Millipore®
Preparation, Separation,
Filtration & Monitoring Products

White Paper

Bio4C™ Orchestrator Software Data Integrity Assessment

Bio4C™ Orchestrator software connects different unit operations or skids to a centralized server (the Bio4C™ Orchestrator server) and collects data and displays it on a centralized Process Dashboard. Bio4C™ Orchestrator supports centralized management of Alarms, Users, Recipes, and Reporting through a browser-based user interface.

In Release 1.0.1, Bio4C™ Orchestrator software connects to Common Control Platform® (CCP®) skids only.

The CCP® Windows 10 OS controlled unit operations are as follows:

- Mobius® Single-use Bioreactors
- Mobius® FlexReady Solution with Smart Flexware® Assemblies for Chromatography and TFF
- CoPrime® Biochromatography Systems

In future releases, Bio4C™ Orchestrator can be adapted for connectivity to 3rd party skids as well as additional CCP® enabled skids or other control platforms. The connectivity strategy is governed by data exchange through industry standard protocols.

This document describes Bio4C™ Orchestrator's adherence to the Food and Drug Administration's (FDA) data integrity guidance set out in Data Integrity and Compliance With Drug CGMP Questions and Answers Guidance for Industry published December 2018.

What is Data Integrity?

This paper is focused on identifying some key aspects of the latest data integrity guidance that are applicable to Bio4C™ Orchestrator, the preventative and detection controls provided.

Data integrity definition: "The extent to which all data for its entire lifecycle is complete, consistent, and accurate." (MHRA). The World Health Organization and Food and Drug Administration add to it using the principles of ALCOA and ALCOA+:

- Attributable: who acquired the data or performed the action
- Legible: can you read and understand the data entries
- Contemporaneous: documented at the time of the activity
- Original: first recording of data or a true copy
- Accurate: reflects what took place.
- Complete: all recorded data requires an audit trail to show nothing has been deleted or lost
- Consistent: ensuring data is chronological
- Enduring: ensuring data is available long after it is recorded
- Available: ensuring data is accessible

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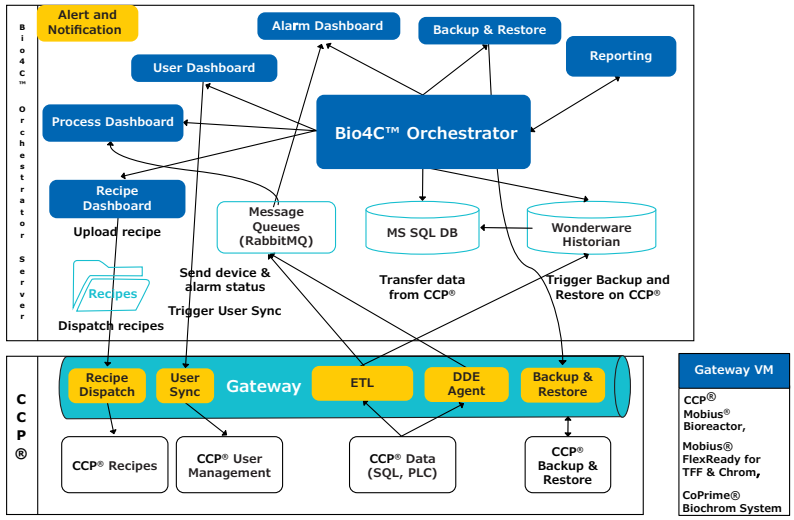
Data Integrity Requirements

In the following table the relevant sections of 21 CFR Part 211 and 212 regarding data integrity requirements are summarized and how Bio4C™ Orchestrator is compliant with these requirements is explained.

This summary is for informational purposes only and is by no means comprehensive. You should contact a company representative if further detail is required.

