HSE PRIMARY CARE

REIMBURSEMENT SERVICE

REIMBURSEMENT LIST OF

CLINICAL NUTRITIONAL PRODUCTS

GUIDELINES FOR MANUFACTURERS/DISTRIBUTORS

October 2017 Version 2.0

INDEX

1.0 INTRODUCTION

1.1 These Guidelines have been prepared by the HSE for the information of Manufacturers /Distributors of Clinical Nutritional Products. The list of Clinical Nutritional Products reimbursable under the GMS and Community Drug Schemes will be maintained in compliance with the Health (Pricing and Supply of Medical Goods) Act 2013.

1.2 Applicants should note that the interchangeability or substitution clause in the Act is intended for those medicinal products deemed interchangeable by the Health Products Regulatory Authority (HPRA) and it is not intended to be applied to Clinical Nutritional Products.

1.3 There are three types of Application Forms for products:

TYPE 1

New formulations which the applicant perceives to have well characterised and substantiated advantages in terms of nutritional composition and patient tolerance / acceptability.

NOTE: These applications will require a full submission. Please refer to the Information Notes (Section 4)

TYPE 2

Formulations which are broadly similar in composition to existing products already on the market and which could be considered to be suitable alternatives.

NOTE: Full clinical trials will not be required. However, a full copy of two key reference papers must be provided as supporting evidence. In addition, appropriate acceptability information must be provided in line with the requirements outlined in Section 6.

TYPE 3

Existing products to which minor changes are proposed

1.4 It will be a matter for the professional judgement of the HSE to determine whether the evidence/supporting documentation/samples provided with the application meet the criteria and level of performance specified in these Guidelines and are suitable for the intended clinical use.

1.5 Products must be cost effective. It will be a matter for the HSE to determine whether a product application is cost effective. The HSE reserves the right to request a mini Health Technology Assessment (HTA) on any product application received. Applicants will be required to submit additional supporting documentation if requested to do so by the HSE in order to evaluate the cost effectiveness of a product. Examples of this additional documentation may include reports of reducing wastage; comparisons with similar products; value for money analysis etc.

1.6 Applicants should note that samples of products and/or packaging for Type 1 and Type 2 applications **will** be requested by the HSE following initial review of the application.

1.7 Applicants should note that samples of products and/or packaging for Type 3 applications **may** be requested by the HSE following initial review of the application.

1.8 Categorisation of Nutritional Products submitted for Health Service Executive Reimbursement Approval

NOTE: All the following categories can include formulations intended for both adult and paediatric use.

Category 1 Non disease specific enteral tube feeds

Category 2 Non disease specific oral nutritional supplements

Category 3 Nutritional products for specific clinical conditions

Category 4 Nutritional products designed for the specific management of inherited metabolic disorders

Category 5 Low Protein Foods

Category 6 Nutritional products designed to enhance the safety and / or acceptability of foods or feeds which are prescribable in any of the above categories

NOTE: While a degree of choice of all the above items may be important to facilitate compliance, it is not intended that an infinite variety of broadly similar products should be available on prescription. Other factors being equal, price will, in the normal course of events, be an important determinant for inclusion on the Reimbursable List.

The above Categories contain a number of Sub Categories which are outlined in Appendix D

The Category and Sub Category of products listed may be reviewed by the HSE in line with emerging clinical practice.

1.9 The HSE operates a strict no price increase policy in relation to contract and reimbursement prices for goods and services. The reimbursement prices will remain in place unless otherwise agreed between the HSE and the Applicant.

1.10 The HSE intends to review the reimbursement pricing in line with each Application Process. The review will be based on the published pricing rules and will seek to ensure that the reimbursement prices continue to underpin the availability of quality products and services for eligible patients while delivering affordability and value for money for the Irish State. Applicants will be informed of the outcome of each pricing review and may submit additional data to the HSE at the time of the review in order to provide supplementary evidence in relation to their pricing arrangements.

1.11 Applicants are advised that clarifications in relation to particular points contained in these instructions may be requested. No face to face meetings/telephone conversations will be held with Applicants. Correspondence must be conducted via e-mail, through

NonDrugReimbursement.Applications@hse.ie . This is to ensure transparency and a clear audit trail.

1.12 Application forms must be submitted to the following:
NonDrugReimbursement.Applications@hse.ie

1.13 Application Fees will be applied in line with Health (Reimbursement List) (Application Fees) Regulations 2016. The HSE will notify the Supplier when their application is in order and will then request that the Supplier pay the relevant application fee by EFT. The Supplier must submit a copy of the receipt (demonstrating that the relevant fee has been paid in respect of their application) to NonDrugReimbursement.Applications@hse.ie within 10 working days of the notification. The relevant fee must be paid to the HSE before the application will be considered by the National Expert Group.

Once the required documentation (including confirmation that the relevant prescribed fee(s) have been paid) is confirmed, the HSE will request the Supplier to submit samples and packaging of the proposed new Products.

The text of the proposed labelling / artwork should be final (though it may be presented in mock-up form if the finally produced version is not available). However, an item will not be added to the Reimbursement List until the HSE has received final copies of the Product labelling/artwork

1.14 Approval for any product to be reimbursed will be valid for a maximum of 5 years. In the case of all reimbursable products, the HSE reserves the right to request an Applicant to conduct a new trial at any time if additional research produces information which may challenge its clinical efficacy. In exceptional circumstances e.g. information/instruction from the Department of Health or the Food Safety Authority of Ireland (FSAI), the HSE reserves the right to delete any product from the Reimbursement List of Clinical Nutritional Products with immediate effect.

1.15 Representations:

Where an Applicant is not satisfied with the decision of the National Expert Group on a product application e.g. rejection of a product or the proposed reimbursement price, they may submit a representation to the HSE with relevant additional information. The National Expert Group will assess the additional information provided with the representation at the next scheduled review meeting to determine whether the decision should be changed.

1.16 The HSE Expert Group would like to acknowledge that these guidelines were adapted from the guidance written by the Advisory Committee on borderline substances.

2.0 GENERAL CRITERIA FOR ALL CLINICAL NUTRITIONAL PRODUCTS

The following General Criteria applies to all Type 1, Type 2 and Type 3 Clinical Nutritional Products submitted for inclusion on the HSE Reimbursement List. This list is not exhaustive and merely describes some of the key legislative instruments. Food businesses/ distributors are responsible for ensuring that their products comply with all the relevant food legislation. The competent Irish authority is the Food Safety Authority of Ireland (FSAI). Further information can be accessed at www.fsai.ie

2.1 Submissions must include evidence that the products have been notified to the FSAI and to date no concerns have been raised regarding the placing of the product on the Irish market.

2.2 The Food Safety Authority of Ireland (FSAI) is a statutory body charged with the regulation and enforcement of food law in Ireland. The principal function of the FSAI is to take all reasonable steps to ensure that food produced, distributed or marketed in the State meets the highest standards of food safety and hygiene reasonably available. Furthermore, the FSAI aims to ensure that food complies with legal requirements, or where appropriate, with recognised codes of good practice.

2.3 All food products (including Foods for Specific Groups and Foods for Special Medical Purposes) must be compliant with all relevant aspects of food law. This includes legal requirements specific to the product in addition to the legal requirements applicable to all foodstuffs. Regulation 178/2002/EC establishes the common basis for food law in Europe. It sets out very general legislative requirements for food and states that:

- the primary responsibility for ensuring compliance with food law rests with the food business operator (the manufacturer or distributor in Ireland)
- food must not be placed on the market if it is unsafe (i.e. injurious to health or unfit for human consumption)
- labelling and advertising of foods must not mislead the consumer

In addition to general food law, many foodstuffs have specific legal rules applicable to them with which they must comply. Specific rules for food products covered by the reimbursement scheme are outlined below[1]*:

2.4 Directive 2009/39/EC** on foodstuffs intended for particular nutritional uses (transposed into national legislation by S.I. No. 579 of 2006 (as amended)) was repealed on the 20th July 2016 by Regulation (EU) No 609/2013 on Food intended for Infants and Young Children, Food for Special Medical Purposes, and Total Diet Replacement for Weight Control (commonly referred to as Foods for Specific Groups)

2.5 Food which falls under the scope of this new Regulation but which complies with Directive 2009/39/EC and which is placed on the market or labelled before 20 July 2016 may continue to be marketed after that date until stocks of such food are exhausted.

[1] Food legislation is continuously being developed and updated*. For the most accurate and up-to-date reference to and requirements of food legislation, please see the FSAI website at http://www.fsai.ie/legislation/food_legislation.html. The FSAI provide an advice line (1890 336677 or info@fsai.ie) which can be contacted with any query on food legislation). *Reference to legislation is correct as of October 2016

2.6 Regulation 953/2009/EC on substances that may be added for specific nutritional purposes in foods for particular uses.

