Good Measuring Practices

When Quality Really Matters
for Pharmaceutical Labs

Why you need to read this White Paper

Operating precision instruments in pharmaceutical research labs and manufacturing plants always means walking a narrow path between high process efficacy and significant process risks. In few industries is working with out-of-specification measuring instruments as critical as on pharmaceutical workbenches.

Particularly with highly potent, active substances both accuracy and precision are absolutely paramount to safety — safety for both the consumers who take final products in either prescription or over-the-counter form, and safety for the operators charged with handling and tracking these potent ingredients throughout research and production processes.

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1. The Quality Umbrella: Good Measuring Practices

Guided by considerations on process safety, METTLER TOLEDO has published a series of seven guidelines specific to various product lines under the umbrella of the Good Measuring Practices program. They were developed as a tangible means of translating the well-established and widely enforced, albeit rather generic working instructions, such as good laboratory practice (GLP) or good manufacturing practice (GMP), into specific sets of guiding principles for its own product portfolio, which are, however, also fully applicable for any other manufacturers’ instruments.

Recognizing the paramount importance of standardized and fully controlled pharmaceutical methods, various industrial guidelines were established between 2007 and 2013, covering technologies used for standard chemical and physical measurements and analysis such as weighing, titration or pipetting, conductivity or pH measurement, determining density or refractive indexes, or thermal analysis.

“Quality First” Throughout the Entire Instrument Lifecycle

The guidelines are pooled under the umbrella of the Good Measuring Practices program and comprise a consistent set of recommendations, supporting operators in systematically managing quality assurance measures for their instrument fleet during its complete lifespan.

The guidelines address all critical interactions between the instrument, its location and environment and the operator, starting by evaluating the application-specific needs and then selecting the models best suited to comply with these requirements. Next, the program provides standard procedures for equipment installation and qualification and for extensive operator training, guaranteeing a smooth start – free of application errors and complications. Finally, the guidelines recommend appropriate routine operations, such as frequent verification testing by the operator and regularly scheduled maintenance services with subsequent calibration executed by the manufacturer’s field service technicians. These measures are recommended to ensure optimized operating hours, to guarantee accuracy of the measuring processes and thus to minimize the risk of out-of-specification results.

While meeting these guidelines can sometimes be cumbersome, not meeting them can cause products to be either ineffective or even toxic – neither of which is desirable, particularly when lives literally hang in the balance. The Good Measuring Practices program provides continuous proactive support throughout the entire lifecycle of laboratory equipment, giving the user the confidence that he can run the instrument at any time within proper operational conditions and thus always fully rely on the results without any compromise on quality.

Risk-Based Management Approach

Ensuring that pharmaceutical manufacturing processes critical to product quality generate results within predefined tolerance windows is fundamental. The potential risk for economic damage related to not meeting such quality requirements is specific to each process step and therefore needs to be thoroughly assessed together with the responsible manager. Appropriate quality assurance measures are then to be identified, implemented, documented and continuously monitored.

Ensuring that the final results are always within these very often rather narrow process tolerance ranges requires an in-depth knowledge of the applications, a thorough understanding of the underlying measuring principles, and – most importantly – a continuous control of the operational state of the equipment in use. Anything less means leaving results to chance.
All Good Measuring Practices guidelines involve a scientific process-specific risk check. The assessment of the risk associated with each measuring process provides the instrument operator with detailed recommendations on frequency and method for regular performance verifications, and proposes intervals for preventive maintenance visits. Only such a holistic view of the entire measuring process allows proper instrument performance day-in, day-out, all year around.

Implementing a systematic and scientific evaluation approach for optimal equipment selection, installation and maintenance is the only way to safeguard consistent adherence of critical manufacturing standards to process requirements across various production locations — and even throughout the industry. This ensures not only manufacturing accuracy but consistent product quality for enhanced safety industry-wide.

The Seven Guidelines

METTLER TOLEDO’S Good Measuring Practices program currently hosts six different guidelines, each specific for a group of instruments, all of them providing application-driven, risk-based management advice for laboratory equipment commonly found on pharmaceutical workbenches. This includes

- **GWP®** – Good Weighing Practice™ for laboratory balances, scales and moisture analyzers;
- **GTP®** – Good Titration Practice™ for titrators;
- **GPP™** – Good Pipetting Practice™ for pipettes;
- **GDRP™** – Good Density and Refractometry Practice™ for density meters and refractometers;
- **GEP™** – Good Electrochemistry Practice™ for pH, redox, conductivity, ion and dissolved oxygen meters;
- **GTAP™** – Good Thermal Analysis Practice™ for thermal analysis instruments;
- **GMDP™** – Good Melting and Dropping Point Practice™ for melting and dropping point instruments.

