

March 19, 2013

The Honorable Margaret A. Hamburg, M.D.
Commissioner
Food and Drug Administration
10903 New Hampshire Avenue
Silver Spring, MD 20993

Re: The Use of Caffeine In Energy Drinks

Dear Commissioner Hamburg:

Recent reports of health complications, emergency department visits, injuries, and deaths related to energy drink consumption have spawned widespread concern among scientists, health professionals, legislators, state and local law enforcement officials, and consumers regarding the safety of highly caffeinated energy drinks. As researchers, scientists, clinicians, and public health professionals who have studied and conducted research on energy drinks, we are writing this letter to summarize the scientific evidence on this issue and encourage action.

Given the evidence summarized below, we conclude that there is neither sufficient evidence of safety nor a consensus of scientific opinion to conclude that the high levels of added caffeine in energy drinks are safe under the conditions of their intended use, as required by the FDA's Generally Recognized as Safe (GRAS) standards for food additives. To the contrary, the best available scientific evidence demonstrates a robust correlation between the caffeine levels in energy drinks and adverse health and safety consequences, particularly among children, adolescents, and young adults.

DESCRIPTION OF ENERGY DRINKS AND RELATED PRODUCTS

Energy drinks are a relative newcomer to the U.S. marketplace and have surged in popularity in recent years, particularly among adolescents. Energy drinks are flavored beverages that contain added amounts of caffeine as well as other additives such as taurine, guarana (a natural source of caffeine), and ginseng.¹⁻³

The U.S. energy drink industry has grown rapidly since the drinks were first introduced,^{3,4} and is projected to reach \$19.7 billion in sales by 2013.² Between 2006 and 2012, Monster Energy®, the largest U.S. energy drink manufacturer, tripled its sales.⁵ As a result of aggressive marketing, energy drinks are particularly popular among adolescents.^{4,6,7} As noted in a 2010 study commissioned by the FDA,^a “[e]nergy drinks are typically attractive to young people,” and 65% of energy drink consumers are 13- to 35-year-olds.⁸ More recent reports show that 30 to 50% of

^a This report discusses the mean per capita daily caffeine intake from energy drinks as calculated by estimates from data provided by the Beverage Marketing Corporation. The mean per capita daily intake tells us nothing about the number of individuals who are ingesting large quantities of these products. The report relied on data that is now out of date and made assumptions based on caffeine levels in 16 oz serving sizes, rather than the new 24 oz sizes. Further, the report also acknowledged that “very limited reliable information is available of the number and age distribution of regular energy drink consumers” and “there may be underreporting for young person[s]”.⁸

adolescents and young adults consume energy drinks.^{7,9-11} According to *Monitoring the Future*, the federally funded national annual survey of students in grades eight through twelve, 35% of eighth graders and 29% of both tenth and twelfth graders consumed an energy drink during the past year, and 18% of eighth graders reported using one or more energy drinks every day.¹²

Energy drinks vary with respect to caffeine content and concentration.^{1,13} The caffeine content of many energy drinks is not disclosed on the product label,² and in these cases, information about caffeine content must be derived from Internet sources of unknown validity. In general, the caffeine concentration of energy drinks is much higher than that of sodas, for which the FDA has recognized 200 parts per million of caffeine (approximately 71 mg per 12 fl oz serving) as GRAS.¹⁴ By contrast, the most popular energy drinks, like Monster Energy®, contain between 160 and 240 milligrams of caffeine per can. Many energy drinks contain as much as 100 mg of caffeine per 8 fl oz serving² with some containing as much as 300 mg per 8 fl oz serving.¹³ In addition, many energy drink brands are sold in larger, containers that hold multiple servings (16 to 24 fl oz/473 to 710 mL).¹ While some energy drink manufacturers properly classify their drinks as beverages, others label their beverages as dietary supplements.^b

Although some brands of coffee contain amounts of caffeine that exceed the FDA's established GRAS levels for soda, energy drinks differ from coffee in three important ways. First, the caffeine in coffee is naturally occurring, while the caffeine in energy drinks is added by the manufacturer and is thus subject to regulation by the FDA as a food additive. Second, many energy drinks and related products containing added caffeine exceed the caffeine concentration of even the most highly caffeinated coffee.^{13,15} Third, coffee is typically served hot, tastes bitter, and is consumed slowly by sipping. By contrast, energy drinks are typically carbonated, sweetened drinks that are served cold and consumed more rapidly. Indeed, energy drinks are often marketed in a manner that encourages consumers to ingest large quantities quickly (*e.g.*, “pound down,” “chug it down”^c). Unlike coffee, energy drinks are marketed in a manner designed to appeal to youth and are highly popular with youth. A scientific review funded by the National Institutes of Health has concluded that the risk for energy drink overdose is increased by the combination of marketing that specifically targets youth and the developmental risk-taking tendencies of adolescents.⁷

^bEnergy “shots” are a subset of energy drinks that come in smaller containers (usually 1.4 to 3 oz) and have even higher caffeine concentration than regularly-sized energy drinks. Many contain B vitamins, taurine, flavoring, and sweeteners. Other “energy products” available for purchase include gel packs, candies, gum, snacks, energy powders, inhalers, and strips, all containing various amounts of added caffeine.

