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HEKUMA

HIGH-END PREFILLABLE SYRINGES FOR INNOVATIVE BIOPHARMACEUTICALS

In this article, HEKUMA, the German specialist for high-performance automation equipment, describes how, in developing a system for Becton Dickinson (BD) to manufacture a high-end prefillable syringe for innovative biopharmaceuticals, it exceeded BD's requirements. HEKUMA provides detailed insights into how specific process challenges arose and were met, and describes a resulting manufacturing line that excels in precision, technical reliability and cleanliness of the manufacturing environment to produce a syringe featuring highest product performance attributes.

As a worldwide leading manufacturer of medical devices, BD is the partner of choice for major biopharmaceutical companies looking for delivery solutions for injectable drugs. BD has a history of leadership in design and innovation, addressing key industry trends and customer needs with novel product and process solutions. Currently, BD is introducing a novel prefillable COP (cyclo-olefin polymer) syringe for biopharmaceuticals. The syringe has a staked needle design (with pre-attached needle) featuring ultra-low silicone, ultra-low tungsten and ultra-low particle values. In order to realise this design input, the challenge was to combine the moulding of the syringe barrel with the insertion of the needle into a single processing step.

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HEKUMA developed a dedicated manufacturing line with breakthrough technologies to individualise the needle cannulas, feed them to the insertion moulding stem where the syringe barrel is moulded around the needle. The syringe barrels then undergo multiple visual inspection steps and finally the needle shield is assembled. All manufacturing steps are fully integrated and conducted in a hermetically closed environment to minimise the risk of any contamination. This manufacturing process has been designed and systematically optimised for the precision, cleanliness and performance of the prefillable syringe aiming for highest patient safety and comfort and best therapeutic outcomes.

EXTENSIVE KNOWLEDGE IN SEPARATION SOLUTIONS

By teaming up with HEKUMA, BD has a strong partner company that has the capabilities to integrate the complex production requirements of these new prefillable syringes into a working equipment concept and to implement it into a practical solution. The company, located in Eching, near Munich, Germany, was the perfect match for building equipment of this kind, because of its ability to bundle a whole array of competencies, which were a sure guarantee of the equipment's quality and the parts that it produces.

HEKUMA not only has the extensive knowledge required for separation solutions for "difficult" or very small components, but also employs a highly developed gripper and robot technology for insertion and

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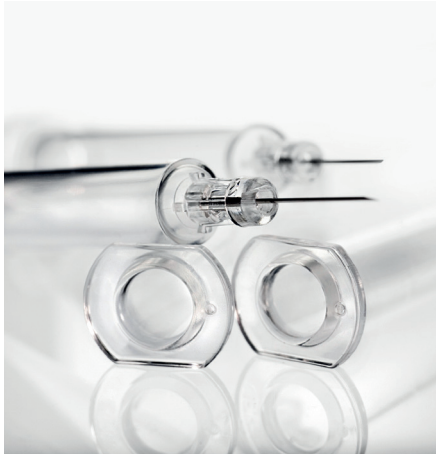

Figure 1: After the plastic body is cooled and cured, the result is the completed syringe barrel and needle.

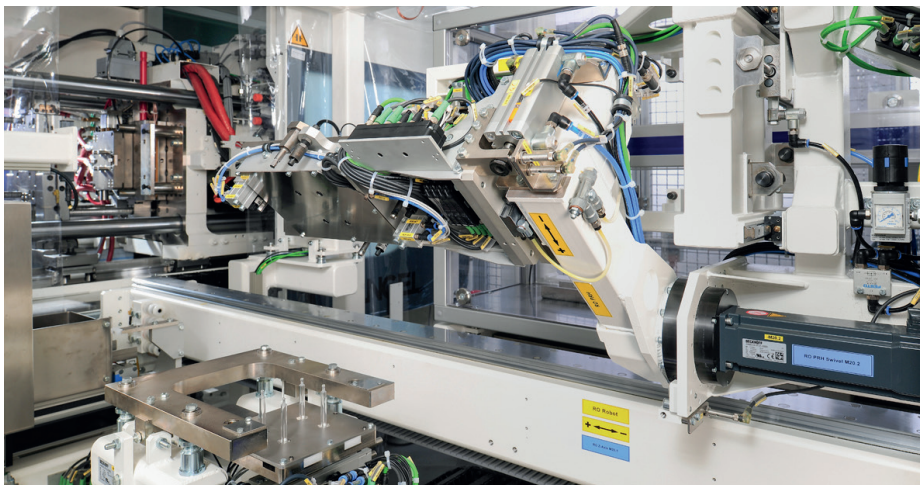

Figure 2: The take-out module includes a 4+4 insert, a take-out robot, and a shuttle system.

take-out processes that are both fast and highly precise. Moreover, HEKUMA boasts extensive experience in setting up highly sensitive quality inspections, especially in optical camera inspections.

