

Small test efforts for large production plants

Sanofi uses filling and closing machines from Syntegon Technology to determine ideal manufacturing parameters for development and life cycle management products.

The cards are constantly reshuffled in pharmaceutical development. Especially the production of clinical samples and the technology transfer to existing commercial equipment require manufacturers to adapt processes continuously to meet the needs of new preparations. Sanofi, for example, relies on the MRD 1010 filling and closing machine from Syntegon Technology to define suitable manufacturing processes for synthetic and biologic drugs, such as peptides, oligonucleotides, or antibodies. The company tests filling and closing parameters of cartridges and vials on a small scale, before they are transferred to larger equipment for clinical samples and commercial products.

The French pharmaceutical company Sanofi arose out of the merger of Sanofi-Synthelabo and Aventis in 2004. Today, over 100,000 employees in more than 100 countries contribute to medical progress; about 8,000 of them in Germany. At the site in Frankfurt-Höchst, they develop different active ingredients in indications such as immunology, inflammation, and rare diseases and are constantly facing new challenges. Clinical samples for antibodies and other synthetic and biologic modalities are administered in different ways, for example with the help of injection devices such as pens. Primary packaging materials vary depending on the drug. The same accounts for the requirements on filling and closing processes, which must constantly be redefined by pharmaceutical manufacturers like Sanofi. Ideally, this is done as flexibly and cost-effectively as possible, and without interrupting commercial production.

Securing medicine supply

“Process adjustments for different preparations require long test phases, which are difficult to realize on commercial equipment in terms of time and logistics,” explains Dr. Daniel Wagner, Head of the Drug Product development department for peptides, oligonucleotides and large synthetic molecules at Sanofi. „Our large commercial filling lines are operating continuously in shift models with minimized stop times. Stopping commercial production for test purposes would interrupt the supply of vital drugs to patients. Moreover, process adaptations would change the complex GMP configurations and would lead to further costs, for instance for revalidation efforts.“ Hence, Sanofi was looking for an additional solution to test parameters for robust development processes, while the commercial lines could continue to run without interruption.

The pharmaceutical company turned to Syntegon for support. The two companies look back on a long-standing partnership. “We already use several filling and closing machines for cartridges and vials in



commercial and clinical sample production from Syntegon,” Wagner explains. “So the idea of purchasing another filling and closing machine for R&D test purposes seemed obvious.”

Tests on a small scale

Sanofi and Syntegon Technology developed a special filling line, which is used to carry out small-scale test series on a pilot plant, before transferring the defined parameters for each preparation to commercial equipment. Sanofi selected the standard MRD 1010 filling and closing machine. The platform was then specially adapted by the experts from Syntegon Technology to meet Sanofi’s requirements for the planned applications. The focus was on flexibility: the entire line is suited for small-batch filling of up to 50 liters and covers different cartridge and vial sizes.

Its three filling systems are another special feature of the MRD line. In addition to the time-pressure filling system, the versatile platform is equipped with a peristaltic pump and a rotary valve piston pump. They make it possible to fill and close up to 30 different types of vials and cartridges – a crucial prerequisite for Sanofi’s wide range of development and commercial products. Thanks to an intermittent rotary star wheel which features an inclined infeed chute, the system also saves space, is easy to clean and simple to operate.

Successful test operations

Sanofi started test operations for small batches in autumn 2017. „The small machine has proven to be the right choice. We can flexibly test process parameters during filling, stoppering and capping of cartridges and vials,“ says Dr. Mandy Mohnicke, who was involved in planning and commissioning of the plant. Amongst others, Sanofi tests the influence of filling speed, filling pressure and contact pressure on product quality during capping, as well as the influence of the piston stopper position in cartridges regarding its functionality in injection devices. Only if all the critical parameters are correct, the scale-up to commercial equipment can begin. „The flexible MRD helps us to thoroughly check relevant process parameters so that we can later manufacture our products with robust processes,“ says Mandy Mohnicke.

Patient safety has top priority

The correct speed and exact position are particularly important when inserting the stoppers: they must neither be placed too high nor too low inside the cartridge to enable patients to dose their medications correctly. Otherwise, the pressure in the container might be too high or too low. This would lead to an undesired leakage of drug product when the needle is positioned, or to an insufficient dosage. In the interest of patient safety, Sanofi also pays great attention to optimum capping parameters such as height and contact pressure. These parameters are crucial for leakproof and sterile injection products.

A specially integrated data logger helps to record the parameters. It bundles the data of different pressure and temperature sensors of the MRD 1010 filling line. Operators have full transparency of the line and can improve processes in a more targeted manner. „The customer-specific data collection and the fact that the equipment is suited for a great number of different containers ensures a high degree of flexibility. Personal discussions with colleagues from other pharmaceutical companies reveal that not every pharmaceutical manufacturer is able to work with such a special pilot line in the development area,“ Dr. Daniel Wagner explains.

Valuable advice

Sanofi was not only satisfied with the advice and support provided during the acquisition and installation phase of the MRD 1010 pilot line, Syntegon Technology also offered the operators competent on-site introductions regarding functions and controls of the line. „The cooperation between Syntegon Technology and Sanofi was exemplary, from ordering to start-up and subsequent service support. We can definitely imagine continuing our cooperation in future projects,“ Wagner says. The pilot plant in Sanofi’s R&D department is paving the way for the drug products of tomorrow.

Get in touch with us!



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