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FFHD
Functional Foods in Health and Disease

# Can functional foods reduce the risk of disease? Advancement of functional food definition and steps to create functional food products

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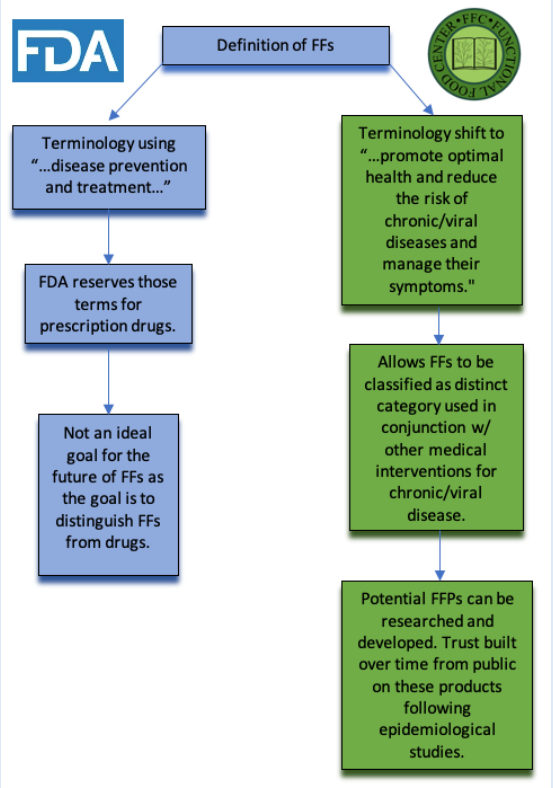
**ABSTRACT**

The definition of functional foods (FFs) has been in development for many years by the Functional Food Scientists of the Functional Food Institute/Functional Food Center (FFC). The status of the FFC's definition is currently unrecognized by the Food and Drug Administration (FDA), but recognition is important for the safe, uniform development and disbursement of functional food products (FFPs) that could improve the health of Americans and people around the world struggling with chronic and viral diseases. If functional foods were to be properly termed using the FFC's current definition, they would be classified as a drug according to the FDA. Thus, the FFC is in communication with governmental representatives to determine the next steps for functional foods to be properly acknowledged. To that end, the FFC is revising its current definition of functional foods to fit a more accurate and encompassing idea of the nature of what functional foods do. This includes a shift to stressing how functional foods promote optimal health, reduce the risk of chronic/viral disease, and manage their symptoms.



Additionally, the process of developing a functional food product must be standardized to ensure the safety of administering bioactive compounds as a health optimization tool. This process follows the methodology of functional food science, which is a potential new form of life science proposed by the Functional Food Center. Over time, the FFC has been developing the appropriate steps to create a functional food product, however, in this article, new steps are emphasized, such as epidemiological studies and after-market research—vital steps to ensuring the safest and most efficacious product is released to the public. Functional foods are not meant to take the place of conventional medicine. They can, however, be used in conjunction with Western medicine and serve as an aid to health optimization for people with chronic/viral diseases and prioritize the management of symptoms associated with those diseases.

**Keywords:** functional foods, bioactive compounds, biomarkers, functional food science, functional food products, epidemiological studies



## INTRODUCTION

It is known that certain food components provide health benefits that can potentially aid in disease risk and symptom management. This leads to several food products on the market claiming to have special health benefits which are regulated by the Food and Drug Administration to ensure that foods are safe to consume and properly labeled [1]. While the FDA does recognize the efficacy of certain food compounds having disease-related health benefits, they have not recognized functional foods as a separate category. However, the Functional Food Center is actively seeking to establish a definition for these types of foods with special bioactive compounds, termed "functional foods."

Since its establishment in 1998, the FFC has been working to develop a definition for functional foods that will be accepted by the FDA to create effective FFPs. Currently, Dr. Martirosyan and the FFC define FFs as:

*"Natural or processed foods that contain biologically active compounds; which, in defined, effective non-toxic amounts, provide a clinically proven and documented health benefit utilizing specific biomarkers for the prevention, management, or treatment of chronic/viral disease or its symptoms"* [2].

