SAFE, CONVENIENT AND EFFICIENT: INDIVIDUALISING PREFILLED SYRINGES

In this article, Ursula Hahn, Team Leader, Product Management, Sanner, discusses the value of individualised prefilled syringes and explains how small changes in design or components can make a huge difference for doctors, patients and pharmaceutical manufacturers alike.

The market for prefilled syringes is growing steadily. Although forecasts vary significantly depending on the issuers of market reports and the respective interpretations, they share one common conclusion: the prefilled syringes market is projected to expand at a rapid pace over the coming five to 10 years.[1,2] A key driving factor is the ongoing boom in the development of biopharmaceuticals, as well as rising life expectancy and an increasing move towards self-medication for the treatment of chronic diseases.

In this context, prefilled syringes allow patients and physicians both a more accurate dosage and a more convenient way of handling drugs. Prefilled syringes are also used in ophthalmology, orthopaedics and cosmetic medicine, for example in therapies based on botulinum neurotoxin (e.g. Allergan's Botox®) or hyaluronic acid. In these sectors, a rapidly growing trend towards individualisation can be observed. This trend is not just about designing prefilled syringes to make them attractive and the brand recognisable; easy handling and safe usage are just as important.

The increasing demand for individualised solutions leads to pharmaceutical manufacturers employing different procuring strategies. Many companies no longer purchase prefilled syringes as system solutions, but instead combine the glass or plastic syringe with individually adapted components to increase both customer and patient orientation. With small changes such as individually adapted piston rods or backstops, manufacturers manage to differentiate themselves from the competition both visually and in terms of user comfort.

CONVENIENCE AND SAFETY FOR DOCTORS AND PATIENTS

For Botox or hyaluronic acid therapies, convenient handling and dosage safety are both very important, both during administration by a doctor and during a patient's self-medication. Particularly in highly sensitive therapeutic areas, such as ophthalmology, ensuring the maximum possible precision and accuracy are essential when it comes to injected treatments. In strabismus and blepharospasm (dystonia of the eyelid), injections with Botox are good alternatives to eye surgery. During this treatment, the doctor injects the neurotoxin into the target muscle close to the eye. However, neurotoxins might migrate from the target muscle to other eyeball-engaging muscles or into the eyelid muscle, resulting in undesirable side effects, such as transient double images. Individualised syringes facilitate a more convenient injection procedure for the physician by sustaining a flexible range of motion and at the same time a clear view of the puncture site.

The same need for accuracy and precision applies to the treatment with Botox or hyaluronic acid in cosmetic medicine. It is easy to come by pictures of people after inaccurate (self-) treatment of Botox. Such is a nightmare scenario – but also a very plausible one. As a highly viscous substance, hyaluronic acid is particularly challenging to administer, especially because its viscosity changes with acting mechanical

