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BEYOND TECHNOLOGY

2850 & 3850

CFR 21 PART 11 / ANNEX 11 EU GMP

GEFRAN SPA

Via Sebina, 74
25050 Provaglio d'Iseo (BS)
Italy

Tel. +39 030 9888.1
Fax +39 030 9839063
www.gefran.com
info@gefran.com

Cap. Soc. €
14.400.000 i.v.
Reg. Imprese Brescia
03032420170
R.E.A. 313074 BS
Mecc. BS 016227

C.F. 03032420170
P.IVA (TVA-VAT-MWS)
IT03032420170
n. iscrizione Registro
AEE: IT18080000010658

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Electronic Records Requirement

References	Name	Description	Result	Notes
CFR21: 11.10(a) **ANNEX11**:4.1	**System validation**	The systems shall be validated to ensure accuracy, reliability, consistent intended performance, and the ability to discern invalid or altered records. The system validation should consider the system's intended use and its context.	N.A.	Customer's responsibility
		The IT infrastructure should be qualified.	N.A.	Customer's responsibility
		The production equipment should be qualified, calibrated and maintained.	N.A.	Customer's responsibility
CFR21: - **ANNEX11**:4.7	**Qualification tests**	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.	N.A.	Customer's responsibility
CFR21: - **ANNEX11**: 1, 4.1, 4.4, 6, 9, 12.2, 16	**Risk assessment**	A justified and documented risk assessment of the computerized system shall be performed (e.g., in the Validation Plan and/or in the URS document) taking into account patient safety, data integrity and product quality. Validation effort and data integrity controls (audit trail) should be based on it.	N.A.	Customer's responsibility
CFR21: 11.10(g) **ANNEX11**: 2	**Access Levels**	All personnel should have appropriate level of access and defined responsibilities to carry out their assigned duties.	**Pass**	Individual strong password protected each user accounts. Each user group have a unique set of access permissions or privileges.

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CFR21: - **ANNEX11**:-	**Separation of duties**	Appropriate separation of duties should be established so that highly privileged system administrator accounts should be reserved for designated technical personnel fully independent of the personnel responsible for the records' content (e.g. business process owners, or other users who may have a conflict of interest). Where these independent security role assignments are not feasible (e.g. in small businesses with few employees), other control strategies should be used to reduce data validity risks, such as usage of different user accounts, or double check of a second operator when the system configuration is modified.	**Pass**	Customer's responsibility. 4 configurable levels of users available: operator, service, supervisor, admin
CFR21: 11.10(g) **ANNEX11:**-	**Logical security**	Use of authority checks to ensure that only authorized individuals can use the system, access the operation or computer system input or output device, alter a record.	**Pass**	-
CFR21: - **ANNEX11**:-	**SW Personal Access Credentials**	Logon credentials for the application software should be personal. The use of shared and generic logon credentials should be avoided to ensure that actions documented in electronic records and on the system can be attributed to a unique individual.	**Pass**	Customer's responsibility. For security reason account will automatically lock if a user enters several incorrect passwords

References	Name	Description	Result	Notes
CFR21: - **ANNEX11**:-	**Operating System Access Credentials**	Logon credentials for the operating system should be personal if the users can perform actions on the data outside of the application software. The use of shared and generic logon credentials for the operating system is allowed only if the users do not access with administrator credentials, if they cannot perform actions on the data outside of the application software, and if the application software access credentials are personal.	N.A.	Not applicable
CFR21: - **ANNEX11**:-	**Antivirus**	There should be controls to prevent and detect virus or other potentially dangerous code.	N.A.	Not applicable
CFR21:- **ANNEX11:** 12.3	**Access management SOP**	Creation, change, and cancellation of access authorizations should be recorded. An updated list with the indication of the users authorized to access the system and their privileges should be available.	N.A.	Customer's responsibility
CFR21: 11.10(d) **ANNEX11:** 12.1 e 12.2	**Physical security**	Physical and/or logical controls should be in place to restrict access to computerized system to authorized persons by means of physical and/or logical controls (e.g. keys, pass cards, personal codes with passwords, biometrics, restricted access to computer equipment and data storage areas).	N.A.	Customer's responsibility
CFR21: 11.10(f) **ANNEX11:**-	**Operational checks**	Operational system checks shall be used to enforce permitted sequencing of steps and events, as appropriate.	**Pass**	-
CFR21: - **ANNEX11**:-	**Data saving**	The system should enforce the saving of electronic data at the time of the activity and before proceeding to the next step of the sequence of events.	**Pass**	-

