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White Paper

Bio4C ACE™ Software for Mobius® Cell Retention System Data Integrity Assessment

Bio4C ACE™ software is an application control engine software that provides robust control and monitoring of bioprocess unit operations. It automates manual tasks, enables remote monitoring of critical process parameters, supplies advanced process control, and facilitates regulatory compliance. Designed to be intuitive and secure, it allows users to run their processes in either manual or automated mode.

With Bio4C ACE™ software, recipe-driven automation eliminates manual operations, increases reproducibility, and minimizes risk of errors. An interactive piping and instrumentation diagram (P&ID) allows users to visually monitor the process and control each component (e.g., pumps, sensors) in the unit operation's Human Machine Interface (HMI) or from anywhere through a browser-based application.

The Mobius® Cell Retention System uses Bio4C ACE™ software which allows real-time monitoring and control of all process parameters, ensuring reproducibility of your perfusion process.

This document describes Bio4C ACE™ software for Mobius® Cell Retention System'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 the Bio4C ACE™ software for Mobius® Cell Retention System, the preventative and detection controls provided.

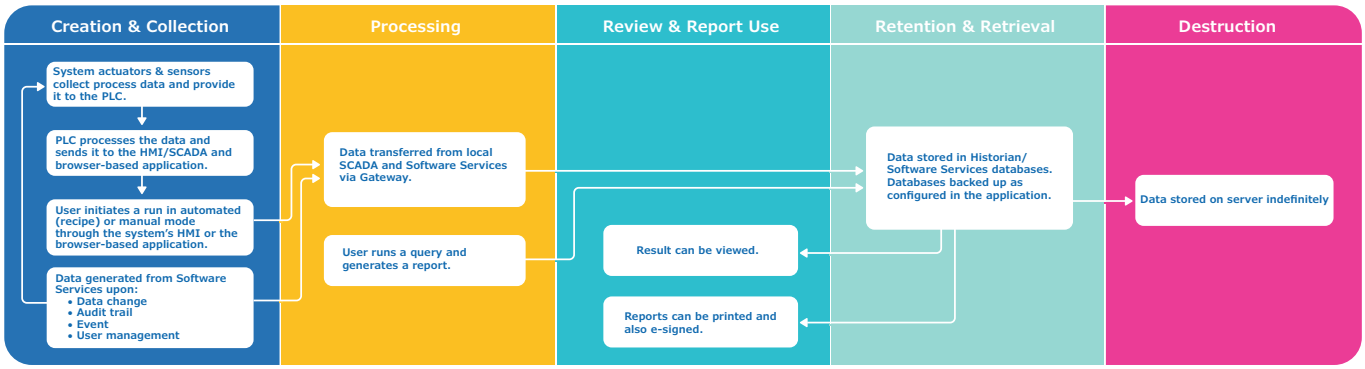
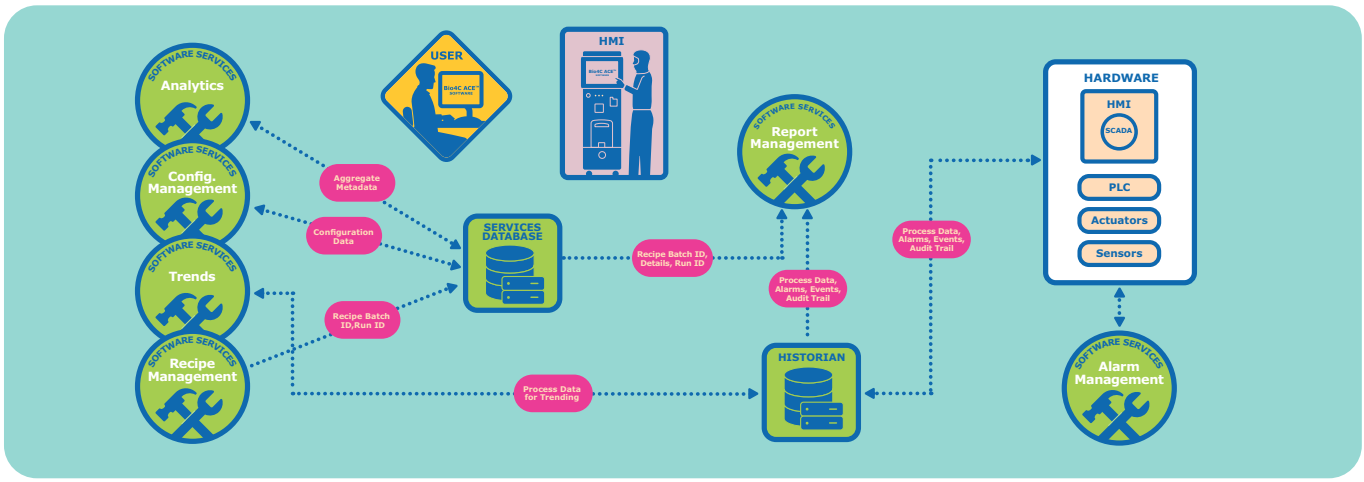
Data integrity definition: "The extent to which all data for its entire lifecycle is complete, consistent, and accurate." (Medicines and Healthcare Products Regulatory Agency, MHRA). The World Health Organization (WHO) and FDA add to the definition by using the principles of ALCOA and ALCOA+:

- **A**ttributable: who acquired the data or performed the action
- **L**egible: can you read and understand the data entries
- **C**ontemporaneous: documented at the time of the activity
- **O**riginal: first recording of data or a true copy
- **A**ccurate: reflects what took place
- **C**omplete: all recorded data requires an audit trail to show nothing has been deleted or lost
- **C**onsistent: ensuring data is chronological
- **E**nduring: ensuring data is available long after it is recorded
- **A**vailable: ensuring data is accessible

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 ACE™ software for Mobius® Cell Retention System facilitates compliance 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 ACE™ software for Mobius® Cell Retention System 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 (this is accomplished with the assistance of a Merck service engineer). The diagram that follows illustrates Bio4C ACE™ software for Mobius® Cell Retention System's process data flow: **Bio4C ACE™ Software Process Data Flow**  **Data Lifecycle Process Flow**  **Hardware Process Flow** When a backup is triggered for Bio4C ACE™ software for Mobius® Cell Retention System, database files are backed up and the restore function checks the integrity of these files during the restoration. Audit trail data flow: data are generated in local SCADA (supervisory control and data acquisition), stored in a local SQL database, transferred to Bio4C ACE™ software for Mobius® Cell Retention System SQL database, and backed up using the Bio4C ACE™ software for Mobius® Cell Retention System backup function.
212.110(b)	Requires that data be "stored to prevent deterioration or loss"	A restore feature is available within Bio4C ACE™ software for Mobius® Cell Retention System, but it is the customer's responsibility to execute a restore action on a regular basis to prove that no data is lost (this is accomplished with the assistance of a Merck service engineer).

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 ACE™ software for Mobius® Cell Retention System audit trails, functionality is available in accordance with 21 CFR Part 11 requirements. Using this functionality, the customer is able to trace 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 generated and stored by the system are original records and created at the time the action is performed. During operation any ungraceful shutdown could trigger a data loss of up to 18 minutes. It is the customer's responsibility to prevent any sudden power loss or shutdown by putting in place an uninterrupted power supply (UPS). Application does not support daylight savings time. 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.
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"	Bio4C ACE™ software for Mobius® Cell Retention System creates and stores the complete data from run summaries, audit trails, alarm events, event summaries, and logins and logouts performed within the system database. Application login and logout information is available in the system logs and can be accessed with the assistance of a Merck service engineer.
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 ACE™ software for Mobius® Cell Retention System data can be reviewed in the Report Management feature by an authorized user. Bio4C ACE™ software for Mobius® Cell Retention System 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. Merck policies and standards are followed in this case and are based on GAMP® 5. It is the customer's responsibility to have a process in place where 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 ACE™ software for Mobius® Cell Retention System, audit trail logging is available to show a timestamped record of 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. Merck policies and standards are followed in this case and are based on 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 and that are applicable to Bio4C ACE™ software for Mobius® Cell Retention System.

All the data integrity requirements are covered in the processes we follow and in the Bio4C ACE™ software for Mobius® Cell Retention System product.

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To learn more, please visit sigmaaldrich.com/control-software

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