

# MICROBIAL FOOD CULTURES: A REGULATORY UPDATE

Starter cultures and probiotics are important food components with numerous product applications, and understanding the regulations that govern their use is critical.

**M**icrobial food cultures include bacterial food cultures, fungi, and yeast. The scope of this article is bacterial food cultures, which can be subdivided into “starter cultures” and “probiotics.” Starter cultures are those traditionally used by the fermented food industry. Probiotics refer to “live microorganisms which, when administered in adequate amounts, confer a health benefit on the host” (FAO/WHO Joint Working Group, 2002).

The presence of living organisms in traditional fermented foods is well known and has been the subject of scientific inquiry for over a century. The organisms in many cases determine the characteristics of the fermented food, e.g., acidity, flavor, and texture, as well as health benefits that go beyond simple nutrition. These characterizing organisms may be present as natural

microflora of the food, or as a result of the intentional addition of the organisms as starter cultures in an industrial food fermentation process. In the discussion below, the regulatory status of these essential components of fermented foods is discussed. Tools that are available to producers of starter cultures and fermented foods for use in evaluating a particular starter culture of interest under U.S. regulations also are presented.

## **Food Ingredients in the U.S.**

Food additives were first subjected to regulation in the United States under the Food and Drug Act of 1906. The act states that a food shall be deemed adulterated: “If it bears or contains any poisonous or deleterious substance, which may render it injurious to health; but in case the substance is not an added substance, such food shall not be considered adulterated under

this clause if the quantity of such substance in such food does not ordinarily render it injurious to health” (Food and Drug Act, 1906).

The basic Food, Drug, and Cosmetic Act was last updated in 1958 and defines a “food additive” as “any substance the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of any food (including any substance intended for use in producing, manufacturing, packing, processing, preparing, treating, packaging, transporting, or holding food; and including any source of radiation intended for any such use) (FFDCA, 1958).

Congress passed the Food Additives Amendment, Section 409 of the Food, Drug, and Cosmetic Act, in 1958, as well. This amendment exempts two

The image shows two white plastic containers of pink yogurt. The top container is partially filled and has three cherries on top. The bottom container is more full and has two cherries on top. The background is white with a soft shadow under the containers.

important groups of substances from the food additive definition. Those are (a) substances generally recognized as safe (GRAS) among experts qualified by scientific training and experience to evaluate safety and (b) substances that either the Food and Drug Administration (FDA) or the U.S. Dept. of Agriculture (USDA) had sanctioned for use in food prior to 1958 (so called “prior sanction” substances). (More information on the U.S. food ingredient approval process is available in a companion article on the Web at [www.foodtechnology.org](http://www.foodtechnology.org).)

### Fermented Dairy Foods

Lactic acid-producing bacteria, as components of traditional fermented dairy foods, predate written history (Sandine, 1979). The presence and activity of the bacteria can be said to define the food in that the culturing action of the bacteria has a fundamental effect on the acidity, moisture content, texture, and shelf life of the fermented food. From a historical perspective, such bacteria naturally present in a fermented food such as yogurt can be viewed as natural components of the traditional food in the same way that acetic acid is a natural component of lemon juice. Neither the bacteria in the traditional fermented food nor the acetic acid in the lemon are ingredients of the food; they are, in all respects, the traditional food. These traditional fermented foods carry names such as “yogurt” but if named today could just as easily be called, in the

case of yogurt, “*S. thermophilus* and *L. delbrueckii* ssp. *bulgaricus* cultured milk” or “*S. thermophilus* and *L. delbrueckii* ssp. *bulgaricus*.” The intentional addition of these bacteria to produce fermented dairy foods in the modern production facility does not change this fundamental fact. In general, regulations worldwide recognize that a large number of bacteria, which provide a wide variety of functions in fermented foods, are foods and, thereby, not explicitly regulated (Wessels, 2004). These uses must conform in most cases to general food safety standards such as the European General Food Law (European Parliament and the Council, 2002).

The recognition of the linkage between the fermented food and the bacteria that provide the culturing function is implicit in U.S. regulations. The natural presence of culturing bacterial species and the intentional use of these organisms are provided for in FDA standards of identity of a number of foods (CFR, Title 21, Part 133, 2007), and the general recognition of safety and suitability of such uses is supported for some organisms in the International Dairy Federation’s *Partial List of Microorganisms And Microbial-Derived Ingredients That Are Used In Foods* (IDF, 2002). Within the U.S. standards for fermented milk products, such bacteria are variously described as “lactic acid-producing bacterial culture” or “harmless lactic acid-producing bacteria” or “characterizing bacterial culture” or “propionic

*Lactic acid-producing bacteria* present in yogurt may be viewed as a natural component of the product. Photo copyright © iStockphoto.com/OlgaLIS

acid-producing bacteria.” The function of the bacteria is described as “culturing” or “action.”

