A REVIEW OF FOODS FOR MEDICAL PURPOSES:
SPECIALLY FORMULATED PRODUCTS FOR
NUTRITIONAL MANAGEMENT OF
MEDICAL CONDITIONS

June 1977

Prepared for

BUREAU OF FOODS
FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
WASHINGTON, D.C. 20201

under

Contract Number FDA 222-75-2000
ADDENDA

The following corrections should be made to the attached report:

p. 39  Phenylketonuria, second column, paragraph should read:
       "protein restricted diet;
       specifically, phenylalanine
       restriction; Lofenalac, (Correct
       ........)"  (Correct spelling)

p. 53  First paragraph, first line, correct the spelling to
       "Lofenalac".

p. 80  Table 9: "Lonalac" (Correct spelling)

p. 84  Table 11:
       Under Product: "Dryco": Delete "Mead Johnson," enter a question mark.
       Under Product: "Enfamil": Delete "Lactose free"

       Under Product: "Lactic Acid Milk," "Lactum," and "Olac" should be noted as no longer available.
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DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
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under

Contract Number FDA 223-75-2090

by

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FEDERATION OF AMERICAN SOCIETIES
FOR EXPERIMENTAL BIOLOGY
9650 Rockville Pike
Bethesda, Maryland 20014
FOREWORD

The Life Sciences Research Office (LSRO), Federation of American Societies for Experimental Biology (FASEB) provides scientific assessments of topics in the biomedical sciences. Reports are based upon comprehensive literature reviews and the scientific opinions of knowledgeable investigators engaged in work in specific areas of biology and medicine.

This technical report was prepared for the Bureau of Foods, Food and Drug Administration (FDA), by the staff of the LSRO, FASEB, in accordance with the provisions of Contract No. 223-75-2090.

The authors acknowledge the contributions of all the consultants who have assisted in this review of the scientific literature and current research and the commercial organizations that have supplied information on their products. The report was reviewed by a number of consultants; however, the listing of the consultants' names in Section X does not imply that they endorse the study. The authors accept responsibility for the contents of the report.

The report was reviewed and approved by the LSRO Advisory Committee (which consists of representatives of each constituent society of FASEB) under authority delegated by the Executive Committee of the Federation Board. Upon completion of these review procedures the report was approved and transmitted to FDA by the Executive Director, FASEB.

While this is a report of the Federation of American Societies for Experimental Biology, it does not necessarily reflect the opinion of each individual member of the FASEB constituent societies.

Kenneth D. Fisher, Ph.D.
Director
Life Sciences Research Office
SUMMARY

In this report, the history, current status, and expected development of special dietary products intended for use under medical supervision are reviewed. Proposed definitions are presented for these products, which have been designated medical foods. The nutritional rationale for use and examples of their utility in the nutrition of patients with medical, surgical, and traumatic conditions are presented along with an inventory of available products. Although there is ample evidence of the clinical superiority of certain medical foods over common foods in the dietary management of a number of specific and nonspecific diseases and disorders, uncertainty prevails about their relative advantages in other clinical conditions. In the United States there are approximately 113 commercially available items that have been identified in this study as medical foods, and it is anticipated that the number and variety will increase as their functional design improves and their therapeutic advantages become more widely recognized. Suggested guidelines on the composition, labeling, and use of medical foods are discussed.
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I. INTRODUCTION

The Bureau of Foods, Food and Drug Administration (FDA) has a continuing interest in the nutritional quality of the American diet. The agency is responsible for evaluating and monitoring the safety of foods, establishing regulations, and providing nutrition information to consumers. In addition, this agency encourages a regulatory climate designed to stimulate development of foods for special dietary use and to offer protection from nutrition fraud and misleading labeling.

In keeping with these responsibilities, FDA requested that the Life Sciences Research Office review the commercial availability of medical foods and the current scientific information and technologic developments related to specially formulated preparations useful in the diagnosis or in dietary management of patients with special or unique nutritional requirements related to specific diseases and disorders. These substances, commonly referred to as medical foods because of their nutritional composition, formulation, and use, are usually administered under direct or indirect medical supervision.

This report is a review of the current status of development and utilization of medical foods as a basis for analysis of any potential need for guidelines on composition, use, and labeling of such products. Clinical applications of medical foods in management of medical, surgical, and traumatic conditions as well as in diagnosis are described. In addition, an inventory of commercial products has been assembled.
II. BACKGROUND

A. HISTORICAL PERSPECTIVE

While special diets and liquid formulations have been a part of therapeutic management of patients for centuries, a major stimulus to development of specific products with high nutritional efficacy was the desire to enhance tissue repair and shorten convalescence during World War II (Kark, 1974). During the decade prior to 1940, several investigators had shown that animals and humans could be maintained in positive nitrogen balance by oral and parenteral administration of high calorie, high protein liquid formulas (Bury et al., 1974; Kark, 1974; Russell, 1975).

Further impetus for development of orally administered complete nutrient diets came from the availability of modified sources of nutrients such as protein hydrolysates, and development of methods for rapid preparation of blended products. The needs of the aerospace program for easily consumable, low residue, high calorie dietary products have resulted in development of special foods that also are useful in the dietary management of patients with certain diseases and disorders. Finally, evolution of modern health care systems has provided mechanisms to support prolonged use of these nutritional products. During the past twenty years there has been a steady increase in the technical development and commercial availability of specially formulated preparations that are useful in the dietary management of patients. Low phenylalanine products (e.g., Lofenalac®) for phenylketonuric patients and products for patients who require liquid diets with minimal residue (e.g., Compleat-B®, Flexical® and Vivonex®) are typical examples.

Several investigators have characterized the important properties of specially formulated complete diets for use under medical supervision in terms of their nutritional and physiological impact on the patient (Bury et al., 1974; Kark, 1974; Russell, 1975). They included a number of properties that should be considered in effective dietary management of various diseases:

- **High Nutritional Efficacy**: Preparations can provide 3000 kcal or more daily and at least 25 percent of the water requirement for extended periods. Nutritionally complete products would supply, in addition to caloric needs, adequate amounts of essential fatty acids, minerals and vitamins, and essential and nonessential nitrogen.
• **Uniform Composition:** Use of chemically identifiable ingredients provides control of product uniformity, allowing modification or supplementation to meet special nutritional needs of individual patients as required. However, deletion, substitution, or reduction of certain nutrients is not possible with commercial preparations.

• **Low Residue:** Most products contain little or no fiber or complex carbohydrates; consequently, gastrointestinal contents and fecal volume are reduced considerably.

• **Ease of Digestibility:** Dietary components may be supplied as readily digestible low molecular weight substances. Absorption in the duodenum and jejunum occurs readily, and in addition, biliary, pancreatic, and enteric secretions are less than normal. If lipids are either absent, at a low level, or of medium chain length, the need for fat-micelle formation is minimized.

• **Microbial Flora Alterations:** Qualitative and quantitative changes in fecal flora suggest that gastrointestinal microbial flora may be altered by consumption of special dietary foods. In general, stool bulk is markedly reduced, but concentration of aerobic and anaerobic stool flora per gram of feces is relatively unchanged.

• **Alteration of Serum Lipid Levels:** While the nature and amount of carbohydrate or other components in the product may affect the rate of decrease, reduction of serum cholesterol levels has been observed (Kaminski, 1976; Winitz *et al.*, 1970).

• **Reduction of Blood Pressure:** Decreased systolic and diastolic blood pressure levels have been reported in normal subjects maintained several days on special dietary products (Winitz *et al.*, 1970). Blood pressure levels returned to baseline values after normal diets were resumed.

• **Gastric Effects:** Consumption of such diets reduces gastric acid secretions and delays gastric emptying (Bury and Jambunathan, 1974).

• **Hypoallergenicity:** The ability to eliminate protein components or alter their composition provides a convenient method of supplying nonallergenic nutrients to patients with food allergies.

• **Water Solubility or Dispersibility:** Liquid preparations allow either tube feeding or consumption without mastication which can be important in pediatric and geriatric patients and in patients
with oral, dental and other head and neck surgical problems. Some can be administered through extremely small (No. 4 French) feeding tubes (Kaminski, 1977).

- **Stabilization of Nutritional State:** The uniformity of types of special dietary products facilitates establishing a stable nutritional status and accurate measurements of the intake of all nutrients. There may be an opportunity to utilize medical foods for critical metabolic balance studies. For example, Young (1970) and Young and colleagues (1971) fed healthy human volunteers diets of known composition prepared from pure chemicals, and observed, among other effects, that urinary electrolytes, urea, and uric acid decreased to lower, but stable values after four days, compared with values during ingestion of a random diet.

- **Storage Properties:** Most products in the dry state or in vacuum packages can be stored up to 12 months at temperatures below 15 C. When reconstituted, they should be kept refrigerated and used within 24 hours because of the possibility of microbial contamination.

### B. CURRENT TERMINOLOGY

Exact definition of these types of products is difficult because of their composition and manner of use. Many currently available products and formulas include widely used foods, food ingredients, and substances that are generally recognized as safe (GRAS) (Office of the Federal Register, 1977; 21 CFR 182.1, 184.1, and 186.1, formerly 21 CFR 121.101, 121.104, and 121.105, respectively). Similarly, a broad array of regular dietary items is useful in feeding patients with disorders amenable to dietary management. On the other hand, some nutritionally complete products were developed originally to facilitate digestion, provide less bulk and thus lower fecal volume, and at the same time, provide nutrients in amounts equivalent to the estimated requirements of a normal adult. In current practice, these latter formulations are being used in such diverse conditions as obesity and weight reduction, acute and chronic pancreatitis, preoperative preparation for intestinal surgery, enteral nutrition of cancer and terminally ill patients, extensive body burns, radiation enteropathy, and the short bowel syndrome.

Regardless of composition or use, products prepared for dietary management of diseases, disorders or related medical conditions are types of foods for special dietary use (Office of the Federal Register, 1977; 21 CFR 105.3, formerly 21 CFR 125.1). The term, food for special dietary use, or colloquially, special dietary foods, is an umbrella term for any food intended
to be used as the sole item of the diet, as a supplementary source of nutrients to increase total dietary intake of the nutrients, or to supply a special dietary need that exists by reason of a physical, physiological, pathological, or other condition, including but not limited to the condition of disease, convalescence, pregnancy, lactation, infancy, allergic hypersensitivity to food, underweight, overweight, or the need to control the intake of sodium (Office of the Federal Register, 1977; 21 CFR 105.3, formerly 21 CFR 125.1).

This definition developed by FDA is designed for regulatory purposes so that certain kinds of information, in addition to that required for conventional foods, can be required on labeling of these special foods. Such supplementary information is needed to inform users about special properties or values of the products. The inclusion of "medical foods" within this definition of special dietary foods is appropriate because of the need for more detailed and specific information on the particular intended use of such preparations. For example, products for dietary management of inborn errors of metabolism require precise quality control of nutrient content and information about those nutrients.

"Medical foods" is a term employed to indicate commercially prepared or other products consumed or administered enterally under direct or indirect medical supervision. The clinical literature contains several related terms for these types of special dietary foods.

The term "elemental diet" has been coined to refer to diets that provide the major nutrients either in easily digestible form or as relatively low molecular weight substances (Russell, 1975). Typically, protein hydrolysates or mixtures of amino acids are present as the nitrogen source. Carbohydrate and lipids are also available in relatively easily digestible forms such as glucose, sucrose, and medium chain triglycerides (MCT). Vitamins and minerals are added to insure complete nutritional adequacy of the product. Elemental dietary products, such as Compleat-B®, Flexical®, Isocal®, Vivonex 100® and Vivonex-HN® are claimed to be almost entirely absorbed in the duodenum and jejunum with little or no residue reaching the large intestine.

Kark (1974) suggested that the term "elemental diet" may be misleading as chemical elements per se are not used as ingredients. He and others have favored the term "chemically defined diets" (CDD). While this term is more precise, it is somewhat inaccurate in that the actual specifications as to chemical content are not always readily available. For instance, protein hydrolysates are frequently used in CDD, but they vary quantitatively and qualitatively in amino acid and peptide content (SCOGS, 1977); similarly, polysaccharide ingredients may exhibit different physical and chemical properties.
Shils (1977) has proposed the term "defined formula diets" (DFD) for oral nutritional preparations. This term is intended to convey the fact that chemically discrete nutrients or materials meeting specifications for composition and purity are used as ingredients. However, exact definition of ingredient composition may not always be possible. Shils et al. (1976) have also used the term "liquid formulas for oral and tube feeding" to describe these products.

C. PROPOSED DEFINITIONS

While each of the terms in current usage has some advantages, for purposes of this report the term "medical foods" has been used and it is defined as follows:

Medical Foods are foods that are specially formulated or prepared products consumed or administered enterally under direct or indirect medical supervision in the dietary management of individuals with specific diseases, disorders, or medical conditions in which the existence of associated special nutritional requirements is established by medical evaluation.

Regardless of composition, medical foods are foods for use by patients who require professional medical counsel and supervision to meet special or unique nutritional requirements. Use of the term, "medical foods," should connote reference to special dietary foods intended for use solely under medical supervision to meet nutritional requirements in specific medical conditions which may be potentially life-threatening or critically disabling.

The proposed definition of medical foods is flexible but sufficiently precise to include all types of special dietary foods designed for the dietary management of diseases and disorders as well as surgical and traumatic conditions. It implies that the food is formulated and intended for use on the basis of sound, generally accepted principles of nutrition. It is based on the concept of use solely under medical supervision but also includes use by dietitians and paramedical personnel. Finally, the definition is sufficiently broad to encompass both commercially prepared products as well as special formulations from suitable ingredients by medical personnel responsible for patient care on an as needed basis.

To provide maximum information on composition and nutritional efficacy, medical foods may be classified further in terms of nutritional adequacy rather than medical use. Many types of medical foods have multiple uses and their usefulness would be dictated by nutritional needs of the patient which can only be determined after medical evaluation. For this
reason, it is suggested that medical foods be categorized as:

1) Nutritionally complete;
2) Nutritionally incomplete; and
3) Components.

Nutritionally complete medical foods are available either as commercial preparations or as products produced on an as needed basis in a hospital diet kitchen, pharmacy, or following instructions of a physician or dietitian. In both cases, these products supply caloric, nitrogen, vitamin, and mineral requirements known to be essential to normal growth, development, and maintenance of health. Medical foods are usually formulated to supply adequate quantities of essential nutrients in terms of daily requirements when fed in reasonable volumes each day. Actual caloric needs of the patient would be determined by the physician, but as a guideline, nutritionally complete medical foods ought to supply at least 1250 to 1450 kcal per m² body surface (2000 to 2700 kcal) per day for the average adult female or male respectively. This guideline makes no allowance for increments related to age, activity, body mass, or physical condition. Such factors would be interpolated in medical design and formulation of the diet. These types of medical foods ought to provide sufficient nitrogen (e.g., a minimum of 0.8 g of protein per kg body weight per day or the equivalent in essential and nonessential amino acids, about 0.1 to 0.2 g as amino acid nitrogen) to ensure a reasonable probability that positive nitrogen balance could be achieved based on the amount fed daily and adequate caloric intake (Randall, 1973; VanItallie et al., 1974). In addition, nutritionally complete preparations would supply sufficient quantities of most (preferably all) of the vitamins, minerals and other essential nutrients known to be required by man within the ranges for the Recommended Dietary Allowances (RDA) as suggested by the Food and Nutrition Board (1974). Other essential vitamins, minerals, and nutrients for which no RDA are specified, may also be included.

Nutritionally incomplete medical foods would include products and formulations that, depending on the volume ingested, may supply less than daily caloric requirements, essential amino acid needs, vitamins, and mineral requirements as defined by the Recommended Dietary Allowances (Food and Nutrition Board, 1974). In most cases, nutritionally incomplete products lack one or more essential nutrients and would be formulated on the basis of medical indications for specialized dietary modification. Such products would not supply all essential nutrients for growth or maintenance of healthy individuals but would contribute to providing complete nutrition for patients requiring special diets. For example, Lofenalac® is formulated only for use by individuals who require low levels of dietary phenylalanine because of an inborn error of metabolism. There are a number of specially formulated, nutritionally incomplete medical foods for use in treatment of patients with inborn errors of metabolism. These are products developed
primarily for infants and children and are available either commercially or through special metabolic centers in North America. The American Academy of Pediatrics Committee on Nutrition (1976) has recently summarized the status of the special diets for infants with inborn errors of amino acid metabolism.

Components. Medical foods in this category would include products and preparations that supply nutrients meeting only one or a few essential nutritional requirements. Components should be distinguished from nutritionally incomplete medical foods because they would contain one, two, or at the most only a few types of nutrients. It is assumed that the physician might make use of several components in formulating a complete diet for a patient depending upon the diagnosis and determination of nutrient needs. Components would be formulated or prepared for oral use under medical supervision in the dietary management of specific diseases or disorders. For example, these would include chemically distinct sources of calories, protein, vitamins and mineral preparations, or electrolyte mixtures.

It should be noted that components of medical foods may include special dietary foods that, by reason of their particular constituents, are selected by certain individuals in the absence of direct or indirect medical supervision. Indeed, components may have other nutritional purposes not directly related to use as medical foods, e.g., Hycal®, a source of readily available calories. Similarly, there are a number of low protein and gluten-free products marketed for use by persons whose medically diagnosed conditions require restricted intake of protein, gluten, or certain amino acids. For example, gluten-free bread is generally available as a product useful in the medical management of gluten enteropathy. Yet consumption of gluten-free bread by individuals for reasons not associated with a medically diagnosed need for dietary management would pose no serious nutritional imbalance, provided other sources of nitrogen were included in the diet. Clearly delineated guidelines for components which are freely available in the market place may be more expeditiously approached by labeling for use as medical foods when necessary.

The Appendix (Section IX) provides a compilation of products classified on the basis of these three definitions and a discussion of issues related to interpretation of the definitions.
Since the passage of the Pure Food and Drugs Act in 1906, the regulatory status of substances that may be both foods and drugs has undergone repeated modification. As the law was amended in 1938 and again in 1962, requirements for premarketing proof of safety and efficacy were mandated for drugs. For drugs, safety implies that the preparation is safe in relation to the possible risks related to the condition being treated. Further, the drug is safe relative to the safety of other drugs available to treat a given disease or disorder. However, food regulations focus primarily on standards of identity and quality. Food additives are prohibited except as specifically indicated in regulations. Safety of foods has traditionally been defined as safe and generally free of risk.

Thus, current regulations for new foods and food ingredients require absence of adverse health effects. Standards of identity and quality or similar regulations on quality are specified, based on assimilation of data derived from studies on safety and suitability. In addition, nutritional information on package labels must meet certain criteria. In an analogous manner, new drug applications require extensive documentation of the chemistry, biological effects, apparent efficacy and lack of toxicity (Office of the Federal Register, 1976a). The data required are specified in considerable detail and include specific mention of preclinical and clinical studies as well as documentation of reference materials. In addition, an evaluation of safety and effectiveness, together with proposed labels, package inserts, manner of use statements, full reports of all published and unpublished preclinical and clinical studies, and identification of all investigators are required before FDA approval of the drug for medical use.