The FFC continues to advance this definition as more research on functional foods and bioactive compounds is done and as we learn more about how this definition can encompass the true meaning of what a functional food does. At the moment, the FFC has proposed a new definition which states:

***"Natural or processed foods that contain biologically-active compounds, which, in defined, effective, non-toxic amounts, provide a clinically proven and documented health benefit utilizing specific biomarkers, to promote optimal health and reduce the risk of chronic/viral diseases and manage their symptoms."***

**Why is the Definition Changing?** As we learn more about the power that functional foods hold, it is important for the Functional Food Center to continue updating the definition to be as reliable and specific as possible to aid in its ability to become official. The

former definition specified "..utilizing specific biomarkers for the prevention, management, or treatment of chronic disease or its symptoms." However, the most recent advancement reflects a shift in focus from chronic/viral disease treatment and prevention to *promotion of optimal health, risk reduction, and management of symptoms.* With this change, the FFC clarifies that they understand functional foods will never replace conventional medicine in terms of disease treatment. Rather, there will always be an intersection of the two in order to generate the best outcomes for diseased individuals' health. Moreover, this definition promotes the possibility of involvement from the food industry in research and development.

Another aspect of the definition modification is that currently, the FDA reserves the terminology of "treatment and prevention" for the description of drugs. Personal communication between the FFC and the FDA says that even if certain foods contain compounds proven to treat disease, a FFP containing those compounds will be viewed as a drug, not a food. Creating a standardized definition of functional foods means that functional food product development would become more effective and ultimately end up having a larger impact on chronic and viral diseases worldwide. Functional food developments could start being used for the management of symptoms associated with chronic and viral diseases and would ideally not be viewed as a drug, or medicine, but rather a functional food. By agreeing to a standardized definition of functional foods and establishing functional food science as a distinct field in life sciences, functional food products can be created and trusted by the public. This creates a whole new category of symptom management and risk reduction for chronic and viral diseases.

**What Is the Goal**: Functional food science is focused on the rigorous, systematic research and production of functional food products [3]. The goal of updating the definition of functional foods is to create a clearer understanding of how a functional food product must be developed, evaluated, and used for general health, risk reduction of chronic/viral disease, and management of their symptoms. If this goal is met, there is a greater chance that food will become a common part of frontline, preventative medicine. Science shows that there are foods with documented health benefits that are effective at reducing disease risk and managing symptoms. For example, fruits and vegetables are associated with a lower risk of cancer, coronary heart disease, and stroke, and coffee has been associated with a lower risk of developing type 2 diabetes [4]. There will always be a need for medication in disease treatment, but the idea behind the FFC's definition of FFs is that we will have legitimate means, aside from only Western medicine, to manage the symptoms of diseases.

**How to Accomplish the Goal**: After having spoken with governmental agencies and representatives, it is clear that they all feel that functional foods would be classified as a drug with the current definition proposed. So, to further the efforts to have a recognized definition of functional foods, the FFC continues to speak with governmental agencies about what can be done to improve our system for functional foods and how we can continue working with functional foods to get them acknowledged. In addition, a unified definition allows for a step-by-step process to be developed in which potential functional foods are researched, strict trials are presented showing efficacy and safety, and functional food products are officially established to be marketed to the public.

**Steps for Developing Functional Food Products (FFPs):** In addition to defining functional foods, it is also very important to define functional food science. Functional food science clarifies the definition of functional foods, the development of new functional food products with specific food bioactive compounds for specific health improvement, and the risk reduction of chronic and viral diseases. This will give a groundwork for not only being able to identify what functional foods are, but will also include a guide for how to study, develop, and market a FFP. Functional food science encompasses the process of developing a functional food product through rigorous, systematic research, to determine the extra-nutritive components of the food that promote positive effects on health [3].

Product development is a long process but ideally, one that, if it begins gaining recognition, can serve as a guide for functional food scientists and researchers all around the world to develop their functional food products. Dr. Martirosyan and the FFC outline the procedural steps to achieve this goal (Figure 1):

1. Establish the goal of the FFP. Specifically, explore the data of recent or past studies using history, ethnobotany, anthropology, archeology, and other fields that may give us insight into potential applications of FFs. The goal needs to be specific, such as alleviating certain symptoms or restoring balance to diseased or imbalanced areas of the mind, brain, and body.
2. After establishing a specific goal, conduct literature reviews to determine the relevant bioactive compound(s) (BC) that effectuates the goal. Concerning FFs, the FFC states that BCs are "...or secondary metabolites are molecules in food, usually in small amounts, that act synergistically to benefit health" [5].
3. Establish the appropriate dosage of the BC needed for the desired goal of the FFP.
4. Determine the specific molecular mechanism or biological pathway that the BC exerts on the body or brain.
5. Discover the relevant biomarker(s) related to the mechanism and pathway. This step is vital in providing scientific evidence for the efficacy of the FFP. The biomarkers provide the ability to have a measurable and quantifiable variable that can be tested.
6. Create or choose the food vehicle best appropriate for the administration of the BC. A food vehicle is a food in its natural state, or a food product developed to deliver BCs to the consumer.
7. Perform or provide preclinical in vitro and in vivo studies using animals to determine safe and efficacious dosages of the BC.
8. Perform or provide clinical human trials to refine the dosage appropriate for humans utilizing the relevant biomarker(s). These trials must be done with strict compliance to determine safety and efficacy.
9. Create a special label for the FFP that sufficiently informs consumers of the most effective way to consume the product. This includes consumption instructions and dosage recommendations, as well as the shelf life of the BC(s) to ensure effective bioavailability.
10. Marketing of the FFP must be done to educate the public on the potential health benefits and biomarkers that can be seen and felt from proper usage and to persuade its use of the original goals of the FFP.
11. After marketing, epidemiological studies need to be conducted to determine the FFP's efficacy, dosage, and safety in an

