2023-01-09

Submission of comments on 'Concept Paper on the revision of Annex 11' (EMA/INS/GMP/778340/2022)

Comments from:

Name of organisation or individual
ECA Foundation / European QP Association

Please note that these comments and the identity of the sender will be published unless a specific justified objection is received.

When completed, this form should be sent to the European Medicines Agency electronically, in Word format (not PDF).

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1. General comments

Stakeholder number *(To be completed by the Agency)*	General comment (if any)	Outcome (if applicable) *(To be completed by the Agency)*
	1 – Purpose and Objectives: Regulation vs Q&A vs Guidance ■ Regulation i.e. Annex 11 ► Establishes overall requirements and expectations applicable to Computerised Systems from a long term perspective ■ Q&A ► When necessary, clarifies and/or explains particular topics. ► Q&A can be revised and enhanced to reflect current thinking and technical developments in a faster (more agile) manner than the regulations themselves. ■ References to external standards ► E.g. ISO 27001 shall not be referred to in a GxP regulation since it will make the standard mandatory within a GxP context. ■ Recommendation ► Guidance shall not be part of a regulatory text; avoiding creating confusion between "*must*" and "*could*". ► Regulation i.e. **Annex 11 must remain as <u>technology agnostic</u> as possible**.	

	2 – Observation: CSV objective ■ CSV objective is to ensure that the regulated user can provide evidence that their computerised systems are fit for their intended use. ■ **Recommendation** ► The following revision to the Annex 11 Principle (paragraph 3) is proposed: ◆ *Where a computerised system replaces a manual process or an existing computerised system, there should be no resultant decrease in product quality, **integrity of data**, process control or quality assurance. There should be no increase in the overall risk of the process.*	
	3 – Observation: Computerised Systems in GMP Environments ■ Computerised systems used in manufacturing environments are not only IT systems, but also include OT (Operational Technology) systems; e.g.: ► Automated equipment in production ► Automated equipment in laboratory ► Automated facility equipment (e.g.: energy, fluids, HVAC, etc.) ■ **Recommendation** ► Please avoid overemphasis on IT systems and applications when writing computerised system regulation and supporting documents (Q&A, Position Paper, Reflection Paper, …)	

	4 – Observation: Data Integrity ■ A primary objective of CSV is to ensure Data Integrity, see for instance 21CFR11.10(a): ► "***Validation of systems to ensure*** *accuracy, reliability, consistent intended performance, and* ***the ability to discern invalid or altered records***." ■ Annex 11 already explicitly mentions "*data integrity*" as part of the risk-based approach. ■ Since data integrity is an overall expectation impacting every process and record in a GxP environment the appropriate place for its consideration should be in a revised Chapter 4. ■ **Recommendation** ► Data Integrity should not be specifically developed in Annex 11.	
	5 – Observation: Risk-based Approach ■ Within the scope of Annex 11, risk management should cover: ► Patient safety ► Product quality ► Data integrity ► **Business capability** ■ About "*business capability*" ► Availability and resilience of computerised systems are vital for securing product availability (supply chain). ► ICH Q9 R1 already recognises the need for extending the scope of Quality Risk Management to the whole supply chain; this	

	implies that the involved computerised systems must be considered within the scope of the capability of pharmaceutical organisations. ▶ Cyberattacks as well as IT service outsourcing show how crucial it is to proactively secure data availability and record legibility throughout the complete data life cycle. ■ **Recommendation** ▶ **Business capability** should be formally added as a risk-based approach consideration.	
	6 – Observation: Criticality (*see as well comment on Item #13*) ■ It is the regulated user's duty to know and to understand its processes, systems, and data. ▶ On a regulatory level, it is not possible to provide a "*one-size-fits-all*" statement regarding what is critical, since criticality is the result of a science-based risk assessment of product, process, data, and regulatory requirements – in particular to process traceability and to data integrity. ▶ It is not because a system, an equipment, an application is "*GxP relevant*" that it is necessarily "*critical*". As mentioned above, criticality is an outcome of the science-based Quality Risk Management. ■ **Recommendation** ▶ The terms "*criticality*" and "*critical*" should be avoided since in the most cases the better	

