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COMPLIANCE RESPONSE ERES

Siemens Opcenter Execution Pharma V2305

Electronic Records / Electronic Signatures

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Execution Pharma V2305 ERES Compliance Response

Product Information

Electronic Records /
Electronic Signatures (ERES)

10/2023
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Legal information

Warning notice system

This manual contains notices you have to observe in order to ensure your personal safety, as well as to prevent damage to property. The notices referring to your personal safety are highlighted in the manual by a safety alert symbol, notices referring only to property damage have no safety alert symbol. These notices shown below are graded according to the degree of danger.

⚠ DANGER

indicates that death or severe personal injury **will** result if proper precautions are not taken.

⚠ WARNING

indicates that death or severe personal injury **may** result if proper precautions are not taken.

⚠ CAUTION

indicates that minor personal injury can result if proper precautions are not taken.

NOTICE

indicates that property damage can result if proper precautions are not taken.

If more than one degree of danger is present, the warning notice representing the highest degree of danger will be used. A notice warning of injury to persons with a safety alert symbol may also include a warning relating to property damage.

Qualified Personnel

The product/system described in this documentation may be operated only by **personnel qualified** for the specific task in accordance with the relevant documentation, in particular its warning notices and safety instructions. Qualified personnel are those who, based on their training and experience, are capable of identifying risks and avoiding potential hazards when working with these products/systems.

Proper use of Siemens products

Note the following:

⚠ WARNING

Siemens products may only be used for the applications described in the catalog and in the relevant technical documentation. If products and components from other manufacturers are used, these must be recommended or approved by Siemens. Proper transport, storage, installation, assembly, commissioning, operation and maintenance are required to ensure that the products operate safely and without any problems. The permissible ambient conditions must be complied with. The information in the relevant documentation must be observed.

Trademarks

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Disclaimer of Liability

We have reviewed the contents of this publication to ensure consistency with the hardware and software described. Since variance cannot be precluded entirely, we cannot guarantee full consistency. However, the information in this publication is reviewed regularly and any necessary corrections are included in subsequent editions.

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Introduction

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Life science industry is basing key decisions on regulated records that are increasingly generated, processed and kept electronically. Reviews and approval of such data are also being provided electronically. Thus the appropriate management of electronic records and electronic signatures has become an important topic for the life science industry.

Accordingly, regulatory bodies defined criteria under which electronic records and electronic signatures will be considered as reliable and trustworthy as paper records and handwritten signatures executed on paper. These requirements have been set forth by the US FDA in 21 CFR Part 11 (21 CFR Part 11 Electronic Records; Electronic Signatures, US FDA, 1997; in short: *Part 11*) and by the European Commission in Annex 11 of the EU GMP Guideline (EU Guidelines to Good Manufacturing Practice, Volume 4, Annex 11: Computerised Systems, European Commission, 2011; in short: *Annex 11*).
Since requirements on electronic records and electronic signatures are always tied to a computerized system being in a validated state, both regulations also include stipulations on validation and lifecycle of the computerized system.

Application of *Part 11* and *Annex 11* (or their corresponding implementation in national legislation) is mandatory for the use of electronic records and electronic signatures. However, these regulations are only valid within their defined scope.
The scope of both regulations is defined by the regional market to which the finished pharmaceutical product is distributed and by whether or not the computerized systems and electronic records are used as part of GMP-regulated activities (see Part 11.1 and Annex 11 Principle).

Supplemental to the regulations, a number of guidance documents, good practice guides and interpretations have been published in recent years to support the implementation of the regulations. Some of them are referred to within this document.

To help its clients, Siemens as supplier of Opcenter Execution Pharma has evaluated the system with regard to these requirements and published its results in this Compliance Response.

Siemens Opcenter Execution Pharma version V2305 fully meets the functional requirements for the use of electronic records and electronic signatures.

Operation in conformity with the regulations is ensured in conjunction with organizational measures and procedural controls to be established by the regulated user. Such measures and controls are mentioned in chapter "Evaluation List for Opcenter Execution Pharma (Page 19)" of this document.

This document is divided into three parts:

1. Chapter "The Requirements in Short (Page 7)" provides a brief description of the requirement clusters.
2. Chapter "Meeting the Requirements with Opcenter Execution Pharma (Page 9)" introduces the functionality of Siemens Opcenter Execution Pharma as means to meet those requirements.
3. Chapter "Evaluation List for Opcenter Execution Pharma (Page 19)" contains a detailed system assessment on the basis of the individual requirements of the relevant regulations.

The Requirements in Short

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The requirements of Annex 11 and Part 11 have the purpose of protecting regulated electronic records and electronic signatures (short: ERES) against manipulation, misinterpretations and incomprehensible changes.

The term "electronic record" means any combination of text, graphics, data, audio, pictorial or other information representation in digital form, that is created, modified, maintained, archived, retrieved or distributed by a computer system for use in a regulated process.

The "electronic signature" is a legally binding equivalent of a handwritten signature. The submission of the signature is a technical process for identifying the signatory, whereas the representation of the signature in connection with the signed action becomes part of the electronic documentation. Since electronic signatures are also considered as being electronic records by themselves, all requirements for electronic records are applied to electronic signatures too.

The following table provides an overview of the requirements from both regulations.

Requirement	Description
Lifecycle and Validation of Computerized Systems	Computerized systems used as a part of GMP-related activities must be validated. The validation process should be defined using a risk-based approach. It should cover all relevant steps of the lifecycle and must provide appropriate documented evidence. The system's functionality should be traceable throughout the lifecycle by being documented in specifications or a system description. A formal change control procedure as well as an incident management should be established. Periodic evaluation should confirm that the validated state of the system is being maintained.
Suppliers and Service Providers	Since competency and reliability of suppliers and service providers are considered key factors, the supplier assessment should be decided on a risk-based approach. Formal agreements should exist between the regulated user and these third parties, including clear responsibilities of the third party.
Data Integrity	Under the requirements of both regulations, electronic records and electronic signatures must be as reliable and trustworthy as paper records. The system must provide the ability to discern altered records. Built-in checks for the correct and secure handling of data should be provided for manually entered data as well as for data being electronically exchanged with other systems. The system's ability to generate accurate and complete copies is essential for the use of the electronic records for regulated purposes, as well as the accessibility, readability, and integrity of archived data throughout the retention period.
Audit Trail, Change Control Support	Besides recording changes to the system as defined in the lifecycle, both regulations require that changes on GMP-relevant data are being recorded. Such an audit trail should include information on the change (before / after data), the identity of the operator, a time stamp, as well as the reason for the change.

