Nutritional Genomics and the Future of Food Labeling in the United States

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INTRODUCTION

Advancements in nutrigenomic research may lead us to a time when genetic testing may enable each of us to know which foods would help us achieve optimal health. In the meantime, nutritional genomic research such as that discussed in the other chapters of this book may provide the basis for understanding specific biochemical constituents of food that may promote health. Yet, how will such information be conveyed to consumers? Could the data discussed throughout this book be used to make claims on food products or at least lay the foundation for such claims? This chapter evaluates the current state of science-based food labeling and then describes the potential for future changes as data from nutritional genomics continues to come forth.

Most Americans encounter food and beverage labels on a daily basis. According to U.S. Department of Agriculture (USDA) food expenditure data, Americans spent over $500 billion ($565,284,000,000) on food products in 2008 (USDA ERS 2009a), the equivalent of $2141.00 per
person per year (USDA ERS 2009a). In the year 2000, U.S. consumers had about 40,000 food products to choose from in the typical supermarket (Harris et al. 2002). Over the past several years over 20,000 new food products were introduced into the U.S. market (USDA ERS 2009b) and several thousand others were retired. In 2008, over 5.5% or 1389, of these new products included the claims “high vitamin” or “low trans fats” (USDA ERS 2009b).

The Nutrition Labeling and Education Act of 1990 (NLEA 1990) required most food products to bear labels that included nutrition information beginning in 1994. While a recent Food and Drug Administration (FDA) health and diet survey (USDHHS 2008) found that 61% of the people surveyed reported that nutrition information was important to them and another 35% reported that nutrition information is somewhat important when shopping for food, a study by the Economic Research Service of the USDA found that consumer use of food labels for making purchasing decisions declined by 10% from 1995 to 2006 (Todd and Variyam 2008). Among adults over 20 years of age the decline was greatest (17.2%) for the use of health claims and was significant for use of the ingredient list, health claims, and all nutrients except for fiber and sugars. Interestingly, the FDA released results of a 2008 survey showing a 10% increase in respondents who reported reading a food label the first time they buy a product but that 56% of those surveyed believed that only some or none of the nutrient content claims on labels are accurate (FDA 2008, 2010a; 21 CFR 1.3 (a)).

Common sense tells us that what we eat affects our health and that whole foods and a quality diet can provide nutrients and bioactive components for good health. We have many common expressions about food and diet: “You are what you eat”; “An apple a day keeps the doctor away”; and “Through the lips and on the hips.” The effects of diet on gene expression were the topics of discussion presented at the nutritional genomics conference held at Cal Poly Pomona in November 2009. From these discussions it is clear that the potential exists for the understanding of these interactions to one day enable good health and prevent the onset of disease. If current research results further support this potential and individual genotypic susceptibilities to diet related diseases are elucidated, what will food manufacturers be allowed to say on food labels?

Most of us know people with medical conditions such as diabetes or high blood pressure that are responsive to diet. Hippocrates said, “Let food be your medicine and your medicine be your food.” Consumers report that reading food labels could be a tool in helping them improve their health (Borra 2006). Yet, in spite of common knowledge and this sage advice, food labeling regulations generally do not permit foods to be marketed as products that may treat, cure, or prevent disease. In fact, had there been an FDA and if Hippocrates had offered food products for sale to his patients, the agency would likely have responded with a warning letter including a statement similar to “Because of these intended uses, these products are drugs within the meaning of the Food, Drug and Cosmetic Act.” Recently, the FDA’s National Center for Toxicological Research created an initiative to look at personalized nutrition and medicine, appointing Jim Kaput, PhD, as director. He has an established career in the rapidly evolving field of nutritional genomics.

LABELING

Labeling is the intersection between the nutritional genomic scientists and the world of consumers. Labeling refers not only to information affixed to the immediate container of a product but also “includes all written, printed, or graphic matter accompanying [a product]…in interstate commerce” (21 CFR 1.3(a)) and so extends to any promotional material or advertising. Federal regulations allow for several types of claims on food product labels, including nutrient content claims, health claims, qualified health claims, and Food and Drug Administration Modernization Act (FDAMA) claims. Each of these types of claims must comply with FDA regulations and must be truthful, not misleading, and supported by scientific evidence.
Nutritional Genomics and the Future of Food Labeling in the United States

Nutrient Content Claims

Nutrient content claims are statements that discuss the level or range of a particular nutrient in a food product (21 CFR 101.13). Examples of nutrient content claims include “contains vitamin C,” “high fiber,” “low fat,” and “healthy.” FDA regulations spell out the requirements that must be met for foods to bear particular nutrient content claims in sections 101.54 through 101.67 of title 21 of the Code of Federal Regulations (Table 22.1).

A main dish food product bearing the nutrient content claim, “healthy” must meet the following nutritional criteria:

1. Low in fat, containing less than 3 g of fat per 100 g of product and no more than 30% of the calories may be from fat
2. Low in saturated fat; containing no more than 1 g of saturated fat per 100 g of the food and no more than 10% of the calories may be from saturated fats
3. No more than 90 mg of cholesterol per serving
4. Must contain at least 10% of the recommended daily intake (RDI) per serving of two nutrients from the list of vitamin A, vitamin C, calcium, iron, protein, or fiber
5. May not exceed 480 mg of sodium per serving

It should be noted that the brand name “Healthy Choice” is exempted from this definition since the name was in use prior to promulgation of the regulation in October of 1989 (21 CFR 101.13 (q)(1)).

