STATEMENT OF JANET WEINER,
CHIEF OPERATIONS OFFICER AND CHIEF FINANCIAL OFFICER,
ROCKSTAR, INC.
BEFORE THE UNITED STATES SENATE
COMMITTEE ON COMMERCE, SCIENCE, AND TRANSPORTATION

Wednesday, July 31, 2013
2:30 P.M.

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Chairman Rockefeller, Ranking Member Thune, and members of the Committee, my name is Janet Weiner, I am the Chief Operations Officer and Chief Financial Officer for Rockstar, Inc., the manufacturer of Rockstar Energy Drink products. I am also co-owner of the company.

I thank the Committee for inviting Rockstar to speak at today's hearing, and I welcome this opportunity to discuss with this esteemed panel Rockstar's commitment to the safety of our products and the responsibility of our brand marketing practices.

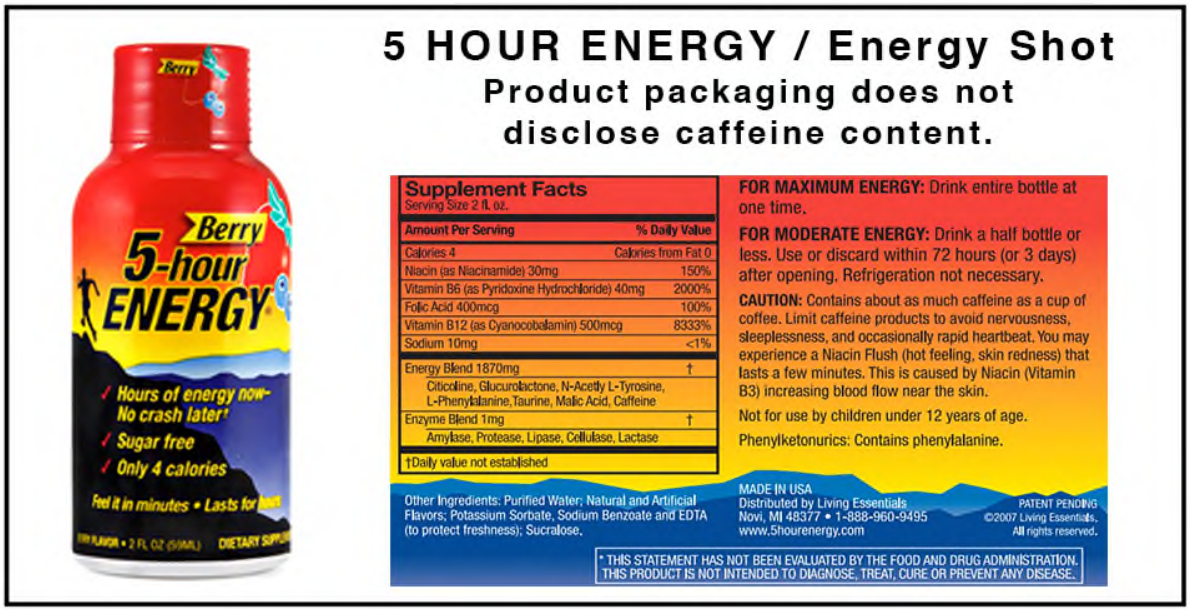
Rockstar represents a model of entrepreneurial enterprise that has grown from an ambitious idea into an American success story, from a small drink manufacturer to a major force in the beverage industry.

Founded in 2001 with a single product, the Rockstar Energy Drink portfolio now consists of over 20 flavors and is currently sold in more than 30 geographies around the world including the United States, Canada, Europe, Asia, Australia, and the Middle East. Rockstar's current market share in the United States is roughly 15 percent of the overall energy drink market.

Energy drinks are an extremely popular and growing product category, having sold more than 34 billion units in the United States since 2000. As such, energy drinks are very much a mainstream product with broad participation from a range of companies within the beverage industry. Following on the next page is chart showing a sample of energy drinks marketed by some of the largest beverage manufacturers in the U.S., which are all in addition to the products manufactured by the companies present here today.

The energy drink market is made more competitive by concentrated “energy shots,” such as 5-Hour Energy and similar products. These products account for approximately 11 percent of the

energy market.[1]



Rockstar's commitment to consumer safety is the company's number one priority, and I will outline for the Committee the steps we have taken to insure this objective.

Before I do that, I would like to make the following assertions, which are based upon a recent Rockstar submission to the U.S. Food and Drug Administration ("FDA"),[2] and which address certain inaccurate or questionable claims regarding the safety of the use of caffeine in our energy drinks products and, specifically, such claims regarding the health of children and teenagers.

First, the use of caffeine within our energy drink formulations has been determined, based upon the consensus of a highly qualified expert panel (hereinafter "GRAS panel"),[3] to be Generally Recognized as Safe ("GRAS") under FDA standards. As part of this determination, the panel specifically considered the effect of caffeine on children.

As we stated in our recent letter to the FDA:

> Various sub-populations were considered during the GRAS determination including evaluation of age or sex specific effects of caffeine. The effect of caffeine on children was considered, and it was determined, based on limited studies, that there is no evidence to support the conclusion that children display

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[1] *See* Food and Drug Administration, Laszlo P. Somogyi, *Caffeine Intake by the U.S. Population* 2 (updated Dec. 2012) (hereinafter "Somogyi Report").

[2] Letter from Kathleen M. Sanzo, on behalf of Rockstar, Inc. to Michael M. Landa, Director, Center for Food Safety and Applied Nutrition, U.S. Food and Drug Administration (June 18, 2013) (hereinafter "Landa Letter").

[3] Rockstar's GRAS panel was comprised of the following individuals: Dr. John Doull Ph.D., M.D. (University of Kansas Medical Center); Dr. Stanley M. Tarka Ph.D. (Consultant); Dr. John A. Thomas Ph.D. (University of Indiana School of Medicine).

> increased sensitivities to dietary caffeine. For example, as reported by Tema Nord, the Nordic Council of Ministers Working Group on Food Toxicology and Risk Evaluation, "Studies on caffeine dependency and withdrawal symptoms in children and adolescents, although few, draw the same picture of the physical and psychological findings as in adults" (Meltzer et al., 2008). Dietary exposure to caffeine in children and the corresponding potential to affect neurodevelopment in children was considered. Studies conducted under placebo controlled settings using large populations of healthy children with asthma or attention deficit disorder demonstrate that consumption of large dietary quantities of caffeine on a daily basis (i.e., 5 to 10 mg/kg body weight per day) for extended durations is without adverse effects on various developmental measures (e.g., motor function, cognition, behavior, general health, deafness, blindness) (Lindgren et al., 1992; Stein et al., 1996; Schmidt et al., 2006, 2007, 2012). Although the current published information provides no evidence that children display increased sensitivities, Rockstar notes that caffeinated Rockstar energy drinks are not intended for use by children . . . , nor are Rockstar products directly marketed to this population group. Caffeinated energy drinks manufactured by Rockstar are clearly labeled not recommended for children . . . . It was therefore concluded that the intended use of caffeine within Rockstar energy drinks does not represent a risk to children under the age of 12 as this population group is not an intended user of Rockstar energy drink products.[4]

Second, case reports purporting to link energy drink consumption with severe adverse effects do not demonstrate a causal relationship between caffeine and the effects that were reported. As explained in our June 18, 2013 letter to the FDA:

> During the GRAS determination, Rockstar, and the Expert Panel, recognized the increasing concerns expressed by the media and scientific community pertaining to the safety of caffeinated energy drinks. It was determined that these concerns were exclusively driven by various case reports in which the consumption of an energy drink was associated with severe adverse reactions and alleged death in some individuals. A critical review of published case-reports documenting incidences of severe adverse effects in association with energy drink consumption was conducted during the GRAS determination. It was concluded that case-reports do not represent cause-effect relationships as such information is subject to many other significant confounding events/information (e.g., lack of information on exposures, the presence of pre-existing or undiagnosed conditions, or improper and falsely documented use patterns of the drink and/or other substances such as drugs and alcohol). This view was supported by the U.S. FDA as reflected within the statement on the Agency CAERs database (for which reports of energy drink associated adverse effects have been documented) that "the adverse effect report itself about a particular product only reflects information AS REPORTED [FDA's emphasis] and does not represent any conclusion by FDA regarding a causal relationship or association with the product

[4] Landa Letter at 7.

> or ingredient." The potential for confounding that is implicit within these types of case report studies is significant, and this limitation has in many instances not received proper consideration.[5]

Additionally, as I will discuss at greater length below, a report released on July 25, 2013, by Pinney Associates further calls into question the reliability of certain data that has been cited to suggest a causal link between energy drinks and emergency room visits.[6]

I. Rockstar's Commitment to Consumer Safety

Rockstar Energy Drink products contain levels of caffeine that are GRAS under FDA standards. In August 2012, the FDA stated that for healthy adults, caffeine intake up to 400 milligrams per day is not associated with general toxicity, cardiovascular effects, effects on bone status and calcium balance, changes in adult behavior, incidence of cancer, or effects on male fertility.

In addition to caffeine, Rockstar contains other ingredients that are consistent with FDA GRAS guidance and are safe for consumption. These other ingredients include B-Vitamins, Ginseng, Milk Thistle, L-Carnitine, Inositol, and Taurine. The caffeine contribution to the finished drinks from the inclusion of Guarana is less than 1 milligram per serving. Taurine is an amino acid that is naturally present in human flesh, and is in meat, mother's breast milk, and popular baby formulas. As explained in an April 25, 2013 scientific white paper signed by John Doull, Ph.D., M.D., a Professor in the Department of Pharmacology at the University of Kansas Medical Center, addressing the safety of Rockstar's products – a copy of which is attached to this statement as Attachment 1 – the expert panel commissioned by our company has concluded that under the conditions of intended use in Rockstar Energy Drink products, the combination of ingredients as used in Rockstar is safe for consumption and GRAS based on scientific procedures.[7]

The caffeine content in Rockstar Energy Drink products is well below this threshold and considerably lower than that contained in a sixteen ounce cup of premium brand coffee.

For example, a sixteen ounce can of Rockstar Energy Drink will contain either 160 milligrams of caffeine or 240 milligrams of caffeine, depending on the product. By contrast, the same sixteen ounces of Starbuck's Pike Place coffee is identified on the company's web site as containing 330 milligrams of caffeine.[8]

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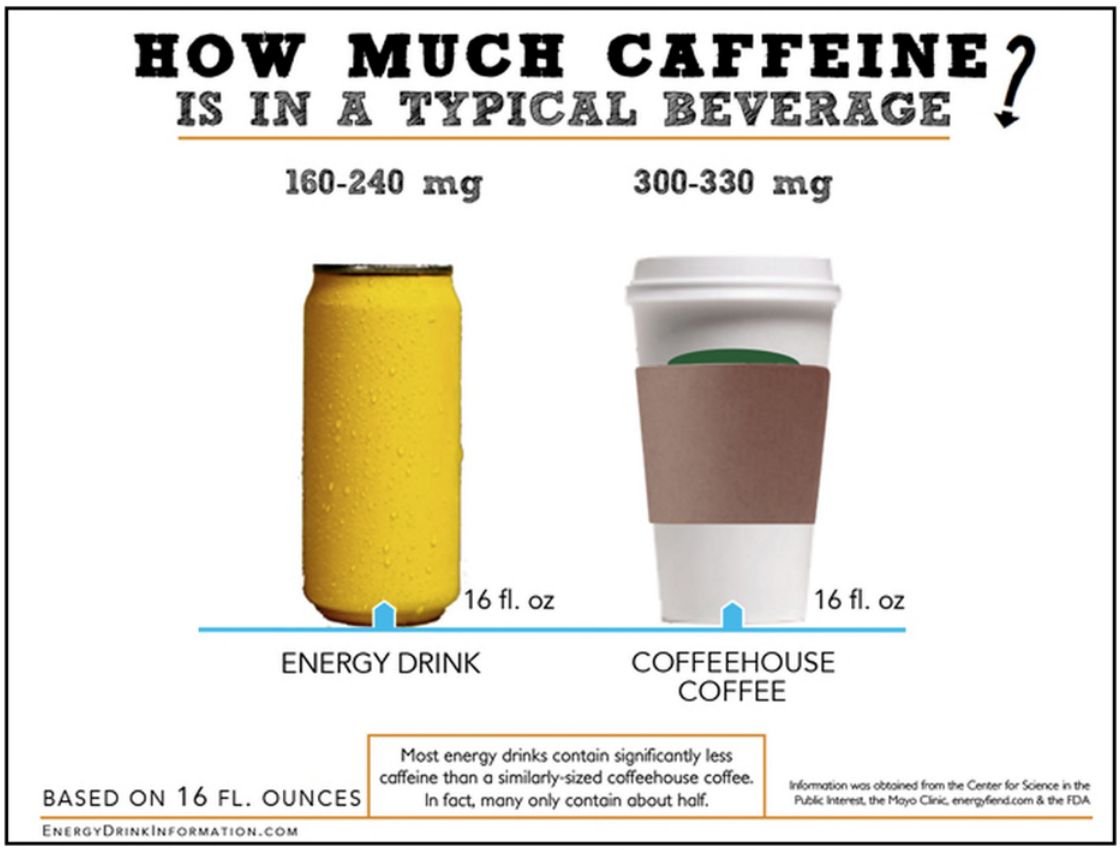
[5] *Id.* at 5-6.

[6] Pinney Associates, *Emergency Department Visits Involving Energy Drinks and Limitations of the Drug Abuse Warning Network (DAWN)* (July 25, 2013) (hereinafter "Pinney Report").

[7] Intertek Cantox, Scientific White Paper: Summary of Data Supporting the Safety of Rockstar Energy Drinks 3, 21-23 (April 25, 2013) [hereinafter Scientific White Paper].

[8] Starbucks Corp., Pike Place Roast Nutritional Information, http://www.starbucks.com/menu/drinks/brewed-coffee/pike-place-roast (last visited July 28, 2013).



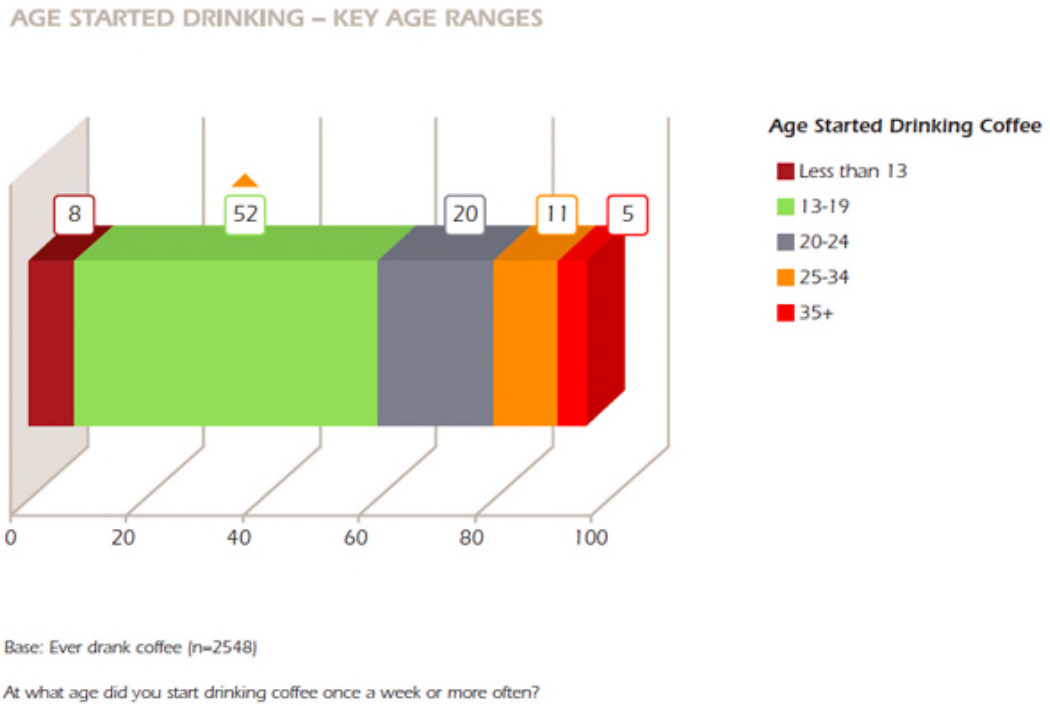
Coffee and tea, rather than energy drinks, are the most significant sources of caffeine for Americans, including teens and children. A FDA-commissioned report authored by Laszlo P. Somogyi on caffeine consumption among the U.S. population in 2009, and then updated in 2010 and again in 2012, indicated that teens and young adults ages 14 to 21 years consume, on average, approximately one-third the amount of caffeine as people over 21 – about 100 milligrams per day. Importantly, the 2012 report also showed that the average amount of caffeine consumed has remained constant. Further, the report found that "'energy drinks' contributed only a small portion of caffeine consumed by teenagers." and that the most significant source of caffeine for both children aged 2 to 13 and teens aged 14 to 17 was coffee, tea, and soft drinks.[9]

Based on data gathered from 2009 through 2010, the U.S. National Center for Health Statistics' National Health and Nutrition Examination Surveys ("NHANES") reported very low energy drink consumption among adolescents, including just 1.1% consumption of energy drinks among adolescent girls and 4.5% among adolescent boys. A similar conclusion was reached by researchers at Pennsylvania State University and the Diet Assessment Center, who found that the percentage of energy drink users reported in the Kantar Worldpanel Beverage Consumption Survey was low, and that energy drinks "were minor contributors to overall caffeine intakes in all age groups."[10]

[9] Somogyi Report at Dec. 2012 update.