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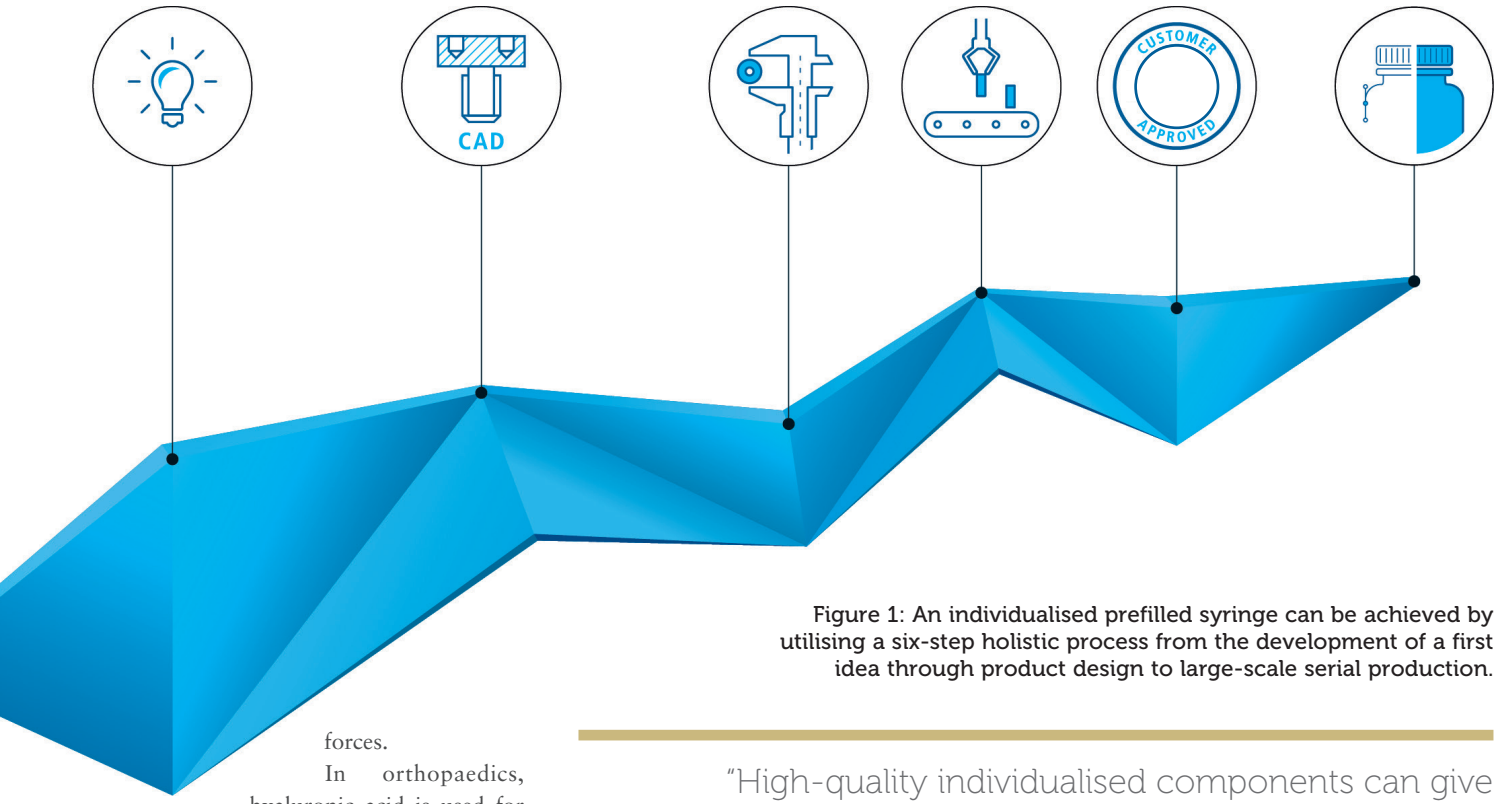

Figure 1: An individualised prefilled syringe can be achieved by utilising a six-step holistic process from the development of a first idea through product design to large-scale serial production.

forces.

In orthopaedics, hyaluronic acid is used for treatments in rheumatology or arthritis, as it is the main component of synovial fluid and acts as a lubricant in all joint movements. Most often, orthopaedic injections are performed by physicians. To avoid injuries during treatment despite the high viscosity of the substance, they require devices that are designed to be both as simple and as safe as possible, allowing for easy administration.

INDIVIDUALISATION WITH VISUAL AND TECHNICAL BENEFITS

The possibilities to individualise prefilled syringes are manifold. Most importantly, individualisation not only benefits the end users, but also the pharmaceutical manufacturers. As far as safety and handling aspects are concerned, the design of individualised syringe components focuses on ergonomics. However, how a device looks also plays an important role for both parties involved: while end users, especially in the cosmetic field, prefer to undergo their expensive treatment by means of a high-quality and visually appealing device, pharmaceutical companies want to make their products distinctive and thereby gain a competitive advantage.