Since 1962, investigational new drug data have been required for vitamin and mineral preparations promoted for use as drugs; and notwithstanding the nutritional purposes of use, some special dietary products were considered drugs because they were originally regulated to ensure their use under medical supervision. However, in 1972 the FDA reclassified these types of special dietary foods from drugs to foods for special dietary use to enhance their development and availability (Office of the Federal Register, 1972). This policy covers all special dietary foods that are intended for use under medical supervision to meet the nutritional requirements of patients who require professional counsel to meet their specialized or unique nutritional requirements because of specific medical conditions. These products are referred to as "medical foods"; however, the term was not precisely defined (Office of the Federal Register, 1973).
The term "for special dietary use" as applied to human food means a food for a particular use which is represented or purports to be used, including but not limited to the following three categories of use (Office of the Federal Register, 1977; 21 CFR 105.3, formerly 21 CFR 125.1):

a. foods that supply a special dietary need existing by reason of a physical, physiological, pathological, or other condition including but not limited to the condition of disease, convalescence, pregnancy, lactation, infancy, allergic hypersensitivity to food, underweight, overweight, or the need to control the sodium intake;

b. foods that supply a vitamin, mineral, or other ingredient for human use to supplement the diet by increasing the total dietary intake; and,

c. foods that provide a special dietary need by reason of being the sole item of the total diet.

Nutritionally complete and nutritionally incomplete medical foods, as well as components of medical foods are foods for special dietary uses under the meaning of these definitions. In addition, medical foods would be foods represented for use solely under medical supervision to meet nutritional requirements in specific medical conditions (Office of the Federal Register, 1977; 21 CFR 105.85, formerly 21 CFR 80.1).

Revisions of regulations related to foods for special dietary uses also require certain scientific data and information on labeling, but exclude those foods represented for use solely under medical supervision to meet nutritional requirements in specific medical conditions from certain of these requirements (Office of the Federal Register, 1976b). With respect to labeling statements for foods for special dietary uses, regulations require that references to essential nutrients be in a specific manner and that reference to non-nutrients must not imply any nutritional, dietary, or therapeutic value (Office of the Federal Register, 1976c). However, foods represented solely as special dietary foods for use under medical supervision in the dietary management of specific diseases and disorders are not prohibited from indicating that the components (as nutrients) are adequate or effective in the dietary management of a disease or symptom of disease (Office of the Federal Register, 1976c). While not stated explicitly, the existence of this provision in the regulations suggests that the scientific rationale and the purposes for use of the food under medical supervision are based on established principles of sound nutrition in health and disease.

The current regulations imply that the rationale for use of medical foods is based on existing scientific knowledge and deductive medical
reasoning and not necessarily on clinical investigations utilizing the medical food in controlled studies involving human subjects with the specific disease or disorder in question. Because the use of these special dietary products is meant to be restricted primarily to situations where clinical management is well controlled, it is evident that medical foods should be labeled to indicate qualitative and quantitative composition as well as the relation of ingredients to known human nutritional requirements. Obviously, the primary purpose of such preparations is to provide essential nutrients; it is generally assumed that use of prepared oral or tube fed diets is predicated upon extant medical knowledge of the disease or disorder present, its possible duration, a rationale for treatment, alleviation or mitigation by dietary management, and possible tolerance or intolerance for the nutrients in the modified dietary regimen.

The FDA is responsible for insuring that these special dietary foods marketed in the United States are safe, efficacious for the intended purpose, and properly labeled. In addition, the FDA has a legal mandate to ensure that advertising of these products conforms to standards of accuracy and reliability. This information, whatever the form of label or advertisement, should provide the physician and the patient with the best possible information about the product, its uses, indications, contraindications and precautions.
IV. NUTRITIONAL ASPECTS

The daily energy and nutrient allowances recommended by the Food and Nutrition Board (1974) of the National Research Council and other national and international organizations (Food and Agriculture Organization of the United Nations, 1974; Health and Welfare Canada, 1974; ICNND, 1963) are accepted universally as general guidelines for the nutritional well being of healthy persons (Table 1). These suggested norms or ranges of energy and nutrient allowances vary with age, sex, and body size, but are considered adequate for persons within a broad category of occupations performed without unusual environmental stresses. In addition, most authorities recognize that individual nutrient needs also vary depending on the quality of the diet, nutrient absorption efficiency, use of pharmaceuticals, and most importantly the basal metabolic rate, physical activity level, and health status of the person.

The Food and Nutrition Board (1974) has also emphasized that the Recommended Dietary Allowances (RDA) not be confused with nutrient requirements and that the RDA do not cover therapeutic nutritional needs and that patients with particular nutritional needs require special dietary treatment on an individual basis. Nevertheless, the RDA and the United States Recommended Daily Allowances (U.S. RDA) (Office of the Federal Register, 1977; 21 CFR 105.3, formerly 21 CFR 125.1) are used, in a practical sense, as the minimum allowance of nutrients necessary for adequate nutrition of patients recovering from surgery or other medical conditions. That is, it is generally assumed that the nutritional needs of an individual with a disease, disorder, or other medical condition are probably either greater than those of a normal healthy person or are unique because of the medical condition. For example, Berdanier and Kaminski (1976) have suggested that traumatized patients have increased nutrient requirements that are related to increased energy and caloric needs. They indicated that caloric requirements could increase up to 200 percent and protein catabolic responses might increase protein requirements from 50 to 500 percent. Berdanier and Kaminski (1976) also noted increased needs for electrolytes, other minerals and vitamins in traumatized patients but pointed out that additional research was necessary to quantify the elevated needs of traumatized patients.

However, the generalization of an overall greater need for energy and nutrients by the sick or injured individual may be less accurate than the potentially unique nutritional needs dictated by the patient's condition. A dietary regimen appropriate to the specific needs of each patient appears to be the usual clinical approach. The energy and nutrient needs of an adult are usually expressed as the sum of calories required by basal metabolism,
Table 1. Recommended Nutritional Allowances for Normal Healthy Adult Males in Terms of Units Per Kg Body Weight per Day

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Units</th>
<th>FAO(^1)</th>
<th>FNB(^2)</th>
<th>Canada(^3)</th>
<th>ICNND(^4)</th>
<th>Goodhart(^5)</th>
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<tr>
<td>Water</td>
<td>1</td>
<td>(1.0 ml/kcal/ day)</td>
<td>4.0</td>
<td>42.8</td>
<td>41.4</td>
<td>2.5 to 4.5(^a)</td>
</tr>
<tr>
<td>Energy</td>
<td>kcal</td>
<td>46.2</td>
<td>38.6</td>
<td>42.8</td>
<td>41.4</td>
<td>40.0</td>
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<tr>
<td>Nitrogen (as protein)</td>
<td>mg</td>
<td>570.0</td>
<td>800 to 928</td>
<td>671.0</td>
<td>1000 to 1500</td>
<td>928.0</td>
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<td>Mineral Elements</td>
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<tr>
<td>Calcium</td>
<td>mg</td>
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<td>11.4</td>
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<td>5.7 to 10.0</td>
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<tr>
<td>Phosphorus</td>
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<td>12.9 to 15.7</td>
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<td>Magnesium</td>
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<td>5.0</td>
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<td>Iron</td>
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<td>142.9</td>
<td>142.9</td>
<td>142.9 to 157.1</td>
<td>142.9</td>
</tr>
<tr>
<td>Iodine</td>
<td>µg</td>
<td>2.0</td>
<td>2.1</td>
<td>1.9</td>
<td>1.9</td>
<td></td>
</tr>
<tr>
<td>Copper(^7)</td>
<td>µg</td>
<td>28.6</td>
<td></td>
<td></td>
<td>28.6</td>
<td>28.6</td>
</tr>
<tr>
<td>Manganese(^8)</td>
<td>µg</td>
<td>67.8</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Zinc</td>
<td>mg</td>
<td>0.2</td>
<td>0.1</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aluminum</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Molybdenum</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cobalt</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sodium(^9)</td>
<td>mg</td>
<td>65.7</td>
<td></td>
<td></td>
<td></td>
<td>65.7</td>
</tr>
<tr>
<td>Potassium</td>
<td>mg</td>
<td>35.7</td>
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<td></td>
<td></td>
<td>79.0</td>
</tr>
<tr>
<td>Chloride(^10)</td>
<td>mg</td>
<td>40.7</td>
<td></td>
<td></td>
<td></td>
<td>40.7</td>
</tr>
<tr>
<td>Vitamins</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thiamin, B(_1)</td>
<td>µg</td>
<td>18.5</td>
<td>20.0</td>
<td>21.4</td>
<td>12.4 to 16.6</td>
<td>2.0</td>
</tr>
<tr>
<td>Riboflavin, B(_2)</td>
<td>µg</td>
<td>27.7</td>
<td>22.9</td>
<td>25.7</td>
<td>17.1 to 20.0</td>
<td>24.3</td>
</tr>
<tr>
<td>Pyridoxine, pyridoxal, B(_6)</td>
<td>µg</td>
<td>28.6</td>
<td>28.6</td>
<td>28.6</td>
<td>14.8</td>
<td>28.6</td>
</tr>
<tr>
<td>Cobalamin, B(_12)</td>
<td>µg</td>
<td>0.03</td>
<td>0.04</td>
<td>0.04</td>
<td>0.04</td>
<td>0.07</td>
</tr>
<tr>
<td>Pantothenate</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Folacin, Folic acid</td>
<td>µg</td>
<td>3.1</td>
<td>0.57</td>
<td>2.9</td>
<td>0.04 to 1.4</td>
<td>0.57</td>
</tr>
<tr>
<td>Niacin</td>
<td>µg</td>
<td>304.6</td>
<td>257.1</td>
<td>285.7</td>
<td>142.9 to 200.0</td>
<td>257.1</td>
</tr>
<tr>
<td>Choline</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Biotin</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Vitamin A(^11)</td>
<td>RE</td>
<td>11.5</td>
<td>14.3</td>
<td>14.2</td>
<td>15.0 to 21.4</td>
<td>21.4</td>
</tr>
<tr>
<td>Vitamin D</td>
<td>µg</td>
<td>0.04</td>
<td>0.1(^12)</td>
<td>0.4</td>
<td>0.01</td>
<td></td>
</tr>
<tr>
<td>Vitamin C, Ascorbic acid</td>
<td>mg</td>
<td>0.46</td>
<td>0.64</td>
<td>0.43</td>
<td>0.42 to 0.70</td>
<td>0.86</td>
</tr>
<tr>
<td>Vitamin E(^13)</td>
<td>µg</td>
<td>214.3</td>
<td>128.6</td>
<td></td>
<td>428.6</td>
<td></td>
</tr>
</tbody>
</table>
Blanks indicate no figure given by reference source cited.

1 Food and Agriculture Organization of the United Nations (1974); for moderately active adult male, 65 kg body weight.
2 Food and Nutrition Board (1974); 23 to 50 year old male, 70 kg body weight.
3 Health and Welfare Canada (1974); 19 to 35 year old male, 70 kg body weight.
4 ICNND (1963); physically active 25 year old male, 70 kg body weight.
5 Goodhart, R.S. (1973); 23 to 50 year old male, 70 kg body weight. Except for water, Goodhart refers to the RDA as revised by the Food and Nutrition Board in 1968.
6 2.5 to 4.0 l or 1.0 ml per kcal.
7 Not an RDA, present in the diet at 2.0 mg per day, an amount considered adequate.
8 Not an RDA, present in the diet at 4.75 mg per day, an amount considered adequate.
9 Not an RDA, present in the diet at 2.3 to 6.9 g per day, an amount considered adequate.
10 Not an RDA, present in the diet at 1.4 to 4.2 g per day, an amount considered adequate.
11 One retinol equivalent (RE)=1 µg retinol = 3.33 IU retinol or 10 IU β-carotene.
12 Females only.
13 One mg of d-α-tocopherol is 1.49 IU.
expended in physical activities, and an additional caloric increment for specific dynamic action. Age, sex, body size, and body shape will affect basal metabolism rate; but in general individuals that are similar in these respects will have approximately the same energy and nutrient requirements. In the ostensibly healthy individual physical activity is the most important source of variations in energy expenditures. In the patient, energy and nutrient needs are a function of his tissue reserves, condition, and ability to absorb and utilize nutrients. The ability to absorb and metabolize nutrients may be compromised by genetically determined enzyme deficiencies that may be prevalent in certain segments of the population; for example, disaccharidase deficiency in races other than Caucasian.

Kinney et al. (1968) studying hospitalized surgical patients without sepsis, long bone fractures, or burns found that these patients expended only 15 to 20 percent energy above the basal metabolic requirements because of reduced physical activity. These values suggest energy requirements of approximately 28 to 32 kcal per kg body weight per day for adult female and male patients as compared to 30 to 40 kcal per kg body weight per day for normal, healthy, moderately active adult females and males (Food and Nutrition Board, 1974). Shils (1972) concluded that 30 kcal per kg body weight per day would meet the daily caloric requirements of a resting patient without significant fever or hypermetabolic state. When loss of lean tissue mass was evident, caloric intake could be increased to 50 kcal per kg per day or more if tolerated. Shils (1972) also pointed out that continued catabolism of body protein may occur despite the existence of fat reserves or administration of parenteral nutrition in certain conditions such as severe burns, trauma, and infection.

On the basis of a review of many studies of parenteral feeding, Randall (1973) concluded that high caloric intakes may be necessary to reduce or even reverse the catabolic loss of protein and fat in chronic illness and surgical convalescence. Intakes of 35 to 50 kcal per kg body weight with 0.1 to 0.2 g of amino acid nitrogen per kg body weight per day were suggested as effective in reducing or preventing nitrogen loss in the postoperative patient (Randall, 1973). Enteral feeding at equally high levels will achieve similar results (Kaminski, 1977). Thus caloric needs of hospitalized adults may vary from as low as 28 to more than 50 kcal per kg body weight per day. The fact that this range exceeds the suggested range for normal, healthy adults is indicative of the need for precise management of dietary intake based on individual patient requirements.

For example, patients with extensive burns have special nutritional problems. The damage or loss of the integrity of the skin leads to an inability to retain body heat. Consequently increased caloric expenditures occur in addition to elevated electrolyte and protein losses. During the early postburn period, patients may be in negative caloric and nitrogen
balance even though supposedly adequate oral intakes are provided (Curreri, 1972). Thus in burn patients the use of medical foods usually follows or supplements parenteral nutrition.

Wilmore et al. (1971), in a study of 26 severely burned patients, demonstrated that 4000 to 8000 kcal per day could be delivered by a combined intravenous (3000 to 5000) and enteral (2500 to 3000) regimen. Septicemia and other complications made nutrient delivery by both routes difficult, and water loss was the major problem. However, weight stabilization was achieved in most patients, and body weight increases were evident in several during the 30 day postinjury period.

Spady et al. (1976) studied energy balance of 11 children ranging in age from 8 to 18 months who were hospitalized for severe protein energy malnutrition diagnosed as either marasmus or kwashiorkor. The initial diet of skim milk, glucose, and coconut or peanut oil provided 91 kcal and 0.6 g of protein per kg body weight per day and was fed for 4 to 5 days. Subsequently, Pelargon® plus coconut or peanut oil were fed to provide 1350 kcal and 31 g protein per 1000 ml. In 9 of the 11 children, daily intakes averaged 165 kcal per kg body weight; however, intakes of up to 250 kcal per kg body weight per day were observed during 14-day segments of the 3-month recovery period.

Stephens and Randall (1969) have reported that several patients with severe malnutrition resulting from various gastrointestinal disorders or surgery were able to achieve positive nitrogen balance and weight increases when fed a commercial preparation at levels ranging from 2400 to 4500 kcal per day. Caloric intake depended on individual patient needs, but provided adequate nutrition for periods of up to 83 days.

Bury et al. (1971) observed essentially similar results in another series of patients with gastrointestinal disorders. Thirteen patients with fistulas were nutritionally supported for 5 to 50 days by oral administration of Vivonex® or Codelid®. The liquid diet at approximately 1 kcal per ml (as fed), provided nitrogen intakes of 0.27 to 0.48 g per kg per day and caloric intakes of 43 to 125 kcal per kg body weight per day.

Voitk et al. (1973a) and Rocchio et al. (1974) reported successful nutritional maintenance of individuals with inflammatory bowel disease. Rocchio et al. (1974) were able to provide 2500 to 3000 kcal and 20 g of nitrogen per day to adult females and 3000 to 4000 kcal and 24 g of nitrogen to adult males. The individual caloric and nitrogenous requirements were determined by balance studies. Patients in both studies received the liquid diet by slow, continuous administration via nasogastric tube.

However, there are few reports of nutritional needs or actual balance studies of persons with specific diseases or disorders. This is no doubt
related to the primary concern for therapy and the technical difficulties involved. Nevertheless, medical management of any disease or disorder includes evaluation of tolerances for fluid, nitrogen, glucose and minerals, particularly sodium, potassium, magnesium and phosphorus, where cardiovascular, hepatic, renal or endocrine dysfunction may be present or suspected. These data appear in clinical reports but are rarely collated and analysed from the standpoint of nutrition. As a corollary, clinical and investigational reports on the use of medical foods rarely provide comparative data on evaluation of several formulations with differing composition for efficacy in a given medical condition. Studies, such as those of Kaminski (1977) on nitrogen balance with two regimens of enteral hyperalimentation, are examples of the type needed.

An additional parameter of nutritional efficacy of medical foods is the possible occurrence of some interaction between the administered diet and the therapeutic regimen (Carr, 1977). Patients requiring medical foods would probably be receiving drugs. Physicians customarily consider the influence of foods on absorption and utilization of oral therapeutic drugs. With respect to administration of medical foods, the pharmacologic properties of drugs given concomitantly must be considered. For example, absorption of L-dopa is slower and peak blood levels are reduced when the drug is ingested with food (Calne and Reid, 1972). Patients with Parkinson's disease exhibited a wide range of plasma levels (average = 1 µg per ml) following ingestion of 3 to 8 g of L-dopa daily with meals. While the relationship between plasma levels and clinical efficacy of L-dopa is unclear, a short period of symptomatic improvement occurs after each dose but usually disappears within five hours. The inter- and intra-patient variability in peak plasma levels and symptom alleviation suggests that interactions between L-dopa and consumed foods affect drug utilization. Such interactions could be critical to the progress of patients receiving medical foods.

The possibility that food and drug interactions might be hazardous to the patient must be considered because the metabolism of drugs often depends upon the nutritional status of the patient (Basu and Dickerson, 1974). For example, low protein diets could affect gastrointestinal and hepatic enzyme activity. A reduced capacity for induction and enzyme activity might alter drug metabolism and produce drug toxicity. However, low protein diets would not increase the toxicity of all drugs; for example, some foreign chemical compounds are less toxic to young animals fed protein-free diets for only seven days (Basu and Dickerson, 1974).

The exact cause of these results is unknown, but may be an adaptive enzyme response. Further, mineral or vitamin deficiencies are known to change the toxicity of numerous drugs; for example, ascorbic acid is presumed to have a significant role in drug metabolism. Thus, medical foods must be considered as potential components of food - drug interactions that could affect the therapeutic effectiveness of drugs.
V. CURRENT USE

A. INTRODUCTION

The purpose of this chapter is to provide information that may aid in determining the possible need for regulations for development and use of medical foods. No attempt has been made to assemble a comprehensive, documented treatise on instances of their clinical use. Diseases, disorders, and other clinical indications in which medical foods have been or may possibly be used advantageously to achieve a desired therapeutic or diagnostic objective are listed in Appendix A. Documentation exists for most, but not all, of the listed items. The lists are intended to be exemplary and indicate the wide scope of clinical applications of medical foods.