Allowable Health Claims

FDA regulations permit the use of certain health claims that characterize the relationship between a food and disease. Such claims are the subject of petitions submitted by interested parties and are based on strong supporting evidence in publically available information from numerous, well-controlled studies. Allowable health claims are authorized by the FDA when there is significant scientific agreement over the interpretation of the data supporting the claim. In a guidance document the FDA states, “The assessment of significant scientific agreement then derives from the conclusion that there is a sufficient body of sound, relevant scientific evidence that shows

TABLE 22.1

Selected Nutrient Content Claims

<table>
<thead>
<tr>
<th>Claim</th>
<th>Eligible Nutrients</th>
<th>Level Required to Use Claim</th>
</tr>
</thead>
<tbody>
<tr>
<td>Contains, good source, provides*</td>
<td>Nutrients with RDI/DRV</td>
<td>10% to 19% of the RDI or DRV</td>
</tr>
<tr>
<td>Rich in, high, excellent source*</td>
<td>Nutrients with RDI/DRV</td>
<td>20% or more of the RDI or DRV</td>
</tr>
<tr>
<td>Fortified, enriched, added, extra, plus</td>
<td>Nutrients with RDI/DRV</td>
<td>10% or more of the RDI or DRV</td>
</tr>
<tr>
<td>Sodium free, no sodium, zero sodium,</td>
<td>Sodium</td>
<td>The food contains less than 5 mg of sodium per labeled serving</td>
</tr>
<tr>
<td>without sodium**</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Low in saturated fat; low saturated fat;</td>
<td>Saturated fat</td>
<td>The food contains 1 g or less of saturated fatty acids per</td>
</tr>
<tr>
<td>little saturated fat***</td>
<td></td>
<td>reference amount customarily consumed and not more than 15% of</td>
</tr>
</tbody>
</table>

This table contains a partial listing of the requirements for the selected nutrient content claims.


*21 CFR 101.54
**21 CFR 101.61
***21 CFR 101.62
consistency across different studies and among different researchers and permits the key determination of whether a change in the dietary intake of the substance will result in a change in a disease endpoint” (FDA 1999).

Once authorized, the health claims are codified in regulation that describes the relationship between the nutrient and disease, the requirements for and limitations on use of the claim, as well as model claim language. The model language for two authorized health claims are given below and a list of all allowable health claims is provided in Table 22.2.

- Calcium and vitamin D for osteoporosis: Adequate calcium and vitamin D throughout life, as part of a well-balanced diet, may reduce the risk of osteoporosis (21 CFR 101.72).
- Folic acid and neural tube defects: Healthful diets with adequate folate may reduce a woman’s risk of having a child with a brain or spinal cord birth defect. (21 CFR 101.79).

On March 22, 1995, the Quaker Oats Co. submitted a health claim petition to the FDA requesting that the agency authorize a health claim on the relationship between the consumption of oat products and the risk of coronary heart disease. Thirty-seven human studies on oat bran and oatmeal and serum cholesterol were included in the petition. In 2001 a Quaker Oats petition to expand the oats and cholesterol claim to include extracted beta glucan included 80 references (Quaker Oats and Rhodia, Inc 2001). The resulting allowable health claim is shown below.

- Oats and cholesterol: Diets low in saturated fat and cholesterol that include 3 grams or more per day of [beta]-glucan soluble fiber from whole oats may reduce the risk of heart disease. One serving of [name of food] provides ______ grams of this soluble fiber.

The health claim regarding the relationship between oats and cholesterol was in the news in May of 2009 after the FDA issued a warning letter to General Mills regarding the use of unauthorized language discussing oats and cholesterol on boxes of Cheerios (Figure 22.1). The letter stated in part,

Based on claims made on your product’s label, we have determined that your Cheerios® Toasted Whole Grain Oat Cereal is promoted for conditions that cause it to be a drug because the product is intended
for use in the prevention, mitigation, and treatment of disease. Specifically, your Cheerios® product bears the following claims on its label:

- “you can Lower Your Cholesterol 4% in 6 weeks”
- “Did you know that in just 6 weeks Cheerios can reduce bad cholesterol by an average of 4 percent? Cheerios is … clinically proven to lower cholesterol. A clinical study showed that eating two 1.5 cup servings daily of Cheerios cereal reduced bad cholesterol when eaten as part of a diet low in saturated fat and cholesterol.”

These claims indicate that Cheerios® is intended for use in lowering cholesterol, and therefore in preventing, mitigating, and treating the disease hypercholesterolemia. Additionally, the claims indicate that Cheerios® is intended for use in the treatment, mitigation, and prevention of coronary heart disease through, lowering total and “bad” (LDL) cholesterol. Elevated levels of total and LDL cholesterol are a risk factor for coronary heart disease and can be a sign of coronary heart disease. Because of these intended uses, the product is a drug within the meaning of section 201(g)(1)(B) of the Act [21 U.S.C. § 321 (g)(P)(B)]. The product is also a new drug under section 201(p) of the Act [21 U.S.C. § 321(p)] because it is not generally recognized as safe and effective for use in preventing or treating hypercholesterolemia or coronary heart disease. Therefore, under section 505(a) of the Act [21 U.S.C. § 355(a)], it
may not be legally marketed with the above claims in the United States without an approved new drug
application.

(FDA Minneapolis Office 2009)

General Mills responded to this letter by submitting studies to support the cholesterol-lowering
claims. Dr. Barbara O. Schneeman, director of the Office of Nutrition, Labeling and Dietary
Supplements at the Center for Food Safety and Applied Nutrition, responded after assessing the
newly submitted studies and concluded that,

In determining whether to amend 21 C.F.R. § 101.81 to authorize the soluble fiber/coronary heart dis-
ease claim to include a statement about a specific percentage reduction in LDL cholesterol, FDA would
need to consider the totality of the publicly available scientific evidence to support such a statement and
also how to convey information in a way that is not misleading (Schneeman 2009a).

This remains an active issue and only time will tell what happens here. General Mills has stated
they have not misrepresented the data. As of this writing, claims regarding Cheerios® and chole-
sterol reduction remain on the company website (General Mills 2010). In a private conversation a
former FDA staff member stated that the only court cases FDA has lost have been based on First
Amendment principles. It will be interesting to see whether such arguments are made in this case.

