

# ADVISORY COMMITTEE ON BORDERLINE SUBSTANCES

## APPENDIX 4

### CLINICAL TRIAL INFORMATION TO BE PROVIDED FOR TYPE 1 (NEW PRODUCTS) NUTRITIONAL APPLICATIONS

**Note: These studies must conform with the principles of good clinical practice. All legal declarations must be completed.**

#### References:

**EC Directive 2001 / 20 / EC  
Guidance for Industry**

**E6 Good Clinical Practice: Consolidated Guidance  
US Department of Health and Human Services: Food and Drug Administration  
April 1996**

Trials should, preferably be carried out within the UK with patients in the targeted age and clinical condition for the proposed indication. If this is not possible there must be a statement to confirm that the study methodology complies with the standards described in the references shown above.

Applicants are advised that further information may be sought if a company wishes to clarify particular points contained in this Appendix. No face to face meetings / telephone conversations will be held with Applicants. Correspondence must be conducted via e-mail, through the Secretariat. This is to ensure transparency and a clear audit trail.

In addition, the ACBS will expect to see the following as a minimum requirement for a product to be considered.

- 1.** Evidence for the efficacy of a nutritional product must be based on human and not animal studies, and must clearly demonstrate the clinical efficacy and safety of the product in question. Ideally such trials should be carried out in the community. However, it is recognised that in some cases this may not be possible. In these situations, trials may be carried out within the hospital setting but the results must be translatable into the community and a rationale be given about the transfer ability to community practice. Trials should, preferably, be carried out within the UK.
- 2.** Two copies of the trial protocol must be attached to the product application for the ACBS's information. The application must state both the intention of the trial and the outcome. Outcome variables within the trial must be relevant to the product and its indications. Whenever possible, the trial product must be

compared with a standard formulation in a controlled trial protocol. There must be an explicit statement about ethical considerations and approval.

Data and other information must be presented in a similar format as would be submitted for a peer reviewed journal. Appropriate references must be given and original (not raw) data generated by the trial must be appended. Statistical analysis must be conducted and details about how this has been conducted should be included.

3. The endpoints must be practical, appropriate, meaningful and not extrapolated. Primary and secondary endpoints must be outlined and the trial must include relevant observations e.g. appropriate anthropometric / biochemical measurements of the patients involved. The trial must meet accepted statistical requirements and, with a statistical analysis and discussion, demonstrate the efficacy and safety of the new product.

For products intended for rarer disease states e.g. the management of inherited metabolic disorders where a randomised controlled trial is not feasible and patient numbers will be low, a cross-over study, case study or an n=1 clinical trial design should be considered instead using published methodologies.

4. There should be a specific statement that the trial meets GCP requirements including an explicit statement of consent of participants. This should be included within the trial protocol.

The trial reports should provide, as a minimum:

- (a) The sex, age and, usually, ethnic origin of each patient
- (b) The number of days during the trial on which each patient received the product and the control product
- (c) Whether the product was given as a sole source of nutrition or as a supplement and, if the latter, the other products or food(s) concerned
- (d) Measurements of each patient's weight (in kilograms), and, for infants and children, length / height (cm) and head circumference (cm) in the under 2's. Relevant anthropometric and biochemical measurements such as weight, mid-upper arm circumference, haemoglobin, renal function, and serum electrolytes should be given both at the beginning and at the end of the trial period. All laboratory electrolyte and mineral results must be provided in SI units.

**Note:** This is not an exhaustive list: results should reflect the objectives of the trial

- (e) Whether or not the patients were oedematous and to include the degree of oedema and the timescale involved

- (f) The acceptability of the feed - for further information, see Appendix 5
- (g) Any additional laboratory investigations which are relevant to the use of the product
- (h) An indication of any growth and / or development (if relevant) in any children studied
- (i) An indication of functional improvements in the patients investigated
- (j) Information about the g protein per kilogram of body weight and k/cal per kilogram of body weight provided by both the proposed new product together with the control product and a statement of the electrolyte constituents in the new product related to current recommendations. Information will also be needed about the total nutritional intake from all sources

**Note:** This requirement will apply whether or not the new product is used as the sole source of nutrition

**GENERAL NOTE:** The data generated by any trial should properly reflect the objectives of the trial and this list is not exhaustive. The ACBS cannot be responsible for the design of any trial or any component thereof.