AFI, the Italian Association of Industrial Pharmacists, is a scientific society representing the scientists and the professional people working in the pharmaceutical fields in Italy. AFI welcomes the opportunity to submit the following contributions in response to the public consultation on "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.

The here under reported table is the results of some meetings held by the working group on "Manufacture of Investigational Medicinal Products" on the questions highlighted inside the proposed document.

Milan, 24 November 2015

Alessandro Rigamonti

Prof. Alessandro Rigamonti
President of AFI

°#	Question	Comment
PRODUCT SPECIFICATION FILE		
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	**Specification management is a mandatory requirement of the quality system applied by the pharmaceutical company. According to the**
1b	Do product specification files exist for manufacture of all investigational medicinal products in the EU?	**It is mandatory that the compliance of the batch with the PSF should be assessed prior to releasing the batch. The PSF exists for all IMPs manufactured in EU.**
RETENTION PERIOD OF BATCH DOCUMENTATION		
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 end of the clinical trial in line with the retention period of the clinical trial master file. Please indicate the preferred option with justification.	**It would be useful to specify what is "batch documentation" and the list of documents that should be included in the "batch documentation".** **As far as the question about the retention period, it seems not relevant to store the batch documentation for 25 years in line with the clinical trial master file.** **Storing batch documentation for such a long time even though the clinical trial is already discontinued or complete is unnecessary. So, option a is preferred.** **To support this preferred option, it has to be underline that, nowadays, the manufacture of IMPs is contracted out to external companies that have a GMP approach to the archive.**

CERTIFICATE OF ANALYSIS		
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.	**The CoA may list information that should be undisclosed or it may contain technical information not understandable to non-technical staff. For these reasons, it not necessary to include the CoA in the shipping documentation. Imported products are already subject to local and GMP arrangements.** **In case of an unauthorized investigational medicinal product, it would be feasible to have a Certificate of Analysis accompanying every batch imported.** **In case of an authorized investigational medicinal product, typically a comparator product, not always is feasible to obtain a Certificate of Analysis by the comparator's provider.**
RETENTION SAMPLE		
4	Should retention samples also be required to be retained by the manufacturer?	**Since retention samples ("a sample of a packaged unit from a batch of finished product for each packaging run/trial period") are stored for identification purposes, the manufacturer responsible for the packaging operations should store them.** **The meaning of "manufacturer" in the question needs to be clarified.** **Where the manufacturer is not responsible for the packaging operations, it not necessary for the manufacturer to store retention samples.** **In case the manufacturer is also responsible for the batch certification and final release, it could be defined in the Quality Agreement where the retention samples should be stored.**

	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.	**A requirement for photos of the investigational medicinal product, the packaging and the labelling to supplement the reference sample would be useful, provided that all part of the patient kit are captured in the pictures (i.e all clinical trial labels attached both on the primary and secondary packaging and the final presentation of the kit). In any case there should be a**
CERTIFICATION ACCORDING TO ART 13.3		
5 a	In how many clinical trials authorised under the Clinical Trials Directive[3] has Article 13(3)(c) of that Directive been used? Please provide figures both as actual number of trials and as a percentage of the trials authorised, if available	**There is no experience reported for the application of the art. 13.(3)©.**
5 b	In how many clinical trials authorised under the Clinical Trials Directive, is the comparator product not authorised in an ICH country (EU, US, Japan, Canada and Switzerland)? Please provide figures both as actual number of trials and as a percentage of the trials authorised, if available	**There is no experience documenting the use of comparator products not authorised in an ICH country.**