Orally administered enzymes for replacement therapy in digestive disorders such as those which may result from pancreatic insufficiency were not included with medical foods in this review even though a case might be made for them on the basis of their proteinaceous nature and their sources. They are currently regulated as drugs (Office of the Federal Register, 1974), and are available mostly in tablet or capsule form as mixtures of amylolytic, proteolytic, lipolytic and cellulolytic enzymes, sometimes combined with bile salts, antispasmodics and other ingredients.

B. EXAMPLES OF CLINICAL UTILIZATION

Certain diseases of the kidneys, gastrointestinal tract, and the liver and biliary system were chosen as examples to explain the rationale and highlight some of the clinical experiences with medical foods that have been reported in the literature. Tables 2 through 6 list data from individual reports of clinical experiences with a representative array of diseases and disorders. All product names in these tables are registered trademarks unless otherwise noted. It should be noted that this listing is not intended to represent an exhaustive collection of the literature.

1. Chronic Renal Failure (See Table 2)

Chronic renal insufficiency is an example of a clinical disorder in which dietary management has proved to be an important part of the treatment (Giordano et al., 1966; Giovannetti and Maggiore, 1964; Walser, 1976). This serious form of kidney dysfunction is caused by many diseases, any of which may result in a drastic reduction of functioning nephrons and consequent decreased efficiency of glomerular filtration, with attendant severe systemic, metabolic, and functional derangements.
Table 2. Medical Foods in Management of Renal Disease.

<table>
<thead>
<tr>
<th>Disease or disorder</th>
<th>Special dietary objectives</th>
<th>Foods used including commercial items</th>
<th>Comments</th>
<th>Efficacy</th>
<th>Safety</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Chronic renal insufficiency (chronic renal failure)</td>
<td>reduce nitrogenous end-products of protein catabolism; reduce excess electrolytes; replace protein, sodium, other substances lost via impaired renal function; adequate nutrition, reduction of uremia, rest for the kidneys; lengthen intervals between dialyses</td>
<td>low protein (e.g., 20-40 g daily), high energy diet, controlled electrolytes and fluid volume; vitamin and mineral supplements plus supplement of 10-20 g essential amino acids; use low protein flours (e.g., Paygel, Aproten), high energy, protein restricted items such as HyCal, Cal Power, Controlyte</td>
<td>nonnitrogenous analogues of certain essential amino acids, useful supplements in protein-restricted diets</td>
<td>good (but varies with degree of renal impairment); dialysis or renal transplant ultimately necessary</td>
<td>clinical surveillance required to avoid azotemia, acidosis, electrolyte imbalance and malnutrition</td>
<td>Anderson et al., 1973; Blagg and Scribner, 1972; Burton, 1974; Chan, 1973; Ford et al., 1969; Giordano et al., 1966; Giovannetti and Magottre, 1964; Kopple et al., 1968; Shaw et al., 1965; Walser, 1976</td>
</tr>
</tbody>
</table>
The most common cause of chronic renal failure is chronic glomerulonephritis (Blagg and Scribner, 1972). Other frequently reported causes include chronic pyelonephritis, cystic disease of the renal medulla, bilateral hydroureteronephrosis, the nephrotic syndrome* (Anderson et al., 1973), arteriolar nephrosclerosis, diabetes mellitus, certain collagen diseases, drug-induced interstitial nephritis (Blagg and Scribner, 1972), crystalline deposits of uric acid and salts (Burton, 1974), and obstructive nephropathies. Becker (1973), Brenner and Rector (1976) and McClusky (1973) list other causes of chronic renal insufficiency.

The conservative management of the uremic patient has been comprehensively reviewed by Walser (1976). Specially formulated diets for patients with chronic renal failure have proved effective in reducing uremia and its complications and in delaying the need for dialysis or surgical intervention (Anderson et al., 1973; Burton, 1974; Chan, 1973; Giordano et al., 1966; Giovannetti and Maggiore, 1964; Walser, 1976; Walser and Mitch, 1977). Overall objectives of such treatment are to control the unpleasant symptoms of uremia, to maintain protein nutrition, and to retard or possibly reverse the progress of the disease until dialysis or renal transplantation becomes essential.

Principles of dietary management include controlled intake of protein and essential amino acids (or their analogues) to reduce the nitrogenous and acidic residues of protein metabolism; adequate nonprotein caloric intake to conserve nitrogen; and supplementation with individually determined vitamin mixtures. With restricted protein diets, a high caloric intake minimizes catabolism, maintains positive nitrogen balance, and prevents further increase in nitrogenous wastes and unpleasant symptoms of uremia. Uremia, *per se*, does not call for salt restriction; however, careful attention to sodium as well as potassium and fluid balance is essential. Dietary restriction of potassium may be needed in advanced stages of the disorder, but occasionally a patient may be hypokalemic as a result of anorexia, nausea, vomiting, and diarrhea. Prevention of acidosis via sodium bicarbonate supplements may be critically important in patients with severe chronic renal failure (Walser, 1976). Hypocalcemia and hyperphosphatemia, which are frequently associated with chronic renal failure, may require calcium and vitamin D supplements and dietary phosphate restriction or the use of phosphate-binding antacids.

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*The nephrotic syndrome is usually characterized by moderate to massive proteinuria, which requires a high protein intake; it is listed here because in unresolved cases, chronic renal insufficiency is a common sequela.
The decision to use dietary therapy is serious because the attendant restrictions may affect the quality of the patient's life. Quantitative restriction of dietary protein to about 0.5 g per kg body weight per day can be a practical aid in managing nitrogen balance in nonsevere uremic patients. In addition, careful attention to the patient's food preferences and compliance is an essential part of management. For patients with renal function impaired to less than 20 percent of normal, the importance of protein quality has been recognized since the time that Giovannetti and Maggiore (1964) pointed out that daily intake of as little as 20 to 25 g of protein containing a high proportion of essential amino acids ("high quality" proteins; high biologic value proteins) resulted in positive nitrogen balance. Subsequent experience has shown that daily diets with as little as 0.3 g per kg body weight of high quality protein accompanied by adequate nonprotein calories provided nitrogen equilibrium in most uremic patients (Carmena and Shapiro, 1972; Kluthe et al., 1972). However, other investigators reported the majority of their patients were in negative nitrogen balance despite the use of high biologic value protein (Ford et al., 1969; Hyne et al., 1969; Kopple et al., 1968; Kopple and Coburn, 1973).

Knowledge gained during the last decade indicates a wide variability in total dietary nitrogen requirements among patients with chronic renal failure. There apparently is no "standard" nitrogen requirement in uremia; thus, patients should be studied individually to determine the minimal dietary protein intake to prevent progressive nitrogen depletion, consistent with patient preferences and compliance (Walser, 1976).

Mixtures of essential amino acids appear more efficient as sources of nitrogen than proteins, including proteins of high biologic value. Optimal mixtures of amino acids are theoretically possible in terms of minimum urea formation and maximum nitrogen retention for anabolism. However, the technical problems of devising optimal mixtures are severe with regard to the numbers of amino acids involved, the individual differences in amino acid requirements, and other variables. Nevertheless, essential amino acid supplements are considered highly effective in the dietary treatment of chronic renal failure even though their advantages over high biologic value proteins are small in terms of nitrogen conservation.

During the past decade, laboratory animal experiments and clinical trials have shown that the alpha-keto analogues of the branched chain amino acids and the hydroxy analogues of phenylalanine and methionine are useful as nonnitrogenous precursors of the corresponding essential amino acids and are effective in sparing nitrogen (Richards et al., 1967; Schloerb, 1966; Walser, 1975; Walser et al., 1973; Walser and Mitch, 1977). For example, in uremic patients fed the calcium salts of the analogues of valine, leucine, isoleucine, methionine and phenylalanine given in conjunction with the four other essential amino acids, the urea appearance rates declined compared
with the rates in patients fed a complete mixture of essential amino acids even though total nitrogen intakes were essentially constant (Walser, 1975). In addition, among some uremic patients fed the analogues in place of the corresponding amino acids, a small number of patients with chronic uremia who otherwise would have required dialysis were maintained for many months and some patients showed a sustained improvement in renal function.

In their recent review of the dietary management of renal failure, Walser and Mitch (1977) concluded: "... the administration of a diet containing 15-20 g of protein, unrestricted as to quality, in conjunction with adequate calories and vitamins, plus a dietary supplement consisting of 10-20 g of essential amino acids and/or their nitrogen-free analogues shows promise of playing a major role in the therapy of chronic renal failure ..." However, the authors caution that much more experience is needed to evaluate the long-term effects of dietary therapy on the progression of chronic renal failure.

Medical foods that are useful in these diets include preparations of essential amino acids as well as those that provide high energy, low-protein and no excess sodium and potassium. Examples are Amin-aid® (essential amino acids), the low-protein flours for breads and pastries such as wheat starch flour (Aproten®, Paygel-P®, Resource Baking Mix®) and high energy products containing carbohydrate with or without fat, but with little or no nitrogen or electrolytes, such as Modified Mor-Rex®, Polycose®, Hycal®, Cal Power®, and Controlyte® (See Appendix B).

When properly used, such diets are said to alleviate the symptoms of chronic renal failure, improve the deranged biochemical parameters and promote a feeling of well being and resumption of normal activities while simultaneously increasing the time between dialyses. Patient acceptance of the diets in terms of palatability, attractiveness, and flavor fatigue, especially the high energy supplements, is reported to be a problem (Anderson et al., 1973).

2. Gastrointestinal Disorders (See Tables 3 and 4)

Diseases and disorders of the alimentary canal have had the major influence on medical foods development, and they will undoubtedly continue to stimulate improvements in the means for dietary management. Work Group VII of the Second Conference on Digestive Disease as a National Problem (Fordtran, 1975) emphasized the inadequacies of nutritional knowledge and listed examples including mechanisms of nutrient absorption and the effect of medium chain triglycerides (MCT) on water and electrolyte movement in the small and large bowels, on gastrointestinal protein synthesis and degradation, and on the absorption of fat-soluble vitamins and minerals. Janowitz and Sachar (1975), reporting the deliberations of Work
<table>
<thead>
<tr>
<th>Disease or disorder</th>
<th>Special dietary objectives</th>
<th>Foods used including commercial items</th>
<th>Comments</th>
<th>Efficacy</th>
<th>Safety</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bowel complications of 5-fluorouracil cancer therapy (5-FU enteropathy)</td>
<td>maintain nutrition and prevent degeneration of rectal mucosa, diarrhea, and melena using elemental diet</td>
<td>Mead Johnson 3200-A.S.</td>
<td>taste objectionable to some patients</td>
<td>good</td>
<td>no problems reported</td>
<td>Bounous et al., 1971, 1972</td>
</tr>
<tr>
<td>Catabolic states¹</td>
<td>emphasis on decreasing digestive demands and achieving positive caloric and nitrogen balance</td>
<td>Codelid (40-, 41-, 42H) 40-H: 41% glucose 41-H: 21% glucose 42-H: 41% sucrose</td>
<td>negative nitrogen balance and weight loss initially in these patients</td>
<td>good</td>
<td>supplemental parenteral feeding used in some patients</td>
<td>Stephens and Randall, 1969</td>
</tr>
<tr>
<td>Celiac disease (gluten-sensitive enteropathy)</td>
<td>prevent bowel intoxication by gluten</td>
<td>gluten-free diet</td>
<td>diets can be made using readily available foods</td>
<td>good</td>
<td>no problems reported</td>
<td>Dissanayake et al., 1974</td>
</tr>
<tr>
<td>Collagenous sprue</td>
<td>prevent bowel intoxication by gluten</td>
<td>gluten-free diet</td>
<td>authors suggest this may be most severe form of celiac disease; prednisolone part of therapy</td>
<td>successful combined therapy</td>
<td>no problems reported</td>
<td>Holdstock and Olesky, 1973</td>
</tr>
<tr>
<td>Crohn's disease</td>
<td>correct diarrhea, steatorrhea and malabsorption; restore caloric and nitrogen balance</td>
<td>low fat diet (30 to 40 g daily)</td>
<td>4 of 5 patients improved promptly and markedly</td>
<td>good</td>
<td>no problems reported</td>
<td>Andersson, 1973</td>
</tr>
<tr>
<td>Dermatitis herpetiformis with enteropathy</td>
<td>prevent gluten intoxication of small bowel</td>
<td>gluten-free or low gluten diet</td>
<td>diets can be made using readily available foods; corticosteroids used instead of diet in some patients</td>
<td>good</td>
<td>no problems reported</td>
<td>Fry et al., 1969; Kumar et al., 1973</td>
</tr>
<tr>
<td>Condition</td>
<td>Recommendations</td>
<td>Nutritional Support</td>
<td>Complications</td>
<td>Reference(s)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>-----------------------------------------</td>
<td>--------------------------------------------------------------------------------</td>
<td>---------------------</td>
<td>--------------------------------------</td>
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<tr>
<td>Fistulas of alimentary tract</td>
<td>restore and maintain positive nitrogen and caloric balance; reduce dietary stimulation of biliary pancreatic, and intestinal secretion and thus, fistula drainage</td>
<td>Vivonex and Codelid and variations of each; virtually fat-free and nutritionally complete except for cobalt and vitamin K</td>
<td>mostly by nasogastric tube, gastrostomy tube or feeding jejunostomy; some ingested the diets; spontaneous closure in 7 of 13</td>
<td>possible complications listed; no serious problems reported</td>
<td>Bury et al., 1971; Hill et al., 1976; Voitk et al., 1973a</td>
<td></td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td>correct nutritional depletion; rest the bowel; minimize biliary and pancreatic exocrine secretion; shorten primary disease; improve wound healing; decrease infections</td>
<td>Vivonex, High Nitrogen; Codelid 72 H</td>
<td>diseased bowel absorbs simple sugars and amino acids given at slow, constant rate</td>
<td>good</td>
<td>no problems reported</td>
<td>Rocchio et al., 1974</td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td>provide adequate enteral nutrition; simultaneously permit bowel rest</td>
<td>Flexical</td>
<td></td>
<td>good in 12 of 13 patients</td>
<td>Voitk et al., 1973a</td>
<td></td>
</tr>
<tr>
<td>Maldigestion/ malabsorption of the elderly (various clinical disorders)</td>
<td>reduce or bypass preliminary digestion; achieve positive caloric and nitrogen balance</td>
<td>Portagen (caloric supplement with 87% MCT®); Vivonex, Flexical, Sustacal, MCT.</td>
<td>elemental diets are &quot;completely pre-digested&quot;; low residue</td>
<td>good</td>
<td>no problems reported; but theoretical problem of using MCT in cirrhosis</td>
<td>Balacki and Dobbins, 1974</td>
</tr>
<tr>
<td>Radiation enteritis</td>
<td>control diarrhea by diet that reduces digestive demands, exocrine secretions and stool volume; reduce long chain triglycerides in diet</td>
<td>Mead Johnson 3200 A.S. Mead Johnson 3200 A.U.</td>
<td>3200 A.S. has hydrolyzed casein and MCT; 3200 A.U. has whole casein and LCT; patient ate 3200 A.S. exclusively for 8 months</td>
<td>fair with 3200 A.U. good with 3200 A.S.</td>
<td>no adverse effects reported</td>
<td>Haddad et al., 1974</td>
</tr>
</tbody>
</table>
Table 3. (Continued)

<table>
<thead>
<tr>
<th>Disease or disorder</th>
<th>Special dietary objectives</th>
<th>Foods used including commercial items</th>
<th>Comments</th>
<th>Efficacy</th>
<th>Safety</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Radiation enteritis</td>
<td>gluten-free, milk protein- free, low residue diet</td>
<td>apparently custom made for small series of pediatric patients</td>
<td>rationale based on similar intestinal mucosal changes as in malabsorption syndrome</td>
<td>good</td>
<td>no problems reported</td>
<td>Donaldson et al., 1975</td>
</tr>
<tr>
<td>Short gut (short bowel) syndrome</td>
<td>minimize digestive demands during postsurgical adaptation; restore caloric and nitrogen balance</td>
<td>nutritionally complete, low residue diet: Flexical</td>
<td>nasogastric tube, slow, controlled rate 24 hr per day; precise tube placement to prevent aspiration</td>
<td>good</td>
<td>of 8 patients 1 died of aspiration pneumonia</td>
<td>Voitk and Crispin, 1975; Voitk et al., 1973b</td>
</tr>
<tr>
<td>Sugar malabsorption in children and postsurgical neonates</td>
<td>correct/prevent dehydration; provide ample nutrition; control intake of offending sugar</td>
<td>CF₄ sugar-free formula, milk-based; mono- or disaccharide may be added as needed</td>
<td>Nestle Co. (Australia) product</td>
<td>16 of 20 good to excellent</td>
<td>adequate with vigilance for hypoglycemia and hypokalemia</td>
<td>Walker-Smith et al., 1973</td>
</tr>
<tr>
<td>Sugar malabsorption in infants and children</td>
<td>same as above</td>
<td>CF₄ formula; glucose and fructose</td>
<td>1 percent increments glucose and fructose added periodically to achieve maximum of 4% of each</td>
<td>good</td>
<td>no problems reported</td>
<td>Davidson and Townley, 1973</td>
</tr>
</tbody>
</table>


13 patients: fistulas at 7 sites, esophagus to colon, including pancreatic and biliary.

40 patients: acute exacerbations of chronic inflammatory bowel disease; diagnoses included ileocolitis (15), ulcerative colitis (9), diverticulitis (5), granulomatous enterocolitis (5) and ulcerative proctitis (1).

13 patients: regional enteritis, ulcerative colitis, radiation enteritis (4 with associated short gut syndrome; 3 with intestinal fistulas).

MCT means medium chain triglycerides.
Table 4. The Use of Medical Foods in Diseases of the Pancreas.

<table>
<thead>
<tr>
<th>Disease or disorder</th>
<th>Special dietary objectives</th>
<th>Foods used including commercial items</th>
<th>Efficacy</th>
<th>Safety</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cystic fibrosis of the pancreas</td>
<td>adequate nutrition with minimum digestive demand; correct malabsorption, diarrhea, steatorrhea</td>
<td>Probana, MCT oil&lt;sup&gt;1&lt;/sup&gt;, Nutramigen, Portagen</td>
<td>good (however, see Gupte, 1974; Taubin and Spiro, 1973)</td>
<td>no adverse effects reported</td>
<td>Allan &lt;i&gt;et al.&lt;/i&gt;, 1973; Bender &lt;i&gt;et al.&lt;/i&gt;, 1975; Gupte, 1974; Newmanberger and Howard, 1973; Taubin and Spiro, 1973</td>
</tr>
<tr>
<td>Exocrine pancreatic insufficiency in acute, subacute, and chronic pancreatitis</td>
<td>adequate nutrition with minimum digestive demand; correct malabsorption, diarrhea, steatorrhea</td>
<td>Codelid; Vivonex-HN</td>
<td>good (however, see Taubin and Spiro, 1973)</td>
<td>adequate in clinical setting</td>
<td>Bury &lt;i&gt;et al.&lt;/i&gt;, 1974; Stephens &lt;i&gt;et al.&lt;/i&gt;, 1972; Stephens and Randall, 1969; Taubin and Spiro, 1973; Votik &lt;i&gt;et al.&lt;/i&gt;, 1972, 1973d.</td>
</tr>
</tbody>
</table>

<sup>1</sup>See footnote 5 in Table 3
Group VIII (Colonic and Inflammatory Bowel Diseases) noted that problems of nutrition in inflammatory bowel disease need controlled clinical investigations to determine basic nutritional data in sick patients and to realize the potential of dietary treatment.