	appropriate term would be "*relevance*" or "*relevant*".	
	7 – Observation: Terminology ■ **Recommendation** ► If particular terms are necessary, they must be clearly defined; otherwise avoid the introduction of new (unnecessary) terms, e.g.: ◆ Data in motion ◆ Data at rest ◆ Digital transformation ◆ Volatile media ◆ True time ► **To be defined**: ◆ Clear printouts (see [A11:8.1]) ◆ Data flow (see [A11:4.3, 4.8, 5]) ◆ Data Owner (see Process Owner) ◆ Durable electronic record (otherwise in Chapter 4) ◆ OT – Operational Technology (see Observation #2) ◆ OTS – Off-the-shelf (without "*commercial*", see comment on Item #8) ◆ RPO – Recovery Point Objective (see also comment #16) ◆ RTO – Recovery Time Objective (see also comment #16)	

8 – Missing points / Possible improvements

In addition to the remarks provided in direct relation to the Concept Paper content.

- **Reference to Annex 15**
  - For consistency, since Annex 15 refers to Annex 11 when computerised systems support processes, it is meaningful that Annex 11 refers to Annex 15 regarding equipment qualification and the validation of processes supported by the computerised system.
- **Personnel** [A11:2]
  - Beside "*Process Owner, System Owner, Qualified Persons and IT*", it is important to explicitly mention "engineering".
    - In particular in a manufacturing context (including QC laboratory), (site) engineering plays an important role for securing availability as well as adequacy of the involved automated equipment and systems.
- **Adequacy** [A11:4.7]
  - "*Automated testing tools and test environments should have documented assessments for their adequacy*".
  - It would be meaningful not to limit the statement scope to automated testing tools, but to extend it to engineering and qualification tools (e.g. requirement management tools, paperless qualification tools, configuration reporting tools, network management tools, incident management

tools, etc.).
    - When tools and applications are used to support engineering, qualification or validation activities, in particular when such tools generate records being considered as "evidences", it is important that such tools are assessed for adequacy and maintained under control, covering for example:
        - Access control
        - Data management (backup, restore, archiving, retrieval, disaster recovery)
        - Configuration management
        - Change management
    - Otherwise the generated evidences could be jeopardised, compromising the ability to prove the qualification status of the concerned equipment or the validation status of the concerned process.
- **Data** [A11:5]
    - For clarity, the title could be changed to "*Data Interfaces*".
- **Accuracy Checks** [A11:6]
    - "*This check may be done by a second operator or by validated electronic means*."
        - While the idea behind this statement is interesting – i.e. replacing a second person review by a validated electronic control – it is not fully practicable.
            - The validated electronic control can

verify that the entered value is in the expected range, but the system has no possibility to ensure that the entered value is correct (i.e. no typo); otherwise, why would the value be entered manually?
    - It is important that the system shall support possible validated controls for range and format correctness, but it is not possible to rely only on the system without second person review, because the system cannot verify on its own if the correct value has been entered manually.
- **Configuration Management** [A11:10]
  - In the current version of Annex 11, configuration management is only part of the title of Item #10 but finally not really covered in this section.
  - It is important to state that change management is only possible if configuration management is accurately conducted, since a change request is always related to a formal configuration baseline.
    - Consequently the result of an executed change request is the generation of a new configuration baseline.
    - Configuration management also includes documentation.
- **Security** [A11:12] (*see also comment on Item #27*)
  - It could be meaningful to add an item 12.5

