This article summarizes the history of the regulation of caffeine, a key component of caffeine-containing energy drinks and other caffeine-containing energy products, in the United States. Caffeine as an ingredient in food has been regulated by the US Food and Drug Administration (FDA) since 1958, when the Food Additives Amendment to the Federal Food, Drug and Cosmetic Act was enacted. It is listed as a substance that is generally recognized as safe by experts for its intended use in cola-type beverages at levels not to exceed 200 parts per million. Here, the history of FDA evaluations of the safe use of, as well as consumer exposure to, caffeine in food in the United States is outlined. Finally, the FDA's current concerns about caffeine and caffeine-containing energy products are reported, along with the current activities to address those concerns.

Published 2014. This article is a U.S. government work and is in the public domain in the USA.

INTRODUCTION

In August 2013, the National Institutes of Health held a workshop entitled “The Use and Biology of Energy Drinks: Current Knowledge and Critical Gaps” at the Neuroscience Center Building in Rockville, Maryland. The US Food and Drug Administration (FDA) participated by giving a presentation on the regulatory status of caffeine, a key component in energy drinks and other energy products. This article builds on that presentation and extends the discussion of caffeine’s regulatory status and history as an ingredient added to food.

Caffeine, chemically known as 1,3,7-trimethylxanthine, occurs naturally in the leaves, fruits, and seeds of numerous plant species, most notably in coffee and cocoa beans, tea leaves, kola nuts, and guarana. Caffeine can be produced synthetically, but when added to food, it is most commonly derived as a byproduct of decaffeination. Historically, caffeine has been added to certain foods, beverages, dietary supplements, and medications; however, coffee and tea, in that order, are the primary sources of caffeine in the diet of the US population.1

Caffeine-containing products may be classified as either conventional foods or dietary supplements. Using caffeine-containing energy drinks as an example, some products are labeled as conventional foods and others are labeled as dietary supplements. This is an important distinction because ingredients added to conventional foods and dietary supplements are subject to different regulations. The manufacturer can decide whether to position a product as a conventional food or a dietary supplement. These regulatory classifications are different with respect to ingredient regulation, labeling, and good manufacturing practices. Manufacturers must meet the applicable regulatory requirements, which depend on whether a product is positioned as a conventional food or a dietary supplement. Manufacturers have been steadily moving towards classifying their energy drink products as conventional foods (i.e., beverages), with the possible exception of energy shots. This article focuses on the use of caffeine as an ingredient added to conventional food. Currently, beverages are the most popular category of food for caffeine addition.

With a few exceptions, an ingredient added directly to food is either a “food additive,” which requires...
premarket review and approval by the FDA, or its intended use must meet the statutory requirement for generally recognized as safe (GRAS) status. Discussed below is the legal basis for food additive approval and for determination that the use of a food ingredient is GRAS. The implementation of the GRAS provision over time and the history of caffeine regulation are also outlined. Finally, the basis for the FDA’s decision to reconsider the safety of caffeine added to foods in the current marketplace is discussed, and the various regulatory options available to the FDA to protect consumers from inadvertent overconsumption of caffeine are noted.

DEFINITION OF FOOD ADDITIVE

In 1958, in response to public concern about the increased use of chemicals in foods and food processing and with the support of the food industry, the US Congress enacted the Food Additives Amendment of 1958 (the 1958 amendment) to the Federal Food, Drug, and Cosmetic Act. The 1958 amendment requires that, before a new additive can be used in food, its producer demonstrate the safety of the additive to the FDA. The 1958 amendment defined the term “food additive” as follows (emphasis added):

“The term “food additive” means 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), if such substance is not generally recognized, among experts qualified by scientific training and experience to evaluate its safety, as having been adequately shown through scientific procedures (or, in the case of a substance used in food prior to January 1, 1958, through either scientific procedures or experience based on common use in food) to be safe under the conditions of its intended use . . .”

Congress recognized that, under this scheme, the safety of an additive could not be established with absolute certainty and thus provided a science-based safety standard that requires producers of food additives to demonstrate to a reasonable certainty that no harm will result from the intended use of an additive. The FDA has incorporated this safety standard into its regulations. If the FDA finds an additive to be safe, ordinarily on the basis of data submitted by the producer to the FDA in a food additive petition, it issues a regulation specifying the conditions under which the additive may be safely used.

