Response to public consultation on the 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

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General comments

In response to the public consultation seeking stakeholders views on the content of the detailed Commission guideline on good manufacturing practice for investigation products for human use, pursuant to the second paragraph of Article 63(1) of regulation (EU) No. 536/2014, the UK National Pharmacy Clinical Trials Advisory Group (NPCTAG) wishes to express the following views to help the Commission develop its thinking in preparing the required guidelines. NPCTAG welcomes the opportunity to review this draft guideline. In general, the guideline is well-written and reasonably detailed; the NPCTAG is pleased to see that the European Commission has taken a number of steps to provide additional guidance and clarification in a number of areas. However, we would like to make the following specific comments:

Sections	Comments
Batch records retention	Batch records retention for 25 years is likely to present some practical challenges in terms of storage space. Furthermore, it may be difficult to provide assurance on the ability to access and read electronic documentation over such long period of time. While NPCTAG do not object to the retention period of 25 years, we ask the Commission to consider these practical issues.
Labelling	NPCTAG support the revised guidelines on labelling, in particular the requirement for expiry date to be presented on the primary container. Such provision will facilitate IMP dispensing and administration at investigator sites, and NPCTAG believe that this will enhance patient safety. However, NPCTAG believe that the inclusion of the detailed requirements for label information within the Commission Guidelines, rather than a reference to Regulation EU No 536/2014, would provide a more comprehensive guideline.
Shipping	NPCTAG is surprised that the section titled "Shipping" has been completely removed in the consultation document, and strongly disagree with its removal. The two stage release process that is referenced in the current published version of Annex 13 is critical

	for subject safety, as such system provides a safeguard and minimises the possibility of unauthorised dosing at investigator sites before site approvals are in place. To minimise the possibility of uncontrolled IMP distribution, NPCTAG believe that only the sponsor can have full knowledge of approvals status at investigator sites, and should thus be responsible for authorising when an IMP can be released for use once QP certification has been completed. NPCTAG strongly believe that such provision is fundamental to GMP and GCP. That same section in the current published Annex 13 also includes that "The Sponsor should ensure that the details set out in the clinical trial application and considered by the Qualified Person are consistent with what is finally accepted by the Competent Authorities. Suitable arrangements to meet this requirement should be established." Again, NPCTAG believe that such provision should be retained in order to safeguard the safety of the subject and the reliability and robustness of clinical data generated in the clinical trial. The arrangement needed to ensure that the Qualified Person is certifying the IMP against the latest regulatory approval and any conditions specified within it can only be achieved with commitment from the sponsor to provide the relevant information together with a robust feedback mechanism between manufacturer and sponsor. NPCTAG consider GMP guidelines concerning IMP distribution to be important and should be retained.
Others	NPCTAG noted that limited reference to sponsor responsibilities has been included in the consultation document. NPCTAG do however believe that reference to the sponsor is appropriate and should be retained, as there is no other obvious guideline for the relevant tasks of the sponsor to be described in relation to IMP responsibilities. As a manufacturer or a number of manufacturers may be contracted by the sponsor to perform various IMP related activities, NPCTAG believe there should be emphasis on sponsor's responsibility on GMP oversight as it is a fundamental requirement of GMP to define responsibilities of all parties in a written agreement.
Others	The exemption to the holding of an authorisation to manufacture and import of investigational medicinal product as stated in Article 61(5)(c) of Regulation (EU) No. 536/2014 has been extended to include **"**the preparation of medicinal products referred to in points (1) and (2) of Article 3 of Directive 2001/83/EC for use as investigational medicinal products, where this process is carried out in hospitals, health centres or clinics legally authorised in the Member State concerned to carry out such process and if the investigational medicinal products are intended to be used exclusively in hospitals, health centres or clinics taking part in the same clinical trial in the same Member State". Our interpretation is that this is a new provision and is not included in Directive 2001/20/EC. While we welcome the widening of the exemption, the introduction of such provision without specific GMP guidance addressing such provision has already led to differences in interpretation. The introduction of magistral formula, in particular, as investigational medicinal product is concerning given the inherent risks associated with these products, and thus its impact on the robustness of the clinical trial data. NPCTAG regard such provision as a significant change and believe that more detailed GMP guidance is warranted.