AIR. NOTHING ELSE.

VALIDATION SUMMARY
MAS-100 SIRIUS®

The life science business of Merck KGaA, Darmstadt, Germany
operates as MilliporeSigma in the US and Canada.

Millipore®

INHALT

1. INTRODUCTION

This summary documents the validation of the MAS-100 Sirius® microbial air sampler. This instrument is developed following GAMP® 5 guidelines.

1.1. DESCRIPTION OF THE MAS-100 SIRIUS®

The MAS-100 Sirius microbial air sampler is a portable, active impaction type air sampler, able to collect viable airborn microorganisms on a wide range of nutrient plates. The instrument is developed as the next generation air sampler and is the direct successor of the MAS-100 NT.

It is a precision instrument offering reliable and traceable air sampling for quality control purposes in demanding applications ranging from pharmaceutical manufacturing environments to medical device production, hospitals, food and beverage or indoor air quality industries.

It fulfils all important regulatory standards including ISO 14698/ EN 17141 and EU GMP Annex 1. The instrument can be configured to various different use cases ranging from manual sampling routines to automated processes including control and data transfer to superordinate systems.

The housing and perforated lid are made of stainless steel with a seamless design to facilitate cleaning and decontamination. The perforated lid is magnetically attached and includes a handle to support aseptic handling. With full support for 21 CFR Part 11 workflows and data integrity (ALCOA+), it includes features such as a tamper proof audit trail and optional user management.

1.2. GLOSSARY

ABBREVIATION	MEANING
ASTM	American Society for Testing and Materials
BUI	Browser-based User Interface
CFR	Code of Federal Regulation
EMC	Electromagnetic compatibility
FDS	Functional Design Specification
FW	Firmware
GAMP®	Good Automated Manufacturing Practice
ISO®	International Organization for Standardization
ISPE®	International Society for Pharmaceutical Engineering
MS	Module specifications
NTP	Network time protocol
N/A	Not Applicable
SL	Standard Liter
SLPM	Standard Liter per Minute
SW	Software
TC	Test case
TCP	Transmission Control Protocol
TCX	Executed test case
URS	User Requirement specifications
VHP	Vaporous hydrogen peroxide

1.3. TRACEABILITY DURING PROJECT DEVELOPMENT AT MBV AG

The MAS-100 Sirius software and hardware documentation, including the specifications, requirements and validation documentation, are managed by MBV AG on Aligned Elements (Application Life Cycle Management system to ensure compliant development documentation for regulated products, for efficient design history file management which is fully 21 CFR Part 11 compliant). Each issue is traceable from User Requirement Specification (URS) to Functional Design Specification (FDS) to Module specification (MS) to Test Case (TC) and to Executed Test Case (TCX). The summary of the results in this validation report refers to the information captured in Aligned Elements.

The detailed documentation can be reviewed upon request by authorized agents of a customer during a scheduled audit at MBV AG.

1.4. QUALITY MANAGEMENT DOCUMENTATION REFERENCES

The following documents which support this validation summary may be consulted during a scheduled audit:

DOCUMENT TYPE	TITLE
R&D documents	User requirement specification (URS)
	Functional and design specification (FDS)
	Module specification (MS)
	Failure mode and effects analysis (FMEA)
	Test cases (TC)
	Executed Test Cases (TCX)
	Traceability matrix
Manuals	MAS-100 Sirius® User Manual
	MAS-100-Sirius® Quick Start Guide
IQ/OQ documents	IQ/OQ MAS-100 Sirius®

1.5. GUIDANCE AND REGULATION REFERENCES

The development and usage of MAS-100 Sirius® relate to following texts and regulations:

- Eudralex Volume 4: European Good Manufacturing Practice guidelines:
  - Annex 1: Manufacture of Sterile Medicinal Products
  - Annex 11: Computerized systems
- United States 21 CFR:
  - Part 210 and part 211 - Current Good Manufacturing Practice
  - Part 11 - Electronic Records; Electronic Signatures
- FDA Guidance for Industry: Sterile Drug Products Produced by Aseptic Processing — Current Good Manufacturing Practice
- ISO Guidelines
  - ISO 14644-1
  - ISO 14698: Cleanrooms and associated controlled environments - Biocontamination control
- EN Guidelines
  - EN ISO 17141: Cleanrooms and associated controlled environments - Biocontamination control
- ISPE® Guidelines
  - ISPE Good Practice Guide: Process Gases
  - ISPE® GAMP® 5 Guide: A Risk-Based Approach to Compliant GxP Computerized Systems

