AIR. NOTHING ELSE.

VALIDATION SUMMARY

MAS-100 Atmos® microbial compressed gas sampler

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

Millipore®

DOCUMENT HISTORY

DOCUMENT ID	VERSION	HISTORY
20754608	1.0	Initial release

TRADEMARKS

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MBV AG	
MAS-100 Atmos®	Switzerland
MAS-100 NT®	

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1. INTRODUCTION

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

2. DESCRIPTION OF THE MAS-100 ATMOS®

The MAS-100 Atmos® microbial compressed gas sampler is a high precision, portable and battery-operated instrument for the collection and enumeration of microorganisms in pressurized gases such as air, nitrogen (N_2), carbon dioxide (CO_2) and argon (Ar).

The instrument is very easy to use and can be operated in a pressure range of 1.2 to 7 bar.a (17.4 to 101.5 Psi). The sampling principle is based on impaction like the Andersen air sampler. At the default flow rate of 100 liter/min (LPM) the instrument provides a physical efficiency with a nominal D50 of 1.1 µm.

The instrument allows flexible adaption to various digitalized levels, including a 21 CFR part 11 compliant software and tamper-proofed audit trail download. Barcode scanners can be connected directly to the instrument to track culture media, sampling head and sampling location. A unique sampling result barcode can be integrated in computerized LIMS or EM workflows.

A broad range of culture media formulations in 90 mm Petri dishes can be selected for the detection of various microorganisms.

3. REFERENCES

3.1 GLOSSARY

ASTM	American Society for Testing and Materials
CFR	Code of Federal Regulation
CFU	Colony Forming Unit
CSV	Computerized System Validation
DDS	Detailed Design Specification
EM	Environmental monitoring
FDS	Functional and design specification
FS	Functional Specifications
GAMP®	Good Automated Manufacturing Practice
HW	Hardware
IQ	Installation Qualification
ISO®	International Organization for Standardization
ISPE®	International Society for Pharmaceutical Engineering

LPM	Liters per Minute
Mango CARA	Merck quality documentation system
MS	Module specifications
N/A	Not Applicable
OQ	Operational Qualification
P	Proceeded
PCB	Printed circuit board
PQ	Performance Qualification
SW	Software
TC	Test case
TCX	Executed test case
UI	User interface
URS	User Requirement specifications
WebUI	Web-based User Interface

3.2 TRACEABILITY DURING PROJECT DEVELOPMENT AT MBV AG

The MAS-100 Atmos® software and hardware documentation, including the specifications, requirements and validation documentation, are managed by MBV AG on Aligned Elements (Life Cycle Management system to ensure compliant development documentation for regulated products, for efficient design history file management which is fully CFR 21. Part 11 compliant). Each issue is traceable from URS to FDS to MS to TC and to TCX.

The detailed documentation can only be viewed upon request by authorized agents of a customer during a scheduled audit.

3.3 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
	Functional and design specification 320_Ceres
	Module specification 320_Ceres
	Failure mode and effects analysis 320_Ceres
	System concept 320_Ceres
	Master Test Plan Ceres
	Test cases (in Aligned Elements)
	Master Test Report Ceres
	Executed Test cases Ceres (in Aligned Elements)
	Ceres traceability matrix (Coverage matrix from RQ (URS) to PS (FS), DDS (Module spec), TC and TCX)
CSV Documents	FRP 180A-TP Test Plan For Verification And Validation of the MAS-100 Atmos® 21CFR11 Compliance
	FRP180A-IQP Installation qualification Protocol For MAS-100 Atmos® 21CFR11 Compliance
	FRP180A-OQP Operational Qualification Protocol For MAS-100 Atmos® 21CFR11 Compliance
	FRP180A-PQP Performance Qualification Protocol For MAS-100 Atmos® 21CFR11 Compliance
	FRP180A-IQR Installation Qualification Execution Report For MAS-100 Atmos® 21CFR11 Compliance
	FRP180A-OQR Operational Qualification Execution Report For MAS-100 Atmos® 21CFR11 Compliance
	FRP180A-PQR Performance Qualification Execution Report For MAS-100 Atmos® 21CFR11 Compliance
	FRP180A-TSR Test Summary Report For MAS-100 Atmos® 21CFR11 Compliance
	FRP 180A-TM Traceability Matrix For Verification And Validation Of The MAS-100 Atmos® 21CFR11 Compliance
	FRP180A - MAS-100 Atmos® 21CFR11/Eu Annex 11 Assessment
	FRP 180A- OBS MAS-100 Atmos® Deviation Handling During Qualification
User Manuals	MAS-100 Atmos® User Manual
	MAS-100-Atmos® Quick Start Guide

