White Paper

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Support for Title 21 CFR Part 11 and Annex 11 Compliance: Agilent VWorks Automation Control Plus 14.1 and AssayMAP Protein Sample Prep Workbench 4.0

Overview

US FDA Part 11 in Title 21 of the Code of Federal Regulations (CFR), and its EU analog, Eudralex Chapter 4, Annex 11, describe the requirements for electronic records and electronic signatures for regulated pharmaceutical organizations. Released in 1997, 21 CFR Part 11 has been enforced since 1999. The intent of these guidelines is to ensure that all appropriate electronic records are attributable, legible, contemporaneous, original, accurate, and maintained with integrity.

This white paper is a resource for users of Agilent VWorks Plus Automation Software version 14.1, AssayMAP Protein Sample Prep Workbench 4.0, and later versions whose organizations must comply with these regulations. VWorks Plus Automation Software controls liquid handling and plate management protocols on Agilent Automation instruments including, but not limited to, the Bravo Liquid Handler and BenchCel Workstations. VWorks Automation Control Software is required for AssayMAP Protein Sample Preparation Workbench, and the VWorks Plus edition is required to enable compliance features. It is the responsibility of the user and their organization to ensure that the functionalities provided by VWorks Plus for Agilent Automation instruments are used appropriately to achieve compliance-readiness for laboratory sample preparation. In addition to the VWorks Plus technical controls, the user organization must establish procedural controls--standard operating procedures (SOPs) to address relevant nontechnical requirements. Governance, for example as an internal audit program, must also be established to assure that system operators follow the SOPs.

Appendix 1 provides a detailed description of how VWorks Plus 14.1 and AssayMAP Protein Sample Prep Workbench 4.0 support users and their organizations in achieving the requirements of each section of 21 CFR Part 11, the related sections of EU Annex 11, and regulations of other countries. The descriptions assume that system access, including instrument hardware and software, is controlled by the staff responsible for the electronic records contained on the system. Thus, the system is designed as a "closed system" as defined in 21 CFR Part 11.3(b)(4).

21 CFR Part 11

21 CFR Part 11 covers three specific elements of a regulated laboratory's operation:

- Security of electronic records
- Attribution of work
- Electronic signatures (if used)

Security

Security refers to the "right people, having the right access, to the right information." Regulated organizations must be able to both verify the identity of system users and limit system access to trained, authorized individuals (11.10(d), (i) and (g); 11.100(b)). Because laboratory staff have different responsibilities based on their job assignments, data access must be able to be segregated and defined such that certain users have certain types of access to certain sets of data while having different access to other data sets.

"Separation of duty, as a security principle, has as its primary objective the prevention of fraud and errors. This objective is achieved by disseminating the tasks and associated privileges for a specific business process among multiple users."

– Botha, Eloff, IBM Systems Journal[1]

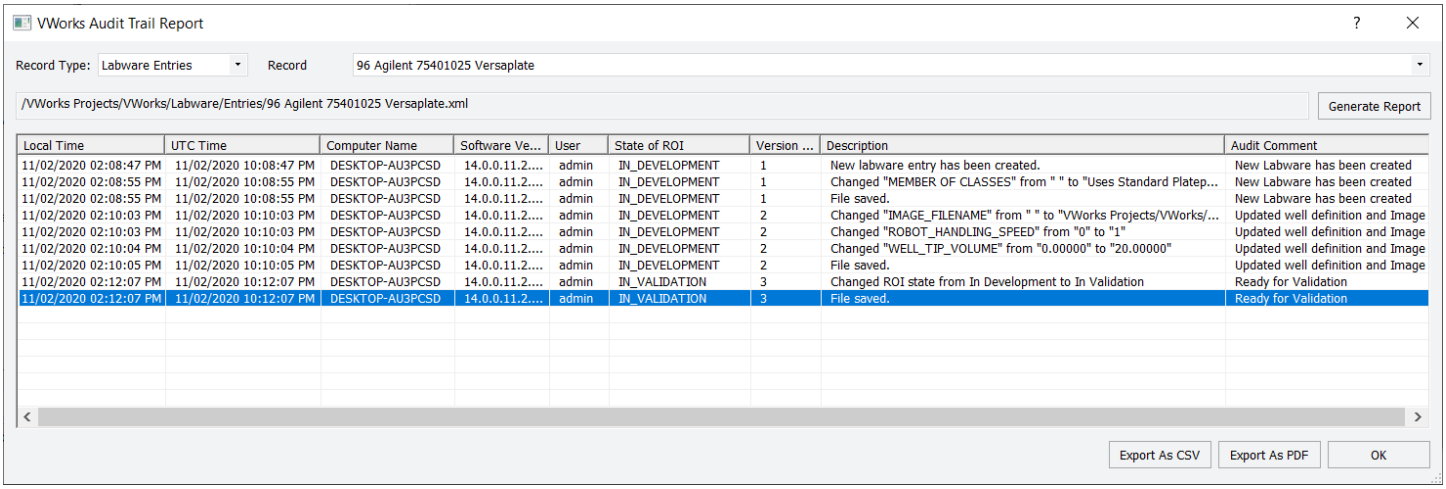
For example, in VWorks Plus 14.1 and AssayMAP Protein Sample Prep Workbench 4.0, it is possible to restrict one user from editing a form, while a different user can create and edit a form.

