evolution in automation

WHITEPAPER

evon XAMControl

21 CFR PART 11

VERSION 2.2

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1 Introduction

FDA regulations 21 CFR Part 11: Electronic Records; Electronic Signature

The US ***FDA*** (Food and Drug Administration) ***21 CFR Part 11*** regulations came into effect on the 20 August 1997. The regulations describe the criteria defined by the FDA under which the use of electronic records and signatures are considered equivalent to traditional paper records. There is also the possibility of a combination of electronic records and records in paper form.

Areas of XAMControl application

XAMControl offers a holistic system platform for automation solutions in the process industry. It covers the complete range of automation and information technology from the field level up to the business control level.

Since 2011, the systems have increasingly been used in the pharmaceutical industry, so that the systems have been adapted and will continue to be adapted to the growing requirements posed by the European and US authorities.

Content of this document

This document describes how the ***21 CFR Part 11*** regulations and appropriate organisational measures can be fulfilled by the ***XAMControl*** system in order to guarantee the user regulation-conform system operation.

2 Principles

2.1 The 21 CFR Part 11 regulations

Title 21 Code of Federal Regulations (CFR), Part 11 contains the legal requirements by the FDA (United States Food and Drug Administration) covering the use of electronic records and electronic signatures. Definitions of the concept ***electronic record*** and ***electronic signature*** are in ***sections 11.3*** (6) and the regulations in (7).

Intention of the regulation

Part 11 was originally released on 21st July 1992 as advance notice of a draft bill. The intention of this initiative was to accelerate the approval process for medication. The subsequent consequences, the acceptance of information as well as signatures in electronic form, were immediately obvious. After a period of cooperation between various administrations and the pharmaceutical industry lasting six years, the regulations came into force on 20th August 1997.

Content of the regulation

Part 11 defines the legal prerequisites under which conditions electronic records and electronic signatures are equivalent to paper records and handwritten signatures.

Part 11 assumes that the danger of manipulation and non-traceable changes to electronic records and signatures is higher than for paper and that this makes additional measures necessary.

The concept electronic record

Electronic record in this document means data that is relevant according to the manufacturer regulation for pharmaceuticals ***(21 CFR Part 210 and Part 211)*** and are recorded (e.g. temperatures), are produced (e.g. limit violation messages), or managed (e.g. material stock levels).

2.2 Nomenclature

The following table contains definitions according to Part 11.

Definition according to the regulation (original) [1]	Position of evon GmbH
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.	XAMControl can be operated as a closed system in that access can be completely controlled by the person responsible (e.g. system operator).
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.	If XAMControl is used together with other systems on a single computer or networks are physically connected, the system operator is responsible for the complete system.
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.	Requires no further explanation.
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 signingwith 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.	Requires no further explanation.
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.	This is a replacement technology for a handwritten signature. Currently user name and password are widely employed. Biometric processes are increasingly being used.
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.	An electronic signature must be able to be unambiguously assigned to a user, whereby the authorisation, e.g. the password, must be stored in encrypted form. The first signature during a session requires entry of user name and password. Further signatures within this session should require at least the input of one of these components. The aim of the signature must be clearly and unambiguously stated.
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.	If required, XAMControl can integrate external systems for biometric measurement.

1 Source: GMP-Gesetze der USA, Maas & Peither GMP-Verlag, ISBN: 3-934971-00-8

3 Electronic Batch Records

3.1 Principally required records by the FDA

3.1.1 21 CFR Part 211

System operators who are subject to the FDA regulations must manage different records about the manufactured products.

Which ones they are is defined in ***21 CFR Part 211, Current Good Manufacturing Practice (cGMP) for Finished Pharmaceuticals, Subpart J.*** These explicitly required records and reports contain the following:

- Report concerning device use and cleaning
- Records concerning raw material, packaging and description
- Central production control records
- Batch, production and control records -
- Laboratory reports
- Sales reports
- Complaints

The required information in a large proportion of these records, such as batch records, is recorded or generated by computer systems.

The requirements on the type of information remain unchanged by ***Part 11.***

3.1.2 Compliance Policy Guide 7132a.15

In addition to these clearly defined records in the ***cGMP***, there is a further group of records that must also be managed.

Part 211 Subpart J references production and control instructions.

In a manually operated process, these instructions exist in paper form as operating procedures. In the case of a computer-operated process, these instructions exist in the form of source code for the application program. The implicit link between source code and records was made in 1987 by the FDA in the ***Compliance Policy Guide 7132a.15***, which states:

Link: Source code and records

We regard source code and its supporting documentation for application programs used in drug process control to be part of master production and control records, within the meaning of ***21 CFR Parts 210 and 211.***

3.2 Additional FDA requirements from 21 CFR Part 11

3.2.1 Validation

All automated systems relevant to GMP must be validated.

3.2.2 Audit-trail

All operations relevant to quality must be recorded in a secure and automatically created ***Audit-trail.***

3.2.3 Access security

Access to electronic recordings must be limited to a qualified and authorised circle of personnel.