It is important to note that there is only one instance (i.e., yogurts) where particular lactic acid-producing bacteria are referenced in U.S. regulations, i.e., “characterizing bacterial culture that contains the lactic acid-producing bacteria, *Lactobacillus bulgaricus* and *Streptococcus thermophilus*” (CFR, Title 21, Part 131, §§131.200, 131.203, 131.206, 2007). In all other standards referring to the presence of lactic acid bacteria, neither the common names nor genus and species names of the lactic acid-producing

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*The standard of identity for Asiago cheese makes a direct reference to the suitability of the presence of the native microflora, harmless lactic acid-producing bacteria. Photo copyright © iStockphoto.com/BassittART*

bacteria are designated, nor is the term “lactic acid-producing bacteria” defined in statute or FDA regulation for such uses.

“Prior sanction” has also been granted for the use of harmless lactic acid-producing bacteria, such as *Lactobacillus acidophilus*, as optional ingredients in specified standardized foods (CFR, Title 21, Part 131, §131.112, 2007), providing additional regulatory basis for the addition of a range of safe and suitable microorganisms to be added to products labeled according to the standards including, but not limited to, *L. acidophilus* and *Bifidobacterium* species that are commonly added to yogurt products in the U.S. market.

the phrase “contains the lactic acid-producing bacteria, *Lactobacillus bulgaricus* and *Streptococcus thermophilus*,” indicating that the intent of the standard is not to limit the inclusion of characterizing bacteria to *L. bulgaricus* and *S. thermophilus*. Current industry practice does not recognize such prior sanctions as explicitly limiting and does not limit the addition of harmless lactic acid bacteria to only those standardized products where prior sanctions exist.

Evidently, enough questions remain concerning which harmless lactic acid bacteria can be added to standardized yogurt, low-fat yogurt and nonfat yogurt to have prompted the National Yogurt Assn. in 2000,

the proposal through an Advanced Notice of Proposed Rule Making, FDA recently published “Milk and Cream Products and Yogurt Products; Proposal to Revoke the Standards for Lowfat Yogurt and Nonfat Yogurt and to Amend the Standard for Yogurt” (FDA, 2009). FDA proposes in this amendment to the yogurt standard to (e) “Permit the use of any safe and suitable cultures in addition to the required characterizing bacterial cultures specified in the standard.”

A further nuance in the regulatory status of harmless lactic acid bacteria for use in cultured dairy products is the fact that such bacteria now provided by starter culture suppliers in single or mixed strain forms were originally isolated from milk or fermented dairy products and are often a part of the natural microflora of raw milk used in fermented products. The standard of identity of Asiago cheese (CFR, Title 21, Part 131, §133.102, 2007), for example, refers to culturing of milk by “harmless lactic acid-producing bacteria present in such milk or added thereto,” a direct reference to the suitability of the presence of the native microflora. In fact, ripening of hard cheeses, such as Cheddar, is due in large measure to the adventitious presence of thermophilic *Lactobacilli*, which

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The necessity for such prior sanction in these limited cases is not apparent given the lack of statutory and regulatory specificity of the term “lactic acid-producing bacteria” or “characterizing bacterial culture” employed in the standards for such foods (CFR, Title 21, Part 131, §131.112, 2007). It may be that the prior sanctions have been granted as clarifications of the meaning of

while acknowledging that the current standards permit the use of lactic acid bacteria in addition to *L. bulgaricus* and *S. thermophilus*, to petition the FDA to revise the yogurt standards to include safe and suitable bacteria cultures as explicitly allowed optional ingredients (National Yogurt Assn., 2000). In response to this petition and after soliciting comments on

survive the pasteurization process and multiply in the cheese during storage, providing a necessary and expected effect in the final product while providing the acceptable functions of culturing and/or action.

As stated above, the use of descriptors such as “harmless lactic acid-producing bacteria,” “characterizing bacteria” or

“harmless flavor-producing microorganisms” refer to bacteria found as active in a fermented food, regardless of the source of the organism—present as normal microflora of the food or as intentionally added starter cultures. Thus, current standards of identity for fermented foods in the U.S. allow for the rich diversity of harmless lactic acid-producing bacteria found in today’s products.