Attribution of work

Attribution of work refers to documenting the "Who, what, when, where and why?" of work performed. This is usually done via the use of automated audit trail functionality. Automated audit trails independently record a user's actions, thus connecting laboratory staff to the work they perform. Audit trail entries enable staff and regulatory inspectors to reconstruct the complete history of an electronic record.

- **Who:** clearly identifies the person responsible for the particular action that creates, modifies, or deletes a record.
- **What:** is the action that took place, including, if applicable, the old value and the new value contained in the record.
- **When:** unambiguously declares the date and time the action took place.
- **Where:** clearly identifies the impacted record.
- **Why:** explains the reason for a change to a regulated record. The reason may be selected from a list of predefined reasons to provide consistency and to enable searching and sorting of entries.

An example of the Who, What, When, Where, and (optionally) Why can be seen in Figure 1 (screencap of an Audit trail report with labels of "Who made the change", "Reason for the change", "When the change occurred", and "What record changed").



Local Time	UTC Time	Computer Name	Software Ve...	User	State of ROI	Version ...	Description	Audit Comment
11/02/2020 02:08:47 PM	11/02/2020 10:08:47 PM	DESKTOP-AU3PCSD	14.0.0.11.2....	admin	IN_DEVELOPMENT	1	New labware entry has been created.	New Labware has been created
11/02/2020 02:08:55 PM	11/02/2020 10:08:55 PM	DESKTOP-AU3PCSD	14.0.0.11.2....	admin	IN_DEVELOPMENT	1	Changed "MEMBER OF CLASSES" from " " to "Uses Standard Platep...	New Labware has been created
11/02/2020 02:08:55 PM	11/02/2020 10:08:55 PM	DESKTOP-AU3PCSD	14.0.0.11.2....	admin	IN_DEVELOPMENT	1	File saved.	New Labware has been created
11/02/2020 02:10:03 PM	11/02/2020 10:10:03 PM	DESKTOP-AU3PCSD	14.0.0.11.2....	admin	IN_DEVELOPMENT	2	Changed "IMAGE_FILENAME" from " " to "VWorks Projects/VWorks/...	Updated well definition and Image
11/02/2020 02:10:03 PM	11/02/2020 10:10:03 PM	DESKTOP-AU3PCSD	14.0.0.11.2....	admin	IN_DEVELOPMENT	2	Changed "ROBOT_HANDLING_SPEED" from "0" to "1"	Updated well definition and Image
11/02/2020 02:10:04 PM	11/02/2020 10:10:04 PM	DESKTOP-AU3PCSD	14.0.0.11.2....	admin	IN_DEVELOPMENT	2	Changed "WELL_TIP_VOLUME" from "0.00000" to "20.00000"	Updated well definition and Image
11/02/2020 02:10:05 PM	11/02/2020 10:10:05 PM	DESKTOP-AU3PCSD	14.0.0.11.2....	admin	IN_DEVELOPMENT	2	File saved.	Updated well definition and Image
11/02/2020 02:12:07 PM	11/02/2020 10:12:07 PM	DESKTOP-AU3PCSD	14.0.0.11.2....	admin	IN_VALIDATION	3	Changed ROI state from In Development to In Validation	Ready for Validation
11/02/2020 02:12:07 PM	11/02/2020 10:12:07 PM	DESKTOP-AU3PCSD	14.0.0.11.2....	admin	IN_VALIDATION	3	File saved.	Ready for Validation

Figure 1. Audit trail report screencapture.

eSignatures

While 21 CFR Part 11 does not require the use of eSignatures, it does provide regulations for their use when they are used. In this case, the system must ensure that eSignatures:

- Are irrevocably linked to their respective records
- Show the full name of the signer, date and time, as well as the meaning of the signature (such as review, approval, responsibility, or authorship)
- Are present whenever the signed records are displayed or printed

VWorks 14.1 and AssayMAP Protein Sample Prep Workbench 4.0 support eSignatures to control record (i.e. a VWorks protocol) progression from "Development", to "Validtion", then to "Released" status. eSignatures are also required to close an Experiment project.

The following outlines the minimum software requirements for VWorks Plus used in compliant environments. The latest shipping software is recommended to enable enhancements and defect fixes. At a minimum, VWorks Plus 14.1 and AssayMAP Protein Sample Prep Workbench 4.0 is required. Please consult your sales representative for a compatibility assessment of your current software.

Appendix—Satisfying the requirements set forth in US FDA Title 21 CFR Part 11 and related global regulations using VWorks Plus

Appendix table notes

Column one

The table addresses 21 CFR Part 11 requirements in the order that they are presented in the US FDA reference document.[2]

Column two

For completeness, column two lists all requirements of 21 CFR Part 11 and other related global requirements.

“System” refers to the analytical system used to acquire and process data.

Most requirements are fulfilled by either technical controls (i.e. software functionality) or procedural controls (i.e. SOPs). Technical controls are controls provided by the software and hence the software supplier, while procedural controls are the responsibility of the user organization. 21 CFR requirements listed in bold are requirements addressed by technical controls. Other global requirements are listed in regular font. Requirements that must be addressed by procedural controls are listed in blue.

