11 November, 2014

Organization for Economic Co-operation and Development
2, rue André Pascal
75775 Paris Cedex 16
France

Subject: Comments on Draft Advisory Document 16, The Application of GLP Principles to Computerised Systems.

Dear Sir or Madam,

Thank you for the opportunity to comment on the above draft guideline. The draft was reviewed by members of the ISPE Good Automated Manufacturing Practices (GAMP®) technical community. We are particularly pleased to note the use of a scalable approach based upon risk, which is to be commended. We hereby offer general and specific comments on the draft as detailed in the attachment to this letter.

The International Society for Pharmaceutical Engineering (ISPE) is an individual membership Society of more than 20,000 professionals involved in the manufacture of pharmaceuticals and related products. All scientific and technical areas of the pharmaceutical manufacturing industry are represented among the ISPE membership. ISPE is committed to creating a forum for uniting the world's pharmaceutical manufacturing community and regulators.

Yours sincerely,

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COMMENTS ON THE PROPOSAL OF THE NEW ☐or REVISED☐ OECD TEST GUIDELINE OR NEW ☐or REVISED☒ GUIDANCE DOCUMENT

Title:

OECD Draft Advisory Document 61
The Application of GLP Principles to Computerised System

Comments submitted by (please fill in below -Name, Country, Organisation)

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National Experts or National Co-ordinators please complete the following:

Name of Expert:	Email:	Mailing Address,Tel/fax	Date comments were received

Expert Comments	National Co-ordinators response
General Comments	
1. The text should reflect that people and processes are also considered as part of a "computerised system". See also comment for Paragraph 5. 2. Discussions of risk should include criticality of the business processes supported by the computer system as well as risk to product quality (for GLP product = study), patient safety and integrity of records. 3. The use of a scalable approach based upon risk is to be commended and is in line with general GAMP principles.	
Paragraph 2	
Including the word "economic" in the approach to validation could lead to a cost based validation approach rather than one purely based upon interpretation of risk. Consider inserting additional text at the end of the first sentence in this paragraph to highlight what risks are being managed: "……..central element of a scalable, economic and effective validation approach with a focus on patient safety and data integrity."	
Paragraph 3	
Consider inserting additional text as follows: "All computerised systems used for the generation, measurement or assessment of data intended for regulatory submission or used to support regulatory decisions……."	

Expert Comments	National Co-ordinators response
Paragraph 5	
The definition of a computerised system is incomplete in this paragraph (it is better in paragraph 6). The computerised system includes hardware, software, interfaced equipment, personnel and procedures (processes) as per PIC/S and FDA definitions.	
Paragraph 7	
Change “computer validation” to “computerised system validation”	
Paragraph 9	
The range of computerised systems should be expanded to include, for example a standalone PC controlling a lab-based instrument or standalone balance. As it stands the range includes either very simple devices or very complex systems but those of medium complexity are not indicated.	
Paragraph 10	
The first sentence provides the wrong focus for the validation approach. Agree that the approach must follow a life cycle but it must be based upon risk. Consider modifying the text as follows: “The validation approach should be risk-based giving the regulated user the freedom to choose any life cycle model.”	
Paragraph 11	
This wording of this paragraph suggests that verification activities are only required in the production environment. Good practices approaches are somewhat different and validation should include verification throughout the life cycle. Therefore it should include testing and / or verification of supplier testing, and appropriate change management should be applied throughout the life cycle and during operations and retirement. Testing is usually necessary in an environment that is representative of the production environment rather than in the production environment (this is impractical as the test data will then be stored in the production	

Expert Comments	National Co-ordinators response
database). Also, it is good practice to monitor the production environment post release of the system and this is not covered. The use of retrospective validation should be clarified, as generally retrospective validation should no longer be required for most recently implemented systems unless the scope of use has changed.	
Paragraph 12	
This paragraph requires further clarification as to the connection to business risk. Additionally it requires clarification as to the extent of the term data management – is it just GCP/GLP data or does it mean all data management?	
Paragraph 13	
The discussion of risk should include criticality of business processes supported by the computerised system as well as risk to product quality (GLP product = study data), patient safety and data integrity. The use of the term “economic (scaled) validation decisions” could be better replaced with “cost effective”.	
Paragraph 14	
Propose this paragraph be modified as follows: “Dual use systems (having both GLP and non-GLP uses and functions) would still require development, validation, operation, and retirement following GLP change control and security process, and should include a clear differentiation of GLP and non-GLP data.”	

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Paragraph 17	
The role of the study director is not usually part of the validation activity and the involvement of quality assurance should be based upon risk.	
Paragraph 18	
The study directors responsibility for data recorded electronically is the same as that for data recorded on paper. This paragraph should be made stronger by including the principles of ALCOA + (see below): ALCOA means: Attributable — who acquired the data or performed an action? Legible — can you read and understand the data entries? Contemporaneous — documented at the time of the activity Original — first recorded observation Accurate — no errors or editing ALCOA + also includes: Complete — all data including any repeat or reanalysis performed Consistent — all elements of the analysis, such as the sequence of events, follow on and are dated or time stamped in expected sequence Enduring — recorded in a permanent, maintainable form for the useful life Available — for review and audit or inspection over the lifetime of the record	