The Five Steps in Each Lifecycle

Each of the Good Measuring Practices guidelines introduced above and described in more detail in later chapters of this paper is structured in five steps that represent key moments in the lifecycle of an instrument. The guidelines present advisory support beginning already with pre-purchase considerations, going all the way to recommendations for testing, calibrating and maintenance interventions during the many years of daily operation.

For all these stages in an instrument’s life, Good Measuring Practices consultants provide a process framework to maximize operational security. Each guideline can therefore be considered as an easy-to-follow sequence to identify appropriate quality assurance measures for handling laboratory instrumentation in any given quality management system.

Keeping an eye on risk and security equilibrates process hazards with testing efforts and operational efficacy in every one of the following five basic steps of an instrument’s lifecycle:
• Evaluation of application, environment and instrument requirements – gaining a detailed understanding of all criteria to be taken into account for setting up an efficient workflow while achieving secure processes and high-quality results, and, last but not least, guaranteeing safe data handling;
• Selection of the instrument – identifying the best suited package of equipment plus service that meets the financial budget and best complies with process requirements over a long period of time;
• Instrument Installation / Operator Training – ensuring professional installation and setup of the instrument followed by an in-depth user familiarization on operational fundamentals by the manufacturer’s experts;
• Initial Qualification / Regular Calibration – testing and releasing the instrument for dedicated routine operations, ensuring full compliance with internal quality standards as well as global and local industrial regulations and norms;
• Routine Operation – providing explicit guidance on optimal frequency and methods of process verification by the operator, and recommendations for scheduling preventive maintenance and re-calibration visits by the manufacturer’s service team.

All Good Measuring Practices guidelines follow this lifecycle consultancy in five steps; however, depending on the very nature of the various instrument groups, the focus of steps 3 and 4 differs slightly between guidelines in order to give more emphasis to topics of superior importance to the instrument’s risk-based lifecycle management.

How Can the Guidelines Assist?

Each step of the lifecycle of the Good Measuring Practices guidelines contains business-relevant deliverables for the responsible managers in various departments of any pharmaceutical company such as the quality assurance manager, the department head, or the procurement officer, who typically focus on both product quality and process profitability.
However, the guidelines also contribute significantly to trouble-free applications and are thus of interest to instrument operators, providing fundamental knowledge and practical tips and tricks for smooth and uninterrupted workflows. The guidelines may assist regarding the following topics:

- **Quality assurance**: The guidelines provide the scientific fundament for top quality, highly accurate measuring results, combining the operator’s application expertise with the manufacturer’s technological proficiency and the built-in test and reminder functionalities of the instruments.

- **Minimized risk**: The guidelines were established to assist with active management of process risks by defining and implementing operational methods that ensure procedural consistency while fulfilling quality assurance and regulatory requirements taking into account environmental influences.

- **Service optimization**: Each guideline issues recommendations for testing and service schemes that are cost-optimized while providing safe margins with regard to process tolerances, following the paradigm “Test as much as needed but as little as possible”.

- **Audit-worthy documentation**: The guidelines further provide information on METTLER TOLEDO’s equipment qualification packages and calibration certificates, obtainable in audit-proof formats, fully compliant with industrial standards and norms under any regulatory regime, professionally documenting the measuring performance of instruments and its interpretation linked to pass/fail criteria.

- **Stability and sustainability**: Last but not least, following the guidelines leads you to increased process stability and lean workflows, thus contributing to ecological sustainability, supporting reduction of process waste due to excessive testing and/or poor product quality.

Each of these guidelines ensures high process quality, particularly when coupled with professional consultation, and thus helps prevent the kind of poor results that causes economic damage due to production delays, rework or recall, or monetary losses in terms of fines and even litigation.

This paper offers a look at each Good Measuring Practices guideline in greater detail, including the benefits they offer to operators at pharmaceutical workbenches.

**Optimized Test Procedures Are Key**

The systematic approach taken in the Good Measuring Practices program seeks to ensure that sufficient action is taken to guarantee accurate and reproducible results without onerous or burdensome over-testing. This helps achieve operational continuity while taking into account process requirements and a potentially negative impact on product quality, and hence consumer satisfaction and environment.

