Challenge

Development and series production of optically sophisticated, cost-effective and reproducible single-use components made of quartz glass

Application

Production of application-specific optical glass components for spectroscopic measurements

Scope

UV spectroscopy
Analytical process applications
Complex shapes in quartz glass

Procedure

Bioprocess Engineering
Process Analytical Technology (PAT)
Quartz Cold Casting

Innovative glass casting process enables customer-specific precision parts made of quartz glass for applications in optical analytics

Joint development of two market leaders of a flow cell for process control in the manufacture of biopharmaceuticals

Situation

Increasingly specific applications in optical analysis require more flexible manufacturing methods

The use of spectroscopic analysis methods for monitoring critical process steps is becoming increasingly important in new areas of application in the manufacturing industry when particularly precise, reliable and reproducible measurement results are required. The requirements for the measurement components regarding measurement and process connection are often so special that established standard solutions cannot be applied. In highly regulated areas of application such as pharmaceuticals, the required standards for optical measuring components in terms of quality, GMP guidelines and reproducibility can therefore often not be achieved with conventional manufacturing processes.

This is also the case in the production of biopharmaceutical active ingredients. Sartorius, a leading international partner to the biopharmaceutical and research industries, has developed a single-use inline sensor interface for UV spectroscopic concentration measurement of biomolecules during the purification process in chromatography systems. As a central measuring component for this interface, an optical single-use flow cell made of quartz glass was required.

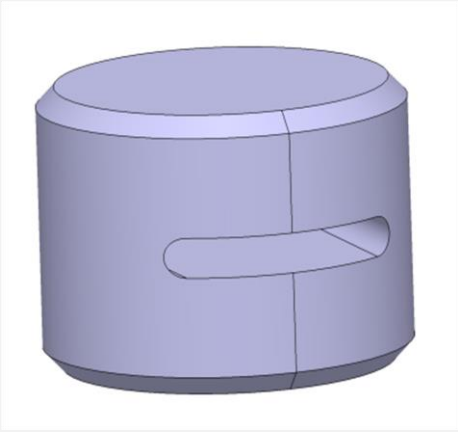
Introduction of UV spectroscopy into biopharma downstream processes

Complex biopharmaceuticals are the drugs of the future. In single-use bioreactors with a capacity of up to 2000 liters, specialized cells produce therapeutic agents that have great application potential, such as monoclonal antibodies or modern vaccines. During purification, these complex biomolecules are separated from starting materials and by-products, e.g. other proteins and DNA. To ensure the purity and thus the safety and efficacy of the drug, the purification steps are monitored using inline flow-through sensors. This provides the user with a constant insight into the operating steps without having to interrupt them for manual sampling. After all, automated processes offer greater process reliability, faster process decisions and more profitable production. To meet the current trend of the market, switching from reusable sensor systems in steel pipes to disposable consumer goods, appropriate sensor technology should be developed as disposable components.

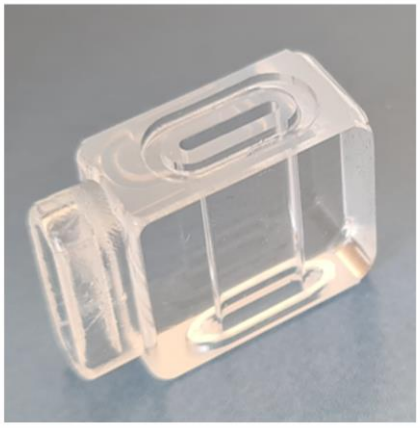
Based on the feasibility of the newly established process at Hellma and taking into account the requirements arising from the process environment, relevant regulations and the required quality, an optical flow cell adapted to the new Sartorius product was then jointly developed and manufactured in the following months as core components for the Sartorius sensor interface.

Challenge

Sartorius strives to offer its customers the best solution on the market. Previously available single-use UV sensors did not meet the requirements expected by Sartorius, especially in terms of dead volume, price-performance ratio and ecological footprint. The key challenge for the successful introduction of UV sensor technology was therefore to develop a cost-effective glass component with challenging dimensions for a single-use sensor interface. Thus, Sartorius was looking for a development partner in the field of precision optics for a joint development in a flexible and competent manner.



first 3-D Model



first prototype

final flow cell

The innovative manufacturing process QCC from Hellma opens up new possibilities

At the ACHEMA process industry trade fair, the Sartorius PAT team first became aware of the quartz cold casting manufacturing process developed by Hellma. After subsequent discussions and further agreements on a joint development project, a feasibility study was agreed, and the first prototypes molded.

Collaborative project management and a partnership on an equal footing were also important.

A special challenge was the high geometric and optical requirements for the central single-use glass component. A consistent, reproducible gap width of 1 mm in a tolerance range of <0.05 mm is of central importance. At the same time, the sides of the glass body must always be parallel and of high optical quality.

The high demands on the quality of the very small flow cell made of quartz glass must be continuously monitored, for example by a 100% control of the gap width, applying the high-quality standards for the biopharmaceutical industry. It became apparent early on that it needed a new production process to meet these challenges.

During the project, the requirements changed

The aim of the joint project was to produce a single-use flow cell that is as easy to manufacture and cost-effective as possible for the *BioPAT® Spectro UV single-use pipe* sensor interface from Sartorius, which is currently under development.