1.6. VALIDATION PURPOSE

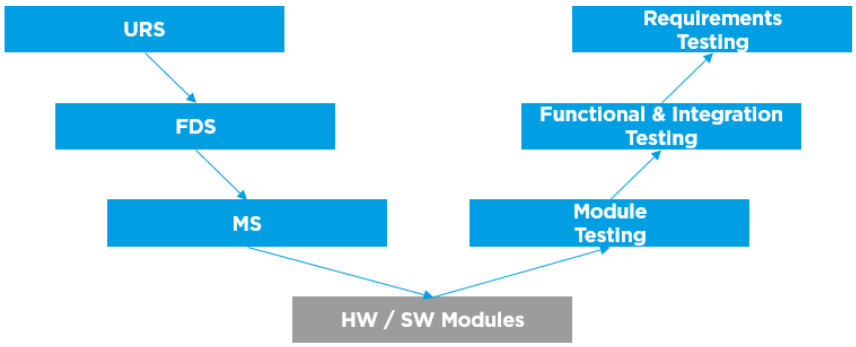
1.6.1. GENERALITIES

Aim of the present validation is to verify that the MAS-100 Sirius air sampler complies with its requirements and specifications.

The validation activities follow good engineering practices and development is managed following GAMP® 5. This includes the following:

- Requirements & Specifications: verify the completeness, correctness, and testability of the MAS-100 Sirius
- Code Verification to verify the compliance with Coding Standards and good coding practices
- Validation of the User Requirement Specification by running Application Test Cases
- Validation of the Functional Specification by running Integration Test Cases
- Traceability Matrix to keep track of the link between the Requirements/Specifications and the tests
- Risk Assessment including a Failure Mode and Effect Analysis.

The structure of the specifications / tests is according to category 3 (off-the-shelf product) as described in the GAMP® guidelines:



1.7. TEST PHASES AND FOCUS

TEST PHASE	TESTER	FOCUS	DEVICE UNDER TEST	EXAMPLE	MANAGED IN / TRACED TO
Requirement Testing	MBV & Validation partner	Testing based on URS & defined use cases (User manual)	Entire instrument & Software (SW)	Transportation test	Aligned Elements / URS
Functional & Integration Testing	MBV & development partners	Combination of individual modules	Entire instrument or combination of multiple modules	Sequential sampling (SQS)	Aligned Elements / FDS
Hardware Module Testing	MBV & development partners	Individual module functioning	Low level access to hardware modules	Performance testing of the real time clock	Aligned Elements / MS
Software Module Testing	MBV & SW development partners	Development tool for SW application	Software application with simulator	Sending and receiving Restful API commands	Aligned Elements / MS
Software Unit Testing	SW Development partner	SW development partners	Individual software class	N/A	SW partner

2. RESULTS

2.1. INSTRUMENT UNDER TEST

All validation activities were performed with the following material:

DESCRIPTION	ARTICLE NUMBER MBV	ARTICLE NUMBER MERCK KGAA, DARMSTADT, GERMANY	PICTURE
MAS-100 Sirius® The validation tests were carried out with a fleet of 12 validation instruments. In order to achieve greater statistical relevance, prototypes were also used where necessary.	200515 (calibrated for 100/200 SLPM, incl. perforated lid type ANS: 100 SLPM, 90mm) 201371 (calibrated for 100/200 SLPM, without perforated lid)	1178800001 1178810001	
Perforated lid type ANS: 100 SLPM, 90mm	201139	1178830001	
Perforated lid type ANR: Lid A 100 SLPM, 55/Growth Direct®	201152	1178850001	
Perforated lid type BNS: Lid B 200 SLPM, 90mm	201263	1178840001	
Perforated lid type BNR: Lid B 200 SLPM, 55/Growth Direct®	201267	1178860001	
MAS-100 Regulus®: Precision tool for adjustment and calibration of MAS-100 Sirius	130.3035	119153	

2.2. REQUIREMENTS AND SPECIFICATIONS VERIFICATION

The requirements and specifications verification was performed by reviews made by the project team before implementation and testing. This table lists an extract of the tests done on the MAS-100 Sirius instrument. The complete list of all test details is available in Aligned Elements.