If operators must continually test their equipment and take it offline, the impact to already thin profit margins in the fast-paced pharmaceutical industry may become business critical if not business threatening. The guidance given in the various Good Measuring Practices frameworks for balancing process risks and testing efforts seeks to ensure optimal uptime while providing greater confidence for smooth internal quality reviews and worry-free external audits.
2. GWP® – Good Weighing Practice™

GWP – The Weighing Standard is a global guideline that applies to all balances and scales from any manufacturer in any industry and at any workplace. METTLER TOLEDO developed GWP as a standardized methodology to guide smart operation and long-term maintenance of all weighing systems. GWP is a scientific weighing benchmark that complies with all quality standards in laboratory and manufacturing. GWP guidelines focus on stable processes, consistent quality, and regulatory compliance as aspects to consider when working with weighing equipment.

For each balance or scale, GWP maintains a highly professional documentation that fully complies with regulatory norms and quality management systems, maintaining a device history throughout the entire lifecycle.

Why Focus on Weighing?

Weighing affects quality. Weighing is critical in very many workflows routinely applied in pharmaceutical processes. Nearly every pharmaceutical formulation is going to require substance weighing to ensure potency and prevent toxicity.

Throughout pharmaceutical manufacturing, including areas such as R&D, production, quality control and logistics, weighing is indeed just one step in a whole process chain, but a step that may strongly influence the final product quality. Accurate weighing is thus essential to ensure continuous adherence to quality requirements. Out-of-specification results may lead to rework or batch disposal, which add up to significant expense for lost manufacturing time and excessive use of raw materials as well as for disposal cost. This risk of economic loss often paired with excessive costs of litigation and enormous fines that are incurred if bad batches reach consumers can be tamed if GWP is applied systematically.

Mastering Process Risk

Strictly following metrological standards, GWP provides a reliable trail for both external quality audits as well as internal quality assurance guidelines such as lean manufacturing. GWP helps enforce standard operational procedures (SOPs), determining intervals for performance verification testing, calibration and maintenance interventions. The GWP guideline supports the quality assurance manager in evaluating weighing processes in a simple, objective way, offering a clear set of criteria that helps assess metrological and environmental conditions and
regulatory requirements. The analysis of these findings allows issuing traceable recommendations for selecting the ideal weighing device and for planning routine quality assurance measures to be documented in the respective SOPs of the laboratory. This ensures uninterrupted weighing processes, satisfying highest reliability and accuracy expectations.

**GWP: The Five Phases**

GWP consultants provide the customer with documented evidence for reproducible weighing results and consistent product quality during the five stages of the GWP lifecycle as described below:

**1 Evaluation**  
**Understanding weighing applications.** GWP provides an initial software-based assessment of the current, but also of the possible future weighing applications based on a concise set of scientific criteria derived from the global weighing standard. Besides other factors, this takes into account the specific environmental conditions of the workbench on which the balance or scale is used, the smallest (net) and the largest (including tare) weight to be weighed, and the specific weighing accuracy required by the application.

**2 Selection**  
**Optimal match based on process risk.** This analysis lets the operator know if a particular balance or scale fulfills these requirements and thus allows managing the risk inherent in the weighing process. It can then be decided whether or not a previously installed weighing device should be utilized or if a device with different accuracy specifications would better match the associated process requirements of your workplace. This also is the right moment to decide on the ideal maintenance and support scheme, assuring optimal weighing accuracy and uninterrupted uptime, avoiding excessive costs for redundant testing activities that may not be relevant.

**3 Installation**  
**The perfect start.** Weighing experts professionally install and qualify your equipment, providing state-of-the-art proof documentation, complying with quality assurance SOPs, and allowing traceability to national or international standards. In-depth, hands-on operator familiarization ensures trouble-free weighing right from day one.

**4 Calibration**  
**Proving continuous performance.** Initial calibration and regular re-calibration including the determination of measurement uncertainty and minimum weight document the accuracy of your weighing process. Its interpretation through pass/fail statements establishes the link between the instrument’s accuracy and the required process tolerance and thus provides evidence for continuous weighing performance, undisputedly securing internal and external audits.

**5 Routine Operation**  
**Optimizing testing efforts.** GWP provides support to the balance responsible in establishing appropriate maintenance and test schemes in such a way that engages test resources when it really matters. Based on the specific process risks, clear recommendations are generated for testing methods and frequency, test weights, and corresponding pass/fail limits. It is not unusual that with GWP in place conventional testing efforts can be significantly reduced while at the same time the applied test procedures are more meaningful so that not only are data reliability and process safety improved but assets are also better protected.