2.7 Directive 1999/21/EC (as amended) on Foods for Special Medical Purposes (transposed into Irish law by S.I. 187 of 2009). This Directive will be repealed by Regulation (EU) 2016/128 supplementing Regulation (EU) No 609/2013 as regards the specific compositional and information requirements for Foods for Special Medical Purposes which will apply from 22 February 2019, except in respect of Foods for Special Medical Purposes developed to satisfy the nutritional requirements of infants, to which it shall apply from 22 February 2020.

2.8 Directive 2006/141/EC (as amended) on Infant Formulae and Follow-on Formulae (transposed into Irish law by S.I. 852 of 2007 (as amended). This Directive will be repealed by Regulation (EU) 2016/127 supplementing Regulation (EU) No 609/2013 as regards the specific compositional and information requirements for infant formula and follow-on formula and as regards requirements on information relating to infant and young child feeding. Regulation (EU) 2016/127 will apply from 22 February 2020, except in respect of infant formula and follow-on formula manufactured from protein hydrolysates, to which it shall apply from 22 February 2021.

2.9 Regulation (EU) No 1169/2011 on the provision of food information to consumers transposed into Irish legislation via S.I. No. 556 of 2014.

2.10 In addition, these foods must comply with legislation applicable to all foods, for example: General hygiene requirements, nutrition and health claims, novel foods, micro-criteria for foodstuffs, additives legislation etc. (this list is not exhaustive).

2.11 Regulation (EU) No 609/2013 (commonly referred to as Foods for Specific Groups) establishes compositional and information requirements for the following categories of food:

(a) Infant Formula and Follow-on Formula;

(b) Processed Cereal-Based Food and Baby Food;

(c) Food for Special Medical Purposes; (d) Total Diet Replacement for Weight Control

This Regulation establishes an EU list of substances that may be added to one or more of the categories of food referred to above and lays down the rules applicable to the updating of that list.

2.12 Formulation

Ingredients & Nutritional Information:

2.12.1 A complete quantitative formulation must be provided including a full list of ingredients, additives and any EU listed allergens together with confirmation that these comply with all relevant RoI/EU legislation. In addition the unique identifiers must be given where applicable

2.12.2 An information/data sheet about the product must be provided. This must also comply with the requirements of the relevant RoI/EC legislation

2.12.3 If the product is to be reconstituted, diluted or otherwise altered, information will be required in respect of the nutritional composition as fed

2.12.4 A statement must be provided, signed and dated by an appropriately competent and authorised individual describing their status and accepting legal responsibility for the accuracy of all the above declarations on behalf of the Applicant.

2.13 **Nutritional Composition**

The following information must be provided in addition:

2.13.1 Composition, percentage and source of nitrogen, sub-groups of sugars, fibres and sub-groups of fats

2.13.2 Information about any protein hydrolysis including:

- whole protein source
- degree of hydrolysis i.e. chain lengths
- source of enzymes used for hydrolysis
- proportion as free amino acids
- whether there is any trace of enzyme or whole protein remaining in the product

2.13.3 Information about any carbohydrate hydrolysis including:

- carbohydrate source
- source of enzymes used for hydrolysis
- whether there is any trace of enzyme remaining or whole protein in the product

2.13.4 Nutrient composition should be provided in mmols (SI/Système Internationale) units as well as in milligrams, SI being the standard unit of clinical measurement in the RoI. This applies specifically to the electrolyte composition and the expectation is that mmols will eventually be stated on the label to improve patient safety

NOTE: Electrolytes in this context include sodium, potassium, chloride, calcium, phosphate and magnesium

2.13.5 Nutritional composition per 100ml or per 100g and per container must be given.

2.13.6 Potential renal solute load.

2.13.7 Osmolality / Osmolarity

2.13.8 Fatty acids

- the total amounts of poly-unsaturated and saturated fatty acids and the ratio between them
- source and ratio of n-6 : n-3 fatty acids
- amount (g) of long chain polyunsaturated fatty acids where added
- amount (g) of medium chain triglycerides where added

NOTE: If the standard data sheet does not contain the above information, it must be provided separately.

2.14 Manufacturing Process and Quality Control Mechanisms

A full manufacturing statement must be provided with reference to appropriate external certification which is recognised by the Republic of Ireland/EC.
This statement must be signed and dated by an appropriately competent and authorised individual describing their status and accepting legal responsibility for the accuracy of this declaration on behalf of the Applicant.

NOTE: If any part of the manufacturing process takes place outside the EU, companies must confirm that manufacturing and quality standards continue to comply with the relevant Republic of Ireland/EC legislation and that equivalent manufacturing accreditations and testing methodologies are in place.

There must also be an absence of pathogenic bacteria in all liquid products, specifically *E.coli* and Salmonella. While sterility cannot be guaranteed, all powdered products must be free from E Coli and Salmonella.

2.15 Special instructions

2.15.1 All powdered products must include a scoop and instructions for reconstitution either using a specified scoop (which must be included) for measuring loose powder or a given weight of powder in a sachet**. The size and weight of powder contained in the scoop must be stated.** There must also be instructions for safe storage after reconstitution.

NOTE: Foods for Specific Groups (including Foods for Special Medical Purposes) require that instructions are provided for appropriate preparation, use/disposal and storage of the products

2.15.2 Standard recipes/baking instructions must be provided if appropriate.

2.16 Shelf life

2.16.1 Information must be provided about the maximum length of time after which the product must not be used

2.16.2 Directions must also be provided about the product storage conditions if opened, prepared for use and unopened states.

2.17 Terminology

2.17.1 For a product to be considered “nutritionally complete”, it must be able to provide the sole source of nourishment (with safe and appropriate levels of all macro/micronutrients) for each 24 hours for the person for whom it is intended when used in accordance with the Applicant’s instructions. No additions will be necessary to maintain optimal nutritional status.

2.17.2 If an Applicant claims that a product is “nutritionally complete” and can be used as the sole source of nutrition, the following information must appear on the product data sheet:

- The dietary values must be referenced to a recognised international standard e.g. RoI/ UK/EU
- Estimated requirements for energy, protein, electrolytes, vitamins and minerals for an adult male must be stated as a comparator
- The volume within which the product meets these requirements and is therefore promoted as being nutritionally complete (rounded up or down to the nearest 50 ml) must be stated

The following additional statements will be viewed by the HSE as helpful:

- These amounts may need to be modified according to the age and clinical condition of the patient.
- Assessment by a dietitian is always recommended when there is any doubt about an individual patient's nutritional requirements

2.17.3 Ingredient listings must use the common name and, where relevant, the unique identifiers for each substance. These are the regulated international non-proprietary names (INN) and the Chemical Abstracts Service (CAS) registry numbers if available. This means that the full chemical name and not just the trade name must be given.

2.18 Administration to the Patient

2.18.1 Where appropriate the dosage, timing and/or frequency of administration for adults, infants and children must be given

2.18.2 Methods and routes of administration must be described i.e. whether for oral consumption and/or to be administered via a tube

2.18.3 Any requirements for reconstitution of the product before administration to the patient must be stated.

NOTE: This information should be provided on the packaging, data sheet and any technical healthcare professional/patient literature.

2.19 Contraindications & Precautions

Details of warnings, contraindications, side effects, potential interactions with medicines (both general and, if known, specific), adverse reactions and guidance on clinical monitoring must be given.

NOTE: This information must be provided on both the data sheet and any technical healthcare professional/patient literature.

Appropriate guidance should be given if the product is not suitable for use by particular ethnic groups and must be provided on both the data sheet and any other relevant technical healthcare professional/patient literature. This information should also appear on the label if possible.

Specific guidance must be provided, if relevant, about the following:

- use during pregnancy/lactation
- use for infants and children
- any potential for overdosing

2.20 Presentation

The following will be required:

2.20.1 Description of the appearance and form of the product e.g. solid, powder, liquid, pasta, bread, biscuit etc.

2.20.2 Whether it will be sold in a bag, bottle, tin, tub etc.

2.20.3 Net weight/volume of each unit as set out above
2.20.4 Secondary/cluster package size and weight/number of units
2.20.5 Whether any additional giving or measuring devices are included. The size/volume and weight of product per device must be stated.

NOTE: All this information can be provided on the data sheet.

2.21 Labelling, Packaging & Samples

NOTE: The following requirements must be submitted with the product samples **when** the HSE requests samples. (See section 1.6 and 1.7)

2.21.1 Samples of each product must be provided to the HSE, **once the Applicant receives a request from the HSE following submission of the electronic application**.