Qualified Health Claims

Qualified health claims represent a class of claims that are also petitioned for by interested parties
but for which the supporting evidence is weaker and does not meet the criteria required for allow-
able health claims. Accordingly, the claims are “qualified” by inclusion of a disclaimer. Rather than
being the subject of regulations, enforcement discretion letters are issued for qualified health claims.
These letters describe the FDA’s assessment of the data submitted in the health claim petition and
also include the language that may be used for the claim. The qualified claim for omega-3 fatty
acids serves as an illustration (see Table 22.3) for a list of health conditions that are the subject of
qualified health claims:

Supportive but not conclusive research shows that consumption of EPA and DHA omega-3 fatty acids
may reduce the risk of coronary heart disease. One serving of [Name of the food] provides [ ] gram of
EPA and DHA omega-3 fatty acids (Hubbard 2004).

The provisions for qualified health claims were created as a result of court decisions in Pearson v.
Shalala, which challenged the FDA’s general health claims regulations and the agency’s decision not
to authorize health claims for four specific substance/disease relationships. A district court first ruled
for the FDA (14 F. Supp. 2d 10 (D.D.C. 1998)). However, on appeal, the U.S. Court of Appeals for the
DC Circuit reversed the lower court’s decision (164 F.3d 650 (D.C. Cir. 1999)). The appeals court ruled
that the First Amendment does not permit the FDA to reject health claims that are deemed potentially
misleading unless the agency also determines that no disclaimer would eliminate the potential de-
ception. In general, qualified health claims are not supported by data that meet the standard of significant
scientific agreement (Hubbard 2004) that is required for health claims and are therefore “qualified”
by inclusion of a statement regarding the strength of the data. In many cases the disclaimer is stronger
than the claim, as is illustrated by the qualified health claim for selenium and prostate cancer.

Two weak studies suggest that selenium intake may reduce the risk of prostate cancer. However,
four stronger studies and three weak studies showed no reduction in risk. Based on these studies,
FDA concludes that it is highly unlikely that selenium supplements reduce the risk of prostate cancer
(Scheenman 2009c).
TABLE 22.3
Qualified Health Claims Describing Nutrient Disease Relationships

<table>
<thead>
<tr>
<th>Nutrient</th>
<th>Disease Relationship</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Omega 3 fatty acids</td>
<td>Coronary heart disease</td>
</tr>
<tr>
<td>2. B-vitamins</td>
<td>Vascular disease</td>
</tr>
<tr>
<td>3. Selenium</td>
<td>Cancer</td>
</tr>
<tr>
<td>4. Antioxidant vitamins</td>
<td>Cancer</td>
</tr>
<tr>
<td>5. Phosphatidylserine</td>
<td>Cognitive dysfunction and dementia</td>
</tr>
<tr>
<td>6. Nuts</td>
<td>Heart disease</td>
</tr>
<tr>
<td>7. Walnuts</td>
<td>Heart disease</td>
</tr>
<tr>
<td>8. Monounsaturated fatty acids from olive oil</td>
<td>Coronary heart disease</td>
</tr>
<tr>
<td>9. Green tea</td>
<td>Cancer</td>
</tr>
<tr>
<td>10. Chromium picolinate</td>
<td>Diabetes</td>
</tr>
<tr>
<td>11. Calcium</td>
<td>Colon/rectal cancer and Recurrent colon/rectal polyps</td>
</tr>
<tr>
<td>12. Calcium</td>
<td>Hypertension</td>
</tr>
<tr>
<td>13. Tomatoes and/or tomato sauce</td>
<td>Pregnancy-induced hypertension</td>
</tr>
<tr>
<td>14. Unsaturated fatty acids from canola oil</td>
<td>Preeclampsia</td>
</tr>
<tr>
<td>15. Corn oil and corn oil-containing product</td>
<td>Prostate, ovarian, gastric, and pancreatic cancers</td>
</tr>
<tr>
<td>16. Folic acid</td>
<td>Reduced risk of coronary heart disease</td>
</tr>
<tr>
<td></td>
<td>Reduced risk of heart disease</td>
</tr>
<tr>
<td></td>
<td>Neural tube birth defects</td>
</tr>
</tbody>
</table>


Appeals of Pearson v. Shalala and new court cases regarding qualified health claims continued through 2009. In May of 2010, the U.S. District Court for the District of Columbia ruled that the FDA had failed to comply with Pearson v. Shalala and the agency’s own guidance document regarding evaluation of scientific evidence for qualified health claims. The Court remanded the case back to the FDA (Alliance for Natural Health U.S. v. Sebelius, 2010).

for the purpose of 1) drafting one or more disclaimers to accompany plaintiffs’ certain cancers, anticarcinogenic, and prostate claims, or, alternatively, setting forth empirical evidence that any disclaimer would fail to correct the claims’ purported misleadingness; 2) determining an appropriate disclaimer to accompany plaintiffs’ lung and respiratory tract claim in light of the SUII.MAX study; and 3) reevaluating plaintiffs’ colon and digestive tract claim and drafting one or more disclaimers.

FDAMA Claims

FDAMA claims were created by passage of the Food and Drug Administration Modernization Act of 1997 (21 U.S.C. § 343). These claims are authorized based on authoritative statements from “a scientific body of the United States Government with official responsibility for public health protection or research directly relating to human nutrition (such as the National Institutes of Health or the Centers for Disease Control and Prevention) or the National Academy of Sciences or any of its subdivisions.” The statement must be “currently in effect” and “[identify] the nutrient level to which the claim refers” (21 U.S.C. § 343). Interested parties are permitted to notify the FDA regarding their intention to make a claim based on an authoritative statement. According to an FDA guidance document the notification must include the language of the intended claims, a description of how it
TABLE 22.4
Seven FDAMA Claims

<table>
<thead>
<tr>
<th>Claim</th>
<th>Source of Statement</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nutrient content claim choline containing foods</td>
<td>Food and Nutrition Board, Institute of Medicine (IOM), National Academy of Sciences</td>
</tr>
<tr>
<td>Fluoride and the risk of dental caries</td>
<td>Centers for Disease Control, Surgeon General, Public Health Service</td>
</tr>
<tr>
<td>Potassium and the risk of high blood pressure and stroke</td>
<td>National Academy of Sciences</td>
</tr>
<tr>
<td>Saturated fat, cholesterol, and trans fat, and the risk of heart disease</td>
<td>Department of Health and Human Services, Department of Agriculture</td>
</tr>
<tr>
<td>Substitution of saturated fat with unsaturated fatty acids and risk of heart disease</td>
<td>National Academy of Sciences</td>
</tr>
<tr>
<td>Whole grain foods and the risk of heart disease and certain cancers</td>
<td>National Academy of Sciences</td>
</tr>
<tr>
<td>Health claim notification for whole grain foods with moderate fat content and the risk of heart disease and certain cancers</td>
<td>National Academy of Sciences</td>
</tr>
</tbody>
</table>


was determined that the requirements for an authoritative statement have been satisfied, a copy of the authoritative statement, and a balanced representation of the scientific literature regarding nutrient disease relationship that is the subject of the claim (FDA 1998). Some sample FDAMA claims are as follows:

- Diets rich in whole grain foods and other plant foods and low in total fat, saturated fat, and cholesterol may reduce the risk of heart disease and some cancers.
- Diets containing foods that are a good source of potassium and that are low in sodium may reduce the risk of high blood pressure and stroke.

Of the seven FDAMA claims (Table 22.4) that are authorized, most derive from statements made by various offices at the National Academy of Sciences. Other agencies that are considered authorities for the purpose of FDAMA claims include the National Institutes of Health (NIH), the Centers for Disease Control and Prevention (CDC), which are both part of the Department of Public Health; the surgeon general as well as the Food and Nutrition Service (FNS), Food Safety and Inspection Service (FSIS), and Agricultural Research Service (ARS), which are part of the Department of Agriculture.

**U.S. FOOD INDUSTRY USE OF FOOD LABEL CLAIMS**

The food industry in the United States has tried to creatively apply the various regulations covering food label claims to come up with ways to inform customers about the quality or benefits of their products (Figure 22.2). Whether this is simply public service or a means to differentiate their products and drive sales, the result has been a plethora of symbols and systems that vary greatly. Ultimately, consumers probably remain confused.

**GUIDING STARS PROGRAM**

The Guiding Stars program, begun in 2006, is described as “objective, based on consumer research, and not influenced by price, brand or manufacturer trade groups” (Guiding Stars 2010). This program was developed by a panel of experts and uses a proprietary algorithm to evaluate data in
the nutrition facts panel to determine the amount of essential vitamins, minerals, fiber, and whole grains per 100 calories for positive value. In addition, the levels of saturated fat, trans fat, cholesterol, added sodium, and added sugars are evaluated and detract from the product’s score and potential rating from zero to three stars. In 2009 the Guiding Stars program modified their algorithm and criteria twice. One adjustment was to account for the fact that naturally occurring trans fat are found in dairy and some meat products—originally any trans fat reduced a food’s eligibility for the program (Guiding Stars 2009a). Another adjustment was made to accommodate the American Heart Association’s recommendation to reduce added sugars (Guiding Stars 2009b). The program lists grocery store chains, food service organizations, and insurance companies among the groups using their system.

**NuVal Program**

The NuVal program provides composite scores—you get positive number scores for good nutrients and “bad” nutrients lower the score by being subtracted from the number.

This program utilized a panel of experts led by Dr. David Katz of the Yale Prevention Research Center to develop an algorithm that converts nutritional information into a numerical score ranging from 1 to 100. The development was funded by the nonprofit Griffin Hospital and Yale University School of Medicine affiliate. According to company information, the algorithm evaluates over 30 nutrients and nutrition factors including protein, calcium, vitamins, sugar, sodium, and cholesterol. Similar to the Guiding Stars program, some nutrients increase the NuVal score and others such as fat and cholesterol lower the score. The company website lists three grocery store partners (http://www.nuval.com/).

**Nutrition at a Glance**

In an unusual twist, Kellogg’s Nutrition at a Glance front of package (FOP) labeling, which lists the amounts of calories and major nutrients such as fat and carbohydrates as well as some vitamins and minerals, uses the United Kingdom’s guideline daily amounts (GDAs) to also present the percentage of each nutrient that that product provides in each serving. It is interesting that the GDAs for fat and sugar are higher than the recommended daily intake (RDI) and percent daily values (DV) used by the FDA for nutritional labeling, while the GDA for fiber is lower than the RDI and DV for this nutrient. It will be interesting to see if this company, beleaguered by reaction to the use of immunity
enhancing claims on several sugary cereals marketed for children, will draw the FDA’s attention for the use of the GDAs as well as the noncompliant nutrient content claims the manner in which the amounts are stated represents. This may well have been one of the programs that FDA views as using “symbols that either expressly or by implication are nutrient content claims” and promised to assess and compare with regulatory criteria in the agency’s letter on point of purchase food labeling (Schneeman 2009b).

SMART CHOICES PROGRAM

The Smart Choices Program made 2009 a very interesting year for nutrition claims on food packages. Created by a group of scientists, academicians, health and research organizations, food and beverage manufacturers, and retailers, this complicated program specified criteria for 19 different product categories, including beverages, cereals, meats, dairy, and snacks.

The program was launched in August of 2009 and quickly came under scrutiny. On September 4, 2009 an article in The New York Times discussed the inclusion of Froot Loops cereal as a Smart Choice (Neuman 2009). The article cited nutritionists who were not part of the Smart Choice program as being appalled by some of the choices, while nutritionists who were part of the program defended standards stating that they were based on government dietary guidelines and widely accepted nutritional standards and influenced by research showing that consumers did not want negative messages or the sense that food choices were being dictated to them. The designation of Froot Loops as a Smart Choice was justified as being a better choice than a donut for a child’s breakfast.

The public outcry over Froot Loops being designated a Smart Choice grew and included a letter to the FDA from Representative Rosa L. DeLauro, chairwoman of the House Appropriations Subcommittee on Agriculture Rural Development, Food and Drug Administration, and Related Agencies. An October 23, 2009 news release from Smart Choice announced that it would “voluntarily postpone active operations and not encourage wider use of the logo … by either new or currently enrolled companies” (Smart Choices 2009). By October 30, companies, including Kellogg’s, Kraft Foods, ConAgra Foods, Unilever, General Mills, PepsiCo, and Tyson Foods, that had been using the Smart Choices logo stated they would cease doing so.