uncontrolled, non-laboratory environment. This step is crucial and will help build trust for the public.

12. Data and information on the epidemiological studies must be sent to trusted third-party organizations and government agencies for approval to market.
13. Release the FFP to the market.
14. Continue to perform aftermarket research to monitor the potential gap between the controlled studies and how the FFP actually affects an individual's health and relevant biomarker(s). This important last working step ensures the product will be refined to maximize efficacy, increase safety, and help future products potentially using the same or similar BC(s) and biomarkers.
15. Official establishment of the FFP.


**Figure 1**. Steps to develop functional food products and bring them to the market

## Examples of Various Steps

***Establishing the Goal of the FFP***: As mentioned, there are many fields at our disposal for discovering potential functional foods. Ethnobotany, for instance, researches the historic, traditional use of plants as medicine in primitive or non-western cultures. While Ethnopharmacology focuses on the bioactivity of traditional remedies [6]. One example of this use comes from the research on Black elderberry (Sambucus nigra), which has been demonstrated to manage the symptoms of influenza and other viral respiratory diseases/illnesses [7]. Researching within these two fields can be a great start to establishing a specific goal of a potential FFP.

***Find Relevant Bioactive Compounds***: The BCs occurring in most fruits and vegetables include phytochemicals such as phenolics and carotenoids, and bananas, for example, contain high amounts of these compounds. Specific phenolic compounds like

gallic acid, catechin, epicatechin, tannins, and anthocyanins are most abundant in this fruit. Furthermore, bananas contain flavonoids, biogenic amines, and even small amounts of phytosterols. Thus, making bananas one of the most powerful antioxidant fruits [8].

***Determine Specific Molecular Mechanism or Biological Pathway***: The BCs previously mentioned with bananas, provide an antioxidant effect on the body. The specific mechanism is that these compounds work to delay or prevent the oxidation or free radical formation of cells [8].

***Find Relative Biomarker(s)***: An example of measurable biomarkers can be seen in the health benefits of the cacao bean. "Cacao (or cocoa) beans are technically not beans or legumes, but rather the seeds of the fruit of the Theobroma cacao tree" [9]. This "super-fruit" has been shown to lower cholesterol levels, reduce resistance to insulin, and improve insulin sensitivity in healthy, obese, and insulin-resistant individuals[10].

***Choose/Develop Appropriate Food Vehicle*:** Sometimes when choosing a food vehicle to administer the BCs, researchers and scientists alter existing products, such as adding or enriching them with vitamins, minerals, or other food products. There are a few different reasons for this, such as making the product more nutritious, making them more desirable for consumers, or even for environmental and economic benefits. One study, for example, conducted how adding pumpkin pulp to wheat bread could bring about these benefits. The pulp provided the bread with, "...potentially bioaccessible phenolics (including flavonoids) and, especially, with peptides" [11]. Furthermore, the pulp "...significantly enriched the bread with potentially bioaccessible angiotensin-converting enzyme (ACE) inhibitors" [11]. Not only did this increase the nutritive component of the food product, but it also made it more palatable and reduced the cost of production. Often, pumpkin pulp is simply disposed of after acquiring the seeds and the flesh of the fruit. So, this process provides environmental benefits as well [11].

***Preclinical Trials*:** One example comes from Seeram and colleagues who tested the effects of six different berry extracts (blackberry, black raspberry, blueberry, cranberry, red raspberry, and strawberry) and their ability to inhibit the growth of human oral, breast, colon, and prostate tumor cells and induce apoptosis in vitro [12]. This study gives credence to furthering the research in vivo with animals to test for the same positive effects.

***Clinical Trials*:** Chen and colleagues (2012) demonstrate a proper human clinical trial with their research on how freeze-dried strawberry powder significantly reduced the risk of esophageal cancer in a high-risk population [13]. In this clinical trial, the researchers were able to adjust and find the proper human dosage to have the desired effects.