Column three

Responsibilities for each requirement are listed in column three. “S” refers to the software system vendor. “U” refers to the user organization. Use of “S” and “U” implies a combination of both technical and procedural controls.

Column four

If available and where appropriate, related global requirements and comments are provided in column four.

Column five

Column five indicates with a “Yes” or “No” whether the requirement can be satisfied using the technical controls provided in VWorks Plus and AssayMAP Protein Sample Prep Workbench. Not applicable (N/A) is used when a requirement must be addressed by procedural controls.

Column six

Column six explains how the regulatory requirement can be satisfied using the technical controls provided by VWorks Plus and AssayMAP Protein Sample Prep Workbench. Column six also provides additional recommendations for the user organization when relevant.

Table 1. Validation.

Part 11 Others	Requirements	S, U	Other Regulations or Comments	Yes/No	If Yes, How, Specifically, is the Requirement Satisfied? or if No, What is the Recommendation?
Part 11 11.10(a)	1.1 Is the system validated to ensure accuracy, reliability, consistent intended performance, and the ability to discern invalid or altered records?	S, U	Required by all regulations. This is a typical example of shared responsibility between the system supplier and the user organization. While the user organization has ultimate responsibility for validation, some tasks can only be done and must be delivered by the software supplier, e.g., validation activities during development and related documentation. 第五章系统 第十三条在计算机化系统使用之前，应当对系统全面进行测试，并确认系统可以获得预期的结果。当计算机化系统替代某一人工系统时，可采用两个系统（人工和计算机化）平行运行的方式作为测试和验证内容的一部分。 第五章系统 第十三条在计算机化系统使用之前，应当对系统全面进行测试，并确认系统可以获得预期的结果。当计算机化系统替代某一人工系统时，可采用两个系统（人工和计算机化）平行运行的方式作为测试和验证内容的一部分。	Yes	Agilent Technologies has verified the performance of VWorks Plus using tests that evaluate accuracy, reliability and consistent performance. However, the user organization is required to validate their sample preparation system according to regulatory expectations. The regulated records for Agilent VWorks Plus and AssayMAP Workbench are: – Protocols – Forms – Device Files – Device Profiles – Runset Files – VWorks Options – Labware Entries – Labware Classes – Liquid Classes – Pipetting Techniques – VWorks Logs – Macro Library Files – Error Library Files – Barcode Files – JavaScript Files – Log Files – Method Files – Method setup tools – Reports VWorks Plus checksums these records to discover any "invalid or altered records." If an invalid or altered record is discovered, an error is displayed, and the user is not able to open the file. Access to Experiment IDs is restricted however modification to the Experiment IDs are the user organization's responsibility.
Annex 11	1.2 Is infrastructure qualified?	U	Annex 11. Principle B Brazil GMP 577	N/A	Qualification of infrastructure such as servers and networks are the responsibility of the user organization.

Table 2. Accurate copies and secure retention and retrieval of records.

Part 11 Others	Requirements	S, U	Other Regulations or Comments	Yes/No	If Yes, How, Specifically, is the Requirement Satisfied? or if No, What is the Recommendation?
Part 11 11.10(b)	2.1 Is the system capable of generating accurate and complete copies of records in both human readable and electronic form suitable for inspection, review, and copying by the FDA?	S, U	第五章系统 第十九条以电子数据为主数据时，应当满足以下要求： （一）为满足质量审计的目的，存储的电子数据应当能够打印成清晰易懂的文件。	Yes	The system generates the following records that can be viewed in VWorks Plus and AssayMAP Workbench. – Protocols – Forms – Device Files – Device Profiles – Runset Files – VWorks Options – Labware Entries – Labware Classes – Liquid Classes – Pipetting Techniques – VWorks Logs – Macro Library Files – Error Library Files – Barcode Files – JavaScript Files – Log Files – Method Files – Method setup tools – Reports For printing, the user organization needs to print using a text editor. It is the user organization's responsibility to maintain the authenticity and integrity of printed records.
Annex 11	2.2 Is it possible to obtain clear printed copies of electronically stored erecords?	S, U	Annex 11.8.1 Brazil GMP 583	Yes	For printing, the user organization needs to print using a text editor. It is the user organization's responsibility to maintain the authenticity and integrity of printed records.

