Expert assessments of the inclusion of ready-to-use therapeutic foods in the World Health Organization Model List of Essential Medicines: lessons learnt from a qualitative evaluation

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Abstract

Nutrition-related health products are a fundamental part of nutrition interventions. While nutrition-related health products comprise a coherent group, products in this category vary in the quality of evidence supporting their use, intended use and composition, which greatly complicates classification and legislation for these products by regulatory agencies around the world. Ready-to-use therapeutic foods (RUTFs) exemplify this problem well, as they have a dual status as medicines and foods. The current proposal to include RUTFs in the WHO Model List of Essential Medicines (EML) brings about a need to clarify where RUTFs fit within the category of nutrition-related health products, and a need to assess the consequences of their inclusion in the list. Drawing from in-depth interviews with experts working in the field of nutrition across different sectors, this study explores where RUTFs fit within the category of nutrition-related health products, and the advantages, disadvantages and trade-offs that key stakeholders would face if RUTFs were included in the EML. The results show that nutrition-related health products are not classified consistently by regulatory agencies around the world, and that experts use various criteria to decide which class of nutrition-related health products RUTFs belong to. There is no consensus among experts about the appropriateness or benefit of including RUTFs in the EML. The advantages and disadvantages, consequences and trade-offs of including RUTFs in the EML are examined and discussed.

Keywords: essential medicines; nutrition products; ready-to-use therapeutic foods; RUTFs; undernutrition

Introduction

Undernutrition creates a substantial burden of disease globally through four main conditions: wasting, stunting, underweight and deficiencies in vitamins and minerals (1, 2). Malnourished children, particularly those with severe undernutrition, have a higher risk of death from common childhood illnesses, such as diarrhoea,
pneumonia and malaria (2). Iodine, vitamin A and iron are the most important micronutrient deficiencies in global public health terms; their deficiency represents a major threat to the health and development of populations worldwide, particularly children and pregnant women in low-income countries (2, 3). Further, for World Health Organization (WHO) Member States committed to achieving the 2030 Sustainable Development Goals, nutrition plays an important role in many of them (4–6), as it is evident that it plays a key role in the healthy and productive development of the population.

There are various evidence-informed interventions to improve nutrition around the world. Many of these essential nutrition actions are recommended by WHO for different population groups across settings and conditions, and nutrition-related health products are a fundamental part of them (1, 7–10).

Nutrition-related health products include products for particular nutrition-related requirements resulting from physical or physiological conditions, which assist, improve or modify the normal physiological growth, development and functions of the body, as well as products that play a role in preventing, treating or curing diseases (10–14). While nutrition-related health products are a coherent group, the category is broad, and contains products with different intended uses, indications, compositions and degrees of evidence supporting their effectiveness (13, 15). Further, nutrition-related health products come in various dosage forms, such as capsules, pastilles, tablets, pills and other similar forms, sachets of powder, ampoules of liquids, drop-dispensing bottles, and other similar forms of liquids and powders (16, 17). These differences complicate a single, straightforward definition of nutrition-related health products, creating confusion and fuelling inconsistent nomenclatures and classifications by regulatory agencies around the world.

Many nutrition-related health products are what the Codex Alimentarius (Codex) calls “foods for special dietary uses”. Several standards relating to foods for special dietary uses have been established by the Codex Committee on Nutrition and Foods for Special Dietary Uses (CCNFSDU) (11, 12, 18–27). Other foods for special dietary uses may exist and are recognized in some national regulations but are not necessarily defined at Codex Alimentarius level. The CCNFSDU defines foods for special dietary uses as:

Those foods specially processed or formulated to satisfy particular dietary requirements which exist because of a particular physical or physiological condition and/or specific diseases and disorders and which are presented as such. The composition of these foodstuffs must differ significantly from the composition of ordinary foods of comparable nature, if such ordinary foods exist (12, 15, 23).

They are also called “foodstuffs intended for particular nutritional uses” by the European Union (28). Definitions of foods for special dietary uses vary slightly across countries and regions (29).

Other nutrition-related health products with therapeutic uses are considered “foods for special medical purposes”. According to the CCNFSDU, these are:

A category of foods for special dietary uses which are specially processed or formulated and presented for the dietary management of patients and may be used only under medical supervision. They are intended for the exclusive or partial feeding of patients with limited or impaired capacity to take, digest, absorb or metabolize ordinary foodstuffs or certain nutrients contained therein, or who have other special medically-determined nutrient requirements, whose dietary management cannot be achieved only by modification of the normal diet, by other foods for special dietary uses, or by a combination of the two (13).

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1 This study has focused on nutrition-related health products included in health-related actions with an impact on nutrition, or what are also known as “specific nutrition interventions.” Many other health interventions and non-health-related interventions outside the health sector can also have an important impact on nutrition but were not included in the scope of this study.

2 For this study, nutrition-related health products were defined as those that aim to cover particular nutritional needs of the target population and impact the health status of this population by modifying priority health outcomes.

3 This includes foods for infants and young children.
They are also called “medical foods” by the United States Food and Drug Administration (US FDA) and “dietary foods for special medical purposes” by the European Union (EU) (30–32). Nutrition-related health products in this category need to meet regulatory requirements for use in chronic conditions (30).

The regulatory framework that defines nutrition-related health products as foods, medicines or foods for special medical purposes varies across countries. Despite the challenges in classification at country level, it is clear that nutrition-related health products are a fundamental part of nutrition interventions. Over the past years, a myriad of nutrition-related health products have been recommended by WHO as part of nutrition interventions, including multiple micronutrient supplements; food fortification with micronutrients or point-of-use fortification with multiple micronutrient powders, iron and folic acid supplements, vitamin A supplements or calcium supplements; and other products such as lipid-based nutrient supplements and therapeutic milks. Some of these interventions, such as the Integrated Management of Childhood Illnesses (33), routine antenatal care (34), and management of severe acute undernutrition (1, 35) are part of integrated public health programmes and have been employed successfully in the management of undernutrition around the world.