Another important advantage is that HEKUMA already had the relevant industry-specific experience in the field of medical technology, for example when it comes to developing equipment used to manufacture disposable items such as cuvettes, Petri dishes and pipette tips. HEKUMA had already proven itself as a highly reliable partner in projects relating to developing and realising Petri dish systems for BD, amongst others. "So, we were able to rely on an existing and working platform for the collaboration," said Klaus Wanner, Director Sales and Marketing at HEKUMA, "The most important communication lines and interfaces between the two companies had already been developed."

EQUIPMENT QUALITY EQUATES TO PRODUCT PERFORMANCE

Over the last two decades an increasing number of innovative therapies have been based on biopharmaceuticals, many of which are administered via injection. Ready-to-use syringes, prefilled with the drug, have become the gold standard.

"On one hand, such prefillable syringes must perfectly protect the highly sensitive and very costly injectable biologics for up to three years. On the other hand, they must flawlessly function as a delivery device, posing high expectations regarding their precision, cleanliness and performance," commented BD Worldwide Strategic Marketing Leader Christian Herget.

High product performance requires high equipment quality: the demands that equipment operators require of the manufacturer are just as high. The quality of the equipment components must be above average, the scrap ratio during manufacturing must be extremely low. The entire system must satisfy cleanroom criteria, i.e. pursuant to GMP it must be easy to be thoroughly cleaned. Last but not least, the syringes must be produced with maximum precision in the shortest possible cycle times.

From the start, the first touchstone in realising the process sequence proved to be one of the greatest challenges: the requirement to over-mould the needles calls for an individualisation of them before a gripper takes them, each between the sizes of 27 to 29 gauges (OD of 0.360 to 0.286 mm), and insert them into the injection mould. The process was structured so it would be fast.

However, the real challenge proved to be the "momentum" of the needles, which were fed into the system in magazines in quantities of close to 100,000 units at a time. This momentum (movement or rather direction of movement in mass) had to be accounted for during the sequence of the entire separation process, and the process sequence had to be structured so that no matter what, the needles remained untouched. This was not solved until after a series of test scenarios and then in such a way that no difficult technical adjustments were needed.

STRICT PREREQUISITES FOR MEDICAL DEVICES

"As far as the actual insertion process into the injection mould is concerned, we were of course able to benefit from our wide range of processing experience from the automotive industry", says Wanner. The visible result can be easily broken down into what is most important: the needles are inserted into the movable side of the injection mould; from the solid side the liquid plastic is injected into the cavity, which completely wraps around the needle. After the plastic body is cooled and cured, the result is the already completed product (Figure 1).

After they are taken out from the mould (Figure 2), the syringe barrels are placed on a transfer shuttle and then they run through various camera inspection stations. Based on the strict specifications for medical devices, here is where the 100% quality inspection takes place, a camera inspection broken down into five single inspections. The first inspection step checks the precision of the flange; the second step is dedicated

Figure 3: Siliconisation of the needle; special attention is given to ensure that the silicone only comes into contact with the needle only, the syringe body.

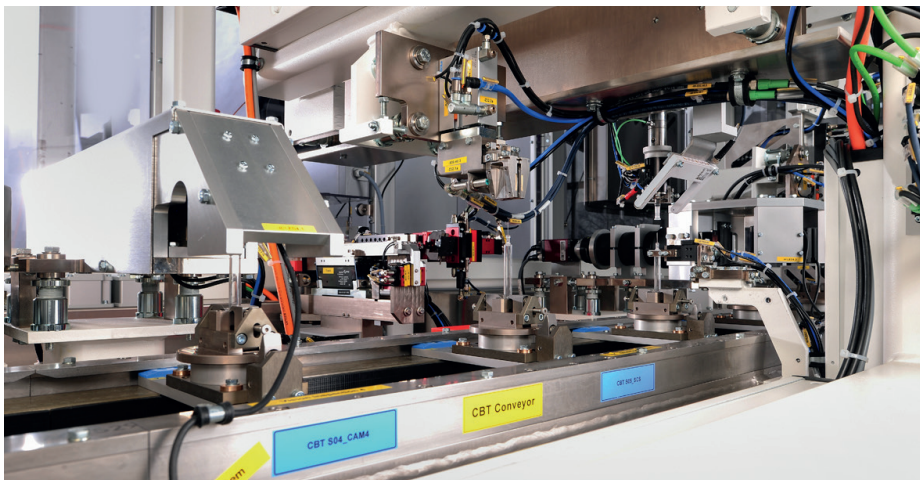

Figure 4: Visual inspection of the short neck, after needle siliconisation and the assembly of the protective cap.

