PDA
Parenteral Drug Association

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July 18, 2016

Dr. S. Kopp
Medicines Quality Assurance Programme
World Health Organization
1211 Geneva 27, Switzerland
kopps@who.int

Reference: QAS/16.666 Guidelines on Validation

Dear Dr. Kopp,

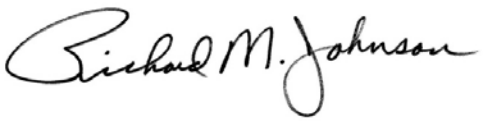
PDA appreciates the opportunity to comment on this draft guideline and commends the WHO for continuing to emphasize harmonization of global requirements. In this draft, PDA notes some terms and acronyms that could be used and defined more consistently with international standards such as : continued process verification(not continuous) and user acceptance testing(UAT).

PDA notes that this guideline does not discuss packaging validation. For clarity PDA recommends this exclusion be clearly stated, especially as this would be different from similar guidelines such as Europe's Annex 15 (2015) and PIC/S guide (2015) which describes validation of packaging in section 7.

PDA is a non-profit international professional association of more than 10,000 individual member scientists having an interest in the fields of pharmaceutical, biological, and device manufacturing and quality. Our comments were prepared by a committee of experts with experience in pharmaceutical and biological manufacturing including members representing the Science Advisory Board, the Regulatory Affairs and Quality Advisory Board, and Board of Directors.

If there are any questions, please do not hesitate to contact me.

Sincerely,



Richard Johnson
President and CEO,PDA

Cc: Denyse Baker, PDA; Richard Levy, PDA

Comments on WHO Working Document QAS/16.666…
Title of the document: Guidelines on Validation

Comments submitted by: Parenteral Drug Association
Telephone number: 301-656-5900,
Address: 4350 E West Highway Suite 600 Bethesda, MD
Email: johnson@pda.org

Date: 12 July 2016

*Kindly complete the table **without modifying the format** of the document - thank you.*

World Health Organization

Template for comments

General comment(s) if any :	**Originator of the comments**

# section	Line no.	Comment / Rationale	Proposed change / suggested text	Classification **L**= low **M**= medium **H**= high	Originator of the comments (for WHO use)
1.2	129-130	Packaging validation is not included, so presumably it is out of scope. Europe's Annex 15 (2015) and PIC/S guide (2015) describe validation of packaging in section 7.	Please clarify if there are intentions of including packaging validation or state clearly that this is out of scope.	H	
1.4	150-151	"Validation often requires… expensive technology..." The expensive technology is due to the manufacturing process or routine testing technology, not necessarily the validation requirement. Most of the time routine or normal personnel and site technical services can perform the validation.	PDA disagrees with the implication that validation has expensive technology needs And suggests the following rewording: Validation **may require** the time of specialized personnel and expensive technology	L	
1.4	154	Various disciplines such as …	Validation is missing as a discipline in the list. Change to (…quality assurance, **validation**, engineering, information technology…	L	
2.1	163	A change was made from the last version, from APIs to starting materials. This may be misinterpreted that the	Change to "This document serves as general guidance only and the principles may be considered useful in its	M	

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		production of API starting materials would require these GMP and validation requirements which is not the case. (See GMP for APIs WHO TRS, 957, 2010, Annex 2.),	application **from the start of** ~~in the~~ manufacture and control of ~~starting materials~~ **active pharmaceutical ingredients (API)** through finished pharmaceutical products (FPPs), as well as other areas."		
3	193	Reference is made to an unpublished draft	PDA recommends this guideline reference only published material and approve versions to ensure ease of access for a general population of readers.	M	
4.1	304	"Qualification and validation are essentially the same." This statement could be a little clearer.	Qualification and validation are essentially the same **and depend on the application (or scope). The term qualification is normally used for equipment and utilities, and validation for systems and processes.**	L	
5.1	317	"… throughout its lifecycle …" could be confusing, since lifecycle is not its own in glossary term. It is used in process validation definition (line 240-243) but not in validation definition (line 269-271).	Change to "throughout **the product** lifecycle…"	L	
5.4	328	Appropriately documented (e.g. in the reports). The use of "e.g. reports" implies that other documentation could exist and reports are not required or needed. Not using or having a validation report is misaligned with FDA Guidance (2011, section PPQ execution and report) and WHO TRS 992 Annex 3, Appendix 7 (2015; last paragraph in Section 5: "fully documented in process validation reports"). Also an e.g. is not aligned with 5.11 in this section.	For clarity expand or remove "e.g." as follows - …**and the results appropriately documented. OR** - **…and the results appropriately documented, i.e. in the reports. …and the results appropriately documented, see section 5.11**.	M	
5.10	349-350	"…for new premises, equipment, utilities and systems, and processes and procedures…" Cleaning and computer systems could be missed so suggest adding parenthetical reference to 1.2 (where they are mentioned). These two types of validation are	Add for new premises, equipment, utilities and systems, and processes and procedures (***Section 1.2)***	L	

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		significant within the industry.			
5.12	363	"worst case …challenge tests should be considered for inclusion in the validation." This is more applicable in qualification than validation. See section 10.9 (OQ) and also validation is typically performed at normal routine conditions (not stressing or challenging the systems)	Change to "…challenge tests should be considered for inclusion in **the qualification** or validation."	M	
7.1		VMP - roles and responsibilities should include organization structure (see also Annex 15, item 1.5) - Lab instruments (IQ/OQ/PQ) is missing but presumed to be under analytical methods validation. Documentation should include record retention	- Roles and responsibilities (including organization structure) - Analytical methods validation (**including lab equipment qualification**) - documentation required in qualification and validation such as SOPs**,** certificates, protocols and reports. **Documentation retention requirements are included**….	M	
9.2	467-471	This appears to state the minimum items ("at least include") in the report. However, it excludes any mention of important items such as: 1) data or summary of data 2) deviation or investigations of OOSs (stated in 9.9) 3) conclusion (stated in 9.6) This 9.2 needs a few items added to be aligned with other international guidances (e.g. FDA PV Guidance 2011)	Add - **data or summary of data** - **deviation or investigations of OOSs, or non-conformances** - **conclusion** (stated in 9.6)	M	
10.1	509, and 550 and 530	V-model has undefined acronyms UAT and PDI. Please define acronyms (user acceptance testing or URS). Where is SAT (lines 530,569) on the diagram?	Define acronyms – add UAT in parenthesis for line 550 and state where SAT is on diagram. Define PDI	H	
10.1	509	Direct impact systems is term used in title of Fig 1 and should be in glossary or referenced	Define "***direct impact systems***" or reference it.	M	
10.22	615	"continuous process verification" should be	Test results should also be collected over a suitable	M	

# section	Line no.	Comment / Rationale	Proposed change / suggested text	Classification L= low M= medium H= high	Originator of the comments (for WHO use)
		"continued" or ongoing process monitoring. Continuous is an alternative approach to process validation (see Annex 15 and PIC/S Guidance). See also WHO Annex 3, Appendix 7 (2015) and US FDA 2011 Guidance. Otherwise add this to definition or change to on-going monitoring	period of time during **continued** process verification, on-going monitoring and/or periodic review…		
10.35	666	Under new approach it states to "See Guidelines on process validation" is not in references or is within one of the references. There is no reference number.	Please clarify where this reference is.	M	
References	734 and 554	These is no reference to WHO Guide on computerized systems stated in line 554	Add reference to WHO item mentioned in line 554e	M	
		Please add rows as necessary (with "copy and paste" empty rows)			