Uncompromising Results With the SevenMulti™

In the pharmaceutical industry, obtaining precise and reliable testing results in a short period of time is undoubtedly important. For this reason, Salutas Pharma GmbH in Barleben, Germany uses a SevenMulti pH Meter to perform their product quality control tests.

Uncompromised Quality

The Salutas Pharma GmbH in Barleben is, with currently about 1350 employees, one of Europe’s most advanced and competitive pharmaceutical production sites. Their portfolio covers pharmaceuticals in the form of tablets, film-coated tablets and hard-gelatine capsules for all solid dosage forms. Besides the production facilities, Salutas also maintains highly modern facilities for analytics, quality control and microbiology.

One important task of the galenics quality control department is the preparation of HPLC-media with a precisely defined pH-value for the subsequent HPLC determinations. Since this is a routine task for the highly-trained lab assistants, the automatic data acquisition is quite a useful and time-saving feature of the SevenMulti™ – a pH value can be automatically determined, while another solution is being prepared in parallel. If another task arises during the analysis which requires attention, the endpoint data acquisition is simply switched to ‘manual’ and the lab assistant retains full control over the entire determination. “We often use the automatic data acquisition for our routine determinations — that saves us a lot of time.” says Katy Brom, lab assistant at Salutas.

Time Saving for Routine Analyses

However, a highly precise determination of the pH value needs much more than a simple measurement alone. Everything starts with the right preparation i.e. calibrating the sensors to be used. The
Salutas’ quality control department uses 3 SevenMulti™ instruments together with multiple InLab® 413 / Expert Pro Sensors. The measurements for the HPLC-solutions cover the pH range from pH 1 to pH 9. Within this regulated environment, it is required that the sensor calibration covers the entire measurement range. With the SevenMulti™, up to 5 calibration points are possible and user-definable buffers, including their temperature dependence, can be stored in the instrument. With one user-defined buffer group utilizing the buffers pH 1.0, pH 5.0 and pH 9.0, the whole range can be covered with a three-point calibration.

The calibration of the sensors is performed every morning before the first determination of the day, therefore the highest degree of precision and reliability for around 20 determinations per day can be guaranteed.

Quality Documentation

The quality of the InLab® 413 and Inlab® Expert Pro Sensors is also checked on a daily basis. After the calibration, the buffer solution with pH 7.0 is measured and the offset of the sensor is documented in the laboratory journal together with the corresponding sensor ID.

The results of the different determinations are printed out together with all sample data on the compact RS-P42 Printer from METTLER TOLEDO and this printout is also later included in the laboratory journal.

A METTLER TOLEDO service technician performed the initial quality certification of the instruments and the necessary equipment. “We are very pleased about the professional service and good cooperation we received.” says Dr. Gerald Ohms, leader of the QC method transfer lab.

www.mt.com/pHlab

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High throughput environments involve many process steps which need to work together smoothly. This can be very time-consuming as well as costly if not managed professionally. RAININ provides a series of products facilitating the workflow of different techniques while at the same time reducing the time needed to process and analyze a large number of samples.

Boosting 96-Well Pipetting
With such a large number of samples to be prepared and analyzed, high throughput is often viewed as a workflow that incorporates a number of techniques that can be integrated to allow a large number of samples to be processed and analyzed in as short a time period as possible.

Quality, Reliability and Reproducibility
The need for higher throughput experiments to deliver meaningful data has continued to grow over the years for a number of scientific disciplines. Reliable and reproducible results are a must and ergonomic features are simultaneously required to minimize injuries and reduce operator errors.

RAININ’s Solutions at Your Fingertips
RAININ’s dedicated high throughput portfolio can be seamlessly integrated into research or routine labs in the pharmaceutical industry, clinical research and diagnostic or academic core facilities. With its patented LiteTouch™ Tip Ejection System (LTS), common multichannel problems are solved and reliability increased for that extra edge in speed and high throughput.

Comprehensive service range including maintenance, calibration, training, quality control, pipette park management and improvement processes to guarantee your continued successful operation on a daily basis.

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Secure and Healthy Pharmaceutical Products
Safeguarded by Good Weighing Practice™ (GWP®)

Staying healthy is top priority for consumers all over the world. Their concern about the quality of pharmaceutical products raises the demand for higher security and more stringent control standards. As a result, companies with a well-established quality management benefit from such market changes.