References	Name	Description	Result	Notes
CFR21: 11.20(h) **ANNEX11:**-	**Device check**	Device (e.g., terminal) checks shall be used to determine, as appropriate, the validity of the source of data input or operational instruction.	**Pass**	-
CFR21:- **ANNEX11:** 3.1	**SLA (Service Level Agreement)**	Formal agreements shall exist between the manufacturer and any third parties (e.g. suppliers, service providers, IT-departments) that are used e.g. to provide, install, configure, integrate, validate, maintain (e.g. via remote access), modify or retain a computerized system or related service or for data processing. These agreements should include clear statements of the third party's responsibilities, including the responsibilities concerning the data integrity requirements.	N.A.	Customer's responsibility
CFR21:- **ANNEX11:** 3.2, 3.4, 4.5	**Supplier assessment**	A supplier assessment shall be foreseen, basing on a risk assessment.	N.A.	Customer's responsibility
CFR21:- **ANNEX11:** 3.3, 4.4	**Traceability matrix**	User requirements should be traceable throughout the life cycle. Documentation supplied with commercial off-the-shelf products should be reviewed by regulated users to check that user requirements are fulfilled.	N.A.	Customer's responsibility
CFR21:- **ANNEX11:**4.2	**Change control & validation deviations**	Validation documentation should include change control records (if applicable) and reports on any deviations observed during the validation process.	N.A.	Customer's responsibility
CFR21:- **ANNEX11:**13	**Incident management**	All incidents 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.	N.A.	Customer's responsibility

References	Name	Description	Result	Notes
CFR21:-ANNEX11:10	**Change and configuration management SOP**	Any changes to a computerized system including system configurations should only be made in a controlled manner in accordance with a defined procedure.	N.A.	Customer's responsibility
CFR21:-ANNEX11:4.3	**System inventory**	The system shall be included in the inventory of GMP systems.	N.A.	Customer's responsibility
CFR21:-ANNEX11:4.3	**System description**	A 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.	-	Requirement satisfied through installation and operation manual
CFR21:-ANNEX11:4.6	**System monitoring (cat. 5)**	For the validation of bespoke or customized computerized systems there should be a process in place that ensures the formal assessment and reporting of quality and performance measures for all the system's life-cycle stages.	N.A.	Not applicable
CFR21:-ANNEX11:4.8	**Data migration**	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.	N.A.	Customer's responsibility
CFR21:-ANNEX11:5	**Interfaces**	Computerized systems exchanging data electronically with other systems should include appropriate built-in checks for the correct, complete, and secure entry and processing of data.	N.A.	Not applicable
CFR21: -**ANNEX11**:-	**Export and import**	There should be tests and controls over the data export and import, including controls on the temporary memory and checks on the integrity of the exchanged files, if modifiable	**Pass**	-

References	Name	Description	Result	Notes
CFR21:- **ANNEX11:**6	**Double check**	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, if required by predicate rules. Fields containing critical data should be blocked after the double check.	N.A.	Customer's responsibility
CFR21: - **ANNEX11**:-	**Data checks**	There should be checks over format and value of the entered data (e.g. drop-down lists, check boxes) to improve the data consistency.	**Pass**	-
CFR21: - **ANNEX11**:-	**Dictionaries**	Standard dictionaries should be used.	N.A.	Not applicable
CFR21:- **ANNEX11:**11	**Periodic reviews**	Computerized systems should be periodically evaluated to confirm that they remain in a valid state and are compliant with GMP regulations. Such evaluations should include, where appropriate, the current range of functionality, deviation records, incidents, problems, upgrade history, performance, reliability, security, data integrity and validation status reports.	N.A.	Customer's responsibility
CFR21:- **ANNEX11:** 12.4	**Records attributability**	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.	**Pass**	The operator ID is always link to any operation entering
CFR21:- **ANNEX11:** 8.2, 15	**Batch release**	Only Qualified Persons shall release batches and the system should clearly identify and record the person releasing or certifying the batches. This should be performed using an electronic signature.	N.A.	Not applicable