2.3. REQUIREMENT TESTING

NAME	DESCRIPTION	EXPECTED RESULT	RESULT
MECHANICAL			
Instrument size and weight	Verify that the instrument (incl. perforated lid) size and weight meets the target dimensions.	- Instrument height is maximum 285mm (MAS-100 NT +15mm) due to optimal working height. - Instrument weight is maximum 2.7kg (MAS-100 NT +15%). Reflects the choice of stainless steel as material	Passed
Agar plate compatibility	Verify compatibility with different agar plate media.	Compatibility with 90mm settle plates, 55mm contact plates and Growth Direct® plates is proven.	Passed
OPERATION			
Cleaning and sterilization of the instrument exterior	Verify that cleaning of the housing and VHP decontamination of the outer instrument has no adverse effect on the handling process.	- Cleaning test with wipe and spray cleaning of the housing with standard agents (Ethanol, 70/30 IPA, Quaternary ammonium, H2O2 + peracetic acid) has no adverse effect on the instrument. - 30 back-to-back VHP decontamination cycles have no adverse effect on the instrument .	Passed
Decontamination of the instrument using VHP	Study the VHP decontamination efficacy at critical locations of the instrument and its internal head volume using bioindicators and enzyme indicators.	- The reference VHP cycle successfully achieved complete microbial inactivation (6-log reduction) at all critical locations on and inside the instrument. - No visual or structural degradation was observed on the tested materials.	Passed
Perforated lid resistance to autoclaving	Verify that the perforated lid can be autoclaved.	Repeated autoclaving cycles (50 cycles at 134°C for 5mins) on the lid of MAS-100 Sirius does not lead to loss of function or rusting.	Passed
Performance test under ambient conditions +/- 2.5%	Verify instrument performance at ambient conditions (i.e. temperature, pressure, humidity) for all variations of the handling process parameters incl. flow rates of 100 and 200 SLPM.	Performance is verified and accuracy meets the specifications +/- 2.5% maximum flow deviation.	Passed
Performance test under environmental conditions	Verify the instrument performance at extremes of operation range (0°C and 40 °C).	Performance is verified and accuracy meets the specifications +/- 2.5% maximum flow deviation under all conditions at the extremes of operation at 0°C as well as at 40°C.	Passed
Minimal battery running time	Verify how many samplings can be performed with one fully charged battery.	A fully charged battery can deliver at least 40 samplings with 1000SL volume at a 100SLPM flow rate with Lid type A*.	Passed
Instrument check	Verify correct lid type used and filter present during sampling	- Warning is issued if wrong lid type is used - Warning is issued if filter is not present - Warnings are display on local user interface during and at end of a sampling - Warning ID's included in result QR code and audit trail	Passed
Tripod mounting	Verify that MAS-100 Sirius can be safely mounted on a tripod using the quick change adapter and adapter plate.	MAS-100 Sirius is securely mounted on the tripod and remains stable during use.	Passed

Audit trail notes	Verify that a pre-selected note can be chosen on the instrument's touchscreen in case of a failed sampling.	- Sampling notes can be added in case of a failed sampling. - Notes can be selected from a predefined list.	Passed
SERVICE			
Warranty seal	Verify the presence of a warranty seal preventing unauthorized access.	A warranty seal prevents the user from opening the instrument base.	Passed
Battery replacement	Verify that the user is able to exchange the battery of the instrument without violating the instruments warranty seal.	Battery replacement possible	Passed
REGULATORY COMPLIANCE			
Transportation test	Verify that transportation does not have an influence on MAS-100 Sirius performance. Packaging of the instrument is done by MBV logistics. The transportation test is done according to ASTM D4169-23e1 DC 13. Climatic stressing preconditioning, Drop test sequence 1, Compression (vehicle stacking), Vehicle vibration, Loose load vibration, Drop test sequence 2.	- Packaging maintains integrity. - MAS-100 Sirius® is not damaged and fully functional.	Passed
EMC Testing	Verify electromagnetic compatibility including emission and immission/immunity by an external lab. Tests were conducted according to IEC 61326-1:2020.	Found to be in conformity with the standard.	Passed
Electrical safety testing	Verify electrical safety by an external lab. Tests according to IEC 61010-1:2010, IEC 61010-1:2010/AMD1:2016, IEC 61010-2-081:2019.	Found to be in conformity with the standard.	Passed
Disturbance of the unidirectional air flow	Verify that the instrument does not disrupt the unidirectional air flow of the cleanroom.	Computational fluid dynamics (CFD) simulations and smoke studies have demonstrated that the instrument does not disrupt the laminar airflow profile.	Passed
Particle emission	Verify the filtering performance of the integrated ISO 35H (HEPA H13) filter with acceptance values that do not exceed the specified ISO 5/ grade A according to ISO 14644-1/EU GMP Annex 1.	MAS-100 Sirius with integrated filter emitted particle levels during operation are below the limits for ISO 5/grade A.	Passed
Noise emission	Verify that the maximum noise emission during instrument operation does not exceed 70dB and fulfils ISO 14644-16 and OSHA.	The maximum noise in operation emission is below 60dB.	Passed
Physical sampling efficiency	Verification of theoretical d_{50} value <2µm according to ISO 14698.	Theoretical d_{50} value of 1.1µm for both 100 as well as 200 SLPM flow rates using corresponding perforated lids.	Passed
Biological sampling efficiency	Determine biological sampling efficiency according to simplified laboratory method of EN 17141.	100 +/- 50% recovery rate compared to qualified reference (MAS-100 NT).	Passed

