



Inside the laboratories of Schülke & Mayr GmbH

The MPS handles the Night Shift

Analytical Quality Control (QC) of pharmaceutical products follows a strict set of guidelines. The quantity of ingredients, standards and solvents used must be accurately determined; stability tests must be performed; analytical methods must be validated, the performance of analytical instrumentation must be verified and certified; and replacement of consumable parts and preventive maintenance must be scheduled at regular intervals. A key element in the analytical Quality Assurance program at the Pharmaceutical producer Schülke & Mayr GmbH in Germany is the GERSTEL MultiPurpose Sampler (MPS) with integrated Weighing Option.

Schülke & Mayr GmbH was founded in 1889 in Norderstedt near Hamburg, Germany and is today a wholly owned subsidiary of Air Liquide. The company is a leading international provider of products for industrial hygiene, infection prevention, Microbiological Quality Management (MQM), as well as chemical preservatives or stabilizers for technical products such as fuels and oil drilling liquids. The company has around 800 employees worldwide, of which 550 are located in Germany. Around ten percent of staff work in R&D at company Headquarters in Norderstedt.

Schülke & Mayr produces and sells disinfectants, antiseptic agents, preservation agents, biocides, medical skin care products, active agents for deodorants, and system cleaning liquids. Among their customers are hospitals and other medical facilities, as well as pharmaceutical companies, cosmetics producers, and food companies. Fuel producers add preservatives from Schülke & Mayr to their diesel fuels, and emulsions from the company are used for oil drilling and production.

Since the bulk of the products from Schülke & Mayr are used for medical, clinical or pharmaceutical purposes, the company is officially classified as a pharmaceuti-



Schülke & Mayr Headquarters in Norderstedt near Hamburg, Germany.

cal company. A requirement for getting and maintaining this classification is that guidelines for product monitoring and quality control must be strictly adhered to:

- Good Manufacturing Practice (GMP)
- German Medicinal Products Act (AMG)
- German Pharmaceutical and Active Ingredient Production Guidelines (AMWHV)
- European Union GMP Guidelines
- EU Regulation 1223/2009 (Cosmetics Regulation)
- EU Regulation 528/2012 (Biocides Regulation).

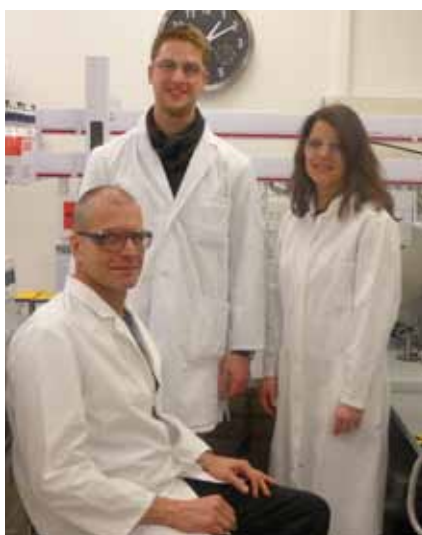
These regulations require strict control of incoming raw materials, continuous monitoring of product intermediates and control of active ingredient concentrations in the final products. Finished products regularly undergo stability testing to ensure that there is no significant change in product safety and performance as a result of aging processes. The regulations also require regular scheduled inspection and validation of measuring and testing equipment.



A view of the Schülke & Mayr laboratories.

No Quality Control without instrumental analysis

Schülke & Mayr perform all chemical analysis in-house. The analytical techniques used for most of this work are Gas Chromatography (GC) and High Performance Liquid Chromatography (HPLC). Analytical methods are developed in the company's Quality Control (QC) laboratory and validated according to regulatory guidelines. Long-time employee Andreas Teevs from the Quality Control and Process Control Department is the key person charged with overseeing analytical method development, method validation, instrument qualification, as well as method implementation and routine analysis. Schülke & Mayr has around 40,000 samples to analyze each year, 90 % of which are performed using GC and HPLC. The GERSTEL MultiPurpose Sampler (MPS) performs automated sample preparation of ten thousand mainly liquid samples every year. "The number of samples has grown dramatically over the past years," reports Mr. Teevs, "and this has been a sizeable challenge for the company and the QC laboratory team. Just in the past five years, the laboratory staff has doubled in size." However, in spite of the growth in the number of samples that must be analyzed, the number of employees in the laboratory will not change in the foreseeable future. In order to increase lab productivity without adding staff, while continuing to meet the required high standards, introducing a night shift was seriously considered. "An extra shift would of course have improved the utilization of the laboratory instrumentation and laboratory productivity, but having to work nights was considered by most to be an unattractive option and an extra burden. Every one of us would have had to make big adjustments," said Andreas Teevs. After considering the alternatives, a more attractive solution was



As part of their daily tasks, Andreas Teevs (left) and his colleagues Michael Bosnak and Beate Teevs-Aschinger are responsible for developing and implementing analytical methods and qualifying the analysis instruments.

found: It was decided to increase the level of automation in the laboratory. Today, the GERSTEL MPS handles the night shift.

No reliable analysis without precise weighing

"Analyzing a large number of samples overnight without the need for a staff presence to prepare samples, generate standards, and to monitor the process is not just a great idea in theory, it actually works!" says Andreas Teevs. But there was one condition that had to be met in order to ensure the success of implementing such a significant amount of automation: The automated sample and standard preparation system had to include an integrated balance. This is required, not only to weigh samples, but also to generate standard and reagent solutions as well as

extensive dilution series for calibration and quality assurance purposes. Today, in many cases, Schülke & Mayr have replaced using standard pipettes with precise liquid dispensing based on the GERSTEL MPS and its automated Weighing Option. "It is easy to see why," says Mr. Teevs: "The accuracy of a 1000 μL syringe is greater than 99.5 % with a relative standard deviation of less than 0.2 %. This means that the MPS provides more accurate results with higher precision than a person using a manual pipette."