**GWP Risk Check**

A free-of-cost process evaluation tool, known as the GWP Risk Check, helps identify whether or not a particular weighing application is likely to cope with the process risk and to provide appropriate quality of the weighing results. Invest five minutes in the online questionnaire of the GWP Risk Check here: [www.mt.com/gwp-riskcheck](http://www.mt.com/gwp-riskcheck).
3. GTP® – Good Titration Practice™

Titration is an analytical technique that allows the quantitative determination of a specific substance dissolved in a sample. It is based on triggering a complete chemical reaction between the analyte and a reagent of known concentration which is added to the sample.

Dependable titration starts with an assessment of the key process requirements, such as the identification of the best suited titration method, the expected degree of process automation comparing a lab's human resources with its daily titration task, and the business criticality for consistently achieving fully accurate results. These are questions to be answered at the outset to guarantee an optimal titration workflow.

Focus on Knowledge Transfer

GTP strongly focuses on providing extensive training and sharing application expertise, supporting the operator in establishing reliable and repeatable workflows. GTP gives tangible instructions for smooth sample preparation and provides free access to a large database with over 500 application methods that significantly minimize the time to routinely operate the titration system.

At the heart of every good automated titration are a variety of sensors. It is crucial to understand how the sensors are properly used, maintained and verified for accurate and repeatable titration. GTP provides knowledge, practical tips and tricks as well as quality guides, ensuring the titration sensors perform in accordance with quality requirements.
Measurement Uncertainty in Titration

In laboratories accredited according to ISO/IEC/EN 17025 (2005) the measurement uncertainty (MU) for titration applications must always be indicated. GTP therefore developed a service known as the MUPac that enables the operator to assess the reliability of titration measurements based on calculating such a confidence interval and at the same time provides a quantitative report assessing all factors influencing the titration results.

GTP: The Five Phases

Here is what the five Good Measuring Practices phases look like for GTP:

1 Evaluation

Thorough workflow analysis. GTP supports assessing the requirements for a titration system, reviewing current and potential future methods, selecting among the various solutions for process automation, but also early planning of commissioning.

2 Selection

Tailored solution. Tailoring a titration system requires full consideration of critical aspects, such as application and methods, choice of reagents and accessories, operator safety, traceable data management, and compliance with industrial norms and regulations. Last but not least, the process productivity can be significantly increased through targeted automation steps from sample preparation to the titration itself and finally cleaning and conditioning electrodes and accessories.

3 Installation

Commissioning for quality. The professional installation of a titration system brings confidence that the instrument is working properly and is utilized in accordance with its intended use. As part of the installation support, an extensive operator familiarization is offered. This training is based on METTLER TOLEDO’s EduPac and provides full insight into the fundamentals of titration, which is crucial to avoid measuring errors in the daily routine and thus expensive follow-up costs.

4 Qualification

Professional deployment. The qualification of a titration system with a corresponding equipment calibration should always be performed by a professional service technician authorized by METTLER TOLEDO. An equipment qualification is completed with a general system suitability test, proving the reliability of the instrument and its proper operational functionality. This allows releasing the system into operation according to the lab’s specific SOPs and quickly start using the instrument for its dedicated analysis.

5 Routine Operation

Optimizing running costs while minimizing risks. GTP suggests an instrument testing regimen and regularly scheduled preventive maintenance visits; the aim is to keep titration systems working correctly at all times and to minimize the risk of equipment failure. Ongoing maintenance visits with calibration of titration system and burettes help ensure years of reliable results from even the most complex titration process.

GTP Risk Check

A 5-minute questionnaire known as the GTP Risk Check can help identify whether or not a particular titration solution is likely to provide appropriate quality. The free-of-cost GTP Risk Check is accessed here: www.mt.com/gtp-riskcheck.
4. GPP™ – Good Pipetting Practice™

Pipetting is a technology widely underestimated in complexity, mainly because using a pipette looks simple and straight-forward at first but liquid handling skills may differ considerably from operator to operator and thus can add significantly to the overall pipetting error. Not only can errors accumulate from the pipette operator technique, but also the selected volume range and the liquid characteristics such as temperature or viscosity can profoundly affect pipetting performance.

GPP emphasizes addressing the appropriate pipetting techniques with professional consultation in refining individual pipetting skills and enhancing liquid handling workflows, both contributing significantly to improved accuracy and reproducibility, and thus improving productivity. By applying the principles contained in GPP, users will better understand the sources of errors in liquid handling, also addressing ergonomic issues to help preserve not only process integrity but also hand health – a serious concern for many pipette operators.

Recognizing Pipetting Risks
GPP provides evidence on the risk of using out-of-calibration pipettes for data quality. Pursuing the resulting GPP recommendations for service measures allows maintaining data integrity of liquid handling applications.