	mentioning explicitly the necessity of pro-active cybersecurity measures to secure system operation. ■ **Electronic Signature** [A11:14] ► In the current version of Annex 11, the meaning of the electronic signature is missing (already reported at publication time in 2011'01). ► To avoid confusion, the signature meaning must be added. ■ **Retirement** ► The current version of Annex 11 does not formally define requirements for the retirement activities of a computerised system. ◆ Verification of the system state-of-control of the system to be retired: »» Verification of the calibration state »» Last periodic evaluation ◆ Necessity to secure availability and readability of the data generated by the computerised system and requiring to be retained beyond the end of system operation.	
	9 – Observation: Chapter 4 ■ In order to keep a clear content for Annex 11, it is necessary to elaborate a similar concept paper for the revision of Chapter 4 and to secure clarity and consistency between both documents, in particular avoiding redundancy and contradiction.	

2. Specific comments on text

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
12-13		Item #1 Comment: ■ See general comments on purpose and objectives Proposed change (if any): ■ See above.	
14-17		Item #2 Comment: ■ Annex 11 already explicitly mentions "*data integrity*" as part of the risk-based approach. ► See as well as the proposed wording improvement for the Annex 11 principle, mentioning explicitly "data integrity" (see "*2 – Observation: CSV Objective*") Proposed change (if any): ■ See general comments on purpose and objectives ► If Data Integrity must be specifically addressed, it should occur in Chapter 4. ► Technical aspects shall not be discussed in a regulatory text, only in guidance or Q&A.	
14-17		Item #2 Comment: ■ Be careful with "buzz words" such as "*data in motion*" and "*data at rest*", in particular because such terms are not unambiguously defined in defined in the industry.	

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		► We don't need new terms causing more confusion than providing clarity. ◆ "*Data in motion*" is finally related to interfaces between systems (see [A11:5]) »» Additionally, "*data in motion*" could refer to data migration (already mentioned in [A11:4.8]) ◆ "*Data at rest*" is covered by the requirements related to protecting data against loss and corruption, including access control (see [A11:7]) Proposed change (if any): ■ Instead of becoming too technical, the mentioned topics in #2 should be summarised – for example in the principles – reminding that the technical implementation of Annex 11 requirements, based on a science-based risk-based approach, must be commensurate and "state of the art" reflecting the current technical development and capability. ► See Directive 2001/83/EC, Article 23, §1 ◆ "*… the marketing authorisation holder shall … take account of scientific and technical progress and introduce any changes that may be required to enable the medicinal product to be manufactured and checked by means of generally accepted scientific methods.*"	

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18-19		Item #3 Comment: ■ Annex 11 does not need to explicitly mention (and develop) the "digital transformation". It should / could be addressed as appropriate in a concept/reflection paper. Proposed change (if any): ■ Please remove any mention to "digital transformation" ■ It would be more valuable that the regulators – aligned with WHO TRS 996 Annex 5 and PIC/S PI 041-1 – would elaborate a Reflection Paper on "hybrid systems", discouraging the regulated industry to still operate such systems in the future.	
20-21		Item #4 Comment: ■ Yes, agree; see general comments. ► Prefer: "*an existing computerised system*" rather than "*another system*" Proposed change (if any): ■ *Where a computerised system replaces a manual process or an existing computerised system, there should be no resultant decrease in product quality, integrity of data, process control or quality assurance. There should be no increase in the overall risk of the process.*	

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22		Item #5 Comment: ■ NO, Q9 is part of the EU GMP in the "non-mandatory" part: Part III ■ Even A15 does not refer to Q9. Proposed change (if any): ■ It is not necessary to explicitly mention Q9 even if QRM is obviously mandatory.	
23		Item #6 Comment: ■ Yes for mentioning IT services, incl. outsourcing of IT activities. ► Cloud should not be mentioned specifically since it is already covered by "outsourcing of IT activities". Proposed change (if any): ■ Please remove any mention to cloud computing.	
24-29		Item #7 Comment: ■ Focusing requirements and effort on the intended use should be sufficient, since Data Integrity is part of the intended use. ► Within the scope of a risk-based approach, "cloud services" shall be considered like any other services according to EU GMP Chapter 7. Proposed change (if any): ■ Please remove any mention to cloud computing. ► Additionally, since "cloud" is a very broad term	