An important aspect for the successful use of nutrition-related health products is that nutrition interventions integrated into public health programmes are associated with issues surrounding the accessibility and cost of these products in-country. The inclusion of a medicine in the WHO Model List of Essential Medicines (EML) (36) conveys the message that some medicines are more important than others, which can facilitate Member States in assuring the availability of these products (37, 38). It is in this context, that the Evidence and Programme Guidance Unit in Department of Nutrition for Health and Development at WHO seeks to understand how nutrition-related health products are defined and classified by experts working on nutrition intervention and programmes. The issues of definition and classification of nutrition-related health products have fundamental implications for how any given product is regulated within countries, which in turn impacts the product availability, cost and specification for use in each country (39).

Owing to this, there is a need to develop a shared understanding of the category of nutrition-related health products and relevant subgroups, and how ready-to-use therapeutic foods (RUTFs) in particular fit into this category. This study conveys perspectives of experts working in the field of nutrition across different sectors about the definition of nutrition-related health products and the criteria they use in their daily work to classify them into subgroups, and inquires further about how RUTFs fit into the broad category of nutrition-related health products.

A key example of this issue is the definition and classification of RUTFs. In 2017, the international nongovernmental organization Action Against Hunger submitted an application to WHO proposing the inclusion of RUTFs in the EML and in the Model List of Essential Medicines for Children (EMLc) (40). RUTFs are high-energy, fortified, ready-to-eat foods for special medical purposes (1, 41, 42) that have a status bordering between foods and medicines. The application to include RUTFs in the EML draws on existing evidence of the efficacy of RUTFs in the management of severe acute undernutrition in children aged 6–59 months (41, 43). The United Nations Children’s Fund, the United States Agency for International Development, and several ministries of health and civil society organizations in Member States supported the inclusion of RUTFs in the EML, citing the body of evidence, practical knowledge and specialist endorsement of these products to treat severe acute undernutrition using a community and integrated model (7, 44–47).

In the application, it is argued that the inclusion of RUTFs in the EML could help alleviate some of the challenges related to the current use of RUTFs to treat severe acute undernutrition around the world, including

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1. The term used in some documents is severe acute malnutrition, although with the WHO broader definition of malnutrition in all its forms, which includes undernutrition (wasting, stunting, underweight), inadequate vitamins or minerals, overweight, obesity, and resulting diet-related noncommunicable diseases, the term undernutrition is used hereewith to convey that reference is made to undernutrition only and not to all other types of malnutrition (2).

2. RUTFs are specially formulated foods for the treatment of infants and children 6 months of age or older, with severe acute undernutrition, who have appetite and do not have medical complications. These health products are nutrient dense, and contain adequate protein and other essential nutrients such as vitamins and minerals. These foods are soft or crushable and can easily be eaten without any additional preparation. They are consumed without adding water, have a low risk of bacterial contamination, require no refrigeration and have a nutritional composition based on the F-100 therapeutic milk used in hospital settings.
challenges related to their availability, accessibility, distribution and cost. This is because the inclusion of RUTFs in the EML can encourage Member States to include them in their national lists of essential medicines, which in turn facilitates the incorporation of RUTFs into national guidelines and public health policies, and their assimilation into the routine delivery system (39, 47). However, the potential inclusion of RUTFs in the EML brings about important considerations about how RUTFs are to be classified and regulated by Member States. One key consideration relates to the bordering status of RUTFs as foods and medicines. While the application to include RUTFs in the EML asked to classify them under the miscellaneous category, this ambiguous status can complicate their classification and approval by country-level regulatory agencies (44). A second key issue is to consider the trade-offs and potential unintended consequences of including these products in the EML.

The overall aim of the project was two-fold. First, it sought to determine the experts’ definitions of nutrition-related health products and the criteria they use to organize products into subgroups; to explore whether they find the category of nutrition-related health products useful; and to understand how they define and classify RUTFs within the category of nutrition-related health products. Second, it sought to evaluate the advantages, disadvantages, and trade-offs key stakeholders would face if RUTFs were included in the EML. Accordingly, the present study asks the following questions:

1. How do RUTFs fit into the conceptual criteria that define nutrition-related health products?
2. What are the advantages and disadvantages of including RUTFs in the EML?
3. What are the criteria and trade-offs considered by stakeholders in their assessment of RUTFs as candidate essential medicines?

Materials and methods

Participants

A total of 18 participants were interviewed across two waves of interviews. Both waves were conducted with experts on nutrition; participants in wave 1 (n = 6) were experts on nutrition products and nutrition programmes, while participants in wave 2 (n = 12) were experts on nutrition programmes and the use of RUTFs in the management of severe acute undernutrition.

Participants were selected using purposive sampling (48). The main sampling criterion was heterogeneity. The researchers sought to interview people with expertise in different domains of the research questions (technical expertise, practical knowledge, decision-makers) and who worked in different sectors. The interviewees were identified through existing lists of experts compiled by the WHO Evidence and Programme Guidance Unit. The experts from these lists are external experts, partners from United Nations agencies or international organizations, or donors with which WHO has been working on the development of undernutrition guidelines, technical notes, and in emergencies. In addition, a small proportion of interviewees were identified via review of publications. The interviewees worked in the following sectors: regulatory agencies, nongovernmental organizations and humanitarian organizations, United Nations agencies and programmes, academia, and private-sector stakeholders that produce RUTFs.