2.21.2 Samples of labels/packaging or proposed labels/packaging for all unit sizes for products to be reimbursed must be provided including labelling for secondary/cluster packaging.

2.21.3 Applicants will be required to provide a sample of "actual size" labels with their samples. Electronic versions will not be acceptable.

2.21.4 Any changes to existing labelling required for the Republic of Ireland market must be submitted to the HSE. A statement must be provided confirming that all labelling complies with Republic of Ireland / EC regulations. This statement must be signed and dated by an appropriately competent and authorised individual describing their status and accepting legal responsibility for the accuracy of this declaration on behalf of the Applicant.

2.22 Descriptive Literature

A statement about how the product will be promoted e.g. whether it will also be promoted as being lactose free, cow's milk protein free, gluten free, soya free etc. must be provided.

Any literature intended for patients must be provided at the time of submission.

NOTE: Medicinal claims (i.e. claims to treat, prevent or cure) are never allowed.

For certain products statements are required to indicate suitability of use (Under European and Irish Food Legislation)

Reference to HSE approval for reimbursement should only be made in technical information specifically designed for the advice of healthcare professionals.

This includes:

- entries in the iMF, BNF and MiMS Ireland
- articles in peer reviewed journals
- the standard company data sheet
- any such information on company websites (which must be password protected)

Any such reference must only be made for the condition for which the product has been approved and not imply that the product has other characteristics which may be beneficial and which the HSE may therefore have also approved by default.

2.23 Promotional Policy

A statement must be provided confirming that the product will be advertised solely to healthcare professionals.

NOTE: Any products approved for reimbursement by the HSE which are placed on the market must comply with current Republic of Ireland/EC food legislation regarding health claims.
Any breach of this provision will result in the product being recommended for de-listing.

2.24 Market Availability

2.24.1 Applicants must state the dispensing unit/pack size

2.24.2 Applicants must state what arrangements are in place to enable approved products to be dispensed by a pharmacist against a prescription. If distribution arrangements are not sufficient to ensure continuity of supply, the product will be recommended for de-listing.

3.0 APPLICATION PROCESS – TYPE 1 (NEW PRODUCTS)

New products which the applicant perceives to have well characterised and substantiated advantages in terms of nutritional composition and patient tolerance / acceptability.

3.1 Applicants should complete the Type 1 Application Form (Appendix A) for each New Product they wish to have included on the PCRS Reimbursement List. A signed copy of the Type 1 Application Form, along with appropriate backup material and Clinical/Acceptability Trials (see Section 4.2) should be sent electronically to the HSE at the email address on the Application Form.

3.2 A single Application Form should be submitted to cover each new product.

A single Application Form should be submitted for each size/volume of a new product.

The HSE will issue an acknowledgement email containing a unique reference number for each new application.

3.3 The HSE will conduct an initial review of the electronic application to ensure that all necessary documentation has been submitted. Once the required documentation is confirmed the HSE will notify the Supplier and will then request that the Supplier pay the relevant application fee by EFT. The Supplier must submit a copy of the receipt (demonstrating that the relevant fee has been paid in respect of their application) to NonDrugReimbursement.Applications@hse.ie within 10 working days of the notification. The relevant fee must be paid to the HSE before the application will be considered by the National Expert Group.

3.4 Once the required documentation is confirmed (including confirmation that the relevant prescribed fee(s) have been paid). The HSE will request the Applicant to submit samples and packaging of the proposed new products

3.5 Product samples should be identical to the final product, though not necessarily from a production run if this is impractical. The text of the proposed labelling/artwork should be final although it may be presented in mock up form if the finally produced version is not available.

3.6 As part of their Application Form, Applicants will be required to identify the appropriate Product Category/Sub Categories from the Product list in Appendix D which best matches their product. This should be based on identifying which Product Category/Sub Categories offers an equivalent nutritional benefit and/or an equivalent level of clinical care for patients.

3.7 In the event that the product requires a new Category/Sub Categories, the Applicant should identify this fact on the application form and submit their reasons for the new Category/Sub Categories in the appropriate section.

3.8 Once all of the required documentation (including confirmation that the relevant prescribed fee(s) have been paid) and product samples/packaging has been received by the HSE, the application will be assessed by the National Expert Group at the next scheduled review meeting.

3.9 The HSE will convene a National Expert Group for the purposes of assessing each product application, including samples and supporting documentation from a clinical and nutritional perspective in the first instance. This will determine whether the evidence provided justifies the product being included on the HSE Reimbursement List.

3.10 For those products which are approved by the National Expert Group, the reimbursement price will be agreed in accordance with the pricing rules in Section 9.0 of this document.

3.11 The HSE will aim to ensure that the reimbursement price of the new product is equivalent or less to that of the products already listed in the appropriate product Category/Sub Categories, having regard to difference in presentation, indications for use etc. Where an Applicant is requesting a price premium for their new product, they are required to outline in their application the factors which they believe justify the premium.

3.12 The National Expert Group shall be authorised to make the final recommendation to the HSE for the inclusion or otherwise of products on the HSE Reimbursement List.

4.0 INSTRUCTIONS FOR CLINICAL TRIALS OF NUTRITIONAL PRODUCTS TYPE 1

4.1 The Clinical Trials must conform to the principles of good clinical practice (Ref: EC Directive 2001 / 20 / EC and Regulation EU No 536/2014 when applicable).

4.2 Evidence in relation to the efficacy of the product must be based on human and not animal studies and must clearly demonstrate the clinical efficacy and safety of the product in question.

4.3 Ideally Clinical 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.

4.4 Clinical Trials should, preferably, be carried out within the Republic of Ireland, UK or EU. In the absence of such Clinical Trial data, the population from which clinical data is derived should be clearly described accompanied by its relevance to the Irish population.

4.5 Details of the Trial protocol must be submitted. The protocol must state both the intention of the trial and the outcome including fallout rates. Outcome variables within the trial must be relevant to the product and its indications.

4.6 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.

4.7 The endpoints must be practical, appropriate and meaningful. Primary and secondary endpoints must be outlined and the trial must include relevant observations e.g. appropriate anthropometric/biochemical measurements of the patients involved.

4.8 The Trial protocol, sample size, and length must meet accepted statistical requirements to demonstrate the efficacy and safety of the new product. All statistical methods should be clearly outlined. Randomised Controlled Trials (RCTs) are the preferred study methodology. Specific Trial requirements in relation to Acceptability (GI Tolerance, Palatability and Compliance are listed in Sections 4.11). For products intended for rarer disease states e.g. the management of inherited metabolic disorders, where a randomised controlled trial is not feasible, and exception may be made at the discretion of the HSE. The Trial data analysis should be gathered by person's independent from the company who intend to market the product.

4.9 The Trial reports should provide, as a minimum:

4.9.1 The sex, age and ethnic origin of each patient

4.9.2 The number of days during the trial on which each patient received the product and the control product

4.9.3 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

4.9.4 Measurements of each patient's weight in kilograms and grams 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.

4.9.5 Whether or not the patients were oedematous and to include the degree of oedema and the timescale involved

4.9.6 The acceptability of the feed (See Section 4.11 Acceptability Trials)

4.9.7 Any additional laboratory investigations which are relevant to the use of the product

4.9.8 An indication of any growth and/or development (if relevant) in any children studied

4.9.9 An indication of functional improvements in the patients investigated

4.9.10 Information about the grams 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

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

4.9.11 The nutritional composition of the proposed product and the control product as appropriate.

4.9.12 Information will also be needed about the total nutritional intake from all sources

4.10 Financial or other interests between trial investigators and the manufacturer of the product should be clearly described.

4.10.1 Where an independent (i.e. not sponsored by manufacturer) trial is cited as support, full details of any linkages, competing interests or conflicts of interest between any of the authors and the product manufacturer (or related companies) must be disclosed.

4.10.2 A suggested form of disclosure would be to use the criteria identified in the International Committee of Medical Journal Editors (ICMJE) Uniform Disclosure Form for potential conflicts of interest. http://www.icmje.org/coi_disclosure.pdf

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

4.11 **Acceptability Studies**

4.11.1 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.

4.11.1.1 Acceptability Studies must conform to the principles of good clinical practice. Ref: EC Directive 2001/ 20/EC and Regulation EU No 536/2014 when applicable.