In addition to the, for quartz glass components, very demanding geometry and the required high optical accuracy in the very small component, further specific challenges arose in the course of the project, such as ensuring the sealing of the quartz component to the plastic body into which it is to be integrated. Together, these requirements turned out to be very complex and could not be satisfactorily met using conventional glass processing technology.

Integration into a highly regulated production environment required the establishment of new processes

In order to eliminate risks related to the purity and efficacy of the future biopharmaceutical drug, it is necessary that each process step can be precisely monitored, that there is a high level of measurement accuracy, and that it is ensured that the measurement components used do not interfere with the process.

High demands are therefore placed on the accuracy of the gap dimension of the flow cell used in the downstream process. At the same time, it must be guaranteed that the quartz components cannot come into contact with foreign substances that could contaminate the pharmaceutical manufacturer's product before packaging.

Application

BioPAT ® Spectro UV Single-Use Pipe with integrated flow cell from Hellma

The flow cell made of quartz glass is the central component of the *BioPAT ® Spectro UV Single-Use Pipe* sensor interface developed by Sartorius. This is integrated into a single-use tubing set for the purification of biopharmaceuticals.

UV light is sent through the flow cell by a specially developed probe head. The light interacts with molecules in the flow cell, it is absorbed in wavelength ranges specific to the respective molecules. The unabsorbed light is passed through the probe head back to the spectrometer and processed there. The resulting absorption spectrum provides information about the composition of the mixture as well as the concentration of target molecules and impurities.

Depending on the application, UV spectroscopy can be used to effectively determine the concentration of the biopharmaceutical active ingredient and track it during the purification process. In other applications, contaminants can be detected, quantified, and tracked in a targeted manner. UV spectroscopy is therefore an effective means of process monitoring and control in purification processes such as chromatography and concentration processes by means of cross-flow filtration.

Solution

QCC enables the efficient production of high-quality optical components in series production

The customer-specific single-use flow cell for Sartorius is produced using the Quartz Cold Casting (QCC) manufacturing process developed by Hellma.

In the QCC technique, a silicon-containing casting compound is poured into molds at room temperature, cured and converted in a thermal process into pure quartz glass that meets optical requirements.

Thus, the manufactured flow cell is monolithic, i.e. it consists of only one piece. This eliminates some of the work steps that would be required in the conventional production of quartz glass measurement cells, making production much more efficient and traceable.

The new manufacturing technology enables a high degree of flexibility and easy adaptability

Since the molds can be flexibly designed, the measuring cell can be constructed in such a way that it can be installed particularly easily and precisely in the customer's flow pipe. Structures for sealing between the glass and plastic parts can also be integrated directly into the quartz part.

For the refinement of the component, established optical processing methods were used. Hellma was able to offer complete production, including testing and packaging, under controlled conditions, so that the cells could be installed directly at Sartorius.

Agile project management methods and the solution-oriented cooperation of the innovation partners Hellma and Sartorius contributed significantly to the success of the project

The close exchange within the competence teams of the two market leaders Sartorius and Hellma as well as the agile and very frequent testing of material samples and integration into the process enabled rapid error detection and correction.

Dr. Jürgen Ell coring the silicon molds

» It was a pleasure to work with Sartorius, even under tougher conditions during the Corona period. Impressively professional project management on the part of Sartorius. Exactly the right partner for us to further develop our new innovative process at Hellma to market maturity « (Dr. Jürgen Ell, Head of Production Technology Development, Hellma)

Due to the high adaptability of the manufacturing processes at Hellma, the customer-specific requirements for the testing process as well as traceability can be fully met.

With the help of batch processes, the orders can be channeled through production in batches. According to the "Purchased Part Approval Process" (PPAP), it is ensured that all specifications are permanently met.

» As part of the good cooperation with Hellma, we succeeded in jointly iteratively developing an optical sensor core component from the first draft to series production under the highest quality requirements.« (Dr. Christian Grimm, Head of Product Development Embedded Hardware, Sartorius Stedim Biotech GmbH

Advantages

Reliable process for reducing effort and costs in the production of optically and geometrically demanding structures

Quartz Cold Casting, developed at Hellma, is a tried-and-tested manufacturing process for implementing complex customer-specific shapes in quartz glass at moderate costs. It can be used in a wide range of applications, even in difficult and highly regulated areas.

Everything from a single source - shaping, finishing and qualification

To save the project partner additional effort in qualifying additional suppliers, actions were taken at Hellma not only to build the Sartorius flow cell isolated from other Hellma products, but also to refine, visually inspect and package it.

Extension of the application scope for this procedure to other areas

With the successful implementation of this customer project, the new cold casting manufacturing process was successfully used for the production of cost-effective single-use optics for UV spectroscopic analysis in biotechnology. The flexibility and efficiency in the realization of customer requirements also make the QCC technology interesting for a variety of other applications. This applies in particular to chemistry, pharmaceuticals, biotechnology, life sciences and the food industry.

Significant optimization of the manufacturing process

The use of precisely manufactured monolithic optics massively simplifies the manufacturing process and ensures a constant optical path length with simultaneous parallelism of the optical windows.

The highest optical quality enables usage in complex spectroscopic applications

Compared to conventional UV flow cells, the SARTORIUS single-use flow cell offers an identical and precisely known optical path length for all connection sizes. With the optical quality achieved, spectroscopic instead of simple photometric methods can also be used for concentration determination.

The flow characteristics of the BioPAT® Spectro UV sensors are practically not affected by the compact design while at the same time ensuring minimum dead volumes. These outstanding results were possible due to the collaboration with Hellma.