APIC Active Pharmaceutical Ingredients Committee

Volume 4

EU Guideline for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use - Annex 15

Section	Revision Document	Proposed Amendments	Comments
General Comments			
The overall content of the Annex 15 is very good. APIC has some minor comments and several typographical error corrections to recommend (presented in red).			
Specific Comments			
Principle, 2nd sentence	It is a GMP requirement that manufacturer's control the critical aspects of their particular operations through qualification and validation over the life cycle of the product and process.	It is a GMP requirement that manufacturers control the critical aspects of their particular operations through qualification and validation over the life cycle of the product and process.	"Manufacturers" should not be possessive , it should be plural
1.3	Validation personnel should report as defined in the pharmaceutical quality system although this may not necessarily be to a quality management or a quality assurance function, however there should be appropriate oversight over the whole validation lifecycle.	Validation personnel should report as defined in the pharmaceutical quality system although this may not necessarily be to a quality management or a quality assurance function, however there should be appropriate Quality oversight over the whole validation life cycle.	It is recommended that clarification for Quality oversight is expected for the whole validation lifecycle.
1.5 k)	k) Confirmation that the materials used for validation are of the required quality and suppliers are qualified to the appropriate level. .	k) Confirmation that the materials used for validation are of the required quality and suppliers are qualified to the appropriate level.	Extra punctuation removed at end of sentence.
4.4 Page 14; Glossary "Bracketing Approach"	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/examples 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.
4.20 e) & f); and g) through n)	e) List of the equipment/facilities to be used (including measuring/ f) monitoring/recording equipment) together with the calibration status. g) List of analytical methods and method validation, as appropriate. h) Proposed in-process controls with acceptance criteria and the reason(s) which	e) List of the equipment/facilities to be used (including measuring/monitoring/recording equipment) together with the calibration status. f) List of analytical methods and method validation, as appropriate. g) Proposed in-process controls with acceptance criteria and the reason(s) which each in-process control is selected.	Points e) and f) were split in two, but are really one item. Therefore, the formatting of points is off by one and require re-lettering.

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	each in-process control is selected. i) Additional testing to be carried out, with acceptance criteria. j) Sampling plan and the rationale behind it. k) Methods for recording and evaluating results. l) Process for release and certification of batches (if applicable). m) Functions and responsibilities. n) Proposed timetable.	h) Additional testing to be carried out, with acceptance criteria. i) Sampling plan and the rationale behind it. j) Methods for recording and evaluating results. k) Process for release and certification of batches (if applicable). l) Functions and responsibilities. m) Proposed timetable.	
5.1 Verification of transport	Finished medicinal products, investigational medicinal products, bulk product and samples should be transported in accordance with the conditions defined in the Marketing Authorisation, product specification file or by the manufacturer.	Finished medicinal products, investigational medicinal products, bulk product and samples should be transported in accordance with the conditions defined in the Marketing Authorisation, product specification file or **as justified** by the manufacturer.	In Marketing Authorisations, product files and other documents, normally storage conditions are defined, only. These do, however, not necessarily reflect possible transport conditions, e.g. biotech APIs are usually stored between -15°C and -25°C. However, during transport temperatures may go down to -60 °C due to the use of dry ice as cooling media without any harm to the product.