Part 11 Others	Requirements	S, U	Other Regulations or Comments	Yes/No	If Yes, How, Specifically, is the Requirement Satisfied? or if No, What is the Recommendation?
Brazil	2.3 Are there controls to make sure that the data backup, retrieving and maintenance process is duly carried out?	S, U	Brazil 585.2 第五章系统 第十九条以电子数据为主数据时，应当满足以下要求： （三）应当建立数据备份与恢复的操作规 程，定期对数据备份，以保护存储的数据供将来调用。备份数据应当储存在另一个单 独的、安全的地点，保存时间应当至少满足本规范中关于文件、记录保存时限的要求。	Yes	It is the responsibility of the user organization to control data backup, retrieving and maintenance. Detailed instructions are available for backup of all relevant files.
Part 11 11.10(c)	2.4 Does the system protect records to enable their accurate and ready retrieval throughout the records retention period?	S, U	China GMP 163	Yes	The following records generated by VWorks Plus and AssayMAP Workbench are stored and managed in secure storage. – Protocols – Forms – Device Files – Device Profiles – Runset Files – VWorks Options – Labware Entries – Labware Classes – Liquid Classes – Pipetting Techniques – VWorks Logs – Macro Library Files – Error Library Files – Barcode Files – JavaScript Files – Log Files – Method Files – Method setup tools – Reports It's the user organization's responsibility to manage the physical security and controlled access to secure storage.
Annex 11	2.5 Are data checked during the archiving period for accessibility, readability and integrity?	U	Annex 11.17	N/A	It is the responsibility of the user organization to ensure that data are checked during the archival period for accessibility, readability, and integrity.
Annex 11	2.6 If relevant changes are made to the system (e.g. computer equipment or programs), is then the ability to retrieve the data ensured and tested?	S, U	Annex 11.17	Yes	The system is designed to read data from legacy versions of VWorks. The user organization is responsible for ensuring readability of this data during their implementation and validation processes.
Annex 11	2.7 Are data secured by both physical and electronic means against damage?	S, U	Annex 11.7.1 Brazil GMP 584 第五章系统 第十条系统应当安装在适当的位置，以防止外来因素干扰。 第五章系统 第十九条以电子数据为主数据时，应当满足以下要求： （二）必须采用物理或者电子方法保证数 据的安全，以防止故意或意外的损害。日常运行维护和系统发生变更（如 计算机设备或其程序）时，应当检查所存储数据的可访问性及数据完整性。	Yes	All the regulated records generated by the system are stored within VWorks Plus secure storage. Physical security is the responsibility of the user organization.
Clinical Guide	2.8 Are there controls implemented that allow the reconstruction of the electronic source/raw documentation for FDA review of the (clinical) study and laboratory test results?	S	Clinical Computer Guide F2 FDA Q&As	Yes	All records are maintained in secure storage to allow reconstruction as needed.
Clinical Guide	2.9 Does the information provided to FDA fully describe and explain how source/raw data were obtained and managed, and how electronic records were used to capture data?	U	Clinical Computer Guide F2 FDA Q&As	N/A	It is the responsibility of the user organization to describe how source/raw data were obtained and managed, and how electronic records were used to capture data.

Part 11 Others	Requirements	S, U	Other Regulations or Comments	Yes/No	If Yes, How, Specifically, is the Requirement Satisfied? or if No, What is the Recommendation?
Annex 11	2.10 Does the system allow performing regular backups of all relevant data?	S, U	Annex 11.7.1 China GMP 163 Brazil GMP 585 Part 211, 68 b	Yes	Backing up data is the responsibility of the user organization. Detailed instructions are available for creating the appropriate backups of all relevant files.
Annex 11	2.11 Is the integrity and accuracy of backup data and the ability to restore the data checked during validation and monitored periodically?	U	Annex 11.7.2 China GMP 163 Brazil GMP 585 Part 211, 68 b	N/A	It is the responsibility of the user organization to ensure the integrity and accuracy of the backed up data, and to check, validate, and monitor restored data periodically.
Clinical Computer Guide	2.12 Are procedures and controls in place to prevent the altering, browsing, querying, or reporting of data via external software applications that do not enter through the protective system software?	S, U	Clinical Computer Guide E	Yes	VWorks Plus is preconfigured with FTP services enabled to facilitate bulk data operations. Due to the inherent limitations of FTP services, permissions may not be consistent with the permissions granted in VWorks Plus. It is the user organization's responsibility to disable FTP services when not needed. See the Administrator's Guide for details.
Clinical Computer Guide	2.13 Are there controls implemented to prevent, detect, and mitigate effects of computer viruses, worms, or other potentially harmful software code on study data and software?	U	Clinical Computer Guide F	N/A	Agilent has tested VWorks Plus in conjunction with industry standard antivirus applications. However, it is the responsibility of the user organization to implement anti-virus software.

Table 3. Authorized access to systems, functions, and data.

Part 11 Others	Requirements	S, U	Other Regulations or Comments	Yes/No	If Yes, How, Specifically, is the Requirement Satisfied? or if No, What is the Recommendation?
Part 11 11.10(d)	3.1 Is system access limited to authorized persons?	S, U	China GMP 183 163 Brazil GMP 579, ICH Q7.5.43	Yes	VWorks Plus has both Windows domain and user-based access controls requiring a unique username and password combination. It is the user organization's responsibility to configure and manage these users.
	3.2 Is each user clearly identified, e.g., through his/her own user ID and Password?	S, U	Several Warning Letters	Yes	Each user is identified by a unique user ID and password combination. Entry of both is required to access the system.
Clinical	3.3 Are there controls to maintain a cumulative record that indicates, for any point in time, the names of authorized personnel, their titles, and a description of their access privileges?	S, U	Clinical Computer Guide 4	Yes	VWorks Plus authenticates users via either the Windows Domain or locally in the application itself. Access privileges are set in the application and any changes are recorded in the activity log. Reports are available that show users' individual and inherited group privileges. These reports are useful for organizations required to perform periodic security reviews.

Table 4. Electronic audit trail.