METTLER TOLEDO runs a global network of ISO/IEC 17025 calibration laboratories equipped with highly sophisticated devices to calibrate any pipettes at any volumes. A dedicated pipette calibration software package controls every step of the calibration process and ensures full data traceability, ensuring compliance with ISO 8655 and FDA 21 CFR Part 11.
**GPP: The Five Phases**

Again, while the basic Good Measuring Practices steps remain the same, GPP focuses on the following key topics relevant to the performance of any liquid handling task:

1 & 2 Evaluation & Selection

**Quality and productivity needs.** The GPP guideline provides crucial information on the type of pipettes (single-channel vs multi-channel; air-displacement vs positive displacement; electronic vs manual) and the type of tips (various tip shapes and shaft designs) recommended for any given liquid and planned pipetting task, to ensure high data quality.

GPP further supports lab technicians in optimizing sample throughput with different source and destination formats while maintaining high pipetting performance through risk-based performance testing and service plans. Ensuring smooth workflows and controlling costs for liquids and disposables are key factors to high process productivity.

3 Training

**Focus on pipetting techniques.** The ability of the pipette user has a major influence on the quality and accuracy of pipetting results. Proper training in ergonomics and recommended pipetting techniques will enhance accuracy and reproducibility of liquid handling tasks. This includes knowing which methods to use for various tasks such as serial dilutions and ensuring correct and consistent pipette handling, i.e. appropriate immersion angle, depth and time, aspiration and dispense speed, or pre-rinsing tips.

4 Calibration

**Risk-based pipette testing.** High-quality pipettes always come with a traceable calibration certificate when purchased and should then be put on a schedule for regular re-calibration based on the intensity of use and the process risk, taking the criticality of out-of-specifications results into consideration.

High value service providers you maintain a high level of accuracy by providing manufacturer-recommended measures during all the stages of your pipette’s life cycle on most common brands. In addition to this professional calibration services ensure that the pipettes are calibrated and in compliance with quality and regulatory regulations. Normally know-how and audit proof documentation are supplied by these providers as well.

5 Routine Operation

**Ensuring ongoing accuracy.** Ensuring every pipette in a lab receives regular maintenance service is essential to sustain high pipetting quality, preventing subtle performance creep that can significantly affect accuracy in sensitive pharmaceutical production processes.

For critical applications, this needs to be complemented with gravimetric performance verification tests regularly performed by the operator between pipette calibrations. This helps detect out-of-specification pipettes at an early stage. An example is a damaged sealing system that can have a negative effect on the precise delivery of liquids.

**GPP Risk Check**

As with all other Good Measuring Practices guidelines, the GPP team also developed its online Risk Check that allows determining significant risks embedded in any given pipetting process. To get started with the 5-minutes GPP Risk Check and for more information on GPP, visit: www.mt.com/gpp
5. GDRP™ – Good Density and Refractometry Practice™

Measurements of density and refractive index are included in the same Good Measuring Practices guideline as both methods are often used for the same application. GDRP provides tangible support long before the daily routine starts in the laboratory. Ensuring the right equipment is being used in a suitable environment by well-trained people is the prerequisite to reliable and reproducible results, forming the basis for dependable and error-free measurement of density and refractive index analysis throughout the complete lifecycle.

**Fingerprinting Samples**

Instruments of the most recent product lines can be used stand-alone or in combination as a multi-parameter measuring system to determine density and refractive indices and automatically convert these values into units such as Brix, alcohol concentration and API degrees. These are key parameters to characterize liquid samples, frequently used for determining concentrations in binary mixtures.

In combination with instruments that determine pH values or color codes of liquid samples, density meters and refractometers are important in quality control and production. When combined in the same workflow with other instruments through connecting kits, a comprehensive and unique “fingerprint” of a particular sample is the result.
**GDRP: The Five Phases**

Built upon the Good Measuring Practices foundation, GDRP focuses on the following activities:

1 **Evaluation**

*The big picture of quality control.* GDRP starts by compiling a recommendation for an analytical system and a corresponding service plan based on the operator’s process requirements. Investing in liquid sample analysis not only involves understanding current quality control requirements but also takes into account future needs, hence the increasing demand for data traceability and automation of sample transfer. In addition, system modularity allows connecting to devices that analyze liquid characteristics other than density and refractive index.

2 **Selection**

*Simplicity through modularity.* When combined with automated sample changers and rinsing pumps, or when upgraded with connecting kits to pH meters and color measurement systems, sample analysis based on density meters and refractometers can be significantly extended and simplified at the same time. GDRP supports the selection of the most suitable system for a given process, an important step to minimize overall production costs and enhance the significance of the sample characterization.