[10] Diane C. Mitchell, et al., *Beverage Caffeine Intakes in the U.S.* abstract (April 2012).

According to the National Coffee Association, "[t]he teenage years are the key entry point into the coffee market."[11] Of Americans who drink coffee, 52% reported that they began consuming coffee one time per week or more between the ages of 13 and 19, with another 8% that began to consume coffee regularly before they turned 13.[12]



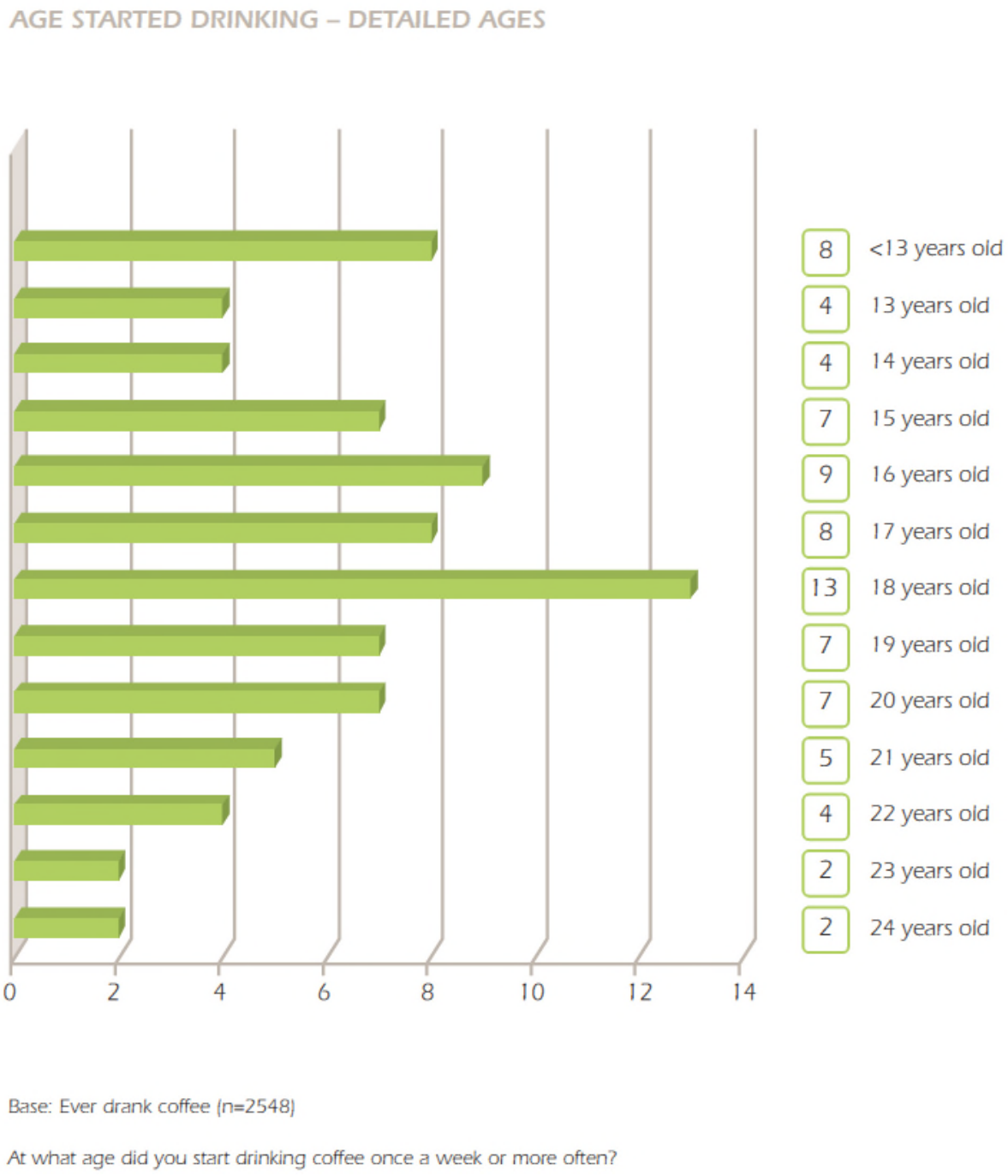
Source: National Coffee Assoc., *2012 National Coffee Drinking Trends* at 52.

Looking at the years in greater detail, the National Coffee Association found that the ages of "16-18 emerge as the most important – 34% of coffee consumers began drinking coffee weekly or more often in those years."[13] Factoring in all ages, the mean age at which consumers started drinking coffee is 19 years old.

[11] National Coffee Assoc., *2012 National Coffee Drinking Trends* 52 (2012).

[12] *Id.* at 52-53 (2012).

[13] *Id.* at 52.



Source: National Coffee Assoc., *2012 National Coffee Drinking Trends* at 53.

Rockstar has been extremely distressed by the proliferation and amount of inaccurate information that has appeared in the media based upon erroneous reports and manipulated data. We hope that this hearing will help to debunk the misinformation that has been unfortunately perpetuated by the media, by questionable methodology in reports prepared by the Drug Abuse Warning Network ("DAWN"), and by the distorted information presented in the "Arria Letter." Although the DAWN report has attracted significant attention, careful analysis of the report and

the public data relied on by the authors, does not appear to be consistent with a signal of substantial medical harm.

As identified in a recent analysis by Pinney Associates, commissioned by the American Beverage Association ("ABA"), reports of energy drink-related Emergency Department ("ED") visits need to be viewed in a broader context, as an analysis of DAWN public use data indicates that drug-related ED visits have also increased (both by a similar proportion and absolute magnitude as compared to energy drinks) for a number of other products, including infant formula, vitamins, and laxatives. In 2011, energy drink-related visits were estimated to comprise only 0.41% of all drug-related ED visits.[14]

Further, Pinney Associates noted the DAWN report's findings rely on extrapolated sample data which can distort the estimate and skew the reported national statistics regarding emergency room visits associated with energy drinks.[15]

Additionally, as the ABA has recently noted, the Authors of the Arria Letter paint a distorted and highly inaccurate picture of caffeine use and safety, ignoring the vast body of robust and reliable scientific evidence that has, for decades, established the safety of caffeine at the levels presented in energy drinks, including for younger consumers.

A copy of both the ABA-commissioned Pinney Report analysis of the DAWN report and the ABA's response to the Arria letter have been submitted with these statements for the Committee's hearing record as Attachments 2 and 3, respectively.

The opportunity to discuss the ABA and Pinney Report's recent findings regarding the DAWN report and the Arria Letter would not only be welcomed, but is imperative, as these two documents call into question the majority of recent reports in the media that claim there is a discernible pattern of adverse effects related to energy drink consumption and caffeine consumption patterns by adolescents.

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[14] Pinney Report at 4 (citing Substance Abuse and Mental Health Services Administration ("SAMHSA") extrapolated estimates that energy drink related visits totaled 20,783 in 2011 whereas all drug related visits totaled 5.1 million for the same year).

[15] PinneyAssociates specifically found that:

> DAWN projects to a national estimate of cases based on combining results from two sources: approximately 183 hospitals in 13 major metropolitan areas, and approximately 50 supplementary hospitals in 2011. Although the metropolitan hospitals actually report more cases, the supplementary hospitals actually exert greater influence on the projected national estimate. On average, one case in the supplementary sample represents 135 weighted cases, whereas one case in any of the 13 main metropolitan areas represents, on average, fewer than 5 weighted cases. Therefore, a single case from a supplementary hospital can count 27 times more than a case from one of the metropolitan hospitals that report data to DAWN. This can distort the estimate. For example, a small 'outbreak' at a community hospital could potentially skew the national statistics; a single case of energy drink use presenting to a hospital in the supplementary sample could be counted as though it were 863 cases (the maximum weight for a single case in 2011), possibly seriously skewing the national statistics and resulting in misleading trend data.

Pinney Report at 9.

In considering such claims, it is important to note again that an ordinary cup of coffeehouse coffee, such as Starbucks' Pike Place blend, contains more caffeine than our products. Moreover, setting quantity aside, the caffeine contained in our products is the same in terms of benefits and effects as the caffeine contained in ordinary coffee. It is important to recognize that caffeine is a well-studied, widely-used, and safely consumed ingredient.

II. Rockstar's Labeling and Marketing Practices

Rockstar Energy Drink product labels clearly state the ingredients in our products, including caffeine, vitamins, sugars, and amino acids.

In addition to clearly listing ingredients, Rockstar Energy Drink products also list the amount of total caffeine per serving and the total caffeine from all sources per container. We take pride in the fact that Rockstar product labeling is as transparent and clearly defined as possible.

Further, Rockstar Energy Drink product labels contain the consumer advisory statement ***"Not recommended for children, pregnant or nursing women, or those sensitive to caffeine."***

Below is an example of a label from a Rockstar Energy Drink, which demonstrates the full range of information that is stated clearly on each container of our product:

Like other foods and beverages, Rockstar Energy Drink products are regulated by the FDA. Rockstar complies with applicable laws and regulations related to the manufacture, labeling,

sale, and distribution of consumable products. Additionally, as part of its commitment to consumer safety, Rockstar has voluntarily committed to report to the FDA any serious adverse events reported to us by consumers that are alleged to be associated with consumption of Rockstar products Rockstar conforms to the adverse reporting system and will continue to do so.

As a member of the ABA, Rockstar has also committed to refrain from marketing its products to children under 12. In addition to our clearly-labeled consumer advisory that Rockstar Energy Drinks are not intended for children, we also do not promote our products to children via our company website. Simply put, Rockstar does not market products to children under 12 years of age. Similarly, as a member of the ABA, Rockstar has committed not to market or sell its products in K-12 schools, including high schools.

Rockstar's target demographic is persons 18 to 35 years of age. Rockstar engages in marketing activities, including event and athlete sponsorship and promotion in action sports, motor sports, and live music events that target the 18 to 35 age group.

III. Conclusion

In conclusion, I reiterate that Rockstar Energy Drink products are safe for consumers and fully compliant with FDA regulations. According to a review conducted by Professor John Doull of the University of Kansas Medical Center, the combination of ingredients contained in Rockstar is safe for consumption. Moreover, contrary to certain inaccurate allegations, our products contain *less* caffeine than Starbucks ordinary house blend, on a per ounce basis, and our products clearly display the caffeine content from all sources per container. Finally, the target audience for Rockstar's marketing initiatives is persons 18 to 35 years of age.

I thank the Chair and members of the Committee for providing Rockstar the opportunity to discuss our commitment to product safety and responsible marketing practices, and I look forward to answering any questions you may have.

ATTACHMENT 1

Scientific White Paper:
Summary of Data Supporting the Safety of ROCKSTAR Energy Drinks

Prepared for:

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April 25, 2013

Summary of Data Supporting the Safety of ROCKSTAR Energy Drinks

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Summary of Data Supporting the Safety of ROCKSTAR Energy Drinks

EXECUTIVE SUMMARY

Energy drinks have been targeted in the U.S. media recently in response to reported adverse events - which have been inaccurately reported by the media - and the fact that two U.S. Senators have requested that the U.S. Food and Drug Administration (FDA) investigate the energy drink category. In response to these concerns, Rockstar, Inc. (manufacturer of Rockstar energy drink products) would like to report that an independent Expert Panel has reviewed key ingredients and use levels in Rockstar energy drink products and concluded that the intended use of the key ingredients in all Rockstar products is "Generally Recognized As Safe" (GRAS) based on scientific procedures. The Expert Panel evaluation was provided under the guidance of Dr. John Doull Ph.D., M.D., also the signatory of this White Paper, while the GRAS process was conducted by Dr. Ashley Roberts (Ph.D.) of Intertek Cantox. Intertek Cantox is a global leader in providing regulatory, scientific, and toxicology consulting services specific to the areas of food safety and nutrition. For over 25 years, Intertek Cantox experts have successfully resolved complex scientific issues, developed effective regulatory compliance plans, and facilitated global regulatory approvals for new products.

The safety of Rockstar energy drink products is further supported on the basis that:

1. Rockstar energy drink products contain either 160 mg or 240 mg of caffeine per 16 ounce can, depending on product, which is less than that of the following Starbucks® coffee:

   Starbucks® "Pike Place® Roast" (standard house blend) 16 ounce Grande coffee contains 330 mgs of caffeine. *(source: Starbucks® website - web link here)*

2. Rockstar fulfills all requirements stipulated by the FDA to sell products labelled as either Conventional Foods or as Dietary Supplements.

3. Rockstar energy drink products indicate the total amount of caffeine from all sources on all product labels.

4. Rockstar energy drink products include the following statement on all product labels: ***"Not recommended for children, pregnant or nursing women, or those sensitive to caffeine."***

5. A Panel of independent experts qualified by training and experience to assess the safety of food and food ingredients (the Expert Panel) has critically evaluated the intended conditions of use including use levels and estimated dietary intakes of caffeine in Rockstar energy drink beverages. The Expert Panel applied the requisite safety standard, i.e., there must be a reasonable certainty of no harm under the conditions of intended use of the substance. The Expert Panel unanimously concluded that such use of caffeine is safe and GRAS based on scientific procedures.

6. The Expert Panel also evaluated the intended conditions of use including use levels and estimated daily intakes of taurine, L-carnitine and inositol in Rockstar energy drink products. The Expert Panel unanimously concluded that such uses are safe and GRAS based on scientific procedures.

7. Upon evaluating the intended use included use levels and estimated daily intakes of guarana extract, milk thistle extract and ginseng extract, the Expert Panel unanimously concluded that the use of these extracts in Rockstar energy drink products is safe, and GRAS based on scientific procedures.

8. In evaluating these ingredients, the Expert Panel considered the potential for synergistic effects of the ingredients as well as any known adverse health effects.

9. Claims that the American Academy of Pediatrics recommends no more than 100 mg caffeine per day for adolescents are inaccurate. Neither Rockstar nor the U.S. FDA (FDA letter dated November 21, 2012) has been able to verify this purported recommendation.

10. Adverse event reports do not establish a cause and effect relationship, and the number of such reports for Rockstar is very low in comparison to retail sales of approximately 3 billion cans of Rockstar energy drink products in the USA since Rockstar brand inception in 2001.

The above points are addressed more fully in the following sections of this report.

“Energy drinks” are popular drinks available for purchase at most supermarkets, box stores, grocery stores, convenience stores and gas stations, with current annual unit sales in USA for all brands estimated to be 4.4 billion units (Rockstar personal communication). There are numerous brands of energy drinks currently on the market containing caffeine. Caffeine is the constituent of teas, coffees and colas that is responsible for the increased alertness following consumption. Since inception in 2001, Rockstar has produced over 3 billion cans of Rockstar energy drink products for the U.S. market. Rockstar energy drink products in the 2013 portfolio contain either

160 mg or 240 mg of total caffeine from all sources per 16 oz. ounce can (with one 16 oz. can containing two 8 oz. servings), depending on product.