Part 11 Others	Requirements	S, U	Other Regulations or Comments	Yes/No	If Yes, How, Specifically, is the Requirement Satisfied? or if No, What is the Recommendation?
Part 11 11.10(e)	4.1 Is there a secure, computer- generated, time-stamped audit trail to independently record the date and time of operator entries and actions that create, modify, or delete electronic records?	S	China GMP 163 第五章系统 第十六条计算机化系统应当记录输入或 确认关键数据人员的身份。只有经授权人员，方可修改已输入的数据。每次修改一个已输入的关键数据均应当经过批准，并应当记录更改数据的理由。应当根据风险评估的结果，考虑在计算机化系统中建立一个数据审计跟踪系统，用于记录数据的输入和修改。	Yes	VWorks Plus has a secure, computer-generated, time-stamped audit trail for the following records: – Protocols – Forms – Device Files – Device Profiles – Runset Files – VWorks Options – Labware Entries – Labware Classes – Liquid Classes – Pipetting Techniques – VWorks Logs – Macro Library Files – Error Library Files – Barcode Files – JavaScript Files – Log Files
FDA GLP	4.2 Does the audit trail record who has made which changes, when, and why?	S	FDA 21 CFF 58.130 e Clinical Computer Guide 2 Clinical Source Data 3	Yes	The audit trail includes the unique user ID, date and time of the change, and the before and after values together with the reason why the change was made.
Annex 11	4.3 Can the system generate printouts indicating if any of the erecords have been changed since the original entry?	S, U	Annex 11, 8.2	Yes	Audit trail reports can be generated and must be saved either in pdf or in txt format. Once saved, these reports can be opened either in a pdf reader or text editor for printing. It is the user organization's responsibility to maintain the authenticity and integrity of printed records.
FDA GMP	4.4 Does the audit trail include any modifications of an established method employed in testing? 4.5 Do such records include the reason for the modification?	S	Part 211.194 8b	Yes	Methods (VWorks protocols) have full audit trails, including the reason for any method modification.
	4.6 Is the audit trail function configured to be always on and can it not be switched off by system users?	S, U	Warning Letter	Yes	Each record created within the system will go through the following three states: – Development – Validation – Released For records that are in Development state, the audit trail function can be configured to be ON or OFF. For records that are in Validation state, the audit trail will be always ON. It cannot be turned OFF. For records that are in Released state, the system will not allow any modifications.
Annex 11	4.7 Is the audit trail available to a generally intelligible form for regular review?	S	Annex 11, 9	Yes	Audit trails are readily available in human readable format accessed from VWorks Plus.
	4.8 Can audit trail contents be configured such that only relevant activities are recorded for realistic and meaningful review of audit trail information?	U	Implicitly required by Annex 11 and many warning letters related to review of audit trail.	No	Audit trail contents are preprogrammed and cannot be configured.
Part 11 11.10(e)	4.9 Is previously recorded information left unchanged when records are changed?	S		Yes	Changes are stored as a new version of the original record, and the original is left unchanged.
Part 11 11.10(e)	4.10 Is audit trail documentation retained for a period at least as long as that required for the subject electronic record?	S, U		Yes	Audit trail information is stored within the electronic record and cannot be separated from it. It is the user organization's responsibility to maintain the authenticity of electronic records that are backed up.
Part 11 11.10(e)	4.11 Is audit trail available for review and copying by the FDA?	S		Yes	Audit trail reports can be exported as pdf files. These exported reports can be copied/printed for review.
Annex 11	4.12 Is it possible to obtain clear printed copies of electronically stored erecords (e.g., e-audit trail?)	S	Annex 11, 8.1	Yes	Audit trail reports can be exported as pdf files. These exported reports can be copied/printed for review.

Table 5. Operational and device checks.

