<November 20th, 2015>

Leem comments on *Detailed Commission guidelines on good manufacturing practice for investigational medicinal products for human use, pursuant to the second subparagraph of Article 63(1) of Regulation (EU) No 536/2014*

1. Comments

Line number(s) of the relevant text	Comment and rationale; proposed changes
Line 151	N° 536/2015 should be replaced by 536/2014
Line 207	To avoid any confusion between Sponsor and Manufacturer when they are different, could you please specify who is supposed to write the Product Specification File
Line 260	Time to keep batch records not specified (However this is one of the questions posed by the *Commission Delegated Act on Principles and guidelines on GMLP for IMP and inspection procedure* document, which might mean that the Commission will, depending of the answers collected, bring in this information.)
Line 266	Could you please confirm the reference to the first subparagraph of article 63 (1)
Line 270	For consistency, please refer to our response to question 2 of the Delegated Act below
Line 349	Reference to Annex IV should be replaced by Annex VI "Labelling of IMP"
Line 373	QC "including comparator" is not specified on the current Annex 13. What is expected by the authority?
Line 375	Could you please confirm the reference to Article 25 of Regulation (EU) N° 536/2014?
Line 487	Current Annex 13 (sections 43 to 47) Shipping. This section is not maintained in the proposed Guideline whereas the term 'Shipping" is defined in its glossary. Where will this Shipping information be available from now on?
Line 532	Why is the term of transportation in the glossary, while there is no dedicated paragraph in the proposed guideline
Attachment 3	Other: Will Table 1, table 2 and attachment 3 of the current GMP annex 13 be maintained or not?

Answers to questions on text ***Commission Delegated Act on on good manufacturing practice for investigational medicinal products for human use, pursuant to the second subparagraph of Article 63(1) of Regulation (EU) No 536/2014***

Line number(s) of the relevant text	Comment and rationale; proposed changes
Lines 120 to 126- Question 1	Q1a : on the requirement for a **product specification file** = a document containing all information to draft detailed written instructions This document should not be a stand-alone reference file. We agree with being referring to files containing all the information… One reason is that updates would be required between clinical phases Q1b: Does PSF files exist for manufacture of all investigational medicinal products in the EU Response: yes This question could be positioned as Q1a and Q1a as Q1b
Lines 130 to 137- Question 2	Q2: on the different options for the retention period of batch documentation Option b) is preferred, since the biosafety risk is already specified in Annex 2. The relevant information is already available in IMPDs, retained for longer periods
Lines 174 to 177- Question 3	Q3: on the feasibility to require Certificate of Analysis should accompany each shipment of imported IMP No, there is no additional value for our pharmaceutical nor quality activities.
Lines 189 to 193- Question 4	Q4a: on the need for the manufacturer to retain retention samples (in addition to samples of each batch of formulated product and of key packaging components) Q4b: if only reference samples are required is there a value for photos of the IMP, packaging and labeling to supplement reference samples? Q4a: yes, except cases where impossible, as rare products (e. g. ATMPs) Q4b: yes in instance of above mentioned cases (e.g. ATMPs)
Lines 219 to 226- Question 5	For industry to provide this information, it would require a full European survey, for which it would be too much of a burden for industry. This information is already available at the national Competent Authorities who each have authorized the clinical trials.