4.11.1.2 A Trial cannot be judged to be satisfactory unless there has been a minimum number of 15 participants completing the Trial. Exceptions will be made in situations where a condition is deemed to be rare and where a minimum number of 15 participants may not be feasible e.g. Inborn Errors of Metabolism

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Aspects of acceptability include:

4.11.2 Gastro-Intestinal Tolerance

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

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

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

- Diarrhoea and/or constipation
- Bloating and/or distension
- Nausea and/or vomiting
- Burping/flatulence/regurgitation
- Abdominal discomfort/pain

4.11.3 Palatability (applies for products taken orally)

4.11.3.1 A formal procedure of assessment must be followed and the results of this must be made available to the HSE.

4.11.3.2 Taste studies must normally be carried out on at least 15 patients in the intended target group for a period of one week.

NOTE: If this is not possible because a rare disease is being studied, this should be highlighted with the application to confirm product categorisation.

Sensory evaluation panels normally comprise healthy individuals. These can be carried out within Europe but must comply with standards acceptable to the HSE.

Taste panels must be composed of patients for whom the product being tested is intended.

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

4.12 Compliance

NOTE: It is very important that data be provided about actual versus prescribed intakes.

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

Examples of compliance could include:

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

4.12.2 How many containers/portions/feeds/volume were taken and how was this measured?

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

4.12.4 How was the product presented e.g. room temperature/heated/chilled/slushed/frozen etc?

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

4.12.6 Were any reasons for non-compliance identified?

5.0 APPLICATION PROCESS – TYPE 2

5.1 Formulations which are broadly similar in composition to existing products already on the market and which could be considered to be suitable alternatives.

5.2 Applicants should complete the Type 2 Application Form (Appendix B) for each Type 2 Product they wish to have included on the PCRS Reimbursement List. A signed copy of the Type 2 Application Form, along with appropriate backup material and Clinical/Acceptability Studies (see Section 6.5) should be sent electronically to the HSE at the email address on the Application Form.

5.3 A single Application Form should be submitted to cover each new product.

A Single Application Form should be submitted for each size/volume of a new product.

The HSE will issue an acknowledgement email containing a unique reference number for each application.

5.4 The HSE will conduct an initial review of the electronic application to ensure that all necessary documentation has been submitted.

5.5 Application Fees will be applied in line with Health (Reimbursement List) (Application Fees) Regulations 2016. The HSE will notify the Supplier when their application is in order and will then request that the Supplier pay the relevant application fee by EFT. The Supplier must submit a copy of the receipt (demonstrating that the relevant fee has been paid in respect of their application) to NonDrugReimbursement.Applications@hse.ie within 10 working days of the notification. The relevant fee must be paid to the HSE before the application will be considered by the National Expert Group.

5.6 Once the required documentation is confirmed (including confirmation that the relevant prescribed fee(s) have been paid). The HSE will request the Applicant to submit samples and packaging of the proposed new products.

5.7 Product samples should be identical to the final product, though not necessarily from a production run if this is impractical. The text of the proposed labelling/artwork should be final although it may be presented in mock up form if the finally produced version is not available.

5.8 As part of their Application Form, Applicants will be required to identify the appropriate Product Category/Sub Categories from the Product list in Appendix D which best matches their product. This should be based on identifying which Product Category/Sub Categories offers an equivalent nutritional benefit and/or an equivalent level of clinical care for patients.

5.9 In the event that the product requires a new Category/Sub Categories, the Applicant should identify this fact on the application form and submit their reasons for the new Category/Sub Categories in the appropriate section.

5.10 Once all of the required documentation and product samples/packaging has been received by the HSE, the application will be assessed by the National Expert Group at the next scheduled review meeting.

5.11 The HSE will convene a National Expert Group for the purposes of assessing each product application, including samples and supporting documentation from a clinical and nutritional perspective in the first instance. This will determine whether the evidence provided justifies the product being included on the HSE Reimbursement List.

5.12 For those products which are approved by the National Expert Group, the reimbursement price will be agreed in accordance with the pricing rules in Section 9.0 of this document.

5.13 The HSE will aim to ensure that the reimbursement price of the new product is equivalent or less to that of the products already listed in the appropriate product Category/Sub Categories, having regard to difference in presentation, indications for use etc. Where an Applicant is requesting a price premium for their new product, they are required to outline in their application the factors which they believe justify the premium.

5.14 The National Expert Group shall be authorised to make the final recommendation to the HSE

6.0 SPECIFIC INSTRUCTIONS RE CLINICAL INFORMATION FOR TYPE 2 APPLICATIONS

6.1 Full clinical trials will not be required for Type 2 Applications. The following is required:

6.1.1 A full copy of at least two peer reviewed publications, directly relevant to the product submitted, must be provided as supporting evidence.

6.1.2 Appropriate acceptability information must be provided in line with the requirements outlined in Section 6.5

6.2 The Acceptability Studies must conform to the principles of good clinical practice (Ref: EC Directive 2001 / 20 / EC and Regulation EU No 536/2014 when applicable)

6.3 Ideally the Acceptability Studies should be carried out in a community setting. However, it is recognised that in some cases this may not be possible. In these situations, Studies may be carried out within the hospital setting but the results must be translatable in to a community setting.

6.4 Studies should, preferably, be carried out within the Republic of Ireland.
If this is not available, the population from which the submitted data is derived, should be clearly described accompanied by its relevance to the Irish population.

6.5 **Acceptability Studies**

6.5.1 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.

6.5.1.1 Acceptability Studies must conform to the principles of good clinical practice. Ref: EC Directive 2001/ 20/EC and Regulation EU No 536/2014 when applicable

6.5.1.2 A Trial cannot be judged to be satisfactory unless there has been a minimum number of 15 participants completing the Trial. Exceptions will be made in situations where a condition is deemed to be rare and where a minimum number of 15 participants may not be feasible e.g. Inborn Errors of Metabolism.

The following aspects of acceptability must be included

6.5.2 Gastro-Intestinal Tolerance

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

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

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

- Diarrhoea and/or constipation
- Bloating and/or distension
- Nausea and/or vomiting
- Burping/flatulence/regurgitation

- Abdominal discomfort/pain

6.5.3 Palatability (applies for products taken orally)

6.5.3.1 A formal procedure of assessment must be followed and the results of this must be made available to the HSE.

6.5.3.2 Taste studies must normally be carried out on at least 15 patients in the intended target group for a period of one week.

NOTE: If this is not possible because a rare disease is being studied, this should be highlighted with the application to confirm product categorisation.

Sensory evaluation panels normally comprise healthy individuals. These can be carried out within Europe but must comply with standards acceptable to the HSE.

Taste panels must be composed of patients for whom the product being tested is intended

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

6.5.3 Compliance

NOTE: It is very important that data be provided about actual versus prescribed intakes.

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

Examples of compliance could include:

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

6.5.4.2 How many containers/portions/feeds/volume were taken and how was this measured?

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

6.5.4.4 How was the product presented e.g. room temperature/heated/chilled/ slushed/frozen etc?

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

6.5.4.6 Were any reasons for non-compliance identified?

7.0 APPLICATION PROCESS – TYPE 3

7.1 The application process for Type 3 should be followed by Applicants when they wish to notify the HSE of a discontinuation or minor change to an existing product on the list of Clinical Nutritional Products on the HSE Reimbursement List.

7.2 For these notifications, Applicants should complete the Type 3 Application Form (Appendix C) for each existing product and submit same electronically to the HSE at the email address on the Application Form.

NOTE: Type 3 Applications must provide a rationale for the proposed changes and include the relevant data sheet.

7.3 Examples of minor changes to existing products would be:

7.3.1 Changes in the manufacturing process which have an impact on the product composition and/or presentation including addition/removal of flavouring

7.3.2 Changes in pack size, labelling etc.

7.3.3 Pro – rata change in cost

7.3.4 Improvements in patient acceptability

7.3.5 Alterations to the fibre source or minor changes in macronutrients, vitamin, mineral, haematinic and trace element composition content to maintain compliance with Republic of Ireland (RoI)/EC regulations

7.3.6 Changes in manufacturing location for either the product in its entirety or for any component of the products

NOTE: If the change(s) are within the EU then a statement confirming that the source of manufacturing has changed, advising of the new location and confirming that all existing Republic of Ireland/EC legislation continues to apply will be required.

If the change(s) are outside the EU then a statement confirming that manufacturing and quality standards continue to comply with relevant RoI/EC legislation and that equivalent manufacturing accreditations and testing methodologies are in place will be required. Appropriate external certification (recognised by the RoI/EC authorities) must be submitted.

7.4 The HSE will issue an acknowledgement email containing a unique reference number for the application.

7.5 The HSE will conduct an initial review of the electronic Type 3 Application Form to ensure that sufficient information has been provided. The HSE reserves the right to request additional documentation and/or product samples/packaging from the Applicant prior to consideration of the application.

