WhitePaper

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Cubis® II Pharma Compliant by Design

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Introduction

The Cubis® II balance series was designed for customizable modularity, which means the user can choose from many hardware and software options for thousands of different configurations. Choose from among 45 weighing modules, seven draft shields, two display and control units, and five software packages, including more than 60 software Apps.

Meet the requirements of the pharmaceutical industry with a combination of the MCA high-end 7" display and specific QApp pharma package, providing all features needed for a full pharma-compliant lab balance system (Figure 1).

Figure 1

The configuration of this package is state-of-the art for the pharmaceutical industry, with a focus on optimal connectivity, data integrity, and data handling by design:

- Comprehensive User Management with an option for "Single Sign-on" centralized user management across the organization
- Full traceability with advanced Audit Trail and a reporting function for efficient reviews
- Requires less effort to go paperless with new print process and electronic signatures
- Automatic Backup/Archiving functionality to ensure data safety

Data generated by the Cubis® II follow the key principles defining data integrity standards for accurate and reliable paper and electronic records as defined by ALCOA (+). Modern data handling enables safe storage in various ways.

The Cubis® II with pharma package contains all the technical controls to support compliance with the FDA directive 21 CFR Part 11 and EU Annex 11. Full compliance can be achieved with additional procedural controls and systems for long-term data storage (Figure 2).

In the following chapters you will find details for those technical solutions.

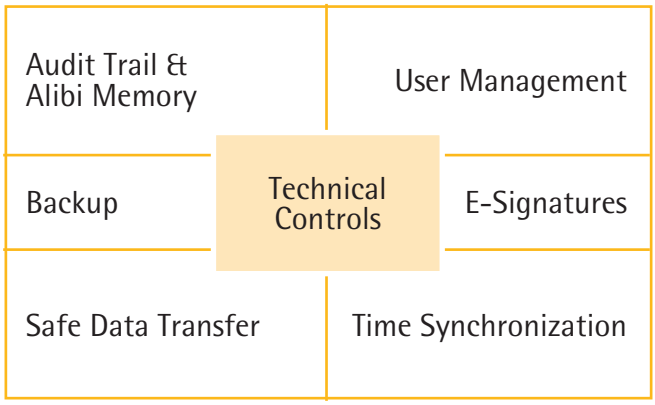

Figure 2

User Management
The Cubis® II balance provides two options for complete user management with access control.

The **local** user management can be configured in accordance with your password policy. User management includes predefined, non-editable roles (e.g. Administrator, Operator), but allows addition of individual roles and configuration of role rights.

Passwords can be configured according to your company's password policy, for instance, by defining password length, complexity, and validity period. In addition, user management allows configuration for exclusion of already used passwords. Also, an auto logout after a specified period of inactivity, and the rules after maximum failed login attempts can be configured.

The rules for 21 CFR Part 11 compliance are easily implemented.

Increase operational efficiency through use of available password rules in the active directory. The Cubis® II system can be integrated into the company's domain to allow use of SSO (single sign on). In this case, **global** defined password rules are implemented automatically. Groups can be defined and maintained centrally, so the whole user management process can be integrated into the company environment. User review can be easily performed by the IT department, without direct access to the balance, and adding or removing a user will follow the already implemented processes.

Electronic Signatures
Electronic signatures are expected to have the same impact as hand-written signatures, so that, based on a secure password, the combination of username and password is accepted in all regulatory instances. In the Cubis® II environment, an electronic signature (ES), based on a secured user name and password, can be used to sign the final report for a weighing process. If your company policy equates the ES and a handwritten signature, a paperless weighing protocol can be produced and integrated, for instance, in the entire batch protocol review process.

Audit Trail
An audit trail is a computer-generated, tamper-protected, time-stamped electronic data file that allows reconstruction of events related to the creation, modification, and/or deletion of records. In general, these data must be recorded in a tamper evident way. A system configured for the regulatory environment should deliver such data in a readable and easy-to- understand way. In the Pharma software package, the audit trail data can be filtered by event categories and exported for display, thus fitting all requirements for a regulated system (Figure 3).