References	Name	Description	Result	Notes
CFR21: 11.10(c) **ANNEX11:**7.1	**Data retention**	Original records (or true copies), including their metadata, shall be protected in order to enable their accurate and ready retrieval throughout the records retention period. Records shall be retained together with the hardware, software and possible other devices needed for their visualization.	N.A.	Not applicable
CFR21:- **ANNEX11:**16	**Business continuity**	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 (e.g. a manual or alternative system). These arrangements should be adequately documented and tested.	N.A.	Customer's responsibility
CFR21: - **ANNEX11**:-	**Disaster recovery**	Disaster recovery plans should be in place.	N.A.	Customer's responsibility
CFR21:- **ANNEX11:**7.2	**Data back-up and restore**	Regular back-ups of all relevant data and their metadata should be done. The back-up data shall have appropriate levels of control and security, in order to avoid unwanted access, alteration or deletion of the data.	**Pass**	Automatic backup with an external tool (Window Application) or automatic backup with an internal FTP Client
CFR21:- **ANNEX11:**17	**Data archiving**	Data may be archived. This data (and their metadata) should be periodically checked for accessibility, readability, and integrity throughout the records retention period. The storage areas shall be validated, secure, maintained in a controlled status and accessible only to the authorized personnel. Indexing of records to permit ready retrieval should be in place.	**Pass**	Data integrity check of all record files

References	Name	Description	Result	Notes
CFR21: - **ANNEX11**:-	**Data physical protection**	Storage and archiving devices should be installed in secure locations, with access limited to the authorized users and properly protected from destruction caused by water, fire…	N.A.	Customer's responsibility
CFR21:- **ANNEX11:**17	**System upgrade**	If relevant changes are to be made to the system (e.g. computer equipment or programs), then the ability to retrieve data should be ensured and tested	**Pass**	Compatibility with new versions will be maintained
CFR21: - **ANNEX11**:-	**System dismissal**	If the original system has to be dismissed, the data should be migrated on a new system or other procedures should be applied to preserve the content and the meaning of the data and their metadata, including the activities that allow the complete reconstruction of the data.	N.A.	Customer's responsibility
CFR21: 11.10(b) **ANNEX11:**8.1	**Copies of records**	The system shall allow generating accurate and complete copies of records in both human readable and electronic form. Copies shall be suitable for inspection, review, and copying by the agency.	**Pass**	-
CFR21: 11.10(e) **ANNEX11:**9	**Audit trail**	Secure, computer-generated, time-stamped audit trails shall be used to independently record the date and time of operator entries and actions that create, modify, or delete electronic records.	**Pass**	Secure, computer generated audit trail is available. Time synchronization via NTP
CFR21:- **ANNEX11:**9	**Audit trail reason**	For change or deletion of GMP-relevant data the reason should be documented.	**Pass**	-

References	Name	Description	Result	Notes
CFR21:- **ANNEX11:**9	**Audit trail review**	The audit trail should be periodically reviewed by a person responsible for the data, and, periodically, by the QA. The modality and frequency of the review should be described in a dedicated procedure and should depend on the criticality of data, type of data, type of process and system complexity. The audit trail review should be documented (if possible, with electronic signature) and each deviation should be investigated.	N.A.	Customer's responsibility
CFR21: - **ANNEX11**:-	**Audit trail review functionality**	The system should be designed to facilitate the audit trail review (e.g. list of relevant data or validated exception reporting process).	**Pass**	Report Utility tool allow Audit Review with filter by time, type, etc..
CFR21: 11.10(e) **ANNEX11:**-	**Audit trail content**	For each registered action, the audit trail should include the following: - Username of the executor; - Date and time of every action executed on the electronic record; - Action type (creation, modification or deletion); - Value of the electronic record before and after the action execution.	**Pass**	-
CFR21: 11.10(e) **ANNEX11:**9	**Audit trail retention**	The audit trail documentation shall be retained for a period at least as long as that required for its electronic record and shall be available for agency review and copying in a generally intelligible form.	N.A.	Customer's responsibility
CFR21: - **ANNEX11**:-	**Non-Modifiability of the Audit trail**	Users should not be able to modify or deactivate the audit trail.	**Pass**	-

References	Name	Description	Result	Notes
CFR21: 11.10(i) **ANNEX11:**-	**Personnel training - Pharma**	Persons who develop, maintain, or use electronic record/electronic signature systems shall have the education, training, and experience to perform their assigned tasks, including specific topics concerning the data integrity.	N.A.	Customer's responsibility
CFR21: 11.10(k) **ANNEX11:**-	**Documentation control**	Appropriate controls over systems documentation shall be used, including: - Adequate controls over the distribution of, access to, and use of documentation for system operation and maintenance. - Revision and change control procedures to maintain an audit trail that documents time-sequenced development and modification of systems documentation.	N.A.	Customer's responsibility
CFR21: 11.30 **ANNEX11:**-	**Open system**	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 (e.g. document encryption, digital signature standards).	N.A.	Not Applicable
CFR21: - **ANNEX11**:-	**Data overwriting**	Configuration settings that allow overwriting should be disabled and forbidden, even during the initial or intermediate phases of data processing (trial runs).	N.A.	Not Applicable
CFR21: - **ANNEX11**:-	**Temporary memories**	Data saved in temporary memories (e.g. buffer or local database) should be committed to durable media upon completion of the step and in any case before proceeding to the next step in the sequence.	N.A.	Not Applicable