Wave 1 interviewees worked in regulatory agencies (n = 3), United Nations agencies (n = 1), the private sector (n = 1) and nongovernmental organizations and humanitarian organizations (n = 1). Wave 2 interviewees were experts from regulatory agencies (n = 2), nongovernmental organizations and humanitarian organizations (n = 2), United Nations agencies (n = 4), the private sector (n = 1) and academia (n = 3).

Procedure

Semi-structured interviews were conducted to gather information on the experts’ definition of the category of nutrition-related health products and how they classify RUTFs within it (wave 1) and to explore the advantages, disadvantages and trade-offs faced by stakeholders in relation to the inclusion of RUTFs in the EML (wave 2).
Informed consent was obtained before collecting any data. This included consent to audio-record the interview. Participants were informed of the evaluation aims and interview objectives, and it was explained to them that participation in the interview was voluntary. All interviews were conducted over Skype and were anonymous and confidential. An identification number (ID) was assigned to each participant to preserve anonymity. This ID, rather than the participant’s name, was used in all study documents and during the data analysis. The interviews lasted between 30 and 45 minutes. Interviews were audio-recorded and transcribed verbatim for analysis.

**Instrument**

Semi-structured interview guides were developed for each wave of interviews. The process for development of interview guides was informed by a desk review, which was conducted in the preliminary phase of the study. Questions in the semi-structured interview guides were designed specifically to gather the informants’ perspectives in a non-leading fashion and help them engage in an exercise of description and reflection of their own practical experience and expert knowledge of the topic of interest in each wave of the interviews. A series of follow-up probing questions were included to expand on the information provided during the interviews, and to give participants the opportunity to elaborate where necessary (49).

The semi-structured interview guide for wave 1 focused on the experts’ definitions of the category of nutrition-related health products; criteria used to classify nutrition-related health products into subgroups; the usefulness and meaningfulness of the category of nutrition-related health products; definition of RUTFs; and classification of RUTFs in the category of nutrition-related health products.

The semi-structured interview guide in wave 2 was designed to identify the potential advantages, disadvantages, domains and trade-offs of including RUTFs in the EML. Based on the desk review, the following criteria were explored: cost and budget impact of RUTFs; cost effectiveness of RUTFs; equity considerations; effectiveness and quality of the evidence available on RUTFs; prioritization of severe acute undernutrition versus other conditions; prioritization of the population group; issues related to the supply chain, particularly product availability and shortages; use of local versus global commercial formulas; and preferences of the target population versus preferences of RUTF experts. The guide also included questions about the management of potential conflicts of interest resulting from the inclusion of RUTFs in the EML, and questions on products that are similar to RUTFs that could be considered for inclusion in the EML. The semi-structured interview guides can be found in Appendices A3.1.1 and A3.1.2.

**Data analysis**

The qualitative data in wave 1 were analysed using thematic analysis, through the following predefined themes: definition of nutrition-related health products; criteria used to classify nutrition-related health products; and classification of RUTFs in the category of nutrition-related health products. Examples of codes are “definition of nutrition-related health products”, “criteria” and “RUTF medicine”. The first code focused on the definition of nutrition-related health products, and explored whether the experts’ definitions of nutrition-related health products included or excluded various groups of products such as supplementary nutrition products, dietary supplements, fortified blended foods, lipid-based nutrient supplements, and others. The second code focused on the criteria experts use to organize the various nutrition-related health products into subgroups. The third code captured the experts’ opinions on the usefulness and meaningfulness of the category of nutrition-related health products, and explored some of the other terms they use to refer to this group of products. The fourth code focused on the definition of RUTFs, exploring any additions experts would make to the definition that was presented to them. The fifth and last code focused on understanding how RUTFs fit into the category of nutrition-related health products.

The qualitative data in wave 2 were analysed using thematic analysis, through the following predefined themes: advantages of including RUTFs in the EML; disadvantages of including RUTFs in the EML; and criteria and trade-offs of including RUTFs in the EML. A coding frame was developed, based on the research questions...
and conceptual framework. An example of a code is “current use of RUTFs”; examples of subcodes are “cost” and “availability”.

Data were analysed using thematic analysis, with the qualitative software NVivo. The evaluator tagged each section of the transcribed interviews with codes (themes) and subcodes (subthemes). The software was used to group together paragraphs tagged with the same code. Viewing the data side by side facilitated the analysis of common elements across all interviews. Next, the data were analysed to identify differences in the answers of participants, by sector.

**Results**

This section presents the results of the qualitative interviews organized by the themes explored. The section begins with the findings on the definition of nutrition-related health products, the criteria experts use to classify nutrition-related health products into subcategories, and the perceived usefulness of the category of nutrition-related health products. Next, it focuses on the definition of RUTFs and the experts’ assessments of how to classify RUTFs in the category of nutrition-related health products.

**Definition of nutrition-related health products**

When asked what the term “Nutrition-related health products” means, most experts converged in saying that it refers to products made of nutritious ingredients that are to be consumed for a specific health reason.

[nutrition-related health products] makes me think of manufactured products containing nutritious ingredients. They are to be consumed for a reason, as part of a healthy diet, or maybe even for treating certain conditions or preventing certain conditions, or expecting nutritional benefits. (W101, United Nations agency)

All experts considered that the category of nutrition-related health products is quite broad and that it includes multiple products with different uses. However, differences across sectors were made evident through the specific “reason” or the use of nutrition-related health products. Experts from nongovernmental organizations and humanitarian organizations and from United Nations agencies tended to include products aimed at improving the quality of nutrition as part of the category of nutrition-related health products. Therefore, products to supplement a healthy diet were considered nutrition-related health products. The category was broadly defined; it included supplements for a healthy diet and products used for the management of health conditions.