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		covering multiple aspects of IT services and multiple complexity levels, mentioning "cloud" without mentioning the related context will generate more confusion than being supportive. ■ For systems operated by service providers, expectations should go beyond that "formal agreements must exist". ► It shall be reminded that an accurate supplier / service provider assessment – or even an audit – represents the necessary condition for being able to leverage supplier's / service provider's good practice.	
30-35		Item #8 Comment: ■ Yes, COTS can induce some confusion. ► OTS – Off-The-Shelf – should be preferred since OTS software components could be commercial or non-commercial, e.g. open source software (OSS). Such OSS should be handled in the same manner than commercial software. ◆ OTS software components cannot be qualified by the vendor / supplier. Suppliers / vendors can only provide a "ready-for-compliance" software component. It remains regulated user's duty to qualify/validate the software component <u>for its intended use</u>. Proposed change (if any): ■ Please use and define "OTS" instead of "COTS"	

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		■ See above comment regarding the qualification of OTS software components.	
36-38		Item #9 Comment: ■ These terms are already defined in Annex 15 and in the EU GMP Glossary. They should not be redefined in Annex 11. ► For consistency reasons, if the definitions shall be improved, it should be made in Annex 15 and in the EU GMP Glossary. ■ Nevertheless the definition is clear: ► Qualification as well as Validation aim to demonstrate the system (and subsequently the process) fitness-for-the-intended-use as defined in the URS. ◆ An equipment is qualified ◆ A process is validated » A validated process requires qualified equipment ► Additionally, a computerised system like process must be kept in a state of control throughout its complete life cycle, i.e. until its retirement. Proposed change (if any): ■ See above	

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39-42		Item #10 Comment: ■ Applying Good Engineering Practice, each specification and configuration item requires to be verified. ► Based on the outcomes of the risk management activities, additional verification activities (e.g. stress tests, worst case tests, or boundary tests) shall be planned for functionalities with particular impact on patient safety, product quality, data integrity, and business capability. Proposed change (if any): ■ **It shall <u>not</u> be emphasised** that the effort should be focused on software parts "*specifically designed or customised*" only.	
43-50		Item #11 Comment: ■ "*User requirements should be traceable throughout the life-cycle*". ► The sentence is very clear; no change is required. ► Criticality should not play any role in the traceability since traceability is required for securing design consistency and implementation completeness. ► It seems that some readers require to be trained. Proposed change (if any): ■ No change is required in [A11:4.4]. ■ **It shall be emphasised that URS** (or equivalent specifications) must cover the system in its full extend in	

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		order to support accurate risk management enabling to consider system and the supported processes in their entirety. ► It is not wise to limit the scope of the specifications – in particular URS – on the "GMP critical functionality" only. ► URS like any other specifications shall be focused at first on the intended use.	
51-53		Item #12 Comment: ■ It is important neither to forbid nor to hinder iterative and incremental project approach (by the way: Agile is only one family of iterative and incremental software development methodologies). ■ The statement "*which may not consist of traditional documents*" is inappropriate since the "documents" are still required but the "format" of those documents could differ from the typical document written using a word processing application. Proposed change (if any): ■ It is not necessary to adapt anything in Annex 11. ► Nevertheless it is important to mention in Chapter 4 that life cycle documentation could consist of documents or of requirement and specification baselines, where the requirement / specification item represents the smallest managed entity.	

