ROTRONIC HygroLab System eCompliance White Paper

Computerized System Validation
Electronic Record
Electronic Signature

Version: 1.0

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Document Name

File name	*HYGROLAB-WP-V270-EN_V1.0.docx*
Version	V1.0
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Review (2)	P. Seliger
Date	7 September 2022

Document History

Version	Date	Document name	Author	Description
V1.0	25.03.2022	HYGROLAB-WP-V270	M. Stozinic	Original version

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1. Introduction

1.1. Purpose

This document presents the current interpretation of **Rotronic AG** concerning regulatory requirements for:

- Computerized system validation
- Electronic record
- Electronic signature

as applicable for the healthcare, food and beverage industries as well as for medical device manufacturing and distribution.

Since US FDA 21 CFR Part 11 and Annex 11 to the European GMP have different scope and structure, this White Paper is articulated as following:

- Body – Overview (chapters 1-3)
- Part 1 – Interpretation and alignment with Annex 11 to European GMP
- Part 2 – Interpretation and alignment with 21 CFR Part 11

The document provides information concerning software functionality (technical solution) and administrative measures (procedural control) which the "*regulated user*"[1] should put in place for a compliant system operation.

1.1.1. Disclaimer

Although the quoted regulation texts are processed carefully, they are mentioned only for information purposes. Only the legal binding original text should be used and referred to for validation and compliance purposes; see:

- https://ec.europa.eu/health/system/files/2016-11/annex11_01-2011_en_0.pdf
- http://www.ecfr.gov/cgi-bin/text-idx?SID=dfff83854c36a4a31a897f96cb4405dc&mc=true&node=pt21.1.11&rgn=div5

This document is part of the *Rotronic eCompliance Strategy* and is subject to changes without notice.

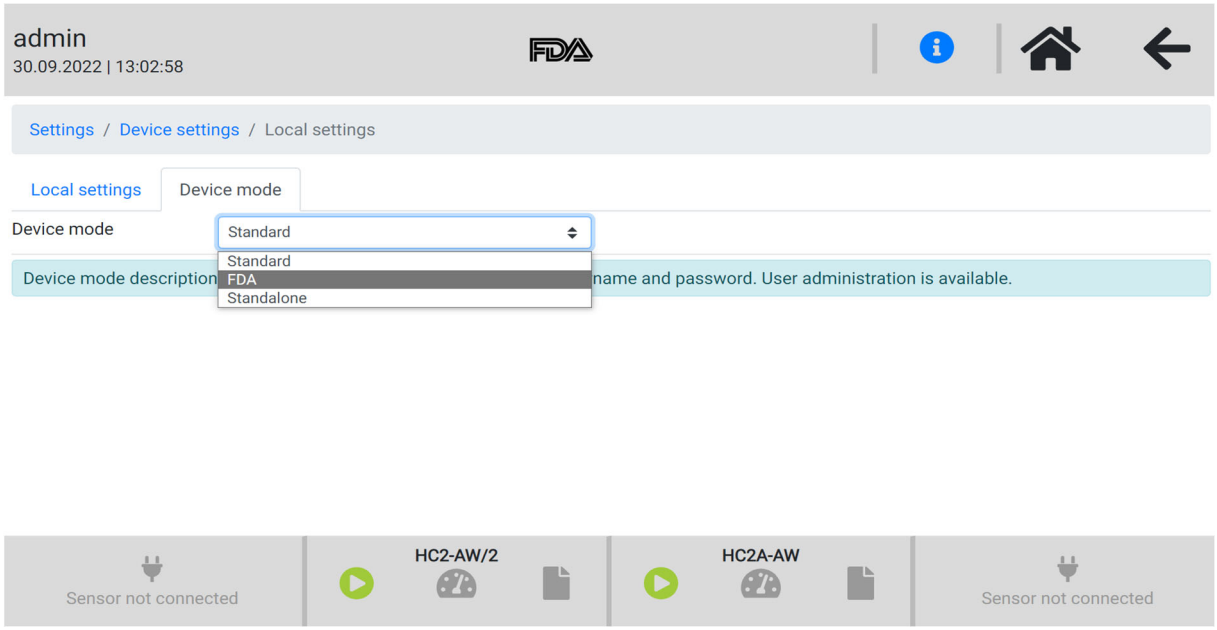
[1] See definition in section 3.3: *Glossary*.