Requirement	Description
System Access, Identification Codes and Passwords	Access to the system must be limited to authorized individuals. Attention should be paid to password security. Changes on the configuration of user access management should be recorded. Periodic reviews should ensure the validity of identification codes. Procedures should exist for recalling access rights if a person leaves and for loss management. Special consideration should be given to the use of devices that bear or generate identification code or password information.
Electronic Signature	Regulations consider electronic signatures being legally binding and generally equivalent to handwritten signatures executed on paper. Beyond requirements on identification codes and passwords as stated above, electronic signatures must be unique to an individual. They must be linked to their respective electronic record and not be copied or otherwise being altered.
Open Systems	Open systems might require additional controls or measures to ensure data integrity and confidentiality.

Meeting the Requirements with Opcenter Execution Pharma

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The Siemens recommendations for the system architecture, conception and installation will assist system users in achieving compliance. For additional information and assistance, refer to Siemens Opcenter Execution Pharma functional and technical documentation from Siemens.

The requirements explained in chapter "The Requirements in Short (Page 7)" can be supported by the system as follows.

The basic data control policies of a regulated company relate to persons, processes and techniques.

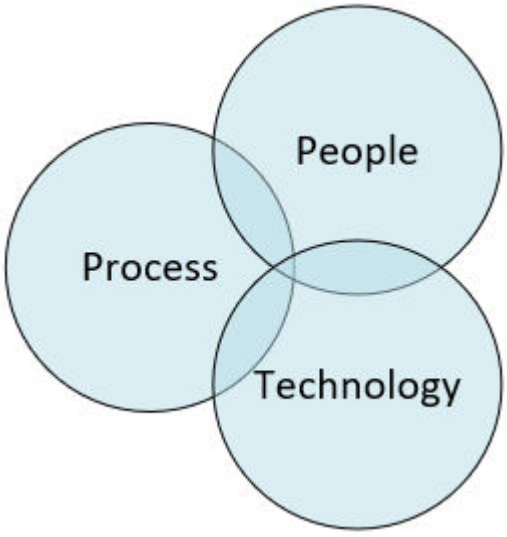

Figure 3-1 Elements of data control

Only the sum of all measures can ensure that the system is operated in compliance with the regulatory requirements.

- Process: Procedures, for example, for operation, change management, validation and archiving
- People: Suitable qualification, training of staff and following the established processes
- Technology: Selection and functionality of the basic components as well as specific configuration for the application

3.1 Lifecycle and Validation of Computerized Systems

In Annex 11 from 1992 and in Part 11 from 1997, the law already required that computerized systems need to be validated. Criteria for the validation of the system and its lifecycle were added in the edited revision of Annex 11 from 2011.

Requirements for the validation of computerized systems and for the maintenance of the validated state are also part of other publications, such as the Baseline Guides, the GAMP Guides and the GAMP Good Practice Guides of the ISPE (International Society of Pharmaceutical Engineers (https://www.ispe.org)) industry association.

Consequently, the system lifecycle and validation approach should be defined taking into account the recommendations of the GAMP 5 Guide (GAMP 5 - A risk-based approach to compliant GxP computerized systems). Topics such as lifecycle management, system development and operation of computerized systems are also dealt with in detail in the GAMP Guides.

3.2 Suppliers and Service Providers

Suppliers of systems, solutions and services must be evaluated accordingly, see GAMP 5 Appendix M2. Siemens as a manufacturer of hardware and software components follows internal procedures of Product Lifecycle Management and works according to a Quality Management System, which is regularly reviewed and certified by an external certification company.

3.3 Data Integrity

Regulated companies should implement integrated data integrity strategies. Of particular interest are the data used to make decisions that have an impact on product quality and patient safety.

The reliability of the data requires a high degree of data integrity over the entire retention period and also extends to the archiving and retrieval of data.

In addition, the system must have the ability to detect invalid or altered records. On the computer system side, functionalities such as access protection, audit trail, data type checks, checksums, data backup/restore, and data archiving/retrieval help maintain data integrity. These measures and technical characteristics are complemented by system validation, appropriate work procedures and staff training.

IT security

IT Security is also essential for achieving and retaining data integrity. Support from Siemens can be found under Industrial Security Services. (https://new.siemens.com/global/en/products/services/digital-enterprise-services/industrial-security-services.html)

Data storage

All data is stored in a database. As described in the security recommendation document it is strongly recommended to activate the security functionality during installation of the database. Encryption of the database and the connection between server and client will therefore be enabled.

It is also possible to link external data, such as pdf files containing material certificates, to a data set. The responsibility for the integrity of all linked documents is with the regulated user.

Siemens Opcenter Execution Pharma can support the user by individually identifying each attached file and generating a checksum in order to detect any alteration to these documents. If an alteration is detected, the system will notify the user and display an error message.

Electronic batch report

Siemens Opcenter Execution Pharma is able to generate a clearly structured electronic batch report in PDF/A file format to allow easy review and archiving of the completed batch record. The electronic batch report contains a comprehensive summary and attachments with detailed information. These attachments consist of weighing and dispensing reports, the execution report which describes the batch manufacturing in detail and the annex collection. Additional records that are provided with the system include list of equipments, list of users or list of deviations, and others may be created individually.

The electronic batch report may be generated either any time manually or at specific events automatically for example when the status of the batch review becomes approved. Siemens Opcenter Execution Pharma can then notify via email the successfully generation of the pdf file containing the electronic batch record.

Archiving

Siemens Opcenter Execution Pharma provides a configurable and scalable archiving function. Messages and measured values are stored continuously to the local database. External files, like for example material certificates, can be stored in a repository folder.

