

QbD and Weighing

Integrating Weighing Process Data

Integration of weighing processes into a manufacturing and management system is essential for consistent monitoring and control of quality-critical attributes. In a Quality-by-Design-based approach, the transfer, integration and storage of weighing-process data are important aspects to consider.

Whether in manual or fully automated manufacturing processes, weighing solutions are an important component in pharmaceutical manufacturing. As weighing is a quantitative measure, weighing results can be statistically analyzed, archived, tracked and traced, integrated into manufacturing and management systems and used for control-feedback loops.

This white paper examines the key factors to consider with regard to data transfer, integration and storage. It also explains how to ensure consistent quality standards.



Contents

-
- 1 Introduction

 - 2 Data Transfer

 - 3 Data Integration

 - 4 Data Storage

 - 5 Custom Programming

 - 6 Summary

1 Introduction

Quality by Design (QbD) is increasingly implemented in pharmaceutical manufacturing, driven by the need to improve final product quality and manufacturing process efficiency.

Build quality into the process

The underlying concept of QbD is that quality should be built into each process step— not only tested at the end. With this scientific, risk-based approach, potential process errors are identified early and proactive steps are taken to ensure safety and efficacy of medications. Weighing processes such as batching, formulating and filling, critically influence product quality and should be considered in a comprehensive QbD concept. Inaccurate weighments can negatively impact the consistency of the blend of ingredients or the correct potency of the final product.

Ensure speed and precision of data transfer

In addition to the accuracy and reliability of the actual weighing equipment, factors, such as the speed and precision of data transfer, can significantly influence the accuracy of the measured result. Other aspects, such as data integration and data storage are required to enable continuous monitoring of the manufacturing process and real-time adjustments. Furthermore, weighing stations are important material ID points. Apart from the weight value, a broad range of information such as raw materials, batch number, responsible operator, and much more can be captured and tracked.

The aim of this white paper is to help understand the parameters that may influence the quality of the weighing result and their relevance for QbD concepts. However, this document does not provide an introduction to Quality by Design and is not intended as a guide on how to integrate QbD in pharma manufacturing.



The Quality by Design Concept

2 Data Transfer – Speed and Precision

Some weighing processes, such as high-speed filling, require ultra-fast transfer of the measurement result at reliable accuracy to ensure consistent process quality.

Depending on the weighing application, measurement speed and speed of data transfer can be critical. In some filling applications, for example, a faster update rate means that the controller can cut off the filling valve more precisely increasing accuracy for the filling system. Therefore, the weighing equipment must be able to provide repeatable high-resolution measurements at a frequency that is higher than the update frequency of the control system.

Ensure measurement speed and update frequency

Some scales and weighing modules with high-quality internal A/D converters¹ are able to process data 300 times per second or faster. Advanced multi-channel weighing terminals can provide fast and repeatable performance for up to four scales, as well as a sum scale. Equipped with fast A/D converters¹ and multi-processor calculating power, they are able to perform concurrent measurement and weight comparisons. But speed alone is not enough; the weighing result must also be precise and repeatable. Filling, batching and formulating are dynamic processes that are often conducted in presence of:

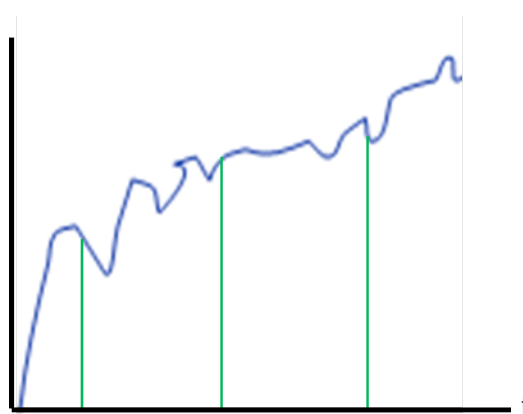
- Mechanical noise (vibration), which is passed through the load cells (e.g. mixers, vibratory feeders, compressors, rotating machinery)

- Electrical noise coupled through the system cables (e.g. line spikes from motors turning on/off, relay/motor starter noise) or
- Internal noise generated by product moving inside a vessel.

