Gerresheimer has a long track record of helping clients navigate the hurdles that stand in the way of transforming a drug delivery system concept into a mass-produced product ready for market. Less well known is the fact that, behind the scenes, one of the secrets of its success is the way it navigates using its own Gate-Model to guide its innovation process.

The Gate-Model is a five-step process covering the crucial stages of product development – from the concept phase through design and development and pre-production development to mass production development and, eventually, mass production. The aim is to develop new and better products that have a higher chance of succeeding in the competitive marketplace.

“...that have a higher chance of succeeding in the competitive marketplace.”

As a full service provider of drug delivery systems, Gerresheimer operates as a one-stop shop for its clients. It has experience across a variety of delivery routes – including inhalers, pen injectors, autoinjectors and prefilled syringes – and works with clients to develop and manufacture both primary and secondary packaging for diverse drug products. Here, Michael Wiglenda, Global Senior Director of the Technical Competence Center & Moldmaking in Germany, explains Gerresheimer’s industrialisation offering and the five-step Gate-Model that guides its innovation process.

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Figure 1: The small batch production facility has a room with a vacuum for filling toxic materials and, depending on the requirement, it may be done in a protective atmosphere.
requirements, the industrial design is drafted, with Gerresheimer taking care of patent management too. Operational concepts are developed as part of the usability engineering, with critical sub-functions considered and models created. In addition, Gerresheimer analyses design concepts as part of usability studies – and performs concept evaluations as well as feasibility studies. The result of the concept phase is a preferred concept, along with a thorough risk analysis and considered market requirements.

Next comes the design and development phase when product requirements are defined, the design is broken down and a client’s product is developed in accordance with the relevant regulations. The process required to manufacture the product is developed – and analysed for potential patenting – and simulations and tests are conducted. Functional samples are also created at this stage.

The Gerresheimer service package also includes preselection of suppliers, selection of materials and design of the packaging. The result of this second stage of the Gate-Model is a completely developed product with defined production processes and a design freeze.

The third phase of the process covers pre-production development, which includes design verification and preparation for product verification. Moulds are developed for small batch production, along with specialised machines, and measuring equipment is developed in Gerresheimer’s quality laboratory. If necessary, development samples, clinical samples or stability batches are manufactured in a small batch production facility (Figure 1) complete with a clean room (Figure 2) – which can also accommodate low-volume commercial production. The result of this phase is a verified product.

Phase four of the Gate-Model is mass production development – involving industrialisation, validation of production means and preparations for introduction of the product. Mould-making and automation engineering experts design, develop and build the high-cavity injection moulds used for mass production (Figure 3), along with any complex robots and systems required. Gerresheimer also qualifies the production equipment, validates the processes and qualifies suppliers – and prepares the product master file. The result of this stage is mass production means and a product validated for mass production.

The fifth and final phase of the process is mass production, when the product is introduced and lifecycle management begins. The result of this phase is ongoing production of the standard parts and/or standard products.

FULL SERVICE PROVIDER

The Gate-Model illustrates how Gerresheimer is a full service provider of drug delivery systems, operating as a one-stop shop for its clients. It has experience across a variety of delivery routes – including inhalers, pen-injectors, autoinjectors and prefilled syringes – administering active substances via pulmonary inhalation, through the skin or via mucous membranes. It works with clients to develop and manufacture both primary and secondary packaging for diverse drug products – ensuring they are convenient, patient-friendly and delivered to where they are needed quickly and efficiently.

Clients starting a project with Gerresheimer will find a plethora of flexible options available, whether they are looking to develop an existing project or begin from an initial idea. However, Gerresheimer is also a partner for industrialisation of completed drug delivery device projects – working with finalised designs and taking them through to mass production. Projects and products looking to be
The integrated approach from Gerresheimer has a number of advantages for clients, including reduced development time and risks – meaning products get to market faster.

“Uncompromising quality assurance has the highest priority across the entire production process.”
production and modification, examining potential changes with test moulds. Furthermore, the department works with replaceable mould inserts for short maintenance and repair times without the need for additional adaptations. Data consistency from the design to all machines and workbenches, as well as the direct link to quality assurance (QA), ensures that moulds are of the highest quality.

Quality Assurance
Uncompromising QA has the highest priority across the entire production process. Precision moulds are ultimately the prerequisite for excellent product quality. As such, only the latest measuring equipment and techniques – for example, computer numerical control (CNC) image processing – are used in the internal measurement lab.

Modern Mould Technologies
More than 65 specially trained employees produce:

- Low- and high-cavity injection moulds, up to 128 cavities, with precision in the micrometre range
- Single- and multi-component moulds
- Indexing plate moulds
- Hot-runner injection moulds
- Moulds for insert moulding – needle and lancet encapsulation
- Stack moulds.