In addition to lactic acid bacteria, “harmless flavor-producing bacteria” and “harmless flavor-producing microorganisms” are provided for in the semi-soft cheeses standard (CFR, Title 21, Part 131, §133.187, 2007). Given the lack of specificity for what constitutes a harmless lactic acid bacteria in the current standards for cultured milk products, one must assume that FDA believes that the traditional bacteria cultures found in the various fermented milk products identified in the standards are safe by virtue of their long history of safe use as both adventitious and fortuitous components of raw milk as well as starter cultures purposefully added during commercial production. Thus, such references requiring the presence of the culturing organism in the food are implicit recognitions of their safety.

#### Other Traditional Fermented Foods

The regulatory situation for starter culture bacteria use in meat, bread, and other traditional fermented foods is similar to that in dairy foods. Lactic acid-producing bacteria are natural components in these foods and have also come to be added intentionally as starter cultures.

Using the example of the lactic acid bacteria and related microorganisms occurring in bread, they are naturally present in the flour, yeast, milk, and other bread-making ingredients, and traditional

processes incorporated a “levain,” “poolish,” or similar pre-fermentation step to favor their growth and flavor contribution. Desirable strains have been selected from the natural microflora and are intentionally added as starter cultures. “Lactic acid-producing bacteria” are included as an optional ingredient in the FDA regulations for specific standardized bakery products (CFR, Title 21, Part 131, §136.110, 2007).

USDA/Food Safety and Inspection Service, in the *Food Standards and Labeling Policy Book*, August 2005, recognizes the use of fermentation as a process in the production of dry and semi-dry sausages and states explicitly: “Dry sausages may or may not be characterized by a bacterial fermentation.” The agency further states: “When fermented, the intentional encouragement of a lactic acid bacteria growth is useful as a meat preservative as well as producing the typical tangy flavor.” With the exception of other references to fermentation as a means for meat preservation, consistent with FDA practice, USDA does not explicitly regulate the specific lactic acid bacteria for use in fermented meat products.

As discussed above, the traditional and FDA references to “lactic acid bacteria” and “lactic acid-producing bacteria” are not carefully defined. The European Food and Feed Cultures Association (EFFCA), recognizing this gap in U.S., EU, and EU member states regulations, developed with the International Dairy Federation (IDF), a list of microorganisms that have a documented safe history of commercial use in foods (International Dairy Federation, 2002). This list provides the genus and species of the organism, the use(s) of the organism, the date of first documented commercial use, and publication references

documenting such use. The IDF/EFFCA list provides the most comprehensive list of microbial food cultures used in food fermentations, but also provides the name of numerous other bacteria, yeast, and fungi that are not characterized by their ability to produce lactic acid but that are used in numerous food applications.

Because neither FDA nor USDA regulations define or describe the particular bacteria being referred to when such descriptors are used, perhaps in recognition of the fact that a complete inventory of organisms present in fermented foods is not available for every food, fermented food manufacturers and starter culture manufacturers have determined the scope of such descriptors for the purpose of determining which organisms can be added to fermented foods.

#### U.S. Regulatory Framework

Microbial food cultures naturally present in fermented foods are not ingredients for the purposes of food labeling. When microbial food cultures are intentionally added to foodstuffs to produce

*Intentionally encouraging lactic acid bacteria growth may contribute to meat preservation and flavor.* Photo copyright © iStockphoto.com/stanislafl



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fermented foods, they are considered to be ingredients for the purposes of labeling and may be declared on the product label as “cultured” followed by the name of the substrate, e.g., cultured milk (CFR, Title 21, Section 101.4(b)(5), 2007) recognizing again the substantial equivalence of the microbial food cultures and the fermented foodstuff. As this is the only instance in U.S. regulations where the common

industry to list particular organism names (genus and species) on the food label when probiotic bacteria are added to food.

A “Partial List of Microorganisms and Microbial-Derived Ingredients That Are Used in Foods” is available on the FDA Web site (<http://www.cfsan.fda.gov/~dms/opa-micr.html>). FDA states, however, that the list is not comprehensive and does not represent all those microorganisms that may qualify as “harmless lactic acid-producing” bacteria.

Strictly speaking, if microbial food cultures or “cultured milk” are ingredients as provided for in U.S. regulations (CFR, Title 21, Section 101.4(b)(5), 2007), they are either food additives or GRAS for the use in foods. While not specifically affirmed by FDA, because of the requirement for the presence of harmless lactic acid-producing bacteria in the standards of identity of certain fermented foods, we can consider such uses, specifically referred

to in product standards of identity, to be GRAS. The basis for a GRAS determination can either be a history of presence in food prior to 1958 or by scientific procedures. Because microorganisms are an integral part of traditional fermented foods, the consumption of which predates 1958 by many centuries, the microflora of these products can be said to be GRAS.