THE GRAS PROVISION

Section 201(s) of the Federal Food, Drug and Cosmetic Act (codified in U.S Code Title 21 section 321) excludes from the definition of food additive any substance the intended use of which is generally recognized, among experts qualified by scientific training and experience to evaluate its safety (qualified experts), to be safe under the conditions of its intended use. This exclusion from the definition of a food additive is known as the GRAS provision. Congress recognized that many substances intentionally added to food would not require a formal premarket review by the FDA to assure their safety, either because their safety had been established by a long history of use in food or because the nature of the substances, their customary or projected conditions of use, and the information generally available to scientists about the substances precluded the need for a formal review. According to the Federal Food, Drug, and Cosmetic Act, the same standard of safety exists for food additives and GRAS substances, but a substance that is GRAS for a particular use may be marketed for that use without formal FDA premarket review and approval. Thus, informing the FDA of a GRAS determination has always been voluntary.

Many substances, such as vinegar, vegetable oil, baking powder, and spices, are lawfully marketed without being subject to a food additive regulation on the basis of their common use in food. The GRAS provision also provides for a GRAS determination on the basis of scientific procedures. Previously, it was not unusual for a GRAS determination to be based on common use. This is not the case today, as most determinations are based on scientific procedures, meaning that a substantial body of scientific data supports the intended use, and there is consensus among qualified experts that the use is safe.

Both food additives and GRAS substances, by law, must be safe for their intended uses, and they are both subject to the same standard of safety, i.e., reasonable certainty of no harm. Although premarket review by the FDA is not required for a GRAS determination, other statutory requirements must be met. GRAS criteria require that qualified experts evaluate the safety of the substance for its intended use and that the information used to support the safety evaluation is in the public domain and generally available. When there is no food additive regulation in effect to establish safe conditions of use and the use does not meet the criteria for GRAS, the use of the substance is deemed an unapproved food additive use. Under US law, foods containing an unapproved food additive are adulterated and are subject to enforcement action by the FDA. Other exceptions to the
food additive definition in the law, other than those outlined in the GRAS provision, include ingredients approved by the FDA or the US Department of Agriculture prior to the enactment of the 1958 Food Additives Amendment (also called prior sanction; for more detail, see the section entitled "Regulatory History of Caffeine" below) and color additives and pesticides, to which other legal premarket approval requirements apply.

The FDA first proposed a list of GRAS substances in the Federal Register of December 9, 1958. While the agency considered it impracticable to list all substances that are GRAS for their intended use, it created a list to illustrate common food ingredients that would be regarded as safe for their intended use. In 1959, a slightly altered version of this list was incorporated into the FDA's regulations as 21 CFR 121.101(d). This original listing of substances came to be called "the GRAS list." Currently, uses of GRAS substances for human food appear in Parts 182, 184, and 186 of Title 21 of the Code of Federal Regulations (CFR). Because there is no requirement to notify the FDA of a GRAS determination, there is no single exhaustive GRAS list.

GRAS REVIEWS AND THE SELECT COMMITTEE ON GRAS SUBSTANCES

On October 30, 1969, largely as a result of a recommendation in the report of the 1969 White House Conference on Food, Nutrition, and Health, President Richard M. Nixon, in his consumer message to Congress, directed the FDA to conduct a critical reevaluation of the safety of GRAS food substances. The GRAS review became a major project at the FDA’s Bureau of Foods (now the Center for Food Safety and Applied Nutrition). The FDA contracted with Life Sciences Research Office, part of the Federation of American Societies for Experimental Biology, to make scientific assessments about the health aspects of GRAS substances (as well as "prior sanctioned" substances), to summarize the available scientific literature, and to provide a recommendation on what restrictions, if any, would be needed to ensure the safe use of these substances in food.

The Life Sciences Research Office formed the Select Committee on GRAS Substances (SCOGS), giving due consideration to the selection of the committee to ensure balance and breadth in the appropriate professional disciplines. SCOGS’s evaluations were made independently of the FDA or any other group, governmental or nongovernmental. By 1982, after 10 years of work and significant costs, the SCOGS had produced 151 detailed reports covering over 400 substances, including caffeine. Information from the SCOGS reviews and detailed reports are posted on the FDA’s website.

THE GRAS AFFIRMATION PETITION PROCESS

In 1976, the FDA promulgated regulations to establish the procedures it would use, on its own initiative, to affirm the GRAS status of substances that were the subject of the SCOGS reviews. The affirmed uses of these substances are listed in Parts 184 and 186 of Title 21 of the CFR.

The SCOGS reviews did not cover all GRAS substances (e.g., they did not cover many substances that were marketed on the basis of a manufacturer’s independent conclusion that a use of a substance was GRAS). Consequently, the FDA’s regulations included a mechanism whereby an individual could petition the FDA to review the GRAS status of substances not being considered as part of the agency’s GRAS review under SCOGS. This established the voluntary GRAS affirmation petition process. The substances currently listed in Part 184 (e.g., menhaden oil) of Title 21 of the CFR were affirmed as GRAS as a result of an industry-sponsored GRAS affirmation petition or SCOGS review.