3.2.4 Storage

The system must archive and protect the electronic recordings and be able to retrieve them on request.

3.2.5 Documentation

The storage, access, distribution and use of documentation created during the validation must be controlled by a process.

3.3 Recordings and datasets controlled by XAMControl

The following table lists the recordings and datasets recorded by XAMControl.

Recording according to system component	Example
System configuration	– Definition of the user and their access rights – Process chain logic – Alarm configuration – Type of control – Graphical representations - Audit-trail
General operator interventions	– Changes in demand and other values – Alarm acknowledgement
Batch management	– Definition of devices and plant – Phase definitions – Recipes
Batch operator interventions	– Interventions in batch operation (start, stop, abort) – Changes in formulae, parameters and sequences
Batch reports	– Phase messages and operator reactions – Batch reports
Process history Process report	– Configuration of trend recording for trends and views – Curve definition – Curve data

4 Evaluation of XAMControl according to 21 CFR Part 11 requirements

4.1 Application specific requirements

The FDA has stipulated guidelines for the implementation of ***21 CFR Part 11*** in the ***Compliance Policy Guide 7153.17*** in which they allow their own inspectors a large amount of discretion regarding regulatory measures.

The FDA does not publish certificates for products, for example such as XAMControl, and no other independent body is authorised to do this.

The regulations in ***21 CFR Part 11*** must always be fulfilled in an applications-specific manner by the plant operator. The decision as to whether prerequisites are met is decided on a case-by-case basis.

4.2 Evaluation table

The following table contains the requirements according to ***21 CFR Part 11*** and the evaluation by evon GmbH regarding the requirements are fulfilled by the system XAMControl and/or by organisational measures.

Definition according to the regulation (original) [1]	Position of evon GmbH
§ 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).	All data XAMControl are saved in MSSQL – Database.. There are four different ways to access to the data: Integrated tools of XAMControl as: Report Generator, Archive revision, Alarmadminsitration. Data can be exported into different formats (dBase, Ascii/CSV, XML) and then be processed in external programs. Data is directly stored in a relational SQL database. External programs can access data there. Data can be printed in PDF format and then be archived.

Definition according to the regulation (original) [1]	Position of evon GmbH
§ 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.	Each audit trail record includes the name of the operator linked to the specific activity. Customers should also establish policies and procedures to prevent unauthorized access to audit trail Table in MSSQL-Database, which can be done with the security system of the MSSQL-Dadabase.
§ 11.100.a Each electronic signature shall be unique to one individual and shall not be reused by, or reassigned to, anyone else.	Windows security and the XAMControl internal security do not permit the creation of duplicate user IDs. Customers using XAMControl applications in FDA-regulated environments must be responsible for ensuring that electronic signatures are unique to one individual and not reused by or reassigned to any other individual.
§ 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.	Customers using XAMControl applications in FDA-regulated environments must be responsible for verifying the identities of individuals using electronic signatures.
§ 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.	Customers using XAMControl applications in FDA-regulated environments must be responsible for verifying the identities of individuals using electronic signatures.
1. The certification shall be submitted in paper form and signed with a traditional handwritten signature, to the Office of Regional Operations (HFC-100), 5600 Fishers Lane, Rockville, MD 20857.	Customers using XAMControl applications in FDA-regulated environments must be responsible for certifying to the agency that the electronic signatures in their system are intended to be the legally binding equivalent of traditional handwritten signatures.
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.	It is the responsibility of the customer to, upon agency request provide additional certification or testimony that a specific electronic signature is the legally binding equivalent of the signer's handwritten signature.

Definition according to the regulation (original) [1]	Position of evon GmbH
§ 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.	The XAMControl user adminsitration as well as the Windows user adminsitration demand the input of user-id (name) and password. Additionally logging in with an electronical ident system can be integrated (e.g. chipcard).
1.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.	To indicate the start of a continuous period of controlled system access, the user must use User-Id and Password to log into XAMControl. For subsequent signatures during this period the XAMControl security requires the user to enter all signature components. The XAMControl User Login Timeout period should be configured to limit the extent of a continuous period of controlled system access. Customers should also implement policies and procedures requiring users to log out of the application during periods of non-use.
1.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.	The XAMControl User Login Timeout period should be configured to limit the extent of a continuous period of controlled system access. Customers should also implement policies and procedures requiring users to log out of the application during periods of non-use. The user has to enter all signature components for all signings by default.
2. Be used only by their genuine owners	Customers using the XAMControl applications in FDA-regulated environments must be responsible for ensuring that non-biometric electronic signatures are used only by their genuine owners.
§ 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	Biometric devices are readily available from 3rd party vendors. However, Customers using the XAMControl applications in FDA-regulated environments, or any organization that may develop biometric devices for interfacing with the audited applications, must be responsible for ensuring that electronic signatures based upon biometrics are designed to ensure that they cannot be used by anyone other than their genuine owners.

2 Source: GMP-Gesetze der USA, Maas & Peither GMP-Verlag, ISBN: 3-934971-00-8

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