3.4 GUIDANCE AND REGULATION REFERENCES

The development and usage of MAS-100 Atmos® relate to following texts and regulation:

- Eudralex Volume 4: European Good Manufacturing Practice guidelines:
  - Annex 1: Manufacture of Sterile Medicinal Products;
  - Annex 11: Computerized systems;
- 21 CFR, part 210 and part 211 - US Current Good Manufacturing Practice;
- 21 CFR, part 11 - Electronic Records; Electronic Signatures;
- FDA Guidance for Industry: Sterile Drug Products Produced by Aseptic Processing — Current Good Manufacturing Practice;
- ISO® EN 17141: Cleanrooms and associated controlled environments - Biocontamination control;

– ISO® 8573-7: Compressed air — Part 7: Test method for viable microbiological contaminant content;
– ISPE® Good Practice Guide: Process Gases;
– ISPE® GAMP® 5 Guide: A Risk-Based Approach to Compliant GxP Computerized Systems.

4. VALIDATION PURPOSE

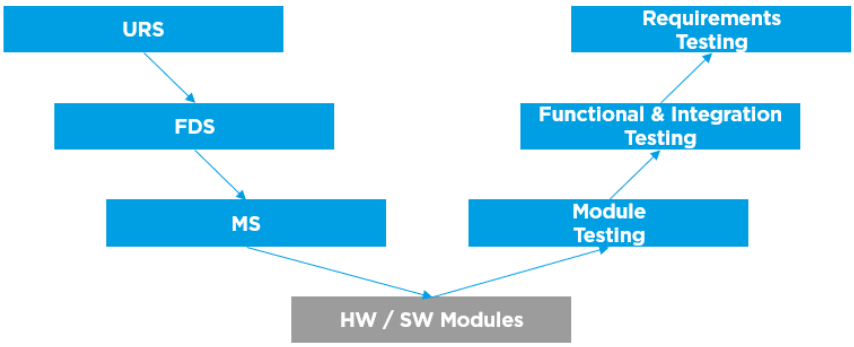
4.1 GENERALITIES

Aim of the present validation is to verify that the MAS-100 Atmos® 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 Atmos®
– Code Verification to verify the compliance with Coding Standards and code Writing Good 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 5 product as described in the GAMP® guidelines:



4.2 TEST PHASES AND FOCUS

TEST PHASE	TESTER	FOCUS	DEVICE UNDER TEST	EXAMPLE	MANAGED IN / TRACED TO
Requirement testing	MBV & Millipore® & Validation partner	End user application: Testing based on URS & defined use cases (User manual)	Entire instrument & Software	21CFR11 assessment Use case derived from User Manual Acceptance test from MBV towards external developers / Millipore®	Aligned Elements / URS Mango
Functional & integration testing	MBV & development partners	Combination of individual modules	Entire instrument or combination of multiple modules and interfaces including control software	Interaction with calibration unit for MAS-100 Atmos Lifetime testing Check performance	Aligned Elements / FDS
Hardware module testing	MBV & development partners	Individual module functioning	Low level access to hardware modules	Performance of individual sensors Battery charging circuit	Aligned Elements / MS
Software module testing	MBV & SW development partners	Development tool for SW application	Software application with simulator	Gas flow control loop Verification of individual commands	Aligned Elements / MS
Software unit testing	SW Development partner	SW development partners	Individual software class	N/A	SW partner

5. RESULTS

5.1. INSTRUMENT UNDER TEST

All validation activities were performed with the following material:

DESCRIPTION	ARTICLE NUMBER		PICTURE
	MBV AG	MERCK KGAA, DARMSTADT, GERMANY	
MAS-100 Atmos® sampler for compressed gases	200162	1173280001	

5.2 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 Atmos® instrument. The complete list of tests is detailed in Aligned Elements.