1.2. Scope

This document applies to **HygroLab software version 2.7.0.0 with activated FDA mode** including the related devices, further referred to as "*HygroLab-based system*".

To activate **FDA mode,** go from the Main Menu into *Settings* → *Device settings* → *Local settings* from there click the *Device mode* register on the top right side and select *FDA* in the Device mode.

By activating the FDA mode, the FDA Logo will appear on top in the middle.



The following functional restrictions are based on the current version of the HygroLab software with activated FDA Mode:

- Sequence of events — Not applicable
- Biometric user identification — Not supported
- Token-based user identification — Not supported

1.3. References

The following documents have been considered during the preparation of this document:

- EU Annex 11, version 2011: "*Computerised systems*"
- 21 CFR Part 11[2]: "*Electronic Record, Electronic Signature*"
- PI 011-3: PIC/S Guidance "*Good Practices for computerised systems in regulated 'GxP' environments*"
- GAMP®5 "*A risk-based approach to compliant GxP computerized systems*"
- GAMP® Good Practice Guide: "*A risk-based approach to compliant electronic records and signatures*"
- *GAMP® CoP Annex 11 Interpretation*

[2] as available at the revision date of this document, see §1.1.1.

2. Definitions & Conventions

2.1. Definitions

See section 3: Source material, Acronyms, Glossary.

2.2. Conventions

2.2.1. Typography

The following typographical conventions are used throughout this document:

Bold	Product name or brand name (first occurrence only)
Italic	Interpretation Document title or section title
Shadowed italic	Original regulatory text
Courier	Software specific or technical information
[DOC]	Literature references
[DOC:xxx]	Reference to a specific document section; in this case section “xxx” of document “DOC”.

2.2.2. Interpretation

The interpretation is structured as follows:

- Paragraph number
- Original rule text
- Rotronic’s interpretation regarding
  - Technical solution
  - Procedural control

3. Source material, Acronyms, Glossary

3.1. Source material

[21CFR11]	Electronic Record, Electronic Signature / US-FDA / Effective from 1 October 2016
[A11]	EU Annex 11 to the EU guidelines of Good Manufacturing Practice for Medicinal Products / European Commission / Effective from 30 June 2011
[GAMP®5]	GAMP®5 "*A risk-based approach to compliant GxP computerized systems*" / ISPE / February 2008
[GAMP®-INT]	*GAMP® CoP Annex 11 Interpretation* / ISPE – GAMP® Community of Practice / 2011-06-07
[GPG-ERES]	GAMP® Good Practice Guide: "*A risk-based approach to compliant electronic records and signatures*" / ISPE / April 2005
[PI011]	Good Practices for computerised systems in regulated "GxP" environments / PIC/S / Version 3 / September 2007

3.2. Acronyms

ERES	Electronic Record, Electronic Signature
FDA	Food and Drug Administration (US Government)
GAMP	Good Automated Manufacturing Practice
GxP	Good x Practice; overall acronyms referring collectively the regulated Good Practices: ■ Good Clinical Practice (GCP) ■ Good Distribution Practice (GDP) ■ Good Laboratory Practice (GLP) ■ Good Manufacturing Practice (GMP)
SCS	System Configuration Specification
SOP	Standard Operating Procedure
OS	Operating System

3.3. Glossary

Regulated User	'Users' (owners of the good practice computerized systems being inspected) are collectively referred to as 'regulated users' for clarity.

Part 1 – Interpretation and alignment with Annex 11 to European GMP

In this section, each paragraph of the rule is reproduced together with the corresponding *Rotronic Interpretation* for a system based on HygroLab. Specific information concerning both the technical solution as well as procedural controls (regulated user's responsibility) is provided separately.

Principle

This annex applies to all forms of computerised system used as part of a GMP regulated activities.

Interpretation

This rule applies to HygroLab-based systems as soon as they are used for collecting and managing data required by GMP and GLP.

A computerised system is a set of software and hardware components which together fulfil certain functionalities.

Interpretation

HygroLab-based systems consist of at least one (1) measurement head (HC2-AW) and at least one (1) HygroLab (HYGROLAB). The software runs on the HygroLab's operating system.

The application should be validated; IT infrastructure should be qualified.

Interpretation

The HygroLab-based system is a standalone system; therefore, the IT infrastructure doesn't need to be qualified.