Part 11 Others	Requirements	S, U	Other Regulations or Comments	Yes/No	If Yes, How, Specifically, is the Requirement Satisfied? or if No, What is the Recommendation?
Part 11 11.10(f)	5.1 Are there operational system checks to enforce permitted sequencing of steps and events, if required?	S, U		Partial	It is the responsibility of the user organization to designate and enforce procedural controls. However Plus has system checks that prevent users from running protocols if they are not in designated states. For example, the system will prevent users from running a protocol that is in Released state if any of its dependent records are in either the Development or Validation state.
Part 11 11.10(g)	5.2 Are there 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?	S	Part 211, 68 b	Yes	The system supports several user roles that control system access at a detailed level. Access can be segregated and defined such that certain users (Administrator, Technician, Operator) have specific types of access (read/write).
	5.3 Is the system designed to record the identity of operators entering, changing, confirming or deleting data including date and time?	S	Annex 11, 12.4	Yes	The identity of operators and related actions are recorded in audit trails, the main log, and the activity log.
Part 11 11.10(h)	5.4 Does the system allow to use device checks to determine, as appropriate, the validity of the source of data input or operational instruction?	S, U	There are two equally valid interpretations of this requirement. Systems should be designed such that: – Proper communication is confirmed between the computer and the "source" of data input (i.e., the instrument) prior to transmission of instructions to or data from the "source." – Regulated records created by the system must unambiguously indicate the "source" of the data (i.e., which instrument or component generated the data.)	Partial	The system has device checks to identify the intended instrument. If during initialization it detects an incorrect instrument, the system will not allow operation to continue. It is the responsibility of the user organization to link the data generated with the instrument that was used to run protocols.
Part 11 11.10(i)	5.5 Is there documented evidence that persons who develop, maintain, or use electronic record/electronic signature systems have the education, training, and experience to perform their assigned tasks?	U	China GMP 18 Brazil 571	N/A	It is the responsibility of the user organization to maintain documented evidence that the persons who develop, maintain, or use electronic record and electronic signature systems have the education, training, and experience needed to perform these tasks.
Part 11 11.10(j)	5.6 Is there a written policy that hold individuals accountable and responsible for actions initiated under their electronic signatures, to determine record and signature falsification?	U		N/A	It is the responsibility of the user organization to establish a written policy (SOP) that holds staff responsible for the actions initiated under their electronic signatures.
	5.7 Have employees been trained on this procedure?	U	Implied requirement of Part 11 11.10(j)	N/A	It is the responsibility of the user organization to train their staff.
Part 11 11.10(k)	5.8 Are there appropriate controls over systems documentation including: – Adequate controls over the distribution of, access to, and use of documentation for system operation and maintenance? – Revision and change control procedures to maintain an audit trail that documents time-sequenced development and modification of systems documentation.	U	China GMP 161 第五章系统 第十一条应当有详细阐述系统的文件（ _必要时，要有图纸），并须及时更新。此文 件应当详细描述系统的工作原理、目的、安全措施和适用范围、计算机运行方式的主 要特征，以及如何与其他系统和程序相接。	N/A	It is the responsibility of the user organization to establish systems documentation.
Part 11 11.10(i)	5.9 Are there revision and change control procedures to maintain an audit trail that documents time-sequenced development and modification of systems documentation?	S, U	第五章系统 第十七条计算机化系统的变更应当根据预定的操作规程进行，操作规程应当包括评估、验证、审核、批准和实施变更等规定。计算机化系统的变更，应经过该部分计算机化系统相关责任人员的同意，变更情况应有记录。主要变更 应当经过验证。	Yes	Agilent maintains development and testing documentation for VWorks Plus and AssayMAP Workbench. Upon request for a vendor audit, documentation can be provided. The user organization is expected to maintain documentation of their system and associated changes *in situ*.

Table 6. Data integrity, date and time accuracy.

Part 11 Others	Requirements	S, U	Other Regulations or Comments	Yes/No	If Yes, How, Specifically, is the Requirement Satisfied? or if No, What is the Recommendation?
Annex 11	6.1 Do computerized systems exchanging data electronically with other systems include appropriate built-in checks for the correct and secure entry and processing of data?	N/A	Annex 11.5	N/A	In this context, VWorks Plus does not exchange data with other systems.
Annex 11	6.2 Is there an additional check on the accuracy of the data? (This check may be done by a second operator or by validated electronic means.)	S, U	Annex 11-6 Brazil GMP 580 ICHQ7-5.45 第五章系统 第十五条当人工输入关键数据时(例如在称重过程中输入物料的重量和批号)_,应当复核输入记录以确保其准确性。这个复核可以由另外一个操作人员完成,或采用经验证的电子方式。必要时,系统应当设置复核功能,确保数据输入的准确性和数据处理过程的正确性。	N/A	VWorks Plus and AssayMAP Workbench allow a second-operator to verify by electronic means through eSignatures.
Clinical Computer Guide	6.3 Are controls established to ensure that the system's date and time are correct?	S, U	Clinical Computer Guide D.3	Yes	Agilent recommends that the system be configured to reference a time server to ensure accuracy of the system date and time. This is configured in and controlled by the operating system.
Clinical Computer Guide	6.4 Can date or time only be changed by authorized personnel, and is such personnel notified if a system date or time discrepancy is detected?	U	Clinical Computer Guide D.3	N/A	VWorks Plus is designed to synchronize with local Windows time. It is the user organization's responsibility to: – Limit access controls of Windows time settings to only authorized personnel. – Maintain procedural controls for setting and maintaining the accuracy of Windows time.
Clinical Computer Guide I	6.5 Are timestamps with a clear understanding of the time zone reference used implemented for systems that span different time zones?	S, U	Clinical Computer Guide D.3	Yes	All time data is time stamped in Coordinated Universal Time (UTC)/Greenwich Mean Time (GMT) and displayed in the local time of the computer used.

Table 7. Control for open systems (only applicable for open systems).

Part 11 Others	Requirements	S, U	Other Regulations or Comments	Yes/No	If Yes, How, Specifically, is the Requirement Satisfied? or if No, What is the Recommendation?
Part 11 11.30	7.1 Are there 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?	N/A		N/A	VWorks Plus and AssayMAP Workbench are not intended to be deployed as an "open" system as per 21 CFR Part 11.3(b)(9).
Part 11 11.30	7.2 Are there 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		N/A	VWorks Plus and AssayMAP Workbench are not intended to be deployed as an "open" system as per 21 CFR Part 11.3(b)(9).

Table 8. Electronic signatures – signature manifestation and signature/record linking.