The FDA posted a summary of adverse effect reports (AER) obtained via the Center for Food Safety and Applied Nutrition Adverse Event Reporting System (CAERS) through October 2012, that related to products marketed as energy drinks or energy shots, which included the brands Red Bull, 5 Hour Energy, Monster, and also Rockstar (U.S. FDA, 2012a). The reports were received under this post-surveillance system between January 1, 2004 and October 23, 2012. It is important to note that these reports cannot determine cause and effect, as stated by the FDA in the summary: "*the adverse effect report itself about a particular product only reflects information AS REPORTED* [FDA's emphasis] *and does not represent any conclusion by FDA regarding a causal relationship or association with the product or ingredient*."

The summary of CAERS reports (through October 2012) released by the FDA included only 13 reports for Rockstar - including zero deaths - over the 7 year time frame of 2006 to 2012. The lethal dose of caffeine in an average person weighing 150 pounds (68 kg) is approximately 10,000 mg of caffeine, which is equivalent to the consumption of 41 cans of 16 oz. Rockstar or 656 ounces of liquid - putting it in perspective this amount of liquid weighs 41 pounds. This volume is 10 times greater than the total amount of fluid that is typically consumed in a day and it is therefore physically impossible to consume this many drinks.

Compared to the over 2 billion cans of Rockstar products sold in the U.S. since 2006 (with over 3 billion sold since brand inception in 2001), the 13 CAERS reports attributed to Rockstar energy drink products between 2006 and October 2012 (and it should be noted that these are only recorded in the AER system, and represent no defined relationship or proof of association with the product or ingredient) represent a very small fraction (0.00000065%) of the overall number of units produced since 2006. It is also important to note that of the 13 CAERS reports received regarding Rockstar energy drink products over the 7 year time frame, 6 of those 13 CAERS reports received allegedly claimed either product spoilage or object in can.

The SAMHSA Drug Abuse Warning Network issued a report (SAMHSA, 2011) on hospital visits involving energy drinks (along with alcohol and/or illegal or legal drug abuse or intake) but the report did not specify how many of the visits cited involved Rockstar products. Greater than 50% of patients in the SAMHSA report aged 18 to 25 admitted to combining drug or alcohol use along with the energy drinks. The SAMHSA study did not present any estimate as to the quantity of energy drinks or amount of caffeine consumed, and it cannot be determined if the other half of subjects, particularly younger subjects, willingly disclosed all other drug or alcohol use. Thus, drug and alcohol use in addition to the energy drinks is likely to have been much higher than the admitted 50% identified in the report.

Numerous multi-ingredient foods and beverages contain caffeine including coffee, tea, chocolate, soft-drinks and ice cream, which have a long history of safe consumption in the U.S. and global diet, and are targeted towards all age groups. Regulating food products on the basis of caffeine content would therefore impact many different product categories. Following a comprehensive evaluation of the literature for caffeine, a panel of independent scientists, qualified by scientific training and relevant national and international experience to evaluate the safety of food ingredients, was convened to evaluate the conditions of use of caffeine in Rockstar energy drink products. The Expert Panel unanimously concluded that the intended use of caffeine, produced in accordance with current good manufacturing practice and meeting applicable *Food Chemical Codex specification*, in Rockstar energy drink products at levels up to 120 mg per 8 oz. serving (a centration of 15 mgs of caffeine per ounce) is safe. One 16 oz. can of Rockstar energy drink contains 2 servings, with total caffeine from all sources at 160 mg or 240 mg depending on the specific Rockstar product. The Expert Panel unanimously found further that use intended use of caffeine in Rockstar energy drink beverages is GRAS based on scientific procedures. The Expert Panel also noted that, in their unanimous opinion, other qualified experts would concur with these conclusions.

The caffeine level in energy drinks currently manufactured by Rockstar, at 80 mg or 120 mg per 8 oz. serving, is considerably less than in that of an 8 oz. serving of Starbucks or Einstein Bros. coffees, which would provide more caffeine at 160 mg and 150 mg respectively, while the 20 oz. Starbucks Pike Place® Roast coffee contains 415 mg of caffeine. Ben and Jerry's Coffee Heath Bar Crunch also contains 84 mg of caffeine per 8 oz. serving.

Some media reports and health group websites have stated that the American Academy of Pediatrics (AAP) recommends that adolescents (persons ages 12 to 19) should not consume more than 100 mg of caffeine per day. However, following a thorough search of the literature a detailed reference for this statement could not be found in these reports.

In the FDA letter dated November 21, 2012 (U.S. FDA, 2012c), it is stated that the FDA contacted the AAP and reviewed their website but was not able to get verification that the AAP has a policy statement supporting an upper limit of 100 mg caffeine per day for adolescents. We also did an independent search of the AAP website and did not identify any such policy statement. Thus, it is incorrect to state that that the maximum safe amount of caffeine for adolescents is 100 mg per day.

In a letter dated August 10, 2012 concerning caffeine, the FDA stated that while the Agency is reviewing recently published safety studies on caffeine, "the available studies do not indicate any new, previously unknown risks associated with caffeine consumption" (U.S. FDA, 2012b). Furthermore, in another letter dated November 21, 2012 (U.S. FDA, 2012c) the FDA stated that it

has “searched the literature but did not find any information that calls into question the safety” of taurine, an amino acid, or guarana, an herb, as currently used in beverages.

Given the above, there is no expectation that consumption of Rockstar energy drink products containing 80 mg or 120 mg of caffeine per 8 oz. serving (160 mg or 240 mg caffeine per 16 ounce can), in adherence with the product label, should be associated with adverse health effects. Also, the Expert Panel convened to evaluate the safety of caffeine also assessed ginseng extract, guarana extract, L-carnitine, milk thistle extract, inositol and taurine, and concluded unanimously that the use of these ingredients in Rockstar energy drink products are safe. The Expert Panel also found such uses to be GRAS based on scientific procedures. Estimates of dietary intakes of these non-caffeine ingredients from consumption of Rockstar energy drink products were determined to be well below estimates of consumption from other food sources and/or orders of magnitude below no-adverse-effect levels determined from safety studies. As all ingredients are present in amounts that are GRAS and/or are found in various foods in comparable amounts, there is no expected safety concern associated with these ingredients alone, or in combination, from consumption of Rockstar energy drink products.

Summary of Data Supporting the Safety of ROCKSTAR Energy Drinks

1.0 INTRODUCTION

"Energy Drinks" are popular drinks with current USA annual sales for all brands estimated to be 4.4 billion units (Rockstar, personal communication). There are numerous brands of energy drinks currently on the market, with the predominant ingredient being caffeine. Caffeine is the constituent of teas, coffees and colas that is responsible for the increased alertness following consumption. The amounts of caffeine in the individual brands of energy drinks are highly variable as are the serving sizes. Since inception in 2001, Rockstar, Inc. (Rockstar) has produced over 3 billion cans of Rockstar energy drink products for the North American market (Rockstar personal communication).

The U.S. Food and Drug and Drug Administration (FDA) posted a summary of adverse effect reports (AER) obtained via the Center for Food Safety and Applied Nutrition Adverse Event Reporting System, (CAERS) through October 2012 that related to products marketed as energy drinks and energy shots, which included the brands Red Bull, 5 Hour Energy, Monster, and also Rockstar (U.S. FDA, 2012a). The reports were received under this post-surveillance system between January 1, 2004 and October 23, 2012. It is important to note that these reports cannot determine cause and effect as stated by the FDA in the summary: "*the adverse effect report itself about a particular product only reflects information AS REPORTED* [FDA's emphasis] *and does not represent any conclusion by FDA regarding a causal relationship or association with the product or ingredient*."

The purpose of this report is to review the CAERS received through October 2012, and to summarize the data supporting the safety of Rockstar energy drinks.

In considering the safety of Rockstar energy drinks, it is important to clarify that these products are not intended for certain populations known to be sensitive to caffeine. Therefore the label includes a statement that Rockstar products are "not recommended for children, pregnant or nursing women, or those sensitive to caffeine." Rockstar considers "children" to encompass individuals under age 12.

2.0 COMPARISON OF CAFFEINE CONTENT OF DIFFERENT FOODS

The amount of caffeine in Rockstar energy drink products is comparable to or less than that of standard coffee, which is widely consumed and purchased in specialty coffee shops.

Numerous foods and beverages contain caffeine including coffee, tea, chocolate, soft-drinks and ice cream that have a long history of safe consumption in the U.S. and global diet and are targeted towards all age groups. Regulating food products on the basis of caffeine content would therefore impact many different products. Energy drinks manufactured by Rockstar contain 80 mg or 120 mg of caffeine per 8 oz. serving. On a per can basis, caffeine levels of 160 mg to 240 mg are present in a 16 oz. can of Rockstar energy drink products. These amounts of caffeine are comparable to brand name coffees that are readily available in the U.S. Concentrations of caffeine present in 16 oz. servings of coffee obtained from common U.S. retailers were found to vary from 206 mg (Dunkin Donuts), 300 mg (Einstein Bros.), to 320 mg (Starbucks). Thus, 8 oz. servings of Starbucks or Einstein Bros. coffees would provide more caffeine (160 mg and 150 mg, respectively) than would be provided in an 8 oz. serving of Rockstar (80 mg or 120 mg, depending on product).

The amounts of caffeine in various energy drinks sold in the U.S. marketplace in serving sizes of 8 oz. or greater are summarized in Table 1. The amount of caffeine in Rockstar energy drink products is comparable to most other energy drink brands but is less than one sixth the caffeine concentration of 5-Hour Energy (a concentrated energy shot).

Table 1 Caffeine Content of Select Energy Drinks Available in the U.S. Marketplace

Energy Drinks	Package Size (oz.)	Caffeine (mg)	Concentration (mg/oz.)
NOS	16.0	260	16.3
Rockstar Energy Drink	16.0	160	10.0
Rockstar Sugar Free	16.0	160	10.0
Rockstar Zero Carb	16.0	240	15.0
Monster Energy	16.0	160 (est.)	10.0 (est.)
Monster Lo-Carb	16.0	160 (est.)	10.0 (est.)
Full Throttle	16.0	200	12.5
RedBull	16.0	154	9.6
RedBull Sugar Free	16.0	154	9.6

The amount of caffeine in energy shots, which are a different type of product than energy drinks, is indicated in Table 2.

Table 2 Caffeine Content of Select Energy Shots Available in the U.S. Marketplace			
Energy Shot	**Package Size (oz.)**	**Caffeine (mg)**	**Concentration (mg/oz.)**
5-Hour ENERY	2.0	200 (est.)	100.0 (est.)

Table 3 lists the caffeine content of other foods and beverages. The amount of caffeine in Rockstar energy drink products on a mg per oz. basis, while about 3 times greater than soft drinks, is less than many coffees and some teas. Ben and Jerry's Coffee Heath Bar Crunch contains as much caffeine as many energy drinks at 84 mg of caffeine per 8 oz. serving.

Table 3 Caffeine Content of Select Food and Beverage Products Available in the U.S. Marketplace			
Product	**Package Size (oz.)**	**Caffeine (mg)**	**Concentration (mg/oz.)**
Starbucks Brewed Coffee (Grande) [Pike Place Roast] (Venti)	16.0 20.0	330 415	20.6
Einstein Bros. Regular Coffee (Medium)[a]	16.0	300	18.8
Dunkin' Donuts Regular Coffee (Medium)	16.0	206	12.9
Starbucks Espresso (solo)	1.0	75	75.0
Jolt Cola	12.0	72	6.0
Coca-Cola	20.0	56	2.8
Mt. Dew	20.0	90	4.5
Ben & Jerry's Coffee Heath Bar Crunch	8.0	84	10.5
Ben & Jerry's Coffee Flavored Ice Cream	8.0	68	8.5
Jolt Caffeinated Gum	1 stick	33	33.0 (per stick)
Hershey's Special Dark Chocolate Bar	1.45	31	20.7

Source: CSPI (2007); source [a] = Turcotte (2010)

3.0 CAFFEINE SAFETY ASSESSMENT

Caffeine is present naturally in coffees, teas and herbs and has a long history of safe use in colas and other foods as an added ingredient.

Caffeine is considered safe for use in stimulant drug products for over-the-counter human use to restore mental alertness or wakefulness during fatigue or drowsiness (21CFR 340) (U.S. FDA, 2012d). Use of caffeine in over-the-counter stimulant products to restore mental alertness or wakefulness during fatigue or drowsiness is acceptable for adults and for children 12 years of age and older (*i.e.*, adolescents) and if used at the maximum allowable levels would be over 1000 mg in a day. This amount of caffeine would equal about 4 Rockstar 16 oz. energy drinks.

Thus, it is incorrect to state that that the maximum safe amount of caffeine for adolescents is 100 mg per day.

The conditions of use of caffeine in Rockstar energy drinks has been evaluated by an Expert Panel in accordance with sections 201(s) and 409 of the Federal Food, Drug, and Cosmetic Act (U.S. FDA, 2010a,b) and FDA's implementing regulations in 21 CFR 170.3 and 21 CFR 170.30 (U.S. FDA, 2012d). Those regulations state that the use of a food substance may be GRAS either through scientific procedures or, for a substance used in food before 1958, through experience based on common use in food. The Expert Panel consisted of the following individuals: John Doull Ph.D., M.D., Stanley M. Tarka, Ph.D. and John A. Thomas, Ph.D.

Under 21 CFR 170.30(b) (U.S. FDA, 2012d), general recognition of safety through scientific procedures requires the same quantity and quality of scientific evidence as is required to obtain approval of the substance as a food additive and ordinarily is based upon published studies, which may be corroborated by unpublished studies and other data and information.

Under 21 CFR 170.30(c) and 170.3(f) (U.S. FDA, 2012d), general recognition of safety through experience based on common use in foods requires a substantial history of consumption for food use by a significant number of consumers.

The Expert Panel unanimously concluded that the intended use of caffeine, produced in accordance with current good manufacturing practice and meeting applicable *Food Chemical Codex* specification, in Rockstar energy drink products at levels up to 120 mg per 8 oz. serving is generally recognized as safe (GRAS) based on scientific procedures. Rockstar energy drink products in the 2013 portfolio contain either 160 mg or 240 mg of caffeine per 16 oz. can depending on product.

The primary data noted by the Expert Panel in their evaluation of the safety of caffeine were as follows.

- The estimated lethal dose for caffeine in adult humans is 10,000 mg (Nawrot *et al.*, 2003). For an adolescent this dose would be expected to be closer to the adult estimate than for a child, given their greater body weight and height by age 12, which is more comparable to adults. Intake of 10,000 mg of caffeine, from the proposed food uses of caffeine in Rockstar energy drink products, would require the consumption of *forty-one* 16 oz. cans, corresponding to 20 liters of fluid **or approximately 41 pounds of Rockstar energy drink, consumed all at one time**. This volume is far in excess of the amount that would be consumed by anyone drinking any beverage, including energy drink consumers.

- Recent comprehensive reviews, conducted by qualified experts, on the reproductive and developmental effects of caffeine in humans have concluded that no adverse

consequences on reproduction or pregnancy have consistently been linked to caffeine (SCF, 1999; IOM, 2001; Peck *et al.,* 2010; Brent *et al.,* 2011). However, the European Commission's Scientific Committee on Food, the IOM, and Health Canada, recommend a reduction in caffeine consumption during pregnancy (SCF, 1999; Nawrot *et al.,* 2003).