The HygroLab offers:

- *Active Directory Connection (LDAP)*
- *Remote Control Connection*
- *SMTP E-Mail Server Connection*

Only with these features it's required the IT infrastructure to be qualified. The regulated user has to ensure that all necessary compliance activities regarding the IT infrastructure have been appropriately carried out before and during operation of a HygroLab-based system.

Where a computerised system replaces a manual operation, there should be no resultant decrease in product quality, process control or quality assurance.

There should be no increase in the overall risk of the process.

Interpretation

The regulated user has to assess and to control the processes supported by an HygroLab-based system in order to ensure that the operation of the HygroLab-based system is neither increasing risk nor jeopardizing process reliability and integrity.

General

1. Risk management

Risk management should be applied throughout the life cycle of the computerized system taking into account patient safety, data integrity and product quality.

As part of a risk management system, decisions on the extent of validation and data integrity controls should be based on a justified and documented risk assessment of the computerised system.

Interpretation *In accordance with GAMP®5, Rotronic AG applies risk management principles during development and maintenance activities.*

It is the regulated user's responsibility to carry out risk management activities when using a HygroLab-based system.

The regulated user should plan and execute configuration, integration, operation, and retirement activities according to a well-established risk management process.

2. Personnel

There should be close cooperation between all relevant personnel such as Process Owner, System Owner, Qualified Persons and IT.

Interpretation *Regulated user's responsibility.*

All personnel should have appropriate qualifications, level of access and defined responsibilities to carry out their assigned duties.

Interpretation *Regulated user's responsibility.*

Rotronic AG is able to provide training to the regulated user's personnel as well as to the involved integrator.

3. Suppliers and Service Providers

3.1. *When third parties (e.g. suppliers, service providers) are used e.g. to provide, install, configure, integrate, validate, maintain (e.g. via remote access), modify or retain a computerised system or related service or for data processing, formal agreements must exist between the manufacturer and any third parties, and these agreements should include clear statements of the responsibilities of the third party.*

Interpretation *Regulated user's responsibility.*

Rotronic AG fully supports the relationship based on a formal contractual Agreement.

IT departments should be considered analogous.

Interpretation *Regulated user's responsibility.*

3.2. *The competence 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.

Interpretation *Regulated user's responsibility.*

Rotronic AG can be audited by regulated users' organizations as appropriate.

Rotronic AG suppliers are undergoing contracts.

3.3. *Documentation supplied with commercial off-the-shelf products should be reviewed by regulated users to check that user requirements are fulfilled.*

Interpretation *Regulated user's responsibility.*

Rotronic AG supports the regulated user by reviewing the HygroLab device documentation in order to ensure that user requirements are fulfilled appropriately.

3.4. *Quality system and audit information relating to suppliers or developers of software and implemented systems should be made available to inspectors on request.*

Interpretation *Regulated user's responsibility.*

Rotronic AG accepts that audit reports could be shown to a regulatory authority on request.

Project Phase

4. Validation

4.1.	*The validation documentation and reports should cover the relevant steps of the life cycle.* *Manufacturers should be able to justify their standards, protocols, acceptance criteria, procedures and records based on their risk assessment.*
Interpretation	*Rotronic AG has been certified according to ISO 9001 since 31 January 1995 and is accredited by the Swiss Federal Office of Metrology (METAS) as a calibration laboratory.* *Rotronic AG development activities for HygroLab-based system occur according to a formal life cycle.* *The regulated user should plan and execute configuration, integration, operation, and retirement activities according to a formal life cycle.*
4.2.	*Validation documentation should include change control records (if applicable) and reports on any deviations observed during the validation process.*
Interpretation	*Rotronic AG works according to a formal change management process.* *The regulated user has to have a change management process in place.*
4.3.	*An up to date listing of all relevant systems and their GMP functionality (inventory) should be available.* *For critical systems an up to date system description detailing the physical and logical arrangements, data flows and interfaces with other systems or processes, any hardware and software pre-requisites, and security measures should be available.*
Interpretation	*Regulated user's responsibility.*
4.4.	*User Requirements Specifications should describe the required functions of the computerised system and be based on documented risk assessment and GMP impact.* *User requirements should be traceable throughout the life cycle.*
Interpretation	*Regulated user's responsibility.* *By performing integration activities by a regulated user, Rotronic AG supports requirement traceability.*
4.5.	*The regulated user should take all reasonable steps, to ensure that the system has been developed in accordance with an appropriate quality management system.* *The supplier should be assessed appropriately.*
Interpretation	*Regulated user's responsibility.*
Procedural control	*Rotronic AG can be audited by the regulated user's organization as convenient.*