The GRAS affirmation petition process was not mandatory, and unlike the process in place for the review of a food additive petition, there was no statutory mandate for the FDA to complete its review in a specified timeframe. Thus, the GRAS affirmation petitions received lower priority than food additive petitions. Uncertainty as to when the FDA would complete its review of a GRAS affirmation petition in many cases led industry to take one of the following actions: 1) Once the FDA accepted a GRAS affirmation petition for review and the filing notice was published in the Federal Register, manufacturers would market their ingredient before the FDA completed its review; or 2) Industry increasingly made independent GRAS determinations without consulting the FDA. In the mid-1990s, the situation worsened as the FDA’s backlog of pending food additive petitions and GRAS affirmation petitions increased. Further, Congress held hearings and issued a mandate to the FDA to complete its food additive petition reviews within statutory requirements.

THE GRAS NOTIFICATION PROGRAM

In an effort to establish a workable, streamlined, predictable, transparent process that would encourage industry to voluntarily submit GRAS determinations to the FDA, a rule to replace the GRAS affirmation petition process with a notification procedure was proposed in 1997. This proposed rule replaced one voluntary process (petitions) with another voluntary process (notices). The FDA issued this proposed rule to enable a more efficient and effective use of FDA resources. In the proposed rule, the FDA also noted that the lengthy rule-making associated with the GRAS petition process had become a deterrent to those wishing to inform the FDA of their independent
GRAS determination. The proposed rule stated that, prior to the publication of a final rule, the FDA was inviting interested persons who conclude that a use of a substance is GRAS to notify the agency of those conclusions in the manner described in the proposal. Although the rule establishing the proposed notification procedure is not yet final, the FDA received its first GRAS notice in 1998. As described in the 1997 proposed rule, the FDA is evaluating whether each submitted notice provides a sufficient basis for a GRAS determination and whether information in the notice or otherwise available to the FDA raises issues that lead the agency to question whether use of the substance is GRAS. Following this evaluation, the FDA responds to the notifier by letter. The FDA maintains the GRAS Notice Inventory on its website, which includes links to the GRAS Notice submitted as well as to the agency’s response letter. To date, the FDA has received over 530 GRAS Notices. The agency reopened the comment period on the 1997 proposed rule in December 2010.

**THE GRAS REGULATION ON CAFFEINE**

Caffeine is listed as GRAS for use in cola-type beverages at levels not to exceed 200 parts per million (ppm) (0.02%). This maximum level of use is equivalent to approximately 71 mg of caffeine in a 12-oz serving of cola, although colas typically contain roughly half this amount. The GRAS regulation for caffeine provides an affirmative statement that the use of caffeine in cola-type beverages at a level of up to 200 ppm is safe. The regulation does not address other conceivable uses of caffeine in food. Other uses of caffeine may or may not be GRAS. Thus, the GRAS status is not an inherent property of a substance. Rather, a GRAS determination is specific to the intended use. However, over the years, the FDA has not challenged the use of caffeine at 200 ppm in non-cola-type beverages.

It should be noted that the GRAS regulation for caffeine appears under an administrative listing in the CFR entitled Subpart B–Multiple Purpose GRAS Food Substances. The term “Multiple Purpose” refers to the intended technical effect and should not be confused with the intended use of caffeine per the regulation, which, as stated above, is limited to cola-type beverages. Nevertheless, considering the history of caffeine use, which dates back to well before the FDA promulgated this regulation, it is likely that the intended effect of caffeine has included its alerting and energizing potential.

**REGULATORY HISTORY OF CAFFEINE**

The regulatory history of caffeine is complex and is not typical of most food ingredients. Caffeine is one of the substances included on the original GRAS list following enactment of the Food Additives Amendment of 1958 (see the final rule). As noted above, the FDA listed caffeine as GRAS when used in cola-type beverages at a level not to exceed 0.02% of the beverage. The only other regulatory recognition of caffeine as an ingredient in human food was in a former standard of identity for soda water, which listed “... caffeine from kola nut extract and/or other natural caffeine-containing extracts” to be included as a mandatory ingredient in soda water products whose names include the word “cola” or “pepper.” This standard of identity was repealed in the Federal Register of January 6, 1989, because “... some provisions of the standard [were] being adequately dealt with by other regulations, while other provisions [were] no longer necessary.” The Federal Register volume 60, page 57076 (November 13, 1995) provides additional discussion of the soda water standard of identity as it relates to cola-type beverages.