2.4. FUNCTIONAL AND INTEGRATION TESTING

NAME	DESCRIPTION	EXPECTED RESULT	RESULT
MECHANICAL			
Impact protection rating of instrument	Verify impact protection as part of electrical safety test.	The IK rating of the instrument is at least IK06.	Passed
Electrical interfaces	Verify that the electrical interfaces of MAS-100 Sirius are clearly described and all functions are tested.	- MAS-100 Sirius has a USB-C port for charging and calibration purposes. - A USB-A port is accessible from the bottom of the instrument and can be used to connect a WiFi dongle to MAS-100 Sirius. - The electrical interfaces are easily accessible by the user. - The functionality of all interfaces is verified.	Passed
OPERATION			
Instrument access on local user interface (LUI) and browser-based user interface (BUI)	Verify the user login process based on user roles and rights.	- Without restricted access: Login not required to access and adapt instrument. - When user management is set up and password-restricted, the access to most of the functionality of the BUI is only possible after login with the System Administrator role and password. - The User management is reserved for the User Administrator role.	Passed
Audit trail	Verify instrument audit trail functionality.	- The Audit Trail can be accessed from the BUI corresponding to the instrument settings; it loads and is displayed correctly; it is tamper proof within instrument. - Each entry has a specific time stamp and the user information. - The exported Audit Trail is provided as a checksum-protected xml format (tamper evident outside instrument). - It is not possible to clear the instrument .log without prior export and a software update does not alter prior entries of the Audit Trail.	Passed
Sensor functionality	Verify whether sensors and blower perform as expected under application conditions.	- The instrument can be initialized. - Sampling is available and the BUI is accessible.	Passed

2.5. MODULE TESTING

NAME	DESCRIPTION	EXPECTED RESULT	RESULT
MECHANICAL			
Housing material	Verify that the instrument housing is made from 316L stainless steel.	With the exception of the display, the base feet and electronic connections, the instrument is made entirely of 316L stainless steel.	Passed
Lifetime testing	Verify that the functionality of all components and the entire system for prolonged use.	Instrument functionality was proven without any issues for a usage equivalent to at least two years of daily sampling (20 samples of 1'000 L at flow rates of 100 or 200 SLPM).	Passed
Instrument operation with cleanroom gloves	Verify that the instrument can be operated using single up to multi layered cleanroom gloves.	- The LUI can be operated with single/double and some triple-layered latex gloves as well as single-layered nitrile gloves. - The instrument does not have sharp edges that pose a risk to the integrity of the gloves.	Passed
OPERATION			
Configuration	Verify configuration submenu for System Administrator: Presence and functionality of all configurations All changes in the configuration submenu are logged in the Audit Trail.	- Time configuration works as expected. - Interface configurations work as expected. - Custom instrument label works as expected. - Handling process parameters works as expected.	Passed
Instrument self test	Verify the instrument self test.	- The BUI allows performing an instrument self-test to verify the instrument and all sensors are functional. - The test output can be displayed as XML format test report.	Passed
Timeout/Logout	Verify the timeout behavior.	- The logged in user is automatically logged out upon timeout. - The timeout time matches the corresponding setting.	Passed
File integrity check	Verify that the BUI offers a validity check for exported MAS-100 Sirius files to ensure their integrity and confirm that the files have not been altered.	- The setting file export can be verified and any manually altered file is detected. - The user list export can be verified and any manually altered file is detected. - The service file export can be verified and any manually altered file is detected. - The Audit Trail export can be verified and any manually altered file is detected.	Passed
Error and warning handling	The instrument detects errors	- In the event of an error, the instrument reports an error on the LUI and writes a corresponding Audit Trail entry. - Warnings are logged in the Audit Trail without additional LUI notification. - When an error occurs during sampling, the error is displayed only after the sampling result screen is shown. An Audit Trail entry is triggered.	Passed
Timer calibration	Verify the accuracy of the instrument timer.	The BUI allows performing a timer calibration to verify the instrument timer against a NTP reference server. Maximum deviation is 0.25%.	Passed

Software update	Verify that instrument application software can be updated through the BUI.	- The BUI has a button on the advanced settings tile to trigger a software update. - After the software update the Audit trail and the instrument configurations are unaffected.	Passed
REGULATORY COMPLIANCE			
Life cycle assessment	The instrument has undergone a detailed life cycle assessment.	The environmental impact of the instrument was evaluated, and the development incorporated measures to maximize sustainability.	Passed
Type label	The instrument type label is checked for conformity.	- Type label is checked by an external regulatory body. - The instrument serial number is displayed at the front in human and machine readable (QR code) format	Passed

MBV AG, Industriestrasse 9, CH-8712 Stäfa, T +41 44 928 30 80, welcome@mbv.ch, www.mbv.ch

2.6. 21 CFR PART 11 AND EUDRALEX ANNEX 11 ASSESSMENT

The following table summarizes the requirements of 21 CFR part 11 and Eudralex Annex 11 along with the technical implementation on how the MAS-100 Sirius is addressing these requirements.

Please note that the applications software of MAS-100 Sirius only manages electronic records and does not cover electronic signatures (as there is no use case requiring a signature).

