Working in Tandem: Formulation Science and Drug Delivery Device Design

The need to continue to innovate with drug delivery devices has been a focus for medical device companies over the past couple of decades. With self-administration of injectables increasingly prevalent, manufacturers must balance the use of new technologies with the need to make products as simple and user-friendly as possible. At Owen Mumford Pharmaceutical Services we acknowledge the importance of understanding the key trends in formulation science and how this may impact the development of new medical devices for subcutaneous administration. We recently conducted in-depth interviews with experts in pharmaceutical formulation science and device development from the US, UK, Ireland, Germany and India to understand where innovations will be directed in the coming years. This article will examine in more detail how these twin areas must work in tandem to create optimal solutions and deliver drug device combination products that can accommodate a wide range of patient needs.

Usability vs Innovation

Usability factors and advances in drug formulation or technology can sometimes be at odds with one another. While medical device manufacturers may want to take advantage of new technologies and create more sophisticated devices, increased adoption of drugs for self-administration mean drug delivery devices must continue to be user friendly for a wide range of patient demographics. More complex electromechanical devices are being developed to include additional features – such as injection speed and depth settings as well as electronic patient notifications. However, devices with increased complexity may be confusing for some patients to understand and use correctly. Simpler, intuitive devices that minimise user steps are more likely to encourage patient adherence to their treatment and minimise the risk of user error. Streamlined products focusing on key features – such as clear end-of-dose indicators – may be more successful than complex, less intuitive devices. However, connectivity and the range of additional benefits it offers not just patients but other stakeholders is still likely to play a key role in the future of medical device development. Pharmaceutical companies will seek to adopt drug delivery devices which incorporate essential elements of connectivity but ensure they remain intuitive and simple for all patients to use.

Injection Frequency vs Injection Experience

Another element in improving the patient experience and potentially therapy compliance is reducing injection frequency. Recent innovations have seen dosage administration reduced to only once a quarter. Efforts to reduce the number of injections required include the development of long-acting and extended-release formulations. Injection frequency can also be reduced by increasing drug volume and/or in case of biologics, viscosity. However, this can make administration more challenging for patients. Changes in needle length and gauge size can impact the user experience as well as the device hold time, all important variables to be considered. Currently, the FDA guidance is to keep injection times to within 10 seconds – companies will need to find ways to deliver large volumes and higher viscosities without exceeding this duration. For larger volumes, formulation scientists will also need to address drug diffusion challenges and the possibility of reverse 'wet injections'. Alternative delivery devices such as transdermal and wearable products can accommodate much larger volumes without presenting the same concerns, and product development is ongoing in this field.

To accommodate higher volume formulations, drug delivery device manufacturers are adapting their device designs. With the increase in biologics there has already been a move from 1mL to 2mL devices with exploration of 3mL-plus volumes well underway. Devices which accommodate 2.25mL pre-filled syringes therefore have a distinct advantage in this market segment. Additionally, two-phase autoinjectors with independent needle insertion and dose delivery provide a more consistent patient experience during administration, even with volumes up to 2mL. Recent pain tolerance studies have shown that increasing fill volumes does not necessarily create a more uncomfortable experience. Introducing novel excipients which numb the injection site and dilate the injection area could reduce discomfort caused by larger volumes.

Both device and pharmaceutical manufacturers realise the necessity of focusing on patient experience at the earliest stages of combination device development. Designing through a patient-centric lens with a thorough human factors process helps to create devices that accommodate the various challenges that patients may face and to adapt devices accordingly. Through this structured approach, manufacturers can refine comfort, convenience and usability of delivery devices for their intended patient population taking into account age and gender as well as any physical or cognitive impairment. Extended-release formulations and novel delivery systems – such as wearable devices – will continue to interest medical device manufacturers moving forward due to their potential to innovatively solve drug delivery challenges for self-administration. However, they can also present additional challenges which need to be overcome such as compatibility with existing primary containers or the need to create novel ones.

Biologic Stability: A Multifaceted Issue

There are a number of elements that affect biologic stability. Manufacturers must bear in mind how a medication will interact with excipients, primary containers, oxygen and light and high extrusion forces. New excipients, such as artificial sugars, can help with biologic stability. For instance, cyclodextrins can prevent protein aggregation, while also reducing the viscosity of biological formulations, and improving injectability.[1] However, novel excipients are being developed with caution as companies seek to avoid exceeding IID (Inactive Ingredients Database) limits,

which would lead to potentially costly and time-consuming efficacy and safety studies. Innovations in primary containers have focused on creating glass coatings to enhance stability or attempting to reduce the risk of protein aggregation caused by silicon through the use of containers made with novel new plastics which do not require a lubricant.

Stability studies conducted after launch can provide a commercial advantage to manufacturers. Successful studies can extend the shelf life of a product beyond the typical 2–3 year mark. One key strategy to increase stability is through lyophilization (freeze drying) but with self-administration becoming increasingly desirable this can create challenges for device design and, hence trends have moved towards liquid biologic formulations for prefilled syringes and auto-injectors. Although storage below room temperature can help to extend the shelf life, it relies on the patient remembering to keep the drug refrigerated and to remove before use. In the case of biologics, this is especially important as low temperature increases viscosity – making user experience more uncomfortable.

Steps Towards Sustainability

Focus on sustainability has increased significantly over the last few years with a variety of groups lobbying for a greener industry. Efforts are being made to develop new reusable devices such as reusable autoinjectors, as an alternative to disposable designs, to reduce the level of wastage especially associated with frequent administration. In addition, there is focus on increasing the use of alternative materials such as upcycled engineering plastics. However, the practicality of these efforts is still to be proven in terms of real-world sustainability and cost across the life of the product from manufacture to disposal. For this reason, environmental initiatives are mainly focused on the manufacturing process and reducing waste as well as formulations allowing for less frequent injection. Reusable drug delivery devices with connectively features are likely to become increasingly common in the drive to produce less waste, however these present challenges for safe disposable or recycling of their electronic components.

This summary of the current developments in drug formulation and device design highlights how intertwined these two areas are, and how important collaboration will be to develop combination products that are cost effective and continually improve the patient experience regardless of the drug formulation. Critically, any innovations should not significantly reduce user comfort, convenience, or ease of use otherwise they may impact therapy adherence and influence the success of a product.

REFERENCE

1. Cyclolab, Cyclodextrin enabled biologics, https://cyclolab.hu/userfiles/Cyclodextrin%20enabled%20biologics_website.pdf

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Julie Cotterell has over 20 years of sales and marketing experience, including regional, national and global roles. She has a wealth of knowledge on different aspects of drug delivery and the associated devices, and is particularly interested in bringing to market products that can allow patients to be treated as simply and effectively as possible. Before joining Owen Mumford Pharmaceutical Services in 2018, Julie worked for both pharmaceutical and medical device companies, including Baxter, BD and Smith & Nephew.