4.6.	*For the validation of bespoke or customised computerised systems there should be a process in place that ensures the formal assessment and reporting of quality and performance measures for all the lifecycle stages of the system.*
Interpretation	*Regulated user's responsibility.*
4.7.	*Evidence of appropriate test methods and test scenarios should be demonstrated.* *Particularly, system (process) parameter limits, data limits and error handling should be considered.* *Automated testing tools and test environments should have documented assessments for their adequacy.*
Interpretation	*According to its risk management process, Rotronic AG can justify its testing strategy.* *By device testing, Rotronic AG uses standard testing procedures. These procedures are tested and maintained under change control.*
4.8.	*If data are transferred to another data format or system, validation should include checks that data are not altered in value and/or meaning during this migration process.*
Interpretation	*Regulated user's responsibility since HygroLab-based systems can only export data.*

Operational Phase

5. Data

	Computerised systems exchanging data electronically with other systems should include appropriate built-in checks for the correct and secure entry and processing of data, in order to minimize the risks.
Technical solution	*Data exchanged between HygroLab and probes are checked by checksum, which is part of the standard communication protocol. Regarding other communication over network, every communication protocol used in HygroLab (HTTP) is having own build in checks or security protocol used.*

6. Accuracy Checks

For critical data entered manually, there should be an additional check on the accuracy of the data.

This check may be done by a second operator or by validated electronic means.

The criticality and the potential consequences of erroneous or incorrectly entered data to a system should be covered by risk management.

Interpretation *The system integrator has to ensure that the configuration of the HygroLab-based system has been performed properly.*

It remains the regulated user's responsibility to ensure that a HygroLab-based system has been correctly installed and that such a system is operated accurately, including data entry as appropriate.

7. Data Storage

7.1. *Data should be secured by both physical and electronic means against damage.*

Interpretation *Regulated user's responsibility.*

Technical solution *Records maintained within the HygroLab-based system should be protected against tampering by user access restriction. The records are stored in internal SQL database which can be accessed only by HygroLab itself. The user access is restricted either by user account management or optionally by LDAP server*

Stored data should be checked for accessibility, readability and accuracy.

Access to data should be ensured throughout the retention period.

Interpretation *Regulated user's responsibility.*

7.2. *Regular back-ups of all relevant data should be done.*

Integrity and accuracy of backup data and the ability to restore the data should be checked during validation and monitored periodically.

Interpretation *Regulated user's responsibility. The user can download the protocols and store them according internal company policies*

8. Printouts

8.1. *It should be possible to obtain clear printed copies of electronically stored data.*

Interpretation *Records stored in or generated by the HygroLab-based system can copied electronically in a legible format and printed out.*

8.2. *For records supporting batch release it should be possible to generate printouts indicating if any of the data has been changed since the original entry.*

Interpretation *Regulated user's responsibility.*

9. Audit Trails

Consideration should be given, based on a risk assessment, to building into the system the creation of a record of all GMP-relevant changes and deletions (a system generated "audit trail").

For change or deletion of GMP-relevant data the reason should be documented.

Audit trails need to be available and convertible to a generally intelligible form and regularly reviewed.

Technical solution	*Every change in the HygroLab-based system will be recorded in the events trail, containing timestamp, username, old and new values.* *Event trail information cannot be deleted or altered by the HygroLab-based system.* *Audit trail information can be exported to CSV or PDF format for each request.*
Procedural control	*The regulated user has to define an operating procedure regarding audit trail review.*

10. Change and Configuration Management

Any changes to a computerised system including system configurations should only be made in a controlled manner in accordance with a defined procedure.

Interpretation *Regulated user's responsibility.*

11. Periodic evaluation

Computerised systems should be periodically evaluated to confirm that they remain in a valid state and are compliant with GMP.

Such evaluations should include, where appropriate, the current range of functionality, deviation records, incidents, problems, upgrade history, performance, reliability, security and validation status reports.

Interpretation *Regulated user's responsibility.*

12. Security

12.1. *Physical and/or logical controls should be in place to restrict access to computerised system to authorised persons.*

Suitable methods of preventing unauthorised entry to the system may include the use of keys, pass cards, personal codes with passwords, biometrics, restricted access to computer equipment and data storage areas.