***Create Special Functional Food Label*:** Currently, the FDA authorizes statements (health claims) made on food or food components that indicate a relationship between the food, an active ingredient, or a compound and a specific disease [14]. This process requires significant agreement among the scientific community and a series of evidence in clinical or observational studies to show a true relationship. The FFC emphasizes, however, the importance and the need for the bioactive compound on the label. This is fundamental in the entire process of establishing a functional food product.

***Market Functional Food Product*:** Marketing is an important step and one that may be carried out by a separate marketing team. Just as research is imperative in the preclinical and clinical trial, it is also so for the marketing process. There needs to be a balanced struck between educating the public of the potential health benefits, as well as showcasing a product worth purchasing by a variety of populations. Huang and colleagues conducted a study to better understand consumer behavior with functional foods in China. They found that "Trust in the food system and health consciousness positively affects purchase intention via purchase attitude" [15]. Furthermore, while price can negatively affect purchase intention, it can be offset by health consciousness. [15]. Another study from Nilova and Malyutenkova sought to develop an algorithm for assessing the competitive abilities of functional foods in marketing, specifically bread and bakery products. This consisted of a combination between the "Harrington method" and the "Triangle of desirability of consumer features" [16]. The former addresses the competitive factors of FFs to be functionality, quality, shelf life, technology, social importance, price, safety, and consumer, while the latter represents safety, quality, and functionality [16].

***Pilot/Epidemiological Studies*:** Epidemiological studies are vitally important for developing trusted functional food products. For example, olive oil has been regarded as a healthy fat and cooking oil, consumed largely in the Mediterranean diet [17]. A large review article investigated the numerous epidemiological studies surrounding the health benefits of olive oil consumption. This review paints a more accurate picture of the true health benefits of olive oil in a real-world, uncontrolled environment, such as strengthening the claims that it has cardio-protective benefits [17].

***Release to Market and After Market Research*:** The final two steps of developing a functional food product include release to market and aftermarket research. To gain the most desirable results from post-market research, it is important to continue marketing even once the product has been released. The higher the consumption rates, the more significant the aftermarket research results are. These kinds of studies allow for continued modification of the functional food product to best meet consumer's health needs.

**Limitations of After Market Research and Epidemiological Studies:** After-market research and epidemiological studies are very time-consuming and costly. Therefore, they can create significant hurdles to the establishment of a FFP. Dr. Martirosyan and the FFC recommend that distinct categories are created so that products can be labeled before these studies and research. This can be represented on the label to inform consumers that long-term studies have not yet been presented but ideally will in the future. This would help products to be marketed in a relatively cost-effective and timely manner. Of course, products that have after-market research and epidemiological studies to back them up would have that categorical distinction.

## CONCLUSION

The FDA currently acknowledges certain health claims on some food products that have demonstrated health benefits to humans [1,14]. They have, however, failed to recognize the category of functional foods as a legitimate category in the food industry. Based on the research reviewed in this article, many different food products hold the potential to reduce the risk of disease and, therefore, could be labeled as official FFPs. The Functional Food Center has been providing updated definitions for

functional foods and requests that the FDA works to accept a unified definition that encompasses the true power of functional foods in disease risk reduction and management of its associated symptoms. Functional foods can be a distinct category used in conjunction with current Western medical practices to help deal with the epidemic of chronic/viral disease plaguing America and most of the developed world.

The FFC has also outlined steps that can be used to research and create FFPs for the public. This systematic, rigorous research is known as functional food science and the FFC hopes for it to be recognized as a distinct form of life sciences. Lastly, and perhaps most important, is the need for epidemiological studies and continuous after-market research that follows up to find any gaps in research between controlled studies and an uncontrolled environment where the products are used by consumers. These new steps included in the process of developing a FFP cannot be stressed enough because they allow for products to be refined to increase efficacy and safety. The FFC is also aware of the limitations and hurdles created by these steps in creating FFPs. So, to address this issue, the FFC is working on developing potential distinct categories of products with and without epidemiological studies and aftermarket research.

**Abbreviations:** FFs: Functional foods, FFC: Functional Food Center, FDA: Food and Drug Administration, FFP/FFPs, Functional food product/Functional food products, BC/BCs: Bioactive compound/Bioactive compounds, ACE: Angiotensin-converting enzyme

**Authors' Contributions:** Danik Martirosyan, PhD: conceived and designed the study, analyzed, and interpreted the data, and actively involved in writing and editing the manuscript; Hunter Kanya, and Camila Nadalet (intern students at FFC): collected the data, wrote the manuscript.

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