The [nutrition-related health products] category, in my mind, would include products across an axis, yes. The diet quality improvement all the way through therapy. And obviously that’s not a black and white classification, there is some grey area. (W103, nongovernmental organization and humanitarian organization)

In contrast, experts from regulatory agencies tended to include in the category of nutrition-related health products only those products that are aimed at preventing or managing health conditions. When prompted, they would accept the idea of a product aimed at aiding a healthy diet as technically being a nutrition-related product, but this was somewhat counterintuitive to them, as they were much more focused on the regulatory framework of their agencies. Such frameworks require stringent assessments of evidence and complex regulations that leave supplements and other nutrition-related products out of the categories they work with. These experts discussed products that often require a formulation by a medical doctor and that are commonly provided to the intended population as part of social, educational or health programmes.
In my mind, nutrition-related products have a medical purpose or a treatment purpose. These include foods for special medical uses. These products include those that are administered through an enteral or parenteral route. Most, but not all of them, are covered by the national health insurance, so we pay particular attention to supporting evidence, cost and safety. (W104, regulatory agency)

In summary, experts from different sectors understand nutrition-related health products to mean slightly different things. While experts across sectors include in the category of nutrition-related health products those nutritious products for the management of health conditions, experts outside the regulatory sector tend to define the category more broadly, to include products aimed at supplementing a healthy diet that are to be consumed by healthy individuals.

Criteria used to classify nutrition-related health products and usefulness of the category

Experts used a combination of criteria to classify nutrition-related health products into subgroups. One prominent criterion was the differential use of products associated with therapeutic or preventive efforts. Nutrition-related health products used to treat or manage disease are different from those used to prevent health conditions. Experts added that nutrition-related health products used by healthy individuals to achieve or support healthy nutrition comprise a third subgroup, but this group was less clearly defined, and experts had more trouble determining the boundaries of this classification. Within the nutrition-related health products with therapeutic or preventive uses, condition-specific use was employed by all experts to classify nutrition-related health products into subgroups.

The (nutrition-related health products) category basically refers to a processed fortified food. And then, there are different types for different uses. You have RUTF for SAM [severe acute undernutrition], RUSF [ready-to-use supplementary food] for MAM [moderate acute undernutrition], and then you’ve got fortified blended foods, which have a special variant for children. There are powdered complementary food supplements and micronutrient powers to be added to food to provide essential nutrients to a diet that is likely low in those nutrients. (W101, United Nations agency)

A second criterion was nutritional composition. Participants considered the composition of the product to categorize different nutrition-related health products, as conveyed in the following quote,

The second way [of classifying nutrition-related health products] is where you have single nutrient versus the complete diet replacement (…) so, there is an objective of what you are trying to accomplish and then there is the problem that underpins the objective that you are trying to accomplish. Is it failure of the entire diet? Energy, micronutrients, macronutrients, or is it an inadequacy of some or several components of that diet? (W103, nongovernmental organization and humanitarian organization)

The quality of evidence supporting the nutrition-related health products, while considered important, was not a criterion used to classify nutrition-related health products into subgroups. This evidence should usually be of high quality, commonly resulting from randomized controlled trials and found in the published literature on the topic. However, none of the experts interviewed considered that nutrition-related health products should be divided into groups according to the amount of evidence supporting them.

It is important to note that all experts relied on a combination of criteria to delineate subgroups of nutrition-related health products, and that these criteria are not mutually exclusive. Therefore, a fixed taxonomy of nutrition-related health products was not present in participants’ answers, although differences across sectors emerged. Experts from regulatory agencies tended to draw from the official or national-level classification of these products. These classifications vary slightly across countries, as has been reported by previous research (30, 50).
I know these terms are kind of confusing, but we are trying to make a clear distinction between products to be used by healthy people and products to be used for health-specific conditions, that being preventing or treating something. If you are sick or have a health condition, and you need a product intended at mitigating or preventing some kind of osteoporosis for example, we are talking about nutrition-related health products that are classified and regulated as medicines as per the country classification system. (W102, regulatory agency)

When asked about how their country had developed a classification system for nutrition-related health products, experts from regulatory agencies explained that the taxonomy was developed drawing from the various classification systems around the world, including Codex, the US FDA and the classification system of the EU, but also the classification system of New Zealand, which was mentioned as a comprehensive classification system for nutrition-related health products. In general, the distinction between nutrition-related health products with therapeutic use and nutrition-related health products aiming to aid diet among healthy people was clear across sectors, yet there was variation in how classification systems dealt with products falling in between these two categories. In various countries, products with “dual status” as foods and medicines (such as RUTFs) tended to be regulated as medicines, since they are meant to be used by people with a health condition.

Lastly, when asked about the usefulness and meaningfulness of the category of nutrition-related health products, experts seemed to agree that the wording “nutrition-related health products” is not that commonly used but it is not hard to understand. However, they pondered whether the non-specificity of the concept could create confusion, given the different names people in the nutrition field already use to refer to these products.

Typically SNF, special nutritious food, which is a name you will most often hear. Partly we have to go with how people already refer to these products. So that's why we say special nutritious food, which at least [is] sort of an overarching category. (W101, United Nations agency)

To me [nutrition-related health products] is not a terminology that I've come across, but it is clear and it communicates the point but I am somebody who has worked in this field for a really long time, so to me it's not necessarily common use but it's not a complex terminology to understand. Although maybe I can see some complexities because, if I were a high-performance athlete I could call some of those supplements that I'm taking nutrition-related health products. And if I'm a health food fanatic and I'm taking alfalfa oil, I might call it nutrition-related health products. I suppose it is for me, who works in the field, I have my own conceptual framework that I would put around that term but probably it's so open that depending on where you're coming from you could make it mean what you want it to mean. I suppose there is some risk in that. (W103, nongovernmental organization and humanitarian organization)