12.2. *The extent of security controls depends on the criticality of the computerised system.*

12.3. *Creation, change, and cancellation of access authorisations should be recorded.*

12.4.	*Management systems for data and for documents should be designed to record the identity of operators entering, changing, confirming or deleting data including date and time.*
Interpretation	*Regulated user's responsibility.*
Technical solution	*HygroLab-based systems are able to manage users based on a two-component user identification:* username *and* password.

13. Incident Management

All incidents, not only system failures and data errors, should be reported and assessed.

The root cause of a critical incident should be identified and should form the basis of corrective and preventive actions.

Interpretation *Regulated user's responsibility.*

In case of relevant customer complaints possibly impacting other regulated users, Rotronic AG would inform them and propose appropriate corrective measures.

14. Electronic Signature

Electronic records may be signed electronically.

Electronic signatures are expected to:

a. *have the same impact as hand-written signatures within the boundaries of the company,*
b. *be permanently linked to their respective record,*
c. *include the time and date that they were applied.*

Technical solution	*Every change in the HygroLab System will by recorded in the event log in the HygroLab-based system. This includes the user, timestamp and values before and after.*
Procedural control	*Regulated user's responsibility.*

15. Batch release

When a computerised 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 batches.

This should be performed using an electronic signature.

Interpretation *The user, Start & Stop time stamps, Status of the measurement, Setpoint and Result are recorded in the document of the batch release.*

Regulated user's responsibility.

16. Business Continuity

For the availability of computerised systems supporting critical processes, provisions should be made to ensure continuity of support for those processes in the event of a system breakdown (e.g. a manual or alternative system).

The time required to bring the alternative arrangements into use should be based on risk and appropriate for a particular system and the business process it supports.

These arrangements should be adequately documented and tested.

Interpretation *It is the regulated user's responsibility to plan appropriate business continuity measures.*

However, Rotronic AG can support the regulated user by elaborating and reviewing business continuity plans for HygroLab-based systems.

17. Archiving

Data may be archived.

This data should be checked for accessibility, readability and integrity.

If relevant changes are to be made to the system (e.g. computer equipment or programs), then the ability to retrieve the data should be ensured and tested.

Interpretation *Regulated user's responsibility.*

Usually Rotronic AG ensures data backward compatibility.

Glossary

Application — *Software installed on a defined platform/hardware providing specific functionality.*

Interpretation *The Software is installed on the HygroLab device.*

Bespoke/ customised computerised system — *A computerised system individually designed to suit a specific business process.*

Interpretation *HygroLab-based systems should be considered as GAMP®5 Category 4 software as defined in [GAMP®5].*

Only the process-specific configuration of a HygroLab-based system is bespoke.

Commercial off-the-shelf software — *Software commercially available, whose fitness for use is demonstrated by a broad spectrum of users.*

Interpretation *HygroLab-based system is commercial off-the-shelf software (COTS) and it should be considered as GAMP®5 Category 4 software as defined in [GAMP®5]. This system is only used in the HygroLab device.*

IT Infrastructure — *The hardware and software such as networking software and operation systems, which makes it possible for the application to function.*

Interpretation *Regulated user's responsibility.*

Life cycle	*All phases in the life of the system from initial requirements until retirement including design, specification, programming, testing, installation, operation, and maintenance.*
Interpretation	*Rotronic AG contributes to support full coverage of the life cycle.*
Process owner	*The person responsible for the business process.*
Interpretation	*Regulated user's responsibility.*
System owner	*The person responsible for the availability, and maintenance of a computerised system and for the security of the data residing on that system.*
Interpretation	*Regulated user's responsibility.*
Third party	*Parties not directly managed by the holder of the manufacturing and/or import authorisation.*
Interpretation	*Rotronic AG should be considered as a "third party" organization.*

Part 2 – Interpretation and alignment with 21 CFR Part 11

In this section, each paragraph of the rule is reproduced together with the corresponding *Rotronic Interpretation* for a system based on HygroLab. Specific information concerning both the technical solution as well as procedural controls (regulated user's responsibility) is provided separately.