However, the cumulative clinical experience with medical foods, intravenous feeding, and combinations of these increasingly demonstrates their efficacy and points the way toward improvement in basic understanding of the nutritional needs of the sick and injured as well as new and better designed medical foods and techniques for their use. Because of the wide scope and large number of entities that may be listed under gastrointestinal disorders, this section is limited to emphasis on principles and objectives of dietary management and typical examples of diseases and disorders that may benefit from medical foods.

The main nutritional objective in diseases and disorders of the gastrointestinal tract is the restoration and maintenance of adequate nutrition during recovery from illness or injury or for the duration of a permanent disorder or incurable disease. From a dietary point of view, probably the most demanding abnormalities affecting physiologic function of the alimentary canal result from interference with digestion, absorption and excretion such as the malabsorption and malabsorption associated with pancreatic insufficiency, malabsorption from damaged intestinal mucosa or sheer lack of sufficient intestinal absorptive area, and disturbed excretion in severe, protracted diarrhea or intestinal obstruction and stasis. Biochemical defects in the small bowel and elsewhere in the body resulting from certain congenital or acquired enzymatic and hormonal deficiencies may adversely influence digestion, absorption, and excretion, as in lactase deficiency, adrenal insufficiency, and uncontrolled diabetes or thyrotoxicosis. Bacterial or viral enteritides and intestinal protozoal infestations may damage gastrointestinal epithelium and change the intraluminal environment thus disturbing nutrition via interference with digestion and absorption and by induction of severe, protracted diarrhea, obstruction, or, in the case of certain intestinal parasites, competition for nutrients.

Primary and secondary malignant neoplasms as well as benign tumors of the bowel cause malnourishment through a variety of effects, including anorexia, stasis, intussusception, and obstruction as well as direct interference with absorptive mechanisms of the gut. Therapeutic radiation of the abdomen and pelvis commonly results in enteritis with damaged blood vessels and mucous membranes of the small intestine, colon, and rectum, decrease in secretion of digestive enzymes, and disturbed absorption. These effects may be intensified when certain chemotherapeutic agents are used in association with radiation (Donaldson et al., 1975). Similarly, some chemotherapeutic agents such as the antimetabolite, 5-fluorouracil, may cause intestinal lesions that result in debilitating diarrhea and malabsorption (Bounous et al., 1971).
Special dietary management in a majority of diseases and disorders of the gastrointestinal tract is intended to nourish the patient while simultaneously minimizing digestive demands on the gut and its appendages, reduce stimulation of digestive secretions, and provide rest to the bowel. These objectives may be met to considerable degree by a nutritionally complete medical food that provides a largely predigested diet with controlled solutes, liquid volume, and low residue. Another significant objective in dietary management is to limit host exposure to nutrients that are toxic or which cannot be metabolized because of an inborn metabolic deficiency. Some primary, secondary and miscellaneous diseases and disorders of the alimentary canal for which medical foods may be useful are listed in the Appendix.

Gluten-sensitive enteropathy (celiac disease, nontropical sprue) is an example of a specific digestive intolerance caused by a toxic effect on the small intestine by the gliadin component of the grain protein, gluten. The basic lesion is atrophy or flattening of the epithelium in the proximal small intestine, with blunted or absent villi, elongation of crypts, and mononuclear infiltration. Associated biochemical disturbances are reduced gut enzyme activities and decreased pancreatic tropic hormone release, with consequent degradation of pancreatic and gallbladder function. A malabsorption syndrome results accompanied by bloating, diarrhea, steatorrhea, and weight loss (Greenberger and Isselbacher, 1974). Although several hypotheses exist regarding etiology of the disorder, its exact pathogenesis remains unknown (Strober et al., 1975; Weiser and Douglas, 1976).

Treatment of gluten-sensitive enteropathy by use of a strict gluten-free diet has been successful in most patients; that is approximately 80 percent of patients according to Greenberger and Isselbacher (1974) and in 100 percent of patients who were judged by Dissanayake and associates (1974) to be observing a strict gluten-free diet. Symptomatic improvement often precedes normalization of the jejunal mucosa by several months. Failure to improve on a gluten-free diet is thought to be related to incorrect diagnosis or the coexistence of another disorder causing maldigestion and/ or malabsorption (Greenberger and Isselbacher, 1974).

Gluten-free flours and other gluten-free products from wheat, rye, oats, and barley are available from regular retail grocery outlets. Rice and corn cereals as well as flours or starches from nongluten-containing edible plants such as rice, corn, lima beans, soybeans, potato, arrowroot, and tapioca are also available. In addition, patients may be instructed on how to avoid dietary items that contain wheat, oats, or rye (including alcoholic beverages derived from wheat or rye) and sauces, and foods made from these sources.

The short gut (bowel) syndrome is a form of malnutrition resulting from an insufficient amount of functioning small bowel; it features intractable diarrhea, steatorrhea, malabsorption, inanition, and weight loss.
This disorder, which usually follows resection of 75 percent or more of the small bowel, causes severe intestinal insufficiency with life-threatening consequences (Voitk et al., 1973b; Voitk and Crispin, 1975; Weser, 1976). With time, the remnant of the small bowel may undergo adaptive changes including lengthening of villi, thickening of the wall, dilation, and a slowing in motility that can result in an increase of absorptive capacity, alleviation of the syndrome and tolerance for a conventional diet (Voitk et al., 1973b). Some investigators suggest that enteric feeding encourages the growth of intestinal mucosa after small bowel resection (Feldman et al., 1974). Voitk et al., (1973b) reported favorable results of using an elemental diet (Flexical®, see Appendix, p 78) in the nutritional management of eight patients with the short gut syndrome. The diet, administered continuously at a controlled rate by nasogastric feeding tube, was well tolerated by all patients. Four were successfully maintained during adaptation for periods of 19 to 52 days; one patient on the medical food alone for 68 days was sufficiently well nourished to tolerate a second operation; three died from causes unrelated to the diet. The authors emphasized the relative safety of oral medical foods versus intravenous hyperalimentation. In patients whose intestinal insufficiency is too great for management with oral feedings alone, intravenous feeding may be advantageously combined with enteric feeding.

Weser (1976) described the usefulness of medical foods as liquid diets in the initiation of oral feeding after small bowel resection; Morgan et al., (1970) reviewed their uses in terms of the abnormal nutritional needs of the sick and injured.

These applications of medical foods take advantage of their pre-digested characteristics (amino acid mixtures, protein hydrolysates, MCT), restricted fat, low residue, and ability for varying dilution and for continuous, controlled rate administration.

Inflammatory bowel disease includes a number of clinical entities, some of which are listed in Table 3. Acute exacerbations may result in a condition of malnutrition from such physiopathologic influences as mal-digestion, malabsorption, severe diarrhea, and steatorrhea. There is an accompanying increase in energy requirements, that is, an excess metabolic demand favoring a catabolic state. In this situation, most patients cannot voluntarily ingest and absorb enough of the high caloric diet needed to compensate for the adverse nutritional state (Rocchio et al., 1974; Stephens and Randall, 1969; Voitk et al., 1973a).

As in the short bowel syndrome, the amount of functional absorptive surface is reduced and a nutritionally complete, predigested, low bulk, low fat, high caloric diet is required to provide the most favorable conditions for enteral nutrition with minimum digestive demands, including minimum
stimulation of exocrine secretion. Ileocolitis, ulcerative colitis, diverticulitis, granulomatous colitis, regional enteritis, and ulcerative proctitis were the diseases of the 40 severely ill patients studied by Rocchiccioli and his coworkers (1974). Dietary management in 22 patients included high caloric intravenous feedings for several days followed by enterically administered medical foods such as Vilonex High Nitrogen® or Codelid® (see Appendix, p 78 and 79); in 18 patients the medical foods were the major source of nutrients. These medical foods were infused at a constant rate via nasogastric feeding tubes. Thus, a total of 40 patients were nourished in this manner for an average of 35 days each.

The medical foods were considered a significant contribution to management of severely ill patients with inflammatory bowel diseases because of the resultant transition from the catabolic to the anabolic state and improved ability to withstand the diseases, their complications, and the associated surgical procedures. For example, a 45-year-old man with a 30-year history of Crohn's enteritis developed partial obstruction with nausea, vomiting, pain, distension, and inanition. Initial treatment included correction of dehydration and electrolyte imbalance, decompression by Miller-Abbott tube, and intravenous feeding. Then, for a period of several weeks, he was fed a medical food by nasogastric tube. During this period he had no obstructive symptoms despite a stenotic ileum, and his nutritional status and psychologic outlook improved remarkably.

It should be recognized that most of the studies reported in this Section were uncontrolled with respect to other diets and the initial treatment of many of the patients included total parenteral nutrition.

3. Liver and Biliary System Diseases and Disorders (See Table 5)

The literature contains few references to the use of medical foods in the management of diseases and disorders of the liver and biliary system. However, certain available medical foods would satisfy the requirement for protein restriction in patients with impending hepatic coma (Koff and Isselbacher, 1974) and for restricting protein and fat in hepatic coma and biliary cirrhosis, respectively. Glucose solutions given by gastric intubation have been used in treating hepatic coma (Tisdale et al., 1974).

For liver diseases such as acute viral hepatitis and uncomplicated cirrhosis, the general dictum of a high caloric, balanced, nutritious diet is readily achieved by use of ordinary foods. Complications and sequelae of certain acute and chronic liver diseases such as portal hypertension with edema, ascites, and hemorrhagic tendency of certain gastrointestinal veins, require a low sodium diet and limited fluid intake; and in hepatic coma and chronic encephalopathy or episodic coma, protein restriction to about 20 to 40 g per day may be helpful (Tisdale et al., 1974). The low protein flours (see Appendix, p 83) are convenient in preparing restricted protein diets.
Table 5. The Use of Medical Foods in Diseases and Disorders Involving the Liver and Biliary System.

<table>
<thead>
<tr>
<th>Disease or disorder</th>
<th>Special dietary objectives</th>
<th>Foods used including commercial items</th>
<th>Comments</th>
<th>Efficacy</th>
<th>Safety</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Biliary fistulas¹</td>
<td>prolonged reduction of blood ammonia, other &quot;toxic&quot; nitrogenous substances; modified amino acid intake to adjust for elevated aromatic amino acids (AAA) and reduced branched chain amino acids (BCAA); substitute alpha-keto analogues of essential amino acids for protein restriction</td>
<td>restrict daily protein to 30 to 40 g; special chemically defined diet to normalize AAA and BCAA in plasma; alpha-keto analogues of valine, leucine, isoleucine, methionine, and phenylalanine</td>
<td>small daily oral doses of neomycin</td>
<td>fair to good; the AAA, BCAA normalization needs validation; the alpha-keto analogue approach experimental</td>
<td>theoretical danger of fatty liver and retarded liver repair on restricted protein diet</td>
<td>Fischer, 1976; Fischer et al., 1976; Maddrey et al., 1976; Tisdale et al., 1974</td>
</tr>
<tr>
<td>Chronicencephalopathy and episodic coma</td>
<td>provide nitrogen-sparing calories; reduce blood ammonia and other &quot;toxic&quot; nitrogenous substances by dietary protein restriction; reduce ammonia formation in gut</td>
<td>20 to 25% glucose solution via nasogastric tube; zero protein at first, then 10 to 20 g increments gradually as patient improves; low protein flours for breads, pastries</td>
<td>use only high biologic value protein; oral neomycin to reduce ammonia formation</td>
<td>fair to good</td>
<td>same as above</td>
<td>Davidson, 1973; Tisdale et al., 1974</td>
</tr>
<tr>
<td>Impending hepatic coma and hepatic coma (hepatoencephalopathy; portal-systemic encephalopathy)</td>
<td>continuous intragastric feeding high dextrin formula at night; frequent oral feedings of high CHO diet daytime to reduce frequency and severity of hypoglycemia</td>
<td>Vivotex at night; high starch oral feedings every 3 hours during the day</td>
<td>status: experimental, continuous nasogastric tube infusion of Vivonex at night</td>
<td>good</td>
<td>needs validation</td>
<td>Greene et al., 1976</td>
</tr>
</tbody>
</table>

¹See fistulas in Table 3.
Catlin (1976) suggested that an amino acid supplement might be helpful in preventing hepatic steatosis in patients with hepatic failure after intestinal bypass surgery for morbid obesity. Greenberger and his associates (1975) reported preliminary experimental data that suggest a role for vegetable protein in treating chronic hepatic encephalopathy, presumably because of its low content of methionine, an apparently encephalopathic amino acid.

A low neutral fat diet limited to about 30 g daily reduced steatorrhea in patients with chronic obstructive jaundice (Rosenoer and Gokim, 1972). The authors recommended that added fats be in the form of MCT from coconut oil. Medium chain triglycerides are easily hydrolyzed in the absence of pancreatic lipase to fatty acids which are absorbed without the need for bile salts, mainly via the portal vein. However, in patients with precoma, MCT may be contraindicated.

Russell (1975) found only one publication related to clinical testing of the concept that nutritionally complete medical foods may reduce the ammonia-producing gut flora and thereby benefit patients with hepatic failure complicating cirrhosis. Blood ammonia levels decreased in four patients fed medical foods; however, the author pointed out that the high amino acid content of many medical foods must be regarded as potentially hazardous in patients with hepatic insufficiency (Russell, 1975).

A patient with a severe malnutrition problem from a combination of chronic pancreatitis, diabetes, and a draining biliary fistula improved significantly on a diet consisting of a nutritionally complete medical food (Stephens and Randall, 1969). The fistula drainage decreased markedly within 72 hours of starting the feeding with Codelid 42 H® (containing 41.2 percent sucrose), thus facilitating surgical correction of the fistula. Currently, these investigators use Vivonex HN®.

Dietary treatment of certain liver diseases, a recognized part of their management, has been accomplished using commonly available foods without a need for medical foods per se. Nevertheless, despite the relative paucity of clinical reports on the use of medical foods in liver and biliary system diseases, certain of them have advantages in preventing and treating some of the serious complications of these diseases and there are indications that their use will increase in these categories as more is learned about the efficacy of the products.
C. DIAGNOSTIC PREPARATIONS

Certain nutrients (mainly simple saccharides and amino acids) are being used in clinical diagnostic tests administered via the oral route. However, the trend in diagnosis is to rely primarily on direct or indirect determinations of substances in blood, other tissues, urine, and feces rather than on loading or tolerance type tests: for example, biochemical and chromatographic determinations of amino acids in the overflow aminoacidurias associated with various disorders of amino acid metabolism.

In some of the rare disorders involving inborn errors of metabolism (Table 6), the diagnostic use of oral nutrients remains investigational as progress is frequently hampered by a scarcity of patients. In many cases such tests are equivocal and require additional validation. Except for certain medical centers with special diagnostic resources, current usage of nutrient preparations in diagnosis appears to be modest. Obviously this does not apply to such long established and widely accepted procedures as the glucose tolerance and xylose tests. However, additional diagnostic uses of orally administered nutrients will probably evolve with an increased understanding of the relationships between diseases and disorders and the digestion, absorption, metabolism and excretion of certain regular dietary components.

Specific nutrients currently used in diagnostic tests are listed in Table 7. A number of these substances, e.g., glucose, sucrose, and starch, are generally recognized as safe (Office of the Federal Register, 1977; 21 CFR 182.1, formerly 21 CFR 121.101). Others, such as amino acids, are otherwise regulated food ingredients (Office of the Federal Register, 1977; 21 CFR 172.852, formerly 21 CFR 121.1004). While special precautions must be observed in some cases, the diagnostic uses of these nutrients are generally without hazard to the patient. Oral doses are administered, and blood or urine samples are monitored over prescribed periods of time.

Although this report does not include consideration of vitamins as medical foods, they are given orally in several diagnostic tests including absorption tests for folic acid, vitamins A and B₁₂, and a tolerance test for vitamin A. Medical foods are not ordinarily used in oral allergy testing.

The specialized use of nutrients for diagnostic purposes appears separate and distinct from the uses of other preparations included in the broad definition of medical foods. While these diagnostic aids are nutrients and are components, they are not administered to meet a well-established nutritional requirement. Similarly, they are not foods for special dietary use in the sense that they supply or supplement a special dietary need. For these reasons, it is suggested that nutrients for diagnostic purposes be set apart from the categories defined as medical foods in a separate regulatory status, "Nutrients for Diagnostic Use."

- 37 -
<table>
<thead>
<tr>
<th>Disease or disorder</th>
<th>Special dietary objectives</th>
<th>Foods used including commercial items</th>
<th>Comments</th>
<th>Efficacy</th>
<th>Safety</th>
<th>References</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fructosemia (hereditary fructose intolerance)</td>
<td>exclude fructose from the diet to prevent malnutrition and severe metabolic derangement in infants and hypoglycemia, gastrointestinal and metabolic disturbances in adults</td>
<td>fructose-free diet, relatively difficult to design because of presence of fructose in most CHO-containing foods</td>
<td>lifetime restricted diet probably necessary; differentiate from benign fructosuria</td>
<td>good</td>
<td>adequate</td>
<td>Bickel et al., 1973; Froesch, 1972</td>
</tr>
<tr>
<td>Galactosemia (galactose-1-phosphate uridyl transferase deficiency type; and galactokinase deficiency type)</td>
<td>exclude milk, lactose, and galactose from diet for infants, lactose-free formulas such as MFB, Lambase, Nutramigen, and CHO-free; for all others, lactose-free common foods</td>
<td>lifetime restricted diet probably necessary</td>
<td>good if diet rigidly observed and started before brain damage</td>
<td>precise clinical and parental monitoring required</td>
<td>Bickel et al., 1973; Koch et al., 1965; Segal, 1972</td>
<td></td>
</tr>
<tr>
<td>Histidinemia</td>
<td>reduce and maintain blood levels of histidine within normal limits</td>
<td>histidine-free amino acid preparation; Histidine-low</td>
<td>diet controls plasma biochemical parameters</td>
<td>questionable needs further study</td>
<td>more data needed</td>
<td>Bickel et al., 1973; Ghadimi, 1974</td>
</tr>
<tr>
<td>Homocystinuria</td>
<td>adequate nutrition; prevent hypermethioninemia; reduce methionine and increase cystine intake; correct homocystinemia and homocystinuria</td>
<td>low methionine chemically defined diet; natural high biologic value protein for minimum methionine; Albumaid X Met, CM-AM, Sobee powder, Metinaid, 3200-K</td>
<td>some patients respond adequately to oral pyridoxine without need for special diet</td>
<td>promising; needs more validation</td>
<td>Bickel et al., 1973; Perry, 1974</td>
<td></td>
</tr>
<tr>
<td>Lactose malabsorption</td>
<td>restrict or exclude lactose in the diet</td>
<td>for infants, same as in galactosemia; for all others, restrict amount of lactose or use lactose-free diet</td>
<td>some persons tolerate moderate amounts of lactose; low lactose skim milk promising</td>
<td>good</td>
<td>adequate</td>
<td>Bickel et al., 1973; Francis, 1974; Turner et al., 1976</td>
</tr>
<tr>
<td>Maple syrup urine disease (a branched chain amino acid disorder)</td>
<td>restrict intake of leucine, isoleucine, and valine to maintain their blood levels in normal limits</td>
<td>protein restricted diet containing low levels or no leucine, isoleucine, and valine; ILV-AM, MSUD-Aid, Gibco product</td>
<td>natural protein or pure amino acids for tolerable intake of the offending amino acids</td>
<td>good if started before brain damage</td>
<td>precise clinical monitoring and parental supervision needed</td>
<td>Bickel et al., 1973</td>
</tr>
<tr>
<td>Condition</td>
<td>Prevention/Management</td>
<td>Outcome</td>
<td>References</td>
<td></td>
<td></td>
<td></td>
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<tr>
<td>Methylmalonic acidemia (vitamin B&lt;sub&gt;12&lt;/sub&gt; unresponsive, types I and II)</td>
<td>prevent ketotic hyperglycinemia, dehydration, restrict protein so that isoleucine, threonine, valine, and methionine limited to growth requirements; synthetic diet low in precursors of propionate and methyl malonate</td>
<td>good; however, clinical experience limited</td>
<td>Giorgio &lt;i&gt;et al.&lt;/i&gt;, 1976; Morrow, 1974; Nyhan &lt;i&gt;et al.&lt;/i&gt;, 1973 Rosenberg, 1972; Shih &lt;i&gt;et al.&lt;/i&gt;, 1976</td>
<td></td>
<td></td>
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<tr>
<td>Phenylketonuria</td>
<td>adequate nutrition; prevent abnormal accumulation phenylalanine, phenyl pyruvic acid, other phenolic compounds; achieve normal phenylalanine blood level; prevent complications of over-restriction of phenylalanine</td>
<td>protein restricted diet; specifically, phenylalanine restriction; Lofenelac, Albumat, Cymogram, Minafen, Aminogran, P-AM</td>
<td>use high biologic value natural protein to meet minimum phenylalanine needs if the medical food contains insufficient phenylalanine</td>
<td>Bickel &lt;i&gt;et al.&lt;/i&gt;, 1973; Hambraeus &lt;i&gt;et al.&lt;/i&gt;, 1971</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tyrosinemia, type II</td>
<td>reduce and maintain blood levels of tyrosine within normal limits; correct eye and skin lesions and possibly prevent mental retardation</td>
<td>low tyrosine, low phenylalanine milk substitute; Mead Johnson 3200 AB</td>
<td>pathogenesis not fully known</td>
<td>Buist &lt;i&gt;et al.&lt;/i&gt;, 1974; Goldsmith and Reed, 1976</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Urea cycle enzyme deficiencies</td>
<td>reduce hyperammonemia, promote growth; prevent mental and physical impairment</td>
<td>keto-analogues of essential amino acids</td>
<td>good for eye and skin lesions; questionable in brain damage</td>
<td>Batshaw &lt;i&gt;et al.&lt;/i&gt;, 1975, 1976; Thoene &lt;i&gt;et al.&lt;/i&gt;, 1977</td>
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</tbody>
</table>
Table 7. Clinical Tests Using Nutrients as Oral Diagnostic Aids.

