Proposed Regulation/Guidance Document: **EU Guidelines for Good Manufacturing Practice for Medicinal Products for Human and Veterinary Use, Annex 15: Qualification and Validation**

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GENERAL COMMENTS ON THE DOCUMENT
The use of the terminology 'Qualification and Validation' is not consistent throughout. For example Section 1.1 states 'All qualification and validation'....etc etc. For the remainder of section 1, the Qualification term is not used. This could be clarified in a note to ensure there is no ambiguity.
Section 3.4 – 3.7 (FAT/SAT). Current best industry practices for equipment qualification is to utilize the data obtained from FAT and SAT to support qualification activities, with the appropriate controls in place to do so *e.g.* change control. Due to utility constraints at vendor sites, it is typically the SAT functional testing that offers the greatest opportunity to support the qualification effort. This section, particularly the statement in 3.7 'FAT may be supplemented by the execution of a SAT....etc' understates the significance of the SAT in current industry best practices.
9.12 For investigational medicinal products or products which are only manufactured infrequently**, cleaning verification** may be used instead of cleaning validation. . The term cleaning verification vs validation should be defined with some guidance in the glossary.

Specific Comments on the Text

Section Number	Current Text	Proposed Change	Rationale and Comment
General	Data supporting qualification and/or validation studies which were obtained from sources outside of the manufacturers own validation programme	Data supporting qualification and/or validation studies which were obtained from sources outside of the manufacturers own **qualification and/or** validation programme	To be consistent with the distinction between Qualification and Validation
1.1	All qualification and validation activities	All qualification and validation activities should	Consistency with 'Principle' section

Section Number	Current Text	Proposed Change	Rationale and Comment
	should be planned and take the life cycle of equipment, process and product into consideration.	be planned and take the life cycle of **facilities,** equipment, **utilities,** process and product into consideration.	
1.5c	...facilities, system, equipment and processes	As 1.1 above	Consistency with 'Principle' section
1.5 i	An assessment of the resources required.	~~An assessment of the resources required.~~	This requirement is a significant variable for a site depending on the workload that typically changes frequently. The resource loading is typically a day to day management function. For a project VMP, a resource loading is more appropriate.
1.5j	The ongoing validation strategy, including revalidation and / requalification, where applicable.	The ongoing validation strategy**, including the process and controls supporting the use of data from outside of the manufacturers own validation program,** revalidation and / requalification, where applicable.	This approach is now 'Best Practice' in industry, a re-emphasis on the controls around these processes is warranted.
3.3	Design Qualification	The requirements of the user requirements specification should ~~also~~ be verified during the design qualification.	The DQ if performed should only be a verification of that the URS requirements are incorporated into the design. There are other engineering design reviews that are typically performed on systems that incorporate for example HAZOP and the requirements of Good Engineering Practices. The DQ could be incorportated into the overall system Design Review as distinct from it needing to be a separate deliverable.
3.4	Equipment, especially if incorporating novel	Equipment, especially if incorporating novel or	Clarifies scope.

Section Number	Current Text	Proposed Change	Rationale and Comment
	or complex technology, should be evaluated at the vendor prior to delivery.	complex technology, should be evaluated at the vendor site **to confirm compliance with the URS/ functional specification** prior to delivery.	
3.5	Prior to installation, equipment should be confirmed to comply with the URS/ functional specification at the vendor site unless otherwise justified.	~~Prior to installation, equipment should be confirmed to comply with the URS/ functional specification at the vendor site unless otherwise justified.~~	This requirement is not consistent with 3.4 re novelty and complexity. Not all equipment requires FAT as it may be a business decision to support the project schedule not to do FAT.
3.6	Where appropriate and justified, documentation review and some tests could be performed at the FAT stage without the need to repeat on site if it can be shown that the functionality is not affected by the transport and installation.	Where appropriate and justified, documentation review and some tests could be performed at the FAT stage without the need to repeat on site if it can be shown that the functionality is not affected by the transport and installation**. In addition, the controls in place during the acquisition of this data must be described.**	Consistent with 'General' section above.
3.7	FAT may be supplemented by the execution of a SAT following the receipt of equipment at the manufacturing site.		See General comments above
4.7	Normally batches manufactured for process validation should be the same size as the intended commercial scale batches and the use of any other batch sizes should be justified. e.g. for a continuous manufacturing process.	Normally batches manufactured for process validation should be the same size as the intended commercial scale batches and the use of any other batch sizes should be justified. ~~e.g. for a continuous manufacturing process.~~	The example is not consistent and perhaps even contradictory.
4.10	It is expected that production personnel are involved in the manufacture of validation batches to facilitate product understanding when commercial manufacture starts.	It is expected that production personnel are involved in the manufacture of validation batches to facilitate product understanding ~~when commercial manufacture starts.~~	Statement implies that validation batches and commercial batches are mutually exclusive. A validation batch can be a commercial batch.

Section Number	Current Text	Proposed Change	Rationale and Comment
4.11	The suppliers of critical starting and packaging materials should be qualified prior to the manufacture of validation batches; otherwise a justification based on the application of quality risk management principles should be documented.	The suppliers of critical starting and packaging materials should be qualified prior to the manufacture of validation batches; ~~otherwise a justification based on the application of quality risk management principles should be documented.~~	Not an appropriate clause for critical, as distinct from non-critical materials.
4.20 e / f	List of the equipment/facilities to be used (including measuring/ f) monitoring/recording equipment) together with the calibration status.	List of the equipment/facilities to be used (including measuring/ **f)** monitoring/recording equipment) together with the calibration status.	Error in document.
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.	The quality of steam, water, air, other inert gases, ~~coolants~~ etc. should be confirmed following installation using the qualification steps described in section 3.	The addition of coolants will lead to confusion re requirement for qualification as they are not direct product contact.
10.2	Furthermore the possibility of incremental changes should be assessed.	Furthermore the ~~possibility~~ **possible impact** of incremental changes **between qualifications** should be assessed.	Clarification
Glossary		Add definition for Critical Aspects	