The stored data in the database can be transferred automatically to the online archive. Archived data can be retrieved within the entire, configured retention period. Data can also be moved from the online archive database to the export database, which is being used as an interface to third party archiving tools. External data needs to be handled accordingly to the archiving strategy of the regulated user and the Siemens Opcenter Execution Pharma functional documentation.

3.4 Audit Trail, Change Control Support

"Audit trails are of particular importance in areas where operator actions generate, modify, or delete data in the course of normal operation." (Guidance for Industry Part 11 – Scope and Application, FDA, 2003)

An audit trail is not required for automatically generated electronic records which can neither be modified nor deleted by the operator. The system provides adequate system security mechanisms for such electronic records.

Changes to the configuration of a validated system are subject to a change procedure and must be controlled accordingly. This can be supported by versioning, system logs and similar means. The following sections therefore distinguish between the requirements for audit trails during operation and the control of configuration changes in engineering.

Recordings during runtime

Siemens Opcenter Execution Pharma supports the requirement for audit trail of GMP relevant operations by recording such actions appropriately (who, what, when, and optionally why) and it provides adequate system security for such electronic records (e.g. access control). The GMP relevant data is defined by the regulated company based on the applicable regulatory requirements. All audit trails can either be printed on paper or be exported in an electronical format.

Operator actions performed in Siemens Opcenter Execution Pharma are being recorded in an audit trail, containing information like old value, new value, user ID, date and time stamp, operation and optionally comments.

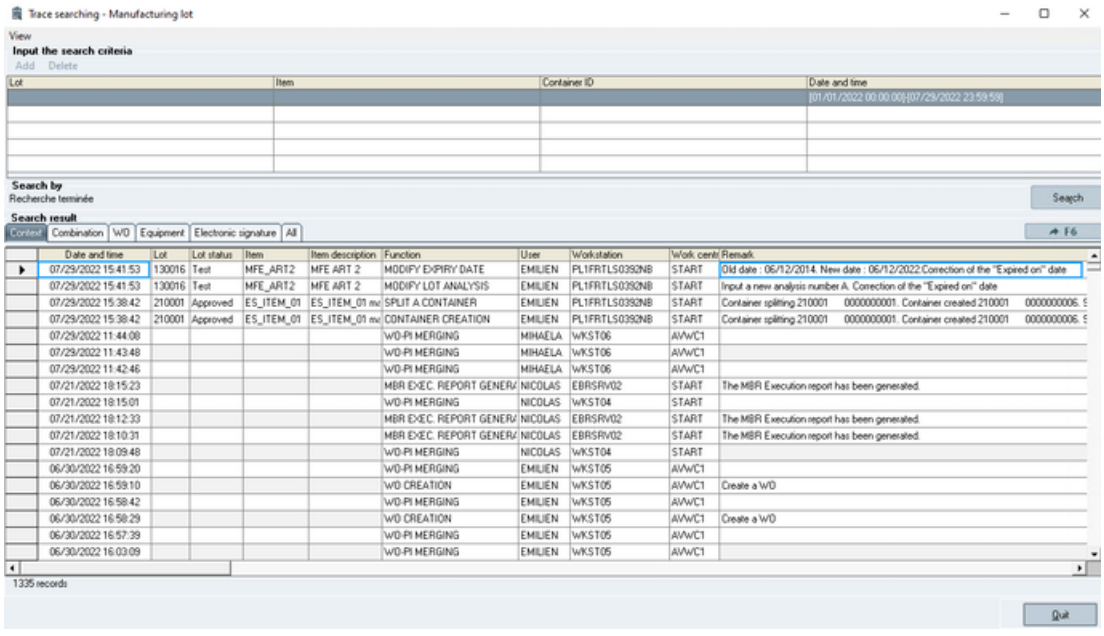

Figure 3-2 Audit trail of a weighing work order

Changes in the item management, sampling rules, labels and scales

All changes for adding, deleting or modifying parameters or in the case of items also validating, invalidating and the activity status of the item master are included in the audit trail.

Configuration control

Changes in the user management

User management can be set up using the Microsoft Active Directory. Any changes made in the course phase of user management (e.g. setup of new users, blocking users, etc.) are recorded in the event log of Microsoft Windows. The event log must be configured accordingly, as described in the Microsoft documentation.

Changes in the configuration

Changes for adding, deleting or modifying parameters are stored.

3.5 System Access, Identification Codes and Passwords

Users must be assigned the required access rights only, to prevent unauthorized access to the file system, the directory structures, and the system data and their unintended manipulation.

The requirements regarding access security are fully met in combination with procedural controls, such as those for "specifying rights and roles".

Adequate security mechanisms are essential for the secure operation of a system. This applies especially to "open paths" which must be protected by additional measures.
For more information on the basic policies of the security concept and configuration recommendations, refer to the Siemens Opcenter Execution Pharma security manual.

The Siemens Opcenter Execution Pharma user management application, a basic functionality of Siemens Opcenter Execution Pharma, is used to set up user management either based on Microsoft Windows security mechanisms or using a custom authentication assembly. The basic functionalities of this application are listed below:

- Management of the system functionalities
- Management of user groups
- Management of user accounts
- Management of audit trail