7.6 Application Fees will be applied in line with Health (Reimbursement List) (Application Fees) Regulations 2016. The HSE will notify the Supplier when their application is in order and will then request that the Supplier pay the relevant application fee by EFT. The Supplier must submit a copy of the receipt (demonstrating that the relevant fee has been paid in respect of their application) to NonDrugReimbursement.Applications@hse.ie within 10 working days of the notification. The relevant fee must be paid to the HSE before the application will be considered by the National Expert Group.

7.7 Once all of the required documentation has been received (including confirmation that the relevant prescribed fee(s) have been paid) by the HSE, the application will be assessed by the National Expert Group at the next scheduled review meeting.

7.8 The National Expert Group will assess each application, and determine whether the discontinuation/minor change can be accepted by the HSE.

7.9 Products that are approved for discontinuation from the Reimbursement List shall remain live on the Reimbursement List for a period of 12 months to allow for patient transition to an alternative product if required.

8.0 SPECIFIC INSTRUCTIONS RE CLINICAL INFORMATION FOR TYPE 3 APPLICATIONS

8.1 Type 3 applications will require the following evidence of efficacy

8.1.1 If the proposed change relates to minor macronutrient content modification I.e. nitrogen, fat or carbohydrate (or any component of these), micronutrient content or concentration, the rationale must be provided and this should be based on clinical studies wherever possible.

8.1.2 If the proposed change relates to changes in the corporate strategy, manufacturing process, ingredient availability, presentation, labelling, patient acceptability or cost, the rationale must be provided.

NOTE: If the proposed changes relate to any aspect of acceptability, the guidance in Section 4.11 must be followed.

8.1.3 If compositional changes are in response to either RoI / EC legislation, then this must be referenced.

8.1.4 If the location in which the product or any component of the product is manufactured is changed, then the following will be required:

8.1.4.1 Within the EU – a statement advising of the new location and confirming that the source of manufacturing has changed and advising of the new location but that all existing RoI / EC legislation continues to apply

8.1.4.2 Outside the EU – a statement confirming that manufacturing and quality standards continue to comply with the relevant RoI / EC legislation and that equivalent manufacturing accreditations and testing methodologies are in place will be required. Appropriate external certification (recognised by the RoI / EC authorities) must also be submitted.

9.0 PRICING RULES APPLYING TO ALL CLINICAL NUTRITIONAL PRODUCT APPLICATIONS

9.1 In the first instance, each Type 1 product application will be assessed from a clinical and technical perspective to determine whether the evidence provided justifies the product being included on the Reimbursement List.

9.2 For Type 1 products which are approved and for all Type 2 products, the reimbursement price will be equivalent or less to the reimbursement price for the relevant product Category/Sub Categories, having regard to differences in sizes, weights etc.

9.3 The reimbursement price for each product Category/Sub Categories will be determined on the basis of whichever is the lowest of:

9.3.1 UK adjusted price (at 12 month average exchange rate), or

9.3.2 Average of the lowest three European countries submitted, or

9.3.3 Price proposed to the HSE

for the lowest price agreed for any product included in the relevant Category/Sub Categories, having regard to differences in sizes, presentation etc.

9.4 The UK adjusted price will be based on the average rate of exchange over 12 months up to date of application, having regard to the prices quoted in the following:

9.4.1 Chemist & Druggists (the most current edition available at the time of pricing);

9.4.2 BNF (the most current edition available), if C&D is unavailable;

9.4.3 Submitted UK Price, if C&D and BNF are not available.

9.5 It will be a matter for the Applicant to supply sufficient supporting evidence to justify a premium above the proposed reimbursement price for the product Category/Sub Categories.

9.6 In the event that a product requires a new Category/Sub Categories, the reimbursement price will be determined using the same criteria as outlined above. The HSE shall in all cases have the final say in relation to the inclusion or otherwise of a premium for new/innovative products.

9.7 The new Reimbursement List will be made available to patients, clinicians and suppliers via the PCRS section of the HSE website.

9.8 The HSE reserves the right to offer a reimbursement price which will be benchmarked against the prices(s) available to the HSE, for products that, in the opinion of the HSE Expert Group, offer an equivalent technical solution and/or an equivalent level of clinical care for patients.

10.0 PRODUCTS WHICH WILL NOT BE CONSIDERED FOR REIMBURSEMENT

Note: This should be read in the context of the entire Guidelines document

Introduction

10.1 The HSE is specifically concerned with products which have proven clinical benefit in the management of formally diagnosed disease states and stringent criteria are applied to regulate the reimbursement of such products. Current awareness of nutrition and its importance in maintaining health has led to the introduction of a range of nutritional products about which many claims are made. However, these may not be clinically substantiated/evidence based in a robust way and their introduction to the Republic of Ireland is market driven with much of the available supporting literature deriving from commercial sources.

Background

10.2 Republic of Ireland food legislation is based on regulations and directives agreed within the European Union (EU). The resulting European Commission (EC) documentation makes repeated reference to the need to ensure a high level of protection for consumers and this includes the requirement that any "health claims for foods should only be authorised for use in the Community after a scientific assessment of the highest possible standard" (Regulation (EC) No 1924/2006). This requirement is not met by many so-called nutraceutical products which some companies wish to bring to the market. A list of approved health claims and conditions for their use, rejected health claims, and permitted nutrition claims have been published by the European Commission and are listed in the Community Register (http://ec.europa.eu/nuhclaims/)

10.3 Some products that are not recognised as medicines (EC Directive 2001 / 83 / EC as amended by EC Directive 2004 / 27 / EC) nor as Traditional Herbal Medicines (Directive 2004 / 27 / EC) and which meet the definition of food as in Regulation (EC) No 178 / 2002 must comply with food law.

There is additional EU food legislation covering the following, more specific, aspects:

10.4 Regulation (EU) No 609/2013 commonly referred to as Foods for Specific Groups

Which is supplemented by:

10.4.1 Commission Delegated Regulation (EU) 2016/128 supplementing Regulation (EU) No 609/2013 of the European Parliament and of the Council as regards the specific compositional and information requirements for food for special medical purposes

10.4.2 Commission Delegated Regulation (EU) 2016/127 supplementing Regulation (EU) No 609/2013 of the European Parliament and of the Council as regards the specific compositional and information relating to infant and young child feeding

10.4.3 Regulation (EC) No 133/2008 on food additives

10.4.4 Regulation (EC) No 1925/2006 on the addition of vitamins and minerals and of certain other substances to foods

10.4.5 Directive 2002/46/EC relating to food supplements Food Supplements Directive 2002/46/EC

It should be noted that this is not an exhaustive list.

10.5 Nutraceuticals

Nutraceuticals have been described as “substances which are not traditionally recognised nutrients but which have positive physiological effects on the human body”. They are generally marketed in the context of health promotion/disease prevention rather than disease management and, as such, have greater appeal for the “worried well”.

Because there is no legal definition of the term “nutraceutical products” nor any separate regulations, products are either regulated as foods or medicines. This means that for any such products to be regulated by the legislation applicable to foods there can be no suggestion that the product can treat or prevent disease. A food (or foodstuff) is defined as “any substance or product whether processed, partially processed or unprocessed intended to be, or reasonably expected to be, ingested by humans” (Regulation (EC) No 178 / 2002)

Regulation (EC) No 1924 / 2006 governs nutrition and health claims made in commercial communications, whether in the labelling, presentation or advertising of foods to be delivered as such to the final consumer. This Regulation placed an obligation on the EU Commission to establish nutrient profiles (Article 4) by 19 January 2009. Recently the European Parliament voted against establishing nutrient profiles. The Commission is now undertaking work to re-consider the requirements for nutrient profiles.

Safe levels of vitamins and minerals have already been established in the case of Foods Used for Special Medical Purposes (Directive 1999 / 21 / EC) which will be replaced by Regulation (EU) 2016/128 supplementing Regulation (EU) No 609/2013 as regards the specific compositional and information requirements for food for special medical purposes from 22 February 2019, except in respect of food for special medical purposes developed to satisfy the nutritional requirements of infants, to which it shall apply from 22 February 2020 Regulation (EC) No 1925 / 2006 on the addition of vitamins, minerals and of certain other substances puts in place provision to set safe maximum levels for fortified foods.

The HSE will only consider applications for such products to be reimbursed in the context of specific clinical conditions and diagnosed disease management where there is robust evidence of clinical efficacy and effectiveness. The HSE will expect any such applications to be clearly defined as disease specific formulations (Category 3) supported by evidence as described in Sections 4 & 6 of this Guidance Document.