- The Expert Panel noted that although infants and children are not intended consumers of energy drinks; consumption by children and potential effects on the developing nervous system of growing individuals should be considered. Caffeine has a long-history of safe use by clinicians for the treatment of apnea in infants. Caffeine and the structurally similar methylxanthine, theophyline, also have been widely used for the treatment of attention deficit disorder (ADHD) and asthma in young and adolescent children (<12 years of age). Under placebo controlled settings, the administration of caffeine (5 mg to 10 mg per kg body weight) to infants within the first 10 days of life for a median duration of 37 days, for treatment of apnea of prematurity, did not affect motor function, cognition, behavior, general health or other developmental measures (*e.g.*, deafness, blindness) during a 5-year follow-up period (Schmidt *et al*., 2006, 2007, 2012). Meta-analyses of controlled studies evaluating the effects of caffeine on development and behavior in children and adolescents administered caffeine, or the structurally similar methylxanthine theophyline, for treatment of asthma or attention-deficit hyperactivity disorder do not support an association between methylxanthine use and adverse effects on cognition or behavior in these individuals (Lindgren *et al*., 1992; Stein *et al*., 1996). The Expert Panel concluded that available evidence do not suggest that dietary caffeine would represent a neurodevelopmental risk to humans of any age group.

- Researchers from the National Institute of Mental Health (Castellanos and Rapoport, 2002) conducted a literature review looking at potential effects of caffeine on developmental and behavior in infancy and childhood. A number of studies conducted from the 1970's to the 1990's were identified including studies in both hyperactive children and normal children. In the hyperactive children, the studies were generally small and adverse effects were noted to be minimal. Expected effects such as dose-dependent insomnia and minor increases in blood pressure and heart rate at doses of 320 mg were observed. In studies in normal children, low doses (~3 mg per kg) were not associated with any effects, while higher doses (~10 mg per kg) were reported to be associated with improvements in vigilance but also "fidgetiness" and "jumpiness". As such effects are typical for caffeine, it was concluded that effects of caffeine at moderate caffeine intakes were "modest" and "innocuous" (Castellanos and Rapoport, 2002). In an earlier review (Leviton, 1992), typical caffeine consumption among children obtained from sources such as coffee, tea, colas and chocolate was not found to be associated with adverse effects. It was noted from a study comparing responses to caffeine in boys and adult men that

children were less likely than men to report caffeine related subjective effects such as faint, flushing or nervous/jittery.

- Coffee has been shown to have hypercholesterolemic properties (Jee *et al.,* 2001) and both coffee and caffeine have been shown to have hypertensive properties (Nurminen *et al.,* 1999; Nawrot *et al.,* 2003; Noordzij *et al.,* 2005); however, there is no definitive evidence to suggest that these effects would result in any long-term adverse effects since available epidemiological data have not demonstrated a clear and consistent association between coffee consumption and risk of coronary heart disease and hypertension. The IOM and Health Canada both state that 'moderate' caffeine intake does not adversely affect cardiovascular health (IOM, 2001; Nawrot *et al.,* 2003) with Health Canada further specifying 'moderate' as ≤400 mg caffeine per day (up to 4 cups of coffee) Nawrot *et al.,* 2003).

- Controlled metabolic studies in healthy adult subjects show that oral doses of caffeine can negatively affect calcium balance (Heaney and Recker, 1982; Massey and Wise, 1984; Bergman *et al*., 1990). The magnitude of this effect is small. Urinary calcium losses of 5.1 mg and 7 mg have been reported in healthy male subjects administered oral caffeine doses of 3 or 6 mg per kg body weight respectively (Massey and Hollingbery, 1988). These urinary losses of calcium are equivalent to the quantity of calcium in 2 tablespoons of milk (Heaney, 2002), and among individuals consuming adequate calcium in the diet the effects of caffeine on calcium balance are nutritionally irrelevant. Comprehensive reviews of intervention and observational studies evaluating the association between caffeine and/or coffee intake and measures of bone health have been conducted by authoritative scientific bodies including the IOM and Health Canada (IOM, 2001; Nawrot *et al*., 2003). The IOM concluded that an association between caffeine consumption and bone health cannot be established (IOM, 2001). Health Canada more specifically concluded that caffeine intakes ≤400 mg per day (up to 4 cups of coffee per day) do not have adverse effects on bone status or calcium balance in individuals meeting their recommended calcium intakes (Nawrot *et al.,* 2003). The Expert Panel similarly concluded that the effect of dietary caffeine from the proposed food uses of caffeine in energy drinks would be negligible among individuals consuming adequate quantities of calcium in the diet.

- Caffeine at doses of 250 mg or more may have a mild, transient diuretic effect, especially among infrequent users. However, regular caffeine users become habituated to the effects of caffeine, diminishing its actions (Armstrong, 2002; Maughan and Griffin, 2003). Overall, beyond a mild transient diuretic effect, there is no substantive evidence to indicate that moderate caffeine consumption in beverage form results in biologically significant changes in hydration status in subjects, either at rest or under exercise

conditions, who consume an otherwise normal diet (Grandjean *et al.*, 2000; Armstrong, 2002; Roti *et al.*, 2006; Goldstein *et al.*, 2010; Campbell *et al.*, 2013). Caffeine doses of 600 mg to 900 mg (approximately 6 to 9 cups of coffee) may increase fluid and electrolyte losses in urine; however, a normal diet will replace these losses (IOM, 2001). Total body water loss depends on the amount of caffeine consumed, the individual's history of caffeine use, the total solute load of food/beverage intake, and environmental/physical stresses (e.g., temperature, level of exercise) (IOM, 2001).

- Caffeine has been shown to have stimulatory effects, increasing performance, vigilance, alertness, memory, and mood (Nehlig *et al*., 1992; Riedel *et al*., 1995; Fredholm *et al*., 1999; ANZFA, 2000; Lieberman *et al*., 2002; Smith, 2002). Higher doses (reported differentially in the literature as >300, >400 or >500 mg caffeine per day) have demonstrated negative effects, such as feelings of anxiety, *nausea*, jitteriness, and nervousness (Greden, 1974; Lader and Bruce, 1986; Lieberman, 1992; Green and Suls, 1996; Garrett and Griffiths, 1997; Childs and de Wit, 2006). Individuals with panic and/or anxiety disorders may be particularly sensitive to the anxiogenic effects of caffeine (Lara, 2010). However, the negative effects of caffeine on anxiety and sleep appear to be self-limiting – *i.e.*, individuals aware of their sensitivities limit their caffeine intakes.

- Caffeine users can become physically dependent on caffeine, demonstrating minor withdrawal symptoms, notably headache, with cessation of intake (Ozsungur *et al*., 2009; Sigmon *et al*., 2009).

- Studies suggest that caffeine has similar anxiogenic and withdrawal effects in younger individuals as seen in adults (Meltzer *et al*., 2008). Health Canada regards children as an 'at risk' subgroup that may require specific advice on moderating their caffeine intake and suggests a caffeine consumption of ≤2.5 mg per kg body weight/day in children under 12 years of age (Nawrot *et al.,* 2003; Health Canada, 2011).

- Concurrent consumption of caffeine and certain medications can result in significant changes in the pharmacokinetics of both caffeine and/or the interacting drug (Durrant, 2002; Broderick *et al*., 2005). It should be noted that the Rockstar energy drink product labels contain the admonition that persons sensitive to caffeine should avoid the product.

The Expert Panel was aware of increasing concerns expressed in the literature by various scientific and medical experts, including regulators, regarding the safety of caffeinated energy drink use by teenagers (*e.g*., Schneider and Benjamin, 2011; Seifert *et al*., 2011; Wolk *et al*., 2012). The dietary intake analyses indicated that, among teenagers, the use of energy drinks was a greater contributor of caffeine intake than the background diet. However, at the 90th percentile, based on NHANES data, the caffeine intakes contributed by the background diet (*i.e.,* food and dietary supplements) and consumption of energy drinks were below the 400 mg per day

level commonly cited by regulatory and authoritative bodies as not associated with adverse effects. The FDA recognizes that "*for healthy adults, caffeine intake up to 400 mg per day is not associated with general toxicity, cardiovascular effects, effects on bone status and calcium balance (with consumption of adequate calcium), changes in adult behavior, incidence of cancer, or effects on male fertility*" (U.S. FDA, 2012b). The Expert Panel also noted that Rockstar products containing caffeine as an ingredient bear the following label statement: "Not recommended for children, pregnant or nursing women, or those sensitive to caffeine." Following the Expert Panel's comprehensive review of all available scientific evidence related to the safety of caffeine, it was unanimously concluded that the intended use of caffeine, produced in accordance with current good manufacturing practice and meeting applicable Food Chemicals Codex specifications, in Rockstar energy drink beverages at levels up to 120 mg per 8 oz. serving, is generally recognized as safe based on scientific procedures. The Expert Panel also noted that, in their unanimous opinion, other qualified experts would concur with these conclusions.

4.0 SUMMARY OF CAERS REPORTS

Adverse events reports are not considered reliable indicators that energy drinks pose safety concerns.

The FDA Center for Food Safety and Applied Nutrition (CFSAN) Adverse Event Reporting System (CAERS) is a post marketing surveillance system. CAERS includes mandatory reports of serious (*e.g.*, death and injury) adverse events related to dietary supplements, and voluntary reports of serious and non-serious adverse events related to beverages or conventional foods. Non-serious adverse events (*e.g.,* reversible non-life threatening effects) linked to dietary supplements also may be voluntarily reported. Voluntary reports may be filed by the public or medical professionals.

A filing of a CAERS report is not sufficient to prove cause and effect. Thus, the CAERS reports do not prove that energy drinks caused any adverse health effects reported. As stated by the FDA "*The existence of an adverse event report does not necessarily mean that the product identified in the report actually caused the adverse event*." The FDA carefully investigates and evaluates other possible causes before deciding whether the product actually caused the reported adverse event.

Deficiencies of CAERS which can preclude identification of a cause and effect relationship, as noted by the FDA itself (http://www.fda.gov/Food/NewsEvents/ucm328536.htm) (U.S. FDA, 2012a), include:

- "*reports with incorrect, incomplete or no contact information, which make following up with the complainant difficult or impossible;*
- *variability among the completeness of the reports. Some reports may consist only of a single sentence with little detail;*
- *reports that list the brand, but do not identify the specific product;*
- *absence of or lack of FDA access to other information related to the report, such as medical records and medical histories (In fact, some state medical privacy laws prevent FDA from obtaining medical records related to the adverse event report.);*
- *use of other supplements or medications at the same time;*
- *pre-existing or undiagnosed medical conditions;*
- *improper use of the product*"

The summary of CAERS reports through October 2012 released by the FDA included only 13 reports for Rockstar and zero deaths (over the timeframe of 7 years – 2006 to October 2012). Among the other energy drink brands there were 21 CAERS reports and zero deaths for Red Bull (from 2004 to October 2012), 40 reports including 5 deaths, for Monster (from 2004 to October 2012), and 92 reports including 13 deaths for 5-Hour Energy (from 2005 to October 2012). More than half of the reports of death for these other brands gave no information on symptoms leading up to death. Other reports provided some description in addition to "death" that was confounding including the following:

- fall and head injury (Report #121679, 5-Hour Energy); this same case seems to have been reported twice (Report #s 121679 & 121680, 5-Hour Energy) as case was for the same date and numbers are sequential)
- pneumonia and acute respiratory failure (Report #129061, 5-Hour Energy)
- suicide (Report #155230, 5-Hour Energy).

Other reports for 5-Hour Energy (Report #s 137118, 144858, 157207) noted that death followed myocardial infarctions (heart attacks) however no information was given on the pre-existing health of the patient. As there are approximately 1.5 million cases of myocardial infarction per year in the U.S., with 30% resulting in death, it is not possible to conclude from the CAERS report alone that the few cases noted were in fact caused by energy drinks.

Furthermore, based on literature reports, the amount of caffeine that would be fatal to humans if consumed all at once is approximately 10,000 mg in adults. To put this into perspective, that is the amount of caffeine in 41 cans of 16 ounce Rockstar can (containing 240 mg caffeine per can), or 656 total ounces **- approximately 41 pounds of Rockstar**. Rockstar energy drink products include a statement on the label that the products should not be consumed by children (<12 years of age). Total fluid (all drinks and water) intake per day is usually 67 oz. (2 liters) for

adults. Therefore, individuals would need to consume about 10 times more energy drinks than the typical full day fluid amounts, and in a short timeframe, to reach fatal levels of caffeine.

Certain media reports have contended that the number of incidents of emergency department visits and adverse events attributable to energy drinks is much higher than that suggested by CAERS. As the basis for this contention, the media has cited a report by the Substance Abuse and Mental Health Services Administration (SAMHSA), dated November 22, 2011, entitled: "The DAWN Report: Emergency Department Visits Involving Energy Drinks" where DAWN stands for Drug Abuse Warning Network. SAMHSA determined that there were 16,053 and 13,114 energy drink-related emergency department visits in 2008 and 2009, respectively, noting that the amount of caffeine in a can or bottle of energy drink can vary from about 80 mg of caffeine to more than 500 mg (SAMHSA, 2011); however precise estimates of caffeine intake associated with each visit are not provided. DAWN is noted to be a public health surveillance system that "monitors" drug related emergency visits where the visit is classified as a DAWN case if it involves drugs. A drug is defined as "alcohol; illegal drugs, such as cocaine, heroin, and marijuana; pharmaceuticals (*e.g.*, over-the-counter medicines and prescription medications); and nutraceuticals, such as nutritional supplements, vitamins, and caffeine products."

The report indicates that for more than half of the visits in which energy drinks were reportedly used (brands not specified) in the 18 to 25 year age range, the subjects also reported using alcohol and other drugs. Since this was likely to have been a self-reporting system it is probable that the use of alcohol and illicit drugs would have been under reported especially in those subjects below the legal drinking age of 21. For the DAWN report, the information is collected from the chart documents. The patient outcomes were not provided. However it was noted that 57 percent of visits involving energy drinks in combination with drugs were classified as "misuse or abuse" while 30 percent were classified as "adverse reactions." No other information, such as the specific energy drinks consumed, or the amounts of energy drinks and drugs consumed were provided in the DAWN report. Likewise, no precise estimate of caffeine intake associated with each visit was provided.

In an update to this report, SAMHSA (2013) reported an increase in emergency department visits to 20,783 in 2011 supposedly attributed to energy drink consumption. In comparison, the number of visits in 2007, 2008, 2009 and 2010 were 10,068, 16,053 13,114 and 15,219 respectively and so over the timeframe from 2007 to 2011, there were both increases and decreases in the number of incidents that occurred annually. In addition, the number of visits involving adverse reactions involving the misuse or abuse of drugs, also approximately doubled with almost half of the total reported incidences being associated with pharmaceuticals, illicit drugs and alcohol. With such confounding factors it cannot be determined from the information provided what role, if any, the energy drink contributed to the visit and/or the symptoms. Furthermore, given that it was a self-reporting system it cannot be determined if those subjects

visiting the emergency department, particularly younger patients disclosed all other concomitant drug or alcohol use. Again, information on the amounts of caffeine intake or the type of energy drink/shot consumed was not determined.

4.1 Incidence of Adverse Reports Versus Volumes Sold

The total number of CAERS reports (through October 2012) over the past 9 years for energy drinks (166) is very low compared to the number of units of energy drinks that have been consumed. It is estimated that the current annual energy drink consumption in the USA is on the order of 4.4 billion units.

Rockstar since inception in 2001 has produced over 3 billion cans of Rockstar energy drink products for the U.S. market, and approximately 2 billion since 2006. The 13 CAERS reports received between 2006 and October 2012 represent a very small fraction (0.00000065%) of the overall number of units produced since 2006, with none proven to be causative to drinking Rockstar energy drinks. It is also important to note that of the 13 CAERS reports received regarding Rockstar energy drink products over the 7 year time frame, 6 of those 13 CAERS reports received allegedly claimed either product spoilage or object in can.

The numbers of visits in the DAWN report estimated for the U.S. are actually based on a "probability sample" of hospitals rather than real numbers. For the visits involving drugs and alcohol, it cannot be determined from the information provided what, if any, role the energy drink would have contributed to the symptoms. For hospital visits attributed to energy drinks alone, it cannot be determined if patients, particularly younger patients, disclosed all other drug use or alcohol. Nevertheless, in the unlikely event that all 20,783 visits in 2011 (the highest number of visits noted) were related to energy drinks, the incidence of visits compared to the annual energy drink consumption estimate, in 2011, of 3.5 billion would be approximately 0.0006% or 1 visit for every 168,400 units sold. Excluding the alcohol and drug combination use (about 50%), the incidence would be approximately 0.0003% or 1 visit for every 336,800 units sold. Further, it should be noted that according to the Centers for Disease Control and Prevention, the number of emergency department visits from all causes in 2011 was 136,100,000 in total.