A. Tests Commonly Listed in Current Clinical Laboratory Texts.

<table>
<thead>
<tr>
<th>Test</th>
<th>Purpose/remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Alanine load</td>
<td>Detection of vitamin B₆ deficiency</td>
</tr>
<tr>
<td>Fructose tolerance</td>
<td>Liver metabolism; diagnosis of fructosuria and fructose intolerance</td>
</tr>
<tr>
<td>Galactose tolerance</td>
<td>Liver metabolism; diagnosis of galactosuria and galactosemia (avoid in small infants; safety of test in galactosemia controversial)</td>
</tr>
<tr>
<td>Glucose-galactose tolerance</td>
<td>Verification of results of lactose tolerance if low; glucose-galactose malabsorption</td>
</tr>
<tr>
<td>Glucose tolerance</td>
<td>Diagnosis and management of diabetes mellitus; diagnosis of von Gierke's disease, infantile celiac disease, hyper- and hypoglycemic states</td>
</tr>
<tr>
<td>Histidine load</td>
<td>Detection of vitamin B₆ deficiency</td>
</tr>
<tr>
<td>Lactose tolerance</td>
<td>Lactase deficiency; lactose intolerance</td>
</tr>
<tr>
<td>Leucine sensitivity</td>
<td>Differential diagnosis of hypoglycemia</td>
</tr>
<tr>
<td>Methionine load</td>
<td>Identification of heterozygotes of cystathioninuria and homocystinuria</td>
</tr>
<tr>
<td>Phenylalanine load</td>
<td>Identification of heterozygotes of phenylketonuria</td>
</tr>
<tr>
<td>Sucrose tolerance</td>
<td>Disaccharidase deficiency; disaccharide malabsorption</td>
</tr>
<tr>
<td>Trytophan load</td>
<td>Detection of vitamin B₆ deficiency; aid diagnosis of Hartnup disease, kynureninase abnormalities and acrodermatitis enteropathica</td>
</tr>
<tr>
<td>Xylose excretion</td>
<td>Carbohydrate absorption; pancreatic insufficiency vs other causes of steatorrhea</td>
</tr>
</tbody>
</table>
B. Tests Listed in Specialty Texts and Clinical Investigative Literature.

<table>
<thead>
<tr>
<th>Test</th>
<th>Purpose/remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Branched chain amino acids tolerance</td>
<td>Maple syrup urine disease; other branched chain aminoacidopathies</td>
</tr>
<tr>
<td>Gliadin sensitivity</td>
<td>Diagnosis of gluten-induced enteropathy</td>
</tr>
<tr>
<td>Kynurenine tolerance</td>
<td>Diagnosis of Hartnup disease</td>
</tr>
<tr>
<td>Lysine tolerance</td>
<td>Diagnosis of cystinuria and its subtypes; Group I hyperlysinemia</td>
</tr>
<tr>
<td>Maltose tolerance</td>
<td>Maltase deficiency</td>
</tr>
<tr>
<td>Radioactive protein absorption test</td>
<td>Estimation of absorption of protein in diagnosis of digestive and absorptive disorders</td>
</tr>
<tr>
<td>Starch tolerance</td>
<td>Amylase deficiency</td>
</tr>
<tr>
<td>$^{131}$I-triolein and $^{131}$I-oleic acid absorption</td>
<td>Estimation of absorption of neutral fats and fatty acids in diagnosis of digestive and absorptive disorders</td>
</tr>
</tbody>
</table>
VI. PROJECTED USE

Research, clinical experience, and technical development during the past three decades have established the value of medical foods in patient nutrition and dietary management of a wide variety of diseases and disorders. Additional research and clinical experience can be expected to provide a basis for continued evolution of products that meet special nutritional requirements of a broader array of diseases and disorders. Similarly, evolving concepts in health care delivery and long-term maintenance of patients with chronic diseases suggest that applications of medical foods will expand substantially.

Most investigators with experience in this field have concluded that medical foods are a significant development that is likely to be of therapeutic value to an increasing number of patients (Kark, 1974; Russell, 1975). In a survey of opportunities and needs in research on digestive diseases, Fordtran (1975), without specifying intravenous or enteral, suggested that hyperalimentation is a major advance and called attention to an urgent need for development of specific alimentation programs for given diseases. Walker-Smith et al. (1973) referred to an improved formula, CF₁, as a versatile and effective preparation which may be used in management of all types of sugar malabsorption in infants.

Among the shortcomings of some of the current products is the relative rigidity of fixed formulas. Flexibility is a highly desirable quality, and it has been suggested that the concept of modularity might be advantageous in this respect. In addition, as was emphasized on page 20, there is an urgent need for data to compare different preparations in terms of their efficacy in dealing with various diseases and disorders in order to improve the scientific bases for the development and use of medical foods. Acknowledging that formulations of medical foods will continue to develop, attain greater flexibility of use in meeting individual patient nutritional needs, and have a wider spectrum of clinical use in the future, Young et al. (1975) have pointed out that optimal utilization of these diets will be achieved when physicians become more aware of their availability and apply such information appropriately to meet patient needs.

The growing significance of medical foods is evident from the recent formation of the American Society for Parenteral and Enteral Nutrition (ASPEN). Organized in 1975, this new professional scientific society has as its primary goal the enhancement of patient care through dissemination of information on parenteral and enteral nutrition. Symposia, workshops, a newsletter and a scientific journal are being used to communicate research findings, clinical experience, and related information. A statement on
their programs and plans is available from the ASPEN National Office, 6900 Grove Road, Thorofare, New Jersey 08086.

A second important development is recognition of the need for increased funding for research on certain topics related to medical foods. For example, the National Cancer Institute (1976) has a Diet, Nutrition, and Cancer Program to develop and disseminate information on the inter-relationships between diet and nutrition, cancer etiology, patient therapy, and rehabilitation. Within the topical areas of therapy and rehabilitation, research on parenteral and enteral nutrition for cancer patients is identified as having high priority.

Butterworth and Blackburn (1975) have called attention to the number of hospital patients that are malnourished, the growing appreciation of the role of nutrition in patient recovery, and the development of products that enhance the ability of the physician and dietitian to provide nutritional support. They suggested that more widespread use of clinical and laboratory methods of nutritional assessment of patient status will lead to significant improvement in quality of health care in hospitals. The expanding role of the clinical dietitian in improving dietary management of patients has been recognized (Bonnell, 1974). Renewed emphasis in teaching and training programs related to clinical and applied nutrition education is evident (Jacobson, 1975).

The observations reported in the preceding paragraphs reflect a growing awareness of the potential for expanded use of parenteral and enteral nutrition in medical management of diseases and disorders. This trend is evident in the several scientific and technical areas involved; that is medicine, dietetics, hospital management and food technology as well as clinical nutrition per se. However, definitive data to document this trend are fragmentary.

Saperstein et al. (1974) noted that the increased clinical use of medical foods has spurred further research to support product development and specific product claims. They estimated the 1974 United States market for sales of medical foods alone was approximately 10 million dollars. If special dietary items for inborn errors of metabolism, allergenic conditions, and parenteral products were included, the total market sales were about 35 to 40 million dollars annually. Saperstein et al. (1974) concluded that the number and total sales of commercial products would continue to grow as hospital personnel became more aware of the convenience, safety, and overall cost reduction (as compared to ad hoc on-site preparation) of commercially prepared medical foods.

Based in part on the successful development of prepackaged blended foods for use in the space flight program, a number of food and pharmaceutical manufacturers have entered or considered entering the medical
foods market. Analysis of the feasibility of developing and marketing a commercially prepared medical food was conducted by Robert S. First, Inc. (New York, N.Y. 10017), market analysts. In a report to their client in August, 1974, they indicated that wider recognition of the benefits and potential of controlled parenteral and enteral nutrition is occurring at an accelerated pace. Sales of nutritionally complete medical foods were estimated to be in excess of $3 million; of other medical foods (sic, semi-synthetic diets), about $10 million; and intravenous protein solutions approximately $4 million. An analysis of marketing patterns in mid-1974 indicated that over half of these products are sold in 16 percent of the U.S. hospital capacity. The majority of total parenteral and enteral nutritional products were administered to surgical patients, primarily those with gastrointestinal diagnoses.

The report concluded that changing patterns of health care delivery and long-term management of patients with certain disorders such as cancer suggest the market for parenteral and enteral nutritional products will expand. In addition, it was noted that the market potential for enteral products is significantly underdeveloped at the present time and is expected to grow much more rapidly in the next decade than the corresponding market for products used in intravenous hyperalimentation. The market for intravenous products in 1980 was estimated at two or three times its 1975 sales volume.

While not strictly a nutritional issue, this market analysis identified palatability and taste fatigue from prolonged use as two important factors that could affect patient acceptability and, consequently, estimates of projected use of medical foods in the next decade.

It seems reasonable to conclude that most evidence indicates the number of products, as well as the volume and frequency of use, can be expected to increase substantially in the foreseeable future.
VII. SUGGESTIONS ON GUIDELINES

A. BASIC ASPECTS

Because specific commercial products are being formulated to meet the nutritional needs of patients requiring close dietary supervision, there is a need for guidelines on the type of information which should be available for nutritionally complete and nutritionally incomplete medical foods. Guidelines for information on components of medical foods would depend on the product and its intended use; however, in all cases, brochures or ancillary information on dietary products and preparations useful in medical management of diseases, disorders, or special conditions should include:

- **Chemical Composition**: including actual ingredients and their sources where possible (e.g., acid modified starch from corn) and nutritional information per container and per 1000 kcal,

- **Physical Properties**: stability, shelflife, dilution directions if necessary, osmolality and physical specifications,

- **Purpose of Use**: indicating conditions, disorders or diseases in which the product was known to be effective and the rationale for its use,

- **Directions, Recommendations, and Suggested Users**: (may be combined with purpose),

- **Effects of Product Use**: including evidence of efficacy, anticipated medical benefits, indications, contraindications and side effects,

- **Tolerances and Effective Use Levels**

- **Pertinent Reference Materials**: including animal studies and clinical reports if appropriate.

As indicated previously, it may not be necessary to indicate all such information on the professional labels, but a statement of its availability should be included on the label. This requirement is essentially no different from the current situation, because most manufacturers do prepare statements which contain this information on the particular product. Furthermore, most of the information on nutrients that would be used in professional inserts or patient labels is already common knowledge and would not require extensive study. There is a need to maintain flexibility because rigid
regulation may be counter-productive to the development and use of these special dietary foods for several readily apparent reasons.

First, current formulation and usage of these products are for the most part, based on generally accepted principles of sound human nutrition. Since their early experimental use nearly 75 years ago, medical foods have been developed as special food products by medical researchers and responsible pharmaceutical or food manufacturers with the intimate cooperation of practicing physicians. Some of these products, during the previous period of classification as drugs, have a long history of clinical study; others have been prepared on an ad hoc basis concomitantly with critical clinical investigations for management of inborn errors of amino acid or carbohydrate metabolism.

Second, physicians have met the special medical dietary requirements of patients with life-threatening or disabling conditions by formulating individual patient diets on an ad hoc basis. In these instances there is no readily available commercial product; indeed, the demand is so small that it may not be economically feasible to manufacture and distribute such special food products. Formulation of these dietary preparations in hospital diet kitchens and other sources of ad hoc preparations is typically under the direction of a dietitian and would be consistent with principles of sound nutrition.

Finally, most preparations that are formulated either commercially or on an ad hoc basis for oral use as medical foods contain materials that are utilized in other processed foods or are naturally present in foods.

Thus, the issue becomes not registration for regulation of medical foods per se, but the regulation, or suggested regulation, of the use of medical foods. If use of medical foods is the issue, then the labeling question becomes one of providing sufficient information with the product so that the user knows what the product contains and how to use it. Similarly, there is an equal need for a label or insert that informs the physician of its composition, its nutritive value, directions for use and any contraindications or other precautions important when treating individuals with specific disorders or diseases.

If the subject of regulation of use becomes the primary issue, then there is a further need to discriminate or to differentiate patterns of usage by normal individuals recovering from surgery or trauma and types of use by individuals that have some specific disease or disorder. In part, this issue has been addressed with respect to nutritionally incomplete medical foods for inborn errors of metabolism. In these instances, products are available that do not have a normal distribution of nutrients in the sense that they have nutrients added or deleted (e.g., Lofenalac® for PKU). Consumption of this product as a sole nutrient source by normal individuals would
be nutritionally unsound; yet as a portion of an otherwise nutritionally ade-
quate diet it would be economically unsound but without nutritional hazard.

B. PRODUCT INFORMATION

Examination of the product labels, package inserts and brochures collected for this study (see p 74), revealed a diversity in scope and content that was usually consistent with the complexity of the product and the degree of caution and special vigilance required in its use. However, some labels and package inserts lacked essential information for the physician and other professional personnel or for the consumer. Frequently consumer information was inadequate or nonexistent.

For some products, information such as file cards, labels, or brochures, reprints of pertinent scientific literature and free professional diet counsel are available from the manufacturer upon request.

As a general guide, it is suggested that labels, package inserts and possible consumer information for all types of medical foods (nutritionally complete, nutritionally incomplete, components) should contain sufficient, but not excessive information. Certain detailed and explicit information is needed by the physician, pharmacist, and the nutritionist. The supervising dietitian requires complete directions on the preparation of certain medical foods, and nurses and technicians require carefully designed instructions on methods of administration, particularly for tube feeding. The patient-consumer needs information about the nature and purpose of medical foods and directions and precautions in their use. The consumer information should be aimed at those with average reading ability and comprehension and should be based in part on the assumption that the consumer will wish to rely primarily on the attending physician, nutritionist or dietitian for detailed professional guidance.

Suggested types of information for professional personnel and patient-consumers of relatively complex medical foods are outlined in the following, which takes into account the currently emphasized principle of consumers' "right to know."

Labels, package inserts and brochures for professional use

Minimum acceptable information should include:

a. Product definition including source of nutrients (e.g., acid modified starch from corn), trade name, manufacturer, type (e.g., nutritionally complete medical
food, low protein, high calorie formula, low phenylalanine formula) and a general description of the product,

b. Complete nutritional composition per package and per 1000 kcal; rationale for use and special characteristics,

c. Clinical indications for use, dosages and methods of administration,

d. Instructions on preparation for use and storage,

e. Precautions and contraindications,

f. Availability and sources of additional information including scientific references and professional diet counsel,

g. Supply information (type, size, weight, etc., of packaged product),

h. Expiration date.

A sample of an adequate professional package insert for a nutritionally complete medical food is shown in Figure 1.

Labels and other sources of information for patients

a. Product trade name and manufacturer

b. In clear lay terms:

(1) Type of product
(2) Purpose of product
(3) Nutritional adequacy (complete or supplement); list of nutrients and percent U.S. RDA (or RDA) by age groups supplied per unit weight or volume; and approximate analysis by protein, fat, carbohydrate, minerals, and vitamins
(4) Directions for use
(5) Precautions, contraindications, and emphasis on use only under supervision of a physician
(6) Availability of additional consumer information from the manufacturer including recipes
(7) Resupply information when appropriate
(8) Expiration date

A sample of an adequate package label for patient use of a nutritionally complete medical food is shown in Figure 2.
Mederga, Inc.

Supermute®. Supermute® is a nutritionally complete, water soluble, low-residue diet formulated for patients with impaired digestion and malabsorption. It is suitable for both oral and tube feeding. Supermute® contains balanced proportions of all essential nutrients in their simplest, readily absorbable forms: pure amino acids, medium chain triglycerides (MCT), simple sugars, vitamins and minerals.

**Composition.** Three packets provide 1000 kcal and 6 g of available nitrogen at 1 kcal per ml at the recommended dilution:

<table>
<thead>
<tr>
<th></th>
<th>amount</th>
<th>energy distribution</th>
</tr>
</thead>
<tbody>
<tr>
<td>Calories</td>
<td>1000 kcal</td>
<td></td>
</tr>
<tr>
<td>Protein (equivalent)</td>
<td>37.5 g</td>
<td>15.0 %</td>
</tr>
<tr>
<td>Carbohydrate</td>
<td>200 g</td>
<td>80.0 %</td>
</tr>
<tr>
<td>Fat</td>
<td>5.5 g</td>
<td>5.0 %</td>
</tr>
<tr>
<td>Inositol acid</td>
<td>2.0 g</td>
<td></td>
</tr>
<tr>
<td>MCT</td>
<td>3.5 g</td>
<td></td>
</tr>
</tbody>
</table>

(composition continued): List all essential and nonessential amino acids and essential vitamins and minerals including amounts and percent. Recommended Dietary Allowances per 1000 calories.

