Response on behalf of the UKCRC Registered Clinical Trials Units Network of, United Kingdom

To the proposals for the content of the summary of the results of clinical trials (Annex IIIa)

The UKCRC Network of Registered Clinical Trials Units supports the international campaign to improve the transparency and unbiased reporting all clinical trials and is a signatory to the ALL TRIALS Campaign http://www.alltrials.net/.

We consider that the issue of transparency in the reporting of unbiased results of all clinical studies, including those outside the scope of this Regulation, is a complicated issue which requires significant further discussion amongst all interested parties, specifically in relation to the practicalities of storing, standardising, the timing and governance of access to data for future research ('data sharing') and suggest a number of key steps are necessary to meet these aims:

- Prospective registration of all clinical studies in a public registry (a requirement of ICMJE Editors since 2005; proposal in the new EU Clinical Trial Regulation)
- Oversight of trial conduct, analyses and reporting by independent committees, including sign off of the final report or publication to confirm compliance with the protocol and Statistical Analysis Plan (or a statement to clarify where there is no sign-off).
- Publication of a Summary Report of the primary outcomes (in line with international standards for reporting unbiased clinical trial results (CONSORT http://www.consort-statement.org/)) produced within 1 year of the trial ending with legitimate postponement if the scientific paper has been submitted and not yet published (unless there is clear undertaking from journal editors that the Summary Report will not interfere with the ability to publish the main paper) (proposal in the new EU Clinical Trial Regulation).
- A commitment always to publish the full trial results e.g. via a peer reviewed journal with a move towards open access publication. Where it is not possible to publish in a peer reviewed journal a forum for publishing results will need to be agreed.
- A commitment to sharing of the trial data-set upon reasonable request to a suitably constituted committee agreed by the trial team. There are differing views and current practices within the Network on the timing, approval and governance of sharing the trial data set.

We caution, however, against trying to use the new Clinical Trials Regulation as the means to this end. Accordingly we agree that it is not appropriate to adopt the ICH GCP E3 Clinical Study Report as the standard of reporting. Instead, we support the proposal to provide a structured and standardised Summary of Results; we note the following in relation to this proposal:

- The international standard for the unbiased reporting of randomised trials is widely recognised, particularly within the non-commercial setting, as CONSORT. In order to reduce the burden of producing the same information in two different formats for trialists who are already working to these standards it would seem advisable to take these into account when determining the precise content and format of the Summary Report for all clinical trials.

- We refer to the EMEA feedback recently given by the MRC in relation to the usability testing of the new EudraCT reporting system 'TECHNICAL GUIDANCE ON THE FORMAT OF THE DATA FIELDS OF RESULT-RELATED INFORMATION ON CLINICAL TRIALS SUBMITTED IN ACCORDANCE WITH ARTICLE 57(2) OF REGULATION (EC) NO 726/2004 AND ARTICLE 41(2) OF REGULATION (EC) NO 1901/2006'. The feedback from the MRC recommends consideration of CONSORT and also expresses concern in regard to the usability of a system which requires data entry of individual data items rather than permitting uploading of summary tables.

- Section 2: Subject disposition (with sufficient detail to allow for replication).

  We suggest using the term 'to validate reproducibility of the trial results' and assume that the intention in this Summary Report is not to enable replication of the primary analyses by the Regulator (or indeed any other person if the Report is made publically available) as is possible with the ICH GCP E3 Clinical Study Report.

- Timing of submission; we advise that the Summary Report should be submitted within 1 year after the End of Trial or in the circumstances that the primary analysis occurs earlier followed by a long period of follow up (for e.g. survival) that the Summary Report is submitted within 1 year after publishing the primary analysis. If the decision is made that the submission be within 1 year after conducting the primary analysis then legitimate postponement be permitted if the scientific paper has been submitted and not yet published (unless there is clear undertaking from journal editors that the Summary Report will not interfere with the ability to publish the main paper).

- We do not support submission of the full Statistical Analysis Plan at the time of authorisation; this document will not be available at the time of CT dossier submission and is typically amended / developed during the trial. We suggest instead that *'A description of the statistical methods to be employed, including the timing of any planned interim analysis(ses)'* as per ICH GCP section 6.9 is more appropriate.

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