5.0 CONSIDERATION OF CAFFEINE CONSUMPTION BY ADOLESCENTS

Caffeine has been used clinically in the treatment of apnea in infants at doses of 5 to 10 mg per kg body weight (*i.e.,* ~100 mg total), as well as in the treatment of attention deficit disorder (ADHD) and asthma in young and adolescent children (<12 years of age). There is no expectation that adolescents (individuals 12 to 18 years of age) should be unduly sensitive to caffeine in comparison to infants and children. Consequently, it is incorrect to state that 100 mg

of caffeine per day is the maximum safe amount for adolescents (12 years of age and older). Literature searches were conducted to identify additional studies specific to adolescents given the recent media concerns about the consumption of energy drinks in this age group.

Some media reports and health group websites have stated that the American Academy of Pediatrics (AAP) recommends that adolescents should not consume more than 100 mg of caffeine per day. However, following a thorough search of the literature a detailed reference for this statement could not be found in these reports.

In the FDA letter dated November 21, 2012 (U.S. FDA, 2012c), it is stated that the FDA contacted the AAP and reviewed their website but was not able to get verification that the AAP has a policy statement supporting an upper limit of 100 mg caffeine per day for adolescents.

We also did an independent search of the AAP website and did not identify any such policy statement. While no policy statement by the AAP was identified, an independent publication in the AAP journal Pediatrics by authors from the Department of Pediatrics and the Pediatric Integrative Medicine Program, University of Miami, Leonard M. Miller School of Medicine, Miami, Florida, Seifert *et al.* (2011), did state that "Adolescent and child caffeine consumption should not exceed 100 mg per day and 2.5 mg per kg BW per day, respectively", with three references provided as support for this intake limit. However, upon close review of the references, none laid out or were proven to recommend this intake limit. The references are summarized below:

1) Babu KM, Church RJ, Lewander W. Energy drinks: the new eye-opener for adolescents. Clin Pediatr Emerg Med. 2008;9(1):35–42. Babu *et al.* (2008) cites to Canadian recommendations that children aged 10 to 12 consume no more than 85 mg per day. No recommendations are given for adolescents aged 12 to 18.

2) BfR Federal Institute for Risk Assessment. Health risks of excessive energy shot intake. December 2, 2009. Available at: www.bfr.bund.de/cm/245/health_risks_of_excessive_energy_shot_intake.pdf. Accessed January 17, 2011. The BfR Federal Institute for Risk Assessment refers to "children" and uses a 10-year-old as an example but makes no reference to "teens" or "adolescents" or a 100 mg per day recommended limit. This reference focuses on energy shots and not energy drinks such as Rockstar. With respect to children, this article states the following: "With portions of 150 mg, children (10 years old, 30 kg BW) reach intake levels of 5 mg caffeine per kg BW. These have been connected with the temporary appearance of arousal, irritability, nervousness and anxiety in several children (SCF, 1999). These products should therefore be labelled as unsuitable for children."

   Interestingly, the SCF (1999) report which is cited by the BfR includes this statement: "Studies on the effects of direct caffeine consumption by pre-school and school children

have given variable results. In experimental studies in which single doses up to 10 mg per kg bw have been given to children, either no effect or small, inconsistent effects have been noted on mood, behavioural, cognitive and motor functions, some of which could be interpreted as beneficial."

3) Heatherley SV, Hancock KM, Rogers PJ. Psychostimulant and other effects of caffeine in 9- to 11-year-old children. J Child Psychol Psychiatry. 2006;47(2):135–142. Heatherley *et al*. (2006) did not evaluate children older than 12 years of age.

Overall, the published literature collected that specifically looked at adolescent populations did not indicate that 100 mg per day of caffeine was likely to be associated with health concerns. In caffeine sensitive individuals, the effects of caffeine may be associated with transient behavioural changes, such as increased arousal, irritability, nervousness or anxiety (SCF, 1999). These are the same effects noted in sensitive adults and would be expected to be self limiting.

A recent letter prepared by the FDA (2012c) noted the following key points with respect to intakes of caffeine among consumers, including adolescents.

- Based on the results of a commissioned consumption study, the mean caffeine consumption by the U.S. population has remained stable, despite the entry of energy drinks on the market, at approximately 300 mg per person per day.
- Among consumers aged 14 to 21 years of age, the mean amount of caffeine consumed was 1/3 of that of adults or ~100 mg per day, with the caffeine contributed predominantly from coffee, soft drinks and teas.
- Caffeine intakes from energy drinks represented only a small portion of daily intakes, even for teens.

In related information, a recent media report ("Moderation key to energy drinks" Hinton Parklander, Mon Dec 3 2012, Byline: ED MOORE EDSON LEADER) cited the Alberta Health Services medical officer of health, Kathryn Koliaska, that older children (>12 years of age) should limit their intake of caffeine to 400 mg per day.

The U.S. National Center for Health Statistics' (NCHS) National Health and Nutrition Examination Surveys (NHANES) most recent data also suggest very low energy drink consumption among adolescents (CDC 2011). The NHANES data are collected and released in 2-year cycles with the most recent cycle containing data collected in 2009-2010. NHANES 2009-2010 survey data were collected from individuals and households *via* 24-hour dietary recalls administered on 2

non-consecutive days (Day 1 and Day 2). Additionally, NHANES respondents provided 24-hour recall data concerning the use of dietary supplements on 2 non-consecutive days.

The results as presented in Table 4 indicate that only 1.1% of adolescent girls and 4.5% of adolescent boys are consumers of energy drinks.

Table 4 Summary of Most Relevant Dietary Intake Assessments Conducted Using 2009-2010 NHANES Data

Population Group	Age Group (years)	Caffeine intakes from background diet[a], Caffeine Users[b] Only (mg/day)			Caffeine intakes from intended uses in energy drinks (120mg/8oz), Energy Drink Users Only (mg/day)			Caffeine intakes from background diet and intended uses in energy drinks (120mg/8oz), Energy Drink Users Only (mg/day)		
		% Users	n	Mean	% Users	n	Mean	% Users	n	Mean
Infants	0 to 2	42.2	648	8	0	0	na	0	0	na
Children	3 to 11	86.1	2,308	18	0.4	8	109*	0.4	8	121*
Female Teenagers	12 to 19	89.2	851	53	1.1	15	143*	1.1	15	172*
Male Teenagers	12 to 19	86.8	908	67	4.5	36	145	4.5	36	164
Female Adults	20 and up	94.1	4,757	155	1.8	65	105	1.8	65	156
Male Adults	20 and up	94.1	4,340	205	3.3	145	140	3.3	145	207
Total Population	All Ages	90.2	13,812	143	2.2	269	129	2.2	269	145

na=not applicable
[a] Background diet includes food and dietary supplements.
[b] A caffeine user is defined as a consumer of a caffeine-containing food and/or dietary supplement.
*low numbers of users diminishes reliability of results

Similarly in Canada, very low consumption estimates have been determined from surveys of adolescents (12 to 17 year olds) in the province of Quebec. The Réseau du sport étudiant du Quebec (RSEQ, 2011) surveyed the energy drink consumption habits of over 10,000 Quebec teens (12 to 17 years of age) and found that 93% of teens rarely or never consumed energy drinks while only 1% consumed them daily. Research by the Institut de la Statistique du Québec (Institut de la Statistique du Québec, 2012) in a survey of more than 60,000 teens (13 to 17 years of age) found that 82.8% of teens rarely or never consumed energy drinks, and only 1.5% consumed them daily. Based on information from Statistics Canada (2009), similar beverage consumption patterns occur all across Canada.

6.0 OTHER INGREDIENTS

There are no safety concerns related to the other ingredients in Rockstar energy drink products, all of which are common in the diet.

As noted in the DAWN Report (SAMHSA, 2011), other ingredients in energy drinks may include vitamins, amino acids, herbs, sugars, and sugar alternatives. The specific ingredients in Rockstar are similar in nature and all are either GRAS ingredients or approved food additives.

The Expert Panel convened to undertake a safety evaluation of caffeine also assessed other ingredients in the Rockstar drinks including L-carnitine, and taurine, and the flavors ginseng extract, guarana extract, and milk thistle extract. The Expert Panel concluded that under the conditions of intended use in Rockstar energy drink products, these ingredients are safe and GRAS based on scientific procedures.

L-Carnitine is a naturally occurring compound found in all mammalian species. It is required for conversion of fatty acyl coenzyme A (CoA) esters for energy. L-Carnitine is produced endogenously by humans, and occurs naturally in the diet as a component of meat and dairy products, and found in negligible amounts in fruits and vegetables. The safety of L-carnitine also is corroborated by the findings of numerous human studies conducted on L-carnitine that included endpoints relevant to safety. In these studies, no adverse effects attributable to the consumption of L-carnitine were reported following daily oral ingestion at doses ranging from 2 to 3 g L-carnitine per day for up to 3 months and at a dose of 2 g per day for up to 6 months. L-Carnitine is also acceptable for use in baby foods and infant formula (EFSA, 2003).

***Panax* Ginseng Extract**: The safety of *P.* ginseng extract is corroborated by the findings of numerous human studies in which *P. ginseng, P. ginseng* rootlets, body, and extracts (aqueous or ethanolic), *P. quinquefolius* root, *P. notoginseng* root, panaxtriol saponin from *Radix/Rhizoma notoginseng* extract, *P. japonicas* root, and *P. vietnemensis* root were consumed by generally healthy subjects or those with various underlying diseases or conditions. Although the various species may differ quantitatively in ginsenoside content, qualitatively, many of the ginsenosides are common to all of the species. Thus, the human studies conducted with various ginseng species also are directly relevant to the safety of the *P. ginseng* extract intended for use in Rockstar energy drink products. The overall absence of treatment-related differences in any of the safety-related parameters assessed following the consumption of up to 9 g per day *P. ginseng* or up to 2 g per day *P. ginseng* extracts for periods of up to 24 weeks further supports the safety of the intended use of *P. ginseng* extract in energy drinks.

Guarana Extract: Guarana extract is an approved food additive permitted for use as a natural flavoring substance and natural substance used in conjunction with flavors (21 CFR 172.510). Guarana also is considered to be Generally Recognized as Safe (GRAS) for use as a flavoring

agent by the Flavor and Extract Manufacturers' Association of the United States. Of the ingredients in Rockstar energy drink products, only the guarana seed extract contains some minor amounts of caffeine. The maximum guarana seed extract present in each 8 oz. serving of Rockstar energy drink products would contribute less than 1 mg of caffeine, which is insignificant in comparison to the 80 mg or 120 mg of caffeine added directly to the drink.

Milk thistle extract: As a food, several parts of the milk thistle plant are consumed, including the flowers (seeds), leaves, heads, and roots. In Canada, the NHP monograph for milk thistle extract considers intakes of 140 mg to 600 mg per day silymarin (calculated as silybin/silibinin), not to exceed 200 mg per dose, safe for consumption (Health Canada, 2009). In the monograph published by the German Commission E, 200 mg to 400 mg per day silymarin (calculated as silibinin) are considered safe (Blumenthal *et al.*, 1998). The lowest of these intakes (*i.e.,* 140 mg per day silymarin), is 41-fold greater than the estimated 90th percentile intake of silymarin in energy drink users from all sources (*i.e.,* from the intended use of milk thistle extract in energy drinks plus the intake of milk thistle from dietary supplements).

Taurine occurs naturally in the diet as a component of meat and poultry, seafood, and dairy products. It also is present in breast milk and infant formula (4 mg to 7 mg per 100 mL) (Laidlaw *et al.*, 1990; Hayes and Trautwein, 1994). The presence of taurine in cow's milk-based infant formula is attributed to its natural occurrence in the milk, whereas taurine is added to infant formula formulated from soy protein (Laidlaw *et al.*, 1990). Infants cannot produce taurine and require it from breast milk or formula, therefore taurine is a conditionally essential amino acid. Safety is corroborated by the findings of numerous human studies conducted on taurine that included endpoints relevant to safety. In these studies, no adverse effects attributable to the consumption of taurine were reported. The European Food Safety Authority (EFSA) reviewed the available human data and concluded that daily oral ingestion of taurine at doses ranging from 3 g to 6 g per day for up to 1 year did not produce adverse health effects (EFSA, 2009). More recently, EFSA's Panel on Additives and Products or Substances used in Animal Feed estimated the observed safe level of taurine in humans to be 6 g per person per day (EFSA, 2012).

It should also be noted that taurine does not have any stimulatory activity. Thus, there is no potential enhanced activity of caffeine due to the presence of taurine. L-Carnitine which is a derivative of the amino acid lysine is not a stimulant and therefore does not compound caffeine activity.

Estimates of exposure to these non-caffeine ingredients from consumption of energy drinks were determined to be well below estimates of consumption from other food sources and/or orders of magnitude below no-adverse-effect levels determined from safety studies. As confirmed by the independent Panel of food safety experts, the above described ingredients, there is no expected

safety concern associated with these ingredients alone, or in combination, from consumption of Rockstar energy drink products.

7.0 CONCLUSIONS

There is insufficient information presented in the CAERS summaries (through October 2012) or the DAWN report to demonstrate that energy drinks were the cause of the adverse events noted therein. Furthermore, there are no data to indicate that Rockstar energy drinks containing 80 mg or 120 mg of caffeine per 8 oz. serving (160 mg or 240 mg of caffeine per 16 oz. can), caused any adverse events. Some of the other brand energy drinks on the market have more than twice this amount of caffeine per ounce. The amount of caffeine in various coffees is higher than the same volume of Rockstar energy drink products. Concentrations of caffeine present in 16 oz. servings of Einstein Bros. and Starbucks coffee were 300 mg and 320 mg, respectively. The 20 oz. serving of Starbucks Pike Place Roast contains 415 mg of caffeine. Thus, 8 oz. servings of Starbucks or Einstein Bros. coffees would provide more caffeine (160 and 150 mg, respectively) than would be provided in an 8 oz. serving of Rockstar products (80mg or 120 mg). Ben and Jerry's Coffee Heath Bar Crunch also contains 84 mg of caffeine per 8 oz. serving.

Rockstar, Inc. has produced over 3 billion cans of Rockstar energy drink products in the USA since brand inception in 2001 and approximately 2 billion cans since 2006. The incidence of alleged adverse events reports in CAERS (through October 2012) citing Rockstar products is incredibly low at 13 total, or 0.00000065%, compared to 2 billion cans sold during the timeframe (through October 2012) that the CAERS reports were received. There has never been an incidence of a reported death from consumption of a Rockstar energy drink product. Current annual energy drink consumption in the USA, total category, is estimated at 4.4 billion units. The number of hospital visits listing energy drinks with and without alcohol and drug substances as reported by SAMHSA in 2011 was 20,783. These events are taken from hospital charts at emergency rooms and they do not appear to be substantiated for legitimacy (*i.e.*, reports are anecdotal and appear not to have been medically vetted). The incidence of visits in 2011 compared to the annual energy drink consumption at that time total category, estimated at 3.5 billion units, would be approximately 0.0006% or 1 visit for every 168,400 units sold. Excluding the visits where there was admission of alcohol and drug combination use (about 50%), the incidence would about 0.0003% or 1 visit for 336,800 units sold.

Any substance if administered at high enough doses may be fatal. The amount of caffeine that is reported in the literature to be fatal to adults is approximately 10,000 mg. Therefore, an adult would need to consume 41 cans of 16 oz. (at 120 mg caffeine) Rockstar energy drink products to reach fatal caffeine levels. The total volume of fluid required to be consumed to reach these levels is 656 oz. (41 pounds of fluid) or about 20 L, which is 10 times the typical amount of total fluid consumed in a full day by an adult.

It is acknowledged that there are certain populations that are potentially sensitive to caffeine. However, all Rockstar energy drink product labels recommend against consumption of energy drinks by children, pregnant or nursing women, or those sensitive to caffeine.