Actions and Uses. Supermute® complete medical food is a partially pre-digested, easily absorbed, low residue diet that provides adequate nutrition, minimizes digestive demands, and facilitates nutrient absorption with minimal alimentary tract activity.

Supermute® is useful in the dietary management of patients with impaired digestion and absorption secondary to a variety of diseases and disorders such as short bowel syndrome, inflammatory bowel disease, gastrointestinal tract fistulas, acute pancreatitis and pancreatic insufficiency. In convalescents, it fills the need for a transition diet between parenteral and normal oral feeding; it is also useful as an aid in preparing the bowel for diagnostic and surgical procedures.

Six packets of Supermute® mixed thoroughly with ml of water provide a full day's supply for the average adult. One packet of Supermute® diluted with ml of water makes a single serving. Because Supermute® is perishable when diluted, no more than one day's supply should be prepared in advance. Unused portions should be stored in a refrigerator, but not for more than twenty-four hours.

For oral use, Supermute® should be served chilled and swallowed slowly. Sipping through a straw and varying the flavor choices may improve patient acceptability. Supermute® may also be given via nasogastric tube, or via a gastrostomy or jejunostomy.

During the first two days of use, because Supermute® is hyperosmolar at the 1 kcal per ml dilution, it should be further diluted to one-half to three quarters strength until patient tolerance is established (usually within forty-eight hours). At the 1 kcal per ml dilution, Supermute® supplies most of the daily fluid requirements; however, additional fluids should be given when necessary to maintain adequate urinary output. For tube feedings, the diet should be at room temperature and given at a controlled rate of approximately 150 ml per hour, depending on the patient's tolerance.

Precautions and Adverse Reactions. Nausea, vomiting, abdominal cramps and diarrhea have been reported. These reactions may be eliminated or minimized by initial adjustment of the rate of administration and the concentration of the diet to one-half strength, gradually returning to full strength during the first forty-eight hours. Site of individual feedings may require individual patient adjustment. To prevent regurgitation and possible aspiration in tube feeding, precise placement of the tip of the nasogastric tube in the stomach is mandatory. Patients sometimes show poor acceptance of oral feedings with this type of diet because of taste and the lack of the usual appetite cues of normal meals. Varying the available flavors, serving chilled or with ice cubes and sipped through a straw, or serving frozen, and education and motivation of the patient as to the therapeutic importance of this form of diet are reportedly effective in improving patient acceptability.

Additional professional and technical information and professional diet advice are available on request to: Director of Research, Clinerg, Inc., (address and telephone number).

Supply Information. Supermute® is supplied in two sizes of packages. For preparing a full day's supply, it is available in cases of twelve g sealed packages, each providing 2000 kcal. For individual servings, it is available in boxes of thirty-six g packets, each providing 333 kcal. Six flavors are available: Chocolate, Bouillon, Vanilla, Strawberry, , , and .

Figure 1. Example of a Professional Package Insert for a Nutritionally Complete Medical Food.
SUPERNUTE® Complete Medical Food. A nutritionally complete special dietary preparation for patients who need an easily digested, readily absorbed low-residue diet that can be consumed by mouth or tube.

SUPERNUTE® is available in two package sizes:  grams (___ oz.) and  grams (___ lb.), in six flavors: chocolate, bouillon, vanilla, strawberry, ______ and ______.

POWDERED MEDICAL FOOD

Use Only Under the Direction of a Physician

Vanilla Flavored

Net Wt. ___ grams (___ oz.)

SUPERNUTE® Complete Medical Food.

Directions. Thoroughly mix one packet of Supernute® in ___ ml (___ oz.) cold water. Chill or add ice cubes before serving. Provides 1 Calorie per ml, 30 Calories per fluid ounce.

Precautions. To prevent abdominal discomfort when starting to use this product, dilute to one-half strength and gradually increase to full strength (one packet in ___ oz. water) during the first two days of use. Unused portion may be safely stored in your refrigerator for up to 24 hours.

Ingredients. List of all nutrients by name only.

CLINERG, INC.
(address and telephone number),

Figure 2. Example of a Package Label Suitable for Patient use of a Nutritionally Complete Medical Food.
For the nutritionally incomplete medical foods such as Lofenelac®, similar amounts of professional and consumer information would suffice but contraindications for use should be emphasized. For example, see the professional package insert information (Figure 3) and other examples of a patient package label for a nutritionally incomplete medical food (Figure 4). Examples of professional and patient information inserts and labels for components of medical foods are given in Figures 5 and 6.

Finally, in all cases the scope and content of required product information depend not only on the complexity of the preparation but also on the nature of the disease or disorder involved and the possible adverse effects of misuse of the product or failure to observe mandatory precautions. This means that, while general guidelines for product information are useful, labels and other information for specific products must be determined on an individual basis.
Metabolics, Inc.

Lo-Pen® Powder. Lo-Pen® Powder is a specially formulated dietary preparation for phenylketonuric infants and children that supplies all essential nutrients except phenylalanine. For use only as directed by a physician.

Composition: (1. A statement of all nutrients including percentage composition by weight of all ingredients that contribute 0.1 percent or more of the total; 2. The estimated phenylalanine content in percent of the total; 3. The approximate analysis of product in percent of protein (equivalent), fat, carbohydrate and minerals; 4. The energy content and the amount of phenylalanine per 100 g Lo-Pen® Powder).

Lo-Pen® is an incomplete diet because it has insufficient phenylalanine for normal growth at certain ages.

Actions and Uses: For the dietary management of infants and children with phenylketonuria. Consult the company brochure for suggestions on diet supplementation.

Preparation: (Directions for mixing with water to make specific amounts of infant formula and mixtures for young children; storage and serving instructions. Include a statement of the amount of phenylalanine provided per kg body weight when fed at a level of 100 kcal., and a comment regarding the need for individualizing food supplements for adequate energy and phenylalanine intake).

Precautions and Contraindications: Lo-Pen® Powder is intended solely for use in the dietary management of infants and children with phenylketonuria. It should not be used for normal persons. Frequent clinical monitoring of patients using this product is mandatory to assure sufficient energy and phenylalanine intake for growth and development. Detailed professional information and diet counseling are available on request to: Medical Director, Metabolics, Inc. (Address and telephone number).

Supply Information: Lo-Pen® Powder (stock number) is available in 1 kg (2.2 lb) cans, sold separately or in cases of six cans.

Figure 3. Example of a Professional Package Insert for a Nutritionally Incomplete Medical Food.
NoCho® powder is a carbohydrate-free diet base supplemented with vitamins and minerals. NoCho® is intended for the dietary management of infants and children with sugar intolerance. When carbohydrates are added as recommended below, NoCho® provides a nutritionally complete diet.

**NOCHO® Powder**

**FORMULA BASE**

Use Only as Directed by a Physician

<table>
<thead>
<tr>
<th>Composition: (A statement of the ingredients contained per 100 g of prepared formula; approximate analysis, giving percent water, protein, fat, carbohydrate and minerals when undiluted and when diluted to 1 liter; and energy supplied per 30 ml (fluid ounce) of prepared product)</th>
</tr>
</thead>
<tbody>
<tr>
<td>A table of vitamins and minerals in both undiluted and diluted modes including percent of U.S. R.D.A. for infants and for children less than four years old in terms of percentage U.S. R.D.A. per 1000 Calories.</td>
</tr>
</tbody>
</table>

**Directions: (Instructions on how to prepare, store, and use including directions for the necessary selected supplemental carbohydrate solution to be combined with NoCho®).**

Pediatrics Specialties, Inc. (address)

Figure 4. Example of a Patient Package Label for a Nutritionally Incomplete Medical Food.
MSUD-TEK®

FOR THE TREATMENT OF MAPLE SYRUP URINE DISEASE

Use only under the supervision of a physician

MSUD-TEK® is a mixture of pure amino acids free from the branched chain amino acids that should not be ingested in excessive amounts by persons with maple syrup urine disease. MSUD-TEK® is not a complete meal, and must be supplemented with sufficient carbohydrate, fat, vitamins and minerals to meet daily nutrient and total caloric needs as advised by a physician.

MSUD-TEK®

Composition per 100 grams or per 1000 Calories (list amino acids and indicate percent U.S. RDA in protein equivalents for infants and children under 4 years old).

HEALTH CHEMICALS, INC.

Precautions: Close laboratory monitoring is mandatory to preclude excess or insufficiency of the branched-chain amino acids. When plasma levels decline to normal it is essential to restore these amino acids to the diet in regulated amounts.

Net Weight: 240 grams (8 oz)

Figure 5. Example of a Professional Package Insert for a Component of a Medical Food.
Speducts, Inc.

ERGS® Liquid.

ERGS® Liquid is a high carbohydrate energy source featuring low electrolytes, low protein and fats, limited fluid volume, and a pleasing taste for patients needing additional Calories.

Composition: ERGS® Liquid contains demineralized, high fructose corn syrup (DE: ___), demineralized water and artificial flavoring. Each 120 ml (4 fluid ounce) can of ERGS® Liquid contains: (list total Calories and all ingredients in percent w/w and actual amounts in terms of amounts per 1000 kcal and U.S. RDA when available).

Actions and Uses: ERGS® Liquid is recommended as a supplemental source of energy for persons on restricted diets such as patients with chronic renal failure or hypermetabolic states. One four-ounce can supplies 1000 kcal, controlled amounts of electrolytes, and only traces of protein. Because of its palatability and the availability of a choice of five flavors, ERGS® Liquid is a psychologic aid in relieving the monotony of restricted diets. Detailed professional literature and dietary advice are available on request from the Medical Director, Speducts, Inc., (address and telephone number).

Directions: (Instructions on how to prepare in various forms, store, and serve).

Precautions: Because ERGS® Liquid is merely a dietary supplement, the basic nutritional needs of the patient must be properly supplied from other sources as directed by a physician.

Supply Information: (size cans, number of cans per case, names and stock numbers of the flavors).

Figure 6. Example of a Patient Package Label for a Component of a Medical Food.
VIII. LITERATURE CITED


Food and Agriculture Organization of the United Nations. 1974. Table 1 in Handbook of human nutritional requirements. FAO nutritional studies no. 28; WHO Monograph series no 61. Rome.


National Cancer Institute, National Cancer Program. 1976. Diet, nutrition and cancer program. Advisory Committee Meeting, January 13-14, 1976, National Institutes of Health, Bethesda, Md. (Available from Dr. Gio B. Gori, Deputy Director, Division of Cancer Cause and Prevention, National Cancer Institute, Bethesda, Md.)


IX. APPENDIX

A. DISEASES, DISORDERS, AND OTHER CLINICAL INDICATIONS FOR USE OF MEDICAL FOODS

The following list of diseases, disorders, and other clinical conditions is a compilation of medically identifiable states in which dietary management through the use of medical foods may be indicated. While comprehensive, it is incomplete, but suggests the broad range of diseases and disorders in which special attention to meeting nutritional needs should be included in the treatment regimen.

1. Diseases and Disorders of or Influencing the Gastrointestinal Tract.

   a. Inflammatory Bowel Diseases

      Colitis
      Crohn's disease (regional enteritis)
      Diffuse inflammatory disease of the small bowel (ileojejunitis, nonstenosing ileojejunitis)
      Diverticulitis of the colon
      Diverticulitis of the small bowel
      Enteropathy from radiation or chemotherapeutic agents
      Granulomatous gastritis
      Granulomatous ileitis
      Ileocolitis
      Irritable colon (bowel) syndrome

      Infestations
      Amebiasis
      Coccidiosis
      Flukes
      Giardiasis
      Nematodes
      Tapeworms

      Subacute and chronic infections
      Actinomycosis
      Cholera
      Enteritis from reovirus-like agents
      Enteropathogenic *E. coli* (enterotoxigenic *E. coli*)
      Epidemic hemorrhagic fever
      Rickettsioses
      Shigellosis
Stasis-induced bacterial overgrowth of small intestine
Tuberculous enteritis
Typhoid and paratyphoid fever
Undulant fever
Viral enteritides
Ulcerative colitis and its complications

b. Malabsorption and Deficiency States

Amyloidosis with malabsorption defect
Disaccharidase deficiency
Drug-induced malabsorption (e.g., neomycin)
Glucose-galactose malabsorption
Intestinal bypass malabsorption
Intrinsic factor deficiency
Lactose intolerance (lactase deficiency)
Malabsorption in progressive systemic sclerosis
Monosaccharide malabsorption
Postgastrectomy malabsorption
Senile maldigestion/malabsorption (many causes)
Sucrase-isomaltase deficiency
Vagotomy malabsorption

c. Miscellaneous

Abetalipoproteinemia
Acute, intractable, nonspecific diarrhea in infants and children
Addison's disease (with protein-losing enteropathy)
Allergic gastroenteropathies
Benign tumors causing stasis and/or malabsorption
Collagenous sprue
Congenital and acquired anatomic anomalies of the gut
Congestive heart failure
Constrictive pericarditis
Dermatitis herpetiformis
Gluten-sensitive enteropathy (celiac disease, celiac sprue, nontropical sprue)
Gunshot and other trauma of the gut
Hypogammaglobulinemia
Hypoparathyroidism
Ileostomy and colostomy (reduce fecal output)
Incontinent and/or bedridden patients
Intestinal lymphangiectasia
Malignant tumors (with stasis, obstruction, maldigestion, malabsorption, malnourishment, debilitation)
Mesenteric vascular insufficiency
Pernicious anemia
Preoperative and prediagnostic bowel preparation
Primary aldosteronism
Protein-losing enteropathy (many causes)
Scleroderma
Short gut (bowel) syndrome
Systemic mast cell disease
Tropical sprue
Uncontrolled diabetes mellitus

2. Diseases and Disorders Involving the Kidney.

Arteriolar nephrosclerosis
Bilateral hydronephrosis
Certain collagen diseases
Chronic glomerulonephritis
Chronic pyelonephritis
Crystalline deposits of uric acid and salts
Cystic disease of the medulla
Diabetes mellitus
Drug-induced interstitial nephritis
Nephrotic syndrome
Obstructive nephropathies

3. Liver and Biliary Diseases and Disorders.

Biliary fistula
Cholestasis with steatorrhea
Chronic hepatic encephalopathy
Episodic hepatic coma
Hepatic coma
Hepatic failure associated with -
   Cirrhosis
   Intoxications
   Postintestinal bypass
Impending hepatic coma

4. Pancreatic Diseases and Disorders.

Abscess
Chronic pancreatitis
Diabetes mellitus
Pancreatic insufficiency (cystic fibrosis, tumor, etc.)
5. Inherited Diseases and Disorders\(^1\) (not listed elsewhere in Appendix A).

Of or related to amino acid metabolism
   Hyperglycinemia\(^2\)
   Homocystinuria
   Maple syrup urine disease (branched chain ketonuria)
   Phenylketonuria
   Tyrosinemia\(^3\)
   Tyrosinosis\(^2\)

Of or related to carbohydrate metabolism
   Galactosemia
   Hereditary fructose intolerance
   Type I glycogen storage disease

Of or related to lipid metabolism\(^4\)
   Phytic acid storage disease (Refsum's syndrome)
   Obesity
   Type I hyperlipoproteinemia


   Adult marasmus
   After head and neck surgery requiring extraoral nutrition
   Basic research in nutrition
   Chyluria
   Electrolyte imbalance
   Epilepsy (myoclonic and akinetic seizures in children)
   Extensive burns
   Failure to thrive
   General cachexia
   In transition from parenteral to normal oral nutrition
   Infants with congenital heart disease
   Low birth-weight infants
   Premature infants
   Postlaryngectomy milk intolerance
   Severe multiple trauma
   Therapeutic fasting

\(^1\)Several hundred inborn errors of metabolism have been recognized; many are rare; some cause no symptoms; some can be treated with drugs, vitamins or other means. Examples that may respond to dietary treatment are listed above.

\(^2\)Effectiveness of dietary treatment requires validation.

\(^3\)Tyrosinemia II responds to low phenylalanine, low tyrosine diet.

\(^4\)In general, medical foods have no role in the lipid storage diseases.
B. COMPILATION OF PRODUCTS

This study includes documentation of the number, types, and composition of available products and manufacturers or suppliers marketing or developing special dietary products that might be considered medical foods. In December 1974, a survey of major pharmaceutical and food manufacturers was initiated. A letter of inquiry (Exhibit 1) was sent to firms selected from a list supplied by FDA and from those listed in the Physicians' Desk Reference (1974) and the AMA Department of Drugs (1973). This survey was continued through December, 1975 with a few additions made in 1976 based on advertisements in relevant scientific journals or citations in journal articles.

In the initial survey, 56 firms were contacted and 48 responded. Eleven firms indicated that they did not produce dietary products and 37 supplied brochures, sample labels, or other information. In all, 47 firms were identified as manufacturers of products they identified as prepared for special dietetic use (Appendix C). The data collected in this survey have been collated and supplied to the Office of the Associate Director for Nutrition and Consumer Sciences, Bureau of Foods, FDA. Because these brochures, labels, and related information are, in several instances, proprietary, of transient interest, or outdated, they are not reproduced in this report. Instead, pertinent information has been abstracted in the following tables. Current information on composition and availability of specific products may be obtained from the respective manufacturers (see Appendix C).

There are two cautions with regard to the survey. First, it should be considered incomplete because only 65 firms were surveyed during the 25-month period, (56 initially plus 9 identified in 1976). Requests were not made to all pharmaceutical and food manufacturers indicated in the source lists (approximately 300) nor was the lack of response from nine firms in the initial survey followed up. In addition, no attempt was made to determine availability of medical foods from hospitals, research centers, or private physicians. Second, the initial letter of inquiry intentionally referred to "products that are prepared for special dietetic uses" rather than "medical foods" because the latter term had no accepted uniform definition among manufacturers, physicians, nutritionists and dietitians and might have excluded certain specialized components of medical foods. In most cases, information about specific products was requested; however, a similar letter without reference to specific products was sent to some firms.

The 47 responding firms identified 134 products that were commercially available at that time. The definitions developed in this report (see page 7), were used to categorize these products as follows:
Gentlemen:

We are currently attempting to gather information on products that are prepared for special dietetic uses. I would appreciate receiving information on:

I am particularly interested in sample labels, product composition, and citations to clinical or other studies on these products.

Thank you for your attention to this request.

Sincerely,

Kenneth D. Fisher, Ph.D.
Research Associate
Life Sciences Research Office
<table>
<thead>
<tr>
<th>Classified as medical foods</th>
<th>113</th>
</tr>
</thead>
<tbody>
<tr>
<td>Essentially nutritionally complete</td>
<td>31</td>
</tr>
<tr>
<td>Nutritionally incomplete</td>
<td>34</td>
</tr>
<tr>
<td>Specialized components</td>
<td>48*</td>
</tr>
<tr>
<td>Classified as nutrients for diagnostic uses</td>
<td>1</td>
</tr>
<tr>
<td>Classified as special dietary foods</td>
<td>(54)*</td>
</tr>
</tbody>
</table>

Data on the products considered to be essentially nutritionally complete medical foods are given in Table 8. Those classified as nutritionally incomplete are listed in Table 9 and components in Table 10. Only one product, Glucola® was identified as a nutrient for diagnostic use; however, various amino acids and other sugars are also used as diagnostic aids (see p 40 and 41).