Therefore, while the category of nutrition-related health products is not a complex term to understand, the lack of specificity of the term could potentially create more confusion among people working in the nutrition field. This is because there are already various names being used to describe this group of products. Another expert explained that most of these names come from the pharmacists, but they lose or change their original meaning as they travel from the medical field to applied work. The expert recommended trying to build some consensus around how these terms are used, and that this is work that needs to be done from the ground up, taking into account how these terms are being used at present.
**Definition of ready-to-use therapeutic foods**

Respondents did not agree on one single definition of RUTFs, but all agreed that they belong to the category of nutrition-related health products. Some experts defined RUTFs as therapeutic foods, as these are products to be used for the management of acute undernutrition, a health condition. This was most often the case for participants in the regulatory sector. In this line of reasoning, experts emphasized that RUTFs are meant to be used for unhealthy children, meaning they are closer to being a medicine than being a food. Participants from outside the regulatory sector found the definition of RUTFs more difficult, given their dual status as foods and medicines. In general, they defined RUTFs as special foods, aimed at the management of a health condition, and they were not considered as medicines. Some experts used concepts such as food for special dietary uses and medical foods. One participant considered RUTFs to be foods, as they are produced in the same manufacturing units where chocolate or peanut butter are produced, with no additional requirements.

*It should not be seen as a medicine because it is still a food but is a therapeutic food, because [it] is a food that should not be consumed by the normal population. [It] should really be targeted to those children, during rehabilitation, which is a very short period of time and for a relatively small number of children compared to the whole population of children. So it is really for a period of two months during rehabilitation. (W202 United Nations agency)*

While most experts agreed with the provisional definition of RUTFs provided by Codex, some raised concerns about the risk of ending with a fixed description once RUTFs are included in the EML. This would constrain innovations in the ingredients and the product recipe. It was argued that innovation of ingredients can help reduce the cost of RUTFs (e.g., by using proteins from fish instead of milk). It was also argued that some flexibility in ingredients would enable the development of recipes that are better received by the target population (e.g., replacing peanuts with local ingredients such as rice). This would not be possible if the description of RUTFs is not flexible. All experts agreed on the importance of maintaining the same nutritional composition regardless of the ingredients used.

**Classification and regulation of ready-to-use therapeutic foods as nutrition-related health products**

Experts were asked about where RUTFs fit in the category of nutrition-related health products. Their answers were slightly different from those for the question about the definition of RUTFs. Experts pondered about the dual status of RUTFs as foods and medicines, but took a pragmatic approach to the question of classification, beyond abstract definitional considerations.

*There are pros and cons of classifying each way, so if it’s classified as a medicine then within countries the whole process to get it included and approved to be used in nutrition programmes is much different, it will need to go through a much more complex and sometimes time-consuming process to have approval. (W105, private sector)*

Therefore, when deciding how to classify RUTFs within the category of nutrition-related health products, all experts weighed the regulatory implications of classifying RUTFs as medicines on the one hand, and as foods on the other. Experts working in regulatory agencies thought that RUTFs should be classified and regulated as medicines, which would help to assure adequate standards of production and monitoring of administration to the intended population. Experts working in other sectors considered that RUTFs should be classified in an in-between category, being “foods for special dietary uses”, “foods for special medical uses”, or “foods for special medical purposes”. Such a categorization would be adequate, as it allows control of the quality of the product without hampering the distribution and availability of RUTFs to be used in nutrition programmes led by Member States. Experts explained that RUTFs should not be classified as medicines or as...
any medical product category requiring medical regulations, as this would create various complications at the country level, with several potential unintended consequences.

I would always advocate for the lighter one, I would advocate for special dietary purposes, if it had to go one way or the other. I don’t think a lot of the governments that use this food would have the capacity to do the risk assessment required, I think they are going to follow the guidelines issued by WHO very closely. I think it’s very much a matter of how WHO is actually defining RUTF and how WHO is advising on the classification. (W206 United Nations agency)

Potential consequences of classifying RUTFs as medicines or any medical product category that would trigger medical regulations included increases in cost, restrictions of access, hampering of local production of RUTFs, and a cascade effect of classifying other products such as RUSFs as medicines, with all the aforementioned potential consequences. In fact, the possibility of medical regulations was the most cited concern about the potential inclusion of RUTFs in the EML.

If RUTF is classified as being the same as conventional medicines, there is a risk that a whole range of new higher standards and demands – which frankly would be unnecessary – they would add no value to consumer safety but they would add to the cost of the product. The biggest barrier probably at the moment to further treatment is the cost of product. (W205, private sector)

However, a minority of participants- all from regulatory agencies- considered that classification of RUTFs as medical products would have the benefit of governments having more control, supervision, and accountability in how the products are used and produced. In evaluating the trade-off between classification as food or medicine, two experts from regulatory agencies in wave 2 agreed that a classification as medical products is better.

Advantages, disadvantages, and trade-offs of including ready-to-use therapeutic foods in the WHO Model List of Essential Medicines

The most cited argument for the inclusion of RUTFs in the EML was that it would make the inclusion of RUTFs in national essential medicines lists more likely. Interviewees explained that this is so because many countries use the EML as guidance for their own list of essential medicines. Inclusion in the country-level list would, in turn, increase the accessibility and availability of RUTFs. Lastly, the inclusion of RUTFs in the EML could increase awareness about severe acute undernutrition and aid its prioritization in countries with a high prevalence of the condition.

