CTAG4 – PRE-MEETING CORRESPONDENCE

After viewing the preliminary agenda, attendees were invited to submit comments prior to the meeting to identify omissions and establish a basis for discussion.

Promoting good analysis practice

Scope of the advice
Raw data from primary research studies may be available to a wide audience with an interest in using them for secondary research or for exploratory analyses. A question arises concerning whether it is desirable or feasible to place restrictions on such research with a view to ensuring its quality.

We might consider:

1. A number of 'quality assurance' checklists exist aimed at specific areas of analysis – meta-analysis, diagnostic studies etc . Can we recommend any of these instruments as generally appropriate or as helpful guidelines, departure from which requires justification and documentation?
    - An initial step towards this discussion would be to compile and review the relevant guidelines
    - If we think a number of guidelines apply, can we simply provide a list or do we need to synthesise them into a single document?
2. Two ubiquitous problems with retrospective analyses are: (i) lack of clarity concerning whether hypotheses were formulated prior to inspection of the data and (ii) whether results are presented for all analyses or for a subset which were considered relevant with hindsight. Once data have been made available it is difficult to verify the production of full analysis protocols prior to data inspection but general guidance can be given regarding good procedures - for instance: ensuring the early production of a formally signed off protocol and an audit trial for any subsequent amendments; splitting data, where possible, into development and validation datasets; use of appropriate statistical corrections when multiple analyses have been carried out.
    - Is there a satisfactory existing guidance on dealing with these problems in retrospective analyses?
    - If not, can a guideline be agreed on high-level principles?
3. Possibly the most important aspect in quality assurance of retrospective analyses is ensuring complete and unambiguous reporting of all procedures. Ideally any analysis report should contain enough information to allow another competent analyst to reproduce the results. Aids to such reporting include references to literature explaining the techniques, statements regarding which analytical software was ùsed, publication of code used in analysis and any prior data transformations or exclusion of data. Interim results`and full analysis datasets – when these differ from the initial data made available – are also very useful in maintaining transparency. It is also

worth considering whether, when the analysis conflicts with a previous one, a summary of differences should be presented.

- The question arising is whether – irrespective of the analysis methods actually used – it is worth stating principles for reporting of analyses that will facilitate later evaluation of the results.

Annex I - Comments from participants below may or may not have been made on behalf of the organisation they are affiliated with.

Comment form

Line Number	Comment and Changes proposed	Name	Affiliation
N/A	Comment: I regard it as essential that analyses of data released under the transparency initiative should be expected to follow guidelines to ensure good practice. The purpose of releasing data is to promote good science and, ideally, debate leading to consensus about the merits of medical interventions, and this can only be achieved if the new analyses performed under this initiative meet appropriate standards. I offer some suggestions below on possible requirements 1. All analyses must be described in a detailed protocol which should be reviewed prior to release of data. 2. A draft protocol (before finalisation) should be sent to the original providers of the data and sufficient time (e.g. 30 days?) allowed for them to comment on the protocol. These comments do not have to be incorporated in the protocol. 3. The results of all analyses undertaken should be made public - if not published in the literature, they should be made available on a website. 4. Any analyses performed in addition to those specified in the analysis protocol should be clearly identified in all reports. 5. Format and layout of analysis reports should confirm to guidelines appropriate to the	Les Huson	Centre for Pharmacology and Therapeutics, Division of Experimental Medicine, Imperial College, London

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	data being analysed. The CONSORT statement in its various forms should provide the basis for this reporting format. This will encourage consistency in the way results are reported which will facilitate their wider use. 6. All program code used in analyses should be made available for scrutiny. 7. Multiplicity is a likely to be a key issue in exploratory analyses of data released under this initiative – analysts must diligently record and report the number of statistical significance test that they undertake and if any reported p-values are not adjusted to compensate for multiplicity this needs to be fully justified. 8. Reporting of p-values alone is not acceptable and all reported analyses should include appropriate point and interval estimates of relevant effects. 9. Use of Bayesian methodology should be encouraged in order to promote the combination of information in the released data with other external information which might inform prior probabilities. 10. Any external information utilised by analysts (i.e. data additional to that provided under the transparency initiative) must also be made publicly available e.g. if analysts compare released data with their own data this data must be made available at the time the results are reported. Proposed change (if any): For consideration at meeting.		
N/A	Comment received; awaiting permission to publish	Gisela Schott	Arzneimittelkommission der deutschen Ärzteschaft, Berlin