10.6 Food supplements

Food supplements are defined as “foodstuffs, the purpose of which is to supplement the normal diet and which are concentrated sources of nutrients or other substances with a nutritional or physiological effect, alone or in combination, marketed in dose form namely

forms such as capsules, pastilles, tablets, pills and other similar forms, sachets of powder, ampoules of liquids, drop dispensing bottles and other similar forms of liquids and powders designed to be taken in measured small unit quantities (Directive 2002 / 46 / EC). Some such products are considered for reimbursement by the HSE. However, this is only within the context of a formally diagnosed clinical condition and any such product would be formally prescribed as an integral part of the clinical management of that disease.

10.7 Conclusions

In summary, there does not appear to be a case for the HSE to include consideration of nutraceutical and other similar products.

The following products will not, therefore, be considered by the HSE;

Those foods which are regulated under Foods for Specific Groups which, although designed for particular life stages or to help in the management of particular conditions , are widely available on a commercial basis e.g. standard infant/follow-on formulae, infant foods and weight reducing products. [NOTE: this does not include Foods for Special Medical Purposes which are designed as specialised products for the clinical management of disorders/disease]

Everyday foods which have been manipulated to enhance their disease prevention/disease management properties e.g. spreads made with plant sterols, yoghurts containing probiotics.

Functional foods or so-called “superfoods” which are naturally occurring but which contain higher levels of specific substances associated with improved health e.g. antioxidants, flavonoids.

Everyday foods which, by virtue of the location from which they are sourced, contain higher than normal levels of identified substances which might be considered to have beneficial nutritional properties.

Foods to which additional nutrients/other substances have been added (sometimes in excess of the maximum permitted safe levels) specifically to enhance their health giving properties.

Food/dietary supplements which are normally available over the counter including minerals, vitamins and other similar products.

“Luxury” foods designed to enhance compliance with the long term management of chronic disease. Although useful, they are not fundamental to disease management.

Any product where, in the opinion of the HSE, there is an equivalent licensed medicinal product.

Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

APPENDIX A

TYPE 1 - NEW PRODUCT APPLICATION FORM:

New Nutritional Products to be added to HSE Reimbursement List

A.1 General Information

Applicant Company Name:	
Product Name:	
Product Description:	
Product Pack Size:	
Product Reference Code:	
Product Specification:	
Manufacturer:	
Distributor to HSE Customers:	
Launch Date for Product in Ireland:	
Identify appropriate product Category/Sub Categories (ref: Appendix D):	
If no product Category/Sub Categories is suitable, please provide justification for creation of a new Category/Sub Categories:	
GMS Code of nearest comparator product:	
Proposed method of distribution for making the product available to HSE Pharmacy contractors:	
Previous use of the product in hospital or community areas in Ireland. Provide	

details of location, duration of use and average annual usage:	

A.2 Clinical Trials [2]

Please confirm (tick) that details of Clinical Trial No. 1 have been provided	
Please confirm (tick) that details of Clinical Trial No. 2 have been provided	
Please confirm (tick) that details of the Acceptability Studies have been provided. (See Section 4.11)	
CE Certificate Submitted[3]:	

A.[3] General Criteria for all Nutritional Products

A3.1	**Please confirm that the product has been notified to the FSAI. (Section 2)** **(Evidence of same must be provided and cross referenced to this question)**	
A3.2	**Please confirm that the product complies with all relevant aspects of Food Law. (Section 2)**	
A3.3	**Please confirm that the product complies with the specific rules for food products covered by the Reimbursement Scheme. (Section 2)**	
A3.4	**Please confirm that the product complies with the Legislation applicable to all foods (Section 2)**	
A3.5	**Please confirm that the product complies with Legislation covering /Foods for Specific Groups and Foods for Special Medical Purposes (Section 2)**	
A3.6		

[2] Please refer to Sections 4, 6 & 8 of this document for Guidelines for Clinical Trials of Nutritional Products

[3] An electronic copy of a valid CE certificate for the product must be submitted with the application.

	Please confirm that a complete quantitative formulation has been provided (Section 2.12.1) **(Please provide as an Addendum and cross reference to this question**	
A3.7	**Where applicable, please confirm that the unique identifiers (Ref: Section 2.17, Terminology) have been provided. (Section 2.12.1)** **(Please provide as an Addendum and cross reference to this question)**	

A3.8	**Please confirm that an information / data sheet about the product has been provided.** **(Section 2.12.2)** **(Please provide an Addendum and cross reference to this question)**	
A3.9	**Please confirm that information has been provided in respect of the nutritional composition as fed, if the product is to be reconstituted, diluted or otherwise altered. (Section 2.12.3)** **(If so, Please provide an Addendum and cross reference to this question)**	
A3.10	**Please confirm that a statement signed by an authorised person accepting legal responsibility for the accuracy of the declarations on behalf of the Applicant has been provided.** **(Section 2.12.4)** **(Please provide an Addendum and cross reference to this question))**	
A3.11	**Please confirm that the information in relation to the Nutritional Composition of the product has been provided.** **(Section 2.13)** **(Please note that if the standard data sheet does not contain any of the information required, it must be provided separately as an Addendum and cross referenced to the relevant question)**	
A3.12	**Please confirm that a full manufacturing statement has been provided.** **(Section 2.14)** **(Please provide an Addendum and cross reference to this question)**	
A3.13	**Please confirm that the requirements in relation to Special Instructions have been provided.** **(Section 2.15)** **(Please provide an Addendum and cross reference to this question**	
A3.14	**Please confirm that the requirements in relation to Shelf Life have been provided. (Section 2.16)**	
A3.15	**Please confirm that the requirements in relation to Terminology have been provided. (Section 2.17)** **Please provide an Addendum and cross reference to this question)**	

A3.16	**Please confirm that the requirements in relation to administration of the product to the Patient have been provided. (Section 2.18)** **(Evidence of same must be provided and cross referenced to this question)**	
A3.17	**Please confirm that the requirements in relation to Contraindications and Precautions have been provided.** **(Section 2.19)** **(Evidence of same must be provided and cross referenced to this question)**	
A3.18	**Please confirm that the requirements in relation to presentation of the product have been provided.** **(Section 2.20)** **(Evidence of same must be provided and cross referenced to this question)**	
A3.19	**Please confirm that the requirements in relation to the Labelling, Packaging and Descriptive Literature have been provided. (Section 2.21 – 2.22)** **(Evidence of same must be provided and cross referenced to this question)**	
A3.20	**Please confirm that the requirements in relation to Promotional Policy have been provided.** **(Section 2.23)** **(Evidence of same must be provided and cross referenced to this question)**	
A3.21	**Please state the Dispensing Unit/Pack size of the product. (Section 2.24.1)**	
A3.22	**Please state what arrangements are in place to enable approved products to be dispensed by a pharmacist against a prescription. If distribution arrangements are not sufficient to ensure continuity of supply, the product will be recommended for de-listing.** **(Section 2.24.2)**	

A4. Product Samples

See Sections 2.21, 3.3, 5.4 and 7.5 of this Guidelines document for information of submission of product samples when requested.

A5. Proposed Price

Reimbursement Price Proposed to HSE **Please specify Pack Size, Unit Price and VAT**	€

United Kingdom Equivalent	
Chemist & Druggists (the most current edition available at time of application)	£
BNF (if C&D price is not available) (the most current edition available at time of application)	£

European Pricing			
United Kingdom	£	Country:	€
Country:	€	Country:	€
Country:	€	Country:	€
Country:	€	Country:	€
Country	€	Country	€

Average of the three lowest European Countries			
Country:	Country:	Country:	Average
€	€	€	€

- United Kingdom price should be quoted in Pound Sterling.
- State the European Country and Reimbursement Price in Euro where this product is marketed and reimbursed under the country's Schemes/Insurance System.
- HSE will require independent validation of the European prices submitted which must accompany this form. Where this information is not available, please provide explanatory footnote/s in the table provided below.
- If this product is not available, specify N.A.

Reason for Price Submitted:

Name and Address in Block Capitals of Key Contact for Application:

Name:

Position:

Address:

I confirm that the information provided in this application is correct.