The Market Calls for More Security
Consumers are highly sensitive to news of pharmaceutical quality problems. They react strongly to scandals by putting their trust in companies with solid and long lasting reputations for high quality standards only. Quality management has become one of the critical success factors in the pharmaceutical market.

Risk Analysis by GWP® Helps to Strengthen the Market Position
The basis of successful, efficient and secure quality management is to identify risks and then to control them throughout the entire process. Good Weighing Practice™ (GWP®) analyses risks caused by inaccurate weighing results (i.e. human errors, the wrong choice of instrument or environmental factors) and recommends measures for risk minimization where they are unacceptably high. This analysis is in line with the requirements of current pharmaceutical standards such as ISO 9001 / GMLP + cGMP / USP / 21 CFR Part 11.

Consequently, GWP® enhances the accuracy of weighing results, the efficiency of the routine test processes and reduces operating costs. Companies who employ GWP® do minimize incalculable risks. All processes are documented sufficiently and prove the company’s awareness and responsibility towards customer needs. Furthermore, GWP® has already secured a worldwide acceptance and is approved by many auditors as the quality standard in the pharma market.

Equipment Operation and Performance Qualification

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<th>GMP/GLP demands…</th>
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<td>…continuous assurance of proper equipment performance.</td>
<td>…proper performance by determining and controlling weighing measurement uncertainty.</td>
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<tr>
<td>…measuring devices to be routinely calibrated and tested.</td>
<td>…test and calibration frequencies based on a risk assessment of the weighing process.</td>
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<tr>
<td>…periodic inspections, maintenance and calibrations according to standard operating procedures.</td>
<td>…SOPs that allow smooth operation and testing of the equipment in order to fulfill GMP/GLP requirements.</td>
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Be secure and request a GWP® consultation:

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Pharmacy quality insights in 2008
• FDA has launched a quality initiative with the goal of implementing the Sentinel System. This is an integrated, electronic system for monitoring medical product safety. It will enable FDA to query data sources, consistent with strong privacy and security safeguards. This historic new system will strengthen FDA’s ability to monitor the performance of a product throughout its entire life cycle, thus enhancing the protection and promotion of public health.
• FDA is warning consumers about the possible danger of buying drugs over the internet. Those medications do not automatically meet the required standards and qualities.
• WHO is addressing the harmonization and enhancement of technical requirements for developing, testing and producing pharmaceutical products.
Benefits for companies using Good Weighing Practice™ (GWP®)

- Use the correct balance with the required accuracy and minimum weight
- Error-free installation, performance qualification and operator training
- Specific recommendation for calibration, routine testing and weights
- Correct measurements during the entire life cycle of the balance
- Standard Operation Procedures (SOPs)
Control of Coating Process on Drug Eluting Stents

Arteries are blood vessels which carry oxygen and nutrients from the heart to the rest of the body. Over time or under certain conditions, so-called ‘plaques’ can build up in and on the artery walls. This process, termed ‘Atherosclerosis’, can restrict or block the blood flow in the artery and is a main cause of heart attacks in humans. One method of treating a blocked artery is the use of drug eluting stents. METTLER TOLEDO offers the stent manufacturers a perfect solution to overcome the challenges during weighing and handling these stents.

Customer Challenges
A stent can be inserted into the artery in order to keep it open and restore unimpeded blood flow. The drug eluting stents are coated with special drugs to avoid fast re-blocking of the artery after implantation.

A stent has a cylindrical shape. In the past, the weighing process has proven challenging for two reasons. Firstly, it was time consuming to place the stent on a standard weighing pan due to its shape and tiny size. Secondly, it was prone to inaccurate readings due to heat transfer from the user, air drafts and the instability of the weighing pan plus its tendency to become contaminated from the drug on the stent surface.

By weighing the stent before and after the coating, the amount of drug is determined to ensure the correct quantity has been applied. This differential weighing approach requires sophisticated and accurate results handling. Moreover, the amount of drug coated onto the stent differs from 50–200 µg, demanding the highest requirements from the weighing devices.

All users in this segment are strictly regulated, forcing them to set up tight SOPs and device testing procedures.