A number of the products identified during the survey were characterized by the manufacturers and suppliers as special dietary foods. As noted in the report (see p 12), not all special dietary foods are medical foods. Examples of special dietary products identified by manufacturers and distributors and not usually considered medical foods, are listed by type in Table 11. Obviously this list is incomplete, includes few over-the-counter weight reduction and other special dietary products, and is presented only because manufacturer representatives provided information on what they considered as "products that are prepared for special dietary uses."

Three additional issues should be noted. First, a total of 34 products considered to be medical foods as defined in this report are generally available as infant foods, hypoallergenic foods or dietary supplements. In the context used in this report, the designation, dietary supplements, is not restricted to supplements containing only vitamins and minerals. These products, listed in Tables 10 and 11 are identified by footnote No. 4. It may be useful to consider those infant foods, hypoallergenic foods, and vitamin and mineral supplements that are specifically formulated to meet a diagnosed nutritional need requiring medical supervision of dietary intake as a subcategory of medical foods rather than infant foods, hypoallergenic foods, or vitamin and mineral supplements per se as they are now defined (Office of the Federal Register, 1977; 21 CFR 105, formerly 21 CFR 125).

Second, the proposed definitions are less than precise and are subject to interpretation. For example, certain products for treatment of inborn errors of metabolism are classified as nutritionally incomplete medical foods because they lack one or more amino acids related to the medical condition. Other products lacking the amino acids are considered components because they do not contain all other nutrients required by

*Thirty-four products were classified as both components of medical foods and special dietary foods.
Table 8. Examples of Nutritionally Complete Medical Foods.

<table>
<thead>
<tr>
<th>Product</th>
<th>Manufacturer or Distributor</th>
<th>Types of Use</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Codelid</td>
<td>Schwarz Mann</td>
<td>Oral or tube feeding in impaired digestion and malabsorption</td>
<td>Product availability unknown</td>
</tr>
<tr>
<td>Compleat-B</td>
<td>Doyle</td>
<td>Blenderized tube feeding formula for continuous total or supplemental feeding by tube</td>
<td>Low cholesterol, controlled sodium</td>
</tr>
<tr>
<td>Ensure</td>
<td>Ross</td>
<td>Oral or tube feeding in impaired digestion and malabsorption</td>
<td>Semi-synthetic preparation</td>
</tr>
<tr>
<td>Flexical</td>
<td>Mead Johnson</td>
<td>Oral or tube feeding in impaired digestion and malabsorption</td>
<td>Semi-synthetic preparation</td>
</tr>
<tr>
<td>Formula 1</td>
<td>Gerber</td>
<td>Primarily for tube feeding in impaired digestion and malabsorption</td>
<td>Supplemented blenderized preparation of common foods</td>
</tr>
<tr>
<td>Formula 2</td>
<td>Cutter</td>
<td>Oral or tube feeding in impaired digestion and malabsorption</td>
<td>Supplemented blenderized preparation of common foods</td>
</tr>
<tr>
<td>HDPC Milk Base Formula 120</td>
<td>Hospital Diet Products Corp.</td>
<td>Primarily for tube feeding where oral ingestion contraindicated</td>
<td>Soya and milk based semi-synthetic preparation</td>
</tr>
<tr>
<td>HDPC Milk Base Formula 125</td>
<td>Hospital Diet Products Corp.</td>
<td>Primarily for tube feeding where oral ingestion contraindicated</td>
<td>Soya and milk based semi-synthetic preparation</td>
</tr>
<tr>
<td>HDPC Meat Base Formula 142</td>
<td>Hospital Diet Products Corp.</td>
<td>Primarily for tube feeding where oral ingestion contraindicated</td>
<td>Soya, milk, and beef based semisynthetic preparation</td>
</tr>
<tr>
<td>HDPC Meat Base Formula 145</td>
<td>Hospital Diet Products Corp.</td>
<td>Primarily for tube feeding where oral ingestion contraindicated</td>
<td>Soya, milk, and beef based semisynthetic preparation</td>
</tr>
<tr>
<td>HDPC Meat Base Formula 155</td>
<td>Hospital Diet Products Corp.</td>
<td>Primarily for tube feeding where oral ingestion contraindicated</td>
<td>Soya, milk, and beef based semisynthetic preparation</td>
</tr>
<tr>
<td>Isocal</td>
<td>Mead Johnson</td>
<td>Oral or tube feeding where normal diet not practical or feasible</td>
<td>Lactose free, low osmolality</td>
</tr>
<tr>
<td>Jejunal</td>
<td>Johnson &amp; Johnson</td>
<td>Primarily for tube feeding in impaired digestion and malabsorption</td>
<td>Semi-synthetic preparation, Product availability unknown</td>
</tr>
<tr>
<td>Lolactene</td>
<td>Doyle</td>
<td>Oral or tube feeding, primarily in lactose intolerance</td>
<td></td>
</tr>
<tr>
<td>MBF</td>
<td>Gerber</td>
<td>Oral feeding for infants and children with milk intolerance</td>
<td>Blenderized liquid formulation</td>
</tr>
<tr>
<td>Meritene-Liquid Nutri-1000</td>
<td>Doyle</td>
<td>Oral or tube feeding where normal diet not practical or feasible</td>
<td>Several formulations, e.g., with milk, available</td>
</tr>
<tr>
<td>Peptrex</td>
<td>Syntex</td>
<td>Oral or tube feeding where normal diet not practical or feasible</td>
<td></td>
</tr>
<tr>
<td>Portagen</td>
<td>Mead Johnson</td>
<td>Oral feeding where normal diet not practical or feasible. Impaired fat absorption</td>
<td>Lactose free, Semi-synthetic preparation</td>
</tr>
<tr>
<td>Precision IR</td>
<td>Doyle</td>
<td>Oral or tube feeding where normal diet not practical or feasible</td>
<td>Low residue, Semi-synthetic preparation</td>
</tr>
<tr>
<td>Product</td>
<td>Manufacturer</td>
<td>Description</td>
<td>Characteristics</td>
</tr>
<tr>
<td>-----------------</td>
<td>--------------</td>
<td>-----------------------------------------------------------------------------</td>
<td>----------------------------------</td>
</tr>
<tr>
<td>Precision HN</td>
<td>Doyle</td>
<td>Oral or tube feeding where normal diet not practical or feasible</td>
<td>High nitrogen. Semi-synthetic preparation</td>
</tr>
<tr>
<td>Precision MN</td>
<td>Doyle</td>
<td>Oral or tube feeding where normal diet not practical or feasible</td>
<td>Semi-synthetic preparation</td>
</tr>
<tr>
<td>Pregestimil</td>
<td>Mead Johnson</td>
<td>Disaccharide deficiency and related intolerances, primarily for infants and children</td>
<td>Semi-synthetic preparation</td>
</tr>
<tr>
<td>Prosobee</td>
<td>Mead Johnson</td>
<td>Oral feeding where milk intolerance a problem</td>
<td>Soy based liquid formula for hypoallergenic diets</td>
</tr>
<tr>
<td>Sustacal</td>
<td>Mead Johnson</td>
<td>Oral or tube feeding where normal diet not practical or feasible</td>
<td>Several liquid formulations available Powder</td>
</tr>
<tr>
<td>Sustagen</td>
<td>Mead Johnson</td>
<td>Oral or tube feeding where normal diet not practical or feasible</td>
<td>Powder</td>
</tr>
<tr>
<td>Vivonex SD</td>
<td>Eaton</td>
<td>Oral or tube feeding in impaired digestion and malabsorption</td>
<td>Semi-synthetic preparation; product availability unknown Vivonex SD with additional nitrogen</td>
</tr>
<tr>
<td>Vivonex HN</td>
<td>Eaton</td>
<td>Oral or tube feeding in impaired digestion and malabsorption</td>
<td>Semi-synthetic preparation; availability unknown Product availability unknown</td>
</tr>
<tr>
<td>W-T Peptide L 4</td>
<td>Warren-Teed</td>
<td>Oral or tube feeding in impaired digestion and malabsorption</td>
<td>Semi-synthetic preparation; product availability unknown</td>
</tr>
<tr>
<td>W-T Protein L 4</td>
<td>Warren-Teed</td>
<td>Oral or tube feeding where normal diet not practical or feasible</td>
<td></td>
</tr>
<tr>
<td>W-T Low Residue Food</td>
<td>Warren-Teed</td>
<td>Oral or tube feeding in impaired digestion and malabsorption</td>
<td></td>
</tr>
</tbody>
</table>

1 All names are copyrighted or registered trademarks unless otherwise noted.
2 Refer to Appendix C for full name and address of manufacturer or distributor.
<table>
<thead>
<tr>
<th>Product</th>
<th>Manufacturer or Distributor</th>
<th>Types of Use</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Albumaid X P</td>
<td>Milner</td>
<td>Phenylketonuria</td>
<td>High calorie essential amino acid supplement</td>
</tr>
<tr>
<td>Albumaid L H</td>
<td>Milner</td>
<td>Histidinemia</td>
<td>Protein supplement</td>
</tr>
<tr>
<td>Amin-Aid</td>
<td>McGaw</td>
<td>Renal insufficiency</td>
<td></td>
</tr>
<tr>
<td>BSPD (Albumaid Complete)</td>
<td>Milner</td>
<td>Malabsorption states</td>
<td></td>
</tr>
<tr>
<td>Carnation Slender</td>
<td>Carnation</td>
<td>Control of calorie intake</td>
<td>High protein low calorie food</td>
</tr>
<tr>
<td>CHO-Free</td>
<td>Syntax</td>
<td>For sugar intolerances</td>
<td>Carbohydrate free formula base</td>
</tr>
<tr>
<td>Citrolein</td>
<td>Doyle</td>
<td>Postoperative and chronic illness</td>
<td>Lactose, gluten and cholesterol free dietary supplement</td>
</tr>
<tr>
<td>HDPC Low Sodium Milk Base Formula 128</td>
<td>Hospital Diet Products Corp.</td>
<td>Primarily for tube feeding where sodium restriction required</td>
<td></td>
</tr>
<tr>
<td>HDPC Cat Base Formula 130</td>
<td>Hospital Diet Products Corp.</td>
<td>Primarily for tube feeding</td>
<td>Protein and sodium content less than U.S. RDA Calcium, phosphate, and sodium less than U.S. RDA</td>
</tr>
<tr>
<td>HDPC Low Sodium Meat Base Formula 160</td>
<td>Hospital Diet Products Corp.</td>
<td>Primarily for tube feeding</td>
<td></td>
</tr>
<tr>
<td>HDPC Low Protein Formula 165</td>
<td>Hospital Diet Products Corp.</td>
<td>Primarily for tube feeding where protein restriction necessary, e.g., renal insufficiency</td>
<td></td>
</tr>
<tr>
<td>HDPC Lactose Free Formula 175</td>
<td>Hospital Diet Products Corp.</td>
<td>Primarily for tube feeding where intolerance an indication</td>
<td>Protein, calcium, and phosphate less than U.S. RDA</td>
</tr>
<tr>
<td>HDPC Milk Base Formula 325</td>
<td>Hospital Diet Products Corp.</td>
<td>Primarily for tube feeding</td>
<td>Protein and several vitamins and minerals less than U.S. RDA</td>
</tr>
<tr>
<td>HDPC Meat Base Formula 355</td>
<td>Hospital Diet Products Corp.</td>
<td>Primarily for tube feeding</td>
<td>Protein and several vitamins and minerals less than U.S. RDA</td>
</tr>
<tr>
<td>HDPC Low Sodium Meat Base Formula 360</td>
<td>Hospital Diet Products Corp.</td>
<td>Primarily for tube feeding</td>
<td>Protein and several vitamins and minerals less than U.S. RDA</td>
</tr>
<tr>
<td>Lambase</td>
<td>Gerber</td>
<td></td>
<td>Primarily a hypoallergenic infant food where tolerance to cow's milk is a problem</td>
</tr>
<tr>
<td>Liprotein</td>
<td>Upjohn</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lofenalac Lonolac</td>
<td>Mead Johnson</td>
<td></td>
<td>Low phenylalanine</td>
</tr>
</tbody>
</table>

Table 9. Examples of Nutritionally Incomplete Medical Foods.
<table>
<thead>
<tr>
<th>Product</th>
<th>Manufacturer</th>
<th>Data/Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Low Methionine Isomil³</td>
<td>Ross</td>
<td>Homocystinuria</td>
</tr>
<tr>
<td>Mullsoy³</td>
<td>Syntex</td>
<td>Hypoallergenic formula</td>
</tr>
<tr>
<td>Neo-Mull-Soy³</td>
<td>Syntex</td>
<td>Hypoallergenic formula</td>
</tr>
<tr>
<td>Nursoy⁵</td>
<td>Wyeth</td>
<td>Hypoallergenic formula</td>
</tr>
<tr>
<td>Nutramigen³</td>
<td>Mead Johnson</td>
<td>Hypoallergenic formula</td>
</tr>
<tr>
<td>Probanza</td>
<td>Mead Johnson</td>
<td>Celiac disease, cystic fibrosis of pancreas</td>
</tr>
<tr>
<td>Product 3200 AB</td>
<td>Mead Johnson</td>
<td>Hereditary tyrosinemia</td>
</tr>
<tr>
<td>Product 3200 K</td>
<td>Mead Johnson</td>
<td>Homocystinuria</td>
</tr>
<tr>
<td>Product 3229 Rezolve</td>
<td>Mead Johnson</td>
<td>Phenylketonuria</td>
</tr>
<tr>
<td>Similac PM 60/40</td>
<td>Hospital Diet Products Corp., Ross</td>
<td>Oral or tube feeding in impaired digestion and malabsorption</td>
</tr>
<tr>
<td>S-14</td>
<td>Wyeth</td>
<td>For infants requiring lowered mineral and protein intake</td>
</tr>
<tr>
<td>S-29</td>
<td>Wyeth</td>
<td>Leucine sensitive hypoglycemia in infants</td>
</tr>
<tr>
<td>S-44</td>
<td>Wyeth</td>
<td>Renal disease, cardiac malfunction in infants</td>
</tr>
<tr>
<td>SMA</td>
<td>Wyeth</td>
<td>Infants with low renal solute tolerance and hypercalcemia</td>
</tr>
<tr>
<td></td>
<td></td>
<td>For infants requiring lowered mineral and protein intakes</td>
</tr>
</tbody>
</table>

Low cysteine, low methionine, soy based formulation
Primarily a hypoallergenic infant food where tolerance to cow's milk a problem
Primarily a hypoallergenic infant food where tolerance to cow's milk a problem
Primarily a hypoallergenic infant food where tolerance to cow's milk a problem
Primarily a hypoallergenic infant food where tolerance to cow's milk a problem
Gluten free, high protein

Similar to Lofenalac
Soy isolate infant formula, low methionine
Phenylalanine free formula
Low residue, semi-synthetic preparation
Protein source 60% lactalbumin and 40% casein
Low leucine infant formula
Low renal solute infant formula
S-29 with no added vitamins

¹ All names are copyrighted or registered trademarks unless otherwise noted.
² Refer to Appendix C for full name and address of manufacturer or distributor.
³ Primarily designed for infant feeding but can be used as complete medical foods.
### Table 10. Examples of Components Employed in Formulating Medical Foods or in Special Diets.