If you include [RUTFs] in the list of the country, it obviously will create awareness on the [severe acute undernutrition] condition, investment of the government, responsibility, and it comes with mutual sustainability, it could help to improve access and also acceptance from the population. (W201, United Nations agency)

Yet, experts also expressed a number of concerns about the inclusion of RUTFs in the EML. As mentioned before, the most common concern was that it would trigger medical regulations, which would aggravate current challenges related to accessibility and cost, while potentially creating new challenges such as harming smaller companies that could produce RUTFs locally.
There were other arguments against the inclusion of RUTFs in the EML. One pertained to the risk of medicalizing child feeding. Participants considered that including RUTFs could create incentives for these products to be used as replacement for real food (both on the part of parents and on the part of the industry), and that prevention efforts targeting severe acute undernutrition would see their budget strained as the result of the resources’ need to provide RUTFs as essential medicines. In particular, concerning the idea of including a food (if RUTF is defined as a food) in the EML:

It’s a dangerous precedent where we are putting a food onto the EML and I think that could lead, rightly or wrongly, to interpretation, it could still change how they’re regulated, how they’re made available. I think it’s very easy to assume that would happen for the RUSF and potentially for all the [lipid-based nutrient supplements] product categories and then I would become extremely concerned if that started happening for all complementary foods. (W206, United Nations agency)

A second argument was about the lack of conclusive evidence that RUTFs are indeed the best approach to manage severe acute undernutrition. One expert argued that the current estimates of RUTFs’ effectiveness are inflated, and that RUTFs are not necessarily better than other interventions. In particular, this expert argued that RUTFs have not been proven to be better than preventive efforts against severe acute undernutrition. In this line of reasoning, pushing RUTFs into the EML alongside country-level essential medicines lists, would put governments in a position where they need to prioritize RUTFs over other essential medicines or other public health problems. In addition, and in open contradiction with the main argument for the inclusion of RUTFs expressed by other experts, participants from academia and the private sector converged in considering that the health system would face an unnecessary burden, which, combined with budget constraints in countries with a high prevalence of severe acute undernutrition, would have the consequence of decreasing the accessibility of RUTFs.

Putting it on the EML, people think that is going to increase access, think that somehow health budgets are going to automatically increase by doing so and that’s simply not the case. Health budgets are going to remain constant and now the people within that sector are going to take prioritization decisions. So with the budget that exists in that sector, they are going to have to now prioritize RUTF versus other essential medicines. (W206, private sector)

Criteria and trade-offs related to the inclusion of ready-to-use therapeutic foods in the WHO Model List of Essential Medicines

The interviews were designed to explore the criteria involved in the trade-offs stakeholders would face should RUTFs be included in the EML. These criteria relate to the current use of RUTFs and inform about the strengths and challenges faced by stakeholders in using RUTFs. Table A3.1.1 shows the factors considered to be a challenge in relation to the current use of RUTFs, broken up by sector. The findings suggest some commonalities across sectors, most notably that availability and cost are current challenges in relation to RUTFs.

In general, respondents mentioned that RUTFs are expensive; this was true for experts across all sectors. All experts discussing this challenge agreed on the need to seek ways to reduce the cost of RUTFs. However, there was no consensus about the type of impact that the inclusion of RUTFs in the EML would have on cost. Most respondents thought that the inclusion in the EML would increase the cost of RUTFs, most likely as a result of stringent, medicine-like regulations and more complex requirements of production, alongside a hampering of locally produced RUTFs. Because RUTFs are perceived as costly products, experts expressed concern about potential consequences of prioritizing RUTFs over other strategies to manage severe acute undernutrition. In addition, they doubted that currently strained health systems would increase their budgets to prioritize and cover the costs of RUTFs, if they were included in the country-level essential medicines lists.
A second criterion perceived as a current challenge was the availability of RUTFs. Experts in nongovernmental organizations and humanitarian organizations, and those working in United Nation agencies and country-level regulatory agencies, thought that the availability of RUTFs needs to be improved to assure treatment of severe acute undernutrition around the world, particularly in those countries with the highest prevalence of severe acute undernutrition and in emergency situations.

[The inclusion in the country EML] will increase national government involvement and the appropriation of the management of SAM and RUTF that is used for treatment, it will mean that the government will increase the awareness, and the acceptance from the population will increase the accessibility and availability of the product, if we talk about availability, that means that we are going to have more coverage of the programme. W201, United Nations Agency]

United Nations agency experts discussed the benefit of having governments rather than international agencies take on the responsibility to assure the provision and availability of RUTFs in contexts where they are needed. An important trade-off involved balancing the cost and availability of RUTFs. If RUTFs were to be included in the essential package, then experts would expect this to bring about an increase in funding to assure their availability. However, some experts were not sure that an increase in funding would necessarily result from the inclusion of RUTFs in the EML or in national essential medicines lists. An industry stakeholder expressed concern about the inclusion of RUTFs in the EML negatively affecting the availability of the products. This participant cited the trade-off between channelling distribution through the health system and through other routes such as community programmes, and ways of distributing RUTFs that run in parallel to the health system. In this case, the expert argued, the inclusion of RUTFs in the EML would restrict their availability to channels belonging to the health system and would have the effect of decreasing the availability of RUTFs through other channels.

### Table A3.1.1. Challenges in the current use of ready-to-use therapeutic foods, by sector

<table>
<thead>
<tr>
<th>Factor</th>
<th>Nongovernmental organizations and humanitarian organizations</th>
<th>United Nations agencies</th>
<th>Private sector</th>
<th>Academia</th>
<th>Regulatory agencies</th>
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<tr>
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<td>Accessibility</td>
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<tr>
<td>Manufacturing</td>
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<tr>
<td>Cost effectiveness</td>
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<tr>
<td>Regulation</td>
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<tr>
<td>Requirements for medicines</td>
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<tr>
<td>Other considerations</td>
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Discussion

This article has sought to explore how experts define the category of nutrition-related health products, and the criteria they use to classify nutrition-related health products into subgroups. In addition, the study has sought to understand how RUTFs fit in the broader category of nutrition-related health products, as well as experts' perspectives on the advantages, disadvantages and trade-offs of including RUTFs in the EML.