^cLabels of Monster Energy® products.

HEALTH COMPLICATIONS ASSOCIATED WITH THE CONSUMPTION OF ENERGY DRINKS

We are particularly concerned about the health effects of energy drink consumption by children and adolescents. Younger individuals tend to have greater sensitivity to a given serving of caffeine than adults because they are more likely to have a lower body mass and are less likely have already developed a pharmacological tolerance from regular caffeine consumption. The American Academy of Pediatrics' Committee on Nutrition and the Council on Sports Medicine and Fitness recently concluded that "rigorous review and analysis of the literature reveal that caffeine and other stimulant substances contained in energy drinks have no place in the diet of children and adolescents."¹⁶

The Institute of Medicine has similarly recommended that any drinks containing caffeine should not be sold to children at school.¹⁷ Pediatric professionals concur and further state that energy drinks "are not appropriate for children and adolescents and should never be consumed."¹⁶ Other experts have concluded that children and adolescents should not consume more than 100 mg of caffeine per day,⁷ less than the amount in a single can of most energy drinks.

With respect to adults, the FDA has noted that consumption of 400 mg of caffeine by healthy adults in the course of a day is not associated with adverse health effects.¹⁸ That standard for "healthy adults" does not take into consideration that individuals have varying sensitivities to caffeine.¹⁹⁻²⁴ Moreover, consumption of 400 mg "in the course of the day" is an important qualification because consumers can ingest 400 mg of caffeine from energy drinks very quickly. Metabolism of caffeine appears to be non-linear at high doses. In one study using caffeine-experienced human subjects, an increase in caffeine dose from 250 to 500 mg was associated with significant increases in the half-life as well as a decrease in the clearance of caffeine from the blood, resulting in higher caffeine levels that were sustained much longer compared with the lower dose.²⁵ An additional consideration is that the negative effects of caffeine at high blood levels could be compounded by the accumulation of its metabolites (e.g., paraxanthine, theophylline, theobromine), which are active stimulants themselves.^{25,26}

Our work as public health professionals has included examination of the surveillance methods used to track adverse health effects associated with energy drink consumption (e.g., emergency department visits for caffeine-related cardiac events). Despite widespread use of energy drinks, there are no systematic data collection methods to ascertain the prevalence of possible adverse health complications related to energy drinks and related products. Therefore, the following information likely underestimates the actual prevalence of adverse health effects associated with these beverages.

Fatalities and Injuries: According to information submitted to the FDA through its voluntary Adverse Event Reporting System, consumption of Monster Energy® was implicated in the deaths of five individuals, and reports of 13 deaths have cited the possible involvement of 5-Hour Energy®.²⁷ The FDA has not disclosed the ages of the deceased individuals in these cases. However, details reported elsewhere indicate that in one case, a 14-year-old girl reportedly died of a cardiac arrhythmia induced by caffeine after consuming two 24 oz Monster Energy®

beverages over two consecutive days.²⁸ Also reported to the FDA were 21 claims of adverse reactions, some requiring hospitalization, which were reportedly associated with the consumption of Red Bull®.²⁹ These reports only refer to three of the energy products on the market, and of course do not include injuries and deaths that were not voluntarily reported to the FDA. Also, between October 2010 and September 2011, about half of all calls to the National Poison Data System for energy-drink-related caffeine toxicity concerned children under 6 years old. This incidence is far greater than for accidental ingestion of other forms of caffeine.³⁰

Emergency Department Visits: The Drug Abuse Warning Network (DAWN) reports U.S. emergency department (ED) visits using a probability sampling strategy. DAWN conducted a special analysis of the data related to energy drink consumption, which revealed a ten-fold increase in ED visits from 2005 to 2009 (1,128 to 13,114).³¹ DAWN recently issued an update to that report which showed that the number of energy-drink-related ED visits doubled between 2007 and 2011, from 10,068 to 20,783.³²

Cardiovascular Complications: Caffeine produces a number of cardiac effects, which appear in a more pronounced manner in caffeine-naïve subjects and in those consuming higher doses of caffeine. The consumption of highly caffeinated energy drinks has been associated with elevated blood pressure, altered heart rates, and severe cardiac events in children and young adults, especially those with underlying cardiovascular diseases. A few studies have examined the effects of caffeine consumption on heart rate and blood pressure in children and adolescents.^{33,34}