<table>
<thead>
<tr>
<th>Product</th>
<th>Manufacturer or Distributor</th>
<th>Types of Use</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>A/G PRO</td>
<td>Miller</td>
<td>Adjunct in meeting post-operative nutritional needs</td>
<td>Contains protein hydrolysates, amino acids and minerals</td>
</tr>
<tr>
<td>Aproten</td>
<td>General Mills</td>
<td>Renal insufficiency, celiac disease</td>
<td>Low protein, gluten free flour and pasta</td>
</tr>
<tr>
<td>Caloreen</td>
<td>Miner</td>
<td>Supplemental energy source where sodium restriction desirable</td>
<td>Low sodium, carbohydrate preparation; availability unknown</td>
</tr>
<tr>
<td>Cal-Power</td>
<td>General Mills</td>
<td>Renal insufficiency</td>
<td>High calorie, low electrolyte supplement</td>
</tr>
<tr>
<td>Casec</td>
<td>Mead Johnson</td>
<td>Source of protein</td>
<td>Milk based product, carbohydrate free</td>
</tr>
<tr>
<td>Cellu-Gluten</td>
<td>Chicago Diet. Suppl.</td>
<td>Diets requiring reduced protein, amino acids, and gluten intake, e.g., renal insufficiency and celiac disease</td>
<td>Gluten-free wheat starch</td>
</tr>
<tr>
<td>Free Wheat Starch</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cellu-Lo/Pro Pasta</td>
<td>Chicago Diet. Suppl.</td>
<td>Diets requiring reduced protein, amino acids, and gluten intake, e.g., renal insufficiency and celiac disease</td>
<td>Gluten-free wheat starch</td>
</tr>
<tr>
<td>Cellu-Lo/Pro Protein</td>
<td>Chicago Diet. Suppl.</td>
<td>Diets requiring reduced protein, amino acids, and gluten intake, e.g., renal insufficiency and celiac disease</td>
<td>Gluten-free wheat starch</td>
</tr>
<tr>
<td>Protein Baking Mix</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Controlyte</td>
<td>Doyle</td>
<td>For conditions requiring low protein, low electrolyte, calorie supplement such as renal insufficiency</td>
<td>High calorie, low protein, low electrolyte preparation</td>
</tr>
<tr>
<td>Dexin</td>
<td>Burroughs Wellcome</td>
<td>Starch hydrolysate carbohydrate modifier for infant formulas</td>
<td>Pure carbohydrate infant preparation</td>
</tr>
<tr>
<td>Dextrot-Maltose</td>
<td>Mead Johnson</td>
<td>Starch hydrolysate carbohydrate modifier for infant formulas</td>
<td>Pure carbohydrate infant preparation and dietary supplement</td>
</tr>
<tr>
<td>General Protein</td>
<td>Lederle</td>
<td>High protein, vitamin, mineral supplement for oral or tube feeding for various protein deficiency states</td>
<td>Sodium restricted</td>
</tr>
<tr>
<td>Gibco Product</td>
<td>Grand Island Biol. Miner</td>
<td>For use in formulation of diet for MSUD patients</td>
<td>Mixture of nonbranched amino acids</td>
</tr>
<tr>
<td>Histimid</td>
<td></td>
<td>Histidinemia</td>
<td>Histidine free mixture of amino acids, water soluble vitamins and minerals</td>
</tr>
<tr>
<td>Hycal</td>
<td>Beecham-Messengill</td>
<td>High carbohydrate, protein and fat free, high calorie supplement</td>
<td>Low electrolytes</td>
</tr>
<tr>
<td>Kaochlor</td>
<td>Warren-Teed</td>
<td>For hypokalemia</td>
<td>Currently available on prescription only</td>
</tr>
<tr>
<td>Kaon</td>
<td>Warren-Teed</td>
<td>For hypokalemia</td>
<td>Currently available on prescription only</td>
</tr>
<tr>
<td>Kato</td>
<td>Ingram</td>
<td>For hypokalemia</td>
<td>Currently available on prescription only</td>
</tr>
<tr>
<td>Kaycel</td>
<td>Cooper</td>
<td>For hypokalemia</td>
<td>Currently available on prescription only</td>
</tr>
<tr>
<td>K-Lor</td>
<td>Abbott</td>
<td>For hypokalemia</td>
<td>Currently available on prescription only</td>
</tr>
<tr>
<td>Klorvess</td>
<td>Dorsey</td>
<td>For hypokalemia</td>
<td>Currently available on prescription only</td>
</tr>
<tr>
<td>K-Lyte</td>
<td>Mead Johnson</td>
<td>For hypokalemia</td>
<td>Currently available on prescription only</td>
</tr>
<tr>
<td>Product Name</td>
<td>Manufacturer</td>
<td>Description</td>
<td></td>
</tr>
<tr>
<td>------------------------------</td>
<td>---------------</td>
<td>-----------------------------------------------------------------------------</td>
<td></td>
</tr>
<tr>
<td>Kolyum</td>
<td>Penwalt</td>
<td>For hypokalemia</td>
<td></td>
</tr>
<tr>
<td>Lipomul-Oral</td>
<td>Upjohn</td>
<td>Prolonged convalescence of chronically ill and malnourished patients</td>
<td></td>
</tr>
<tr>
<td>Lytefren</td>
<td>Mead Johnson</td>
<td>Fluid and electrolyte balance</td>
<td></td>
</tr>
<tr>
<td>MCT Oil</td>
<td>Mead Johnson</td>
<td>Substitute for ordinary lipid components of diet</td>
<td></td>
</tr>
<tr>
<td>Metamin</td>
<td>Milner</td>
<td>Source of essential minerals</td>
<td></td>
</tr>
<tr>
<td>Metinoid (Meitinoid)</td>
<td>Milner</td>
<td>Homocystinuria</td>
<td></td>
</tr>
<tr>
<td>Mor-Rex</td>
<td>Corn Products</td>
<td>Major source of USP glucose</td>
<td></td>
</tr>
<tr>
<td>MPF</td>
<td>General Mills</td>
<td>Specialized protein source; hypo-allergenic dietary component</td>
<td></td>
</tr>
<tr>
<td>MSUDaid</td>
<td>Milner</td>
<td>For maple syrup urine disease</td>
<td></td>
</tr>
<tr>
<td>Oral Electrolyte Formula</td>
<td>Wyeth</td>
<td>Fluid and electrolyte balance</td>
<td></td>
</tr>
<tr>
<td>Paygel-P</td>
<td>General Mills</td>
<td>Renal insufficiency, celiac disease, phenylketonuria</td>
<td></td>
</tr>
<tr>
<td>Paygel Baking Mix</td>
<td>General Mills</td>
<td>Renal insufficiency, celiac disease, phenylketonuria</td>
<td></td>
</tr>
<tr>
<td>Pedialyte</td>
<td>Ross</td>
<td>Fluid and electrolyte balance, infants and children</td>
<td></td>
</tr>
<tr>
<td>Pfiklor</td>
<td>Pfizer</td>
<td>For hypokalemia</td>
<td></td>
</tr>
<tr>
<td>Polyose</td>
<td>Ross</td>
<td>Source of calories, easily absorbed</td>
<td></td>
</tr>
<tr>
<td>Potassium Chloride</td>
<td>Phillips Roxane</td>
<td>For hypokalemia</td>
<td></td>
</tr>
<tr>
<td>Potassium Triplex</td>
<td>Eli Lilly</td>
<td>For hypokalemia</td>
<td></td>
</tr>
<tr>
<td>Product 80056</td>
<td>Mead Johnson</td>
<td>Calorie, vitamin, mineral source</td>
<td></td>
</tr>
<tr>
<td>Product Med 71004</td>
<td>Schwarz-Mann</td>
<td>For maple syrup urine disease</td>
<td></td>
</tr>
<tr>
<td>Promix</td>
<td>Brunswick Labs</td>
<td>Protein deficiency states</td>
<td></td>
</tr>
<tr>
<td>Protinex</td>
<td>Brunswick Labs</td>
<td>Protein deficiency states</td>
<td></td>
</tr>
<tr>
<td>Provimalt</td>
<td>Fleet</td>
<td>Protein deficiency states</td>
<td></td>
</tr>
<tr>
<td>Resource Baking Mix</td>
<td>Doyle</td>
<td>Renal insufficiency, celiac disease</td>
<td></td>
</tr>
<tr>
<td>Stuart Amino Acids</td>
<td>Stuart</td>
<td>Source of amino acids</td>
<td></td>
</tr>
<tr>
<td>Sumacal</td>
<td>Hospital Diet</td>
<td>Carbohydrate calorie source</td>
<td></td>
</tr>
<tr>
<td>Support</td>
<td>Mission</td>
<td>Fat free source of carbohydrate and protein</td>
<td></td>
</tr>
</tbody>
</table>

1 All names are copyrighted or registered trademarks unless otherwise noted.
2 Refer to Appendix C for full name and address of manufacturer or distributor.
Table 11. Products Identified by Manufacturers and Suppliers as Special Dietary Foods.  

<table>
<thead>
<tr>
<th>Product</th>
<th>Manufacturer</th>
<th>Infant Foods or Formulas</th>
<th>Hypoallergenic Foods</th>
<th>Dietary Supplements</th>
<th>Remarks</th>
</tr>
</thead>
<tbody>
<tr>
<td>Advance</td>
<td>Ross</td>
<td>X</td>
<td></td>
<td>X</td>
<td>Supplemented Similac for older infants</td>
</tr>
<tr>
<td>A/G PRO</td>
<td>Miller</td>
<td>X</td>
<td></td>
<td>X</td>
<td>Protein hydrolysates, amino acids and minerals</td>
</tr>
<tr>
<td>Betalactose</td>
<td>Syntax</td>
<td>X</td>
<td></td>
<td>X</td>
<td>Product availability unknown</td>
</tr>
<tr>
<td>Biolac</td>
<td>Syntax</td>
<td>X</td>
<td></td>
<td>X</td>
<td>Product availability unknown</td>
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<tr>
<td>Breminil</td>
<td>Syntax</td>
<td>X</td>
<td></td>
<td>X</td>
<td>Product availability unknown</td>
</tr>
<tr>
<td>Carnation</td>
<td>Carnation</td>
<td>X</td>
<td></td>
<td>X</td>
<td>Calcium caseinate protein modifier or supplement</td>
</tr>
<tr>
<td>Instant Breakfast</td>
<td>Mead Johnson</td>
<td>X</td>
<td></td>
<td></td>
<td>Egg substitute with no cholesterol</td>
</tr>
<tr>
<td>Casein</td>
<td>Mead Johnson</td>
<td>X</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>CHONO</td>
<td>General Mills</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Citrolein</td>
<td>Doyle</td>
<td>X</td>
<td></td>
<td></td>
<td>Supplement to diet in pediatric, geriatric and other situations</td>
</tr>
<tr>
<td>Controlyte</td>
<td>Doyle</td>
<td>X</td>
<td></td>
<td>X</td>
<td>For caloric fortification of foods</td>
</tr>
<tr>
<td>Dexin</td>
<td>Burroughs Wellcome</td>
<td>X</td>
<td></td>
<td>X</td>
<td>Starch hydrolysate pure carbohydrate</td>
</tr>
<tr>
<td>Dextrin-Maltose</td>
<td>Mead Johnson</td>
<td>X</td>
<td></td>
<td>X</td>
<td>Starch hydrolysate pure carbohydrate</td>
</tr>
<tr>
<td>Dietene</td>
<td>Doyle</td>
<td>X</td>
<td></td>
<td>X</td>
<td>High protein, fat restricted infant formula; product availability unknown</td>
</tr>
<tr>
<td>Dryco</td>
<td>Mead Johnson</td>
<td>X</td>
<td></td>
<td>X</td>
<td></td>
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<tr>
<td>Egg Beaters</td>
<td>Fleischmann</td>
<td>X</td>
<td></td>
<td>X</td>
<td>Low cholesterol egg substitute; similar products from other firms also available</td>
</tr>
<tr>
<td>Enfamil</td>
<td>Mead Johnson</td>
<td>X</td>
<td></td>
<td></td>
<td>Lactose free, low cholesterol; also available with added iron</td>
</tr>
<tr>
<td>Hyca1</td>
<td>Beecham-Messengill</td>
<td>X</td>
<td></td>
<td>X</td>
<td>High calorie carbohydrate dietary supplement</td>
</tr>
<tr>
<td>Isomil</td>
<td>Ross</td>
<td>X</td>
<td></td>
<td>X</td>
<td>Lactose free, soy protein formulation</td>
</tr>
<tr>
<td>Kaoklor</td>
<td>Warren-Teed</td>
<td>X</td>
<td></td>
<td></td>
<td>For hypokalemia; available on prescription only</td>
</tr>
<tr>
<td>Kao1</td>
<td>Warren-Teed</td>
<td>X</td>
<td></td>
<td></td>
<td>For hypokalemia; available on prescription only</td>
</tr>
<tr>
<td>Kato1</td>
<td>Ingram</td>
<td>X</td>
<td></td>
<td></td>
<td>For hypokalemia; available on prescription only</td>
</tr>
<tr>
<td>Kaycel</td>
<td>Cooper</td>
<td>X</td>
<td></td>
<td></td>
<td>For hypokalemia; available on prescription only</td>
</tr>
<tr>
<td>K-Lor1</td>
<td>Abbott</td>
<td>X</td>
<td></td>
<td></td>
<td>For hypokalemia; available on prescription only</td>
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<tr>
<td>Klorve1</td>
<td>Dorsey</td>
<td>X</td>
<td></td>
<td></td>
<td>For hypokalemia; available on prescription only</td>
</tr>
<tr>
<td>K-Lyte1</td>
<td>Mead Johnson</td>
<td>X</td>
<td></td>
<td></td>
<td>For hypokalemia; available on prescription only</td>
</tr>
<tr>
<td>Kolyum1</td>
<td>Pennwalt</td>
<td>X</td>
<td></td>
<td></td>
<td>For hypokalemia; available on prescription only</td>
</tr>
</tbody>
</table>

1. Supplemented Similac for older infants.
2. Protein hydrolysates, amino acids and minerals.
3. Product availability unknown.
4. Calcium caseinate protein modifier or supplement.
5. Egg substitute with no cholesterol.
6. Supplement to diet in pediatric, geriatric and other situations.
7. For caloric fortification of foods.
8. Starch hydrolysate pure carbohydrate.
9. High protein, fat restricted infant formula; product availability unknown.
10. Low cholesterol egg substitute; similar products from other firms also available.
11. Lactose free, low cholesterol; also available with added iron.
12. High calorie carbohydrate dietary supplement.
13. Lactose free, soy protein formulation.
14. For hypokalemia; available on prescription only.
<table>
<thead>
<tr>
<th>Product</th>
<th>Manufacturer</th>
<th>Availability</th>
<th>Notes</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lactose Acid Milk</td>
<td>Mead Johnson</td>
<td>X</td>
<td>Contains no milk products</td>
</tr>
<tr>
<td>Lactum</td>
<td>Mead Johnson</td>
<td>X</td>
<td>Specifically a low sodium food with high protein</td>
</tr>
<tr>
<td>Lambase²</td>
<td>Gerber</td>
<td>X</td>
<td>Lysine, methionine, and mineral supplement</td>
</tr>
<tr>
<td>Liprotein³</td>
<td>Upjohn</td>
<td>X</td>
<td>Limited calorie source, primarily for weight control</td>
</tr>
<tr>
<td>Lonalac²³</td>
<td>Mead Johnson</td>
<td>X</td>
<td>Soy based formula</td>
</tr>
<tr>
<td>Low Methio-nine Isomí³</td>
<td>Ross</td>
<td>X</td>
<td>Soy based formula</td>
</tr>
<tr>
<td>Lysmína</td>
<td>Miller</td>
<td>X</td>
<td>Soy based formula</td>
</tr>
<tr>
<td>Metrical</td>
<td>Mead Johnson</td>
<td>X</td>
<td>Iron in low molecular weight polysaccharide</td>
</tr>
<tr>
<td>Mullsoy²</td>
<td>Syntex</td>
<td>X</td>
<td>For hypokalemia; available on prescription only</td>
</tr>
<tr>
<td>Neo-Mull-Soy²</td>
<td>Syntex</td>
<td>X</td>
<td>Readily absorbed calorie source</td>
</tr>
<tr>
<td>Nursoy²</td>
<td>Wyeth</td>
<td>X</td>
<td>For hypokalemia; available on prescription only</td>
</tr>
<tr>
<td>Niferex</td>
<td>Central Pharm.</td>
<td>X</td>
<td>For hypokalemia; available on prescription only</td>
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<tr>
<td>Olac³</td>
<td>Mead Johnson</td>
<td>X</td>
<td>Several formulations available</td>
</tr>
<tr>
<td>Pflkor³</td>
<td>Pfizer</td>
<td>X</td>
<td>Special medical use infant formula</td>
</tr>
<tr>
<td>Polycoose⁴</td>
<td>Ross</td>
<td>X</td>
<td>Special medical use infant formula</td>
</tr>
<tr>
<td>Potassium Chloride³</td>
<td>Eli Lilly</td>
<td>X</td>
<td>Special medical use infant formula</td>
</tr>
<tr>
<td>Potassium Triplex³</td>
<td></td>
<td>X</td>
<td>Special medical use infant formula</td>
</tr>
<tr>
<td>Proteínez³⁴</td>
<td>Brunswick Labs</td>
<td>X</td>
<td>Casein hydrolysate derived amino acids fortified with tryptophan</td>
</tr>
<tr>
<td>Provinal³⁴</td>
<td>Fleet</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Similac</td>
<td>Ross</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Similac PM 50/40⁴</td>
<td>Ross</td>
<td>X</td>
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<tr>
<td>S-14³</td>
<td>Wyeth</td>
<td>X</td>
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<td>S-29³</td>
<td>Wyeth</td>
<td>X</td>
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<td>S-44³</td>
<td>Wyeth</td>
<td>X</td>
<td></td>
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<tr>
<td>SMA³</td>
<td>Wyeth</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Soyalac</td>
<td>Loma Linda</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Stuart Amino Acids⁴</td>
<td>Stuart</td>
<td>X</td>
<td></td>
</tr>
<tr>
<td>Support³</td>
<td>Mission</td>
<td>X</td>
<td></td>
</tr>
</tbody>
</table>

¹See text for explanation.
²All names are copyrighted or registered trademarks unless otherwise noted.
³Refer to Appendix C for full name and address of manufacturer or distributor.
⁴Also classified as a medical food, see Tables 9 or 10.
⁵Originally marketed by Borden Pharmaceutical, but may be currently available from Syntex.
individuals with the diagnosed inborn errors of metabolism. With the advice and counsel of knowledgeable experts it may be useful to develop regulatory guidelines for such products. For example, the American Academy of Pediatrics has prepared an evaluative review of specialized medical foods for use by infants and children with inborn errors of metabolism (American Academy of Pediatrics, 1976).

Finally, there are a number of commercially available foods that purport to supply perceived nutritional requirements. These include products that claim to be special sources of essential nutrients or factors considered "nutritious" by segments of the public. In certain instances nutritional claims may be sound; however, the nutritional significance of such products in management of medically diagnosed conditions is frequently unclear.
C. MANUFACTURERS AND SUPPLIERS OF MEDICAL FOODS

Abbott Laboratories
Abbott Park
North Chicago, IL 60064

Baxter Laboratories, Inc.
(see Baxter Travenol Laboratories, Inc.)

Baxter Travenol Laboratories, Inc.
1 Baxter Parkway
Deerfield, IL 60015

Beecham-Messengill Pharmaceuticals
501-551 Fifth Street
Bristol, TN 37620

Bristol Laboratories
P.O. Box 657
Thompson Road
Syracuse, NY 13201

Brunswick Laboratories
5836 W. 117th Place
Worth, IL 60482

Burroughs Wellcome Co.
The Wellcome Research Laboratories
3030 Cornwallis Road
Research Triangle Park, NC 27709

C.B. Fleet Co., Inc.
4615 Murray Place
Lynchburg, VA 24505

Carnation Company
Research Laboratories
8015 Van Nuys Boulevard
Van Nuys, CA 91412

The Central Pharmacal Company
112-128 East Third Street
Seymour, IN 47274

Chicago Dietetic Supply Inc.
La Grange, IL 60525

Cooper Laboratories, Inc.
Parsippany, NJ 07054

Corn Products
A Unit of CPC International, Inc.
International Plaza
Englewood Cliffs, NJ 07632

Cutter Laboratories Inc.
Fourth and Parker Streets
Berkeley, CA 94710

The Delmark Co.
5320 W. 23rd Street
Minneapolis, MN 55416

Dorsey Laboratories
Division of Sandoz-Wander, Inc.
P.O. Box 83288
Lincoln, NE 68501

The Doyle Pharmaceutical Company
Highway 100 at West 23 Street
Minneapolis, MN 55416

The Drackett Products Company
5020 Spring Grove Avenue
Cincinnati, OH 45232

Eaton Laboratories
13-27 Eaton Avenue
Norwich, NY 13815

The Fleischmann Laboratories
Standard Brands Incorporated
Corporate Research Center
Betts Avenue
Stamford, CT 06904
General Mills Chemicals, Inc.
4620 West 77th Street
Minneapolis, MN 55435

Miller Pharmacal Company
P.O. Box 299
West Chicago, IL 60185

Gerber Products Company
445 State Street
Fremont, MI 49412

Milner Scientific and Medical
Research Co., Ltd.
41 North John Street
Liverpool L2 6SE
England

Grand Island Biological Co.
3175 Staley Road
Grand Island, NY 14072

Mission Pharmacal Co.
1325 E. Durango Street
San Antonio, TX 78210

Hospital Diet Products Corporation
205 West Wacker Drive
Chicago, IL 60606

McGaw Laboratories
1015 Grandview Avenue
Glendale, CA 91201

Ingram Pharmaceutical Co.
202 Green Street
San Francisco, CA 94111

The Nestle Company Inc.
100 Bloomingdale Road
White Plains, NY 10605

Johnson & Johnson Research
Laboratory
U.S. Highway 1
New Brunswick, NJ 08902

O'Neal, Jones & Feldman, Inc.
1304 Ashby Road
P.O. Box 21509
St. Louis, MO 63132

Lederle Laboratories
Middletown Road
Pearl River, NY 10965

Pennwalt Corporation
755 Jefferson Road
Rochester, NY 14623

Eli Lilly and Company
307 E. McCarty Street
Indianapolis, IN 46206

Pfizer Inc.
235 East 42nd Street
New York, NY 10017

Loma Linda Foods
Riverside, CA 92505

Philips Roxane Laboratories, Inc.
330 Oak Street
Columbus, OH 43216

Mead Johnson Laboratories
2404 W. Pennsylvania Avenue
Evansville, IN 47721

Ross Laboratories
625 Cleveland Avenue
Columbus, OH 43216

Miles Laboratories, Inc.
Ames Company Division
1127 Myrtle Street
Elkhart, IN 46514

- 88 -
Schwarz-Mann
Mountain View Avenue
Orangeburg, NY 10962

Stuart Pharmaceuticals
3411 Silverside Road
Wilmington, DE 19897

Syntex Laboratories, Inc.
3401 Hillview Avenue
Palo Alto, CA 94304

Travenol Laboratories, Inc.
(see Baxter Travenol Laboratories, Inc.)

The Upjohn Company
Pharmaceutical Research and Development Laboratory
301 Henrietta Street
Kalamazoo, MI 49001

Warren-Teed Pharmaceuticals Incorporated
582 West Goodale Street
Columbus, OH 43215

Wyeth Laboratories
P.O. Box 8299
Philadelphia, PA 19101
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