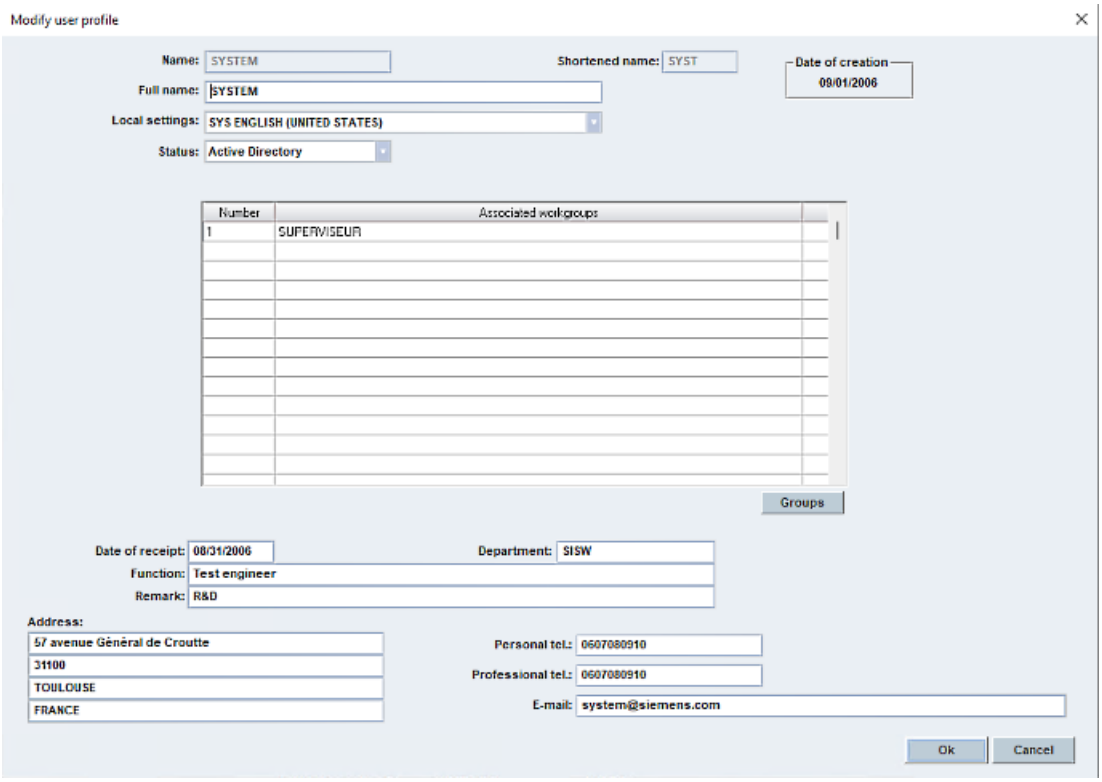

Figure 3-3 View of a user profile

Thereby the following requirements for access protection are fulfilled:

- Central user management (setup, deactivation, blocking, unblocking, assignment to user groups) by the administrator
- Use of a unique user identification (user ID) in combination with a password
- Definition of system functionalities and access for specific user groups
- Password settings and password aging: The password settings are being managed by Microsoft Windows security mechanisms or by a custom authentication assembly
- The user is automatically blocked after a configurable number of failed logon attempts and can only be unblocked by administrators who have the user management rights
- Automatic lock after a configurable idle time of the keyboard and mouse or if the application is running during the idle time as a background task
- Log functions for actions related to access security, such as logon, manual and automatic logoff, input of incorrect user ID or password, user put into not allowed status after several attempts to enter an incorrect password, and password change by user
- Concurrent access in order to enter records is being prohibited by the system

In addition, users must be assigned specific access rights at operating system level to prevent unauthorized access to the directory structure of the Siemens Opcenter Execution Pharma system programs and unintended manipulation.

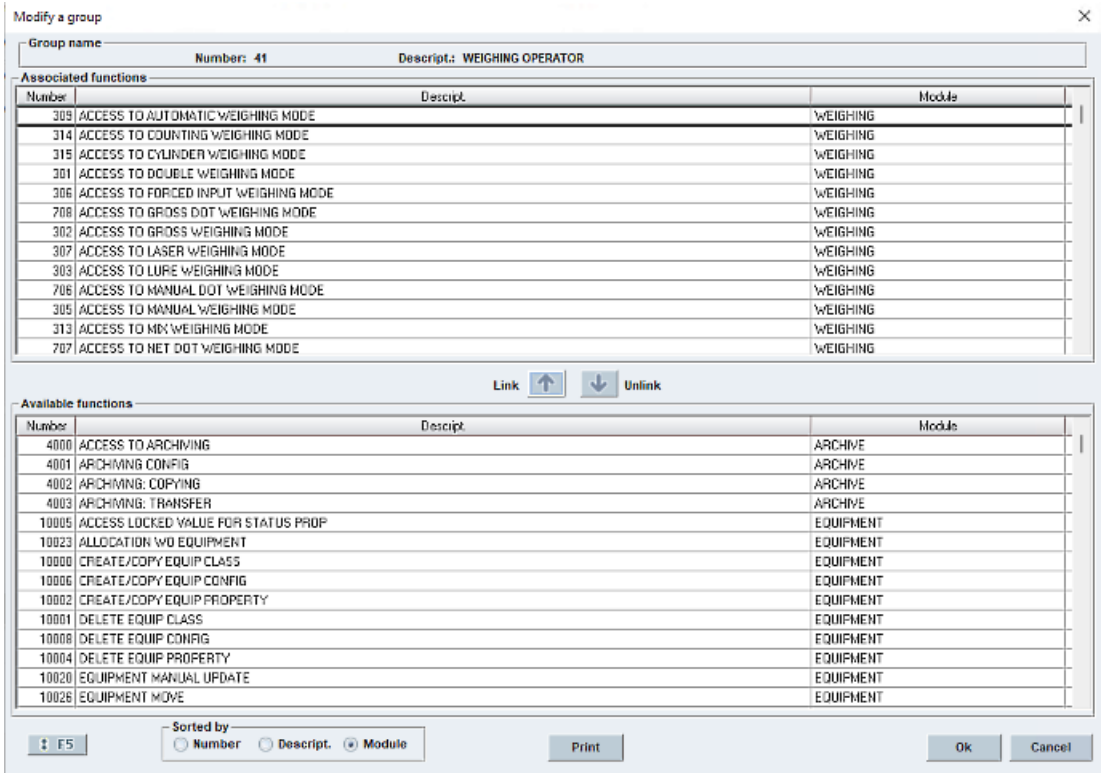

Figure 3-4 Assigning functions to the group "Weighing operator"

3.6 Electronic Signature

In the following section only the electronic signatures performed through the core system are evaluated. Siemens Opcenter Execution Pharma provides functions for configuring an electronic signature. The operations or actions which require an electronic signature, which group is able to sign this action and the sequence of signatures are specified during the configuration phase. In order to meet the individual validation process, four different electronic signature types are predefined:

- Single electronic signature (signature of the user who performed the action)
- Double (conditional) electronic signature (if the original operator does not have the rights to validate the performed action an additional signature of a responsible user is needed)
- Single check electronic signature (signature of a user who differs from the user who performed the action)
- Double check electronic signature (signature of the user who performed the action and a user who did not perform the action)

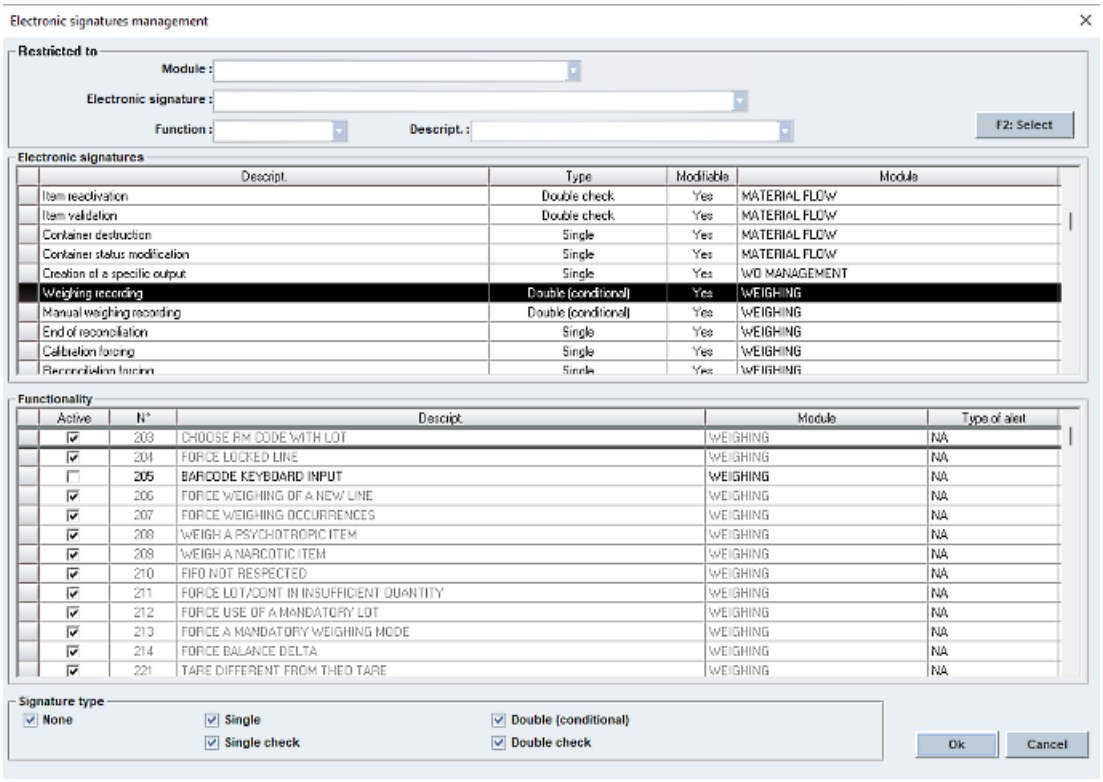

Figure 3-5 Configuring electronic signature for different actions

The electronic signature is being executed in a separate dialog in which the user has to sign electronically by confirming the intended action with entering his password. Subsequently the electronic signature is saved in the audit trail along with the user name, time stamp, and the action performed. Also failed attempts to perform an electronic signature is saved in the audit trail. A mandatory comment is needed to validate the electronic signature. Comments can be free text or predefined text for each electronic signature.

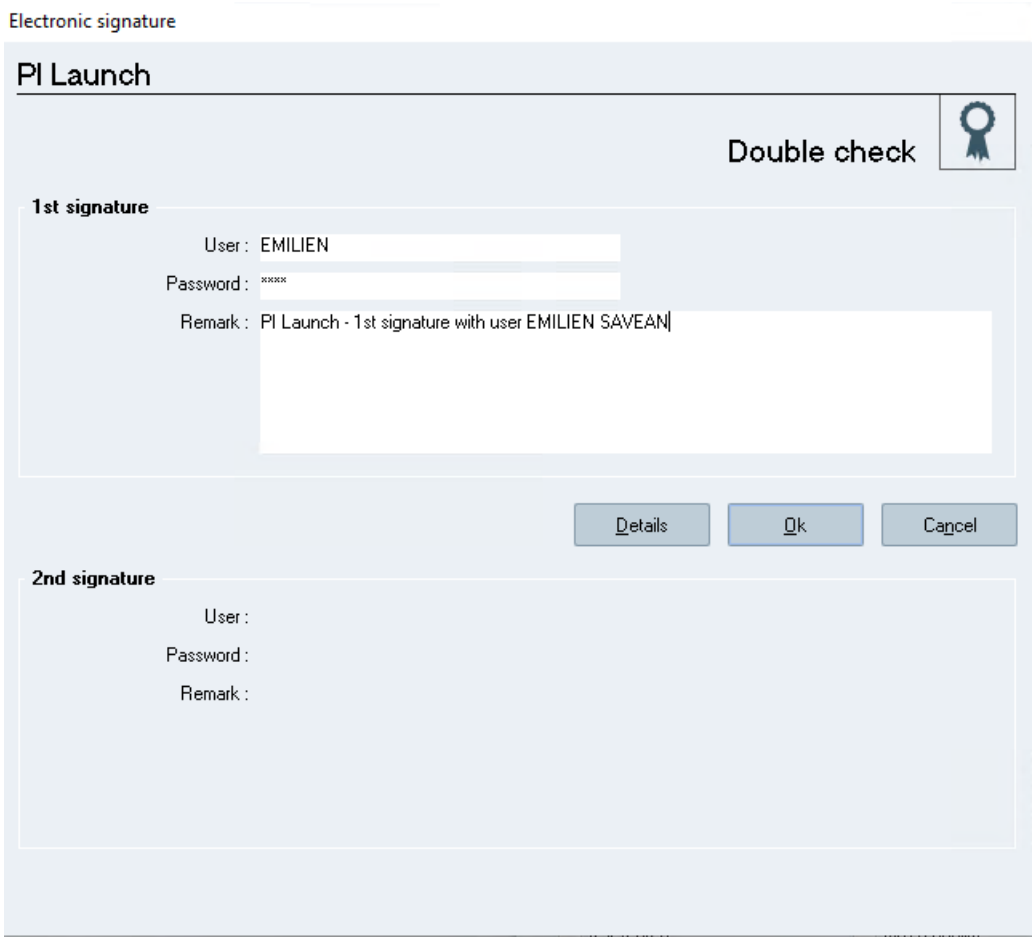

Figure 3-6 Dialog double check electronic signature

Evaluation List for Opcenter Execution Pharma 4

The following list of requirements includes all regulatory requirements from 21 CFR Part 11 as well as from Annex 11 of the EU-GMP Guidelines. All requirements are structured in the same topics as those introduced in the chapter "The Requirements in Short (Page 7)" of this Compliance Response.