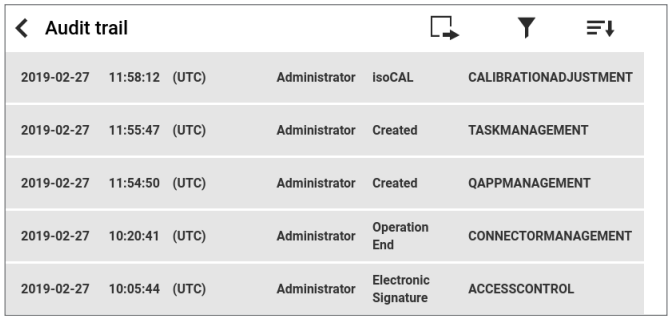

Figure 3

Additionally, the Cubis® II balance contains an alibi memory; the system automatically stores weighing data in a ring buffer that can hold up to 150,000 datasets. These records cannot be deleted or manipulated; however, the list is accessible via the web browser and can be used for additional analyses.

Report Functionality
To create a compliant weighing protocol, additional metadata must be added. Data, such as sample date and time, software version, balance ID, user ID, batch number, and so on, can be configured to include all required metadata for reliable records. Finally, the whole data set can be included in a GxP-compliant weighing report. In the print process, such values are included in the report and can be printed or exported as an electronic, signed PDF.

In case of a mistake, a user is able to mark an incorrect dataset as invalid, with an explanatory comment required before continuing (Figure 4). This dataset will not be deleted or hidden, but rather is displayed, together with the correct dataset, and visibly marked as invalid by crossed-out text.

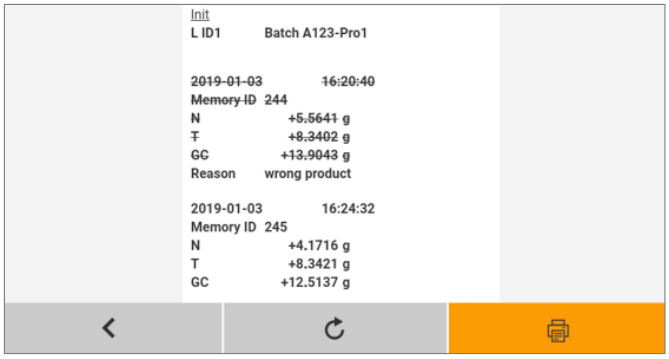

Figure 4

Backup and Archiving
The Cubis® II balance can automatically execute time-controlled actions for backup; the system is able to upload data to a shared file or export the data to other systems. Backups contain audit trail data, printouts, logfiles, alibi memory, and the configuration. All GxP relevant records are stored in a safe way and can be archived by the IT department in their usual manner. In case of disaster, the configuration files are stored in a system-specific way for recovery. All other datasets are stored as PDF files. Archiving is easy and fully compliant because all relevant data are readable without the need for a system-specific viewer or separate software.

Time Synchronization
An accurate time, traceable to UTC, is necessary for trustworthy records. Therefore, the Cubis® II balance supports automatic time synchronization via Network Time Protocol (NTP). In most companies, time servers are available and can be provided by the customer's IT department. If a time server is unavailable, a standard time server service can be implemented. All changes to the configuration of the time synchronization are restricted to authorized persons and logged in the audit trail.

Electronic Records
An electronic record should be protected against any manipulation. The Cubis ® II system allows detection of electronic record manipulation by saving a calculated MD5 checksum with all files. The MD5 algorithm is a widely used function to provide a digital fingerprint or unique identifier for each document. The calculated checksum is stored in all audit trail files and additionally in a separate MD5 file. IT systems like a LIMS can calculate the checksum of a document and compare it with the original checksum of the Cubis® II. If they are identical, this indicates the file was not manipulated, thus guaranteeing the trustworthiness of relevant weighing data and corresponding files.

Interfaces
The Cubis® II balance provides nearly all common configurable interfaces through its hardware and software. Additional hardware, such as barcode scanners, printers, or storage devices, can be connected to the balance by Ethernet, USB-A, -B and -C, and the legacy RS 232 serial port. These interfaces are pre-defined to connect the balance to other software systems and devices directly and easily.