The action to curtail the Smart Choices program was not only in response to public outcry about Froot Loops being denoted as a Smart Choice but primarily in response to an October 20, 2009 FDA letter to industry regarding point of purchase and FOP labeling. The letter stated in part that criteria used by the various programs to label the front of packages and store shelves with nutrition information were not consistent and that consumers would be less likely to check the nutrition facts box when such symbols were used. The letter also stated that all label claims and symbols are subject to FDA regulations and that the agency “[was] analyzing FOP labels that appear to be misleading” and “developing a proposed regulation to define the nutritional criteria” for making broad FOP or shelf label claims concerning the nutritional quality of a food. The letter further stated that it is the FDA’s “intent is to provide standardized, science based criteria on which FOP nutrition labeling must be based” (Schneeman 2009a).

On November 3, 2009 Smart Choices Chairman of the Board Michael Hughes published an opinion piece in USA Today in which he stated that leading experts in nutrition, public health, and food science, as well as food industry representatives participated in the process. Government agencies sent observers. “We will gladly participate in the FDA’s process, just as the agency participated with us” (Hughes 2009).

In May of 2009 the American Dietetic Association released a review of various front of package labeling systems (American Dietetic Association 2009) and published a chart comparing the ratings various foods would receive under several of these labeling paradigms. As shown in the portion of the chart depicted in Figure 22.3, Planters® Lightly Salted Cocktail Peanuts would receive disparate ratings from Guiding Stars, NuVal and Smart Choices.
FIGURE 22.3 The differing ratings a single product would receive from various front-of-package labeling programs. (Excerpted from American Dietetic Association, 2009, used by permission.)

**Traffic Light Labeling**

The FDA’s letter to industry on point of purchase food labeling also discussed the United Kingdom’s traffic light FOP labeling program:

The recent experience with FOP labeling in the United Kingdom demonstrates the potential of voluntary initiatives to provide consumers helpful FOP labeling. In that instance, the government set certain criteria for the use of such labeling, and retailers took the initiative to implement FOP labeling in their stores. The agency wants to explore the potential of that approach (Schneeman 2009b).

It should be noted that, unlike in the United States, nutrition labeling is not compulsory on UK food products. In order to help consumers make nutritionally sound food purchase choices, the British government has encouraged the use of a standardized traffic light symbol on the front of food product labels. The levels of various nutrients present in the product are rated as green, yellow, or red (Figure 22.4). According to the UK’s Food Standards Agency, a red light symbol indicates that “the food is high in something we should be trying to cut down on. It’s fine to have the food occasionally, or as a treat, but try to keep an eye on how often you choose these foods, or try eating them in smaller amounts.” The yellow light is neutral and green indicates “the healthier choice” (Food Standards Agency 2010). The number of grams of fat, saturated fat, sugars, and salt in what the manufacturer or retailer suggests as a “serving” of the food is also listed in the graphic.

The traffic light system has not been embraced by industry. According to the thesis of Debra Van Camp at Ohio State University, its adoption on products introduced from January 2002 through December 2008 ranged from 27% among foods not targeted by the agency to 55% of hot cereal, cold cereal, pastry dishes, pizzas, prepared meals, and sandwiches, which were targeted by the Food

**FIGURE 22.4** UK traffic light symbols that may be used voluntarily on food product labels.
Standards Agency (Van Camp et al. 2009). The primary adopters were private label products; none of the major brands used the system (Food Standards Agency 2010).

Even though nutritional labeling is required on food product in the United States, the FDA appears to be intent on adding FOP labeling. In the October 2009 letter to industry on point of purchase labeling the agency stated (Scheenman 2009b),

If voluntary action by the food industry does not result in a common, credible approach to FOP and shelf labeling, we will consider using our regulatory tools toward that end. This effort will include research to assess through consumer studies the likely effects of FOP symbols on information search behavior related to the Nutrition Facts label, which in turn can affect consumer understanding of the full nutrition profile of a product. The foundation of that approach should be a common set of mandatory nutritional criteria that consumers can rely on when they view FOP labels, even if no one symbol is ultimately selected as superior.

In March of 2010, FDA Commissioner Margaret Hamburg published an open letter to industry regarding FOP labeling in which she stated,

I believe we now have a wonderful opportunity to make a significant advancement in public health if we can devise a front-of-pack labeling system that consumers can understand and use. We intend to work closely with food manufacturers, retailers, and others in the design process, and I hope that every food processor will contribute its views on how we can do this in the best way possible. In the meantime, FDA will soon issue new draft guidance relating to front-of-pack calorie and nutrient labeling (Hamburg 2010).

The letter was followed by the April 29, 2010 publication of Docket FDA-2010-N-0210, “Front-of-Pack and Shelf Tag Nutrition Symbols” for comment (FDA 2010b).

Whether such government-mandated FOP labeling would be helpful to consumers or would simply negate product differentiation via food label claims is an open question. It will be important for anyone with an interest in communicating nutrition information on food labels to participate in the policy development process. In fact, the FDA’s statement that it is their “intent is to provide standardized, science based criteria on which FOP nutrition labeling must be based” (Schneeman 2009b), the March 2010 letter (Hamburg 2010) and the April 29, 2010 publication of Docket FDA-2010-N-0210 “Front-of-Pack and Shelf Tag Nutrition Symbols” are calls to action. Nutrigenomic scientists, the food industry, and other interested parties may start their participation by commenting on this and other proposals outlined in the letter to industry. It is imperative to be part of the discussion and shape the future of food labels with an eye on the growing field of nutritional genomics. Otherwise, what the FDA eventually decides could be detrimental to product labeling and the public’s access to important nutritional information.

**OTHER COMMENTS ON NUTRITIONAL GENOMICS AND FOOD LABELING FROM THE FDA**

The FDA’s letter to industry regarding FOP labeling gives us a good understanding of the agency’s view on the subject. Before that letter was published several former and current FDA staff members were interviewed and asked their thoughts on nutritional genomics and the future of food labeling. Their comments ranged widely and are summarized next.