High-quality individualised components can give prefilled syringes a distinctive appearance – from applying the brand name or logo to the use of different colours or the indication of dosage strengths. International and country-specific traceability, safety and information requirements can be met with simple, but effective, means. To simplify complicated logistics in delivering the same product with different dosing strengths to different markets, the syringes can be distinguished in terms of colour, shape and labelling.

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From the technical point of view, a sophisticated design of syringe components, such as the thread, can ensure fast processing on filling lines and simplify the packaging procedure. Thousands of prefilled syringes can be filled and assembled on high-speed lines – provided the single components, such as backstops and rods, are perfectly compatible. An exact design and compatibility with common filling systems is crucial for high process efficiency which, in turn, is decisive for pharmaceutical manufacturers, especially in view of the high time and cost pressure in the pharmaceutical market.

AN INDIVIDUALISED PREFILLED SYRINGE IN SIX STEPS

Component manufacturers with long-term experience in different markets and with varying regulations are uncommon when it comes to prefilled syringes. However, individualised solutions require a high level of packaging and processing expertise, combined with industry knowledge and design know-how. In addition, a component manufacturing partner should not only have a specific process installed that enables detailed product specification, conception and development of individual solutions, but one that does so under competitive conditions.

How can all these requirements be reconciled? Which characteristics must a prefilled syringe solution fulfil to be both convenient and efficient, without sacrificing patient or physician safety? The answer lies in a holistic development process that encompasses several phases: from the development of a first idea through product design to large-scale serial production (Figure 1).

Step One – Concept Phase

At the beginning of the multi-stage development process, different approaches are developed based on customer demands, whilst already considering the criteria for subsequent serial production. This phase

should also include a first, rough cost estimate, as well as a detailed examination of the regulatory requirements and the patent situation. Moreover, first sketches of the proposed solutions are created, giving pharmaceutical companies the option to choose between several possibilities, all of which fulfil the given requirements (Figures 2 and 3).

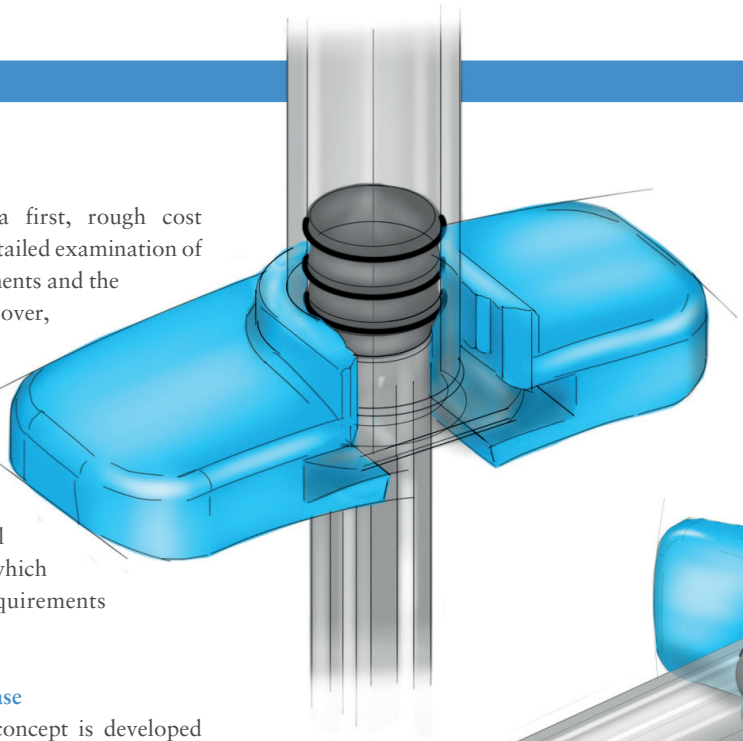

Figure 2: Different approaches are developed based on customer demands, whilst already considering the criteria for subsequent serial production.