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54		Item #13 Comment: ■ **We disagree with this point for the following reasons:** ► It is regulated user's duty to know and to understand its processes, systems, and data. ► It is not possible to define what is critical on regulatory level, since criticality is the result of a risk assessment of product, process, data, and regulatory requirements to traceability and data integrity. Proposed change (if any): ■ **A regulation is not a guideline!** ► See general comments on purpose and objectives	
55-57		Item #14 Comment: ■ **We disagree with this point for the following reasons:** ► It is not the aim of a regulation to provide examples. ◆ If examples are needed they should be provided in training or supporting material. Proposed change (if any): ■ **A regulation is not a guideline!** ► See general comments on purpose and objectives	

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58-63		Item #15 Comment: ■ [A11:7] is correctly worded and doesn't require any improvement. ► The requirement of periodic restore verification is appropriate: ◆ The frequency of periodic restore verification should be defined based on a risk assessment. ◆ This required verification gives opportunity to exercise the restore process. ► Do not forget! ◆ Restore verification of back-up data represents a mitigation measure against data loss. Proposed change (if any): ■ If necessary, it could be useful to mention that this periodic restore verification could be performed in a test environment, providing that this test environment is similar to the production environment.	
61-63		Item #15 Comment: ■ INCORRECT statement: ► Backup and restore processes are directly related to **SHORT TERM** data protection. ► Archiving and retrieval are directly related to **LONG TERM** data retention. ► "Long-term backup (or archival)" is an inaccurate statement.	

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		Proposed change (if any): ■ Please avoid mixing and to confuse short term data protection and long term data retention processes	
64-68		Item #16 Comment: ■ **We disagree with this point for the following reasons:** ► It is regulated user's duty to assess its systems for identifying backup scope, frequency, content, as well as the need for periodic verification. ► See as well comment to #13. Proposed change (if any): ■ If improvement regarding backup & restore processes is needed, explicit references to RPO and RTO could be added: ► RPO – Recovery Point Objective ► RTO – Recovery Time Objective ■ RPO and RTO have a direct impact to the disaster recovery strategy. ► Without an adequate backup strategy, it not possible to elaborate any disaster recovery strategy.	

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69-70		Item #17 Comment: ■ **We disagree with this point for the following reasons:** ► [A11:8] is perfectly clear and no improvement is required. ◆ Obviously it must be possible to perform some data review or investigation outside of the system, if necessary. »» For this reason, it must be necessary to "print-out" (as PDF or on paper) the complete required data. Proposed change (if any): ■ No change is required in [A11:8].	
71-75		Item #18 Comment: ■ [A11:9] is clear but too often (deliberately?) misunderstood. ► Risk management should not be misused for justifying non-compliances (see Q9, section 1). ► A risk-based approach to audit trail means: ◆ If the system does not allow the operator/user to change value at run-time, no audit trail is required. »» Assuming that configuration changes made by the system administrator are adequately covered by the change	

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		management process. ◆ Beside data (creation), modification, and deletion, some operator activities could justify the generation of an audit trail entry. » In such cases, a process risk assessment should be performed for identifying what operator activities require to be audit-trailed. ■ **Audit trail is not equivalent to system log !!!** ► In case of data transfer between systems, a log file can be generated for supporting trouble shooting; **in no way such a log file is an audit trail**. Proposed change (if any): ■ Please remove any mention to system logs since they are not equivalent to audit trail. ■ Additionally, it could be useful to consider the above remark related to <u>some</u> operator activities which might require to be documented with an audit trail entry (see [A11:12.4].	
76-80		Item #19 Comment: ■ On a GMP system, while "*when, who did what*" is a mandatory set of audit trail information, "*why*" should depend on the particular process context. ► For example, a manufacturing formula could foresee the ability for the operator to adjust at runtime a setpoint value within a limited range in order to	

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		compensate some process variability. ◆ Since the particular scenario is formally described in the process specification, it is not necessary to make the reason (why) mandatory for the particular action. ⏩ Finally, it is nothing more than the application of a risk-based approach: ▸ When a reason is (why) required? Proposed change (if any): ■ Be careful (and frugal) with the requirement related to the reason (why).	
81-84		Item #20 Comment: ■ OK ► It is not necessary to explicitly mention these aspects in the regulation. Proposed change (if any): ■ Data Integrity requirements fully apply to audit trail entries like to any other GxP relevant data.	
85-88		Item #21 Comment: ■ The review of process audit trail entries shall be part of the release activities (second person review); e.g.: ► Batch release ► Release of analytical results. ■ The review of administrative audit trail entries shall be part of the periodic evaluation.	