In 1978, as part of its review process (described above), SCOGS completed an evaluation of the safety of caffeine as an additive to nonalcoholic cola-type beverages (Report Number 89, summary available from online database). SCOGS did not consider the safety of caffeine as a natural component of coffee or tea; however, they did consider estimates of caffeine consumption from these sources as “a point of orientation in considering the magnitude of total caffeine consumption from all food and beverages sources. ...” SCOGS rendered a decision for caffeine, which states, “While no evidence in the available information on caffeine demonstrates a hazard to the public when it is used in cola-type beverages at levels that are now current and in the manner now practiced, uncertainties exist requiring that additional studies be conducted.” One concern raised in the report was the potential behavioral effects of caffeine, especially in children. In addition, SCOGS concluded that it was “inappropriate to include caffeine among the substances generally recognized as safe,” noting that “[a]t current levels of consumption of cola-type beverages, the dose of caffeine can approximate that known to induce such pharmacological effects as central nervous system stimulation.”

In the Federal Register of October 21, 1980, the FDA proposed to “delete caffeine used as an added food ingredient from the [GRAS list], to declare that no prior sanction exists for the use of caffeine as an added food ingredient, to restrict the use of caffeine as an added food ingredient to current uses and levels, and to require that the presence of caffeine as an added ingredient be reflected on the product label in the ingredient declaration.” The FDA further proposed to list caffeine as a food additive on an interim basis pending the completion of additional safety studies to resolve issues of concern at the time, including the potential fetotoxic and teratogenic...
properties of caffeine, the potential behavioral effects of caffeine, and the potential carcinogenicity of caffeine. The FDA proposed these actions on the basis of safety concerns that arose during its review, which encompassed both the SCOGS report and additional data. In the proposed rule, the FDA also discussed the SCOGS review, including the data on levels of exposure from added caffeine in cola-type beverages as well as from naturally occurring caffeine present in coffee, tea, chocolate, etc.

The FDA acknowledged that its proposed actions were dependent on a conclusion that the relevant uses of caffeine were not the subject of a prior sanction. Section 201(s)(4) of the Federal Food, Drug, and Cosmetic Act, codified in U.S. Code Title 21 Section 321, exempts from the definition of a food additive "any substance used in accordance with a sanction or approval granted" under the Federal Food, Drug, and Cosmetic Act before the enactment of the Food Additives Amendment of 1958. This type of sanction or approval is known as a "prior sanction." In the 1980 proposed rule, the FDA proposed to declare that no prior sanctions existed for added caffeine, though it noted that evidence of a prior sanction for a particular use of added caffeine could be submitted in response to the proposed rule.

In response to the 1980 proposed rule, comments were submitted providing evidence of a prior sanction for certain uses of caffeine. Thus, because of the prior sanction, the FDA could not regulate the use of caffeine in cola-type beverages as a food additive. Therefore, in the Federal Register of May 20, 1987, the FDA proposed to codify a prior sanction for the use of added caffeine in nonalcoholic carbonated beverages. The documentation submitted in support of the existence of a prior sanction included a letter dated August 20, 1958, from John L. Harvey, then-Deputy Commissioner of Food and Drugs, to Edgar J. Forio of the Coca-Cola Company, stating that the FDA had "long sanctioned the distribution of Coca-Cola and the enactment of [the Food Additives Amendment] would not affect [that] sanction in any way." In the 1987 proposed rule, the FDA noted that the letter was sent less than a week after the US House of Representatives passed the Food Additives Amendment and just before the US Senate passed that legislation. The FDA cited this time line in support of its conclusion that Mr. Harvey understood the significance of his use of the term "sanctioned" in his 1958 letter.

In the same May 20, 1987, proposed rule, the FDA explained that, before recognizing a prior sanction, it must assure that the use is safe. The FDA went on to discuss the safety issues raised in the October 21, 1980, proposed rule and cited the publication of a large number of studies that were conducted in the intervening period, including many that addressed the safety concerns cited in 1980. Upon review of these data, the FDA "...found no evidence to show that the use of caffeine in carbonated beverages would render these beverages injurious to health." The FDA tentatively concluded that "nonalcoholic carbonated beverages containing a maximum level of 0.02 percent caffeine by weight would not be adulterated under section 402 of the act, and that codification of a prior sanction for this use be proposed." On April 22, 2003, the FDA announced its intent in the Federal Register to withdraw the 1980 and 1987 proposed rules (along with other non-caffeine-related proposed rules). Comments were received in the docket, but the FDA did not initiate any further action. Thus, despite these various efforts to further regulate the use of caffeine as an added food ingredient, the regulation at Title 21 page 182.1180 of the CFR remains unchanged. During the 1980s, the FDA focused its regulatory activities on colas and other carbonated soft drinks and did not consider the expanded uses of caffeine that are seen today.

In 2010, the FDA issued a warning letter to manufacturers of caffeinated alcoholic beverages, resulting in the removal of such products from the marketplace.