Subpart A — General Provisions

§ 11.1 Scope

§ 11.1 (a)	*The regulations in this part set forth the criteria under which the agency considers electronic records, electronic signatures, and handwritten signatures executed to electronic records to be trustworthy, reliable, and generally equivalent to paper records and handwritten signatures executed on paper.*
Interpretation	*The HygroLab-based system allow the regulated user to collect, manage, and report GxP relevant data in a compliant manner.*
Technical solution	*All system changes are documented within the events of the HygroLab-based system. Any events generated due to a user manipulation will be traced with the user's signature. All events can be commented/confirmed by a user with access to the system and sufficient rights. Any comments/confirmations will be traced with the user's signature.* *PDF Exports from the HygroLab will be recorded in the audit trail including author, time stamp and batch number.*
§ 11.1 (b)	*This part applies to records in electronic form that are created, modified, maintained, archived, retrieved, or transmitted, under any records requirements set forth in agency regulations. This part also applies to electronic records submitted to the agency under requirements of the Federal Food, Drug, and Cosmetic Act and the Public Health Service Act, even if such records are not specifically identified in agency regulations. However, this part does not apply to paper records that are, or have been, transmitted by electronic means.*
Interpretation	*The HygroLab-based system make it possible to collect, manage, and report regulated data electronically.*
§ 11.1 (c)	*Where electronic signatures and their associated electronic records meet the requirements of this part, the agency will consider the electronic signatures to be equivalent to full handwritten signatures, initials, and other general signings as required by agency regulations, unless specifically excepted by regulation(s) effective on or after August 20, 1997.*
Interpretation	*See also § 11.1(a)*
§ 11.1 (d)	*Electronic records that meet the requirements of this part may be used in lieu of paper records, in accordance with 11.2, unless paper records are specifically required.*
Interpretation	*With the HygroLab-based system, the regulated user is able to manage regulated records in electronic format only.*

§ 11.1 (e) *Computer systems (including hardware and software), controls, and attendant documentation maintained under this part shall be readily available for, and subject to, FDA inspection.*

Interpretation *The regulated user should be aware that HygroLab-based systems can be subject to regulatory inspection whenever they are used for GxP purpose.*

Within the scope of a HygroLab implementation project, the relevant departments of Rotronic AG may be audited by the regulated user.

§ 11.1 (f) *This part does not apply to records required to be established or maintained by 1.326 through 1.368 of this chapter. Records that satisfy the requirements of part 1, subpart J of this chapter, but that also are required under other applicable statutory provisions or regulations, remain subject to this part.*

Interpretation *Prior to deciding to apply (or not apply) 21 CFR Part 11 requirements, the customer should assess how its activities as well as the related generated records fit into the scope of 21 CFR Part 1, Subpart J and if the generated records are required by other applicable regulations.*

§ 11.2 Implementation

§ 11.2 (a) *For records required to be maintained but not submitted to the agency, persons may use electronic records in lieu of paper records or electronic signatures in lieu of traditional signatures, in whole or in part, provided that the requirements of this part are met.*

§ 11.2 (b) *For records submitted to the agency, persons may use electronic records in lieu of paper records or electronic signatures in lieu of traditional signatures, in whole or in part, provided that:*

(1) The requirements of this part are met; and

(2) The document or parts of a document to be submitted have been identified in public docket No. 92S-0251 as being the type of submission the agency accepts in electronic form. This docket will identify specifically what types of documents or parts of documents are acceptable for submission in electronic form without paper records and the agency receiving unit(s) (e.g., specific centre, office, division, branch) to which such submissions may be made. Documents to agency receiving unit(s) not specified in the public docket will not be considered as official if they are submitted in electronic form; paper forms of such documents will be considered as official and must accompany any electronic records. Persons are expected to consult with the intended agency receiving unit for details on how (e.g., method of transmission, media, file formats, and technical protocols) and whether to proceed with the electronic submission.

Interpretation *The regulated user has to define (and document) whether the data collected and the records generated by HygroLab-based systems are used for GxP purposes. The regulated user has also to define the appropriate measures to apply to such data and records.*

§ 11.3 Definitions

§ 11.3

(a) The definitions and interpretations of terms contained in section 201 of the act apply to those terms when used in this part.

(b) The following definitions of terms also apply to this part:

(1) Act means the Federal Food, Drug, and Cosmetic Act (secs. 201-903 (21 U.S.C. 321-393)).

(2) Agency means the Food and Drug Administration.

(3) Biometrics means a method of verifying an individual's identity based on measurement of the individual's physical feature(s) or repeatable action(s) where those features and/or actions are both unique to that individual and measurable.

(4) Closed system means an environment in which system access is controlled by persons who are responsible for the content of electronic records that are on the system.