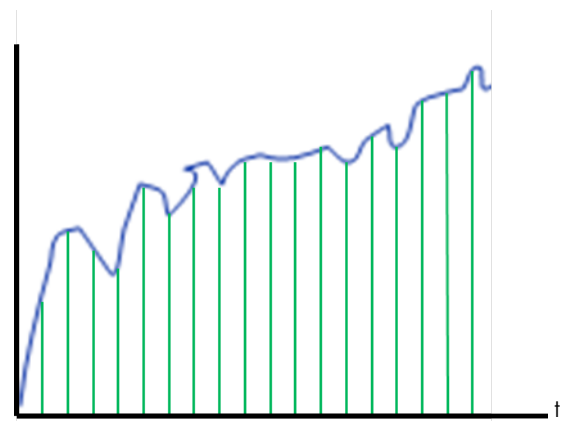
Prevent distortion of the measurement signal

Filters can be used to prevent these fluctuations from reducing the weighing accuracy of the process. It is important to note that traditional vibration filtering, common in weighing terminals, is no more than an averaging functionality with a few fixed settings. Such filters are slow to respond to changes in weight simply because they take the average of a fixed number of weight samples to derive the stable weight.

Sophisticated filtering solutions on the other hand provide tunable multi-stage digital filters and digital signal processing to remove the unwanted noise. They can be specifically adjusted to different weighing conditions to optimize the speed, stability and accuracy of the weight data with updates up to 50 Herz required for fast process control decisions.






A/D sampling 50-100 Hz



High speed sampling 366 Hz

¹ The analog/digital signal converter (A/D converter) converts the analog measurement into a digital signal)

Quality Attributes	Selected Solutions	Key Features
Precise, repeatable measurement data at high update rates	IND560 weighing terminal with TraxDSP digital filtering 	<ul style="list-style-type: none"> • Ultra-fast A/D conversion and I/O bus update rate ensure precise measurement control • Tunable digital filtering suppresses environmental effects on weighing accuracy • Graphical display indicates current weight in relation to target value, reducing operating errors
	IND131/331 weighing terminals with TraxDSP digital filtering 	<ul style="list-style-type: none"> • Ultra-fast A/D conversion rate • Tunable digital filtering suppresses environmental effects on weighing accuracy • Easy integration into process-based network architectures
High accuracy at high speed	WMS Precision Weigh Module 	<ul style="list-style-type: none"> • Ultra-fast A/D conversion rate • Easy integration into plants, machines and instruments

3 Seamless Data Integration

Full integration of weighing solutions into the overall data management system avoids redundant data maintenance and prevents errors.

Scales and weighing terminals can be integrated into the manufacturing process at different levels:

- They can assist control systems by providing fast, accurate information in a dynamic environment or execute local control, and
- They can provide process information to systems above them in the manufacturing plant hierarchy

The key to data integration is having the correct connection to your wider control system. Whether it is a Programmable Logic Controller (PLC), a Manufacturing Execution System (MES) or an Enterprise Resource Planning (ERP) system, the connection requirements for the hardware and software differs. Options include fieldbus interfaces, such as analog output, Profibus, DeviceNet or EthernetIP and data connections, such as Ethernet TCP/IP or serial interfaces. When purchasing a new weighing system, the data integration capabilities must match the data requirements of the wider manufacturing system.

Ensure easy integration of weighing process

Data integration can take two basic forms. If the PLC system is controlling the process, the weighing system must provide fast and accurate weight data continu-

ously for process decision-making. If an advanced weighing terminal is controlling the process directly, the control system will require regular updates of critical process data like current weight, process results, operator ID, or other information. As mentioned in the chapter before, the update rate is most critical for PLC-controlled processes to enable quick decision-making in the PLC. In both systems, accuracy and reliability are critical.

A wide range of interface protocols permits integration of an appropriately configured and effectively networked weighing process with many ERP and MES systems. Seamless data exchange avoids redundant data maintenance and helps prevent errors:

- ERP system data becomes available in the weighing process
- Production data is sent back without manual intervention.

Integrate weighing process to prevent operating errors

All consumption data is available in the ERP/MES system without manual interaction. Based on this data exchange, stock levels are automatically adjusted.

