EIPG Response to Consultation on Annex 13.

The following represents the consolidated response from the Member Associations of the European Industrial Pharmacists Group;

Amended Text	Response
PERSONNEL 3. All personnel involved with investigational medicinal products should be appropriately trained in the requirements specific to these types of product. In cases where the number of staff involved is small, there should be, for each batch, separate people responsible for production and quality control making the final release	This paragraph deals with qualification rather than giving requirement for a specific activity. It would be more appropriate to add a sentence such as: " in cases where the number of staff involves is small, the personnel should be adequately GMP trained both in manufacturing and quality control aspects". We suggest this topic could be more appropriately addressed in a Q&A session of the EMEA WEBSITE .
36. Samples are retained to fulfill two purposes; firstly to provide a sample for analytical testing and secondly to provide a specimen of the finished product. Samples may therefore fall into two categories, Reference samples and Retention samples, see annex 19 for definitions. Reference and retention samples of investigational medicinal product, including blinded product should be kept 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. Consideration should be given to keeping retention samples until the clinical report has been prepared to enable confirmation of product identity in the event of, and as part of an investigation into inconsistent trial results. *Reference samples* of finished product should normally be stored within the EEA or in a third country where appropriate arrangements have been made by the Community with the exporting country to ensure that the manufacturer of the investigational medicinal product applies standards of good manufacturing practice at least equivalent to those laid down by the Community. In exceptional circumstances the reference samples of the finished product may be stored by the manufacturer in another third country, in which case this should be justified, and documented in a technical agreement between the sponsor, importer in the EEA and that third	1. If limited quantities are available, retention samples should be limited for similar packaging. 2. The possibility of using an electronic system to document the final packaging should be stressed. 3. We have debated whether the proposed definitions of "Reference sample" and "Retention sample" should be deleted in the core text of Annex 13. If the proposed definitions are (or ought to be) identical with the definitions stated in Annex 19, a reference to Annex 19 seems to be more appropriate. However, if there are intended differences in the definitions of "Reference sample" and "Retention sample" used in Annex 13 and Annex 19, the definitions should be shown separately in both Annex 13 and Annex 19.

country manufacturer. In the case of *retention samples*, (of both unblinded and blinded product) it is acceptable to store information related to the final packaging as written or electronic records if such records provide sufficient information. In the case of the latter, the system should comply with the requirements of Annex 11.	
44. Investigational medicinal products should remain under the control of the sponsor until after completion of a two-step procedure: certification by the Qualified Person; and release by the sponsor for use in a clinical trial following fulfillment of the requirements of Article 9 (Commencement of a clinical trial) of Directive 2001/20/EC. Both steps should be recorded and retained in the relevant trial files held by or on behalf of the sponsor. The Sponsor should ensure that the details set out in the clinical trial application and considered by the Qualified Person is consistent with what is finally accepted by the Competent Authorities. Suitable arrangements to meet this requirement should be established. In practical terms, this can best be achieved through a change control process for the Product Specification File and defined in a Technical Agreement between the QP and the Sponsor.	Further clarification is required to provide guidance regarding the roles and responsibilities of the QP and legal representatives (e.g. in the content of quality defects) The content of QP declarations and Batch Release Certificates should be defined in the Annex

Concern was expressed that the following possible amendments to Annex 13 had not been included and that they should be noted in the final version

Section & text in Annex 13	Comment
PREMISES AND EQUIPMENT 5. The toxicity, potency and sensitizing potential may not be fully understood for Investigational medicinal products and this reinforces the need to minimize all risks of cross-contamination. The design of equipment and premises, inspection / test methods and acceptance limits to be used after cleaning should reflect the nature of these risks. Consideration should be given to campaign working where appropriate. The choice of cleaning solvent is made.	1. The solubility of the product needs to be considered in decisions about the choice of cleaning method and cleaning solvent. Account should be taken to ensure that all product contact surfaces are cleaned appropriately.

Labelling 28-30	Storage conditions and period of use should be included on the label of the outer packaging only. The period of use is subject to frequent revision. Storage conditions may also change during development. Re-labelling of the immediate containers in a kit requires a re-packaging operation which poses a high risk for potential error. Therefore re-labelling operations should be limited to the outer packaging.
42. Where, permitted in accordance with local regulations, packaging or labeling is carried out at the investigator site by, or under the supervision of a clinical trials pharmacist, or other health care professional as allowed in those regulations, the Qualified Person is not required to certify the activity in question,	1. Clarification is required to establish what type of operations constitute dispensing as opposed to manufacturing carried out at the investigator site, which should not require local QP release. 2. There should be an improvement in the classification of what activities (e.g. reconstitution) fall under GMP and require GMP authorization, and what do not.

Acknowledgement.

The response quoted was prepared from comments provided by the Industrial Pharmacist Associations of;

- Belgium Vereniging der Apothekers van de Pharmaceutische Industrie
  Union des Pharmaciens de l'Industrie Pharmaceutique
- Denmark Pharmadanmark and IndustriFarmaceutForeningen
- Great Britain Industrial Pharmacists Group, Royal Pharmaceutical Society
- Greece Panhellenic Association of Pharmacists
- Italy Associazione Farmaceutici dell'Industria
- Netherlands Nederlandse Industrie Apothekers
- Sweden Sveriges Farmacevtförbund