The idea that FDA draws a bright line separating food and drug was stated several times along with the idea that the agency would be very wary about the sorts of claims that potentially could arise if a person could have their DNA assayed and learn what nutrients could be particularly beneficial to them. One interviewee commented, “The agency would not want to allow the line between foods and drugs to be blurred.” The concept of claims needing to meet the criteria of significant scientific agreement was stated by several interviewees.
One person interviewed stated that, “From a regulatory standpoint and FDA; there is none more conservative in regard to being pessimistic or wary of new developments in nutrition than nutritionists and people at CFSAN” (Center for Food Safety and Applied Nutrition). He went on to explain that CFSAN staff are very skeptical because “there is a history of fraud and that charlatans are always there before the science.” He said, “If companies wanted to discuss links between genomics and food, FDA would be very wary and would like the evidence to be very strong due to history of fraud.”

One interviewee revealed that a former FDA commissioner said, “There are people who do molecular biology and there are people that feed animals and look for lumps and bumps—which attracts the smartest people?” The interviewee went on to explain, “Nutrition and toxicology studies are done in a black box. The studies involve broad groups and vague findings. Nutritional genomics may change that. Studies on pharmacology and genomics of disease have provided lots of evidence that people respond to drugs differently and the future may lead us to similar knowledge about food.”

Other interviewees noted that regulations change to accommodate the science and that regulations are not prescriptive but are permissive and are changed via petition, some by legislation or via legislative authority given to the agency by Congress. Other interviewees noted that drugs must go through an approval process to show safety and effectiveness and suggested that in a similar fashion, the industry would need to show validity for nutrigenomic claims. The potential need for a process similar to generally regarded as safe (GRAS) notifications or new dietary ingredient (NDI) notifications was noted. These notifications must include safety data and exposure estimates in order to determine whether the use of the ingredient would pose health risks to consumers.

Another interviewee suggested that the best approach would be to make claims about obtaining a benefit versus avoiding harm, supporting health versus disease prevention, and went on to state,

The idea that you have information that someone with a [genetic] tendency to develop a certain disease if they consume your product leads to ethical questions. Should you note on the label that certain folks should avoid this food? (Alcoholic beverage labels include warnings to pregnant women.) The idea that you would have material information regarding the effect of your product when used as intended gets right to the heart of the concept of misbranding. One aspect of misbranding is when the information presented is misleading in a particular. But if you have certain information and do not reveal it; that could also be misbranding.*

The most interesting comment from those interviewed was “FDA certainly will not lead the way [to nutrigenomic claims on food labels] but may be dragged kicking and screaming.” Ultimately, knowledge changes and people’s choices change, but the FDA is charged with protecting consumers and this responsibility will figure greatly in the process of responding to the science and industry attempts to inform consumer of the benefits of certain foods. Will future food labels guide individuals to select foods for optimizing their health? Will we have a series of color codes for those susceptible to diseases? Perhaps we will end up with a “eat right for your type” system. Or perhaps only general positive statements will be permitted, such as, “Great for people who require plenty of omega-3s,” or “Formulated for people who require high levels of antioxidants.”

Possible Pathways to Nutritional Genomics Claims

So far, various types of claims that food products may qualify for have been discussed along with the applications of these claims and the FDA’s response to some of them. So far all the claims discussed—nutrient content claims, allowable health claims, qualified health claims, and FDAMA claims—are authorized via the petition processes and are based on the level of scientific agreement in publically available information about the nutrient and disease states. In order to take advantage of

*Misbranding is prohibited by the Federal Food, Drug, and Cosmetic Act (FD&C Act), which states, “The introduction or delivery for introduction into interstate commerce of any food, drug, device, or cosmetic that is adulterated or misbranded.” A product is misbranded if it is incorrectly labeled either by the inclusion of false or misleading information or it fails to include information required by law.
these regulatory mechanisms as applied to nutritional genomic advancements, industry must not only watch the literature in order to gather publicly available information to support these petition processes but must also fund, conduct, and publish studies to add to the body of data. It is also important for scientists and industry to comment on FDA rulemakings. The FDA's letter on FOP labeling asked for comments, and these can be provided from a group or anonymously through attorneys or regulatory consultants. It is important for parties interested in influencing food labeling regulations to understand the regulations and to use real science and sound principles of nutrition when commenting on FDA guidance documents or call for comments. In order to effectuate future claims relevant to nutritional genomics, it will also be helpful to watch for authoritative statements from federal experts.

**Other Routes to Nutritional Genomics Claims**

We have reviewed the various petition processes that may be used to gain approval for various types of claims that discuss the relationship between diet and health. There are also mechanisms that rely on public information that are not subject to premarket FDA review or approval but that may be useful for disseminating information about nutritional genomic advancements. It may be possible to market medical foods or foods for special dietary uses based on advancing science; it may also be possible to market products using structure function claims.

**Medical Foods**

Medical foods are formulated for the dietary management of a disease or condition with distinctive, established nutritional requirements (Table 22.5). The definition of medical foods as extracted from the Orphan Drug Act can be found in 21 CFR 101.9(j)(8):

A medical food is a food which is formulated to be consumed or administered enterally under the supervision of a physician and which is intended for the specific dietary management of a disease or condition for which distinctive nutritional requirements, based on recognized scientific principles, are established by medical evaluation.