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Paragraph 21	
Consider modifying the text to clarify the minimum requirement: "The person's training and experience should correlate in a plausible way with the complexity of the validation project (minimal training for simple systems / processes; in depth training / experience for complex systems / processes). There should be a basic understanding for all personnel and it should be added to if the system or process is more complex."	
Paragraph 28	
Consideration should be given to expanding the possible suppliers to specifically include data storage and cloud services.	
Paragraph 29	
Add the following to the paragraph: ".....evidence of formal assessment and / or vendor audits should be available at the test facility. The need for, and extent of vendor assessment should be based upon the risk and complexity of the computerised system and the business process supported by the computerised system."	
Paragraph 31	
The term "validation system" could be confusing and it should be defined or the term / wording changed.	
Paragraph 38	
Consider modifying the text as follows: ".....according to the user manual or other suitable documentation"	

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Paragraph 39	
Disagree with the statement "As the qualification of the underlying COTS product has no relevance for the application". It is still relevant and will require an appropriate form of qualification and documentation to support the application.	
Paragraph 40	
This paragraph appears to relate COTS with Infrastructure software as defined by GAMP Category 1. This statement is not strictly true. Application COTS will require validation against user requirements as a minimum and should certainly be approached based upon a formal risk assessment.	
Paragraph 43	
This paragraph needs to include a reference to the complexity and criticality of the business process supported by the computerised system.	
Paragraph 47	
Unsure of the value for the source code being made available to the test facility unless it is being maintained and / or modified by the test facility.	
Paragraph 48	
Not all of the elements in this list are value-added for COTS, for example application programming language of file structure. Knowing the programming language for COTS is not relevant as the user has, or should have, no control over the code. This list needs to be reviewed for its relevance for COTS or for bespoke (custom) systems.	

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Paragraph 49	
The system type determines the nature and scope of the documentation. It is not true to say that SOPs are the main documentation of all systems. This may be OK for COTS but not in the case of configured / custom LIMS. e) Periodic testing of functionality is not necessary. Periodic Review of system operational controls is more appropriate. Retesting is only necessary for systems that are subject to variance e.g. calibrated instruments f) For some COTS equipment, the Vendor would do all routine preventative maintenance and fault repair. In that case they would have their own policies and procedures for performing the work. This could be reflected in SOPs or more appropriately be specified in an SLA. h) In the event of a breakdown there should also be Business continuity procedures	
Paragraph 50	
Although the list of examples is not exhaustive, it should include SOPs governing how and when vendor or third party assessments are required (e.g. Vendor Management)	
Paragraph 53	
In addition to functionality, the inventory should also contain: make, model or version as relevant, Business System Owner and IT Owner (persons or roles who have responsibility or accountability for the system)	
Paragraph 66	
There should be a statement that those functions and / or functionality that are out of scope (i.e. not intended to be used) should be identified and not tested.	

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Paragraph 67	
Not only could the URS be used in this instance but also a functional specification approved by the business	
Section Heading 2.7	
The more widely understood term is “Customised Systems” rather than “Bespoke Systems”	
Paragraph 80	
Conversion of data to a different format should be considered as data migration (e.g. from a proprietary raw data format to PDF). Printouts of electronic records usually do not meet ALCOA requirements (see paragraph 18 above). There are cases where this is the only option, but there should be a risk assessment as the records will not meet all of the requirements for maintaining data integrity. The paragraph indicates that checks to ensure data are not altered; perhaps this should be clarified to state that “statistical spot checks” would be acceptable, based upon risk.	
Paragraph 104	
Consider adding the following: “However, the test facility should have a documented overview of how data are stored, how these requirements are fulfilled and which studies are affected. This information should be part of the system validation documentation set.” Suggest changing the use of the word “migrates” to “transfers” in the final sentence.	
Paragraph 106	
Some commercially available systems might not enable all of the requirements of this paragraph. In such situations it may need to	

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be addressed based upon a risk assessment and may require a hybrid solution.	
Paragraph 110	
Review of the audit trail should be based upon an understanding of the use of the system, the ability to modify the record and the controls preventing malicious alteration of the records. The periodic review of the audit trail should ensure that required records are configured and the audit trail is working. Periodic review of the audit trail content is of limited value and is a time consuming activity. The frequency of audit trail review should be based upon risk to the integrity of the records. Audit trail content should be reviewed as a result of a suspected data integrity issue or as part of in-process record reviews.	
Paragraph 123	
The reference to "test results" in this paragraph suggests the need for testing as part of periodic evaluation. This may be true for instruments but not for other systems such as LIMS. Periodic evaluation may determine the requirement to perform additional regression testing.	
Paragraph 124 & 129	
These two paragraphs should be combined. Creation, change and cancellation of access authorisations should be recorded. Authorisation records need to be periodically reviewed based upon the criticality of the business process supported by the computerised system	
Paragraph 137	
The use of the wording "element of" is confusing. Incident management should be interfaced with, or integrated with change management, configuration management, periodic review and training.	

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Paragraph 141	
The study director will not usually have a role in establishing an adequate electronic signature system.	
Paragraph 146	
Most paper printouts of an electronic record do not contain all of the information (e.g. certain meta data). Based upon a risk assessment it may be the only option, but this has to be done based upon an understanding of the process and the information that will not be captured in the printout.	
Paragraph 152	
This may, for example, include producing hard copy printouts or transferring the data to another system. Most paper printouts of an electronic record do not contain all of the information (e.g. certain meta data). Based upon a risk assessment it may be the only option, but this has to be done based upon an understanding of the process and the information that will not be captured in the printout.	
Table 2: Glossary	
Correct the information regarding GAMP 5, which is a registered trade mark: GAMP® 5 Published in 2008	