5.2.1 REQUIREMENT TESTING

REQUIREMENT TESTING	DESCRIPTION	EXPECTED RESULT	RESULT
Adjustment and calibration	Verify the adjustment and calibration of MAS-100 Atmos® according to its Service Manual	– Adjustment and calibration are conducted without errors – Calibration certificates are generated: – Pressure calibration – Mass flow calibration	Passed
Performance test under ambient conditions	Verify instrument performance at ambient conditions (i.e. temperature, pressure, humidity)	– MAS-100 Atmos® can be adjusted – 10 successive calibrations are successful. – Sampling at lower pressure range (1.2 bar pressurized air) is in the specifications. – Sampling at higher pressure range (7 bar pressurized air) is in the specifications. – Specifications: Flow rate ± 5% and Pressure ± 2%	Passed
Performance test under environmental conditions	Verify the instrument performance at extremes of operation range (4°C and 50 °C)	MAS-100 Atmos® calibration is within specifications (Flow rate ± 5% and Pressure ± 2%)	Passed

REQUIREMENT TESTING	DESCRIPTION	EXPECTED RESULT	RESULT
Cleaning and sterilization	Verify that cleaning and of the housing and autoclaving of the sampling head has no adverse effect	Cleaning test with wiping of the housing with standard agents (Ethanol, 70/30 IPA, Quaternary ammonium, H_2O_2 + peracetic acid) has no adverse effect. Autoclaving of the sampling head has no adverse effect	Passed

Verification off the physical sampling efficiency (D50)	Verify the expected physical sampling efficiency is met by design	– Distance between Agar plate and perforated lid is same as for the MAS-100 NT®
		– Same number of holes and arrangement as for MAS-100 NT® perforated lids
		– Nominal D50 values:
		  – 300 x 0.6 mm lid: 1.1 µm at 100 LPM and 1.6µm at 50 LPM
		  – 300 x 0.47mm head: 0.8 µm at 100 LPM and 1.1 µm at 50 LPM
			Passed

Sampling with gases other than air	Verify instrument performance for gas types other than air	– Calibration with air is within specifications – The gas correction factor is determined for N_2, CO_2 and Argon – The corrected gas flows for N_2, CO_2 and Argon are within specifications Specification: The gas flow deviation is less than 5% over all tested flows (60 to 700 SLPM)	Passed
Minimal battery running time	Verify capacity of battery pack	– A fully charged instrument can run 32 samplings with 2 bar absolute air input, at 100% flow mode with 1000 L per sample. – It is still possible to run the decompression after battery warning shows up.	Passed
Operating and configuration	Verify all user functions regarding configuration and operation of MAS-100 Atmos® according to its user manual.	– The configuration and operation of MAS-100 Atmos® described in the user manual is verified and meets the user manual.	Passed

Transportation test	Verify that transportation does not have an influence on MAS-100 Atmos® performance	– Initial calibration results are within the specifications, Packaging of the instrument is done by MBV logistics
		– Transportation test is done according to ASTM D4169-16 DC 13
		  – Climatic stressing preconditioning
		  – Drop test sequence 1
		  – Compression (vehicle stacking)
		  – Vehicle vibration
		  – Loose load vibration
		  – Drop test sequence 2
		– MAS-100 Atmos® is not damaged and fully functional
		– Calibration results are still within the specifications
			Passed

REQUIREMENT TESTING	DESCRIPTION	EXPECTED RESULT	RESULT
Sampling with different parameters (volume and gas type)	Verify that it's possible to sample at the volume lower and upper ranges and with other types of gas selected	– It's possible to select 50 or 3000 among the volumes displayed on the Local UI – It's possible to perform a sampling of 50 NL with N_2 gas selected – It's possible to perform a sampling of 3000 NL with N_2 gas selected – It's possible to perform a sampling of 50 NL with CO_2 gas selected – It's possible to perform a sampling of 3000 NL with CO_2 gas selected – It's possible to perform a sampling of 50 NL with Ar gas selected – It's possible to perform a sampling of 3000 NL with Ar gas selected – All relevant information is displayed in the audit trail	Passed
Sampling compressed air under aseptic conditions	Ability to perform the complete c workflow: run several samplings with different nutrient plates, using autoclaved sampling head, and record growth of microorganisms.	– A biocontamination test sequence can be completed, from sampling until CFU count on agar – The sampling archives and the audit trail are exported – The data in the sampling archive exports (CSV and XML) meet the data in the audit trail	Passed

