Scientific Archivists Group
Promoting excellence in records management

Commission Delegated Act on principles and guidelines on good manufacturing practice for investigational medicinal products and on inspection procedures, pursuant to the first subparagraph of Article 63(1) of Regulation (EU) No 536/2014 can be downloaded here

Line	Text	Comment
53	*"…medicinal products for human sue…"*	Change to: should read *"…medicinal products for human use…"*
70-72	*"The manufacturer shall regularly review his manufacturing methods in the light of scientific and technical progress and the development of the investigational medicinal product."*	There is no definition of what is meant by "*regularly*". The appropriate period between reviews is open to interpretation. There should be a requirement to maintain a record of any reviews, the decisions made, and the actions undertaken to change or not to change manufacturing methods. Add: *"Records shall be maintained of reviews of manufacturing methods, any decisions made to change or not to change the method(s), and any corrective action or preventive action subsequently taken."*
77-79	*"The manufacturer shall establish, implement and maintain an effective pharmaceutical quality system, involving active participation of the management and personnel of the different departments."*	The nature and purpose of the *"effective pharmaceutical quality system"* is not clearly defined and so open to interpretation on what might be appropriate. There should be a requirement to maintain a record of any decisions made and actions arising as a consequence of implementation of the quality system. Add: *"Records shall be maintained of the pharmaceutical quality system, any decisions made, and any actions subsequently taken."*
80-98	Entire section	There is no requirement to provide evidence that personnel are *"competent and appropriately qualified"*

Line	Text	Comment
99-108	Entire section	There is no requirement to provide evidence that facilities and equipment are *"designed, constructed, adapted and maintained"* appropriately or are *"subjected to appropriate qualification and validation".* Add: *"Records shall be maintained to provide evidence that facilities and equipment are designed, constructed, adapted and maintained appropriately and are subjected to appropriate qualification and validation."*
120-124	*"Question 1a: Would a requirement for a product specification file (a reference file containing, or referring to files containing, all the information necessary to draft the detailed written instructions on processing, packaging, quality control testing, batch release and shipping of an investigational medicinal product) be useful to be introduced?"*	Yes.
127-129	*"The manufacturer shall retain batch documentation for at least five years after the completion or formal discontinuation of the last clinical trial in which the batch was used."*	It may be difficult to comply with this requirement as the manufacturer – when different from the clinical trial sponsor – may not be aware of the date of completion or discontinuation of the last clinical trial for which the batch was used. Furthermore, detention periods based upon a currently unknown future trigger date are notoriously difficult to implement. Change to: *"The manufacturer shall retain batch documentation for 15 years after expiry of the batch."*
130-136	*"Question 2: Different options exist for the retention period of batch documentation:* *a) Retention for at least five years after the completion or formal discontinuation of the last clinical trial in which the batch was used, whichever is the longer period.* *b) Retention for at least 25 years after the*	The requirement to retain batch documents for 25 years after the end of the clinical trial seems excessive taking due account of risk factors and common statutes of limitation. Conversely, the existing requirement to retain batch records for only 5 years after batch expiry may be considered too short.

Line	Text	Comment
	end of the clinical trial in line with the retention period of the clinical trial master file. *Please indicate the preferred option with justification.*	We recommend 15 years after batch expiry. As already noted, fixing a retention period based on completion/discontinuation of clinical trials is difficult to implement effectively. Batch expiry trigger date is a more practical solution.
140-141	*"…provided to the competent authorities at their request."*	I believe the standard wording is *"…provided to the competent authorities upon request."*
142-145	*"The electronically stored data shall be protected, by methods such as duplication or back-up and transfer on to another storage system, against loss or damage of data, and audit trails shall be maintained"*	Suggest rewording to *"The electronically stored data shall be protected against loss or damage through the use of appropriate technical checks and (where relevant) preservation techniques, and appropriate audit trails shall be maintained."*
174-176	*"Question 3: Would it be feasible to require that Certificates of Analysis should accompany each shipment of imported investigational medicinal products as a means to ensure that analytical control had been carried out in the third country? Please elaborate your answer to this question."*	This would seem to be an appropriate requirement, ensuring that a CofA is always available on file.
184-188	*"Sufficient samples of each batch of bulk formulated product and of key packaging components used for each finished investigational medicinal product batch shall be retained by the manufacturer for at least two years after completion or formal discontinuation of the last clinical trial in which the batch was used, whichever period is the longer."*	Align the retention of these records with the retention requirement for batch documentation. As noted, using the date of completion or discontinuation of a clinical trial in which the batch was used is a difficult trigger point to implement effectively. A standard 15 year retention following batch expiry is more practical.
189-193	*"Question 4a: Should retention samples also be required to be retained by the manufacturer?* *Question 4b: If only reference samples are required, would a requirement for photos of the investigational medicinal product, the packaging and the labelling to supplement the reference sample be useful? Please justify."*	Yes, retention samples should be required.
194-198	*"…the manufacturer shall retain samples of*	Given that the retention requirement

Line	Text	Comment
	starting materials, other than solvents, gases or water, used in the manufacturing process for at least two years after the release of the product. That period may be shortened if the period of stability of the material, as indicated in the relevant specification, is shorter."	includes shortening of the period of the shelf life is shorter, it seems more appropriate to set the initial retention requirement to be the same as batch documentation i.e. up to 15 years if the shelf life supports this.
231-235	*"The register or equivalent document must be kept … for at least five years after the completion or formal discontinuation of the last trial in which the batch was used. The retention period of the register will follow that of the batch documentation mentioned in section 2.6."*	Align the retention of these records with the retention requirement for batch documentation (see comments above)
288-290	*"The manufacturing process is not expected to be validated to the extent necessary for routine production but shall be validated in its entirety in so far as appropriate, taking into account the stage of product development."*	Add: *"Where carried out, records shall be maintained to provide evidence that the manufacturing process is subjected to appropriate qualification and validation."*
309-311	*"If a product is modified, data should be available…"*	Change to *"If a product is modified, the modification should be documented and data should be available…"*
515-516	*"Inventory records of returned products should be kept."*	No defined retention period