Higher doses of caffeine have been associated with caffeine intoxication, resulting in tachycardia, elevated blood pressure, vomiting, hypokalemia (from beta-adrenergic stimulation), and cardiac arrhythmias (atrial flutter, atrial fibrillation, atrioventricular nodal reentrant tachycardia, and ventricular fibrillation).^{1,3}

A study of young adults found that the consumption of a sugar-free energy drink containing 80 mg of caffeine was associated with changes in platelet and endothelial function great enough to increase the risk for severe cardiac events in susceptible individuals.³⁵ These findings show how acute effects of caffeine administration on heart rate might result in cardiovascular events requiring hospitalization, especially in at-risk youth. Caffeine's effects on blood pressure have been found to be more pronounced among African American children than White children.^{36,37}

The consumption of energy drinks before or during exercise might be linked to an increased risk for myocardial ischemia. In healthy individuals who consume caffeine and then exercise afterwards, significant reductions in myocardial blood flow have been noted by indirect laboratory measures.³⁸ Several mechanisms have been postulated to explain this effect, including the ability of caffeine to block adenosine receptors that modulate coronary vasomotor tone.³⁸ This vasoconstrictive effect might be more pronounced among caffeine-naïve individuals or those who acutely ingest higher doses of caffeine, such as are present in energy drinks.

Seizures: In addition to cardiac events, cases have been reported of new-onset seizures attributed to energy drink consumption among 15- to 28-year-olds.³⁹⁻⁴² In all of these cases, seizures ceased after the individuals abstained from consuming energy drinks.

Childhood Obesity: Energy drinks have also been shown to contribute to youth obesity due to their high calorie and sugar content.^{7,43} One 24-oz can of Monster Energy® contains 81 grams of sugar, which is equivalent to 6.75 tablespoons.² The American Academy of Pediatrics' Committee on Nutrition reports findings that the consumption of excessive carbohydrate calories from energy drinks increases risk for pediatric overweight and that "energy drinks have no place in the diet of children and adolescents."¹⁶ In addition, adolescents are at risk for increased consumption of high-calorie energy beverages due to marketing claims that they enhance physical and mental performance and increase energy.¹³

Other Health Issues: Youth with higher caffeine intake commonly report troubling neurological symptoms, including nervousness, anxiety, jitteriness, and headache.⁴⁴⁻⁴⁶ In one review, youth consuming 100 to 400 mg of caffeine daily from dietary sources report jitteriness and nervousness.⁴⁴ Studies have also linked high caffeine intake to reduced sleep, poor academic performance, daytime sleepiness (falling asleep at school), aggressive behavior, and social and attention problems among youth.⁴⁷⁻⁵³ With regard to energy drinks in particular, studies have shown negative behavioral effects among youth including jitteriness, anxiety, and dizziness, which might undermine students' ability to stay on task, focus, and perform well.⁶ Although many energy drink manufacturers assert that additives such as taurine and B-vitamins improve physical or cognitive performance, current evidence does not support these claims.⁵⁴ Finally, energy drinks that have higher titratable acidity levels than sports drinks have been associated with comparatively more tooth enamel loss.⁵⁵

Health and Safety Effects of Combining Energy Drinks with Alcohol: Energy drinks also pose unique dangers when combined with alcohol. Although the FDA and CDC have concluded that the combination of alcohol and energy drinks is unsafe and poses serious health risks,^{18,56} the latest available national data from *Monitoring the Future* indicated that 26% of high school seniors consumed an alcoholic beverage containing caffeine during the past year.¹² Because individuals who consume energy drinks with alcohol underestimate their true level of alcohol-related impairment (*i.e.*, a "wide-awake drunk"),⁵⁷⁻⁵⁹ the bulk of scientific evidence suggests that individuals who combine energy drinks with alcohol are more likely to engage in risky behavior than if they were only consuming alcohol.⁶⁰⁻⁶⁴ Accordingly, consuming energy drinks mixed with alcohol is associated with serious alcohol-related consequences such as sexual assault and driving while intoxicated.⁶⁰ One study found that individuals who mix alcohol and energy drinks are more likely to report heavy drinking,⁶⁵ while another study documented a link between frequent consumption of energy drinks and increased risk for alcohol dependence among college students.⁶⁶

CONCLUSION

Based on our own research and our review of the published literature cited herein, we conclude that there is no general consensus among qualified experts that the addition of caffeine in the amounts used in energy drinks is safe under its conditions of intended use as required by the GRAS standard, particularly for vulnerable populations such as children and adolescents. On the contrary, there is evidence in the published scientific literature that the caffeine levels in energy drinks pose serious potential health risks, including increased risk for serious injury or even death. We therefore urge the FDA to take prompt action to protect children and adolescents from the dangers of highly caffeinated energy drinks, including applying the existing GRAS standard for sodas to energy drinks and other beverages that contain caffeine as an additive. We also urge the FDA to require that manufacturers include caffeine content on product labels.

Sincerely,



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