3 **Installation**

*Making the right connections.* Maximum performance requires more than excellent instrumentation: correct installation is crucial to guarantee the best working conditions as well as longevity for the selected system. Trouble-free operation starts with the proper selection of the working location, the best suitable tube connections, as well as correct connection to other measuring cells, automation units and/or computer.

4 **Qualification**

*Providing operational confidence.* After installation, the system has to be qualified for the operations it needs to fulfill. Professional commissioning and qualification of the instrument is required. The GDRP guideline ensures that these activities are documented in a way that is easy to understand but traceable and audit-proof at the same time. Professional training provides the necessary skills to operate the instrument with full confidence.

5 **Routine Operation**

*Ensuring consistent results.* GDRP suggests periodic preventive maintenance visits, but also provides the operator with system performance verification tests using traceable liquid reference standards certified for density and refractive index at varying temperatures. These are the two main measures providing confidence that sample analysis continuously yields consistent and reliable results. Well-trained users and regularly maintained instruments reduce the likelihood of day-to-day measurement errors, preventing potentially expensive follow-up costs.

**GDRP Risk Check**

The GDRP team also developed its online risk assessment tool. Visit the free GDRP Risk Check and see in less than 5 minutes if there are significant areas where your process may need enhanced safety measures: [www.mt.com/ggrp-riskcheck](http://www.mt.com/ggrp-riskcheck).
6. GEP™ – Good Electrochemistry Practice™

In many laboratories, pH measurement is a common analysis; however, many things can go wrong in this highly sensitive process - needless to say, the same applies to various other measurement parameters, such as conductivity, ORP, ion concentration or dissolved oxygen.

GEP helps guide operators through the whole product lifecycle, detecting possible risks and finding the right tools to address these risks and obtain consistently good results from the outset.

Sensor Selection is Key to Success

Undoubtedly the highest hurdle to overcome in preparing for any of these electrochemical applications is the right sensor selection, not only because of the large range of sensors that are available on the market to best address the widely varying needs of applications, but also because of regulatory requirements and process safety challenges that need to be considered, particularly for applications on pharmaceutical workbenches.

GEP™ – Good Electrochemistry Practice™
for pH, redox, conductivity, ion and dissolved oxygen meters
**GEP: The Five Phases**

Taking into account the complexity of sensor selection and identifying appropriate quality assurance measures, the five Good Measuring Practices phases for GEP focus on:

1 **Evaluation**
   **Thorough workflow analysis.** GEP starts by collecting the current and potential future requirements of your laboratory’s routine analysis, also assessing conceivable benefits and risks of process automation and software-based data management.

2 **Selection**
   **Optimal system selection.** Based on the GEP guideline, a sales specialist assists you in selecting the right sensors for your samples and tailoring the ideal system, taking into consideration criteria like ease-of-use, operator safety and secure data transfer.
   To facilitate sensor selection, GEP refers to a very comprehensive, yet highly useful sensor guide that helps you to select the right sensor based on technical and applicative criteria. For more details see www.mt.com/electrode-guide.

3 & 4 **Installation & Qualification**
   **Reliable right from the start.** Engaging the expertise of the manufacturer’s service team for the installation and qualification of a newly acquired device not only saves time, but provides you with the certainty of having your instrument setup in an appropriate location and taken to operation according to well-proven checklists, thus fulfilling all release criteria.
   It is only the professional qualification of both the measuring system through intensive testing and of the operator through practical training that ensures full conformity with regulatory norms and internal quality standards. Hands-on training helps to avoid very many user errors, which have unconsciously become part of the daily routine.

5 **Routine Operation**
   **Consistent performance and accuracy.** Regular performance verification tests executed as documented in application-specific SOPs in combination with periodic preventive maintenance visits reduce the likelihood of measuring out-of-specification. These measures sometimes seem onerous, but they are the only safe way to establish reliable workflows and thus achieve consistently high-quality, trustworthy results.
   GEP helps assess process risks to ensure that the systems maintain accuracy and the sensors’ active lifespans are extended. It emphasizes in particular the proper handling of sensors as it has been reported in the past that probably more than half of all sensor problems are due to incorrect storage or otherwise poor usage.

**GEP Risk Check**

The first step towards high-quality electrochemical processes is to learn about possible risks. The 5-minute GEP Risk Check is free of charge and discusses potential sources for measurement deviations and suggests methods to enhance accuracy of your electrochemical analysis.
Access the GEP Risk Check online here: [www.mt.com/gep-riskcheck](http://www.mt.com/gep-riskcheck).
7. GTAP™ – Good Thermal Analysis Practice™

Thermal analysis systems offer a wide range of highly sensitive techniques that allow accurate measurement of various material characteristics. Thermal analysis is well-established in research, production and quality control laboratories of the pharmaceutical industry, where materials have to be characterized with regard to their components.