5.2.2 FUNCTIONAL AND INTEGRATION TESTING

FUNCTIONAL AND INTEGRATION TESTING	DESCRIPTION	EXPECTED RESULT	RESULT
Date format	Verify date formats in dependence of selected language	Whatever the language selected: English, German, French, Italian, Spanish, Russian: – Date format on local UI and browser UI dashboard is yyyy-mm-dd – Date format in audit trail and sampling archive is yyyy-mm-dd	Passed
User management	Verify specified user roles and rights	User roles and rights as defined in user manual section 2.11.2: – Clearly separated user roles are defined (operator, system administrator, user administrator, service engineer) – Instrument access is possible using a file key or hardware key – Optional use of Login for operator – Advanced functions of system administrator and user administrator are only accessible via user login	Passed

FUNCTIONAL AND INTEGRATION TESTING	DESCRIPTION	EXPECTED RESULT	RESULT
Instrument access	Verify login process based on user roles and rights	– When not logged in and browser UI is opened: only access to Device Info and Writing key file to HW key – When “no login” is selected in the settings, access to the **local** UI is not restricted meaning that a sampling can be started – When “Login with user key (for operator)” is selected in the settings, access to the local UI is only possible with a hardware key or a key file – When “Login with user key and PIN” is selected in the settings, access to the local UI is only possible with a hardware key and PIN, or key file and PIN – Each user role can only access the menus in the browser UI associated with his role. – The login and logout information is correctly logged in the audit trail – The measurement is logged correctly and the operator information in the audit trail log file is correct	Passed
Audit trail	Verify audit trail functionality	– Audit trail loads and is displayed correctly. – The audit trail can be filtered by categories; user role; name of a user; date and time; or combination of different filters. – The language setting changes apply to the audit trail title row. – The audit trail can be printed and saved in .pdf using the Print function of the web browser. – All the audit trail information loaded in the browser page previously to the print command is saved in the .pdf. – "Audit trail / sampling archive export" sub menu loads and is displayed correctly. – It’s not possible to clear the audit trail without exporting it first. – The audit trail can be exported in a zip file. The .zip file contains the audit-trail.xml, the errors-warnings.xml, the measurements.xml, the public key and the signature. – The content of the document should be displayed correctly and easily readable. – The audit trail on the instrument can be cleared after it has been exported. – In the instrument’s audit trail there is only one log entry: "Delete log".	Passed
Electronics and wiring	Verify PCB architecture and cable connections	All components are connected as designed	Passed

Sensor and actuator functionality	Verify whether sensors and actuators perform under application conditions	When the device is connected to a gas system the sensors and actuators perform as expected: – The device can automatically switch to 50% flow mode and complete the sampling when the gas supply is not sufficient – Decompression step is available and system pressure is back to ambient pressure after decompression is finished – Sampling is possible as long as the system pressure is between 1.2 and 7 bar.a	Passed
Shutdown under pressure is not possible	The software shall inhibit the shutdown (or standby) of the instrument when there is still pressure detected. This shall apply for a manual request via power button (single tab, double tab) or via the automatic standby timer	The device does not go into sleep mode when the system is under pressure	Passed

5.2.3 MODULE TESTING

MODULE TESTING	DESCRIPTION	EXPECTED RESULT	RESULT
Pressure indication	Verify pressure indication on the local UI	– Pressure indications on local UI (status bar and gauge) show the current pressure in the device – When pressure is below 1.2 bar.a, no frame displays on the local UI – When pressure applied is between 1.2 and 7 bar.a, a yellow status frame displays on the local UI – When pressure applied is above 7.2 bar.a, a red status frame displays on the local UI. Decompression is possible to release overpressure from the system. A warning is logged in the audit trail	Passed
Status bar	Verify content and functionality of status bar	– The battery charging level is correctly displayed – The battery charging indication is correctly displayed – The pressure is correctly displayed – The date and time are correctly displayed	Passed