Part 11 Others	Requirements	S, U	Other Regulations or Comments	Yes/No	If Yes, How, Specifically, is the Requirement Satisfied? or if No, What is the Recommendation?
Annex 11	8.1 When electronic signatures are used, do they have the same impact as hand written signatures within the boundaries of the company? Are they permanently linked to their respective record? Do they include the time and date that they were applied?	S, U	Annex 11.14 ICH Q7.6.18 第五章系统 第二十三条电子数据可以采用电子签名的方式，电子签名应当遵循相应法律法规的要求。	N/A	– The user organization must establish the legal impact of electronic signatures. – Electronic signatures are permanently linked to their respective records. – Signed electronic records include the date and time the signature was executed.
Part 11 11.50 (a)	8.2 Do signed electronic records contain information associated with the signing that clearly indicates all of the following: – The printed name of the signer? – The date and time when the signature was executed? – The meaning (such as review, approval, responsibility, or authorship) associated with the signature?	S, U		N/A	Signed electronic records show: 1. the name of the signer, 2. the date and time the signature was executed, and 3. the meaning of the signature
Part 11 11.50 (b)	8.3 Are the items identified in paragraphs (a)(1), (a)(2), and (a)(3) of this section subject to the same controls as for electronic records and are they included as part of any human readable form of the electronic record (such as electronic display or printout)?	S, U		N/A	All the items identified in paragraph (a)(1), (a)(2), and (a)(3) are subject to the same controls as for electronic records and they are included as part of a human readable form of the electronic record.
Part 11 11.70	8.4 Are electronic signatures and handwritten signatures 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?	U		N/A	Handwritten signatures are not addressed by the system and must be managed by procedurally by the user organization. Electronic signatures are embedded in the electronic record and cannot be modified, overwritten or deleted.
Part 11 Preamble	8.5 Is there a user specific automatic inactivity disconnect measure that would "de log" the user if no entries or actions were taken within a fixed short timeframe?	S, U	Part 11 Preamble section 124	No	The system enables the user's organization to configure automatic session locking after a specified period of inactivity.

Table 9. Electronic signatures general requirements and signature components and controls.

Part 11 Others	Requirements	S, U	Other Regulations or Comments	Yes/No	If Yes, How, Specifically, is the Requirement Satisfied? or if No, What is the Recommendation?
Part 11 11.100(a)	9.1 Is each electronic signature unique to one individual and not reused by, or reassigned to, anyone else?	S, U		N/A	VWorks Plus can be configured to authenticate users with Windows Active Directory. It is the user organization responsibility to configure Active Directory authentication method and define security policies to prevent duplication and deletion of user accounts.
Part 11 11.100(b)	9.2 Does the organization verify the identity of the individual before the organization establishes, assigns, certifies, or otherwise sanctions an individual's electronic signature, or any element of such electronic signature?	U		N/A	It is the responsibility of the user organization to verify the identify of staff before it establishes, assigns, certifies, or otherwise sanctions an individual's electronic signature, or any element of such electronic signature.
Part 11 11.100 (c)	9.3 Are persons using electronic signatures, prior to or at the time of such use, certified 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? 9.4 Do persons using electronic signatures, upon agency request provide additional certification or testimony that a specific electronic signature is the legally binding equivalent of the signer's handwritten signature?	U		N/A	It is the responsibility of the user organization to verify that staff using electronic signatures meet these requirements.
Part 11 11.200(a) (1)	9.5 Do electronic signatures that are not based upon biometrics employ at least two distinct identification components such as an identification code and password?	S, U		Yes	Both identification (user name) and password are required to make an electronic signature.
Part 11 11.200(a) (1) (i)	9.6 When an individual executes a series of signings during a single, continuous period of controlled system access, is the first signing executed using all electronic signature components?	S		Yes	The first signing executed requires both identification (user name) and password are required to make an electronic signature.
Part 11 11.200(a) (1) (i)	9.7 When an individual executes a series of signings during a single, continuous period of controlled system access, are subsequent signings executed using at least one electronic signature component that is only executable by, and designed to be used only by, the individual?	S		Yes	Both identification (user name) and password are required to make an electronic signature.
Part 11 11.200(a) (1) (ii)	9.8 When an individual executes one or more signings not performed during a single, continuous period of controlled system access, is each signing executed using all of the electronic signature components?	S		Yes	Both identification (user name) and password are required to make an electronic signature.
Part 11 11.200(a) (2)	9.9 Are controls in place to ensure that electronic signatures that are not based upon biometrics are used only by their genuine owners?	S, U		Yes	Both identification (user ID) and password are required to make all electronic signatures. It is the user organization's responsibility to ensure that user names and passwords are known only by the assigned individuals and are traceable to individual users.
Part 11 11.200(a) (3)	9.10 Are the electronic signatures 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?	U		N/A	Misuse of electronic signatures by anyone other than the owner would require intentional co-operation of a user and the System Administrator. It is the user organization's responsibility to ensure that user names and passwords are known only by the assigned individuals and are traceable to individual users.
Part 11 11.200(b)	9.11 Are electronic signatures based upon biometrics designed to ensure that they cannot be used by anyone other than their genuine owners?	U		N/A	Biometric authentication is not supported in VWorks Plus.

Table 10. Controls for identification codes and passwords.