ID	Description	Implementation
211.68	Requires that "backup data are exact and complete" and "secure from alteration, inadvertent erasures, or loss" and that "output from the computer … be checked for accuracy"	Bio4C™ Orchestrator has backup and restore features in place to perform a full system backup and restore. Evidence is created that the backup is exact and complete. It is the customer's responsibility to define the backup schedule and to prove that restore from backup is possible without loss of data. Process flow: data generated by the instruments are recorded to the CCP® Historian. When a backup is triggered for CCP®, the Historian data files are transferred from CCP® to the Bio4C™ Orchestrator Server location where it is stored and when a restore is triggered it is again transferred back from the Bio4C™ Orchestrator Server to CCP®. Bio4C™ Orchestrator's Restore function checks the integrity of these files while copying back. CCP®'s Restore function manages restoring these files. The same process is applicable for CCP® SQL database files. When a backup is triggered for Bio4C™ Orchestrator, MS SQL database and Wonderware Historian files are backed up and stored in a user specified location. Bio4C™ Orchestrator's Restore function checks the integrity of these files during the restoration. Audit trail data flow: data is generated in local SCADA (supervisory control and data acquisition), stored in local SQL database, transfer to the orchestrator SQL database, backed-up using the Bio4C™ Orchestrator backup function. 
212.110(b)	Requires that data be "stored to prevent deterioration or loss"	A Restore feature is available within Bio4C™ Orchestrator, but it is the customer's responsibility to execute on a regular basis a restore action to prove that no data is loss.
211.100 and 211.160	Requires that certain activities be "documented at the time of performance" and that laboratory controls be "scientifically sound"	Within Bio4C™ Orchestrator audit trails, functionality is available in accordance with the 21 CFR Part 11 requirements. Using this functionality, the customer is able to prove that each action is executed at the time of performance.
211.180	Requires that records be retained as "original records," or "true copies," or other "accurate reproductions of the original records"	All the records created during validation are original records and created at the moment of test execution. Regarding backups, functionality exists to create a full copy of the system. It is the customer's responsibility to archive these copies in a safe place. When CCP® is connected to Bio4C™ Orchestrator certain functions are restricted on CCP® with access privileges like accessing Recipe Editor, Reporting module, User Management and Restore to ensure these functionalities are done through Bio4C™ Orchestrator and avoid duplication. Bio4C™ Orchestrator reads the data from the CCP™ SQL database as it is and displays it in Reports.

211.188, 211.194, and 212.60(g)	Requires “Complete information”, “complete data from all tests”, “complete record of all data”, and “complete records of all tests performed”	A complete validation package (including a Validation Summary Report) is available with all the required test protocols, test results and evidence such as screen shots.
211.22, 211.192, and 211.194(a)	Requires that production and control records be “reviewed” and that laboratory records be “reviewed for accuracy, completeness, and compliance with established standards”	Bio4C™ Orchestrator User Management (including privilege management) allows implementation of segregated duties or user roles. It is the customer’s responsibility to implement user roles. As part of validation activities, all the deliverable parts of the validation package are reviewed and approved by defined stakeholders. MilliporeSigma policies and standards are followed in this case. They are based on GAMP® 5. It is the customer’s responsibility to have a process in place that all records are reviewed for accuracy.
211.182, 211.186(a), 211.188(b)(11), and 211.194(a)(8)	Requires that records be “checked”, “verified” or “reviewed”	Within the Bio4C™ Orchestrator audit trail logging is available to show what has been done and by whom. Also, role management is in place to ensure that records can be “checked”, “verified” or “reviewed”. As part of the validation activities, all the deliverables which are part of the validation package are reviewed and approved by the defined stakeholders. The MilliporeSigma policies and standards are followed in this case. They are based on the GAMP® 5.

CONCLUSION

This document includes all requirements related to data integrity as described in the FDA’s “Data Integrity and Compliance With Drug CGMP Questions and Answers Guidance for Industry” guideline published in December 2018.

All the data integrity requirements are covered in the processes we follow and in the Bio4C™ Orchestrator R1 product.

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To place an order or receive technical assistance

Please visit: **EMDMillipore.com/contactPS** or email **OrchestratorSupport@EMDgroup.com**
For additional information, please visit: **EMDMillipore.com/Bio4COrchestrator**

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