Economy Spring

THE SECRET TO A SINGLE AUTOINJECTOR DESIGN FOR MULTIPLE MEDICATIONS

The autoinjector market is booming and is predicted to continue doing so for some time to come. In order to capitalise on this, pharma companies are looking to use their autoinjectors for multiple medications. David Philbrick, Business Development Manager, Economy Spring (MW Industries), presents the case for bringing on metal component manufacturers in the initial design phase to make the most out of the crucial expertise they can offer.

This article is based on an MW Industries white paper: "Designing Auto-Injectors for Multiple Drug Viscosities".

The global injectable drug delivery market and, more specifically, the autoinjector market is booming. That growth is predicted to continue throughout the coming decade. According to a June 2016 report by Roots Analysis, the global autoinjector market is predicted to grow at a rate of more than 8% per year for the next 10 years. Mordor Intelligence estimated the global injectable drug delivery market to be US$40 billion (£29 billion) in 2016. The market is expected to experience a $CAGR_{2016\text{-}2021}$ of about 18.1% and so reach around $93 billion by the end of 2021.

These predictions are borne out in the real world as evidenced by increases in production at Economy Spring, a metal spring supplier and a division of MW Industries. Specifically, in 2016, Economy Spring produced 40-60 million springs across all of the drug delivery systems it supplies (including autoinjector devices), whereas the company is now producing 250-300 million springs.

With such a huge market in play, taking into account the range of physical properties exhibited by drugs and biologics being administered via autoinjectors, it is crucial for pharma and biopharma industry original equipment manufacturers (OEMs) to optimise device designs to be as adaptable, and thereby as cost-effective,

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Figure 1: Recent history has seen an inexorable trend towards at-home self-administration of injectable drugs for patients with chronic conditions.

as possible. And that means bringing metal spring component manufacturers on board in the initial design phase.

HOW AN AUTOINJECTOR COMES TO MARKET

A major factor of the global injectable drug delivery market's predicted growth is the widespread increase in the self-administration of drug therapies, propelling the manufacture of autoinjectors like the EpiPen (Mylan, PA, US). The proliferation of this practice is due to the influence of health insurance and managed care companies, which aimed to reduce the number, and expense, of physician office visits by enabling patients to inject themselves with treatments for chronic conditions (Figure 1). While the medical community pushed back, the pharmaceutical and biopharmaceutical industry saw the writing on the wall.

Pharma and biopharma OEMs (e.g. AbbVie, UCB, Eli Lilly) began investing in the research and development of devices that could safely and effectively accommodate the self-injection of drugs and biologics. They enlisted and aligned world-class new product development firms (NPDs) and plastics and moulding contract manufacturing organisations (CMOs) to design and produce new autoinjectors. Soon, that practice became routine.

Typically, a pharma OEM would contract an NPD to create an autoinjector around a new drug or biologic it is bringing to the market. The NPD would then begin research to plan the device design. The OEM would also contract a CMO (e.g. Nemera, West) to mould the plastic components, specify and source the metal components, and send those to the OEM for final assembly, at which point the syringe is installed and the drug loaded. Alternatively, final assembly and drug-loading can take place at the CMO, provided it has the capability to maintain the drug in a stable, climate-controlled environment. However, due to their extreme sensitivity, biologics are nearly always loaded at the OEM. Once the NPD locks down a working design, the CMO typically manages manufacturing while the NPD shifts into a support and consulting role.

CREATING ONE DESIGN FOR MULTIPLE DRUGS AND BIOLOGICS

Proper design of the plastic housing and specification of the material and size of the springs are essential for any single-drug autoinjector, but those tasks become even more vital and complex if an OEM wants to repurpose that same device for multiple drugs and biologics with varying formulation characteristics, particularly viscosity. And that's where experienced metal component manufacturers are invaluable. The springs that control the introduction of the surgical sharp or syringe needle, the delivery rate or dosage of the drug, and the automatic retraction of the needle are the most critical metal components of any autoinjector.