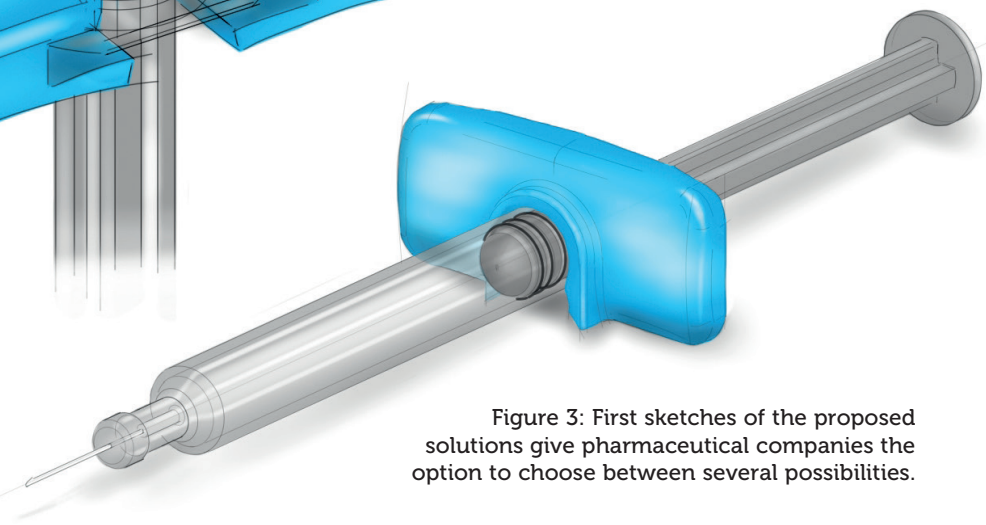

Figure 3: First sketches of the proposed solutions give pharmaceutical companies the option to choose between several possibilities.

Step Two – Design Phase

The selected product concept is developed in further detail during the design phase, while the manufacture of close-to-production product samples is prepared. A physical 3D model as well as detailed elaboration of the data help demonstrate the basic functionalities of the concept (Figure 4). In parallel, the materials are selected in line with regulatory requirements and long-term availability.

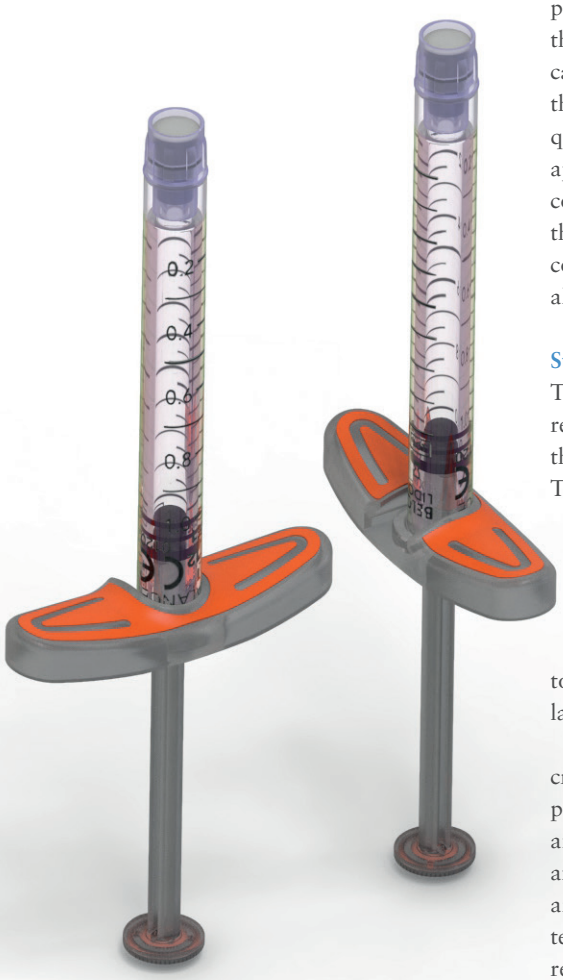

Figure 4: In the design phase, a physical 3D model demonstrates the basic functionalities of the concept.