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		Proposed change (if any): ■ The content of audit trail review shall be based on the assessed risks: ► Process risks ► Risk to data integrity ► Product quality risks ► Patient safety. ■ It is not the regulation aim to provide examples.	
89-92		Item #22 Comment: ■ **We disagree with this point for the following reasons:** ► It is regulated user's duty to assess its systems for defining when (how frequently) audit trail entries have to be reviewed. ■ See as well comment to #13, #16. Proposed change (if any): ■ It is not the regulation aim to provide examples.	
93-97		Item #23 Comment: ■ **We disagree with this point for the following reasons:** ► It is definitively an overkill to provide a full traceability by typo. ► Only after confirmation of a data capture (i.e. data are committed), an audit trail entry must be generated if the value is changed.	

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		Proposed change (if any): ■ It is not the regulation aim to provide examples.	
98-102		Item #24 Comment: ■ **We disagree with this point for the following reasons:** ► Storing and displaying process events (e.g. batch history file) differently or at another place than audit trail entries will over-complicate the review of the complete data (for example for batch release purpose, or for releasing analytical results) and will cause that some entries will be forgotten or overlooked. ► It is meaningful (but it should not be mandatory) to store administrative audit trail entries separately, since these entries are not related to the process (only to system configuration, and system management) and they will be reviewed within the scope of the periodic evaluation. Proposed change (if any): ■ See remark regarding the possibility to store administrative audit trail independently on the process relevant audit trail.	

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103-106		Item #25 Comment: ■ **We disagree with this point for the following reasons:** ► It is only necessary to remind that the main objective of periodic evaluation is to formally ensure that the system remains in the qualified state. ► Configuration review could be part of the periodic evaluation depending on system size and complexity. Proposed change (if any): ■ See above comment ■ Configuration review shall cover the entirety of the configuration of the computerised system, including: ► (External) services being part of the computerised system / application ► Services supporting system operation and maintenance.	
107-109		Item #26 Comment: ■ Instead of reference to ISO 27001 (which can represent an overkill depending on system size and complexity), it is much more efficient to add a fourth risk management topic for computerised system: "*business capability*". ► This includes the ability to keep systems in operation and to secure data integrity – in particular data availability – throughout the system life cycle.	

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		Proposed change (if any): ■ Please add "*business capability*" as the 4th criterion for a risk-based approach to computerised systems. ■ ISO 27001 shall not be referred to in a GxP regulation.	
110-114		Item #27 Comment: ■ **We disagree with this point for the following reasons:** ► [A11:12] is perfectly clear and no improvement regarding technology is required. ◆ Computerised systems in manufacturing environment are not only IT systems, but at first OT systems: » Automated equipment in production » Automated equipment in laboratory. ◆ Physical and logical security measures are mandatory and they must be defined and implemented based on the identified risks. Proposed change (if any): ■ It could be meaningful to add an item "12.5" mentioning explicitly the necessity of pro-active cybersecurity measures to secure system operation and business capability. ■ It is not the regulation aim to specify technology.	