The *requirements* listed fully consider both regulations, regardless of whether technological or procedural controls or a combination of both are needed to fully comply with Part 11 and Annex 11.

The *answers* include, among other things, information about how the requirement is handled during the development of the product and which measures should be implemented during configuration and operation of the system. Furthermore, the answers include references to the product documentation for technical topics and to the GAMP 5 guide for procedural controls that are already considered in the guide.

4.1 Lifecycle and Validation of Computerized Systems

The fundamental requirement that a computerized system, used as a part of GMP related activities, must be validated is extended in the revision of Annex 11 from 2011 by requirements detailing expectations on a system's lifecycle.

	Requirement	Reference	Answer
4.1.1	Risk management should be applied throughout the lifecycle of the computerized system.	Annex 11, 1	The PLM process (Product Lifecycle Management) is the development process of Siemens software products. This process incorporates risk management accordingly. During the validation and operation of the system, risk management must be ensured by the regulated user.
4.1.2	Validation of a system ensures its accuracy, reliability, consistent intended performance, and the ability to discern invalid or altered records.	21 CFR 11.10 (a)	Yes, the development of the software product (COTS, see Annex 11, glossary) is under the control of the Siemens QMS and the PLM process. The regulated user should take appropriate measures to validate the application (see Annex 11, glossary), as well as maintaining its validated state.
4.1.3	Validation documentation covers relevant steps of the lifecycle.	Annex 11, 4.1	Yes. The PLM process includes all relevant documents. The responsibility for the validation of the application (see Annex 11, glossary) is with the regulated user.
4.1.4	A process for the validation of bespoke or customized systems should be in place.	Annex 11, 4.6	Customer-specific applications are verified in the scope of realization according to the responsibilities agreed upon in the project. The validation process is the responsibility of the regulated user.

	Requirement	Reference	Answer
4.1.5	Change management and deviation management are applied during the validation process.	Annex 11, 4.2	Yes. The PLM process includes change management, deviation management and fault corrections. The regulated user should ensure appropriate change management and deviation management (see GAMP 5, appendices M8 and D5).
4.1.6	An up-to-date inventory of all relevant systems and their GMP functionality is available. For critical systems an up-to-date system description [...] should be available.	Annex 11, 4.3	The regulated user should establish appropriate reporting, a system inventory as well as system descriptions (see GAMP 5, appendix D6).
4.1.7	User Requirements Specifications should describe required functions, be risk-based and be traceable throughout the lifecycle.	Annex 11, 4.4	Yes. Specification of requirements is part of the PLM process. For the project-specific configuration, the regulated user must appropriately describe the user requirements in the system's lifecycle (see GAMP 5, appendix D1).
4.1.8	Evidence of appropriate test methods and test scenarios should be demonstrated.	Annex 11, 4.7	Ensuring the suitability of test methods and scenarios is an integral part of the PLM process and test planning. The regulated user should be involved in the agreement of testing practice (see GAMP 5, appendix D5) for the application.
4.1.9	Appropriate controls should be used over system documentation. Such controls include the distribution of, access to, and use of system operation and maintenance documentation.	21 CFR 11.10 (k)	Yes. During the development of the product the product's documentation is treated as being part of the product. As such, appropriate controls are ensured by the PLM process. The regulated user should establish appropriate procedural controls during development and operation of the production system (see GAMP 5, appendices M9 and D6).
4.1.10	A formal change control procedure for system documentation maintains a time sequenced record of changes.	21 CFR 11.10 (k) Annex 11.10	During the development of the product changes are handled according to the PLM process. The regulated user should establish appropriate procedural controls during development and operation of the system (see GAMP 5, appendices M8 and O6).
4.1.11	Persons who develop, maintain, or use electronic record/electronic signature systems should have the education, training and experience to perform their assigned task.	21 CFR 11.10 (i)	Siemens' processes do ensure that employees have according training for their tasks and that such training is properly documented. Furthermore, Siemens offers a variety of training courses for users, administrators and support staff.
4.1.12	Computerized systems should be periodically evaluated to confirm that they remain in a valid state and are compliant with GMP.	Annex 11, 11	The regulated user should establish appropriate procedural controls (see GAMP 5, appendices O3 and O8).

	Requirement	Reference	Answer
4.1.13	All incidents should be reported and assessed.	Annex 11, 13	The Siemens Opcenter portfolio offers functionalities to support reporting on different system levels. The regulated user should establish appropriate procedural controls (see GAMP 5, appendix O5).
4.1.14	For the availability of computerized systems supporting critical processes, provisions should be made to ensure continuity of support for those processes in the event of a system breakdown.	Annex 11, 16	The regulated user should appropriately consider the system in his business continuity planning (see GAMP 5, appendix O10).

4.2 Suppliers and Service Providers

If the regulated user is partnering with third parties for planning, development, validation, operation and maintenance of a computerized system, then the competence and reliability of this partner should be considered utilizing a risk-based approach.