**CAFFEINE LABELING**

Under US law and regulations, neither caffeine nor caffeine-containing ingredients (e.g., coffee- and tea-derived flavoring ingredients) have special regulatory status with regard to labeling on food products or dietary supplements. Under the Code of Federal Regulations, all ingredients, including caffeine, in a retail food product must be listed by their common and usual name in the ingredients list on the product label. The ingredients are also required to be listed on the packaging of food products in descending order of predominance by weight, when present at levels above 2% by weight (with exceptions; see references for examples of exceptions).

While the FDA requires nutrient content labeling on food, caffeine is not a nutrient and the FDA does not require the amount of either natural or added caffeine to be labeled. On dietary supplements, the amount of caffeine used as a dietary ingredient must be listed, but if caffeine is part of a proprietary blend, only the total amount of the blend is required to be listed.

Although quantitative labeling of added caffeine in a food or dietary supplement is technically feasible, the amount of caffeine that occurs in plant-based products, such as coffee or chocolate, varies. Thus, it would be difficult to label the amount of naturally occurring caffeine in different products accurately on a consistent basis. For this reason, quantitative labeling of naturally occurring caffeine in products is challenging because numerous label changes would be needed to reflect batch-to-batch variations.
Manufacturers may voluntarily label the caffeine content of their products. As early as 2007, the amount of caffeine was labeled on some brands of cola-type beverages. Many members of the American Beverage Association voluntarily provide the content of caffeine on their products’ labels and have done so for some time. More recently, the American Beverage Association developed guidelines for their members on caffeine labeling of energy drinks. The Council for Responsible Nutrition and the American Herbal Products Association, two trade groups for the dietary supplements industry, have also issued guidelines for members on labeling of caffeine. These industry guidelines also recommend quantitative labeling of caffeine on the product as well as an advisory statement cautioning against use by children, pregnant women, and individuals sensitive to caffeine.

MAJOR SOURCES OF CAFFEINE IN TODAY’S MARKETPLACE

Caffeine occurs naturally in certain foods such as coffee, tea, and cocoa. Caffeine is also added directly or indirectly to some beverages, such as caffeine-containing energy drinks and soda-type beverages, as well as to some nonbeverage foods. The amount of caffeine in a food product varies, depending on multiple factors that include serving size, product type, the method of preparation, and the source of caffeine (e.g., purified caffeine, tea, coffee, guaraná). The caffeine content in coffee beans (Coffea spp.) varies widely, depending on geographical origin, growing conditions, and the effects of processing, storage, and roasting. Published chemical analyses of coffee beverages have demonstrated wide ranges of caffeine content (e.g., 143–259 mg per 16-oz serving), even in the same coffee beverage obtained from the same outlet over consecutive days (i.e., 259–564 mg per 16-oz serving). In general, a serving of espresso (about 1 oz or 30 mL) provides 64 mg of caffeine, and an 8-oz cup (237 mL) of automatic drip coffee provides 145 mg of caffeine. Tea (Camellia spp.) beverages contain a variable quantity of caffeine, depending on species, variety, processing method (green, black, etc.), origin, and method of preparation (e.g., water temperature and volume, steeping time, mixing). Typically, tea beverages contain 20–80 mg of caffeine per 8 oz (237 mL). Caffeine is also found in cocoa-based products, kola nuts, guaraná, and yerba maté. Cocoa (Theobroma cacao) contains a small amount of natural caffeine. Cocoa is a major ingredient in chocolate, but chocolate products may contain a wide range of cocoa levels. Chocolate candy, for example, may contain 11–115 mg caffeine per 1-oz serving. Cocoa beverages contain approximately 5 mg caffeine per 6-oz serving.

More than 60% of carbonated soft drinks sold in the United States, including colas, contain caffeine. Carbonated soft drinks containing added caffeine typically have approximately 30–40 mg per 12-oz serving. Caffeine-containing energy drinks typically contain 17–224 mg caffeine per serving (or 1.5–32.5 mg/oz). Caffeine-containing energy drinks often contain other ingredients in addition to caffeine, such as vitamins, L-carnitine, taurine, glucuronolactone, guaraná, kola nut, yerba maté, and/or other botanical extracts. Some of these ingredients, such as guaraná and yerba maté, are additional sources of caffeine and may contribute to overall dietary exposure to caffeine. “Energy shots” are a specialized form of caffeine-containing energy drinks and are often marketed as a dietary supplement, whereas caffeine-containing energy drinks are typically marketed as a conventional food. Energy shots are usually sold in 2-oz containers, but they normally contain the same amount of caffeine as their larger-sized, caffeine-containing energy drink counterparts. Energy shots account for approximately 11% of the caffeine-containing energy drink market, and as of June 2009, there were approximately 250 brands in the United States. More recently, caffeine has been added to other food products such as chewing gum, waffles, and candies that have not been traditional sources of caffeine in the US food supply.