We note specifically that the taxonomy of microbial food cultures is constantly evolving, changing the name, but not the organism itself, and in the

process creating opportunities for confusion as to which organisms have a safe history of use. This GRAS determination for culturing bacterial species such as *Lactococcus lactis*, which is generally recognized as part of the characteristic mesophilic microflora of various hard cheese types, is obvious. And, certainly, *Lactococcus lactis* is GRAS for this use based upon presence in the food prior to 1958, even though it at that time was called *Streptococcus lactis*, as well as by scientific procedures, given that the safety of the organism has been well documented. In this shifting world of taxonomy, the key to documenting the safe use of a particular culture at the genus and species level is to be able to demonstrate the use regardless of the currently employed name. For this, the standard reference for use is recognized, i.e. the International Code of Nomenclature (<http://www.bacterio.cict.fr/>), where the recognized synonyms for a particular organism are cataloged.

However, other less-well-known organisms commonly found in fermented foods may require more specialized knowledge as they are isolated and introduced into foods for industrial food fermentation. Or, organisms with a safe history in food may be employed for different uses or at significantly higher dosage in foods, thereby increasing human exposure—for example, probiotics added to food for their health benefits rather than for the fermentation of foods. In such cases, a GRAS determination may be warranted for these new uses.

Three GRAS notices have been submitted to FDA that relate to the addition of live microorganisms to food (<http://www.cfsan.fda.gov/~rdb/opa-gras.html>). GRN 000049 provides the evaluation that *Streptococcus thermophilus* strain Th4 and *Bifidobacterium lactis* strain Bb12 are GRAS for use in infant



**Emerging scientific research** is identifying the hidden potential of microbial starter cultures to deliver health benefits to consumers. Photo courtesy of DMI

and usual name for microbial food cultures is addressed, it is only natural to ask “to which microbial cultures does the term ‘cultured milk’ refer?” In circular fashion, one might reasonably respond that the term refers to those organisms used in the production of cultured milk, which is not useful if one is trying to determine which microbial food cultures may be added to a specific standardized food. It is also common practice in the food

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formula intended for use by infants 4 mo and older. GRN 000171 states that *Lactobacillus acidophilus*, *L. lactis*, and *Pediococcus acidilactici* are GRAS for use in meat and poultry products to control pathogens. And, GRN 000231 provides that *L. casei* subsp. *rhamnosus* strain GG is GRAS for use in infant formula.

Two tools have been developed that are available to assist manufacturers in determining the scope of the descriptors, “lactic acid-producing bacteria,” “harmless flavor-producing microorganisms,” etc. As noted above, the International Dairy Federation, with the support of the European Food and Feed Cultures Assn., has published a list of microorganisms with a documented history of use in food. Also, recently, the European Food Safety Authority (EFSA) has reviewed organisms that are commonly used in food and feed, and EFSA has proposed a list of organisms that have been determined to qualify for Qualified Presumption of Safety (QPS) status based on historic usage and the available scientific data (EFSA, 2008). Taken together, these tools

provide important guidance to manufacturers as part of a determination, in addition to corroborating scientific evidence, whether a particular organism is GRAS for a specified use.

Microbial food cultures have a long, safe history of use in food, and have generally been considered safe and suitable for myriad uses. As long as cultures are used for traditional fermentation and their metabolism and effect on food substrate is well constrained by the substrate and growth conditions, there is a reasonable expectation of safety. Today, however, scientific studies are unlocking the hidden potential of microbial starter cultures to deliver not only functionality in a food matrix but also to provide a health benefit to consumers. In addition, microbial cultures without a history of use in food may be discovered to have health benefits to consumers. It is incumbent on the food industry to insure that these newly discovered microbial food cultures are safe, as well as to insure that new uses of cultures with a safe history of use in food are safe where

these new uses envision new levels of exposure to specific consumer groups such as children, older people, and other at-risk populations. Understanding the regulatory requirements for microbial food cultures and the tools available for the determination of safe history of use can assist the food industry in making this obligation a reality. **FT**

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*This paper was prepared by the Cultures Committee of the International Food Additives Council (IFAC). IFAC represents companies that make high quality substances used worldwide as food ingredients. Cultures Committee members make microbial food cultures used by the dairy, bakery, and other segments of the food industry.*

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