designing connectivity into drug delivery devices, it is also important to ensure that cybersecurity risks are addressed so that the vulnerability of a device, to hacking or malware, for example, is minimised. Only when it meets a user or business need should connectivity be added to a device. However, in the future the changing technology landscape could make the decision to connect much simpler.

HARNESSING THE AVAILABLE CONSUMER TECHNOLOGIES

There are technologies already being used in the consumer market which can be applied to the medical industry generally, including drug delivery. The most commonly used technologies include Wi-Fi, Bluetooth, cellular and NFC (near-field communication). However, there are limitations to these technologies in their current form which have prevented wider use within drug delivery devices. For instance, wireless technologies require the device to be in range of a particular location or other device, and NFC requires a particularly close range. Bluetooth requires a hub to send data to (and so works best with a companion device). Cellular technologies need a SIM and are pay-to-use. Most technologies require some sort of set-up, either by the user or HCP.

Despite these issues, technologies are widely available in the home which could be harnessed to develop new drug delivery use cases:

- The user interface (UI) for a drug delivery device is central to ensuring that it is being used correctly, so there are always opportunities for improvement and to cater better for those less able to use standard UIs (for instance, those with visual impairments or dexterity issues). Voice recognition provides an opportunity to be more inclusive and is already widely used in the consumer market.

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- User expectations could lead drug delivery devices to become a part of the Internet of Things (IoT) for those managing chronic conditions. Home assistants could be key in enabling this, as they could provide updates on device status (for instance, if a drug needs reconstituting or warming) and potentially pass instructions to the device from the user (when functions are not safety critical). More simply, they could provide patient reminders, particularly useful for elderly patients who need to take enteral medication at a particular time of day.
- Bluetooth beacons can help to remind users to use their device once they are in a particular location, such as their home (more on beacons later). For those with multiple, complicated therapies, such as elderly patients, this could provide a real opportunity to make their therapy more manageable.
- An augmented reality device (like Google Glass) could provide instructions during use to a novice user. This could even be tailored to individual devices and their patients. Augmented reality could also help those who need more training and assistance in using their devices, such as children or those with learning difficulties.

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These scenarios rely on technologies consumers are familiar with (although in the case of augmented reality, still not widespread). These technologies are not available to all users, however, and this has been a major stumbling block to creating devices with connectivity as a major feature. Where the consumer sector can allow users to self-select through access to technology, the medical industry has to ensure coverage for the entire patient population (for most devices). However, should an environment of ubiquitous and reliable connectivity arise, this could be a game-changer.

EVALUATING EMERGING TECHNOLOGIES

The medical device industry is generally slower to take on new technologies than the consumer industry. This is understandable due to the increased regulation and safety considerations. Therefore, emerging technologies often take longer to appear. Such is the case with Bluetooth 5 – the newest version of Bluetooth which (for context) is in only the Samsung S8 smartphone onwards.

Up until recently Bluetooth came in two distinct flavours: Bluetooth and Bluetooth Low Energy (BLE). Bluetooth was used for wireless keyboards and mice, wireless headsets and speakers. BLE uses a lot less power and was designed for areas like healthcare, fitness and beacons. An example is wearables which use BLE rather than Bluetooth. In the summer of 2016 the Bluetooth Special Interest Group (Bluetooth SIG) announced Bluetooth 5, which will likely become the *de facto* version of Bluetooth over the next few years. It has twice the speed and four times the range of Bluetooth 4.2. Bluetooth 5 has the ability to replace BLE in low-power devices as the increased communication throughput means communication time is reduced. This means less compromise in drug delivery devices when it comes to how the connectivity feature is utilised.

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Bluetooth 5 allows devices which are already connected to transmit even more data. Since there is less need to worry about energy consumption or data volumes, it's now possible to collect all the data you may possibly want and broadcast it back to a smartphone or other hub, even if there is no current use for it. For example, if using a patch pump, more than just the delivery time can be logged. An entire profile of the delivery can be recorded, including varying flow rates and any pauses to be sent for analysis. There is usually also a concern about when Bluetooth can broadcast and for how long – with a longer range and faster communication this would no longer be an issue.

Beacons are also being given a boost with the introduction of Bluetooth 5, and they have applications in the drug delivery space as part of the IoT. Beacons are small Bluetooth radio transmitters which are visible to Bluetooth-enabled devices once in range. If the device recognises the beacon's ID it will then trigger a pre-set event, such as in the example given earlier where a reminder is triggered when a user gets home.

As the amount of data which can be transferred with a beacon is larger (with Bluetooth 5) than just the beacon's ID, it can also transmit sensor data such as temperature. This could be used to track the temperature of a drug and keep users informed of time left before their injection can be performed. Beacons could potentially be used alongside a drug right from dispensing, enabling a batch of drugs to be tracked from the filling line to the patient as an anti-counterfeiting measure. Information on the drug, such as dose, could be conveyed to the device itself, which could automatically set the injection profile for that user. The use of beacons also goes beyond the home environment – tracking drugs' movement through a hospital is already happening with barcode readers, but beacons would be a more time-efficient, less manual solution.

When it comes to tracking drugs, particularly when there are concerns about counterfeiting, NFC has been the go-to technology to date. Various drug packages have been supplied with RFID tags which either allow the user to track their therapy or allow devices to authenticate the drug prior to use. Beacons perform this task automatically, in that they require no user interaction once set up. Therefore, the authentication step would become more user-friendly if beacons replaced NFC in these cases.