In practice, several big pharma OEMs have successfully launched a new autoinjector for a specific drug. However, the attempt to repurpose that device to accommodate other injectables, particularly biologics, encountered problems largely due to differences in the viscosity of the different medications. Drugs with different viscosities require springs with different physical characteristics – composition, length and thickness – to create spring rates that provide enough power to push higher viscosity drugs and biologics through the syringe to the needle, in order to deliver precisely the correct amount of drug. This includes the specified length of time for the syringe to be fired and the timely retraction of the needle at the end of that time period. Without knowledge of this complex science of metal performance and how it translates into the successful and accurate delivery of injectables with dissimilar viscosities, pharma OEMs (and their NPDs and CMOs) inevitably struggle to repurpose existing autoinjector designs for different drugs.

> "Most autoinjectors contain a main spring and a return spring. With each application, a delicate dance occurs between the two. The rates of both springs work in concert to control the amount of medication delivered and the duration of the administration."

THE CRITICAL ROLE OF METAL SPRINGS

Autoinjectors come in many forms – pen-injectors (e.g. EpiPen), trigger-activated, twist-and-depress and more – but the majority require metal spring components designed to control the needle and achieve precise delivery of the drug.

Most autoinjectors contain a main spring and a return spring (Figure 2). With

Figure 2: Most autoinjectors are driven by a delicate balance between a main spring and a return spring.

"Given the vast number of autoinjectors projected to be produced in the future, the cost-savings that can be realised by using a single injector design with interchangeable springs is indeed remarkable. That given, the importance of having a collaborator that understands the material science of spring design at the initial design phase cannot be understated."

each application, a delicate dance occurs between the two. The rates of both springs work in concert to control the amount of medication delivered and the duration of the administration. When engaged, a main spring must provide the necessary force to depress the syringe plunger within a specified time frame and surmount the device assembly friction to properly deploy the needle into the skin. A return spring must be able to counterbalance the remaining force of the main spring to safely retract the needle at an exact time. Both must be designed so they don't damage the plastic parts that comprise the rest of the device. If the metal springs are not meticulously fabricated to accommodate the viscosity of the specific drug or biologic involved, as well as to work smoothly within the confines of the device's plastic components, then the medication simply cannot be self-administered accurately and safely.

When you understand the interplay between the metal springs in an autoinjector and the correlation of their characteristics to the viscosity of the drug or biologic being delivered, it becomes obvious that there's no such thing as a one-size-fits-all autoinjection device. But that doesn't mean that a pharma OEM with a variety of drugs eligible for self-administration needs to design a completely unique device for each medication.

In the circumstance of designing an autoinjector that will ultimately be used for multiple medications, the plastic housing and components of a device can be designed to accommodate springs with rates that vary by as much as 30-40%. Simply put, an autoinjector can be designed so that the metal spring components are interchangeable. In such cases, OEMs need to be thinking from the get-go about these possibilities and need to get a qualified metal component manufacturer involved in the device design process as early as possible. Doing so can save millions of dollars in R&D and production costs.

INTERCHANGEABLE DESIGN

According to the US National Center for Biotechnology Information (NCBI), "Recent studies confirm that the incidence of anaphylaxis ... is increasing worldwide." The first line of defence for an anaphylactic reaction is the administration of epinephrine, often via an EpiPen. That rising need – combined with the growing trend to treat other common chronic conditions such as diabetes, rheumatoid arthritis and multiple sclerosis via injectable self-administration – translates to an escalating demand for autoinjection devices.

Given the vast number of autoinjectors projected to be produced in the future, the cost-savings that can be realised by using a single injector design with interchangeable springs is indeed remarkable. That given, the importance of having a collaborator that understands the material science of spring design at the initial design phase cannot be understated. That knowledge allows for:

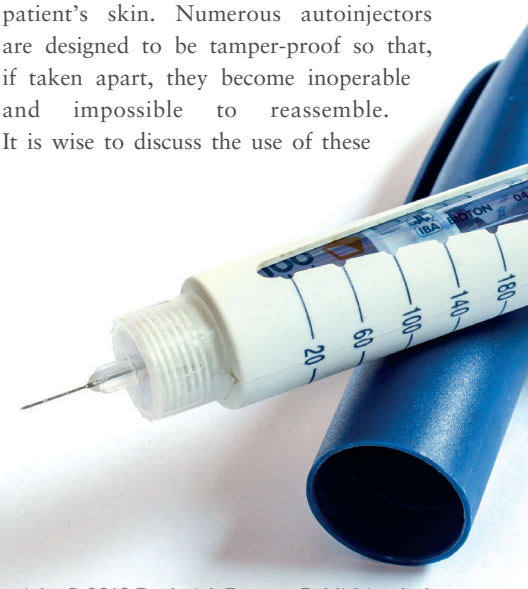
- Producing precision springs and other metal components that perform consistently from device to device without failure
- Specifying springs with metal characteristics that allow for the precise and accurate delivery of a drug or biologic of a given viscosity
- Understanding how springs with varying rates impact plastic housing and component design.

All of that (and so much more) requires years of specialised experience, investment and research, in an area of expertise not traditionally held by NPDs or plastics and moulding CMOs. Only an experienced, highly-qualified metal component manufacturer can offer that knowledge. It is incumbent upon pharma and biopharma OEMs to directly engage such firms at the onset of device design. As OEMs come to understand the importance of springs and other precision metal components in autoinjector design, the advantages of direct access to those fabricator-suppliers at the earliest stages of product development become clear.

Using an example from Economy Spring, the company was brought on board early to work with a high-profile pharma OEM, its NPD and moulding CMO on a device design project, now entering its final phase. With the metal spring manufacturer's help, the NPD conceived an autoinjector to use with two completely different drugs under the OEMs purview. Economy Spring fabricated and is now supplying two different main springs with distinct rates to the CMO to assemble into the same plastic device housing. The springs look exactly the same, so Economy Spring came up with a brilliantly straightforward solution to prevent mix-up during assembly: it delivers the springs to the CMO in different coloured trays. The CMO's automation system can then detect if the correct spring is being used simply by monitoring the tray colour on the line. This example clearly illustrates the importance of including the spring manufacturer in the initial design, resulting in substantial savings in time and money.

NOT ONLY SPRINGS

Autoinjectors often have other metal components, such as anti-fire mechanisms that prevent the device from accidentally triggering if dropped or prematurely activating during self-administration and harming the patient (Figure 3). Many autoinjectors must be cocked or twisted to release these safety components so the trigger is free to release. Others have a built-in tip that acts as a trigger so the device won't fire until a certain level of force is achieved by pushing it against the patient's skin. Numerous autoinjectors are designed to be tamper-proof so that, if taken apart, they become inoperable and impossible to reassemble. It is wise to discuss the use of these



types of components at the beginning of the design cycle so that the device can successfully accommodate all safety and performance requirements necessary.

CONCLUSION

The inclusion of the metal spring component manufacturer, along with the NPD and CMO, in the initial design phase of injectable drug delivery systems, particularly autoinjectors, represents a huge potential saving in time and money for pharmaceutical and biopharmaceutical industry OEMs. It's a methodology that is being repeated more often today and will continue to spread in step with the market boom.

ABOUT THE COMPANY

Economy Spring, a division of MW Industries, is a manufacturer of advanced medical device components, including highly-engineered, precision metal components and assemblies such as springs, surgical sharps, needles, laser machined tubing, staples, titanium clips and complex assemblies. The company deploys its end-to-end product lifecycle know-how and design expertise to shorten product development time and lower costs. Economy Spring's >40-years' track record helps deliver product reliability and performance in demanding surgical and drug delivery applications. The company is registered with the US FDA and has ISO9001 certified and ISO13485 compliant quality processes.

ABOUT THE AUTHOR

Dave Philbrick is Business Development Manager & Lead Product Engineer for Economy Spring, an MW Industries Company. For more than 38 years he has been involved in supporting new product development for medical instrumentation & drug delivery systems for Medical / Pharma OEM's. He is a specialist in metal component development, design and integration.