Signature: _____ Date: _____

Telephone No: _____ E-mail: _____

The completed form along with application information should be submitted to:

NonDrugReimbursement.Applications@hse.ie

Feidhmeannacht na Seirbhíse Sláinte
Health Service Executive

APPENDIX B

TYPE 2 - PRODUCT APPLICATION FORM:

New Nutritional Products to be added to HSE Reimbursement List

A.1 General Information

Applicant Company Name:	
Product Name:	
Product Description:	
Product Pack Size:	
Product Reference Code:	
Product Specification:	
Manufacturer:	
Distributor to HSE Customers:	
Launch Date for Product in Ireland:	
Identify appropriate product Category/Sub Categories (ref: Appendix D):	
If no product Category/Sub Categories is suitable, please provide justification for creation of a new Category/Sub Categories:	
GMS Code of nearest comparator product:	
Proposed method of distribution for making the product available to HSE Pharmacy contractors:	
Previous use of the product in hospital or community areas in Ireland. Provide	

details of location, duration of use and average annual usage:	

A.2 Reference Papers [4]

Please confirm (tick) that details of Reference paper No. 1 have been provided (See Section 6.1)	
Please confirm (tick) that details of Reference Paper 2 have been provided (See Section 6.1)	
Please confirm (tick) that details of the Acceptability Studies have been provided. (See Section 6.5)	
CE Certificate Submitted[5]:	

A.3 General Criteria for all Nutritional Products

A3.1	**Please confirm that the product has been notified to the FSAI. (Section 2)** **(Evidence of same must be provided and cross referenced to this question)**	
A3.2	**Please confirm that the product complies with all relevant aspects of Food Law. (Section 2)**	
A3.3	**Please confirm that the product complies with the specific rules for food products covered by the Reimbursement Scheme. (Section 2)**	
A3.4	**Please confirm that the product complies with the Legislation applicable to all foods (Section 2)**	
A3.5	**Please confirm that the product complies with Legislation covering /Foods for Specific Groups and Foods for Special Medical Purposes (Section 2)**	
A3.6		

[4] Please refer to Sections 4 , 6 & 8 of this document for Guidelines for Clinical Trials of Nutritional Products

[5] An electronic copy of a valid CE certificate for the product must be submitted with the application.

	Please confirm that a complete quantitative formulation has been provided (Section 2.12.1) **(Please provide as an Addendum and cross reference to this question)**	
A3.7	**Where applicable, please confirm that the unique identifiers (Ref: Section 2.17, Terminology) have been provided. (Section 2.12.1)** **(Please provide as an Addendum and cross reference to this question)**	
A3.8	**Please confirm that an information / data sheet about the product has been provided.** **(Section 2.12.2)** **(Please provide an Addendum and cross reference to this question)**	
A3.9	**Please confirm that information has been provided in respect of the nutritional composition as fed, if the product is to be reconstituted, diluted or otherwise altered. (Section 2.12.3)** **(If so, Please provide an Addendum and cross reference to this question)**	
A3.10	**Please confirm that a statement signed by an authorised person accepting legal responsibility for the accuracy of the declarations on behalf of the Applicant has been provided.** **(Section 2.12.4)** **(Please provide an Addendum and cross reference to this question)**	
A3.11	**Please confirm that the information in relation to the Nutritional Composition of the product has been provided. (Section 2.13)** **(Please note that if the standard data sheet does not contain any of the information required, it must be provided separately as an Addendum and cross referenced to the relevant question)**	
A3.12	**Please confirm that a full manufacturing statement has been provided. (Section 2.14)** **(Please provide an Addendum and cross reference to this question)**	
A3.13	**Please confirm that the requirements in relation to Special Instructions have been provided.** **(Section 2.15)** **(Please provide an Addendum and cross reference to this question)**	
A3.14	**Please confirm that the requirements in relation to Shelf Life have been provided.** **(Section 2.16)** **(Please provide an Addendum and cross reference to this question)**	

A3.15	**Please confirm that the requirements in relation to Terminology have been provided.** **(Section 2.17)** **(Please provide an Addendum and cross reference to this question)**	
A3.16	**Please confirm that the requirements in relation to administration of the product to the Patient have been provided. (Section 2.18)** **(Evidence of same must be provided and cross referenced to this question)**	
A3.17	**Please confirm that the requirements in relation to Contraindications and Precautions have been provided.** **(Section 2.19)** **(Evidence of same must be provided and cross referenced to this question)**	

A3.18	**Please confirm that the requirements in relation to presentation of the product have been provided.** **(Section 2.20)** **(Evidence of same must be provided and cross referenced to this question)**	
A3.19	**Please confirm that the requirements in relation to the Labelling, Packaging and Descriptive Literature have been provided. (Section 2.21 – 2.22)** **(Evidence of same must be provided and cross referenced to this question)**	
A3.20	**Please confirm that the requirements in relation to Promotional Policy have been provided.** **(Section 2.23)** **(Evidence of same must be provided and cross referenced to this question)**	
A3.21	**Please state the Dispensing Unit/Pack size of the product. (Section 2.24.1)**	
A3.12	**Please state what arrangements are in place to enable approved products to be dispensed by a pharmacist against a prescription. If distribution arrangements are not sufficient to ensure continuity of supply, the product will be recommended for de-listing.** **(Section 2.24.2)**	

A4. Product Samples

See Sections 2.21, 3.3, 5.4 and 7.5 of this Guidelines document for information of submission of product samples when requested.

A5. Proposed Price

Reimbursement Price Proposed to HSE **Please specify Pack Size, Unit Price and VAT**	€

United Kingdom Equivalent	
Chemist & Druggists (the most current edition available at time of application)	£
BNF (if C&D price is not available) (the most current edition available at time of application)	£

European Pricing			
United Kingdom	£	Country:	€
Country:	€	Country:	€
Country:	€	Country:	€
Country:	€	Country:	€
Country	€	Country	€

Average of the three lowest European Countries			
Country:	Country:	Country:	Average
€	€	€	€

- United Kingdom price should be quoted in Pound Sterling.
- State the European Country and Reimbursement Price in Euro where this product is marketed and reimbursed under the country's Schemes/Insurance System.
- HSE will require independent validation of the European prices submitted which must accompany this form. Where this information is not available, please provide explanatory footnote/s in the table provided below.
- If this product is not available, specify N.A.

Reason for Price Submitted:

Name and Address in Block Capitals of Key Contact for Application:

Name:

Position:

Address:

I confirm that the information provided in this application is correct.

Signature: _____ **Date:** _____

Telephone No: _____ **E-mail:** _____

The completed form along with application information should be submitted to:

NonDrugReimbursement.Applications@hse.ie

APPENDIX C

TYPE 3 – MINOR CHANGE

This form has been prepared to enable manufacturers/distributors to inform the HSE of any of the following in relation to existing Clinical Nutritional Products on the HSE List of Reimbursable Items:

a) Intention to Discontinue Clinical Nutritional Products on the HSE Reimbursement List:

b) Minor Changes of Clinical Nutritional Products on the HSE Reimbursement List.

1. Product Details

Applicant Company Name:	
GMS Code:	
Manufacturer:	
Distributor to HSE Customers:	
Product Name:	
Product Description:	
Product Pack Size:	
Product Reference Code:	
Product Category/Sub Categories: (See Appendix D):	

2. Notification

(a) Intention to Discontinue Nutritional Products on the HSE Reimbursement List
Applicants should complete this section if they wish to notify the HSE of their intention to discontinue the listing of a Clinical Nutritional Product on the HSE Reimbursement List.

In the interest of maintaining an uninterrupted supply of Clinical Nutritional Products to patients, it is a requirement that products that are approved for discontinuation from the HSE Reimbursement List shall remain live on the Reimbursement List for a period of at least 12 months to allow for patient transition to an alternative product if required.

Proposed date for product discontinuation:	
Date (month and year) of expiry of last batch	
Date (month and year) when it is estimated that stocks of product will be depleted:	
Where the product discontinuation is of a particular pack size within a range of products provide details of those products that will continue to remain available:	
Give reasons for the proposed product discontinuation of the product (s) with appropriate substantiating information:	
If there is a reimbursed alternative to the product being discontinued please provide details:	
Provide an evaluation of likely impact that the proposed discontinuation will have on the quality of patient care, including an estimate of the number of patients it will affect:	
Provide details of the current status and availability of the product in the various Member States of the European Union:	
A copy of any letter(s) sent or proposed to be sent to Irish Health Care Professionals in relation to the discontinuation of the product (Confirmation that same is enclosed):	

(b) Minor Changes of Clinical Nutritional Products on the HSE Reimbursement List

Applicants should complete this section if they wish to notify the HSE of a proposed Minor Change to a Clinical Nutritional Product on the HSE Reimbursement List.

Note: Examples of Minor Changes to the product are set out in Section 7 of this Guidelines document.