The Automated Weighing Process
The Automated-S Microbalances are perfect for automating weighing processes. The stent is transferred onto the weighing pan within the balance and speeds up the weighing process and increase form keeps the sample in a defined position for robotic arm to the balance.
In order to simplify data collection, LabX balance software is the ideal system part-ner. All data can be easily transferred to a server, enabling full traceability and easy calculation of all results.

In addition, due to the user management, the weighing process can be programmed by an administrator and the complete SOP for the weighing process can be run on the balance screen. All technicians therefore strictly follow the SOPs and store all results without touching a PC.

The design of the Automated-S Microbalances has been highly welcomed by stent manufacturers as they increase productivity by speeding up the process and reducing errors. Benefits include:

- Automated sample handling and weighing process
- Hands-free sample handling
- Short process times, fast stability times
- Highest repeatability and highest precision performance
- Designed for seamless integration into an automated process incl. data storage
- Robust stainless steel cover to prevent influences of temperature shifts and to protect against contaminations

LabX balance
- LabX balance offers fast and easy application programming and ensures defined SOPs application.
- The RapidAccess function of LabX links the balance with a server. All data are stored directly onto the server. This process is easy, fast and secure from manual transferring processes.

www.mt.com/micro
Peace of Mind Through Faultless Traceability

Traceable results and the reliability of password-protected and hassle-free user management are of paramount importance, especially in the production area where pharmaceuticals are compounded under strict regulations, METTLER TOLEDO’s XP Precision Balance is the perfect partner for such applications where utmost productivity and unique flexibility are essential.

Traceability and Reproducibility for Maximum Security
Pharmaceutical companies face several challenges in their production areas where chemical solution reactions take place in base compartments. Whilst operators monitor chemical reactions against any kind of frothiness during synthesis, lab managers need the peace of mind that these operators add the right mix of antifoam in relation to required tolerance settings. For example, a Swiss pharmaceutical company informed us that the proportion of antifoam mixture in their production area is 100 grams of concentrate to 900 grams of water, which must adhere to a tolerance of plus/minus 4 grams of each antifoam concentrate. As the recipes of such concentrates must be reproducible and traceable at any time, a balance with a formulation application is needed. It should also be user-friendly and offer a sophisticated user management system in order to protect the balance against any kind of modifications. Pharmaceutical companies work in a strongly regulated environment and compliance with regulations such as GMP is a must. The XP precision balance offers everything pharmaceutical companies require.

Programmed Security and Tailor-Made Documentation
The programming of a recipe is simplified in the formulation application of the XP Precision Balance due to the easily comprehensible touch-screen user guidance. If a recipe is pre-programmed, the operator will be guided through the tasks of weighing and formulating and is automatically warned if tolerance limits are violated. This eliminates errors and guarantees a safe routine operation. Thanks to an intelligent User Management, the administrator can define individual access rights for each user by means of a password and therefore protect the balance against unwanted modifications. This company’s lab manager reported that, “With the XP Precision Balance, I have full control of the tasks my employees carry out on the balance and I can check all measurement results on the detailed printouts. When we are audited by the FDA, I feel confident in the knowledge that all samples and measurements are traceable and comply with GMP and other regulations.”
Cover and Protect your Precious Samples

At the quality control lab of a major pharmaceutical producer, titration plays a key role in testing raw materials. Due to the large number of samples, the Rondo 20 sample changer from METTLER TOLEDO is being used as a way of increasing productivity. Samples that give off unpleasant or even harmful smells are covered by an automatically removable cover. The CoverUp™ lid removal system is the ideal solution.

Automated Titration for Efficient Raw Material Quality Control
As well as determining the water content (using specialized Karl Fischer titrators), acid/base titrations, argentometric chloride measurements and complexometric titrations for determining the calcium and magnesium content, are also performed for quality control of the raw materials.

With around 20 samples daily, it was definitely worth supplementing the titrator with a Rondo 20 sample changer. It has not only improved reproducibility, but has also made it possible to perform multiple analyses simultaneously, which has further improved productivity.