Seamless exchange supports batch release in the MES/ERP system, simplifies data handling and avoids manual input errors.

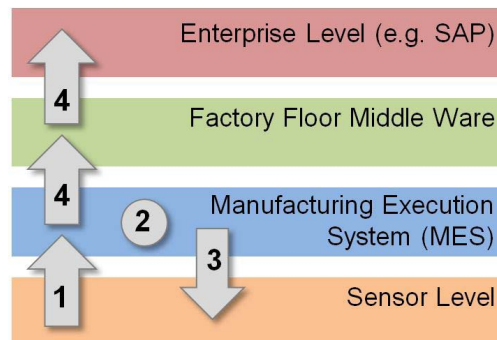
Key benefits of seamless connectivity include:

- Elimination of paper records through automatic data collection

- Direct feedback from sensors to control systems to trigger alarms and indicators and automate process control
- ERP data integration
- Centralized database management
- Decentralized process intelligence
- Simplified wiring

Typical Weighing Process Control in Manufacturing Plant

- 1) Read Inputs: The weight value is sent to master controller.
- 2) Solve Logic: The controller logically interprets this value.
- 3) Write Outputs: The next event is determined by comparing the weight to required tolerances and user requirements.
- 4) Data Transmission: Data is transferred in the network for real-time availability.



Quality Attributes	Selected Solutions	Key Features
Fast and reliable communication of weighing data	IND131/331 weighing terminals 	<ul style="list-style-type: none"> • Ultra-fast A/D conversion rate with digital filtering • Easy integration into process-based network architectures • Support for a wide variety of options, including DIO, additional Com port, and PLC interfaces
Full integration of input and output signals with wide range of protocols	IND780 weighing terminal 	<ul style="list-style-type: none"> • Connectivity for multiple sensor technologies, PLCs database connections, FTP capabilities, and more • Communications from basic serial protocols up to custom PLC data templates • Control up to 40 inputs and 56 outputs using optional internal or external modules.

4 Data Storage

Seamless capturing, exchange and documentation of production and master data provides track and trace capabilities and fulfills regulatory requirements


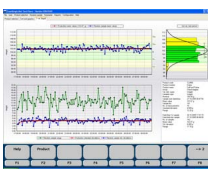

In pharmaceutical manufacturing, documentation and storage of specific process data is essential to comply with requirements of regulatory authorities, such as the U.S. Food and Drug Administration (FDA) or European Medicines Agency (EMA). This is required for auditing purpose but also, in case of quality issues, to track back to the specific point within the process where the issue occurred. In addition, the stored data can be used to continuously analyze and adapt the manufacturing process to improve product quality.

Ensure compliant storage of relevant process data

When a central data storage system is in place, the connected weighing equipment can simply transfer the captured data, such as measured weight, weighing station ID, materials used, operator name, and much more. If such a central data storage system is not available, advanced weighing solutions can provide this functionality. Solutions range from basic storage of weight data to a wide range of values going beyond simple weighing. A broad range of accessories, such as barcode readers and label printers help identify and track materials along the process.

Typical Data Management Solutions



Quality Attributes	Selected Solutions	Key Features
<ul style="list-style-type: none"> Reliable storage of process data Full traceability Regulatory compliance 	<p>FormWeigh.Net formulation software</p> 	<ul style="list-style-type: none"> Storage of recipes, work procedures, results and traceability data in a centralized database Extensive validation documentation and flawless validation records for pharmaceutical production. Full functionality for implementation of 21 CFR Part 11 compliant production processes.
	<p>FreeWeigh.Net in-process control software</p> 	<ul style="list-style-type: none"> Functionality supports compliance with 21 CFR Part 11 in pharmaceutical production Centralized test planning and decentralized data acquisition Automatic and manual exchange of product, statistics, user data and more
	<p>IND780 weighing terminal</p> 	<ul style="list-style-type: none"> Internal alibi memory for storage of up to 256,000 transaction records Internal tare, SQL CE database, custom tables

5 Custom Programming

The ability to customize the weighing solution to the specific process requirements improves overall process flow and control.