FDA CONCERNS ABOUT CAFFEINE

The FDA is concerned about the indiscriminate use of caffeine as an ingredient in food. The number of products with added caffeine, such as caffeine-containing energy drinks and confectionaries, has increased since 1958 and since the FDA last proposed regulatory changes for the use of caffeine in the 1980s. Although estimates of exposure to caffeine since the 1990s have been relatively stable, there are more recent reports suggesting that significant numbers of individuals in the US population consume more than the commonly cited health reference value of 400 mg/d for healthy adults. In addition, while the patterns of use of caffeine-containing products appear to be changing, the implications of these changes for public health are not well understood. For example, while it is commonly stated that different types of caffeinated products are substituted for each other (e.g., caffeine-containing energy drinks for coffee, and vice versa), there are few data documenting this assertion.

Another concern is that caffeinated products are readily available and attractive to children and adolescents. Products with added caffeine, such as caffeine-containing energy drinks, chewing gum, snack foods, candy, and flavorings added to water, may be particularly attractive to young consumers. There is an ongoing debate about caffeine’s health risks to children and ado-
lescents, largely related to incomplete development of the nervous system in youth. The marketing of caffeine-containing energy drinks to children was a topic of congressional interest in 2013.47

Caffeine is likely one of the earliest known examples of functional ingredients sought after by consumers, and consumption from natural sources for central nervous system stimulation has been culturally accepted throughout the ages. Although a wide range of opinions exist about the safety of adding caffeine to food or dietary supplements, most consumers perceive caffeine as safe, which may mitigate their concerns about excessive consumption. There is wide individual variation in sensitivity to caffeine, even among healthy consumers.48 The interpretation of studies on caffeine intake and its potential effects are confounded by such factors as variability in consumer sensitivity, habituation versus nonhabituation, the timing of consumption in relation to the circadian rhythm, and the use of consumer recall data to estimate intake. Although a variety of complex issues must be considered in assessing the safety of caffeine added to food, as for all ingredients added to food, any use of added caffeine must meet the safety standard of the Federal Food, Drug, and Cosmetic Act. In light of the ongoing questions raised about caffeine in caffeine-containing energy drinks and other novel products, the FDA is reevaluating the uses of caffeine.

**FDA ACTIVITIES RELATED TO THE SAFE USE OF CAFFEINE**

The FDA has been engaged in several activities to increase understanding of any potential public health consequences that may be associated with increased caffeine consumption, particularly by children and adolescents, and to determine whether further regulatory actions are needed. These activities include evaluating caffeine exposure by consumers, compilation and monitoring of published scientific literature, review of adverse event reports, and review of other public health signals. In addition, the FDA has reached out to the food industry and other stakeholders and did contract with the Institute of Medicine (IOM) to hold a public scientific workshop. These efforts are described briefly below.

**Estimates of caffeine exposure**

The FDA considers the estimation of caffeine exposure as one of the most important aspects to address in evaluating the safety of various uses of caffeine. In 2009, the FDA contracted with an outside expert to produce an independent assessment of caffeine exposure, using data from all available sources.40 Daily caffeine consumption was first estimated using data from the National Health and Nutrition Examination Survey (NHANES), a nationwide survey conducted jointly by the US Department of Health and Human Services and the US Department of Agriculture. NHANES includes data on the content of caffeine, along with that of 62 other common components, in foods consumed in the United States. The calculated per capita mean caffeine exposures, based on NHANES datasets from 2001 to 2006, for consumers aged 2 years and older is provided in Table 1. The mean daily exposure to caffeine for the total population ranged from 142.1 to 150.8 milligrams per person per day (mg/person/d).40 The author of the FDA’s commissioned assessment notes that those between ages 2 and 19 years consumed less caffeine than adults. This was attributed to increased consumption of cola beverages among younger age groups relative to adults, who consume more coffee, which contains more caffeine. Female adults consumed less caffeine than males, and caffeine intake increased in an age-dependent manner for both males and females. Males aged 40–59 years consumed the highest daily amounts of caffeine, followed by a substantial decrease for males in older age groups. According to NHANES data from 2005–2006, the highest mean per capita caffeine intake was 295.6 mg/day, recorded for males aged 50–59 years.40

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<th>Age groups by gender</th>
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<td>20 y and over</td>
<td>153.4</td>
<td>155.1</td>
<td>165.3</td>
</tr>
<tr>
<td>Males and females</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2 y and over</td>
<td>142.1</td>
<td>150.8</td>
<td>149.8</td>
</tr>
</tbody>
</table>