The safety of the amount of caffeine used in Rockstar energy drink products (up to 120 mg per 8 oz. serving) is supported by the findings of an Expert Panel convened to evaluate the conditions of use of caffeine in Rockstar products. The Expert Panel unanimously concluded that the intended use of caffeine, produced in accordance with current good manufacturing practice and meeting applicable *Food Chemical Codex* specification, in Rockstar energy drink products at levels up to 120 mg per 8 oz. serving is both safe and generally recognized as safe (GRAS) based on scientific procedures (Rockstar energy drink products contain either 160 mg or 240 mg of caffeine per 16 oz. can, depending on product).

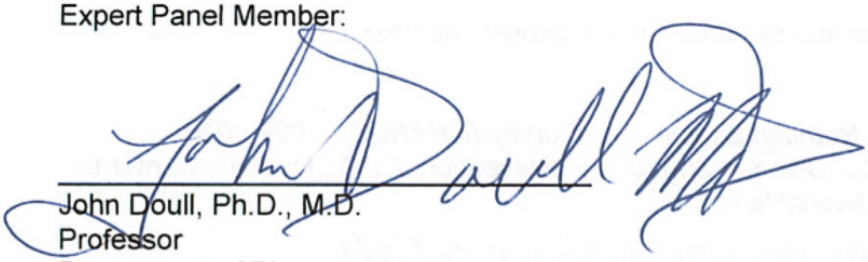
The FDA (2012b) has stated in a letter dated August 10, 2012, that, while the Agency is reviewing recently published safety studies on caffeine, the available studies do not indicate any new, previously unknown risks associated with caffeine consumption.

Given the above, there is no expectation that consumption of Rockstar energy drink products containing 80 mg or 120 mg caffeine per 8 oz. serving, in adherence with the product label, should be associated with adverse health effects.

Also, the Expert Panel convened to assessment caffeine also assessed *Panax* ginseng extract, guarana extract, L-carnitine, inositol, milk thistle extract, and taurine, and concluded that under the conditions of intended use, including use levels and estimated dietary intakes, in Rockstar energy drink products, these ingredients are both safe, and GRAS, based on scientific procedures. The guarana extract ingredient does not significantly increase caffeine amounts. The caffeine content of the guarana seed extract is 0.75 to 1.25%; provides an additional 0.0875 mg which is insignificant compared to the 80 mg or 120 mg of caffeine added directly to an 8 oz. serving). Estimates of exposure to these non-caffeine ingredients from consumption of Rockstar energy drink products were determined to be well below estimates of consumption from other food sources and/or orders of magnitude below no-adverse-effect levels determined from safety studies. Thus, there is no expected safety concern associated with these ingredients alone, or in combination, from consumption of Rockstar energy drink products.

Furthermore, scientific research that has compared caffeine consumer to non-consumers, has found that the consumption of caffeine enhances mental and physical performance (Smith, 2002; Ruxton, 2008).

Expert Panel Member:



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CFR Sections Referenced (Title 21—Food and Drugs)		
Part	Section §	Section Title
170—Food additives	170.3	Definitions
	170.30	Eligibility for classification as generally recognized as safe (GRAS)
172—Food additives permitted for direct addition to food for human consumption	172.510	Natural flavoring substances and natural substances used in conjunction with flavors
340—Stimulant drug products for over-the-counter human use	All sections	All sections

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ATTACHMENT 2

Pinney Associates

Emergency Department Visits Involving Energy Drinks and Limitations of the Drug Abuse Warning Network (DAWN)

Prepared for the American Beverage Association by PinneyAssociates

July 25, 2013

Table of Contents

1 Executive Summary

The Substance Abuse and Mental Health Services Administration (SAMHSA) released a report in January 2013, based on data from the Drug Abuse Warning Network (DAWN), suggesting an increase in the number of emergency department (ED) visits involving energy drinks and concluding that the consumption of energy drinks is a "rising public health problem". At the request of the American Beverage Association, Pinney Associates (PA) was asked to conduct a review of the DAWN report and its findings.

Overall, reports of energy drink-related ED visits need to be viewed in a broader context, as an analysis of DAWN public use data indicates that drug-related ED visits have also increased (both by a similar proportion and absolute magnitude as compared to energy drinks) for a number of other products, including infant formula, vitamins, and laxatives. Furthermore, the vast majority of energy drink-related ED visits appear to have been occasioned by non-serious medical conditions: 84.4% of visits related to caffeine/multivitamins resulted in discharge home, rather than admission to a treatment facility. In comparison, only 75.5% of alternative medicine-related ED visits resulted in home discharge. Given that there are a number of other products demonstrating comparable increases in ED visits, and that these products appear to be associated with a less benign profile than that associated with energy drinks, it is unclear why energy drinks have been singled out by SAMHSA as a public health concern. The DAWN public use data do not support the public health concern flagged by SAMSHA.

2 Drug Abuse Warning Network (DAWN)

DAWN is a public health surveillance system that monitors "drug-related" visits to hospital EDs. Each year DAWN produces estimates of such visits for the nation as a whole and for selected metropolitan areas. To be a DAWN case, the ED visit must involve a drug, either as the direct cause of the visit or as a contributing factor. Such a visit is referred to as a "drug related visit." The reason a patient used a drug is not part of the criteria for considering a visit to be drug-related. Drugs include: alcohol[1]; illegal drugs, such as cocaine, heroin, and marijuana; pharmaceuticals (e.g., over-the-counter medicines and prescription medications); and nutraceuticals, such as nutritional supplements, vitamins, and caffeine-containing products. DAWN cases are identified by the systematic review of ED medical records in participating hospitals. DAWN cases broadly encompass all types of drug-related events, including accidental ingestion and adverse reactions, as well as explicit drug abuse. SAMHSA noted in its report on energy drinks that although energy drinks are not treated as drugs by the FDA, ED visits involving energy drinks were classified as adverse reactions if the chart documented them as such.[2]

[1] Alcohol is considered a reportable drug when consumed by patients aged 20 or younger. For patients aged 21 and older, alcohol is reported only when it is used in conjunction with other drugs.

[2] Within DAWN, an ED visit is categorized as an adverse reaction when the chart documents that a prescription or over-the-counter pharmaceutical, taken as prescribed or directed, produced an adverse drug reaction, side effect, drug-drug interaction, or drug-alcohol interaction.

The exact DAWN survey methodology has been adjusted over time in order to, according to SAMHSA, "improve the quality, reliability, and generalizability of the information produced by DAWN" (Source: DAWN 2010 Codebook). The current approach, which was developed based on recommendations from a 1997 panel of experts and a 2-year SAMHSA evaluation of design alternatives, was introduced in 2003, but not fully implemented until the 2004 data collection year.

3 Data Analysis Approach

In order to put the SAMHSA findings on energy drinks into perspective, PA conducted a number of additional analyses using the DAWN public-use dataset. However, there is an important caveat to these analyses that must be acknowledged; namely, information on the use of energy drinks *per se* is not currently available in the public-use data file. Rather, the public-use data file only contains information on the larger category of "caffeine/multivitamins," of which the "energy drinks" category is a subset. As this larger category appears to be mostly comprised of energy drink-related visits (about 80% overall, from 2005-2011) information pertaining to caffeine/multivitamin-related ED visits are used as a proxy for energy drink-related visits in all reported analyses. Outreach to SAMHSA revealed that the agency has received several requests for the specific energy drink data, but thus far has declined to make these data public.

4 Increasing Number of Energy Drink-Related ED Visits: Real Phenomenon or Artifact?

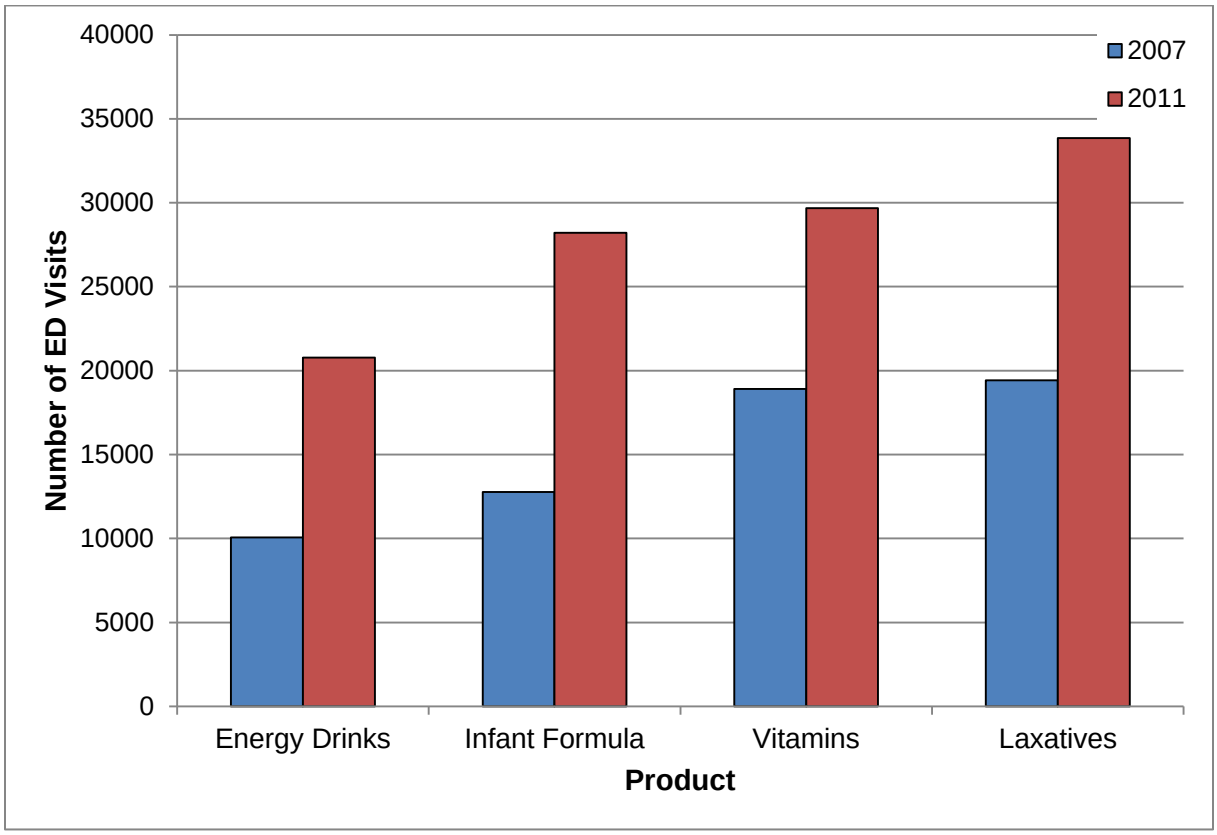
According to the SAMHSA report, the number of ED visits involving energy drinks doubled from 10,068 visits in 2007 to 20,783 visits in 2011.[3] Notably, however, an analysis of DAWN public-use data indicates that the total number of overall drug-related ED visits (regardless of the specific drug/s involved) also increased between 2007 and 2011, rising from 3.9 million visits to 5.1 million visits. Therefore, the increase in energy drink-related visits should be understood in the context of an increase in overall drug-related ED visits. It is not known whether this reflects a real increase in the utilization of EDs, or an artifact perhaps resulting from change in the data collection or case identification methodology. In 2007, energy drink-related visits comprised 0.25% of all drug-related ED visits. In 2011, energy drink-related visits comprised 0.41% of all drug-related ED visits.

Furthermore, as shown in Table 1 below, estimated drug-related ED visits appear to have increased not only for energy drinks, but for a number of other drugs/products, including infant formula, alternative medications, and other miscellaneous products such as dermatological agents (e.g., Vick's, hand lotion), gastrointestinal agents (e.g., laxatives), isopropyl (rubbing) alcohol, and ophthalmic preparations (e.g., eye drops, contact solution). Not only have drug-related ED visits increased for these other products by similar proportions as for energy drinks, for many, their absolute magnitude is similar, too (see Figure 1 below). In addition, energy drink-related ED visits appear to

[3] It is important to note that these are not raw numbers of visits, but estimates projected to a national sample. The limitations of the weighting system used to derive these projected estimated are discussed in Section 4.1.1 below.

be more likely to be associated with non-serious complaints that do not require further medical follow-up, compared to ED visits related to other product/medications. Yet, increasing ED visits associated with these other products have not been identified as a public health concern.

Figure 1 Number of ED Visits Related to Specific Products



It is unclear whether these data reflect an increase in the levels of accidental and/or intentional exposure to substances and drugs in general, including energy drinks, or if there are methodological and statistical processes that may give the appearance of notable increases in drug-related ED visits. It is possible, for example, that the observed increases in some categories could be due to increased awareness by health professionals of certain substances, or increased perception of certain categories as problematic. This could lead to either increased detection of such substances (e.g., if the medical interviewer asks about them more than previously) or increased attribution of ED visits to the substance (e.g., if the medical interviewer is more likely to record the substance or to name it as a factor in the ED visit).

Table 1 Number of ED Visits Related to Specific Products

Drug	2007	2008	2009	2010	2011	% Change, 2007-2011
Total drug-related ED visits	**3,998,228**	**4,383,494**	**4,595,263**	**4,916,328**	**5,067,374**	26.74%
Total drug reports	**6,248,023**	**6,957,634**	**7,270,914**	**7,808,492**	**8,046,258**	28.78%
Caffeine/multivitamin	12,750	18,970	14,415	18,734	29,379	130.42%
Energy drinks	*10,068*	*16,059*	*13,119*	*15,219*	*20,783*	*106.43%*
Nutritional products	59,389	74,437	80,724	93,749	95,089	60.11%
Iron products	7,800	8,885	11,020	12,982	12,711	62.96%
Minerals and electrolytes	11,140	16,364	15,088	16,094	14,946	34.17%
Electrolyte replacement solutions, oral[a]	673	689	855	1,282	1,824	171.03%
Oral nutritional supplements	15,388	15,919	20,835	26,014	33,855	120.01%
Infant formula	12,764	12,019	16,582	22,242	28,212	121.03%
Vitamin and mineral combinations	9,499	13,566	13,847	16,369	14,834	56.16%
Vitamins	18,915	26,905	28,857	29,381	29,672	56.87%
Alternative medicines	13,320	15,892	15,951	20,806	24,222	81.85%
Herbal products	8,603	6,661	8,864	11,915	12,508	45.39%
Nutraceutical products	4,385	8,975	7,356	8,600	10,087	130.03%
Probiotics	330	485	128	752	1,760	433.33%
Gastrointestinal agents	78,826	94,468	104,390	101,940	103,358	31.12%
Antidiarrheals	6,947	8,462	8,526	12,113	10,859	56.31%

Drug	2007	2008	2009	2010	2011	% Change, 2007-2011
Laxatives	19,424	28,053	27,621	29,668	33,861	74.33%
Dermatological agents	30,072	30,438	36,016	44,262	50,632	68.37%
Topical emollients	2,832	2,937	2,972	5,622	4,836	70.76%
Hydrocortisone, topical	2,019	2,817	4,206	4,284	3,997	97.97%
Camphor[b]	460	1,402	238	1,032	2,204	379.13%
Hydrogen peroxide, topical	593	471	957	2,361	1,503	153.46%
Miscellaneous						
CNS Stimulants	48,732	53,169	53,652	66,888	93,457	91.78%
Caffeine[c]	6,434	5,930	7,293	8,633	8,936	38.89%
Isopropyl alcohol, topical	2,252	4,504	2,473	2,779	3,219	42.94%
Ophthalmic preparations[d]	9,137	9,125	11,828	13,653	14,506	58.76%

[a] Electrolyte replacement solutions include products such as Gatorade, Powerade, Pedialyte, etc.
[b] Camphor includes products such as Vick's, Biofreeze, etc.
[c] Caffeine includes coffee, as well as other caffeine-containing products, including caffeine pills and diet pills.
[d] Ophthalmic preparations include contact solution, eye drops, etc.