Award-Winning Mould-Making Department
The quality of Gerresheimer’s mould-making department was recognised by its top placement in the renowned Excellence in Production competition, organised by the Laboratory for Machine Tools (RWTH Aachen University, Germany) and the Fraunhofer Institute for Production Technology (Aachen, Germany). The TCC of Gerresheimer Regensburg GmbH was named Mould Maker of the Year 2014.

PILOT PLANT
The TCC pilot plant is the practice-oriented competence centre for all injection moulding processes. Here, Gerresheimer proves moulds to check performance and measures, optimises and qualifies moulds. Moulds are sampled using special machinery under near-series conditions and subjected to comprehensive application and processing tests to get them ready for large-scale production.

The sampling and mould optimisation process in the entire component verification. An important stage during this process is the set-up of stable parameter settings for injection moulding, based on a fractional factorial design of experiments (DoE). Additionally, it is at this point that the optical and dimensional component measurements take place in the certified measuring lab, which are then documented in a comprehensive sample test report. Machine and process-capability documentation and mould trials over set time lengths (e.g. four or 24 hours) complete the pilot plant phase.

ANALYSIS AND TESTING

Quality Laboratory
When it comes to drug delivery systems, safety is of the utmost priority. The pilot plant therefore carries out extensive testing in the areas of materials, geometry and function. Gerresheimer has a measuring lab for the geometric measurement of components, assembly units and finished products, a lab for material analyses and a lab for functional testing with product-specific testing equipment.

Optical & Tactile Measurement Technology and Industrial Computer Tomography
By using a measurement lab with the most modern measuring equipment, Gerresheimer ensures that complex mould inserts and filigreed injection moulding parts or assembly units can be measured to extreme levels of precision. The complete set of component measurements is documented in an initial sample test report. The measurement equipment includes:

- Various multi-sensor co-ordinate measuring machines for optical and tactile component measurements
- Universal co-ordinate reading microscopes
- An industrial computer tomograph for the destruction-free measuring and testing of individual drug delivery components or entire assemblies.

Material-Specific, Physical and Chemical Analyses
The material analysis lab is responsible for the inspection and approval of incoming goods and raw materials worldwide. The standard spectroscopic and thermal analyses are:

- Fourier-transform infrared spectroscopy (FTIR)
- Melt mass-flow rate (MFR)/melt volume-flow rate (MVR)
- Differential scanning calorimetry (DSC)
- Thermogravimetric analysis (TGA).

In addition to these, Gerresheimer’s extensively equipped lab also offers the possibility of a physical-chemical analysis of viscosity, residual moisture and density, as well as an infrared spectrometer and a thin section microscope. In-house expertise enabling development and execution of customer-specific methods rounds off Gerresheimer’s analysis portfolio.

Product-Specific Functional Testing
In the functional testing lab, Gerresheimer develops and qualifies test methods to guarantee compliance with product-specific requirements. It ensures enhanced safety for patients via comprehensive testing of physical product characteristics, product-specific performance tests and statistical data analysis during the product development cycle.

Individual Qualification Packages
The pharmaceutical and medical product industry requires proof of process capability and the reproducible production of an injection mould. QA is therefore given critical importance in both national and international laws and guidelines, signifying a requirement for increased effort and expense with respect to the qualification and validation of moulds in the development and industrialisation phases. As a result of these regulations however, there is less wear on moulds and a higher quality of parts overall, resulting in less waste. But mould qualifications are time and cost intensive. This is why Gerresheimer offers its customers various
mould qualification levels depending on the product, its area of application and the regulatory requirement level.

AUTOMATION ENGINEERING

Together with the development and construction of special-purpose machines associated with moulds, Gerresheimer Medical Systems offers its customers high-performance automation solutions. In the pharma and healthcare industries, automation co-ordinated precisely with the product, project and processes has a decisive influence on the quality and economic efficiency of production. The technicians, mechanics, electricians, designers, qualification experts and programmers from the automation engineering department are responsible for this task at the TCCs.

The automation engineering department provides automation competency; develops automation solutions; and specifies, designs, builds,procures and qualifies the following:

- Customer- and part-specific assembly lines
- Testing robots (pressure, flow rate, optical features, force deflection systems)
- Rotary table systems
- Linear systems
- Robots to insert and remove parts
- Packaging systems
- Pre-production equipment
- Pharmaceutical assembly systems
- New generations of glass forming lines (Figure 4).

All the production systems produced by Gerresheimer meet good automated manufacturing practice (GAMP) requirements, as well as US FDA 21 CFR Part 11, and are designed for production in clean rooms in accordance with ISO 14644-1 Class 7/8 or GMP Grade C/D. Being an international manufacturer, Gerresheimer also monitors and assists the start-up of its production equipment on the client’s site.