Applicant Company Name:	
GMS Code	
Details of Proposed Minor Change:	
Proposed date for Minor Change:	
Date (month and year) when it is estimated that stocks of currently listed product will be depleted:	
A copy of any letter(s) sent or proposed to be sent to Health Care Professionals in relation to the discontinuation of the product (Confirmation that same is enclosed):	

NOTE: For ALL Minor Change notifications, an electronic copy of the outer packaging artwork, CE certification and patient information leaflet for currently listed product AND proposed minor change product must be submitted with the application.

Name and Address in Block Capitals of Key Contact for Application:

Name:

Position:

Address:

I confirm that the information provided in this application is correct.

Signature: _____ Date: _____

Telephone No: _____ E-mail: _____

E-mail: _____

The completed form along with information should be submitted to:

NonDrugReimbursement.Applications@hse.ie

APPENDIX D

PRODUCT CATEGORY/SUB CATEGORIES

NOTE: All the following categories can include formulations intended for both adult and paediatric use

CATEGORY 1: NON-DISEASE SPECIFIC ENTERAL TUBE FEEDS

1.1 Overall Description: ≥1.0 kcal / ml and <20% P:E (Protein: Energy Ratio)

Flat Rate Sub-Categories

1.1.1 Standard Tube Fee
1.1.2 d
(1.0 kcal / ml and <20% P: E with fibre)
1.1.2 Standard Tube Feed
(1.0 kcal / ml and <20% P: E without fibre)
1.1.3 Standard Formula Paediatric Tube Feed
(1.0 kcal / ml and <5.0g protein / 100ml) with fibre
1.1.4 Standard Tube Formula for Children
(1.0 kcal / ml and <5.0g protein / 100ml) without fibre
1.1.5 Nutrient Enriched Formula for Infants. Suitable from birth to 18 months (Suitable for Enteral or Oral)

1.2 Overall Description: Protein and Energy Rich Products (with/without fibre)

Flat Rate Sub-Categories

1.2.1 Standard Energy, Increased Protein Tube feed
(1.2 kcal/ml/, P: E< 20%) with fibre
1.2.2 Standard Energy Increased Protein Tube Feed
(1.2 kcal/ml/, P: E <20%)) without fibre
1.2.3 Standard Energy Increased Energy Protein Tube feed
(1.0-1.2kcal/ml/>20% P: E) with or without Fibre
1.2.4 High Energy, Standard Protein Tube feed
>1.2kcal/ml <20% P: E) with fibre
1.2.5 High Energy Standard Protein Tube Feed
(>1.2kcal/ml.<20% P: E) without fibre
1.2.6 High Energy, High Protein Tube Feed
(>1.25kcal/ml.<20% P: E) without fibre
1.2.7 Very High Energy, Standard Protein (>1.75kcal/ml.<20%P:E) with/without Fibre
1.2.8 High Energy, Formula Paediatric Tube Feed ;(1.5kcal/ml) with Fibre
1.2.9 High Energy, Formula Paediatric Tube Feed: (1.5kcal/ml) without fibre

1.3 Overall Description: Protein and Energy Reduced Products (with/without fibre)

1.3.1 Reduced Energy Products Adults: < 1.0 kcal/ml and / or ≤ 4.0g protein / 100ml
1.3.2 Reduced Energy Products Paediatric Children :< 1.0 kcal/ml and / or ≤ 2.4g protein / 100ml

CATEGORY 2: NON-DISEASE SPECIFIC ORAL NUTRIONAL SUPPLEMENTS

NOTE: The nutrients provided in these products will not, on their own, meet all the identified daily nutritional needs of the persons for whom they are intended.

2.1 Overall Description: ≥1.0 kcal / ml and <5.0g protein /100ml, with or without fibre

Flat Rate Sub-Categories

2.1.1 Standard Sip Feeds for Children with fibre
2.1.2 Standard Sip Feeds for Children without fibre

2.2 Protein and Energy Rich Products, with or without fibre

- Adults: ≥ 1.5 kcal/ml and / or ≥5.0g protein / 100ml
- Children: >1.0 kcal/ml and / or ≥4.0g protein / 100ml

Flat Rate Sub-Categories

2.2.1 High Energy, Standard Protein Juice Based Sip Feed
2.2.2 High Energy, Standard Protein Powdered Milkshake
2.2.3 High Energy, Standard Protein Sip Feed: (<20% P: E) with Fibre
2.2.4 High Energy, Standard Protein Sip Feed: (<20% P: E) without Fibre
2.2.5 High Protein Sip Feed: (>20% P: E)
2.2.6 Very High Energy, Sip Feed (≥ 2kcals/ml) with/without fibre
2.2.7 Textured Modified High Energy, High Protein Sip Feed
2.2.8 High Energy, Semi Solid
2.2.9 High Energy, Paediatric Sip Feed with Fibre
2.2.10 High Energy, Paediatric Sip Feed without Fibre
2.2.11 Protein Concentrate Powder
2.2.12 Other

2.3 Protein and Energy Reduced Products, with or without fibre

- Adults: < 1.0 kcal/ml and / or ≤4.0g protein / 100ml •

Children: <1.0 kcal/ml and / or ≤2.4.g protein / 100ml

CATEGORY 3: NUTRITIONAL PRODUCTS FOR SPECIFIC CLINICAL CONDITIONS

NOTE: If these products, when used in accordance with the manufacturer's instructions, are claimed to provide the sole source of nutrition (with safe and appropriate levels of all macro / micronutrients for each 24 hours for the persons for whom they are intended, they must comply with the guidance in the Information Notes (Sections 4,6 or 8 as applicable)

3.1 **Diabetes Specific Products**

Products in which there is removal or modification of energy and / or nutrients or where there is supplementation with energy and / or nutrients which are considered to confer significant clinical benefits in the management of disease and specific clinical conditions e.g.
respiratory disease, liver disease, prematurity, glucose / galactose malabsorption

Flat Rate Sub-Categories

3.1.1 Diabetes Specific Sip Feed
3.1.2 Diabetes Specific Tube Feed

3.2 **Cancer Specific (EPA enriched) Products**

Products which have been specifically designed to enhance immune function, to reduce infection rates and, by virtue of specific metabolic effects on metabolism, to improve nutritional statues in disease e.g. pancreatic cancer.

Flat Rate Sub-Categories

3.2.1 Cancer Specific (EPA enriched) Sip Feed
3.2.2 Cancer Specific (EPA enriched) tube Feed

3.3 **Renal Specific Products**

3.3.1 Renal Specific Sip Feed
3.3.1 Renal Specific Tube Feed

3.4 **Milk Substitute**

Products for the clinical management of conditions of proven dietary allergy or intolerance in infants and children e.g. allergy to whole protein and / or disaccharide intolerance

Note: this does not apply to foods in cases of dietary avoidance in adults when alternative dietary sources are available.

3.5 **Other**

CATEGORY 4: NUTRITIONAL PRODUCTS DESIGNED FOR THE SPECIFIC MANAGEMENT OF INHERITED METABOLIC DISORDERS

These products are specifically designed for use in the following indicative conditions and will not, on their own, meet all the identified daily nutritional needs of the persons for whom they are intended.

4.1 **Inherited Metabolic Disorders**

a. Glutaric aciduria (Type 1)
b. Homocystinuria or hypermethioninaemia
c. Hyperlysinaemia
d. Isovaleric acidaemia
e. Maple syrup urine disease
f. Methylmalonic or propionic acidaemia

g. Phenylketonuria
h. Tyrosinaemia
i. Urea cycle disorders (other than arginase deficiency)
j. Fatty Acid Oxidation Disorders
k. Galactosaemia
l. Histidinaemia
m. Other

CATEGORY 5: **LOW PROTEIN FOODS:** For use when a low protein diet is an essential part of the clinical management of an inherited metabolic disorder.

NOTE: The nutrients provided in these products will not, on their own, meet all the identified daily nutritional needs of the persons for whom they are intended.

Flat Rate Sub -Categories

5.1.1	Biscuits
5.1.2	Bread Rolls
5.1.3	Bread
5.1.4	Low Protein Mix
5.1.5	Egg Replacer
5.1.6	Pasta in Sauce
5.1.7	Pasta
5.1.8	Other

CATEGORY 6: NUTRITIONAL PRODUCTS DESIGNED TO ENHANCE THE SAFETY AND / ACCEPTABILITY OF FOODS OR FEEDS WHICH ARE PRESCRIBABLE IN ANY OF THE ABOVE CATEGORIES

NOTE: The nutrients provided in these products will not on their own, meet all the identified daily nutritional needs of the persons for whom they are intended.

6.1 **Thickeners**
For the management of dysphagia, infantile vomiting, nausea and vomiting in pregnancy.

6.2 **Flavourings**
To improve the acceptability of unpalatable formulations.