	Requirement	Reference	Answer
4.2.1	When third parties are used, formal agreements must exist between the manufacturer and any third parties.	Annex 11, 3.1	The regulated user is responsible to establish formal agreements with suppliers and third parties (see GAMP 5, appendix O2).
4.2.2	The competency and reliability of a supplier are key factors when selecting a product or service provider. The need for an audit should be based on a risk assessment.	Annex 11, 3.2 Annex 11, 4.5	The regulated user should assess its suppliers accordingly (see GAMP 5, appendix M2).
4.2.3	The regulated user should ensure that the system has been developed in accordance with an appropriate Quality Management System.	Annex 11, 4.5	The development of Siemens Opcenter products follows the PLM process stipulated in the Siemens Quality Management System.
4.2.4	Documentation supplied with commercial off-the-shelf products should be reviewed by regulated users to check that user requirements are fulfilled.	Annex 11, 3.3	The regulated user is responsible for the performance of such reviews.
4.2.5	Quality system and audit information relating to suppliers or developers of software and implemented systems should be made available to inspectors on request.	Annex 11, 3.4	Matter and extent of the documentation affected by this requirement should be agreed upon by the regulated user and Siemens. The joint non-disclosure agreement should reflect this requirement accordingly.

4.3 Data Integrity

The main goal of both regulations is to define criteria under which electronic records and electronic signatures are as reliable and trustworthy as paper records. This requires a high degree of data integrity throughout the whole data retention period, including archiving and retrieval of relevant data.

	Requirement	Reference	Answer
4.3.1	The system should provide the ability to discern invalid or altered records.	21 CFR 11.10 (a)	Yes. Based on the database security settings, access is only possible via Siemens Opcenter Execution Pharma. An entry in the audit trail will be generated for any operator action (for example, the operator changes set points / alarm thresholds / the monitoring mode or acknowledges alarms). All relevant changes are recorded including time stamp, user ID, old value and new value and comment. Unauthorized changes are prevented by the system through access control. A finalized electronic batch record and archived data can be accessed in read only mode and cannot be altered. The handling of external files which might be attached to data of Siemens Opcenter Execution Pharma is in the responsibility of the regulated user. It is possible to implement security functionalities within Siemens Opcenter Execution Pharma to ensure the integrity of external files.
4.3.2	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.	Annex 11, 8.2	Yes. Operational modification of data is recorded in the general audit trail and can be printed out in a report.
4.3.3	The system should provide the ability to generate accurate and complete copies of electronic records in both human readable and electronic form.	21 CFR 11.10 (b) Annex 11, 8.1	Yes. Accurate and complete copies can be generated either manually or automatically in electronic formats or on paper.
4.3.4	Computerized systems exchanging data electronically with other systems should include appropriate built-in checks for the correct and secure entry and processing of data.	Annex 11, 5	Yes. The exchange of data is ensured via the gateway database. In this module a built-in data type check validates the correctness of incoming data.
4.3.5	For critical data entered manually, there should be an additional check on the accuracy of the data.	Annex 11, 6	Yes. The system has built-in plausibility checks for data entry. In addition, a multiple signature or operator dialog can be realized as an additional check.
4.3.6	Data should be secured by both physical and electronic means against damage.	Annex 11, 7.1	In addition to the system's access security mechanisms, the regulated user should establish appropriate security means like physical access control, backup strategy, limited user access authorizations, regular checks on data readability, etc. Furthermore the data retention period should be determined by the regulated user and appropriately considered in the users processes (see GAMP 5, appendices O3, O4, O8, O9, O11 and O13).

	Requirement	Reference	Answer
4.3.7	Regular backups of all relevant data should be done.	Annex 11, 7.2	Yes. The regulated user should establish appropriate processes for backup and restore (see GAMP 5, appendix O9).
4.3.8	Electronic records must be readily retrievable throughout the records retention period.	21 CFR 11.10 (c) Annex 11, 17	Yes. When exporting archives, the regulated user must establish procedural controls for archiving and retrieval of data (see GAMP 5, appendix O13).
4.3.9	If the sequence of system steps or events is important, then appropriate operational system checks should be enforced.	21 CFR 11.10 (f)	Yes. For example allowances can be made for a specific sequence of operator actions by configuring the work order accordingly.

4.4 Audit Trail, Change Control Support

During operation, regulations require the recording of operator actions that may result in the generation of new relevant records or the alteration or deletion of existing records.

	Requirement	Reference	Answer
4.4.1	The system should create 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.	21 CFR 11.10 (e) Annex 11, 9	Yes. Changes during operation can be traced back by the system itself via audit trail and contain information with time stamp, user ID, old and new value and comment. The audit trail is secure within the system and cannot be changed by a user.
4.4.2	Management systems for data and documents should be designed to record the identity of operators entering, changing, confirming or deleting data including date and time.	Annex 11, 12.4	Yes. The requested information is part of the user management and audit trail functionality.
4.4.3	Changes to electronic records shall not obscure previously recorded information.	21 CFR 11.10 (e)	Yes. Recorded information is not overwritten and is always available in the database.
4.4.4	The audit trail shall be retained for a period at least as long as that required for the subject electronic records.	21 CFR 11.10 (e) Annex 11, 9	Yes. This is technically feasible and must be considered in the procedural controls for backup and archiving by the regulated user (see GAMP 5, appendices O9 and O13).
4.4.5	The audit trail should be available for review and copying by regulatory agencies.	21 CFR 11.10 (e)	Yes. The audit trail can be made available and also be exported in electronic formats.

4.5 System Access, Identification Codes and Passwords

Since access to a system must be restricted to authorized individuals and the uniqueness of electronic signatures also depends on the authenticity of user credentials, user access management is a vital set of requirements regarding the acceptance of electronic records and electronic signatures.