Part 11 Others	Requirements	S, U	Other Regulations or Comments	Yes/No	If Yes, How, Specifically, is the Requirement Satisfied? or if No, What is the Recommendation?
Part 11 11.300(a)	10.1 Are controls in place to maintain the uniqueness of each combined identification code and password, such that no two individuals have the same combination of identification code and password?	S, U		Yes	VWorks Plus can be configured to authenticate users with Windows Active Directory. It is the user organization responsibility to configure Active Directory authentication method and define security policies to prevent duplication and deletion of user accounts.
Part 11 11.300(b)	10.2 Are controls in place to ensure that identification code and password issuance are periodically checked, recalled, or revised (e.g., to cover such events as password aging)?	S, U		Yes	Password expiration is configurable via either the Windows Domain/Active Directory or locally in the application itself. The user organization should configure password expiration based on a documented risk assessment.
Part 11 11.300(c)	10.3 Are there 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? Are there procedures to issue temporary or permanent replacements using suitable, rigorous controls?	S, U	第五章系统 第十四条数据的输入或修改只能由经许 可的人员进行。杜绝未经许可的人员输入数据的手段有：使用钥匙、密码卡、个人密码和限制对计算机终端的访问。应当就输入和修改数据制订一个授权、取消、授权变更，以及改变个人密码的规程。必要时，应当考虑系统能记录未经许可的人员试图访问系统的行为。对于系统自身缺陷，无法实现人员控制的，必须具有书面程序，相关记录本及相关物理隔离手段，保证只有经许可的人员方能进行操作。	Yes	VWorks Plus has the ability to deactivate user accounts as needed. However, it is the responsibility of the user organization to establish these transaction safeguards. Windows Domain/Active Directory can be used to control access to the system outside of the application.
Part 11 11.300(d)	10.4 Are there transaction safeguards in place to prevent unauthorized use of passwords and/or identification codes? Are there safeguards 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?	U	第五章系统 第十四条数据的输入或修改只能由经许 可的人员进行。杜绝未经许可的人员输入数据的手段有：使用钥匙、密码卡、个人密码和限制对计算机终端的访问。应当就输入和修改数据制订一个授权、取消、授权变更，以及改变个人密码的规程。必要时，应当考虑系统能记录未经许可的人员试图访问系统的行为。对于系统自身缺陷，无法实现人员控制的，必须具有书面程序，相关记录本及相关物理隔离手段，保证只有经许可的人员方能进行操作。	N/A	It is the responsibility of the user organization to establish these transaction safeguards.
Part 11 11.300(e)	10.5 Are there controls for 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?	U		N/A	It is the responsibility of the user organization to establish controls to test devices initially as well as periodically to ensure they function properly and have not been altered in an unauthorized manner.
Annex 12.3	10.6 Creation, change, and cancellation of access authorizations should be recorded.	S	所有授权的建立、授权的更改和授权的取消都应有记录	Yes	Creation, change, and cancellation of access authorizations are managed locally by the system and recorded in the activity log. If the organization chooses to authenticate users with Windows Active Directory, then the user's organization has responsibility to configure Active Directory authentication method and define security policies to prevent duplication and deletion of user accounts.

Table 11. System development and support.

Part 11 Others	Requirements	S, U	Other Regulations or Comments	Yes/No	If Yes, How, Specifically, is the Requirement Satisfied? or if No, What is the Recommendation?
Annex 11	11.1 Has the software or system been developed in accordance with an appropriate quality management system?	S, U	Annex 11 4.5 Brazil GMP 577 GAMP This is a shared responsibility between the system supplier and the user organization. The user should require the supplier to provide documented evidence that software is developed within the framework of a quality management system (QMS). 第二章原则 企业应当能够提供与供应商质量体系和审计信息相关的文件。	Yes	VWorks Plus is developed within the ISO 9001 Quality Management Standard (Ref. section 2.2 of the LSCA Quality Manual).
Brazil	11.2 Is there a formal agreement in case the software supplier subcontracts software and maintenance services? Does the agreement include the contractor's responsibilities?	S, U	Brazil GMP 589 第二章原则 第四条企业应当注重计算机化系统供应商的管理，制定相应的操作规程。供应商提供产品或服务时（如安装、配 置、集成、验证、维护、数据处理等），_企业应当与供应商签订正式协议，明确双方责任。	Yes	Agilent requires formal agreements with all suppliers. (Ref. section 7.4 of the LSCA Quality Manual).
ICH Q10	11.3 For outsourced (development and support) activities, is there a written agreement between the contract giver and contract acceptor?	S, U	ICHQ10, 2.7 c	Yes	Agilent requires formal agreements with all suppliers (Ref. section 7.4 of the LSCA Quality Manual).
ICH Q10	11.4 Are the responsibilities and communication processes for quality related activities of the involved parties (contractors) defined?	S, U	ICHQ10, 2.7 c	Yes	Agilent requires formal agreements with all suppliers (Ref. section 7.4 of the LSCA Quality Manual).
Part 11 11.10(i)	11.5 Is personnel developing and supporting software trained?	S, U	第三章人员 第五条计算机化系统的“生命周期”中所涉及的各种活动，如验证、维护、管理等，需要各相关的职能部门人员之间的紧密合作。在职责中涉及使用和管理计算机化系统的人员，应当接受相应的使用和管理培训。确保有适当的专业人员，对计算机化系统的设计、验证、安装和运行等方面进行培训和指导。	Yes	All Agilent personnel are required to be trained (Ref. section 6.0 of the LSCA Quality Manual).

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