Tool engineering for near-serial product samples is particularly important during this phase. By means of mould-flow simulation, the engineers analyse the filling of the cavities and the temperature conditions in the planned tool to achieve an optimum quality. This way, the number of subsequent approval loops can be reduced, leading to considerable time and cost savings. During this phase, the basis of the production concept for later serial production should also be established.

Step Three – Prototype Phase

The third phase of the process contains the realisation of the necessary equipment for the manufacture of near-serial prototypes. This equipment forms the basis of the fabrication tools later required for large-scale production. In this phase, final changes to equipment and design can still be carried out without major costs and time loss. The actual production tool will only be manufactured during a later phase, once series maturity is reached.

The prototype phase is also the most critical and complex phase of the entire process as all requirements must be finalised and tested. Good project management and close co-operation with the customer are crucial during finalisation. Quality tests can only be performed if all quality requirements and deadlines are adhered to. This results in a tested and approved product design for successful transfer into serial production.

Step Four – Industrialisation Phase

The industrialisation phase mainly consists of the production, installation and qualification of serial production equipment, as well as the definition of parameters for a smooth and efficient production process, under cleanroom conditions if required. The manufacturing tool is subjected to a comprehensive qualification process in accordance with cGMP guidelines.

Step Five – Implementation Phase

Next, it is necessary to validate the production processes and finalise all necessary documents for approval and registration. According to a testing plan especially developed by quality management, all relevant functionality parameters are inspected. If the final inspection is successful, constant product quality, and consequently a timely market entry of the pharmaceutical product, is ensured.

Step Six – Roll-Out and Monitoring Phase

To ensure the quality of product and processes during, and especially after, market launch, continuous control of serial production is indispensable. An individual in-process control inspection plan defines test criteria and intervals. In addition to the attributive and variable tests, it is also necessary to test the functionality of the syringes and components and to monitor and safeguard the functions of all production equipment continuously through preventive maintenance.

CREATING TAILOR-MADE SYRINGE COMPONENTS

Throughout the entire product life cycle, a multi-phase process can provide for the highest quality, especially in large order volumes. Integrating all test results, as well as the operating data, into a manufacturing execution system ensures continuous traceability. Thanks to this kind of close-knit quality control and professional process and production management, complaint rates can be kept under 0.5 complaints per ten million delivered parts, while "On Time In Full" (OTIF) levels are high, with a rate of over 98% of all deliveries arriving complete and on time.

The close involvement of the drug manufacturer in the entire development process is extremely important to achieve satisfying and efficient results. High transparency and open communication in all project phases keeps everyone informed about the project's current status at any time. Thanks to professional project management and profound expertise, this multi-stage development processes is able to create successful tailor-made prefilled syringe components with the required focus on ergonomic handling and patient safety, as well cost-effectiveness.

ABOUT THE COMPANY

Based in Bensheim, Germany, the Sanner Group was founded in 1894 and is now in its fourth generation as a family-owned enterprise. Sanner develops and produces high-quality plastic packaging and drug delivery systems for pharmaceutical, medical and healthcare customers. The group gained international recognition for its desiccant know-how and moisture protection solutions. With more than 500 employees, Sanner is present all over the world, including in Germany, China, India and the US. The company produces over two billion plastic units each year for standard and customised packaging and drug delivery solutions.

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ABOUT THE AUTHOR

Ursula Hahn started her career in quality management after graduating in Material Science and Surface Engineering from the University of Applied Sciences (Aalen, Germany) in 1992. She joined Sanner in 1995 and has since held a variety of positions in quality management, engineering/packaging development, innovation management and product management, gaining a wealth of expertise in packaging development. Ms Hahn has been Sanner's Team Leader, Product Management, since 2017 and, amongst other tasks, is responsible for patent management.