In simple terms, all thermal analysis techniques measure the change of physical or chemical properties of a specific material as a function of temperature and/or time. The methods return quantitative data on changes of properties such as mass, dimension, enthalpy or viscoelasticity, while samples are being heated, cooled or held at a constant temperature.

Thanks to its modularity METTLER TOLEDO’s line of modern thermal analysis systems offers the possibility for flexible system enhancements and can thus be extended as needs and processes change over time.

Tailor-made Support

GTAP is an easy-to-follow guideline for handling thermal analysis instrumentation in a quality management system. It provides practical recommendations, tailored to quality requirements and process risks, taking industrial norms and regulations into account. Operators benefit from professional quality assurance measures that help save precious working hours and cost throughout the entire lifecycle of a system.
GTAP: The Five Phases

While the basic Good Measuring Practices steps remain the same as for all the other guidelines, GTAP focuses on the following key topics relevant to the performance of material characterization:

1 Evaluation

**Thorough analysis of system requirements.** Evaluating the current and possible future needs for a thermal analysis solution must not only identify the target applications, but also take into account aspects such as operator safety, compliance with both industrial and internal quality standards, ease of data management, and the potential for higher throughput by means of process automation.

2 Selection

**Tailoring through modularity.** Based on this initial assessment of requirements, professional GTAP consultants support the definition of the most suitable thermal analysis system, including not only the core instrument but also automation options, software solutions, accessories and a customized service plan addressing specific customer needs regarding training and support and guaranteeing maximum instrument uptime. Such a balanced package of maintenance measures provides a clear picture of the recommended testing efforts and its related costs, providing full transparency on the expected total cost of ownership for your thermal analysis solution.

3 Installation & Qualification

**Commissioning for consistency.** Professional installation and operational qualification of thermal analysis instrumentation assure that the instruments are properly set up and configured, and operators are qualified to handle the system according to manufacturer’s instructions and the lab’s specific SOPs. An extensive system suitability test provides procedural security and ensures an efficient release of the thermal analysis solution into operation, thus allowing a successful start of the dedicated analysis. The entire process of equipment installation and qualification is traced in every detail and carefully described in an audit-proof document that further serves as the first chapter of the device history logbook.

4 Training

**Commissioning for consistency.** Training and documentation further enhances operator confidence when applying complex material characterization techniques. Within the framework of system qualification, operators profit from comprehensive application training, providing detailed knowledge and skills on measuring techniques, instrument handling and data analysis to ensure consistently accurate and precise results.

5 Routine Operation

**Full control over maintenance costs.** Periodic preventive maintenance and calibration by the manufacturer’s service engineers ensure years of reliable results for even the most complex thermal analysis set-up. In addition, regular performance verification tests by the operator according to process-specific SOPs using known standards provide the certainty that already minor system deviations will be detected at an early stage. Well maintained and regularly tested instruments reduce the likelihood of day-to-day measurements errors, avoiding unexpected downtime and incorrect analysis leading more often than not to very expensive rework.

GTAP Risk Check

A free, five-minute questionnaire known as the GTAP Risk Check can help identify whether or not a particular solution provides appropriate accuracy for a given thermal analysis process. Access the online GTAP Risk Check questionnaire here [www.mt.com/gtap-riskcheck](http://www.mt.com/gtap-riskcheck).
8. GMDP™ – Good Melting and Dropping Point Practice™

Melting point is a unique parameter that can be used to identify a crystalline substance. Dropping or softening point is used to obtain a quality control parameter for substances that gradually melt or only soften over a large temperature interval. Both methods yield a thermal value based on the same general methodology: controlled heating of a sample until an exactly defined event is detected which is based on the phase transition from a solid to a liquid or semi-liquid state.

GMDP makes sure that the right equipment is used in a suitable environment by appropriately trained operators. Required by melting point determination and especially in dropping and softening point tests the strict adherence to international standards such as Pharmacopeias, ASTM, ISO or IP is imperative to achieve consistent and comparable results. By supporting this and ensuring that the best suitable instrument is selected, GMDP forms the basis for error-free and thus reliable results throughout the complete lifecycle of the instrument.

Secure and Easily Accessible Thermal Values

With respect to accuracy, standard compliancy, measurement reliability and operational security the instruments of the most recent product line form a worldwide standard in automatic determination of the thermal values melt-
ing, dropping and softening point. Innovative sample preparation tools make sure that the most important part of the respective determination is performed efficiently, securely and error-free.