References	Name	Description	Result	Notes
CFR21: - **ANNEX11**:-	**Date and Time Synchronization**	Date and time should be synchronized with a time reference and should not be modifiable by the users.	**Pass**	-
CFR21: - **ANNEX11**:-	**Time zone**	The system time zone should be under control.	**Pass**	-
CFR21: - **ANNEX11**:-	**Report date and time**	When the activity is time-critical (e.g. weighing) printed records should display the date and timestamp.	**Pass**	-
CFR21: - **ANNEX11**:-	**System availability**	The system should be available for the users at the time of the activity execution.	N.A.	Customer's responsibility
CFR21: - **ANNEX11**:-	**Stand-alone systems**	Stand-alone computerized system should ensure proper security restrictions to protect time/date settings and ensure data integrity in all computing environments, including the workstation operating system (e.g. protection of the Windows folders, users that are not PC administrators…).	N.A.	Not Applicable
CFR21: - **ANNEX11**:-	**Data review**	The data and their metadata should be reviewed (if possible, in electronic form) preferably using the electronic signature to certify that the review has been done. The modality and frequency of the review should be described in a dedicated procedure and should depend on the data criticality, data type, process type and system complexity. The data review should be documented (if possible, with electronic signature) and each deviation should be investigated.	N.A.	Customer's responsibility

References	Name	Description	Result	Notes
CFR21: - **ANNEX11**:-	**Data submission**	If the data submission (e.g. scale or zoom of a diagram) affects the data review and possible critical decisions, it is necessary that the review is done in electronic format, or on dynamic true copies, or (if applicable) on static true copies verified for their accuracy and not modifiable by the end users.	N.A.	Not Applicable
CFR21: - **ANNEX11**:-	**Data inalterability**	It should not be possible to alter data outside of the application software, both when they are saved in temporary memory (e.g. buffer or local database) and when they are stored in their final location (e.g. server).	**Pass**	-
CFR21: - **ANNEX11**:-	**True copy generation**	There should be written procedures, training, review and audit, and self-inspection of processes defining the conversion of an original electronic record to true copy, including verifications (by a second person or a technical mean) to confirm successful conversion process.	N.A.	Not Applicable
CFR21: - **ANNEX11**:-	**Dynamic format**	True copies should preserve the record's dynamic format, if necessary, to allow the interaction of the users with the record's content (e.g. for queries, searches, processing…).	N.A.	Not Applicable
CFR21: - **ANNEX11**:-	**Analytical methods**	Analytical methods should be validated.	N.A.	Not Applicable
CFR21: - **ANNEX11**:-	**Production processes**	Production processes should be validated.	N.A.	Not Applicable

References	Name	Description	Result	Notes
CFR21: - **ANNEX11**:-	**Laboratory data**	Laboratory data should be complete, meaning that they should include raw data (diagrams, tables, and spectra obtained from laboratory instruments) and possibly the analytical method used to obtain the result. Appropriate procedures should be in place to define the modality of reprocessing, and each result should be maintained.	N.A.	Not Applicable
CFR21: - **ANNEX11**:-	**Statistical analysis**	Raw data and procedures (e.g. SAS programs) used to obtain statistical analysis used for GxP purpose should be available with the final result of the analysis. Appropriate procedures should be in place to define the reprocessing modality.	N.A.	Not Applicable
CFR21: - **ANNEX11**:-	**Governance**	There should be a governance document, integrated in the business quality system, to describe the policies and the organizational and technical controls used to guarantee the data integrity, including roles and responsibilities of the involved personnel.	N.A.	Customer's responsibility

References

[1] EU GMP - Guide to Good Manufacturing Practice for Medicinal Products, Good Manufacturing Practice, Eudralex – Volume 4 and Annex 11 Computerized Systems - 2011 Edition.

[2] 21 Code of Federal Regulations, Part 11, "Electronic Records; Electronic Signatures ", FDA, March 1997.

[3] Guidance for Industry, Electronic Records and Electronic Signatures, Code of Federal Regulations Title 21 Part 11 (21CRF Part 11), FDA, August 2003.

[4] GAMP Good Automated Manufacturing Practices – A Risk-Based Approach to Compliant GxP Computerized Systems Version 5, ISPE-GAMP Forum, 2008.