An important consideration in the assessment of drug-related ED visits is the health outcomes or consequences associated with such visits. While DAWN does not capture information on the nature of the complaint or symptom severity that prompted the ED visit, there is information available on the disposition or discharge status of ED visits that can serve as a proxy for measuring clinical severity and acuity. Table 2 below shows the results of an analysis of the 2011 DAWN public-use data that was conducted to determine the percentage of visits resulting in discharge home for all drug-related ED visits, caffeine/multivitamin-related visits, and for three groups of selected comparator products (nutritional products, which includes iron products, minerals and electrolytes, oral nutritional supplements, vitamins; alternative medicines, which includes herbal products, nutraceutical products, probiotics; and CNS stimulants) (see Appendix Table 5 for additional information on the visit and demographic characteristics associated with caffeine/multivitamin-related ED visits, as well as the three selected comparator products).

Of the overall caffeine/multivitamin-related ED visits in 2011, 84.4% resulted in discharge home. Considering ED visits related to caffeine/multivitamin use only (i.e., no other drug involvement), the percentage of visits resulting in discharge without any further follow-up was even higher (88.3%), demonstrating that the vast majority of energy drink-related ED visits are for non-serious complaints that do not require further medical care. Notably, home discharge rates for caffeine/multivitamin-related ED visits are substantially higher than those for drug-related ED visits overall (63.8%). These findings are consistent with information from the American Association of Poison Control Centers' (AAPCC) National Poison Data System which indicates that in cases involving energy drink exposure where medical outcome was assessed, the vast majority of cases were considered to be not serious (83% of cases with medical outcomes classified as "none" or "minor").[4] This suggests that ED visits associated with consumption of energy drinks are not as serious as those associated with other drugs.

Table 2 Home discharge rates for selected ED visit types

Visit Type	% of Visits Resulting in Discharge Home
All drug-related ED visits	63.8%
CNS stimulants-related visits	74.2%
Alternative medicines-related visits	75.5%
Nutritional products-related visits	80.3%
Caffeine/multivitamin-related visits	84.4%

[4] Bronstein AC, et al. 2011 Annual Report of the American Association of Poison Control Centers' National Poison Data System (NPDS): 29th Annual Report. Clinical Toxicology 2012;50:911-1164. Note: Energy drinks were added as a generic code to NPDS in 2010. Because only partial year data is available for 2010, it is not yet possible to assess trends related to energy drinks with these data.

4.1 Limitations of DAWN

Though not directly addressing the reported rise in energy drink-related ED visits, there are a number of limitations of DAWN that are worth noting.

4.1.1 Representativeness of the Sample and Validity of Projected Rates for the U.S.

DAWN uses a sample of hospital EDs to estimate national ED visit rates, including 13 major metropolitan areas and a supplementary sample to cover the remainder of the U.S. In 2002, prior to the most recent DAWN re-design, there were 21 metropolitan areas included in the sample. The DAWN redesign methodology report called for an expansion to 48 metropolitan areas in order to provide better national coverage and to increase the reliability and stability of their estimates. However, in 2004 (the first complete year of the redesigned DAWN) only 15 metropolitan areas had sufficient participation to warrant separate, stand-alone estimates. As of 2011 (the latest year for which public use data are available), the number of metropolitan areas with sufficient participation was further reduced to 13. Thus, although the expert panel that evaluated DAWN recommended *more* participating hospitals to increase reliability, in fact there are now *fewer* participating hospitals.

It is important to understand that DAWN's reporting is not based on a straightforward enumeration of cases. DAWN projects to a national estimate of cases based on combining results from two sources: approximately 183 hospitals in 13 major metropolitan areas, and approximately 50 supplementary hospitals in 2011. Although the metropolitan hospitals actually report more cases, the supplementary hospitals actually exert greater influence on the projected national estimate. On average, one case in the supplementary sample represents 135 weighted cases, whereas one case in any of the 13 main metropolitan areas represents, on average, fewer than 5 weighted cases (see Appendix Table 4). Therefore, a single case from a supplementary hospital can count 27 times more than a case from one of the metropolitan hospitals that report data to DAWN. This can distort the estimate. For example, a small 'outbreak' at a community hospital could potentially skew the national statistics; a single case of energy drink use presenting to a hospital in the supplementary sample could be counted as though it were 863 cases (the maximum weight for a single case in 2011), possibly seriously skewing the national statistics and resulting in misleading trend data.

In 2011, the vast majority (85.6%) of weighted caffeine/multivitamin-related ED visits were derived from the supplementary sample. This does not appear to be unique to caffeine/multivitamins, however, as an analysis of selected comparator products (i.e., nutritional products, alternative medicines, and CNS stimulants) revealed that for these three other drug classes/product categories the bulk of the weighted reporting is also coming from the supplementary sample: 83.7% for nutritional products, 83.4% for alternative medicines, and 87.3% for CNS stimulants.

Using the publicly available DAWN data, we examined trends in caffeine/multivitamin-related ED visits by individual metropolitan area and observed a variable pattern. Among the 11 metropolitan areas with available data between 2007-2011, two areas experienced a decrease in caffeine/multivitamin-related ED visits during this time period

(Denver, Phoenix); four areas experienced an increase between 50-100% (Boston, Chicago, Houston, Minneapolis-St. Paul); and five areas (Dade County (Miami), Detroit, New York City, San Francisco, and Seattle) experienced an increase greater than 100%. This may imply that there are regional variations in trends in ED visits related to energy drinks or that there are regional variations in the characterization of ED visits, possibly from a greater local awareness in the higher reporting areas. An analysis of selected comparator products also revealed regional variation in ED visits. For the category of CNS stimulants, for example, one metropolitan area experienced a decrease in ED-related visits between 2007 and 2011; one area experienced an increase of less than 50%; five areas experienced an increase between 50-100% and two areas experienced an increase greater than 100%.

4.1.2 Reliability of Self-Reported Data

The reliability of DAWN data is dependent on information listed by the provider on the ED medical chart, which is typically based on patient self-report taken by the triage nurse. Therefore, the drugs actually involved in ED visits might not all be identified and documented. As noted in the SAMHSA report, of the 20,783 ED visits involving energy drinks in 2011, more than half (58%) were reported to involve energy drinks only. However, it is possible that while some patients presenting to the ED may have readily reported use of an energy drink (a legal product, and thus more likely to be considered socially acceptable), they may have been reluctant to report any other drug use that may have occurred in conjunction with their use of an energy drink (e.g., use of illegal drugs, drugs for which there was no valid prescription or use of alcohol by those under legal age). Further, as described above, the salience of certain drugs/substances and the perception of the drug/substance as a problem could also affect reporting by the provider.

4.1.3 Inability to Determine Causation

Many drug-related ED visits involve multiple drugs. As noted in the SAMHSA report, of the 20,783 ED visits involving energy drinks in 2011, 42% reportedly involved other drugs. Use of pharmaceuticals was most commonly reported in conjunction with energy drink use (27%), with 9% of visits involving energy drinks and central nervous stimulants. About 13% of visits involved energy drinks and alcohol and 10% of visits involved energy drinks and illicit drugs, with 5% involving energy drinks and marijuana. In these instances, it may be difficult or impossible to determine whether a single drug or product is responsible for the visit or if the visit was the result of the interaction between the drugs. Furthermore, important information that could aid in assessing causation is not captured (e.g., nature of the complaint/symptoms that brought the patient to the ED, overall health of the patient, amount used/exposure information). Importantly, there is no specific information on consumption of other caffeine-containing products (e.g., coffee – which is included in the larger caffeine category by DAWN, but not listed as a specific product). This is particularly important given the wide variability in caffeine content of popular brands of coffee. According to an analysis prepared for

the Food and Drug Administration (FDA) on caffeine consumption in the U.S.[5], the mean amount of caffeine consumed by the U.S. population has remained relatively stable between 2003 and 2008 at approximately 300 milligrams per person per day despite the entry of energy drinks into the marketplace. Furthermore, according to the same analysis, energy drinks contribute a small portion of the caffeine consumed, with major sources of caffeine being coffee, soft drinks and tea.

5 Potential Issues

The estimates provided in the SAMHSA report are based solely on number of ED visits, and do not account for the availability of the product (i.e., sales). As shown in Table 3 (which includes data for the years 2007-2011, since as noted by SAMHSA, statistical tests were not used until 2007 when the number of ED visits involving energy drinks exceeded 10,000) and Figure 2 (which displays data for the years 2005-2011, consistent with the figure presented in the SAMHSA report), the increase in energy drink-related ED visits was accompanied by an increase in the number of cases of energy drinks sold. However, ED visits still appear to be increasing at a higher rate than sales.

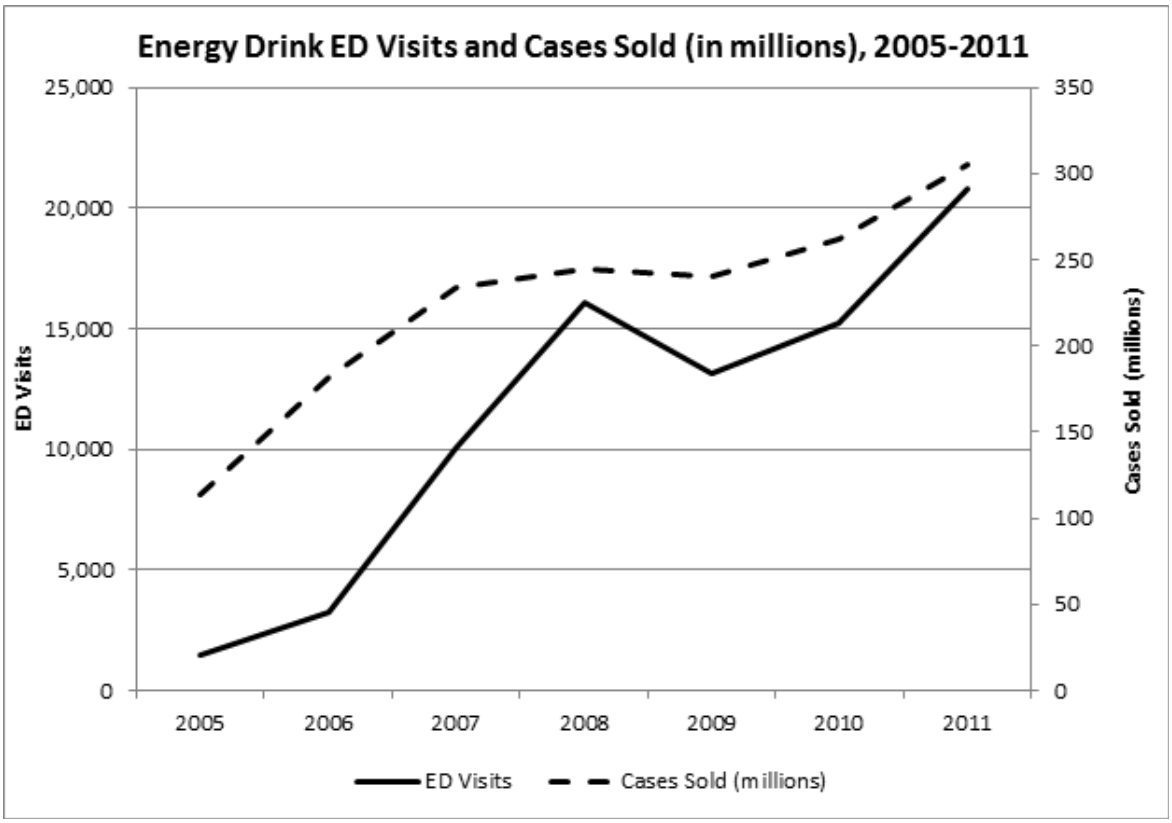
Table 3 Energy drink-related ED visits and number of cases of energy drinks sold (2007-2011)

	2007	**2008**	**2009**	**2010**	**2011**	**% Change 2007-2011**
Number of energy drink-related visits	10,068	16,059	13,119	15,219	20,783	106.4%
Cases sold (millions)[±]	234.1	244.5	240.1	261.5	305.0	30.3%
Number of energy-drink related visits per 1 million cases sold	43.0	65.7	54.6	58.2	68.1	58.4%

[±]Source: Beverage Digest Fact Book

[5] Caffeine Intake by the U.S. Population. Prepared by Laszlo P. Somogyi, Ph.D. for the Food and Drug Administration, Oakridge National Laboratory. Subcontract Number 70000073494. Completed September 2009 and revised August 2010. Available at: http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofFoods/CFSAN/CFSANFOIAElectronicReadingRoom/UCM333191.pdf

Figure 2 Energy drink-related ED visits and cases of energy drinks sold (in millions), 2005-2011



6 Conclusion

Although the DAWN report has attracted a lot of attention, careful analysis of the report and the public data underlying it, do not appear to be consistent with a signal of substantial medical harm. The vast majority of caffeine/multivitamin-related ED visits appear to be associated with non-serious complaints that do not require further medical follow-up, as 84.4% of visits related to these products resulted in discharge home, a higher rate than observed for other products. The reported rate of ED visits related to caffeine/multivitamins remains quite small, representing a tiny fraction of the overall visits to EDs each year. Finally, the limitations of the DAWN system suggest caution in basing public health policy on the results relative to energy drinks.

8 Appendix

Table 4 DAWN weighting by metro area (2011)

	Number of Cases, Unweighted	% of Unweighted Cases	Average Weight	Minimum Weight	Maximum Weight
BOSTON-CAMBRIDGE-QUINCY,MA-NHMSA:(1)	24,889	10.86%	3.86	1.60	8.54
NEW YORK CITY - 5 BUROUGHS (PART OF NEW YORK- NEWARK-EDISON, NY-NJ-PA MSA):(2)	39,776	17.35%	3.13	0.94	22.84
CHICAGO-NAPERVILLE-JOLIET, IL-IN-WI MSA:(3)	21,918	9.56%	6.68	1.42	28.77
DETROIT-WARREN-LIVONIA, MI MSA:(4)	22,502	9.82%	4.20	1.23	11.62
MINNEAPOLIS-ST. PAUL-BLOOMINGTON, MN-WI MSA:(5)	12,049	5.26%	4.50	1.33	8.04
FORT LAUDERALE DIVISION OF MIAMI-FORT LAUDERDALE, FL MSA:(6)	5,352	2.33%	6.15	2.59	14.30
DADE COUNTY DIVISION OF MIAMI-FORT LAUDERDALE, FL MSA:(7)	7,101	3.10%	4.46	2.57	8.57
HOUSTON-BAYTOWN-SUGAR LAND, TX MSA:(8)	9,115	3.98%	10.31	3.32	27.90
DENVER-AURORA, CO MSA:(9)	12,112	5.28%	3.01	1.10	7.34
PHOENIX-MESA-SCOTTSDALE, AZ MSA:(10)	13,166	5.74%	4.76	1.05	15.87
OAKLAND DIVISION OF SAN FRANCISCO-OAKLAND-FREMONT, CA MSA:(11)	2,462	1.07%	13.29	9.22	18.18

SAN FRANCISCO DIVISION OF SAN FRANCISCO-OAKLAND-FREMONT, CA MSA:(12)	8,936	3.90%	4.09	1.14	10.06
SEATTLE-TACOMA-BELLEVUE, WA MSA:(13)	18,973	8.28%	2.86	1.03	7.74
ALL OTHER LOCATIONS:(14) (a.k.a. "*supplementary sample*")	30,860	13.46%	135.13	2.01	862.82

Table 5 Visit characteristics and demographics for caffeine/multivitamin-related ED visits, nutritional products-related ED visits, alternative medicine-related ED visits and CNS stimulant-related ED visits (2011)