The assembly steps and inspection of the modules are done by intelligent camera and inspection systems. As an example, a respiratory patient must be able to easily determine how many doses remain in their inhaler – to avoid the risk of accidentally running out of medication. To facilitate this, Gerresheimer designed an assembly system where the dose-counter function is checked both with a camera inspection system (camera control of the tab position) and a position sensor in the display element after a simulated number of doses, all of which was fully automated.

Automation is an integral component of Gerresheimer’s product and process development, and leverages its expertise and know-how throughout the concept and design phase. This means Gerresheimer doesn’t wait until mass production to develop automation solutions – it develops them in the prototype and pre-production phase, saving a lot of time.

SMALL BATCH PRODUCTION

Prior to series production, pharmaceutical and medical technology products run through an exhaustive approval process, for which small numbers of units need to be produced repeatedly. For example, small batches may be required as clinical samples, development samples or stability batches.

With its TCCs, Gerresheimer offers clients its own production systems for this task, which are capable of quick and uncomplicated production of development samples, clinical samples or small series at any point in the project.

These facilities include the Class 8 clean room and some of the injection moulding machines have integrated laminar flow covers to create a Class 7 clean-room environment in the injection-moulding area. Project-specific assembly units and specific measuring technologies complete the equipment.

Expansion into Glass

Gerresheimer has expanded its Wackersdorf TCC. The company has invested tens of millions of Euros in creating 3,000 m² of additional space for the development and industrialisation of glass products, such as syringes and cartridges. The task area of the TCC has thus been expanded to include working with glass. Construction began in 2018.

One focus of the expansion is the establishment of small batch production for prefilled glass syringes and cartridges. Once the project is complete, it will be possible to produce pre-series modules from glass forming to ready-to-ship, washed and siliconised ready-to-fill systems. The focus is on syringes and cartridges for sophisticated, biotechnologically manufactured medication, clinical samples for approval or prototypes for process and technology development.

At the same time, glass competence is also being established in the automation systems area (special machine engineering) to develop innovative technologies for glass
forming and automation. In the future, new generations of glass forming lines for syringe production will originate in a co-operation between Gerresheimer’s Bünde and Wackersdorf locations, with small batch production and automation systems in Wackersdorf and large batch production in Bünde. This expansion is set to greatly improve Gerresheimer’s capacity to develop, optimise and produce innovative glass-based drug delivery systems.

CONCLUSION

Using the equipment and latest technologies in its TCCs, Gerresheimer handles:

- Concept development
- Concept studies
- Ratings and cost analysis
- Industrial design
- Product development
- Process and manufacturing equipment design
- Mould making
- Production (clinical sample, small batch, large batch)
- Automation engineering
- Product Assembly (manual, semi-automated, automated)
- Product finishing
- Pharmaceutical assembly and filling
- Sterilisation
- Packaging
- International distribution.

Gerresheimer is able to join at any phase of drug delivery system development – from initial concept through to final design – and optimise the product for mass production with specialist knowledge and high-quality processes and facilities.

ABOUT THE COMPANY

Gerresheimer is a leading worldwide partner to the pharmaceutical and healthcare industries. Gerresheimer Medical Systems produces customised injection-moulded plastic assembly units, as well as primary packaging made from glass and plastics, worldwide. Gerresheimer works with global players in the pharmaceutical and medical technology industry, producing drug delivery systems across the spectrum. As a full service provider for drug delivery systems, Gerresheimer handles all the phases of the value-creation chain, beginning from the first idea development through to mass production.

ABOUT THE AUTHOR

Michael Wiglenda holds a Dipl-Ing FH in Mechanical Engineering and has more than 20 years of management experience in the plastics processing industry. Mr Wiglenda heads the Technical Competence Centers of Gerresheimer Medical Systems in Germany, China and the US as a Global Senior Director. He was responsible for the creation of the international competence centres as well as for the extension of the German competence centre with pharmaceutical small batch production capabilities. Additionally, Mr Wiglenda is Senior Director of Internal Tool Making.
Deliver your active substance safely on target!

Gerresheimer Medical Systems offer assistance with customized drug delivery systems

With Gerresheimer Medical Systems as your partner, you profit from more than forty years of experience in the development, industrialization and contract manufacturing of customized drug delivery systems. Each year, we produce over 100 million inhalers which meet the full requirements of modern pharmaceutical packaging. As a system supplier, Gerresheimer develops patient-friendly products that are easy to use, provide precise dosing, and efficiently transport the active substance to its target site. Prior to production, we apply demanding quality standards to material selection, assembly technique and device functionality.

Contract Development  Industrialization  Contract Manufacturing

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