Figure 5: The finished product complete with needle-caps.

to the barrel of the syringe, followed by the inspection of the tip of the syringe. The visual inspection of the main cylinder and the needle are especially thorough. Here, the entire range of the body is inspected for cosmetic defects like spots, scratches or trapped air bubbles.

At the end of the inspection process, the needle and the needlepoint are tested for possible deformations and occlusions using light rays. Once the needle has been successfully tested and proven to be intact, it is siliconised (Figure 3). Special attention is given here to ensure that the silicone only comes into contact with the needle, but not with the syringe body. The silicone ensures that the needle can be inserted into the skin smoothly, and thus without causing pain.

USING PROTECTIVE CAPS

After the siliconisation has been completed successfully, another processing step takes place. Following the various visual inspection steps, protective needle shields are mounted on each syringe, which had been fed to the system from a bowl feeder. The protective caps run through a separating and positioning process, before they are assembled onto the syringes (by way of a light clicking mechanism). Subsequently, a camera inspects to ensure that the needle shields are positioned correctly on the needle (Figure 4). Standing upright, flange showing upward, the syringes (Figure 5) are loaded into a nest in groups of 100 or 160 pieces. The nests on their part are placed into tubs and are transported from there to the packaging unit. The very compact manufacturing line, measuring approximately 4m long and 3m wide (see Figure 6), is being installed in a cleanroom in one of the seven worldwide BD manufacturing facilities for prefillable syringes.

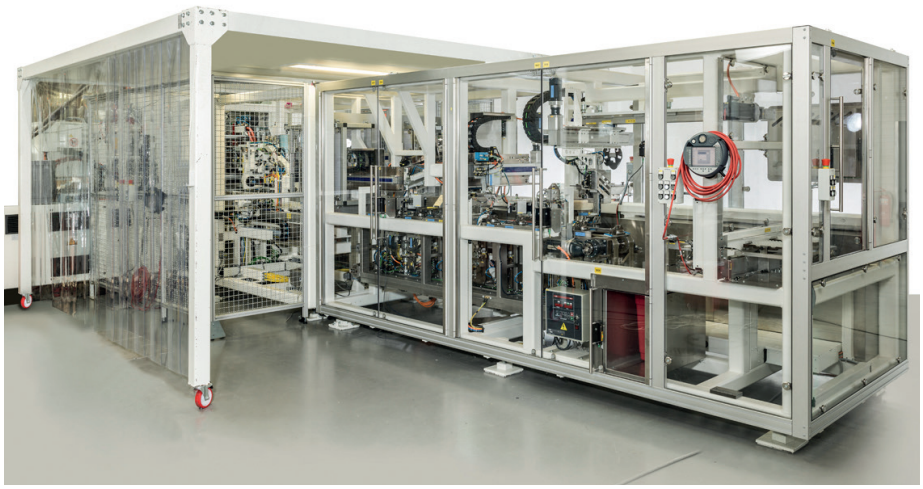

Figure 6: Overview of the whole manufacturing line.

REQUIRED CYCLE TIMES ACHIEVED

The duration of the overall process is in accordance with BD specifications, having cycle times of less than half a minute. Jakob Kammerloher, Technical Director at HEKUMA, commented: “Cycle times, precision, cleanliness standards and tight technical reliability. The requirements profile, which was placed upon us, was extraordinarily ambitious. At the end, we create a very rugged overall system were all these factors are taken into account and all requirements are fully met or even overachieved. Thanks to the intensive, extremely result-oriented collaboration, a system that is able to combine high quality with high volume arose. This way, we support our customer to manufacture a really well marketable product.”

ABOUT HEKUMA

HEKUMA (Eching, Germany) is part of the elexis Group. The company creates a sustainable competitive advantage with its innovative ideas and exciting technology in high-performance automation for customers in the plastics industry. With its dedication and ambition, HEKUMA has established itself as a competent systems manufacturer and proudly look back on more than 40 years of experience. It offers complex grippers for high-performance insert and take-out systems for injection moulding processes with upstream and downstream automation. In addition, the company considers its capability to develop turnkey solutions and production concepts, such as Sigma inside, to be one of its core competencies. HEKUMA focuses on the medical and automotive technology markets as well as the consumer goods industry.