(5) Digital signature means an electronic signature based upon cryptographic methods of originator authentication, computed by using a set of rules and a set of parameters such that the identity of the signer and the integrity of the data can be verified.

(6) 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.

(7) Electronic signature means a computer data compilation of any symbol or series of symbols executed, adopted, or authorized by an individual to be the legally binding equivalent of the individual's handwritten signature.

(8) Handwritten signature means the scripted name or legal mark of an individual handwritten by that individual and executed or adopted with the present intention to authenticate a writing in a permanent form. The act of signing with a writing or marking instrument such as a pen or stylus is preserved. The scripted name or legal mark, while conventionally applied to paper, may also be applied to other devices that capture the name or mark.

(9) Open system means an environment in which system access is not controlled by persons who are responsible for the content of electronic records that are on the system.

Interpretation

The HygroLab was designed to operate as closed system.

Currently, the HygroLab does not support biometric identification devices. If such devices are required, the regulated user should contact Rotronic AG.

Subpart B — Electronic Records

§ 11.10 Controls for closed systems

§ 11.10	*Persons who use closed systems to create, modify, maintain, or transmit electronic records shall employ procedures and controls designed to ensure the authenticity, integrity, and, when appropriate, the confidentiality of electronic records, and to ensure that the signer cannot readily repudiate the signed record as not genuine. Such procedures and controls shall include the following:*
Technical solution	*See also § 11.1(a)*
§ 11.10 (a)	*Validation of systems to ensure accuracy, reliability, consistent intended performance, and the ability to discern invalid or altered records.*
Technical solution	*Every change in the HygroLab-based system setting will be recorded in the event trail, containing timestamp, username, old and new values. Users without sufficient permissions are not able to access or edit HygroLab settings.*
Procedural control	*The regulated user has to plan, validate and operate their HygroLab-based system according to regulatory requirements and, if appropriate, to their own validation standards.* *Rotronic AG makes available to the regulated user the "HygroLab e-compliance package" which includes templates of validation documentation. These templates can be used and adapted by the regulated user for developing specific validation documentation.*
§ 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.*
Technical solution	*The HygroLab-based system allows exporting of records stored in the database of the HygroLab to documents in PDF or CSV format.*
Procedural control	*The regulated user is responsible for the correct handling of records stored in unsecured files (e.g. after exporting to a different format) outside of the HygroLab environment.*

§ 11.10 (c)	*Protection of records to enable their accurate and ready retrieval throughout the records retention period.*
Technical solution	*As long as the records are stored in the internal SQL database, they are protected within the HygroLab-environment.*
Procedural control	*The regulated user has to define the procedural controls applicable to records exported in un-secured files throughout the required retention period until records deletion.* *The regulated user has to define operating procedures regarding backing-up, restoring and archiving the records generated by HygroLab-based systems.*
§ 11.10 (d)	*Limiting system access to authorized individuals.*
Technical solution	*HygroLab has its own access control mechanism which uses a two-component identification method: User-ID and password.* *Access privileges can be freely assigned to each user.*
Procedural control	*The regulated user has to define an operating procedure regarding user management and physical as well as logical access control. Such procedure should cover access conditions to HygroLab, operating system as well as to devices.*
§ 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.*
Technical solution	*Every change in the HygroLab-based system setting will be recorded in the audit trail, containing timestamp, username, old and new values.* *Audit trail information cannot be deleted or altered by the HygroLab-based system.* *Audit trail information can be exported to CSV or PDF format for each request.*
Procedural control	*The regulated user has to define an operating procedure regarding audit trail review.*
§ 11.10 (f)	*Use of operational system checks to enforce permitted sequencing of steps and events, as appropriate.*
Technical solution	*Not applicable*
Procedural control	*Not applicable*
§ 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.*
Technical solution	*See §11.10(d)*
Procedural control	*See §11.10(d)*

§ 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.*
Technical solution	*HygroLab-based systems are identified as follows:* ■ *unique device ID (serial number).* *The unique ID is documented as part of the system configuration. Based on this, confusion between sources of data is avoided.*
Procedural control	*Not applicable*
§ 11.10 (i)	*Determination that persons who develop, maintain, or use electronic record/electronic signature systems have the education, training, and experience to perform their assigned tasks.*
Technical solution	*Members of the Rotronic development department and partners are experienced developers who are trained on a regular basis according to the ISO 9001-based Quality Management System.* ■ *Rotronic service engineers are trained on a regular basis according to the ISO 9001-based Quality Management System.* ■ *Rotronic calibration engineers are trained on a regular basis according to the ISO 9001-based Quality Management System.*
Procedural control	*The regulated user has to ensure that any person using the HygroLab-based system is properly trained.* *The regulated user's personnel can be trained by Rotronic AG.*