The compliance table is built according to the following rules:

- In the first column, preceded by its reference in the 21CFR11 regulation, lists the textual repetition of the requirement stated by the FDA,
- In the second column, preceded by its reference in the Eudralex Annex 11 regulation, lists the textual repetition of the requirement stated by the European Good Manufacturing Practice,
- In the third column, the mode of response to this requirement is given:
  - **'P'** if it must be "Proceeded" by the customer (end user)
  - **'S'** if the **System** (MAS-100 Sirius) must ensure it or is covered through a process at the manufacturer
- In the fourth column, it is described how the system and user address the requirement.
- In the fifth column, the result of test stating is provided. The compliance evaluation is either “Passed” or “Failed” and N/A is used when a requirement is not applicable to the application software.

REQUIREMENT 21 CFR PART 11	ANNEX 11	MODE OF RESPONSE	TECHNICAL IMPLEMENTATION	TEST STATUS
B-11.10.a - Validation of systems to ensure accuracy, reliability, consistent intended performance, and the ability to discern invalid or altered records.	4.1 - Do validation documents and reports cover the relevant steps of the life cycle?	S	Development and validation according GAMP5 (includes SW validation of 21 CFR 11 relevant functionality).	Passed
		S	Approval of setting changes may be enforced.	Passed
		S	Integrity of exported files may be checked. (Applies to Audit Trail including sampling results (replicated in result QR-code), calibration certificates, exported instrument setting, exported user list, service file download.)	Passed
		S	Validation Summary (this document) covers the relevant steps of the life cycle.	Passed
B-11.10.b - The ability to generate accurate and complete copies of records in both human readable and electronic form suitable for	8.1 - Is the system capable of producing clear printed	S	Audit trail may be viewed on the instrument (via BUI), printed and exported to a checksum protected file in. .xml format.	Passed

REQUIREMENT 21 CFR PART 11	ANNEX 11	MODE OF RESPONSE	TECHNICAL IMPLEMENTATION	TEST STATUS
inspection, review, and copying by the agency. Persons should contact the agency if there are any questions regarding the ability of the agency to perform such review and copying of the electronic records.	.copies of electronically stored data? 8.2 - For records supporting batch release it should be possible to generate printouts indicating if any of the data has been changed since the original entry.	S	Altering of data on the instrument possible is not possible.	Passed
B-11.10.c - Protection of records to enable their accurate and ready retrieval throughout the records retention period.	17 - Is data archived? If data is archived, is it checked for accessibility, readability, and integrity? When changes are made to the system, is the ability to retrieve archived data ensured and tested? 7.2 - Are regular back-ups of relevant data done? How is the integrity and accuracy of data and the ability to restore data checked during validation and monitored periodically?	S	No overwriting/altering of data on the instrument possible. Memory warning and memory limit ensure enough free memory remaining to allow export of data. Clearing instrument memory only possible after export.	Passed
		P	Perform regular back-up of data.	customer responsibility
		P	File integrity check may be performed on exported audit trail before deleting the data from the instrument.	customer responsibility
		P	Secure long-term retention of exported audit trails for the legal retention period (manufacturer responsibility ends with successful export of the file).	customer responsibility
		P	Print calibration certificate after every calibration and secure long-term retention for the legal retention period.	customer responsibility
		S	Exported audit trails cannot be imported back onto the instrument.	Passed
B-11.10.d - Limiting system access to authorized individuals.	10 - Are system changes made in a controlled manner in accordance with a defined procedure? 12.1 - Are physical and/or logical controls in place to restrict access to the system? 12.2 - Do the security controls extend depending on the criticality of the system? 12.3 - Is the creation, change and cancellation of access authorizations recorded?	P	Physical access to instrument restricted to concerned employees (e.g. access to production area controlled with employee badge) + password protected access to the device.	customer responsibility
		P	Access to data network restricted to concerned employees (IT access restrictions).	customer responsibility
		S	User management with dedicated user roles, defined access per user role, individual user names and passwords may be setup (no direct access to file system).	Passed

REQUIREMENT 21 CFR PART 11	ANNEX 11	MODE OF RESPONSE	TECHNICAL IMPLEMENTATION	TEST STATUS
		S	Automatic blocking of user after 3x wrong password used.	Passed
		P	The user management shall be setup on the instrument and appropriate password complexity set.	customer responsibility
		P	Create and administer users, including setting password validity periode and manual blocking or archiving users who should no longer have access. Creation, change and cancellation of access shall be recorded.	customer responsibility
		P	Perform and document regular user reviews.	customer responsibility
		S	Automatic standby/logout after time of inactivity.	Passed
		S	Only trained Service engineers are provided login credentials.	Passed
B-11.10.e - Use of secure, computer generated, time stamped audit trails to independently record the date and time of operator entries and actions that create,	14.c - Do electronic signatures include the time and	S	Audit trail automatically records all user action and instrument events with timestamp, username and in case of setting changes the old and new value.	Passed