The study findings indicate that nutrition-related health products are a broad category that means slightly different things to experts across sectors. Those from the regulatory sector had a narrow definition of nutrition-related health products comprising nutritious products to manage health conditions. Experts from other sectors included in the category nutritious products to aid a healthy diet to be consumed by healthy people.

Experts draw from three main criteria to classify nutrition-related health products into subgroups. They determine whether the product is aimed at treating or preventing conditions. Nutrition-related health products to treat or manage conditions are different from those used to prevent health conditions. Within this broad division, experts consider the intended use for specific conditions, such as RUTFs for severe acute undernutrition and RUSFs for moderate acute undernutrition. A third criterion is nutritional composition, which goes from single nutrient to replacement of the whole diet. Importantly, these criteria were not described as mutually exclusive, rather, participants draw from all of them to classify nutrition-related health products.

In relation to RUTFs, most experts highlighted the dual status of these products as foods and medicines and, therefore, were inclined to think that RUTFs belong to a middle-ground category such as foods for special dietary uses or foods for special medical uses. Since a final definition of RUTFs is currently being developed (42), the majority of participants in this study considered that such definition should focus on composition but be flexible otherwise, to allow innovation in the ingredients used to produce RUTFs. This would allow consistency in the nutrient composition of RUTFs across manufacturers, while allowing global and local manufacturers to try new ingredients that could help to reduce the cost of RUTFs. Regarding how RUTFs should be classified in the EML, most experts thought that they should be classified in the “miscellaneous” category. However, they stressed that this classification could lead to inconsistencies in how RUTFs are classified across Member States.

All experts took a pragmatic approach to answering the question of classification and regulation of RUTFs, beyond its conceptual definition. There was no consensus among experts with regard to how RUTFs should be classified and regulated in-country. Some experts considered RUTFs to be foods and thought they should be regulated as such. Other participants stated that RUTFs should be classified and regulated as foods for special dietary uses, as this reflects the fact that RUTFs are meant to be used by a certain population, to treat severe acute undernutrition, and for a specific period of time. Experts outside the regulatory sector considered that RUTFs should not be classified as medicines, as this would bring about complex regulations with the unintended consequence of decreasing their availability and accessibility, and probably increasing their cost. However, experts from regulatory agencies, particularly from low- and middle-income countries, considered it important to classify RUTFs as medicines, to assure stringent and reliable regulation by countries.

In general, the qualitative interviews on the experts' definitions of nutrition-related health products show that the category is thought of as a broad category comprising a myriad of products. Some key criteria used by experts to classify nutrition-related health products into subgroups are the nutritional composition, the intended use, and the division between therapeutic and preventive products. RUTFs belong to the category of nutrition-related health products, but the way in which experts classify them into a subgroup depends on whether experts are concerned with taxonomy or with the regulatory consequences of classifying RUTFs as foods or as medicines.

The experts' assessments of the advantages and disadvantages of including RUTFs in the EML varied according to their expectations of how RUTFs would be classified by regulatory agencies at the country level. The large majority of experts considered that the inclusion of RUTFs in the EML would facilitate their inclusion
In national essential medicines lists. However, there was no consensus among experts about the direction of the consequences (advantages or disadvantages) that this would bring about. Two important considerations in this regard were the issues of regulation and quality of evidence supporting RUTFs, as discussed in the results section. Finally, the potential trade-offs resulting from the inclusion of RUTFs in the EML depended on how experts evaluated the current use of RUTFs, particularly the challenges in relation to the current use of RUTFs in the treatment of severe acute undernutrition. There was a large consensus about cost being a current challenge in relation to RUTFs. Experts agreed that RUTFs are costly, but they also thought that they afford cost-effective interventions. Importantly, the availability of RUTFs was perceived as a current challenge, mostly by experts working in nongovernmental organizations and United Nations agencies. Most cited trade-offs around the issues of cost and the prioritization of RUTFs against other products or interventions to manage severe acute undernutrition, and trade-offs relating to the capacity of strained health systems and the modifications they would have to implement in order to assure the availability of RUTFs if they were included in national essential medicines lists.

In general, the qualitative interviews on the experts’ perspectives on the advantages, disadvantages and trade-offs of including RUTFs in the EML were plural and sometimes contradictory. Most of the divergences found in the experts’ assessments are explained by the lack of a commonly agreed definition of RUTFs and the uncertainties about how RUTFs will be classified and regulated at the country level. Case-studies of countries where RUTFs have been included in their national essential medicines list should be carried out, to learn how different classifications and regulations of these products play out in real life. The present study on the experts’ assessment of the advantages, disadvantages and trade-offs of including RUTFs in the EML shows that this inclusion would probably facilitate adoption of the products in national essential medicines lists, but that the effect of this on cost and availability is deeply entangled with the question of how RUTFs are classified by each country.

References


Appendix 3.1.1

Semi-structured interview guide (wave 1)

The purpose of this interview is to identify the criteria that define nutrition-related products. As you probably know, there isn’t a consensus on what this category of products entails, nor is there a unified nomenclature to refer to them. In this interview, I will be asking a variety of questions that will help me to better understand the criteria you use to define nutrition-related products and which products fall into this category. I will also be asking questions about ready-to-use therapeutic foods that will help me understand how they fit your definition of nutrition-related products.

How this interview will work

I will be asking general questions about nutrition-related products. After each question, there will be some time for you to respond. To begin the interview, I would like to ask for your consent to record our conversation today.