Unfortunately, Bluetooth is not as versatile as cellular technology because it requires a data hub, such as a smartphone, enabled with the correct Bluetooth version. However, these devices continue to become more prevalent and it will not be long until all smart devices are Bluetooth 5 enabled. Additionally, Bluetooth 5 continues to be the lower energy option, perfect for use in a hand-held device to keep battery use to a minimum.

ASSESSING FUTURE TECHNOLOGIES

The connectivity industry is likely to move from a relatively disparate set of technologies to a landscape mapped by one or two. The key technology to watch is 5G. Its benefits should lead to increased coverage compared to 4G as users may start favouring a cellular connection over Wi-Fi. 5G would then be the focus of most efforts to connect those devices which warrant connectivity. From the perspective of designing a device, cellular technologies are already the preferred option as the only way to create a device that can be used anywhere. Additionally, Wi-Fi requires more reliance on the user (or HCP) to set up the device with the network.

5G is estimated to be introduced between 2020 and 2025. Given that it is still some way into the future, there are loose definitions on what it will look like and the benefits it will provide. However, the mobile operators interest group, GSMA, has outlined a number of objectives,[3] and

there are industry expectations on what 5G has to look like. For example, the speed of 5G is anticipated to be 1 Gbit/s, with some estimates as high as 10–50 Gbit/s compared with the average 4G speed of 15 Mbit/s. It is for this reason that we can expect cellular connections to start replacing Wi-Fi (for context, an HD film could be downloaded in seconds over a 5G network). These features will help enhance the use cases discussed earlier as well as create the opportunity for new ones, for example:

- Where an elderly patient has a complicated treatment regimen to manage, it would be beneficial for a carer to be able to monitor the patient's drug delivery activity live. The lower latency of 5G will make this easier.
- Where patient data is being collected to help understand adherence across a patient population, larger volumes of data could be collected and processed. With faster upload and download speeds, each use of an inhaler (for instance, the inhalation profile) could be analysed away from the device with the user or HCP alerted to potential issues.
- It will be easier to integrate drug delivery devices into the IoT. With smoother operation they will meet the demanding ease-of-use requirements of the consumer market, potentially merging with health monitors.
- Wearable drug delivery devices are often connected to allow better management of what is often a complicated treatment. Using 5G, a system can be designed with the expectation that the user will be able to upload or download data continuously as needed.

The spread of 5G among mobile devices (5G is intended to be usable with existing 4G networks) can be combined with the spread of mobile devices themselves to create an image of a highly connected world. Approximately one third of the world's population is projected to be covered by 5G by 2025, and will therefore be in a position to transfer data continuously given the high speeds and reliable connection. This continuous guaranteed connection will help with the rise of autonomous cars, drone delivery systems and widespread adoption within the healthcare industry. What this means in practice for drug delivery is much more frequent uploading and downloading of data, given that the faster speeds of 5G will permit less energy usage for the same or greater data transmission.

It should be noted that the wider reliance of the healthcare industry on a connected world will have a significant impact on how conditions are diagnosed and treated, even when the devices themselves are not connected. Remote appointments with doctors are likely to become more prevalent. Wearable health monitors have the potential to flag early indicators of illness to users and doctors. Where drug delivery devices are connected, it will become important to fit into this new ecosystem, streamlining treatment and improving outcomes for patients. Demand for drug delivery devices to contribute positively to this trend will increase and device designers will have to determine where this fits into their user and business needs. 5G is the key technology which will enable this ecosystem and the industry to keep up with demand.

CONCLUSION

The advancement of connectivity technologies is not slowing down, and many industries are excited about the possibilities that are opening up. Within drug delivery devices, the ability to transmit data faster and more reliably will make it easier for device designers to meet challenging user and business needs. And the spread of coverage among more users, to more distant regions will make it possible to integrate the connectivity function fully with the use of the device.

Healthcare is transitioning out of hospitals, and user expectations and behaviour are changing as they become accustomed to the IoT. Drug delivery devices will need connectivity in order to keep up with these changes and we expect these connected devices to become the new norm. Of course, the implementation of connectivity will require extensive human factors engineering studies to investigate and validate new use cases. Manufacturers need to plan ahead for the changing technology landscapes, taking account of the new use cases enabled by emerging and future technologies.

ABOUT THE COMPANY

Sagentia is a global science, product and technology development company. Our mission is to help companies maximise the value of their investments in R&D. We partner with clients in the consumer, industrial, medical and oil & gas sectors to help them understand the technology and market landscape, decide their future strategy, solve the complex science and technology challenges and deliver commercially successful products.

Sagentia employs over 150 scientists, engineers and market experts and is a Science Group company. Science Group provides independent advisory and leading-edge product development services focused on science and technology initiatives. It has 16 European and North American offices, two UK-based dedicated R&D innovation centres and more than 400 employees. Other Science Group companies include OTM Consulting, Oakland Innovation, Leatherhead Food Research and TSG Consulting.

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Charlotte Harvey is a consultant mechanical engineer within Sagentia Ltd. Her experience lies predominantly in managing medical product developments, specifically those in the surgical and injectable drug delivery fields. Recent projects have included front-end innovation in the drug delivery space, user interviewing for human factors, and several instances of developing reconstitution-based autoinjectors. Charlotte graduated from the University of Cambridge with a Masters in Mechanical Engineering.