The automatic evaluation of the melting and dropping/softening point is based on almost five decades of experience that in the case of dropping and softening point has also been established in five international standards. In both cases, video recording of the respective event yields a hitherto unknown measurement security as it provides comprehensive post-evaluation of the test. Thanks to the easy operation, the innovative sample preparation tools and the reliable automatic determination, the thermal values melting and dropping/softening point are easily and securely available for identity and purity check of active ingredients both in drug development and production as well as for raw materials such as waxes that are used as auxiliary reagents to produce ointments, creams and suppositories.

**GMDP: The Five Phases**

Built upon the Good Measuring Practices foundation, GMDP focuses on the following activities:

1 & 2 Evaluation & Selection

*The sample determines the analytical system.* Based on a thorough analysis of sample properties and standards that determine the respective analytical standard operating procedure, GMDP compiles a recommendation for the most suitable analytical instrument solution and corresponding service plan. This takes into account current and future analytical requirements but also goes beyond towards PC software-based instrument and data management.

3 & 4 Installation & Qualification

*Dependable results right from the beginning.* Skilled members of the service team execute the installation and qualification of the instrument. GMDP ensures that this process is carried out efficiently according to comprehensive and well-established procedures. All activities are logged in audit-proof documentation that fulfills highest standards. GMDP especially focuses on practical training of the operators in order to eliminate one of the major error sources in melting and dropping/softening point determination: the sample preparation. The time invested fosters the operator’s confidence both in the analytical workflow and instrument operation and augments process security and analytical precision in daily routines sustainably.

5 Routine Operation

*Maintain accuracy and reliability.* In order to ensure measurement accuracy and reliability GMDP recommends periodic preventive maintenance visits performed and documented according to application specific SOPs. In addition, system performance verification tests based on certified reference substances that encompass the required temperature measurement range are strongly recommended. Beyond that GMDP provides professional training documentation in order to establish and to maintain the training level concerning correct execution of the complete analytical workflow by operating personnel.

**GMDP Risk Check**

Invest 5 minutes of your time and visit the free GMDP Risk Check in order to identify areas in your melting or dropping/softening point determination processes that require enhanced analytical security:

9. Summary

Precision measurements and chemical analysis applying technologies, such as weighing, titration, or pipetting, are common methods on the pharmaceutical workbenches of various departments, such as R&D, quality control or production.

In order to guarantee adherence to internal and external norms and regulations, to enhance data and product quality, and last but not least to minimize consumer risks, it is crucial to ensure that the instrumentation is selected according to a risk-based evaluation of the application process, professionally commissioned, installed, maintained and calibrated, as well as to make sure that the operators are adequately trained.

Under the umbrella of its Good Measuring Practices program, METTLER TOLEDO has developed seven scientific, risk-based management guidelines for the following technologies relevant in most research, production and quality control laboratories of the pharmaceutical industry:

- **GWP® – Good Weighing Practice™**
- **GTP® – Good Titration Practice™**
- **GPP™ – Good Pipetting Practice™**
- **GEP™ – Good Electrochemistry Practice™**
- **GDRP™ – Good Density and Refractometry Practice™**
- **GTAP™ – Good Thermal Analysis Practice™**
- **GMDP™ – Good Melting and Dropping Point Practice™**

Each of these guidelines can be applied to all respective devices of METTLER TOLEDO but also of any other manufacturer. Additionally, each has been shown to significantly contribute to process quality improvements, focusing on five key stages that cover the entire lifecycle of any instrument:

- Process Evaluation;
- Instrument Selection
- Instrument Instalation & Operator Training;
- Instrument Qualification & Calibration
- Routine Operation.

These systematic process steps contribute to:

- Quality assurance: the scientific fundament combining the operator’s application expertise with the manufacturer’s technological proficiency guarantees top quality results;
- Minimizing risk: the guidelines assist with practical recommendations to manage process risk and thus fulfill regulatory requirements;
- Service optimization: each guideline is optimized for total cost of ownership including testing efforts and service costs while applying safe process margins;
- Audit-worthy documentation: qualification documents and calibration certificates in audit-proof formats ensure compliance with pharmaceutical regulations and norms;
- Process sustainability: whenever possible, these guidelines contribute to environmental stability, avoiding excessive testing and supporting waste reduction.

Applying the holistic approach embedded in all of METTLER TOLEDO’s Good Measuring Practices guidelines is the only way to secure long-term process consistency, performance reliability and overall data quality day-in, day-out. This approach addresses the basic quality needs at all workbenches of pharmaceutical research, production and quality control departments.