The connectors can be used for data transfer to a file server via various protocols like Windows File Server (SMB) or via Secure File Transfer Protocol (FTPS). External hard drives can be attached to standalone systems.

Web Interface
Each Cubis® II balance integrated into the company's network can be accessed by an authorized user with a standard web browser using an encrypted https connection (Figure 5). The web application can be used for reviewing the audit trail data or the alibi memory.

Configure or manage the balance using this web-based functionality. Remote access can be disabled if not needed.

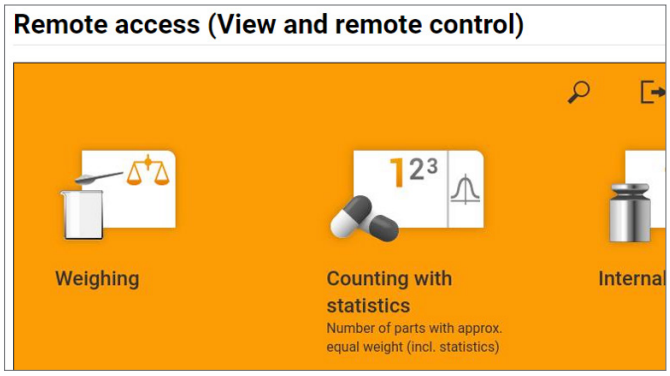

Figure 5

Tasks, Profiles & Connectors
A weighing process is built by the combination of tasks and profiles. Standardize your work by configuring tasks to carry out a certain protocol. For instance, a task can be linked to two different print profiles, so executing this task exports a PDF to a file server for data archiving and also prints out the weighing protocol to a default printer (Figure 6).

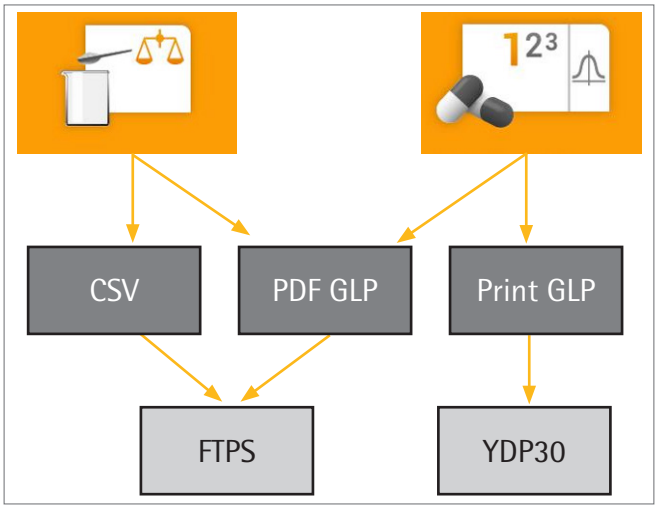

Figure 6

Each print profile is linked to a connector which can utilize all supported interfaces of the Cubis® II.

Save Weighing Protocols
For the execution of weighing tasks, the internal balance adjustment can be set to mandatory to avoid recording weight without proper adjustment of the balance. The result of the latest adjustment is displayed in the balance status center and recorded in the audit trail. Furthermore, the balance measures the leveling status and advises the user to start the automatic leveling procedure if the balance is not properly levelled.

Conclusion
The design of the Cubis® II series combines high-performance weighing with full end-to-end data integrity, supported by the individual QApp-enabled workflows. Furthermore, the technical progress of the new series includes individual sample holders, motorized automatic levelling, an integrated ionizer for elimination of electrostatic charges, and gesture-controlled handling. The control status centre displays information, warnings or errors, as well as environmental conditions. All of the hardware has been designed to improve the ergonomics and efficiency of weighing tasks and ensure error-free results.

The QApp pharma package was developed considering GAMP 5 guidance and fulfills all 21CFR Part 11 demands through an integrated audit trail, a state-of-the-art user management system, and fully-compliant data handling.

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