Cover-Up™ – a Compact and Economic Solution
Tests are often performed on nonaqueous acid/base titrations with perchloric acid as titrant and acetic acid as solvent. This can generate unpleasant smells. To save costly air extraction space, the aim was to find a solution that would allow the samples to be covered with an automatically removable cover. The Cover-Up™ system for Rondo 20 meets the requirements perfectly. The cover is lifted off the sample cup magnetically directly before titration and then replaced immediately after titration. This makes the Rondo 20 with CoverUp™ a virtually closed system. This design has two key advantages over other solutions: it takes up less space and is also much cheaper. In addition to this, no additional programming needs to be performed as the entire procedure is controlled automatically by the METTLER TOLEDO Titrator.
An Excellent Technique for Identifying Thermal Transitions

Differential Scanning Calorimetry is an excellent tool for analyzing phase transitions in materials commonly used in pharmaceutical drugs. Hot-stage microscopy is an advanced technique that is widely used for the characterization of thermal transitions, which has the added advantage that the sensitivity of the system is not influenced by different heating rates.

DSC and Hot-Stage Microscopy

The following example illustrates how sulfapyridine (a component in the sulfasalazine preparation used to treat rheumatic arthritis) can be easily analyzed and characterized using the DSC 1 combined with the FP82 Hot-Stage Microscopy System from METTLER TOLEDO. The combination of techniques allows the user to directly observe how the thermal events relate to the structure of a particular sample material as it is heated. By directly observing morphological changes of a sample, it is much easier to interpret and evaluate the DSC curve in question.

The results in Figure 1 show that Sulfapyridine exhibits crystallization and several solid-solid transitions as soon as it is heated from the glassy state. Although these transitions are easily recognized in the DSC curve, the curve itself cannot show which transition is actually occurring at any moment.

By using the FP82 Hot-Stage Microscopy system in combination with the DSC 1, it is possible to identify the individual processes that correspond to each DSC peak. Figure 2 shows the sample at 120.1 °C. It is now possible to see that spherulite crystals have grown out of the glassy phase. Figure 3 shows that at 176.6 °C, the spherulites have changed through melting and re-crystallization to the new rhombic modification.
Efficient Data Management

The above example was performed using the analySIS® software available for the METTLER TOLEDO FP82 Hot-Stage System. This software enables still and video images to be saved on a PC system; making it easier to document parameters such as the sample temperature, the magnification or scale, the sample name and the time and date besides the actual images themselves. This software also has many additional benefits including 21 CFR Part 11 compliance as well as excellent data availability.

The DSC 1 in collaboration with the FP82 Hot-Stage Microscopy System is an extremely valuable combination for the characterization of polymorphic forms and the study of melting and crystallization processes. The advantages of this technique are greatly improved with the analySIS® image and video recording software. The exchange of image data in electronic form then becomes a very simple matter.

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New Products and Technologies
From METTLER TOLEDO

METTLER TOLEDO delivers powerful solutions that simplify work in laboratories around the world. Combining our state-of-the-art technologies with our applicative competence, we have a strong value proposition to make: accurate results and productivity second to none.

Weighing Solutions and Analytical Instruments

New ErgoClips & Stands
Available from 2009

We are proud to announce the expansion of our ErgoClips portfolio! The ErgoClip small flask, used for enhanced weighing directly into the 10ml volumetric flask, is now also available for analytical XS/XP Balances. Please visit our website for ErgoClip filter holder to improve manual filter weighing process and new ErgoClip stands to prevent damage to ErgoClips and keep the bench space tidy.

New Range of Laboratory Conductivity Sensors
Easier Handling and More Precision

The entire range of laboratory conductivity sensors is replaced by the second generation of InLab® conductivity sensors. The robust sensors have a newly developed open tip design. Therefore, sample carryover is reduced to an absolute minimum. Cleaning and rinsing becomes easier. The linearity over the whole measuring range is maximized and the response time is shortened. All kinds of samples can be measured easily, including pure water.

Manual Multi-Channel Pipetting
Increase productivity with the new Pipet-Lite Adjustable Spacer – the world’s only manual multi-channel pipette with adjustable spacing. Ideal for routine work in genomic, proteomic, tissue culture and cell culture applications, this pipette can easily alter the format spacing from 24-well to 96-well. Just a twist is all that’s required to change spacing!

High-Capacity Evaporation Trap for Pipette Testing on XP/XS Analytical Balances

METTLER TOLEDO has developed a 100ml Evaporation Trap for use with its world-leading range of XP and XS Balances. The 100 ml Evaporation Trap, which is unique in the market, is optimized to achieve minimal evaporation, uninterrupted pipetting even for high volume pipette and high reproducibility without the need for a draft shield to increase handling comfort.

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