RE: Public consultation on Draft Revision 3 of 'Detailed guidance for the request for authorisation of a clinical trial on a medicinal product for human use to the competent authorities, notification of substantial amendments and declaration of the end of the trial'

COMMENTS SUBMITTED ON BEHALF OF THE UKCRC REGISTERED CLINICAL TRIALS UNITS

Amends

- **Typographical errors:**
  - Page 1 – "draft revision"
  - Page 17 – second bullet point – "in case the clinical trials referred to has been performed..." suggest "where a clinical trial referred to has been performed.."
  - Page 18 – 2.8.3 - "Possibility to refer to the" is repeated in section heading.

- **Suggested misplaced text**
  - Page 24 – 3.3.3 – the final paragraph at the end of section 3.3.2 relates to the IMPD – section 3.3.3 would appear to be a more relevant place for this paragraph.

Clarity

- **Queries relating to deletions:**
  - Page 14 – 2.6 – the list of 'information and data required to support the quality of the IMP' has been removed. This was considered a useful checklist to identify documents to accompany CTA applications. What is the reason for its deletion and does this reflect a change in the requirements? If so, we suggest this is stated when the revised guidance is released. (In particular it is noted that there is now no reference in the guidance to the inclusion of example labels with a submission).
  - Page 32 – the table which explained information required by the different member state's competent authorities (previously 'attachment 1') was a useful reference tool. We would encourage the re-insertion of an updated version of the table, or the provision of a link to a dynamic web-based document.

- **Suggested additional information/clarification:**
  - Page 13 – 2.6 – clearer guidance on which SmPC should be used where several are available and where individual sites may use one of several generic versions of a drug.
  - Page 18 – 2.8.3 – this section allows for the use of SmPCs alone for studies where dosing regimens are not covered in SmPC but the same form and indications are involved. Should this particular scenario be detailed in Table 1? Could the submission of an SmPC only also be extended to scenarios where the drug use is outside the licensed indication for other reasons, but can be justified (e.g. in common usage)? These scenarios could then also be added to Table 1.
  - Page 19 – 2.8.3.2 & 2.8.3.3 – these sections are unchanged but we feel it is worth noting that some confusion exists as to the exact scenarios under which a trial is considered to be a CTIMP or non-CTIMP and the example trial scenarios given in these sections do not provide sufficient clarity. Further elaboration on the scenarios would be of great assistance.
  - Page 20 – 2.9 – NIMPs – it would be helpful if the guidance stated where details of NIMPs should be listed for the competent authority when making an application. The current application form does not specifically request or provide space for this information.
  - Page 23 – 3.3.1 – The lists of examples of substantial/non-substantial amendments is very useful. However the last bullet point is not clear – does this refer to an extension of the intended trial duration? If so, is there is a limit beyond which extension would be considered substantial? If so, what is the limit?
  - Page 25 – 3.4 – the inclusion of a list summarising what information is relevant to whom in which member states (i.e. competent authority, ethics committee, or both) would be a useful addition.

- Page 31 – 4.3 – it is noted that the reference to a trial summary report being required 'within one year of the end of the trial' has been removed. However, since there is no explicit requirement under the EUCTD for submission of a clinical trial report we suggest this section could be further amended to provide detail on the content and detail expected in the clinical trial report. Whilst ICH E6 and E3 refer to the details to be included in clinical trial reports, it is widely recognised that the detailed reports required from manufacturers are less appropriate for non-commercial reports and that less detailed reports or a peer reviewed publication might be more appropriate in the non-commercial setting. It would be very helpful to have this stated in the guidance.
- The document contains several references to 'ICH countries'. A definition of this term and/or countries included would be a useful addition.

- **General queries**
  - Page 26 – 3.5 (c) and (d) – a description and justification of amendments are now required as separate documents. Will the amendment notification form be amended accordingly so that these items are no longer required within the form to avoid duplication?

- **Comments on formatting:**
  - Increased use of bulleted lists in general makes the document easier to read and follow. Further editing along these lines would further enhance clarity.