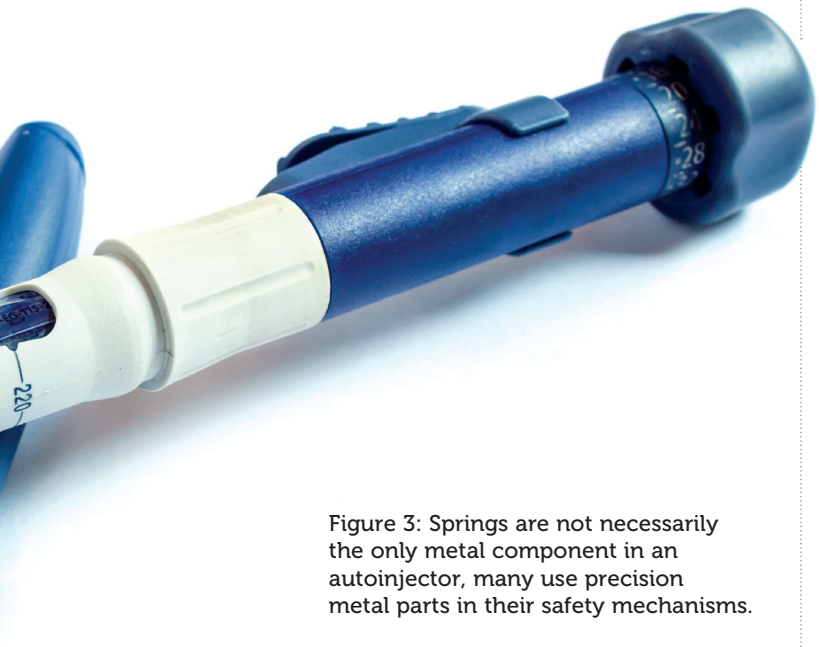


Figure 3: Springs are not necessarily the only metal component in an autoinjector, many use precision metal parts in their safety mechanisms.

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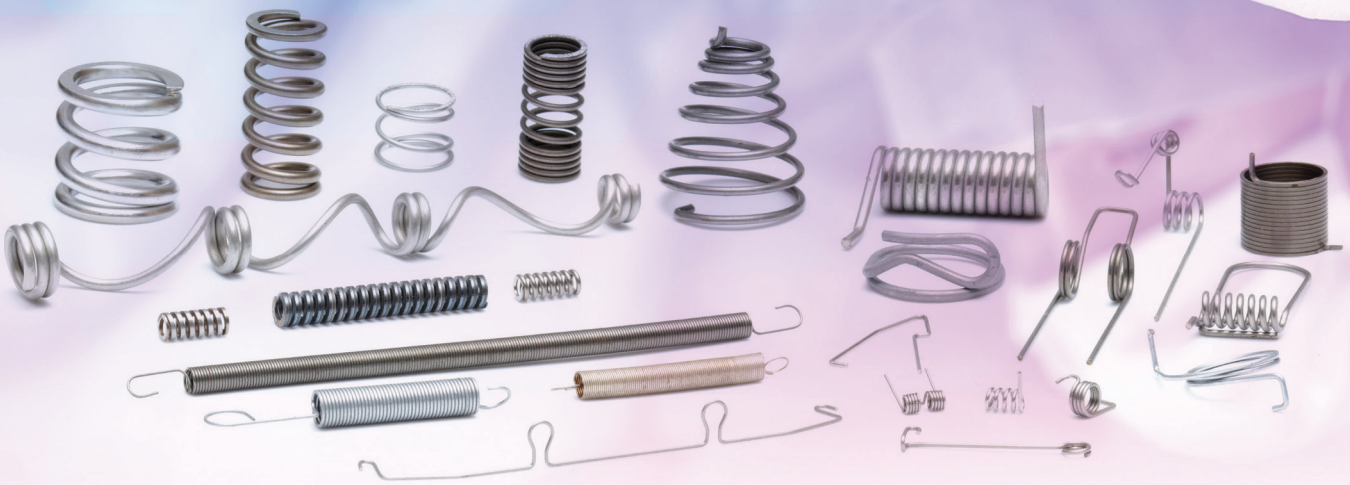

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