REQUIREMENT 21 CFR PART 11	ANNEX 11	MODE OF RESPONSE	TECHNICAL IMPLEMENTATION	TEST STATUS
modify, or delete electronic records. Record changes shall not obscure previously recorded information. Such audit trail documentation shall be retained for a period at least as long as that required for the subject electronic records and shall be available for agency review and copying.	date that they were applied? 12.4 - Is the system designed to record the identity of operators entering, changing, confirming, or deleting data including date and time? 9 - Consideration should be given, based on a risk assessment, to building into the system the creation of a record of all GMP-relevant changes and deletions (a system generated "audit trail"). For change or deletion of GMP- relevant data the reason should be documented. Audit trails need to be available and convertible to a generally intelligible form and regularly reviewed. 7.1 - How is data secured by both physical and electronic means against damage? How is data accessible throughout the retention period?	S	No overwriting/altering of data on the instrument possible. Memory warning and memory limit ensure enough free memory remaining to allow export of data. Clearing instrument memory is only possible after export.	Passed
		S	The instrument time & date synchronization may be configured.	Passed
		P	Secure long-term retention of exported audit trails for the legal retention period (manufacturer responsibility ends with successful export of the file).	customer responsibility
		P	Print calibration certificate after every calibration and secure long-term retention for the legal retention period.	customer responsibility
		S	Audit trail may be viewed on the instrument (via BUI), printed and exported to a checksum protected file in. .xml format.	Passed
		S	Non-volatile memory retaining data independent of state of battery charge or connection of Power Supply.	Passed
		S	Robust stainless steel housing mechanically protects electronics.	Passed
B-11.10.f - Use of operational system checks to enforce permitted sequencing of steps and events, as appropriate	5 - Computerized systems exchanging data electronically with other systems should include appropriate built-in checks for the correct and secure entry and processing of data, in order to minimize the risks. 6 - For critical data entered manually, there should be an additional check on the accuracy of the data. This check may be done by a second operator or by validated electronic means. The criticality and the potential consequences of erroneous or incorrectly entered data to a system should be covered by risk management.	S	Fixed sequence with optional screens to guide user.	Passed
		P	Configure optional screens as needed.	customer responsibility
		S	Manual data entry by the Operator is not supported.	Passed
		P	Enforce settings approval to enforce review of manual entry of setting changes.	customer responsibility
B-11.10.g - Use of authority checks to ensure that only	N/A	S	User management with role based access rights.	Passed

REQUIREMENT 21 CFR PART 11	ANNEX 11	MODE OF RESPONSE	TECHNICAL IMPLEMENTATION	TEST STATUS
authorized individuals can use the system, electronically sign a record, access the operation or computer system input or output device, alter a record, or perform the operation at hand.		P	User Management: generate users, review user lists, block or archive user which are no longer authorized (deleting users is not possible to maintain consistency of records), unblock users which were blocked (e.g. after repeated entry of wrong password or administrative reasons or via Active Directory).	customer responsibility
		P	Enable settings approval in the instrument settings.	customer responsibility
		S	No overwriting/altering of data on the instrument possible.	Passed
B-11.10.h - Use of device (e.g., terminal) checks to determine, as appropriate, the validity of the source of data input or operational instruction.	4.8 - When data is transferred to another data format or system, does the system check the validity to confirm data was not altered in value and/or meaning during migration.	S	Only provides valid options to the user based on user role, user login state and current state of instrument.	Passed
		S	Consistency of downloaded data is verified in the process.	
		S	Integrity of exported files may be checked.	Passed
B-11.10.i - Determination that persons who develop, maintain, or use electronic record systems have the education, training, and experience to perform their assigned tasks.	2 - Is there close cooperation between all relevant personnel such as process owner, system owner, qualified persons, and IT? Do all personnel have appropriate qualifications, level of access and defined responsibilities to carry out their assigned duties?	S	Manufacturer: operation under ISO9001, job profiles include requirements.	Passed
		P	User training and assignment of appropriate role.	customer responsibility
B-11.10.j - The establishment of, and adherence to, written policies that hold individuals accountable and responsible for actions initiated under their electronic signatures, in order to deter record and signature falsification.	N/A	N/A	not applicable – the system does not handle electronic signatures.	N/A
B-11.10.k - Use of appropriate controls over systems documentation including: (1) Adequate controls over the distribution of, access to, and use of documentation for system operation and maintenance. (2) - Revision and change control procedures to maintain an audit trail that documents time-sequenced development and modification of systems documentation.	4.2 - Do validation documents include change control records (if applicable) and reports on deviations observed during the validation process?	S	Development complies with GAMP5, validation of changes.	Passed
		S	User manual available to buyer of instrument.	Passed
		S	Documentation changes are undergoing release process, including document versioning.	Passed
		P	Manage user specific documents and procedures.	customer responsibility
		S	Life Cycle Management Tool (Aligned Elements) tracks changes and deviations.	Passed