The FDA-commissioned assessment also examined food and beverage consumption data issued in February 2008 by the National Eating Trend service of the NPD.
Group, a market research firm. Estimates of caffeine exposure were determined using consumption frequency data from the National Eating Trend service and from caffeine concentration data collected from technical publications, the Internet, trade associations, and industry sources. For all age groups, coffee, tea, and carbonated beverages were the major sources of caffeine, and caffeine exposure tended to increase with age. Children aged 2–13 years were found, on a per capita basis, to consume 28.7 mg/person/d caffeine, which increased to 74.9 mg/person/d and 62.0 mg/person/d among males and females, respectively, aged 14–21 years. The daily per capita caffeine exposure for adults over age 22 years was 161.9 mg/person/d, with women of childbearing age consuming less, at 115.6 mg/person/d. Coffee was noted to be the largest source of caffeine among adults, followed by tea. Soft drinks and tea were the primary sources of caffeine in children aged 2–13 years. The exposure to caffeine for the overall population, using NPD Group data with trade statistics and market information, was in general agreement with estimates of average total daily caffeine intake based on NHANES data.

The FDA has continuously maintained data on food and beverage consumption as a critical component of its mission in reviewing the safety of the components of food. It has used these data in combination with available information on the levels of caffeine (both natural and added) in food to periodically estimate caffeine exposure in the US population. These estimates are consistent with those found in the published literature, which are derived from similar data sources and methodologies. Although published estimates of caffeine exposure are based on a variety of different data sources, depending on the time of publication, they demonstrate relatively constant levels of caffeine exposure over time and reveal similar patterns of exposure. Generally, caffeine exposure is observed to increase with age, with higher exposures reported in men. Pregnant women are reported to consume less caffeine compared with other women of childbearing age. The primary sources of dietary caffeine are coffee and tea for adults and soft drinks for children. Recent sales data have shown increases in sales of caffeine-containing energy drinks and energy shots, though it is unclear whether this indicates higher levels of use by individual consumers or a greater number of consumers using these products.

The FDA will continue to compile data on the use of caffeine as a food ingredient, to track the consumption patterns of caffeine-containing foods and beverages, and to monitor caffeine exposure in the US population. As part of the ongoing review of the safety of caffeine, the FDA is working to identify and fill data gaps to direct further investigation and will continue to evaluate information as it becomes available to better understand the changing patterns of caffeine use.

Compilation and monitoring of published scientific literature

The FDA has compiled previously published literature on caffeine and is monitoring the recent literature on caffeine safety. A comprehensive report was completed in 2011 that summarized the findings of more than 1,500 research articles and more than 300 reviews published in the literature between 1994 and 2009. It covered the cardiovascular, neurological, and reproductive effects of caffeine in the general population and in certain subpopulations such as children, pregnant and lactating women, and adults with underlying disease. Literature on animal studies, experimental studies, and epidemiological studies were included. This report was provided to the IOM and is available on its website.

Review of adverse events reported

The FDA has evaluated adverse event reports submitted to the FDA via the Center for Food Safety and Applied Nutrition Adverse Events Reporting System. Manufacturers of dietary supplements are required to submit MedWatch reports for all serious adverse events associated with their products. Voluntary reports of less-serious adverse events for food or dietary supplements can also be submitted. The FDA evaluated adverse event reports received between January 1, 2008, and December 31, 2012, that were associated with food or dietary supplements containing caffeine. A total of 1,392 events were reported, of which 945 contained minimal information and only 166 contained enough information to conduct an in-depth review. The organ systems affected and the products associated with the adverse events were analyzed, and the most commonly cited systems in descending order of number of adverse events were as follows: gastrointestinal, skin, central nervous system, respiratory, cardiovascular, hepatobiliary, psychiatric, and renal. The FDA concluded that two dietary supplements products, Acacia Cleanse and Jack3D, were most often associated with an adverse event. Additionally, tea, caffeine, and yerba maté were the stimulant-containing ingredients most often involved in adverse events. The FDA’s findings were provided to the IOM and are available on its website.

Review of other public health signals

The FDA is monitoring other reports that may provide signals of possible adverse events relating to caffeine-containing energy drinks. For example, the reports from the Drug Abuse Warning Network, a surveillance system within the Substance Abuse and Mental Health Services Administration that examines emergency room visits.
related to consumption of caffeine-containing energy drinks, are one source of data. Data from the poison control systems (New York City Poison Control and the US National Poison Data System) that have provided summary data to the FDA are another source. The FDA continues to monitor all the scientific literature and other available data for indications of whether caffeine-containing energy drinks pose any threat to the public health.