MODULE TESTING	DESCRIPTION	–	EXPECTED RESULT	RESULT
Configuration	Verify settings sub-menu for System Administrator: -Presence and functionality of all settings - All changes in the settings submenu are logged in the audit trail	–	System administrator can login the browser UI and navigate to the settings sub menu – The system administrator can change the different settings listed in the User Manual section “Changing instrument settings”, the settings are saved to the instrument and the changes are logged in the audit trail	Passed
Time zones and daylight-saving time	Verify that the time zone setting automatically determines summer / winter time	–	Set date and time are correctly displayed on local UI and browser UI – The device automatically switches to summer/wintertime according to selected time zone	Passed
Uniqueness of login information	When renewing or changing the PIN of any file key or hardware key, the new PIN can't be identical to the old one Renewing or changing the PIN gets logged in the audit trail	–	It’s not possible to reuse the same PIN – When the PIN is changed on a file key a new file key is downloaded immediately – When the PIN is changed on a Hardware key, new PIN gets successfully written to hardware key – All actions are logged in the audit trail	Passed
PIN aging	Verify that PIN expires after configured amount of time	–	Hardware keys and key files are created for all PIN expiry options (e.g. 1/3/6/12 month(s) and never) – The PIN expires when time of instrument is set to 1/3/6/12 month(s) later – The PIN does not expire when the key was created with the "never" option	Passed
PIN renewal on browser UI	Verify that PIN can be renewed (i.e. both if expired and valid) for system administrator, user administrator and service engineer	–	It is possible to renew an expired PIN on a key file and on hardware key on the browser UI – It is possible to change a valid PIN on a key file and on hardware key browser UI	Passed
PIN renewal on local UI	Verify that PIN can be renewed if expired	–	Prompt to renew PIN is displayed on local UI as PIN validity period is expired – PIN can be changed on the local UI, it is successfully written on the hardware key and access to local UI is granted – All actions are logged in audit trail	Passed

MODULE TESTING	DESCRIPTION	–	EXPECTED RESULT	RESULT
Creation of new users	Verify process of creating new users (i.e. key files and hardware keys)	–	Hardware key gets successfully written for Operator, user administrator and system administrator	Passed
		–	Key file created for user administrator and system administrator is automatically downloaded to computer	
		–	A PIN validity is selectable	
		–	The created users are able to login the Local UI	
		–	The created users are able to login the Browser UI and access the dashboard corresponding to their user profile	
		–	All actions are correctly logged in audit trail	
Blacklist	Verify that users can be blocked and unblocked by the user administrator.	–	It is possible to block system users: key files and hardware keys appear in the blocked user list	Passed
		–	The blocked users don't have access to the browser UI	
		–	The blocked users don't have access to the local UI	
		–	It is possible to un-block system users.	
		–	The un-blocked users have access to the browser UI again	
		–	The un-blocked users have access to the local UI again	
		–	All actions are correctly logged in audit trail	
False login attempts	Verify that instrument gets locked after three false login attempts	–	The Local UI and browser UI get locked after three successive false login attempts (for hardware keys and key files)	Passed
		–	The system administrator and service engineer (hardware keys and key files) can unlock a blocked device	
		–	All actions are correctly logged in audit trail	
Barcode scanning of sampling parameters	It shall be possible to connect a barcode scanner via USB to MAS-100 Atmos® and scan optional information such as plate ID, location of sampling, and perforated lid. This information is supposed to be stored together with the sampling data in the sampling log	–	Settings can be chosen such that location, plateID, and perforated lid are to be scanned	Passed
		–	Scanning is successful and the sampling is started	
		–	The scanned information is correctly transferred to the sampling log	
		–	All steps logged in the audit trail	

Result barcode	MAS-100 Atmos® shall display a result barcode on its local UI after sampling. The result barcode shall also be saved in the sampling log of the device	– When the setting for Sampling barcode is set to csv, the local UI displays the corresponding screen with a 2D bar code at the end of a sampling. Content is complete and in csv format – When the setting for Sampling bar code is set to xml, the local UI displays the corresponding screen with a 2D bar code at the end of a sampling. Content is complete and in xml format – The result bar code can be scanned and contains all information about the sampling procedure as logged in the sampling log	Passed
Audit trail export	Verify audit trail export and printing	– The current audit trail view (i.e. with applied filters) can be exported to a pdf file with the print function in the browser – The full audit trail can be exported without audit trail clearing – The full audit trail can be exported with audit trail clearing – The full audit trail export and clearing is logged in the audit trail	Passed
Audit trail archive verification	Verify that the user has the possibility to check the integrity of an archive (either downloaded from the browser UI or from via USB dump)	– The integrity of the .zip archive can be checked on the browser UI – The integrity of the audit-trail.xml, the errors-warnings.xml, and the measurements.xml files can be checked on the browser UI – The non-tempered archive is indicated as valid – The tempered archive is indicated as invalid	Passed
Application software update	Verify that firmware can be updated - Verify functionality of firmware update - Verify that updating firmware is logged in the audit trail	– The system administrator and the service engineer can access the Diagnostic sub menu to update the application software – Update successfully finishes and the device reboots with the updated software application version – The previously configured settings have not been changed – All actions are correctly logged in audit trail	Passed
Adjustment and Calibration functions	Verify that adjustment and calibration can be started from browser UI	– System administrator and service engineer have access to the Adjustment and Calibration menu in the browser UI – When a calibration instrument is connected: – It is possible to perform “CALIBRATE AS FOUND”: The browser UI shows: "Leak Test", "Time Check" and "Calibration Status" as passed – It is possible to perform "CALIBRATE AS-LEFT": shows: "Leak Test", "Time Check" and "Calibration Status" as passed and has a button to view adjustment parameters – All actions are correctly logged in audit trail – It is possible to view, print or download the calibration certificate	Passed