The regulation goes on to stipulate that a medical food

- Is a specially formulated and processed product, not a naturally occurring food used in its natural state
- Provides nutritional support specifically modified for the management of the unique nutrient needs that result from the specific disease or condition, as determined by medical evaluation

The regulation describes the patient medical foods as formulated for

- A patient who has limited or impaired capacity to ingest, digest, absorb, or metabolize food or certain nutrients because of therapeutic or chronic medical needs
- A patient who has other special medically determined nutrient requirements which cannot be met by the modification of the diet alone
- A patient who requires medical care on a recurring basis and is receiving active and ongoing medical supervision

Medical foods are exempt from nutrition labeling regulations but are subject to other basic labeling requirements, as well as the food GMP (Good Manufacturing Practice) regulations. In 1996, the FDA published an Advanced Notice of Proposed Rulemaking (ANPR) (FDA 1996) with the intent to regulate medical foods more rigorously. However, after a number of years of inaction, the agency withdrew the proposed rule while stating that the proposed rule could still reflect the FDA’s view on the subject. Chatter in trade publications indicates that some expect the FDA to take up the issues
TABLE 22.5
Examples of Medical Foods

<table>
<thead>
<tr>
<th>Target Disease</th>
<th>Medical Food</th>
<th>Purpose</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kidney disease</td>
<td>Type and quality of protein</td>
<td>Provide adequate nutrition that is minimally taxing for diseased kidneys due to moderate protein levels, low fluid and electrolyte levels, and high caloric content</td>
</tr>
<tr>
<td>Liver disease</td>
<td>Type and quality of protein</td>
<td>Provide adequate protein without inducing or exacerbating hepatic encephalopathy and to overcome malnutrition</td>
</tr>
<tr>
<td>Hypermetabolic states (severe burns, trauma or infection)</td>
<td>Type and quality of protein; added amino acids; elevated levels of specific vitamins or minerals</td>
<td>Provide high calories for increased energy needs; glutamine to aid intestinal cell proliferation to overcome impaired GI function</td>
</tr>
<tr>
<td>Lung disease (chronic obstructive pulmonary disease, acute respiratory distress syndrome, cystic fibrosis)</td>
<td>High fat, low carbohydrate content</td>
<td>Reduce load of carbon dioxide the lungs must clear</td>
</tr>
<tr>
<td>Compromised immune function, human immunodeficiency virus infection, acquired immune deficiency syndrome (AIDS)</td>
<td>Enriched with specific amino acids; fortified with increased levels of vitamins</td>
<td>To support immune function and increase CD4/CD8 ratio</td>
</tr>
<tr>
<td>Oral rehydration solutions</td>
<td>Solutions of water electrolytes and carbohydrate source</td>
<td>To quickly restore fluids and minerals lost in diarrhea and vomiting in infants and children</td>
</tr>
<tr>
<td>Phenylketonuria (PKU)</td>
<td>Restricts dietary phenylalanine</td>
<td>Phenylalanine-req to allow greater intake of complete protein</td>
</tr>
<tr>
<td>Malabsorption as found in inflammatory bowel disease (ulcerative colitis, Crohn’s disease); radiation enteritis; short bowel syndrome</td>
<td>Pre-digested macronutrients; altered type or quantity of fat</td>
<td>To reduce the severity and incidence of diarrhea and abdominal discomfort in individuals with fat malabsorption</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>Type and quantity of carbohydrate; high fiber</td>
<td>To enhance blood sugar control</td>
</tr>
</tbody>
</table>

Source: FDA, 1996, Regulation of Medical Foods.

once again, while others see the overburdened and under-funded agency as unable to address medical foods in light of more pressing concerns.

While the formulation for the medical food must be based on “recognized scientific principles,” under current regulations, there is no explicit requirement that clinical studies be conducted on the medical foods nor must the product be reviewed by FDA prior to market introduction. As stated in the 1996 ANPR, medical foods “may bear claims that have not been evaluated under the 1990 amendments to ensure that they are scientifically valid. Moreover, there is no assurance that the formulation of a medical food has been evaluated prior to sale to ensure that it is suitable for the intended patient population.” However, the requirement that claims must be supported by scientific evidence does necessitate the availability of supporting studies. Under the guidelines of the 1996 ANPR, medical foods would have to be clinically tested and would very likely have to be reviewed and approved by FDA; however, testing is not presently required by FDA regulation.

It is possible that nutritional genomic research could lead the discovery of nutritional dysfunction that may be occurring in many diseases currently treated with pharmaceuticals. If so, these findings could be applied to the production of medical foods that could potentially lead to great
improvements in patient care and outcomes. If supported by scientific data, medical foods may currently be marketed without prior FDA approval of the formula or the claims made about the product providing it conforms to the regulations discussed above. Table 22.5 provides information from the 1996 ANPR on medical foods that were on the market at that time.

**Foods for Special Dietary Uses**

If a food is marketed for a particular dietary need, it is classified as a food for special dietary uses. Special dietary uses are defined in 21 CFR 105.3 as

(i) Uses for supplying particular dietary needs which exist by reason of a physical, physiological, pathological or other condition, including but not limited to the conditions of diseases, convalescence, pregnancy, lactation, allergic hypersensitivity to food, underweight, and overweight;

(ii) Uses for supplying particular dietary needs which exist by reason of age, including but not limited to the ages of infancy and childhood;

(iii) Uses for supplementing or fortifying the ordinary or usual diet with any vitamin, mineral, or other dietary property. Any such particular use of a food is a special dietary use, regardless of whether such food also purports to be or is represented for general use.

The regulation also notes that the use of an artificial sweetener in a food in order to effect caloric value or available carbohydrates, or to make the food suitable for use by diabetics is a special dietary use. Food sold by weight loss programs qualify as foods for special dietary uses as do the ubiquitous low calorie beverages. The Nutrisystem program offers a line of products with double special dietary uses, Nutrisystem D, which are formulated for weight loss and diabetes control.

In the 1996 ANPR on medical foods, the FDA discussed the differences between medical foods and food for special dietary uses (FDA 1996):

The statutory definitions of medical foods and foods for special dietary use overlap to the extent that both categories encompass foods that are intended for use by sick people. The differences in the statutory definitions evidence, however, that Congress intended foods for special dietary use under section 411(c)(3)(A) of the act to be a broader category of foods for use by people with special dietary needs or desires, while it intended medical foods to be a narrower category of foods for use by people with particular diseases or conditions that have distinctive nutritional requirements. Since a medical food must address the “distinctive nutritional requirements” of a disease or condition, a medical food is suitable only for use by patients with that disease or condition. Of course, it is possible for more than one disease or condition to create the same distinctive nutritional requirements. A product that is intended to address the distinctive nutritional requirements of a particular disease is a medical food, even though some of those requirements may also be created by other diseases. A product that is designed to address a problem that is common to several diseases, but not the full range of requirements of any specific disease, would be a food for special dietary use. For example, the distinctive nutritional requirements of burn patients include a greater energy requirement due to hypermetabolism and a requirement for dietary glutamine because endogenous synthesis of this amino acid does not meet the metabolic requirement. Thus, a product formulated to meet the higher energy requirement due to the hypermetabolic state, but which does not meet the requirement for glutamine, would be a food for special dietary use and not a medical food because it does not meet the full range of distinctive nutritional requirements in patients with burn injuries.