[Turn the recorder on]

State the date and participant code

Definition of the category

• In your own words, what are “nutrition-related products”?
• Are there any subcategories of “nutrition-related products”?
• Is the category “nutrition-related products” different from “supplementary nutrition products”? If so, how is it different?
• Do you consider dietary supplements to be “nutrition-related products”? Why?
• Do you consider fortified blended foods to be “nutrition-related products”? Why?
• Do you consider lipid-based nutrient supplements (LNS) products to be “nutrition-related products”? Why?
• Is the category “nutrition-related products” different from “foods for special dietary uses”? If yes, how is it different?
• Lastly, is the category “nutrition-related products” different from “foods for special medical purposes”? If so, how is it different?
• Does the classification of these products in your country differ from the classification provided by the United States Food and Drug Administration and the European Union?
• If so, what are the main differences?
Criteria used to define the category

- In your work, what term do you use to refer to “nutrition-related products”?
- Please list the nutrition products you consider within this category
  ___________________ ___________________
  ___________________ ___________________
  ___________________ ___________________
  ___________________ ___________________
- Thinking of the products you just listed, what criterion (or criteria) did you use to decide which product belongs to the category [name the nomenclature used by the interviewee]?
- Thinking of the products you just listed, were there any products that you ruled out of this list? If so, what criteria did you use to rule them out?

Usefulness of the category

- Do you find the category of nutrition-related health products meaningful? Why/why not?
- Do you find the category of nutrition-related health products useful? Why/why not?
- Do you find the category of nutrition-related health products problematic? Why/why not?
- What would be a good criterion to organize these products?
  - What about condition-specific intended use?
  - What about therapeutic or preventive use?
  - What about nutritional composition?
  - What about the quality of evidence supporting claims?
  - Do you use any other criterion? Please explain.

Ready-to-use therapeutic foods (RUTFs)

I would like to ask you a few questions about ready-to-use therapeutic foods. We define ready-to-use therapeutic foods as:

“High-energy, fortified, ready-to-eat foods for special medical purposes suitable for the dietary management of children from 6 to 59 months with SAM [severe acute undernutrition], typically made from full-fat milk powder, sugar, peanut butter, vegetable oil, and vitamins and minerals.”

- Do you think this definition is sufficient? Why/why not?
- Would you include any other product characteristic in this definition?
- Please list the names of RUTF products you are familiar with:
  ___________________ ___________________
• When you think of RUTFs, do you include F-100 and F-75 in this category? [Please remember these are milk-based therapeutic formulas.] Why/why not?

• Do you consider RUTFs to be nutrition-related health products? Why?

• Do you consider RUTFs to be foods for special dietary uses or medical foods? Why?

Thank you for your participation in the interview!

[Turn the recorder off]
Appendix 3.1.2
Interview guide (wave 2)

The purpose of this interview is to discuss the potential inclusion of ready-to-use therapeutic foods (RUTFs) in the WHO Model List of Essential Medicines (EML). As you probably know, there is an initiative to include RUTFs in the EML. In this interview, I would like to get your perspective on this. I will be asking you about the potential advantages and disadvantages (intended and unintended) of including RUTFs in the list. I will also be asking questions to better understand the trade-offs that key actors across sectors would face should this initiative move forward.

How this interview will work

I will be asking general questions about nutrition-related products. After each question, there will be some time for you to respond. To begin the interview, I would like to ask for your consent to record our conversation today.

[Turn the recorder on]

State the date and participant code

Ready-to-use therapeutic foods (RUTFs)

I would like to ask you a few questions about ready-to-use therapeutic foods. We define ready-to-use therapeutic foods as:

“High-energy, fortified, ready-to-eat foods for special medical purposes suitable for the dietary management of children from 6 to 59 months with SAM [severe acute undernutrition], typically made from full-fat milk powder, sugar, peanut butter, vegetable oil, and vitamins and minerals.”

[ONLY IF REQUESTED BY INTERVIEWEE, SAM criteria: Child has a mid-upper arm circumference <115 mm or a weight-for-height/length <-3 z-scores below the median of the WHO growth standards, or has bilateral oedema.] Following WHO recommendations, RUTFs are intended to treat uncomplicated cases of SAM in phase two of recovery or at home.

RUTFs have a status bordering between foods and medicines. RUTFs may potentially be included in the EML under the “miscellaneous” category. In relation to this application:

- Do you consider RUTFs to be foods for special dietary uses or medical foods? Why?
- What would be your main argument for the inclusion of RUTFs in the EML?
- What would be your main concern about the inclusion of RUTFs in the EML?
- What would be your main argument against the inclusion of RUTFs in the EML?
- What potential conflict of interest do you see resulting from the inclusion of RUTFs in the EML?
- How would you manage the potential conflict of interest you mentioned?
Regarding the current use of RUTFs:

- From your perspective, what are the main advantages of using RUTFs to treat SAM?
- From your perspective, what are the main challenges related to the use of RUTFs to treat SAM?
- Is availability a challenge? If yes: Would the inclusion of RUTFs in the EML help?
- Is accessibility a challenge? If yes: Would the inclusion of RUTFs in the EML help?
- Is distribution a challenge? If yes: Would the inclusion of RUTFs in the EML help?
- Is the cost of these products a challenge? If yes: Would the inclusion of RUTFs in the EML help?
- Is manufacturing a challenge? If yes: Would the inclusion of RUTFs in the EML help?
- Is regulation/classification of these products a challenge? If yes: Would the inclusion of RUTFs in the EML help?
- Do you think that the requirements for medicines/pharmaceutical products should be applied to RUTFs? Why?
- For national registration: Are there any special or additional regulatory requirements that a medicine or pharmaceutical product must comply with in comparison with a food product?
- Would you have any other consideration in relation to the inclusion of RUTFs in the EML? Please explain.
- Overall, do you think use of RUTFs is a cost-effective intervention to treat SAM? Why?
- Do you have any equity-related concerns regarding RUTFs?
- Is there any other product similar to RUTFs that you think should be included in the EML? Please explain

Thank you for your participation in the interview!

[Turn the recorder off]