Although the standard weighing software is capable of handling most applications, there are often opportunities to gain additional benefits for a specific application through custom programming. Advanced weighing terminals already offer a high degree of flexibility for standard applications, but some high-end solutions provide full customization capabilities.



Adapt the weighing solution to your process

With custom programming capabilities, the weighing system may be programmed to capture additional data, provide custom displays for operators, compensate for process specific variables, modify I/O control, and more. Custom programming opens up the weighing system to effectively and exactly meet the requirements of the application. The better the weighing

system can be adapted to the process requirements, the better the conditions for a consistently high-quality product.

Improve process transparency and control

Capturing additional data helps to improve the transparency of the process and enables comprehensive monitoring and control of critical quality attributes. Customized graphical displays help avoid operating mistakes by guiding the operator step-by-step through the process and ensuring results within tolerances. Individually designed noise filters help ensure the accuracy of transferred data by filtering interfering noise from the specific process environment.

Quality Attributes	Selected Solutions	Key Features
Full process control with customized applications and user guidance	IND780 weighing terminal with TaskExpert™ 	<ul style="list-style-type: none"> Graphical programming environment to build on standard applications or create custom solutions Easy to use, flowchart-based system Managing of relational databases with SQL Server 2000 Windows CE functionality
Full integration of input and output signals with wide range of protocols	IND890 PC weighing terminal with Microsoft VisualStudio.Net 	<ul style="list-style-type: none"> Highly flexible PC application with leading software technologies and open interfaces Integrated Microsoft VisualStudio.Net technology enables easy implementation of customized solutions Use of the IND890-API to combine applications with weighing data

6 Summary

The topics of data transfer speed, integration, storage or even customization of applications and processes do not come to mind immediately when evaluating the critical quality attributes of a weighing process. However, depending on the process, these aspects can have a significant impact on the accuracy of the weighing result and ultimately on final product quality.

Data transfer speed, for example, is essential when it comes to controlling dosing and filling applications to ensure an exact cut-off point. Most process equipment introduce vibrations and noise that can disturb the stability and accuracy of the measurement. Sophisticated filtering solutions are needed to remove these disturbances from the data while ensuring consistently high transfer speeds.

Seamless data integration is a key component of a real-time process monitoring and control setup. Automatic electronic data collection and integration reduces paper-based documentation and helps prevent errors from manual data entries. It also enables direct feedback from sensors to control systems to trigger alarms and indicators and automate process control.

Central data storage enables the manufacturer to continuously analyze and improve the manufacturing pro-

cesses and ensure consistent product quality. In case of quality issues, the database helps to quickly track back from the final product to the specific process step where the problem occurred. Finally, central data storage is required by regulatory authorities as part of Good Manufacturing Practices.

Together, these three elements (data transfer speed, integration and storage) constitute an essential pillar of any manufacturing process based on Quality by Design principles. Quality by Design relies on continuous monitoring and real-time control of manufacturing processes to ensure consistent product quality. In modern manufacturing, this can be achieved only through comprehensive data integration.

When selecting the right weighing equipment for a Quality-by-Design-driven manufacturing process, consider the necessary software, interfaces and controlling capabilities to ensure seamless process integration.

Learn more about how METTLER TOLEDO weighing solutions support Quality by Design framework at

► www.mt.com/ind-qbd

Additional References

METTLER TOLEDO white papers

- QbD and Weighing – Ensuring Accurate Measurements
- QbD and Weighing – Building Consistent Processes

METTLER TOLEDO webinar

- QbD and Weighing - Ensure Consistent Weighing Quality in Pharmaceutical Manufacturing

QbD guidance documents

- ICH Q8(R2): Pharmaceutical Development
- ICH Q9: Quality Risk Management
- ICH Q10: Pharmaceutical Quality System
- ICH Q11: Development and Manufacture of Drug Substances
- FDA: Pharmaceutical cGMPs for the 21st Century – A Risk-Based Approach
- FDA: Quality Systems Approach to Pharmaceutical CGMP Regulations

www.mt.com/ind-qbd

Mettler-Toledo AG

Industrial
CH 8606 Greifensee
Switzerland
Phone +41-44-944 22 11
Fax +41-44-944 30 60

Subject to technical changes
©07/2013 Mettler-Toledo AG