REQUIREMENT 21 CFR PART 11	ANNEX 11	MODE OF RESPONSE	TECHNICAL IMPLEMENTATION	TEST STATUS
B-11.30 - Persons who use open systems to create, modify, maintain, or transmit electronic records shall employ procedures and controls designed to ensure the authenticity, integrity, and, as appropriate, the confidentiality of electronic records from the point of their creation to the point of their receipt. Such procedures and controls shall include those identified in § 11.10, as appropriate, and additional measures such as document encryption and use of appropriate digital signature standards to ensure, as necessary under the circumstances, record authenticity, integrity, and confidentiality.	N/A	S	Not applicable – the system is considered a closed system as per definition in A-11.3(b)(4).	N/A
B-11.50.a - Signed electronic records shall contain information associated with the signing that clearly indicates all of the following: (1) The printed name of the signer; (2) The date and time when the signature was executed; and (3) The meaning (such as review, approval, responsibility, or authorship) associated with the signature	N/A	S	Not applicable - no action is possible on the instrument which require a signature.	N/A
B-11.50.b - The items identified in paragraphs (a)(1), (a)(2), and (a)(3) of this section shall be subject to the same controls as for electronic records and shall be included as part of any human readable form of the electronic record (such as electronic display or printout).	N/A	S	Not applicable - no action is possible on the instrument which requires a signature.	N/A
B-11.70 - Electronic signatures and handwritten signatures executed to electronic records shall be linked to their respective electronic records to ensure that the signatures cannot be excised, copied, or otherwise transferred to falsify an electronic record by ordinary means.	14(b) - Are electronic signatures permanently linked to their respective record.	S	Not applicable - no action is possible on the instrument which requires a signature. Changes of instrument settings and parameters are controlled by role based access control.	N/A
C-11.100 a - Each electronic signature shall be unique to one individual and shall not be reused by, or reassigned to, anyone else.	N/A	S	Not applicable - no action is possible on the instrument which require a signature.	N/A

REQUIREMENT 21 CFR PART 11	ANNEX 11	MODE OF RESPONSE	TECHNICAL IMPLEMENTATION	TEST STATUS
C-11.100 b - Before an organization establishes, assigns, certifies, or otherwise sanctions an individual's electronic signature, or any element of such electronic signature, the organization shall verify the identity of the individual	N/A	S	Not applicable - no action is possible on the instrument which requires a signature.	N/A
C-11.100 c - Persons using electronic signatures shall, prior to or at the time of such use, certify to the agency that the electronic signatures in their system, used on or after August 20, 1997, are intended to be the legally binding equivalent of traditional handwritten signatures. (1) The certification shall be submitted in paper form and signed with a traditional handwritten signature, to the Office of Regional Operations (HFC–100), 5600 Fishers Lane, Rockville, MD 20857 (2) Persons using electronic signatures shall, upon agency request, provide additional certification or testimony that a specific electronic signature is the legally binding equivalent of the signer's handwritten signature	14 (a) - Do electronic signatures have the same impact as hand-written signatures within the boundaries of the company?	P	Not applicable - no action is possible on the instrument which requires a signature.	N/A

REQUIREMENT 21 CFR PART 11	ANNEX 11	MODE OF RESPONSE	TECHNICAL IMPLEMENTATION	TEST STATUS
C-11.200 a - Electronic signatures that are not based upon biometrics shall: (1) Employ at least two distinct identification components such as an identification code and password (i) When an individual executes a series of signings during a single, continuous period of controlled system access, the first signing shall be executed using all electronic signature components; subsequent signings shall be executed using at least one electronic signature component that is only executable by, and designed to be used only by, the individual (ii) When an individual executes one or more signings not performed during a single, continuous period of controlled system access, each signing shall be executed using all of the electronic signature components (2) Be used only by their genuine owners; and (3) Be administered and executed to ensure that attempted use of an individual's electronic signature by anyone other than its genuine owner requires collaboration of two or more individuals	N/A	S	Not applicable - there are no activities which require signatures. However, the role-based access control for advanced functions (system administrator and user administrator) consists of a username and a password. The access control for the operator role (which has no change rights on instrument setting) is configurable by the system administrator. A use of credentials by someone other than the genuine user is not allowed by the system. But the task can be performed by someone else with the same user role.	N/A
C-11.200 b - Electronic signatures based upon biometrics shall be designed to ensure that they cannot be used by anyone other than their genuine owners.	N/A	S	Not applicable - There is no biometric access to the system	N/A
C-11.300 - Persons who use electronic signatures based upon use of identification codes in combination with passwords shall employ controls to ensure their security and integrity. Such controls shall include:	N/A	S	Not applicable - there are no activities which require signatures.	N/A
C-11.300 a - Maintaining the uniqueness of each combined identification code and password, such that no two individuals have the same combination of identification code and password.	N/A	S	Not applicable - there are no activities which require signatures. However, the system checks that the user name is unique and hence prevents identical combination of identification code and password.	N/A