When they prepared a laboratory restructuring plan that focused specifically on improving laboratory automation, Mr. Teevs and his team started searching for an autosampler with an integrated weighing option. "We found what we were looking for in the GERSTEL MPS, specifically the Dual Head version, which enables the use of two different syringe sizes that can dispense a wide range of volumes accurately and efficiently without time-consuming syringe changes." The MPS weighing option offers the possibility to monitor, control and document the volumes dispensed. But the MPS also performs all standard sample preparation steps for GC and HPLC and injects the sample into the chromatography system.

A well balanced selection of laboratory equipment

Andreas Teevs and his colleagues currently work with several MPS systems: A stand-alone MPS WorkStation is used to add internal standards and generate dilution series. An XL version of the MPS, called "the bridge", handles sample preparation for two GCs. This is combined with sample introduction to the GC on the left and delivering a vial with a prepared sample into the standard GC autosampler on the right hand side. A third MPS is mounted on another GC system. Each MPS is equipped with

the Weighing Option, i.e. with a laboratory balance, in this case a Sartorius ME 235S OCS. Thermostatically controlled trays are used to store standard and reagent solutions at a constant temperature of 20 °C. Finally, each sampler has two towers (Dual Head version), enabling the simultaneous use of two different syringe sizes. The weighing step is freely selectable in the PrepSequence method settings in the GERSTEL MAESTRO Software (please see workflow diagram). “The resulting weighing protocol can be exported as a Microsoft Excel file or as semicolon separated (CSV) text file for further processing, for example, in a LIMS or Chromatography Data Handling System,” says Andreas Teevs.

“Does the complete automation save time? Probably not a lot in the sense that analyses are finished faster”, says the laboratory manager. “But the MPS with weighing option has enabled us to work both more efficiently and more productively”. The MPS performs analyses overnight without staff watching over it. When the staff comes to work in the morning, analysis results are quickly processed and evaluated and the production batches released. This has led to reduced waiting periods in production, which is of course important. “All in all,” says Mr. Teevs, “the MPS handles the complete analysis, which is something we could only dream of before.” The staff is still trained and able to perform all sample preparation steps manually in case any problems should arise with the laboratory automation system.

Monitoring instrument performance – required and necessary

Where pharmaceuticals or products for medical use are manufactured, a high level of precision and accuracy is required. “All analysis instruments must undergo regular detailed checks and controls in order to

find potential sources of errors and inaccuracies before they develop into something bigger,” says Andreas Teevs. This is another important aspect in which the MPS with automated weighing option plays a key role. Analysis instruments can significantly influence the accuracy of the analysis results, as Mr. Teevs has seen in his 35 years at Schülke & Mayr.

Since the GERSTEL MPS was introduced to the Schülke & Mayr laboratories, it has enabled a more comprehensive control of variations in analytical data resulting from system deviations and instrument wear. As an example, a gas bubble could form inside a syringe when sample is drawn leading to a deviation in sample volume. “This could happen,” says Andreas Teevs, “If the syringe barrel has been worn from extensive use and as a result, air is being drawn in between the barrel and the plunger.” If the sampler is equipped with a balance, the resulting variations in sample volume can be seen directly, trends can be followed and countermeasures such

Stability Test

Pharmaceuticals are subjected to stability tests on a regular basis: During product development, during the approval phase, and after the product has been approved for sale into the market (ongoing stability tests). It is established, whether contamination is formed or introduced into the product and, if so, which compounds are found and in which concentrations. Even after years on the market, product stability can potentially change leading to changes in estimated shelf-life or even product recalls. Samples of different batches of a product are stored under various storage and temperature conditions. During this process, samples are regularly taken and extensive analysis performed.

as replacement of consumable parts can be scheduled. This helps to ensure that the laboratory always delivers reliable and accurate data. “Without a weighing option,” says the expert, “A regular or ongoing system monitoring and control would never be this easy – or even possible.”



Every GERSTEL MPS in the Schülke & Mayr laboratories is equipped not only with a Weighing Option, but also with two towers (Dual Head version) in order to accurately dispense a wide range of volumes without having to go through the process of changing syringes. “The Bridge”, an XL version of the MPS spans two GC systems. Prepared samples can be introduced to the GC on the left and vials with prepared samples can be placed into the autosampler of the GC on the right hand side.

Steps that are performed automatically in the MPS weighing option

Vial is placed in the vial weighing position in the laboratory balance

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Weighing is performed, the value is exported and entered into the weighing protocol

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The vial is returned to the MPS tray and sample is dispensed into the vial

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The vial is returned to the weighing position

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Weighing is performed, the value is exported and entered into the weighing protocol

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The MPS returns the vial to its position in the sample tray



When they prepared their laboratory restructuring, Schülke & Mayr focused on automated sample preparation. Mr. Teevs and his team specifically wanted an autosampler with integrated weighing option that can dispense a wide range of volumes accurately and efficiently without time-consuming syringe changes while offering the possibility to monitor, control and document the dispensed volumes. They found all this and more in the GERSTEL MultiPurpose Sampler (MPS).