Calibration certificate creation	Verify that the calibration certificate can be created from the browser UI and that calibration data is correctly and completely stored on the instrument Also verify that all the data on the certificate is correct and the same as in the browser UI	– In the Adjustment and Calibration menu in the browser UI it is possible to: – display the As Found Mass flow calibration certificate – display the As Found Absolute pressure calibration certificate – display the As Left Mass flow calibration certificate – display the As Left Absolute pressure calibration certificate – Print or download the certificates as .pdf – Data on the certificate is correct and the same as in the browser UI	Passed
Settings approval	Verify settings approval function in browser UI	– The device gets locked once a service engineer changes the settings, if it is configured such that settings approval is required – The device can be unlocked if a system administrator completes the settings approval process – All actions are logged in the audit trail – The device does not get locked if it is configured such that settings approval is not required	Passed
Lifetime testing	Sensor, actuators and other critical components must be subject to stress and lifetime tests	– Regulating valve is fully functional after lifetime test – Flow sensors did not drift more than 5% during one year and is functional for at least 5 years – Pressure sensor did not drift more than 2% during one year and is functional for at least 5 years – The head closure mechanism is fully functional and no safety concerns are raised for more than three years of use (1000 openings and closings) – The safety valve withstands the use of at least three years	Passed

5.3 21 CFR PART 11 CONTROLS

An assessment of the 21CFR part 11 compliance was made by an external company specialized in computerized system validation.

This table outlines the requirements of 21 CFR part 11 and the method of compliance utilized by MAS-100 Atmos® instrument (local user interface (UI) and MAS-100 Atmos® application software. It is a Browser-based User Interface accessible with a web-browser when a computer is connected to the instrument by means of a USB-C (instrument side) to USB-A (computer side) cable.

In this document, only electronics records are considered as MAS-100 Atmos® applications software doesn't manage electronic signatures.

The compliance table is built according to the following rules:

– In the first column, preceded by its reference in the 21CFR11 regulation, the textual repetition of the requirement stated by the FDA,

- In the second column, the mode of response to this requirement:
  - **'P'** if it must be "Proceeded" by the company (end user),
  - **'S'** if the **System** (MAS-100 Atmos®) must ensure it,
- In the third column, the synthetic interpretation of this requirement,
- In the fourth column, the result of test stating if it is “Passed” or “Failed”, N/A is used when requirement is not applicable to the application software.

REQUIREMENT 21CFR PART 11	MODE OF RESPONSE	SYNTHETIC INTERPRETATION	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	P and **S**	The system should be validated for its ability to detect invalid or corrupted records GMP recommendations were followed for validation and qualification of product and equipment. Evidence can be provided during an audit, thus answering to the “P” part of the requirement	Passed
B-11.10.b - The ability to generate accurate and complete copies of records in both human readable and electronic form suitable for 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	**S**	Records must be available: • on the screen, • or in paper form, • or in electronic form via an export for the FDA auditor who only has the most common office automation tools on his computer. The FDA accepts records in PDF format	Passed
B-11.10.c - Protection of records to enable their accurate and ready retrieval throughout the records retention period	P and **S**	Recordings must be protected for the legal retention period	Passed
B-11.10.d - Limiting system access to authorized individuals	P and **S**	The system must be protected against access by unauthorized persons	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, 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	**S**	This point specifies that there must be a timestamp of the data as well as an audit trail on all the actions taken by the users influencing the recorded data An audit trail is a record of all operations performed in the database The system must include a secure audit trail function of each GMP record and user actions. This audit trail must be kept for as long as the records to which it relates It must be available to be inspected or outsourced for the FDA agency	Passed