§ 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.*
Technical solution	*Not applicable*
Procedural control	*The regulated user has to define policies and/or procedures defining behaviour rules and processes for associates having to execute or review electronically-performed signatures.* *Each associate executing electronic signature or having to consider such signature must be trained to ensure the appropriate use of electronic records and electronic signatures.*
§ 11.10 (k)	*Use of appropriate controls over systems documentation including:* *(1) Adequate controls over the distribution of, access to, and use of documentation for system operation and maintenance.* *(2) Revision and change control procedures to maintain an audit trail that documents time-sequenced development and modification of systems documentation.*
Technical solution	*All documents provided by Rotronic AG have a version number and stay under change control.*
Procedural control	*The regulated user has to ensure that engineering and qualification/validation documents are generated and maintained according to Good Documentation Practice recommendations, e.g. unique document identification, version number, change management.*

§ 11.30 Controls for open systems

§ 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.*
Technical solution	*The HygroLab-based system is designed to operate as a closed system.*
Procedural control	*The HygroLab-based system can't be used as an open system.*

§ 11.50 Signature manifestations

§ 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.*
Technical solution	*See also § 11.1(a)*
Procedural control	*PDF Exports from the HygroLab will be recorded in the audit trail including author, time stamp and batch number.*

§ 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).*
Technical solution	*See also § 11.1(a)*
Procedural control	*PDF Exports from the HygroLab will be recorded in the audit trail including author, time stamp and batch number.*

§ 11.70 Signature/record linking

§ 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.*
Technical solution	*See also § 11.1(a)*
Procedural control	*PDF Exports from the HygroLab will be recorded in the audit trail including author, time stamp and batch number.*

Subpart C — Electronic Signatures

§ 11.100 General requirements

§ 11.100 (a)	*Each electronic signature shall be unique to one individual and shall not be reused by, or reassigned to, anyone else.*
Technical solution	*Using HygroLab-based system, applied signatures cannot be removed nor copied.*
Procedural control	*It is the regulated user's responsibility to ensure that each user has a unique user-ID and that users handle their two-component identification confidentially.*
§ 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.*
Procedural control	*The regulated user has to define the required administrative controls to ensure that the identity of each individual is correctly verified.*

§ 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, 12420 Parklawn Drive, RM 3007 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.*
Procedural control	*The regulated user has to ensure that all required administrative tasks are successfully performed prior to using electronic signatures.*

§ 11.200 Electronic signature components and controls

§ 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.*
Technical solution	*Not applicable*
Procedural control	*The regulated user has to elaborate a binding procedure describing the electronic signature process valid for their organization.*
§ 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.*
Technical solution	*Presently, personal electronic signatures as well as biometric user identification are not directly supported by the HygroLab-based system.*
Procedural control	*If biometric user identification is required, the regulated user should contact Rotronic AG.*

§ 11.300 Controls for identification codes/passwords

§ 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:*
§ 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.*
Technical solution	*A HygroLab-based system is able to manage multiple users based on a two-component user identification: Username and Password.*
Procedural control	*Not applicable.*
§ 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).*
Technical solution	*HygroLab supports password aging, password strength and check for reused passwords.*
Procedural control	*The regulated user should configure HygroLab-based system according to the recommendation provided by Rotronic AG as well as to its own information security policy.*
§ 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.*
Technical solution	*HygroLab-based system supports the disabling of a user, manually or automatically after some failed logins as well as the recognition of multiple logins with the same user.*
Procedural control	*It is the responsibility of the regulated user to manage in the appropriate manner tokens used for user identification.* *If token-based user identification is required, the regulated user should contact Rotronic AG for a recommendation.*
§ 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.*
Technical solution	*HygroLab-based system generates an audit trail entry in case of identification failure.*
Procedural control	*In addition to the appropriate system configuration, the regulated user should define a procedure covering the review of audit trails.*

§ 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.*
Technical solution	*HygroLab-based system does not directly support token-based user identification.*
Procedural control	*It is the responsibility of the regulated user to manage in the appropriate manner tokens used for user identification and to define the required controls in a corresponding procedure.*