Line 55	Good manufacturing practice for investigational medicinal products is set out in the	Suggest adding abbreviation (GMP)	Good manufacturing practice (GMP) for investigational medicinal products is set out in the
Line 90	‘This cooperation may be described in a technical agreement”	‘This cooperation should be described in a technical agreement as per Eudralex Vol 4, Chapter 7”	(See also line 222) There should be some formal document where the CT sponsor has indicated the expectations/responsibilities relating to manufacture. A QTA
Lines 128-131	N/A	"Deviations from any predefined specifications and instructions shall be investigated and corrective and preventive action (CAPA) measures initiated as appropriate."	Added 'as appropriate', because CAPA may not always be required.
Line 174	Physic-chemical	Physico-chemical	Typographical error
Line 183	Specifications for starting materials, immediate packaging materials, intermediate products, bulk products and finished products, manufacturing formulae and processing and packing instructions should be as comprehensive as possible given the current state of knowledge.	Suggest consistent terminology to primary container	Specifications for starting materials, primary packaging materials, intermediate products, bulk products and finished products, manufacturing formulae and processing and packing instructions should be as comprehensive as possible given the current state of knowledge.

Lines 191-194	Line 191/192 - minor wording change suggested. Line 192/194 - the additional specification of 'management personnel' is excessive.	Line 191/192 "Any changes should be carried out according to a written procedure which should address any implications for product quality ~~such as stability and bioequivalence~~." Line 192/194: "The approval process for instructions and changes thereof shall include appropriate personnel at the manufacturing site."	Line 191/192: Suggest delete 'such as stability and bioequivalence' since this can impose narrower thinking than 'any implications for product quality'. Line 192/194: The key thing is the involvement of appropriate personnel, not that these are 'management'.
Lines 198-206	See comment on Order definition below. In addition, it would be useful to specify how long the order needs to be retained.	"The manufacturer should retain the order for investigational medicinal products for a period of X years following its receipt."	
Lines 231-235	The proposed wording implies that all manufacturing sites should have access to the whole PSF. This is not appropriate where parts of the manufacture are contracted out. The important thing is that manufacturing sites have access to sections of the PSF relevant to the operations they perform.	"The documentation Relevant sections of the product specification file, including changes, shall be accessible at the manufacturing site."	Limits need for manufacturing site access to relevant sections of the PSF.

Lines 268-273	The clinical trial master file is a GCP document, not a GMP document. There should be no need for a manufacturer to be required to retain a clinical trial master file, just the GMP documents (some of which may be subject to copying and supply to the sponsor for them to include in their trial master file).	Either delete this as not being relevant to GMP or, modify the wording of Lines 271-273 as follows: "If the sponsor and the manufacturer are not the same entity, the sponsor should make appropriate arrangements with the manufacturer to provide copies of any documents required for the clinical trial master file."	N/A
Line 272	If the sponsor and the manufacturer are not the same entity, the sponsor has therefore to make appropriate arrangements with the manufacturer to fulfil his requirement to retain the clinical	Suggestion for gender neutral language	If the sponsor and the manufacturer are not the same entity, the sponsor has therefore to make appropriate arrangements with the manufacturer to fulfil the requirement to retain the
Line 273	“the sponsor has therefore to make appropriate arrangements with the manufacturer to fulfil his requirement”	Include requirement that any such arrangement is recorded in the QTA	Align with Chapter 7 expectations for outsourced activities.

Lines 333-340	Although it is not a change, recommend deletion of the sentence "There should be comparability of expiry dating and clinical trial duration", since this could be read as an expectation to only use products with shelf lives longer than intended clinical trial duration, which is unrealistic. Shelf life extension or resupply plans may be valid and necessary in order to progress a trial.	Delete Line 340.	N/A
Lines 346-349	Typographical error: 'Annex IV' should be 'Annex VI'.	Replace 'Annex IV' with 'Annex VI' in Line 349.	N/A
Lines 355 - 357	The re-labelling operation should be performed by appropriately trained staff in accordance with GMP principles and specific and standard operating procedures and should be checked by a second person.	This section does not include the PIC/S Annex 13 requirements for the operation to be performed at an appropriately authorised manufacturing site or at the investigational site under the supervision of the trial site pharmacist. The change appears less prescriptive than PIC/S Annex 13 requirements.	Current wording in clause 33 of PIC/S Annex 13 provides more specificity which facilitates legislative implementation of this requirement, therefore our preference be retained.
Line 361	“and label reconciliation performed with 100 %”	“and full label reconciliation performed and recorded. Any discrepancy observed during reconciliation should be investigated and satisfactorily accounted for before release”	Clarify reconciliation requirements and ensure discrepancies are fully investigated. If the original text is to be retain we suggest rewording to “and 100% label reconciliation performed.”
Line 368	'Place' should be 'placed'.	N/A	Typographical error

Lines 378 - 381	Samples are retained to fulfil two purposes: firstly, to provide a sample for future analytical testing, and secondly, to provide a specimen of the finished product and may be used in the investigation of a product quality defect. Samples may therefore fall into two categories:	Suggestion for clarity	Samples are retained to provide a sample for future analytical testing, to provide a specimen of the finished product and may be used in the investigation of a product quality defect. Samples may fall into two categories:
Line 414	product applies standards of good manufacturing practice at least equivalent to those	Suggest using abbreviation for consistency	product applies standards of GMP at least equivalent to those
Lines 442 - 448	Where investigational medicinal products are imported from a third country and they are subject to agreements concluded between the Union and that country, such as a Mutual Recognition Agreement (MRA), equivalent standards of good manufacturing practice apply provided any such agreement is relevant to the product in question. In the absence of a MRA, the qualified person should determine that equivalent standards of good manufacturing practice apply through knowledge of the quality system employed at the manufacturer.	Suggest using abbreviation for consistency	Where investigational medicinal products are imported from a third country and they are subject to agreements concluded between the Union and that country, such as a Mutual Recognition Agreement (MRA), equivalent standards of GMP apply provided any such agreement is relevant to the product in question. In the absence of a MRA, the qualified person should determine that equivalent standards of GMP apply through knowledge of the quality system employed at the manufacturer.
Line 502	"…to asses any"	" ….to assess any"	Typo
Line 532	General comment: The Glossary of the new document is rather light.	Suggest add terms back in, or at least cross-reference back to Reg. 536/2014, Article 2 for those that	N/A

N/A	There are a number of points on which clarification on interpretation would be beneficial. It is not necessarily the case that wording needs to change, but it would be good to understand from GMP inspectors how they will interpret these. For example, Line 422/423 adds a requirement that "any exception to [retaining a reference sample of sufficient size to perform duplicate analysis] should be justified to, and agreed with, the national competent authority." To whom and how should this justification be sent for agreement? The wording suggests this is a matter for the national competent authority, not something to be included, and thus agreed, as part of the IMPD. It would also be good to further discuss matters relating to shelf life extension labelling and inter-site transfers, since these are very much at the GMP/GCP interface.	N/A	N/A