Vienna, 28 May 2014

Submission of comments on '< **Qualification and Validation (Annex 15 to EU GMP Guidelines)** >'

Comments from:

Austrian Qualified Person Association (aqpa)

About aqpa: The Austrian Qualified Person Association (aqpa) was founded in 2008. Because of the unique responsibilities and tasks of a Qualified Person in Europe they need a forum to represent the Qualified Person in Austria. The aqpa provides Austrian Qualified Persons with a platform allowing them to exchange their experience, discuss the latest regulatory requirements, identify and address troubles and challenges and to support a harmonised European approach with a special focus on the specific Austrian national requirements.
Today the Austrian Qualified Person Association is led by the following representatives from the industry: Georg Göstl (Chairman), QP, Baxter AG; Gabriela Schallmeiner (dep. Chairwoman), QP, Affiris AG (part-time) and Inspection-Ready Consulting; Wolfgang Zauner (Secretary), QP and Head QA, AFFiRiS AG Austria and Markus Thiel (Treasurer) , QP and Managing Director, Roche Austria GmbH.
Website: www.Austria-QP.at

AQPA, the Austrian Qualified Person Association, appreciates the opportunity from the European Commission to comment the Draft Template for the “Annex 15-Qualification and Validation”.

Our comments to the document are listed below:

General: The terms “continuous process verification” and “ongoing process verification” = “continued process verification” are used through-out the document, however, the conceptual difference between these terms remains vague. A clarification is highly recommended.

3.2 …..stage and any ~~GMP~~ quality risks minimized……

Comment: the main emphasis should be on product quality rather than GMP (compliance). It is understood that the specifications should also comply with GMPs.

3.4 Equipment, especially if incorporating novel or complex technology, ~~should~~ may be evaluated at the vendor prior to delivery.

Comment: Factory acceptance testing (FAT) and site acceptance testing (SAT) should not be mandatory for qualification, FAT/SAT are performed to minimize economical risks and have no GMP aspects.

3.14 b) Tests should cover the operating range of the intended process, unless documented evidence from the development phases, which ~~confirm~~ confirms the operational ranges, ~~are~~ is available.

Comment: The original phrasing is unclear and should be changed to the above.

4.4 Process validation for new products should cover all intended marketed strength……

Comment: the current draft seems to exclude possibility to use a bracketing approach for new products, however, this might be a justifiable approach in certain cases (e.g. prior knowledge from similar products, etc).

4.14 …However, the decision to carry out concurrent validation must be justified, documented in the validation protocol or the VMP and approved by authorized personnel.

Comment: documention of concurrent validation in the validation protocol should also be acceptable.

4.20 Validation protocols should include, but are not be limited to the following:

…

e) List of the equipment/facilities to be used (including measuring/

~~f)~~ monitoring/recording equipment) together with the calibration status.

…

Comment: f) is no separate item; formal correction

5.2 It is recognised that ~~validation~~ verification of transportation may be challenging due to the variable factors involved however transportation routes should be clearly defined. For transport across continents seasonal variations should also be considered.

Comment: there seems to be inconsistent usage of the terms qualification, validation and verification; this should be harmonised.

7. ~~VALIDATION~~ QUALIFICATION OF UTILITIES

Comment: See comment to 5.2

7.1 The quality of media that are in contact with the product (steam, water, air, other inert gases, ~~coolants~~ etc.) should be confirmed following installation using the qualification steps described in section 3.

Comment: There is no need to qualify media which have no contact with the product (e.g. coolants).

7.3 ~~A risk assessment should be carried out where there may be direct contact with the product e.g. HVAC systems or indirect contact such as through heat exchangers tomitigate any risks of failure..~~

Comment: 7.3 should be cancelled, as it is not in context with the preceding paragraphs. A risk assessment should be part of the qualification process and is repetitive here.

8.3 *Where microbial testing of surfaces in clean rooms is carried out, validation should be performed on the test method to confirm that sanitising agents do not influence the result.*

Comment: The meaning of this section is not clear: sanitising agents are used for disinfection and will always have an influence on microbial testing of surfaces.

9.5 ~~Limits for the carry over of product residues should be based on a toxicological evaluation to determine the product specific permitted daily exposure (PDE) value.~~ The justification of cleaning limits ~~for the selected PDE value~~ should be documented

in a risk assessment which includes all the supporting references. The removal of any cleaning agents used should also be confirmed.
Acceptance criteria should consider the potential cumulative effect of multiple equipment in the process equipment train.
Comment: PDE is just one example for the determination of potential effects and other available toxicological/pharmacological data should be taken into account. The risk assessment shall serve as an instrument for the determination and justification of acceptance criteria.

9.7 Where campaign manufacture is carried out, the impact on the ease of cleaning between batches should be considered and the maximum length of a campaign (in ~~both~~ time and/or number of batches) should be the basis for cleaning validation exercises.
Comment: Campaigns are not necessarily defined by the time AND number of batches. Additionally, campaign time and number of batches are not always equally important to ensure the cleanability or detectability of product residues.

9.8 Where a worst case product approach is used as a cleaning validation model, the rationale for selection of the worst case product should be justified and the impact of new products to the site assessed. When there is no single worst case product when using multi-purpose equipment, the choice of worst cases should consider a toxicological assessment ~~toxicity and PDE value~~ as well as solubility. Worst case cleaning validation should be performed for each cleaning method used.
Comment: see comment to 9.5.

9.13 Where cleaning validation has shown to be ineffective or is not appropriate for some equipment, dedicated equipment may ~~should~~ be used for each product or other measures have to be taken to achieve cleanliness of the equipment concerned.
Comment: The section is unclear in its necessity for dedicated equipment. Other measures ensuring cleanliness of equipment should be acceptable.