	Requirement	Reference	Answer
4.5.1	System access should be limited to authorized individuals.	21 CFR 11.10 (d) 21 CFR 11.10 (g) Annex 11, 12.1	Yes. System access can be managed via the user administration. The single user rights must be specified by the regulated user. Also procedural controls should be established by the regulated user, as described in GAMP 5, appendix O11.
4.5.2	The extent of security controls depends on the criticality of the computerized system.	Annex 11, 12.2	System security is a key factor during design and development of Siemens products. Nonetheless, since system security highly depends on the operating environment of each IT-system, these aspects should be considered in security management (see GAMP 5, appendix O11). Recommendations and support is given by Siemens' Industrial Security approach.
4.5.3	Creation, change, and cancellation of access authorizations should be recorded.	Annex 11, 12.3	Changes in the user access management are being recorded and should be subject to change control procedures.
4.5.4	If it is a requirement of the system that input data or instructions can only come from certain input devices (e.g. terminals), does the system check the validity of the source of any data or instructions received? (Note: This applies where data or instructions can come from more than one device, and therefore the system must verify the integrity of its source, such as a network of weigh scales, or remote, radio controlled terminals).	21 CFR 11.10 (h)	Yes. The Siemens Opcenter Execution Pharma work center (workstations) can be configured so that special input data / commands can only be performed from a dedicated work center. All other work centers then have read only access rights at the most.
4.5.5	Controls should be in place to maintain the uniqueness of each combined identification code and password, so that no individual can have the same combination of identification code and password as any other.	21 CFR 11.300 (a)	Yes. It is ensured that every identification code is unique within the system. Every combination of identification code and password is therefore also unique.
4.5.6	Procedures are in place to ensure that the validity of identification codes is checked periodically.	21 CFR 11.300 (b) Annex 11, 11	The regulated user should establish appropriate procedural controls.
4.5.7	Passwords should periodically expire and have to be revised.	21 CFR 11.300 (b)	Yes. Password aging can be configured in the user administration.

	Requirement	Reference	Answer
4.5.8	A procedure should be established for recalling identification codes and passwords if a person leaves or is transferred.	21 CFR 11.300 (b) Annex 11, 12.1	A user account can be disabled or the assigned access rights can be withdrawn for that user. The regulated user must establish appropriate procedural controls.
4.5.9	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.	21 CFR 11.300 (c)	The regulated user should establish appropriate procedural controls.
4.5.10	Measures for detecting attempts of unauthorized use and for informing security and management should be in place.	21 CFR 11.300 (d) Annex 11, 12.1	Yes. Failed attempts to use the system or to perform electronic signatures are recognized and can be logged. The regulated user should establish appropriate procedural controls to ensure a periodic review of security and access control information logs (see GAMP 5, appendix O8).
4.5.11	Initial and periodic testing of devices, such as tokens and 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.	21 CFR 11.300 (e)	Such devices are not part of the Siemens Opcenter Execution Pharma portfolio. The regulated user should establish appropriate procedural controls.

4.6 Electronic Signature

To ensure that electronic signatures are generally accepted as equivalent to handwritten signatures executed on paper, requirements are not only limited to the act of electronically signing records. They also include requirements on record keeping as well as on the manifestation of the electronic signature.

	Requirement	Reference	Answer
4.6.1	Written policies should be established that hold individuals accountable and responsible for actions initiated under their electronic signatures, in order to deter record and signature falsification.	21 CFR 11.10 (j) Annex 11, 14.a	The regulated user should establish appropriate procedural controls.
4.6.2	Signed electronic records should contain the following related information: • The printed name of the signer • The date and time of signing • The meaning of the signing (such as approval, review, responsibility)	21 CFR 11.50 (a) Annex 11, 14.c	Yes. The listed information is available.
4.6.3	The above-listed information is shown on displayed and printed copies of the electronic record.	21 CFR 11.50 (b)	Yes. The listed information is available.
4.6.4	Electronic signatures 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.	21 CFR 11.70 Annex 11, 14.b	Yes. The electronic signatures cannot be removed or used otherwise.
4.6.5	Each electronic signature shall be unique to one individual and shall not be reused by, or reassigned to, anyone else.	21 CFR 11.100 (a) 21 CFR 11.200 (a) (2)	Yes. The electronic signature uses the unique identifiers for user accounts in the Microsoft Windows user administration or is locally defined in the Siemens Opcenter Execution Pharma user management. The re-use or re-assignment of electronic signatures is effectively prevented.
4.6.6	When a system is used for recording certification and batch release, the system should allow only Qualified Persons to certify the release of the batches and it should clearly identify and record the person releasing or certifying the batch.	Annex 11, 15	Electronic signatures are linked to an individual and each individual is allocated to a group. The system allows strict determinations which user group is allowed to perform a signature for which functions.
4.6.7	The identity of an individual should be verified before electronic signature components are allocated.	21 CFR 11.100 (b)	The regulated user should establish appropriate procedural controls for the verification of an individual's identity before allocating a user account and/or electronic signatures.

	Requirement	Reference	Answer
4.6.8	When an individual executes one or more signings not performed during a single session, each signing shall be executed using all of the electronic signature components.	21 CFR 11.200 (a) (1) (ii)	Yes. Performing an electronic signature requires the user ID as well as the user's password.
4.6.9	When an individual executes a series of signings during a single session, the first signing shall be executed using all electronic signature components; subsequent signings shall be executed using at least one private electronic signature component.	21 CFR 11.200 (a) (1) (i)	Yes. Each signature consists of two components (user ID and password) and for each signature both components are required.
4.6.10	The use of an individual's electronic signature by anyone other than the genuine owner would require the collaboration of two or more individuals.	21 CFR 11.200 (a) (3)	Yes. It is not possible to falsify an electronic signature during signing or after recording of the signature. In addition, the regulated user needs procedures that prevent the disclosure of passwords.
4.6.11	Electronic signatures based upon biometrics shall be designed to ensure that they cannot be used by anyone other than their genuine owner.	21 CFR 11.200 (b)	Standard tools of third party manufacturers can be used to create biometric electronic signatures. The integrity of such solutions should be assessed separately.

4.7 Open Systems

The operation of an open system may require additional controls to ensure data integrity as well as the possible confidentiality of electronic records.

	Requirement	Reference	Answer
4.7.1	To ensure the authenticity, integrity, and, as appropriate, the confidentiality of electronic records additional measures such as data encryption are used.	21 CFR 11.30	All communications are performed via SSL encryption. Detailed information about security measures are described in the security manual.
4.7.2	To ensure the authenticity and integrity of electronic signatures, additional measures such as the use of digital signature standards are used.	21 CFR 11.30	Siemens Opcenter Execution Pharma does not provide functionality for digital (encrypted) signatures.

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