Cloud Framework, Regulatory Requirements

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Contents

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This document has been developed by the Pharmaceutical User Software Exchange (PHUSE) Working Group on Cloud Adoption and is subject to ongoing consultation and feedback from all relevant stakeholders.

You may submit comments and suggestions regarding this document to *avid@nnit.com* (Anders Vidstrup, NNIT A/S).

1. Scope

In adopting cloud-based solutions for GxP workloads, understanding the essential characteristics of cloud services and solutions is important for determining the applicability of GxP requirements to specific Cloud Service Providers and/ or cloud-based solution models.

This document outlines the regulatory requirements that govern the use of cloud services in a GxP environment. It is one of three supplements to the "Cloud Services – Pre-Amble" ref [1] which all together form the "Framework for Adoption of Cloud Services in the Regulated Life Science Industry" from the Pharmaceutical User Software Exchange (PHUSE).

Note: *The content in this document is intended to be informative but should not be considered in lieu of appropriate regulatory advice.*

3. Interpretation of regulatory requirements

Many regulations could be covered, but the following are generally in scope when considering Cloud Services for the Life Science Industry:

- US FDA 21 CFR part 11
- US FDA 21 CFR part 211
- US FDA 21 CFR part 820
- EU GMP Annex 11

The list below in section 3.1 does not intend to be comprehensive. It contains examples of applicable rules in the different Cloud Service Models.

In section 3.2 questions from EMA regulators that were asked to the PHUSE cloud adoption group are listed.

3.1. Regulatory requirements traced to IT terms and Cloud Services

For clarification on responsibilities of below topics suggestions are given in "Cloud Services – Pre-Amble" ref [1].

Topic	Regulations	IAAS	PAAS	SAAS
Audit Trail, Electronic records	21 CFR Part 11, §11.10(a) and 11.10 (e) Annex 11, §8.2, §9 and §12.4		X	X
Audit Trail, Time stamp	21 CFR Part 11, §11.10 (e) Annex 11, §8.2, §9 and §12.4	X	X	X
Audit Trail, Record Management	21 CFR Part 11, §11.10(a)		X	X
Backup	21 CFR Part 11, §11.10(c) 21 CFR part 211, §211.68(b) Annex 11, §7.2	X	X	X
Change and Configuration Management	21 CFR Part 11, §11.10(k) (2) Annex 11, §1, §4.2 and §10	X	X	X
Change and Configuration Management, System overview	Annex 11, §4.3	(X)	(X)	X
Incident and Problem Management	21 CFR Part 11, §11.300(d) Annex 11, §13	X	X	X
Periodic Review	21 CFR part 211, §211.22 (implicit by cGMP) Annex 11, §11	X	X	X
Personnel Qualification, electronic signature	21 CFR Part 11, §11.10(j) 21 CFR part 211, §211.25(a) Annex 11, §2 and §14	(X)	(X)	X
Personnel Qualification, general	21 CFR Part 11, §11.10(i) 21 CFR part 211, §211.25(a) Annex 11, §2	X	X	X
Physical Security	21 CFR part 211, §211.28 (and §211.122(d)) Annex 11, §7.1, §12.1 and §12.3	X	X	X
Record Management, availability	21 CFR Part 11, §11.10(b) and §11.10(c) Annex 11, §7.1, 8.1, §8.2 and §17	X	X	X
Record Management, electronic signature	21 CFR Part 11, §11.50(a), §11.50(b) and §11.70 Annex 11, §14	(X)	(X)	X
Record Management, general	21 CFR Part 11, §11.10(k) 21 CFR part 211, §211.180 and §211.182 Annex 11, §1, §5, §7.1, §9, §12.4 and §17	X	X	X
Remote Access, e.g. in clinical trials	21 CFR Part 11, §11.10(f) and §11.10(g) Annex 11, §5 and §6	X	X	X
Systems Development, general	21 CFR Part 11, §11.10(a) Annex 11, §1, §4.1, §4.2, §4.4, §4.6 and §4.7	(X)	X	X
Systems Development, Incident- and pro-blem management	21 CFR Part 11, §11.10(h) Annex 11, §4.2 and §13	X	X	X
Systems Development, Infrastructure	21 CFR Part 11, §11.10(a), §11.10(d), §11.100(a) and §11.200(a) Annex 11, §1, §4.1, §4.2, §4.4, §4.6 and §4.7	X	X	X
Third Party Management	21 CFR part 820, §820.22 and §820.50 Annex 11 - §3.1	X	X	X
User Access Management, general	21 CFR Part 11, §11.10(d), §11.10(g), §11.100(b), §11.300(a), §11.300(b), §11.300(c), §11.300(d), §11.300(e) Annex 11, §12.1, §12.2, §12.3, §15	X	X	X
User Access Management; electronic signature identity	21 CFR Part 11, §11.200(a) and §11.200(b)	(X)	X	X
User Access Management; Record Management	21 CFR Part 11, §11.100(a)	X	X	X

3.2. Questions from Regulators

This chapter contains questions about the use of Cloud Services in the regulated Life Science Industry.

3.2.1. Introduction

At the EMA GCP Inspectors Working Group (IWG) and Interested Parties Joint Meeting November 2015 the PHUSE cloud adoption group was represented. At this meeting a presentation was given outlining the framework of the PHUSE Cloud Service Adoption in Life Sciences ref [1] that was developed by Cloud consumers and Cloud providers under the auspices of the PHUSE/FDA collaboration. Key cloud-related concepts were outlined with focus areas being:

- ISO-based role definitions - moving onto illustrating those roles in specific relationship scenarios
- The "IT supply chain" concept - the positions of SaaS, PaaS and IaaS in the context of those roles (and responsibilities)
- Reference to the PHUSE framework's check listing approach for those roles
- Specific reference, as example, to Electronic Data Capture (EDC) and related apps in a cloud technology stack
- Cloud approaches/solutions providing benefits of innovation, speed of solution adoption, fixed-cost reduction, on-demand usage etc.
- Predicate rules still apply.

3.2.2. Questions

EMA GCP IWG prepared 10 questions in advance of the meeting. They were walked through in detail. Particular areas of interest from those discussions were:

- Contractual relationships along the "IT supply chain" and the inspectors' desire for clarity as well as diligence in formulation and maintenance - including SLA and rights of audit/due-diligence
- Data "Ownership"
- Data (and application) retention/re-use/re-accessibility
- Change control
- Security and access controls
- Emerging best practices and standards
- GxP awareness of providers in the cloud technology stack in the context of the defined roles.

More questions were delivered to PHUSE upfront at the meeting:

1. Who owns the data when stored on vendor's servers?
2. What is the attitude to server farms location and sharing of partitioned server with other clients?
3. What considerations are given to data protection in the countries where servers may be located?
4. How should the cloud data be protected from unauthorised access?
5. What consideration is given to back up and restoration? What are the minimum expectations for this?
6. What are essential components for consideration in contracts with a cloud service provider?
7. What risks do you believe there are in using cloud?
   a. How is it guaranteed that documents and data stored in the cloud are archived and ready for inspection for at least 25 years after the end of the clinical trial (as required by article 58 of the European Clinical Trial Regulation)?
8. How can sponsors audit cloud solutions?
9. What about change control?

4. Glossary

See Glossary in PHUSE, Cloud Services - A Framework for Adoption in the Regulated Life Sciences Industry, Pre Amble, Edition 4, April, 2019.

5. References

1. PHUSE, Cloud Services - A Framework for Adoption in the Regulated Life Sciences Industry, Pre Amble, doc ID WP-23, April, 2019.