REQUIREMENT 21 CFR PART 11	ANNEX 11	MODE OF RESPONSE	TECHNICAL IMPLEMENTATION	TEST STATUS
C-11.300 b - Ensuring that identification code and password issuances are periodically checked, recalled, or revised (e.g., to cover such events as password aging)	11 - Are computerized systems periodically evaluated to confirm that they remain in a valid state? Such evaluations should include, where appropriate, the current range of functionality, deviation records, incidents, problems, upgrade history, performance, reliability, security, and validation status reports.	S	Not applicable - there are no activities which require signatures. However, upon user creation the renewal timeframe can be set by the user administrator.	N/A
C-11.300 c - Following loss management procedures to electronically deauthorize lost, stolen, missing, or otherwise potentially compromised tokens, cards, and other devices that bear or generate identification code or password information, and to issue temporary or permanent replacements using suitable, rigorous controls.	N/A	S	Not applicable - there are no activities which require signatures. However, a user can be blocked by the user administrator. A user is temporarily suspended after 3 unsuccessful login attempts	N/A
C-11.300 d - Use of transaction safeguards to prevent unauthorized use of passwords and/or identification codes, and to detect and report in an immediate and urgent manner any attempts at their unauthorized use to the system security unit, and, as appropriate, to organizational management.	N/A	S	Not applicable - there are no activities which require signatures.	N/A
C-11.300 e - Initial and periodic testing of devices, such as tokens or cards, that bear or generate identification code or password information to ensure that they function properly and have not been altered in an unauthorized manner.	N/A	P	Not applicable - there are no activities which require signatures. However, the access control system is based solely on username and password without tokens or cards.	N/A
N/A	1 - Are decisions on the extent of validation and data integrity controls based on a justified and documented risk assessment?	S	Development and validation according GAMP5.	Passed
N/A	3.1 - When third parties are used to provide, install, configure, integrate, validate, maintain, modify, or retain the system, do formal agreements exist?	S	Operation under ISO9001.	Passed
		P	Ensure appropriate control.	customer responsibility
N/A	3.2 - Are third parties audited? 3.4 - Is quality system and audit information relating to third party suppliers or developers of software & implemented systems available to inspectors on request?	S	Operation under ISO9001	Passed

REQUIREMENT 21 CFR PART 11	ANNEX 11	MODE OF RESPONSE	TECHNICAL IMPLEMENTATION	TEST STATUS
N/A	3.3 - Is documentation from commercial off-the-shelf products reviewed to check that user requirements are fulfilled?	P	Review documentation to ensure user requirements are fulfilled.	customer responsibility
N/A	4.3 - Is an up to date listing of relevant systems and their GMP functionality available? For critical systems, an up to date system description detailing the physical and logical arrangements, data flows and interfaces with other systems or processes, hardware and software pre-requisites and security measures is available.	S	Development and validation according GAMP5.	Passed
		P	Maintain documentation for integrated system.	customer responsibility
N/A	4.4 - Do user requirement specifications describe the required functions of the system? Is URS based on documented risk assessment and GMP impact. Are User requirements traceable throughout the life-cycle?	S	Development URS based on known user requirement, managed in a life-cycel management system.	Passed
		P	Ensure URS aligned to customer process.	customer responsibility
N/A	4.5 - Was the system developed in accordance with an appropriate quality management system?	S	Operation under ISO9001.	Passed
N/A	4.6 - For customized systems, what process is in place to ensure the formal assessment and reporting of quality and performance measures for the life-cycle stages of the system.	N/A	N/A – system is not customized.	N/A
N/A	4.7 - What evidence of test methods and scenarios are available? Were parameter limits, data limits and error handling considered? How are automated testing tools and test environments assessed for adequacy?	S	Test cases are documented in life-cycle management tool. Industry standard tools are used, in alignment with their intended use case.	Passed
N/A	13 - Are all incidents reported and assessed? Is the root cause of critical incidents identified? Does the identified root cause form the basis of corrective and preventive actions?	P	Ensure compliant incident management in operation of the system.	customer responsibility
N/A	15 - Does the system allow only qualified persons to certify the release of batches and clearly identify and record the person releasing or certifying the batches?	S	System is not performing batch release.	Passed
		P	Ensure compliant batch release, based on data and results provided by the system.	customer responsibility

REQUIREMENT 21 CFR PART 11	ANNEX 11	MODE OF RESPONSE	TECHNICAL IMPLEMENTATION	TEST STATUS
N/A	16 - What provisions are made to ensure continuity of support for critical processes in the event of a system breakdown? Is the time required to bring alternative arrangements into use based on risk and appropriate for the system and business process it supports? Are these arrangements adequately documented and tested?	S	Manufacturer: Business Contingency Plan is in place.	Passed

3. CONCLUSION

The conclusion of the MAS-100 Sirius validation is that the requirements and functional specifications have been fully met, and the system is released for operation within the scope of the product specifications.The MAS-100 Sirius instrument is fit for its intended use.

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