Design Requirements for 21 CFR 11 Compliance and Manufacture 4.0 Readiness in a QC Microbiology Instrument

Introduction

With increased Data Integrity scrutiny from regulatory authorities in the quality control lab and manufacturing areas, it is critically important for pharmaceutical manufacturers to meet regulatory requirements as defined in PDA TR80. To design an automated system for use in Pharma QC laboratory the key functions required include:

- Secure password control
- Secure data collection
- Comprehensive easy to view audit trails.
- Security of data transfer to network
- Ability to monitor multiple units through secure network storage

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Technology

The Growth Direct® System is an automated, rapid microbial enumeration platform suitable for in-process product testing, environmental, and water monitoring that integrates digital imaging, robotic cassette handling, incubation, and software control. Samples are loaded into incubators and are moved by a robotic system and illuminated by blue light every four hours. Post imaging, the cassettes are automatically returned to the incubator by the robotic system.

RMBNucleus™ Central Manager is a new standalone software solution which integrates with the Growth Direct® system to enhance micro QC visibility and data integrity through user access management and remote dashboard visibility.

Using proprietary software and graphical user interface (GUI), the Growth Direct® System allows companies to meet ALCOA+ standards

ALCOA+

The guiding principles for Data Integrity can be summarized in the acronym ALCOA+.

- **Attributable** – all records are linked to a person or computer system that performed the activity
- **Legible** – data is permanent and easily read
- **Contemporaneous** – data is documented at the time of the activity
- **Original** – the first recording of data, or raw or source data, not transcription
- **Accurate** – data is correct including context/meaning, complete, truthful, and reflective of the test results
- **Complete** – all data and meta data is included
- **Consistent** – data is created in a repeatable and traceable manner
- **Enduring** – data is recorded and stored on acceptable media – paper or electronic – for the defined lifecycle and retention period
- **Available** – data should be readily available and accessible for review and audit as needed throughout the data lifecycle

Attributable

System admins are trained on the use of the system and software. Each action performed on the Growth Direct® requires authentication using an assigned username and password. The user information is linked to each action and saved, linking an individual to an activity on the system, such as loading tests, unloading tests, and/or approvals.

Authentication is required for all actions on the system.

Legible

Reports and information on the GUI are presented in a clear and easy to read format. Additionally, data and meta data are saved to a database. Coding and naming conventions are standardized to avoid colloquialisms and local vernacular.

Contemporaneous

Distractions, work overload, or forgetfulness can result in completing paperwork significantly after actual occurrence. In many instances, key observations are missed. Automation records incubation and enumeration steps, date and time (to the second), immediately after the action or activity starts/ends, or is performed.

Original & Accurate

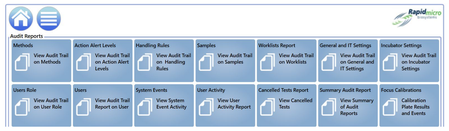
Data and meta data are saved and stored on the system. Access to the database is prohibited. Results, records, and reports cannot be modified or deleted, preventing any attempts at falsification or manipulation of results.

Each individual sample is assigned a unique identifier. Prior to analysis by the system, the Growth Direct® will verify the identity of the sample to prevent mismatching of samples.

Complete

Included default reports hold required data to ensure record completeness. All results are stored and reported, regardless of “pass” or “out of specification” (OOS) status which require additional comments to be entered.

Active audit trails provide details on the user, date, time, action, and associated justification for non-standard actions performed on the system. Audit reports maintain all previous settings, including date of any changes.



Consistent

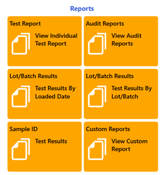
Samples are handled, incubated, imaged, analyzed, and results reported in the same manner every time. Data capture and storage is also performed with the same rigorous consistency due to the automation of every step.

Enduring

The system backs up its database periodically (daily by default). The database and backup are stored locally, but the system is also configured to copy the backup to a defined server on the network designated for centralized storage and protection.

Available

Data are always available via the GUI. The ability to store large amounts of data and quickly sort and search, makes accessibility of data more streamlined than with paper-based processes and is aligned with regulatory expectations.



RMBNucleus™ Central Manager

Central Manager is a new stand-alone software solution which, when used with the Growth Direct® system, further enhances compliance with regulations, and adherence to GMP and ALCOA+ best practices.

Multi System Management

With increasing test volumes leading to a growing number of Growth Direct® systems per site, Central Manager interfaces with each system to ensure Complete, Consistent and Attributable data across the entire fleet.

User Management & Active Directory Integration

Central Manager supports user access and roles across multiple systems to ensure attributable and accurate data collection. Central Manager acts as a reliable source for password management.

Central Manager supports Active Directory integration, with multiple daily updates to support up-to-date password management.

Web LIMS

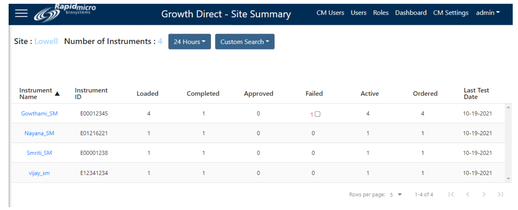
Central Manager enables Web LIMS for constantly updated test management and result reporting.

The Web LIMS interface further supports ALCOA+ compliance through enduring data storage.

Dashboard Visibility

Central Manager includes two dashboards for enhanced visibility – at the system and the site level (in the case of multiple systems). The dashboard database includes customizable date ranges and shows test and system events and alerts.

The system and site level dashboards supports data Availability, by enhancing visibility to QC status anywhere on a company VPN without being limited to being near the system or at a particular site.



Summary

Current (especially paper-based) processes introduce risk as critical data entry points are reliant on the individual recording the data. Growth Direct® greatly reduces the risk in these areas as the data through use of automation and software resulting in greater compliance with data integrity guidelines issued by the FDA, MHRA, EMA and is also consistent with recommendations outlined in PDA Technical Report 80.

RMBNucleus™ Central Manager further supports ALCOA+ compliance through user management and Active Directory Integration, Web LIMS Interface, and remote dashboard visibility.

For additional information on Growth Direct® products and services, please visit www.rapidmicrobio.com.

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