Foods for special dietary uses most likely represent the most straightforward route for incorporating nutritional genomic findings into food labeling because of the provisions from the regulations defining the use of foods “for supplying particular dietary needs which exist by reason of a... physiological condition” and of “foods for supplementing or fortifying the ordinary or usual diet with any vitamin, mineral or other dietary property.” Nutritional genomics will likely lead us to be able to formulate and market foods that contain a particular bioactive nutrient or “dietary property” for particular physiological conditions.
Structure Function Claims

Although originally devised for dietary supplements, in recent years, the FDA has allowed structure function claims to be made about conventional foods. Structure function claims describe the effects that a food or food ingredient has on the normal, healthy structure or normal, healthy function of the body and its systems (21 CFR 101.93). Such claims may not discuss or imply drug actions or abnormal/disease states, must be truthful, not misleading, and must be supported by scientific data. Structure function claims for conventional foods are based on nutritive value such as “fiber supports healthy digestion.” When used on dietary supplement products, structure function claims must be accompanied by the disclaimer, “These statements have not been evaluated by the Food and Drug Administration. This product is not intended to diagnose, treat, cure or prevent any disease.” In addition, dietary supplement manufacturers must notify the FDA of the structure function claims in use within 30 days of market introduction. Food products bearing structure function claims are not required to include the disclaimer and manufacturers do not have to notify the FDA of the claims in use.

Minute Maid recently introduced a series of enhanced juices which are marketed with a number of structure function claims. The pomegranate blueberry variety is marketed for brain nourishment and the front label includes the structure function claims “Omega-3/DHA* Help Nourish Your Brain” and “5 Nutrients to Support Brain and Body” (Figure 22.5). The back of the package includes several other structure function claims:

- DHA is a key building block in the brain.
- Choline and B12 play a role in brain and nervous system signaling.
- Antioxidant vitamin E helps shield the omega-3s in the brain from free radicals.
- Antioxidant vitamin C is highly concentrated in brain nerve endings.

In October of 2009, the National Advertising Division of the Council of Better Business Bureaus announced that they had reviewed the “help nourish your brain” claim and determined that Minute Maid had sufficient data to support the claim. However, the body recommended that a television commercial depicting immediate memory improvement after drinking the product be discontinued due to its implication that people who drink the juice will experience immediately improved memory capabilities (NAD News 2009). Nutritional genomic findings that demonstrate how a particular

* Docosahexaenoic acid.
food or food component supports the normal, healthy structure or normal, healthy function of the body or its systems can be communicated to consumers through structure function claims.

**Dietary Guidance Statements**

Unlike health claims, which were discussed in the section Allowable Health Claims, dietary guidance statements do not require FDA authorization and do not link a particular nutrient to a disease but are general statements regarding health and diet. The distinction between the two types of statements was exemplified in a 1993 federal register docket on food labeling and health claims (FDA 1993):

The following illustration using the National Cancer Institute’s (NCI’s) Five-a-Day Program … exemplifies how the context of the label will determine whether a statement is a health claim or dietary guidance. A cereal label that says “The National Cancer Institute recommends that you eat five servings daily of fruits and vegetables” is not a health claim because the information cannot be reasonably understood to be about a substance. There is neither a nutrient nor a product-specific element in the claim, and there is therefore no characterization between a substance and the disease included in the name or the organization. However, if the statement said, “The National Cancer Institute recommends that you eat five servings daily of fruits and vegetables to increase your intake of fiber,” it would be a health claim because of the reference to a specific nutrient, fiber, and to a disease, cancer.

These statements were succinctly described in a January 2007 guidance document (Schneeman 2007):

Dietary Guidance statements tend to focus on general dietary patterns, practices and recommendations that promote health. Typically “dietary guidance” statements make reference to a category of foods and not a specific substance. An example of a dietary guidance statement is: “Carrots are good for your health.” Dietary guidance statements can be made without FDA review or authorization before use but the statements must be truthful and non-misleading.

**CONCLUSION**

This review has outlined the current regulations governing food product claims, the position of the FDA regarding such claims and the need to watch the science and to participate in FDA discussions on food labeling in order to influence the future of food labels. Emerging nutritional genomic science looks promising and several potential pathways exist for making use of nutritional genomic data. The application of the regulations authorizing the promotion of foods for special dietary uses looks particularly promising as a way to utilize nutritional genomic data for the promotion of public health. The concept that labeling that fails to reveal material facts about a product causes the product to be misbranded, coupled with assertions of First Amendment rights to free speech may provide a path for making nutritional genomic claims.

Whether the regulatory environment is shaped by and keeps pace with nutritional genomic findings will depend largely upon the participation of interesting parties in FDA regulatory processes. While there are current regulatory frameworks that would permit the use of some claims that may be made possible through nutritional genomic research, it may be necessary to completely revamp labeling regulations via petitions to the FDA and to Congress in order to fully communicate useful health messages to consumers. Or, it may be necessary to petition for a mechanism similar to the GRAS process to deal with some nutrigenomic claims, as suggested by a former FDA staff member.

Not only will the future of food labeling as it relates to nutritional genomic data require awareness of the emerging science, it will also require vigilance to ensure that the increasingly enforcement driven FDA does not narrow the use of the claims and food classifications through guidance document and enforcement precedence. Ultimately, we cannot predict the future of food labeling but with knowledge, planning, and effort we can perhaps shape it.
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21 CFR 101.72 Health Claims: Calcium and osteoporosis.
21 CFR 101.93 Certain types of statements for dietary supplements.
21 CFR 105.3 Foods for Special Dietary Use, Definitions and Interpretations, CFR Title 21.


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