EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

28 MAY 2014 FINAL

Submission of comments on 'EU GMP Guide Annex 15: Qualification and Validation, EudraLex, Volume 4'

Comments from:

Name of organisation or individual
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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)*
	The EGA welcomes the EC proposed revision of the EU GMP Guide Annex 15 aim at updating it in line with the significant changes that have occurred in the manufacturing and regulatory environment.	
	The EGA would like to highlight the importance to foster convergence between regulatory requirements from different jurisdiction. Companies operate manufacturing environments supplying different regions and divergences between jurisdictions create an unnecessarily complex environment for manufacturing operations and compliance.	
	The EGA proposes that the final Annex 15 be the object of a break out session or workshop to ensure early harmonisation of interpretation of the regulatory expectations.	

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)*
Point 1.5c		Comment: The summary of the various systems & status on site, should not be detailed within the VMP, but rather should be specified and maintained within specific project plans, one project plan for each specific area, such as facilities, cleaning validation, process validation, etc. Proposed change (if any): Please remove this item.	
Point 1.5d		Comment: Including protocol & report templates would lengthen the VMP unnecessarily and contradict the introductory statement whereby the VMP would be "brief, concise, clear". Proposed change (if any): Please remove this item.	
Point 1.5g		Comment: Typicaly, acceptance criteria are not handled but set. Proposed change (if any): Please amend this section as suggested above.	
Point 1.5i		Comment: This is typically covered by Good Manufacturing Practices and should not unnecessarily lengthen the VMP. Proposed change (if any): Please remove this item.	

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Point 1.5k		Comment: This is typically covered by Good Manufacturing Practices and should not unnecessarily lengthen the VMP. Proposed change (if any): Please remove this item.	
Point 1.6		Comment: There should only be one VMP for a manufacturing site. We however acknowledge that for significant validation projects, a specific, separate, validation project plan could be appropriate. Proposed change (if any): Please amend this section as suggested above.	
Point 3.3		Comment: DQ should not be necessary for off the shelf equipment or standard systems. Proposed change (if any): Please amend wording to reflect this.	
Point 3.4		Comment: It is important that this paragraph covers the below proposed section below. Proposed change (if any): Please add '***With tests performed according to an approved FAT protocol and test results recorded in a report signed by the customer if satisfied that the FAT is a success'***.	
Point 3.9e		Comment: It is proposed that this section further includes text relating to lubricants.	

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		Proposed change (if any): Please add '***Verification of materials of construction and suitability of lubricants used.'***	
Point 3.10a		Comment: We propose the inclusion of additional elements as shown below. Proposed change (if any): Please add ***'such as testing of functionality of the equipment, i.e. start-up and shut-down, parameter control, HMI responsiveness and other features as per the URS/ functional specification/ equipment manual.'***	
Point 3.10		Comment: It is proposed to include an additional point, to cover testing of operation of equipment. Proposed change (if any): Please add ***"c) Tests to confirm correct operation of equipment safety features, alarms, interlocks, etc."***	
Point 4.20		Comment: Editorial change. Proposed change (if any): Please amend the section as follows: *'Validation protocols should include, but* ***should ~~are~~*** *not be limited to the following:'*	
Point 4.20e		Comment: Such detail should be included in the actual PV report, and not within the protocol. Furthermore, point f & g are the same point.	

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		Proposed change (if any):	
Section 4.4 Glossary "Bracketing Approach"		Comment: It is appreciated that based on knowledge a bracketing approach can be applied. We suggest to clarify the number of PV batches required if for the bracketing only the extremes are selected and to give an indication/example for the required number of PV batches if other matrix like approaches are appropriate e.g. in combination of different strengths and different container sizes/filling volumes. Proposed change (if any): Please amend this section to further detail examples of acceptable bracketing approaches.	
Point 6.1		Comment: More focus on qualification of the equipment and in line automated checking devices, needs to be included rather than validating the process. Today's blister packaging lines offer many in line features that afford much more quality assurance than simply validating the process with a certain number of packed batches. Furthermore, determining the critical control points, through a formal risk assessment, within a blister packaging line is essential. Proposed change (if any): Please amend as follows: 6.1 Variation in equipment processing parameters during primary packaging may have a significant impact of the integrity and correct functioning of the pack (e.g. blister strips, sachets and sterile components) therefore primary **&**	

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		secondary packaging **equipment** ~~***processes***~~ should ~~***undergo validation***~~ **be qualified**".	
Point 7.1		Comment: The need to qualify utilities should be restricted to utilities that are in contact with the product or that directly impact the product, such as water, compressed air (some), HVAC, etc. For other utilities that are not product contact, commissioning should suffice. Proposed change (if any): Please amend as suggested: "7.1 The quality of steam, water, air, other inert gases, coolants etc. should be confirmed following installation using the qualification steps described in section 3 ***where necessary (eg, product contactor impact)***".	
Glossary: Cleaning validation		Comment: To include further detail, as shown below: Proposed change (if any): "Cleaning validation is documented evidence that an approved cleaning procedure will remove ~~**all traces of the previous product used in the equipment**~~ **residues to a safe and acceptable level"**	
Glossary: Performance Qualification		Comment: To re-word Proposed change (if any): "The documented verification that **a system or equipment** ~~**the facilities, systems and equipment, as connected**~~	

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		~~**together**~~, can perform effectively and reproducibly, based on the approved process method and product specification"	

Please add more rows if needed.