APPENDIX 5

ACCEPTABILITY STUDIES FOR A NUTRITIONAL PRODUCT

Note: These studies must conform with the principles of good clinical practice.

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

Patient acceptability is fundamental to the successful use of any product. It is important that all relevant aspects of acceptability are included in an application and that all flavours of a product are assessed for acceptability.

The objective of such studies will be to confirm that a product for which consideration has been requested has been found to be acceptable to patients for whom the product is intended, i.e. in accordance with the ACBS clinical indication(s).

Thus studies undertaken in healthy volunteers will be of no value. Similarly sensory panels composed of healthy people will not meet this requirement.

Acceptability studies will not, normally, be required for either gluten free or low protein foods.

In the case of infant feeds, the ACBS does not require palatability studies. Studies of gastrointestinal tolerance and compliance are required. Other aspects of acceptability such as changes in stool consistency may be required depending on the indication.

There is no requirement for these studies to be carried out in the NHS. What is important is the methodology used and the patient group rather than the physical location. However, cultural differences in acceptability should be considered.

All acceptability studies must be for at least 1 week and **at least 15 patients** must complete the study – Please note there are exceptions to this general rule below. A PRISMA/CONSORT type diagram should be included, which references the number of patients approached, the numbers recruited and what happened, particularly to those who did not complete the study.

Where nutritional products are intended for use in very rare conditions, such as inherited metabolic disorders, fewer patients may be acceptable. For acceptability studies regarding products indicated for inherited metabolic disorders, please read the information starting at page 4 below. For other rare conditions, advice on patient numbers should be sought from the ACBS secretariat.

ASPECTS OF PATIENT ACCEPTABILITY INCLUDE:

1. GASTRO-INTESTINAL TOLERANCE

G-I tolerance studies must normally be carried out on at least 15 patients in the intended target group for a period of 1 week.

1.1 Information must be provided about the timing, duration, cause and seriousness / severity of any adverse effects

1.2 The following must be monitored and reported as a minimum:

1.2.1 Diarrhoea and / or constipation

1.2.2 Bloating and / or distension

1.2.3 Nausea and / or vomiting

1.2.4 Burping / flatulence / regurgitation

1.2.5 Abdominal discomfort / pain

An easy to follow table must be included and, where appropriate, scales should be used. Quantitative data should be presented where appropriate. It is not the remit of the ACBS to interpret data.

2. PALATABILITY

2.1 A formal procedure of assessment must be followed and the results of this must be available to the ACBS.

2.2 Taste studies must normally be carried out on at least 15 patients in the intended target group (patients) for a period of 1 week

Palatability applies primarily to products intended for oral consumption although there may be cases when they are helpful in assessing the acceptability of tube feed products.

Sensory evaluation panels normally comprise healthy individuals. However, this is not appropriate when developing products for specific patient groups. These **must** be carried out within the UK and also take due account of cultural differences. Such panels **must** comprise patients for whom the product is intended.

Taste panels **must** be composed of patients for whom the product being tested is intended. These **must** be carried out within the UK and also take due account of cultural differences.

General statements of support from healthcare professionals will not be considered.

3. COMPLIANCE

It is very important that data be provided about actual vs. prescribed intakes

Compliance studies must normally be carried out on at least 15 patients in the intended target group for a period of 1 week

Examples of compliance could include:

3.1 How many containers / portions / feeds / volume was the patient prescribed each day?

3.2 How many containers / portions / feeds / volume were taken?

3.3 What was the size / volume of each container / portion of feed?

3.4 How was the product presented i.e. room temperature / heated / chilled / slushed / frozen?

3.5 Was anything added to the product to make it more acceptable?

3.6 Were any reasons for non-compliance identified?

3.7 Viscosity data

This list is indicative but not exhaustive.

Guidance on acceptability studies for inherited metabolic disorders

1. All rules mentioned above in this document apply unless an alternative rule is specified below.

Type 2 applications for products or product ranges seeking listing on Part XV of the Drug Tariff

2. Table 1 specifies, by metabolic condition, the minimum number of patients that must complete the acceptability study for the study to be considered by the ACBS.

3. Where a product range is developed for the management of more than one condition, for example PKU and MSUD, the minimum number of patients for each condition specified in table 1 must be included and complete the acceptability study.

4. Acceptability data can be gathered for a product range indicated for a number of different metabolic diseases under a single research protocol. The protocol can be used to make a single ACBS submission for the product range.

5. Adults and children should be included in studies, when applicable.

6. At least 3 out of 5 patients for each condition must tolerate and find the product being tested acceptable in order for the study to be considered by ACBS.

7. For products intended for infants with metabolic conditions, it may not be reasonable to collect acceptability data in all rare disorders. Instead data from infants with PKU may be considered acceptable to test the tolerance of specialised infant formulas. In this case, the manufacturer must provide justification to the ACBS for consideration that acceptability data in the rare disorder(s) is not feasible to obtain, and to provide data from infants with PKU that can be extrapolated to the other relevant inherited metabolic conditions of amino acid and protein metabolism.

For type 3 applications or when seeking to change a product already approved for listing on Part XV of the Drug Tariff

8. When a new ingredient is added or an ingredient changed in a product or product range previously approved by the ACBS, it is important that any change is justified by the company.

9. Any change in product composition, that will affect the mouthfeel, taste or texture of the product, will require a palatability study.

10. Where a palatability study is required for a type 3 application, the minimum

number of patients that must complete the study for it to be considered by the ACBS is specified, by metabolic condition, in Table 1.

11. Where a product range approved by the ACBS has previously undergone acceptability testing, applications for new flavour additions to the product range do not require acceptability or palatability data.

12. The applicant is required to complete the declaration in the application form confirming that when a new flavour of a product or an amended formulation that impacts flavour is submitted as a Type 3 application following has been undertaken:

- Consulted both adult and paediatric IMD dietitians (when applicable) and patients from relevant age groups (adult/paediatric) about the current flavour range and any future flavours that are developed. Evidence of such consultations will be made available for the ACBS committee to review on request.

- Ensure that patients have had the opportunity to taste the range of flavours and have agreed their palatability. Evidence of taste testing will be made available for the ACBS committee to review on request.

Table 1 - Patient numbers required for Type 2 applications for patients with IMD

Condition	Prevalence	Min. number of patients
Phenylketonuria	1 in 10,000 to 1 in 12,000	10
Maple Syrup Urine Disease	1 in 150,000	5
Homocystinuria	1 in 65,000	5
Tyrosinaemia Type 1	1 in 100,000	5
Glutaric Aciduria Type 1	1 in 100,000	5
Propionic Aciduria	1 in 100,000	5 (dietary management similar for both conditions)
Methyl malonic aciduria	1 in 60,000	
Isovaleric acidaemia	1 in 50,000 to 1 in 150,000	5
Pyridoxine responsive epilepsy	1 in 100,000	5
Alkaptonuria	1 in 100,000 – 1 in 250,000	5
Urea Cycle Disorders	1 in 35,000	5
Hyperlysinaemia	Extremely rare	Case studies
Histidinaemia	Extremely rare	Case studies
Fatty acid oxidation disorders	1 in 40,000 – 1 in 120,000 (long chain) MCADD: 1 in 10,000	5 LCFAOD 10 MCADD
Glycogen storage disease	1 in 100,000	5: for generic products that are suitable for more than one type of GSD condition.5: for a product that is aimed at one type of GSD only e.g., GSD Type III
Galactosaemia	1 in 45,000	5