**Food industry and other targets of outreach**

In light of the new types of caffeinated products appearing on the market, including many that seem to have special appeal to children and adolescents, the FDA has met with some companies to hear the rationale for adding caffeine to varied products and to express its concern. The FDA has also reached out to the American Beverage Association, which represents the nonalcoholic beverage industry, and the Grocery Manufacturers Association, which represents food, beverage, and consumer-products companies. In May of 2013, following conversations with the FDA, the manufacturer of a caffeinated gum announced that it agreed to halt the production, sales, and marketing of its product while the FDA continues an evaluation. Consistent with this example, the FDA has requested that the industry propose additional self-limiting measures for caffeine added to products. Moving forward, the FDA will continue to look for industry to demonstrate leadership and commitment to public health as it evaluates the latest scientific information on the safe use of caffeine. As always, the FDA will rely on collaboration with the scientific community, consumers, and industry to ensure the use of caffeine added to food is safe.

**FDA-sponsored IOM meeting**

Any FDA action related to caffeine use must be based on sound science, so the FDA contracted with IOM of the National Academies for help in obtaining scientific input on dietary exposure and any health hazards associated with caffeine-containing energy drinks and other food products containing caffeine. The workshop, entitled “Caffeine in Food and Dietary Supplements: Examining Safety,” was held August 5–6, 2013, in Washington, DC. The IOM set the agenda for the meeting to accomplish the following aims: 1) Evaluate the epidemiological, toxicological, clinical, and other relevant literature to describe important health hazards associated with caffeine consumption; 2) Delineate vulnerable populations who may be at risk from caffeine exposure; 3) Describe caffeine exposure and risk of cardiovascular and other health effects on vulnerable populations, including additive effects with other ingredients and effects related to pre-existing conditions; 4) Explore safe caffeine exposure levels for general and vulnerable populations; and 5) Identify data gaps on the stimulatory effects of caffeine, including cardiovascular, central nervous system, or other health outcomes.

The FDA provided reference material to the IOM, including a backgrounder with a series of questions on which the FDA desired input; reports on estimates of caffeine exposure; a compilation of about 15 years of caffeine-related safety studies published in the literature up to 2009; and data on adverse event reports received by FDA. In 2014, the IOM released a summary of the workshop presentations and discussions. While this summary captured the recommendations of individual presenters and the themes raised by individuals, it does not present a consensus view of the workshop as an entity nor does it provide specific recommendations for FDA actions.

The workshop presentations as well as both FDA- and IOM-generated meeting materials are currently available online from the IOM website.

**CONCLUSION**

Over time, the FDA has worked to better understand the public health risk associated with consumption of caffeine and to determine the appropriate response. Most recently, in 2009, the FDA took action on caffeinated alcoholic beverages. The FDA continues to work to better understand the potential risks to public health that may be associated with increased consumption of caffeine added to foods and dietary supplements and to determine what further regulatory actions may be appropriate.

The FDA is committed to addressing the issues and concerns related to the safe use of caffeine. To this end, it is seeking information to address the following questions: 1) Does the FDA have the science right?; 2) Are there clear principles to guide the addition of caffeine to food?; and 3) Is the FDA applying appropriate regulatory oversight?

The FDA considers the assessment of caffeine exposure key to getting the science right. Population-based estimates of caffeine intake do not indicate excessive consumption by the population at large; however, more granular estimates are desired to address consumption by consumers in various age groups and vulnerable subpopulations, such as children and women of childbearing age. In addition, estimates of exposure need to include added caffeine and caffeine from all sources, including naturally occurring caffeine and stealth caffeine present as a component of other added ingredients (i.e., botanicals and extracts). Also key to getting the science right is the identification of those studies from the vast
literature on caffeine that most accurately characterize potential risks. While the science to support the safe addition of caffeine to a broader range of foods is being sorted out, stakeholders and the FDA could develop clear principles to guide the addition of caffeine to food.

In terms of regulatory oversight, the FDA has various options at its disposal to manage risks associated with the potential effects of increased caffeine consumption on public health. Examples of the FDA’s options that will be evaluated include the following: 1) Amending the existing regulation on caffeine; 2) Issuing guidance describing principles for the use of caffeine in food and dietary supplements; 3) Labeling initiatives that would require disclosure of the total caffeine content of foods (including added caffeine and caffeine from natural sources) and a cautionary statement on caffeine-containing products to alert caffeine-sensitive individuals; 4) Developing and implementing a postmarket surveillance plan; and 5) Undertaking an education campaign directed primarily at youth, caffeine-sensitive individuals, and abusive users of caffeine.

In addition, the FDA may need to work with some of its federal partners to take action. For example, the Federal Trade Commission might work to establish greater restrictions on the marketing of caffeinated products.

The agency encourages stakeholders to engage in dialogue with the FDA about uses of caffeine. The FDA has called on companies to show voluntary restraint in marketing caffeinated products. As the situation demands, however, the FDA will take whatever actions are necessary to protect consumers.

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