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115-117		Item #28 Comment: ■ **We disagree with this point for the following reasons:** ► See comment on Item #27. Proposed change (if any): ■ A two-component identification – i.e. User-ID and password – is required. ► When a token is used, it can only replace the manual entry of the User-ID, since the second identification component – i.e. password – must remain private.	
118-121		Item #29 Comment: ■ OK Proposed change (if any): ■ Segregation of duties could be formally mentioned as followed: ► User management strategy must ensure that the segregation of duties is enforced: ◆ Securing second person review of performed activities ◆ Ensuring that the system administrator is not interested in the process/business data. ►► If the organisational constraints require a user to have two roles – i.e. operator and administrator – this user must have two	

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		different user accounts and the audit trail review activities (for release purpose as well as within the scope of periodic evaluation) shall give some particular consideration to the audit trail entries and activities related to these user accounts. - See for example OECD GLP Guide #22, "*System administrator access*" - It is forbidden to perform business process related activities with administrator privileges, excepted system management activities.	

122-126		Item #30
		Comment:
		- OK
		Proposed change (if any):
		- Access control and user management activities must be formalised (SOP) and documented; they must cover:
		  - Creation of user account
		  - Modification of access privileges
		  - Withdrawing of access authorisations
		  - Lock and unlock of user account.	

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127-130		Item #31 Comment: ■ **We disagree with this point for the following reasons:** ► It is impossible for pharmaceutical regulated user to technically qualify media for archiving purpose. ► If additional information / recommendation are necessary, the following points should be addressed: ◆ Media robustness ◆ Necessity to take into account already archived data when assessing system change requests, in particular in case of system update, system upgrade, and system replacement. Proposed change (if any): ■ It is necessary to take into account already archived data when assessing system change requests, in particular in case of system update, system upgrade, and system replacement. ■ It is not the regulation aim to specify technology as well as technical details.	
131-135		Item #32 Comment: ■ There is no urgent need to discuss about Artificial Intelligence (AI) and Machine Learning (ML) in Annex 11. ► AI and ML are rapid evolving technologies. ◆ At this time, a reflection paper on AI and ML would be more appropriate; e.g.:	

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		▸▸ DKMA paper on "*Questions to critical GxP AI/ML applications*" ▸▸ FDA discussion paper on "*Artificial Intelligence and Machine Learning*" Proposed change (if any): ■ Only a mention that, even if AI and ML are implemented for supporting a GxP / GMP process, **Annex 11 principle** – *Where a computerised system replaces a manual process or an existing computerised systems, there should be no resultant decrease in product quality, integrity of data, process control or quality assurance. There should be no increase in the overall risk of the process.* – **remains valid**.	
136-140		Item #33 Comment: ■ The current content of the FDA draft guidance on CSA is: ► Focused on medical device and not on GMP processes ► Not consistent with the current version of Annex 11, i.e.: ◆ Not fitting with the definition of a computerised system according to PIC/S PI 011-3, 6.2. ■ Annex 11 already focuses clearly on system intended use and on the necessity to keep processes under control. ► It is sufficient! Proposed change (if any):	

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		■ Please avoid referring to CSA since its future in a GMP environment is unclear.	
142-150		Section #2 Comment: ■ It not the objective of a regulation to provide guidance. Regulation shall only focus on WHAT must be achieved. Proposed change (if any): ■ See general comments on purpose and objectives	
153-155		Section #3 Comment: ■ NA Proposed change (if any): ■ NA	
158-167		Section #4 Comment: ■ Based on the proposed timetable and considering the current experience by revising Annex 11 and Chapter 4, the authors must keep in mind that what they write between 2023 and 2025 should remain valid at least for 15-17 years: i.e. until 2040 - 2042. Proposed change (if any): ■ For the above reason, Annex 11 shall in no way reflect "current" trends and technology which can become obsolete very quickly. ■ Annex 11 must remain technology agnostic, only defining objectives to achieve.	

Line number(s) of the relevant text *(e.g. Lines 20-23)*	Stakeholder number *(To be completed by the Agency)*	Comment and rationale; proposed changes *(If changes to the wording are suggested, they should be highlighted using 'track changes')*	Outcome *(To be completed by the Agency)*
168-207		Sections #5, #6, #7, #8 ■ No comment	

Please add more rows if needed.