Requirement 21CFR part 11	Mode of response	Synthetic interpretation	Test status
B-11.10.f - Use of operational system checks to enforce permitted sequencing of steps and events, as appropriate	P and **S**	The system must be able to control, when appropriate, the respect of a sequence of steps or operations (Workflow)	Passed
B-11.10.g -Use of authority checks to ensure that only 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 and **S**	The company must be able to control authorized interventions on the recordings (creation, modification, deletion). Direct access to stored data must be controlled as well as direct interventions on the supervised process	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	P and **S**	This point is to secure user command actions step by step (obligation to go through certain steps) during the supervision of a process (alarm acknowledgment, process start, correction of parameters, launch of end report lot,....). Each action must be able to be carried out by the only user(s) authorized to carry it out. Some of these actions must even be checked or validated by another person who is himself authorized to do so, all of which must be traced in an audit trail (see B-11.10.e) On the other hand, it is necessary to record unsuccessful access attempts by an unauthorized user	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	P	People who develop and maintain or use the system must have the initial training, continuous training and experience necessary to perform their tasks	N/A (Out of assessment scope)
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	P and S	The company should establish written policies and obtain adherence to hold individuals responsible and accountable for actions taken under their electronic signature in order to discourage signature tampering	
B-11.10.k - Use of appropriate controls over systems documentation including:	/	System documentation should be checked	
(1) Adequate controls over the distribution of, access to, and use of documentation for system operation and maintenance	P	Distribution and access to system documentation should be subject to appropriate controls	

Requirement 21CFR part 11	Mode of response	Synthetic interpretation	Test status
(2) - Revision and change control procedures to maintain an audit trail that documents time-sequenced development and modification of systems documentation	P	The development and modification of system documentation is conducted according to review and change control procedures which include an audit trail	N/A (Out of assessment scope)
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.	S	Access to open systems must include additional measures such as encryption or digital signing	N/A (Not an open system)
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	S	Electronically signed records must contain the signatory's legal or full name, date and time and meaning of the signature in clear text on all visible forms of the record	N/A (No electronic signature)
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)	S	Data from 11.50.a. must be treated as part of the record and be presented in all legible forms of the record	

Requirement 21CFR part 11	Mode of response	Synthetic interpretation	Test status
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	S	The signature / registration link is impossible to distend by any common means	N/A (No electronic signature)
C-11.100 a - Each electronic signature shall be unique to one individual and shall not be reused by, or reassigned to, anyone else	S	A signature must be: • personal, • unique for each person in each system at a given time, • not reusable • not reassignable	
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	P	Verification of the identity of electronic signature users	
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	P	The commitment of the users and administrator is reaffirmed in the case of the implementation of an electronic signature which must be recognized by the user as the equivalent of his handwritten signature in a letter (postal) addressed to the FDA	

Requirement 21CFR part 11	Mode of response	Synthetic interpretation	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	S	For non-biometric signatures, the system must use at least two distinct means of identification, such as an identifier code and a password, to sign electronically. When an individual performs a series of signatures during a continuous period of controlled access to the system, the system may allow that individual to sign with only one component of their electronic signature, provided that the first signature is performed using all components of the electronic signature The level of security must be such that if a signature is made by a person who does not hold this signature, this necessarily means that the holder has communicated his password to someone The company must guarantee through the system the identity of the people able to sign electronically	N/A (No electronic signature)
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	P and S	The system must be designed to ensure that electronic signatures based on biometrics cannot be used by anyone other than their owner	
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:	/		
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	S	The system must be able to maintain the uniqueness of each username/password combination.	
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)	P and S	The management of passwords linked to the signature must respect the criteria of complexity, lifespan, reset, of the customer's procedure	

Requirement 21CFR part 11	Mode of response	Synthetic interpretation	Test status
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	P and S	The system must provide the possibility of permanently or temporarily deactivating the identification process in place (card or token), in the event of loss. The system must provide the possibility of providing a replacement identification method (card or token) The system administrator can revoke a signature	N/A (No electronic signature)
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	S	The system must be able to detect and trace attempts to use unauthorized electronic signatures	
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	P	The equipment used to generate identification codes or passwords must be tested periodically	

6. CONCLUSION

The conclusion of the MAS-100 Atmos® Validation is that requirements and functional specifications have been fully validated and released to operate per written product specifications. The MAS-100 Atmos® instrument is fit for its intended purpose.

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