	Caffeine/Multivitamin Products	Nutritional Products	Alternative Medicines	CNS Stimulants
Total ED Visits	29,379	95,089	24,222	93,457
Combinations				
Product Only	14,393 (48.99%)	63,780 (67.07%)	11,374 (46.96%)	45,951 (49.17%)
Product, Any Pharmaceutical Combination	11,952 (40.68%)	11,090 (11.66%)	4,497 (18.57%)	40,648 (43.49%)
Product, Any Alcohol Combination	8,615 (29.32%)	1,644 (1.73%)	1,523 (6.29%)	17,118 (18.32%)
Product, Any Illicit Drug Combination	3,701 (12.60%)	201 (0.21%)	1,653 (6.82%)	12,914 (13.82%)
Product, 2+ Substances, Not Misuse/Abuse	3,503 (11.92%)	23,735 (24.96%)	8,870 (36.62%)	14,974 (16.02%)
Visit Characteristics				
Quarter				
First Quarter	5,580 (18.99%)	25,279 (26.59%)	9,059 (37.40%)	20,909 (22.37%)
Second Quarter	7,764 (26.43%)	26,784 (28.17%)	5,738 (23.69%)	25,739 (27.54%)
Third Quarter	8,503 (28.94%)	22,483 (23.64%)	5,485 (22.64%)	26,334 (28.18%)
Fourth Quarter	7,532 (25.64%)	20,542 (21.60%)	3,939 (16.26%)	20,475 (21.91%)
Part of the Day				
Early morning (12:00-5:59 AM)	6,367 (21.67%)	14,965 (15.74%)	3,605 (14.88%)	16,914 (18.10%)
Morning (6:00-11:59 AM)	5,044 (17.17%)	18,738 (19.71%)	4,274 (17.64%)	18,896 (20.22%)
Afternoon (12:00-5:59 PM)	8,236 (28.03%)	29,750 (31.29%)	9,610 (39.68%)	27,655 (29.59%)
Evening/Night (6:00-11:59 PM)	9,733 (33.13%)	31,637 (33.27%)	6,734 (27.80%)	29,993 (32.09%)
Number of Substances				
One	14,393 (48.99%)	63,780 (67.07%)	11,374 (46.96%)	45,951 (49.17%)

	Caffeine/Multivitamin Products	Nutritional Products	Alternative Medicines	CNS Stimulants
Two or more	14,986 (51.01%)	31,308 (32.93%)	12,848 (53.04%)	47,506 (50.83%)
Case Type				
Suicide Attempt	917 (3.12%)	1,473 (1.55%)	1,363 (5.63%)	4,715 (5.05%)
Seeking Detox	364 (1.24%)	5 (0.01%)	14 (0.06%)	2,272 (2.43%)
Alcohol Only (Age<21)	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Adverse Reaction	15,914 (54.17%)	79,638 (83.75%)	16,656 (68.76%)	41,311 (44.20%)
Product Only	13,061 (44.46%)	57,447 (60.41%)	8,528 (35.21%)	28,970 (31.00%)
Product, Any Pharmaceutical Combination	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Product, Any Alcohol Combination	0 (0.00%)	820 (0.86%)	659 (2.72%)	1,594 (1.71%)
Product, Any Illicit Drug Combination	5 (0.02%)	5 (0.00%)	0 (0.00%)	5 (0.00%)
Product, 2+ Substances, Not Misuse/Abuse	2,849 (9.70%)	21,366 (22.47%)	7,469 (30.84%)	10,743 (11.49%)
Overmedication	1,247 (4.25%)	9,240 (9.72%)	1,769 (7.30%)	10,959 (11.73%)
Malicious Poisoning	30 (0.10%)	293 (0.31%)	0 (0.00%)	94 (0.10%)
Accidental Ingestion	232 (0.79%)	2,883 (3.03%)	1,693 (6.99%)	4,510 (4.83%)
Other	10,675 (36.34%)	1,557 (1.64%)	2,729 (11.27%)	29,596 (31.67%)
Disposition				
Discharged Home	24,798 (84.41%)	76,326 (80.27%)	18,295 (75.53%)	69,379 (74.24%)
Product Only	12,714 (43.28%)	58,968 (62.01%)	9,470 (39.09%)	39,000 (41.73%)
Product, Any Pharmaceutical Combination	9,722 (33.09%)	6,949 (7.31%)	2,613 (10.79%)	27,820 (29.77%)
Product, Any Alcohol Combination	6,416 (21.84%)	461 (0.48%)	1,060 (4.37%)	11,016 (11.79%)
Product, Any Illicit Drug Combination	3,103 (10.56%)	101 (0.11%)	767 (3.17%)	7,032 (7.52%)
Product, 2+ Substances, Not Misuse/Abuse	3,431 (11.68%)	14,007 (14.73%)	6,545 (27.02%)	10,506 (11.24%)
Released to Police/Jail	15 (0.05%)	100 (0.11%)	8 (0.03%)	260 (0.28%)
Referred to Detox/Treatment	363 (1.24%)	430 (0.45%)	32 (0.13%)	2,134 (2.28%)
ICU/Critical Care	367 (1.25%)	1,133 (1.19%)	288 (1.19%)	2,074 (2.22%)

	Caffeine/Multivitamin Products	Nutritional Products	Alternative Medicines	CNS Stimulants
Surgery	5 (0.02%)	387 (0.41%)	0 (0.00%)	5 (0.01%)
Chemical Dependency/Detox, Psychiatric Unit	50 (0.17%)	189 (0.20%)	1,056 (4.36%)	2,973 (3.18%)
Other Inpatient	1,804 (6.14%)	13,263 (13.95%)	3,653 (15.08%)	5,608 (6.00%)
Transferred	972 (3.31%)	2,244 (2.36%)	697 (2.88%)	9,401 (10.06%)
Left Against Medical Advice	326 (1.11%)	90 (0.09%)	60 (0.25%)	718 (0.77%)
Died	0 (0.00%)	0 (0.00%)	0 (0.00%)	0 (0.00%)
Other	672 (2.29%)	222 (0.23%)	108 (0.45%)	823 (0.88%)
Not Documented	7 (0.02%)	703 (0.74%)	25 (0.10%)	81 (0.09%)
Demographics				
Sex				
Male	20,502 (69.78%)	40,796 (42.90%)	10,684 (44.11%)	54,926 (58.77%)
Female	8,877 (30.22%)	54,293 (57.10%)	13,538 (55.89%)	38,531 (41.23%)
Age Category				
0-11	668 (2.27%)	32,032 (33.69%)	2,762 (11.40%)	10,926 (11.69%)
12-17	3,082 (10.49%)	2,345 (2.47%)	1,145 (4.73%)	13,859 (14.83%)
18-24	9,260 (31.52%)	2,627 (2.76%)	3,494 (14.43%)	23,543 (25.19%)
25-34	7,038 (23.96%)	6,510 (6.85%)	4,148 (17.13%)	21,486 (22.99%)
35+	9,332 (31.76%)	51,575 (54.24%)	12,673 (52.32%)	23,643 (25.30%)
Race/Ethnicity				
White Only	18,293 (62.26%)	60,953 (64.10%)	17,926 (74.01%)	68,763 (73.58%)
African American Only	3,475 (11.83%)	14,800 (15.56%)	2,284 (9.43%)	9,108 (9.75%)
Hispanic or Latino	7,055 (24.02%)	16,528 (17.38%)	3,140 (12.96%)	14,404 (15.41%)
All Other Races	556 (1.89%)	2,807 (2.95%)	873 (3.60%)	1,181 (1.26%)

ATTACHMENT 3

AMERICAN BEVERAGE ASSOCIATION

July 26, 2013

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

Dear Dr. Hamburg:

We are writing in response to a March 19, 2013, letter ("the Arria Letter") to you from 18 healthcare professionals ("the Authors") concerning the safety of caffeine as an ingredient in energy drinks. The Authors of that letter assert 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."[1] The Authors further assert that the use of caffeine in energy drinks under the intended conditions of use is not generally recognized as safe ("GRAS"). Finally, the authors conclude that "the best available scientific evidence demonstrates a robust correlation between caffeine levels in energy drinks and adverse health and safety consequences, particularly among children, adolescents, and young adults."[2]

The Authors paint a distorted and highly inaccurate picture of caffeine use and safety, ignoring the vast number of robust and reliable scientific publications that has, for decades, established the safety of caffeine at the levels presented in energy drinks, including for younger consumers. Caffeine is a well-studied, widely used, and safely consumed food ingredient. The vast majority of U.S. consumers consume a caffeine-containing beverage daily without any evidence of risk or harm. The amount of caffeine in mainstream energy drinks is typically less than the caffeine in a 12-16 fluid ounce ("medium") coffee-shop brewed coffee.[3] Recent surveys of consumption of caffeine-containing beverages, including a survey sponsored by FDA, consistently demonstrate that coffee drinkers consume the most caffeine. For example, in a recent consumption survey sponsored by the International Life Sciences Institute ("ILSI"), the authors noted that "caffeine intakes were highest for adult

[1] Letter from Amelia M. Arria, Ph.D. et al. to the Honorable Margaret A. Hamburg, M.D., Commissioner, Food and Drug Administration, at 1 (March 19, 2013) (hereinafter "Arria Letter").
[2] *Id.*
[3] A 16 fluid ounce Starbucks™ Grande coffee contains about 330 mg (about 20 mg/fluid ounce). Mainstream energy drinks contain 10 to 15 mg/fluid ounce or about 80 to 120 mg/8 fluid ounce serving. A 16 fluid ounce energy drink container would typically contain 160 to 240 mg of caffeine, less than a 16 fluid ounce cup of brewed Starbucks™ coffee.

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coffee drinkers over 35 years of age."[4] Surveys demonstrate that while more than fifty percent of people consuming caffeine-containing beverages drink coffee, only about four percent drink energy beverages.[5]

The Authors' focus on caffeine intake from energy beverages ignores increased caffeine intake from coffee. Coffee consumption increased by 700% from 1995 to 2000.[6] Furthermore, the National Coffee Association's National Coffee Drinking Trends study for 2012 showed that increases in coffee consumption were most significant among those between 18 and 39 years old: "Among those 18 to 24 years old, daily consumption jumped from 40 to 50 percent and for those 25 to 39 years old, from 54 to 63 percent."[7] The Authors' persistence in attacking energy drinks cannot be reconciled with the data.

About twenty-five years ago, two distinguished academicians, Dr. P.B. Dews and Dr. Jack Bergman, introduced a chapter in a book on Nutritional Toxicology entitled "Dietary Caffeine and Its Toxicity" with the following:

> Caffeine is part of the diet of most people. It is generally accepted that caffeine helps people work and enjoy their days a little better, but that has not been established by rigorous, objective, and quantitative studies. There is much more substantial evidence that dietary consumption is harmless in normal people. There has continued to be a perhaps never-ending series of suggestions of adverse effects which, so far, on further investigation have been shown to be ill-founded. Use of the term toxicity for the effects reported or suggested for caffeine as a component of the diet, the main concern of this review, may therefore be misleading. What is toxic and what is not, what is sought after and what is an unwanted side effect, depends on the circumstances.[8]

In spite of the Authors' attempt to paint caffeine as unsafe, the weight of the scientific evidence clearly establishes that caffeine is a safe food ingredient under the intended conditions of use in energy drinks, and is properly designated as a GRAS food ingredient for

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[4] Mitchell, D.C. et al., *Beverage Caffeine Intakes in the U.S.*, Poster session presented at the American Society for Nutrition Annual Meeting at EB 2013, Boston, MA (Apr. 20-24, 2013).
[5] *Id.*
[6] Lumin Interactive (Designer), *How Coffee Changed America* (Web Graphic), *available at* http://newswatch.nationalgeographic.com/2012/01/19/coffee-changed-america-infographic/ (last accessed May 30, 2013).
[7] National Coffee Association, *2012 National Coffee Drinking Trends Study* (2012).
[8] Bergman, J. and Dews, P.B., *Dietary Caffeine and Its Toxicity, 2* NUTRITIONAL TOXICOLOGY 199, 199-200 (John N. Hathcock ed., 1987).

use in beverages generally and energy drinks in particular. Energy drinks have been marketed worldwide for about three decades and are safely consumed throughout the world. It is estimated that nearly 5 billion cans of energy drinks are consumed in the United States annually and many more billion cans are consumed each year worldwide. Regulatory bodies in Europe and Canada (and elsewhere) have evaluated these beverages previously and concluded that they are safe, as detailed below.

Contrary to the assertion by the Authors that "the best available scientific evidence demonstrates a robust correlation between the caffeine levels in energy drinks and adverse health consequences, particularly among children, adolescents, and young adults,"[9] the scientific evidence demonstrates that: (1) caffeine is safely consumed by virtually all consumers; (2) the effects of "excess" caffeine consumption are self-limiting and reversible; (3) serious adverse events associated with caffeine are extremely rare and typically involve inherent, individual health-related factors beyond caffeine; and (4) for most consumers the benefits of caffeine – increased attention, vigilance, improved productivity, and concentration – are obtained without any adverse effect whatsoever.

We address the principal allegations set forth by the Authors in turn below.

I. Energy Drinks Are Not Typically High in Caffeine in Comparison to Competing Beverages

One of the Authors' principal premises is that energy drinks contain "high levels of added caffeine."[10] The Authors do not define what they mean by "high" levels of caffeine. For purposes of this discussion, we will assume that "high" means substantially in excess of the level of caffeine otherwise widely available in comparable or competing beverages such as coffee. Even with that generous interpretation of the Authors' meaning, their assertion is unsupported by facts.

Most energy drinks are sold in containers ranging from about 8 fluid ounces to 16 fluid ounces with approximately 10-15 mg/fluid ounce of caffeine. A typical container of an energy drink will therefore contain between 80 and 240 mg caffeine.[11] In contrast, prepared coffees often exceed the levels of caffeine in a typical energy drink. For example, a medium Starbucks Coffee (a Grande, in Starbucks parlance), which is a 16 fluid ounce beverage, contains 330 mg caffeine (Table 1). Also, shelf-stable coffees and iced coffees are sold in

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[9] Arria Letter, at 1.

[10] *See, e. g.*, Arria Letter, at 1.

[11] *See* Center for Science in the Public Interest ("CSPI"), *Caffeine Content Of Food & Drugs* (Dec. 2012), *available at* http://www.cspinet.org/new/cafchart.htm (last accessed May 30, 2013).

retail outlets on shelves and in refrigerators, often adjacent to energy drinks. Indeed, some coffee flavored ice creams and frozen yogurts contain about as much caffeine in a serving as would typically be found in an 8 fluid ounce energy drink (Table 1). Therefore, the focus on the caffeine content of energy drinks seems misplaced.

Table 1. Caffeine Content of Select Foods Available in the U.S.			
Product	**Amount**[12]	**mg of Caffeine**[13]	**Mg caffeine/oz.**
Dunkin' Donuts with Turbo Shots	20 fl. oz.	436	21.8
Caribou Depth Charge	16 fl. oz.	370[14]	23.1
Starbucks Coffee (Grande/Medium)	16 fl. oz.	330	20.6
Caribou Coffee of the Day	16 fl. oz.	305[15]	19.1
Panera Frozen Mocha	16.5 oz.	267	16.2
Baskin Robbins Cappuccino Blast	24 fl. oz.	234	9.75
Dunkin' Donuts Coffee (Medium)	14 fl. oz.	178	12.7
Starbucks Iced Coffee	16 fl. oz.	165	10.3
Monster	16 fl. oz.	160	10
Rockstar	16 fl. oz.	160	10
McDonalds Premium Roast Iced Coffee	22 fl .oz.	145	6.59
Ben & Jerry's Coffee Heath Bar Crunch Ice Cream	4 oz.	42	10.5
Red Bull	8.4 fl. oz.	80	9.5
Ben & Jerry's Coffee Flavored Ice Cream	4 oz.	34	8.5
Mio (by Kraft)	1 squirt (1/2 tsp.)	60 per serving; 1080 per 1.62 fl. oz. bottle	
Coca-Cola, Coke Zero, or Diet Pepsi	12 fl. oz.	35	2.9
Hershey's Special Dark Chocolate Bar	1.45 oz.	31	21.4
Brewed tea	8 fl. oz.	30-80	3.75-10

[12] The amounts used in Table 1 correspond to typical serving or container sizes. Where multiple size containers are offered for sale (coffee products, for example), the mid-sized container was used.

[13] *See* CSPI, *Caffeine Content of Food and Drugs*, *supra* note 11 and public industry information. Table 1 includes values from the current version of the CSPI chart, as well as previous versions of the CSPI page.

[14] CARIBOU COFFEE CO., *Depth Charge*, *available at* http://www.cariboucoffee.com/page/1/beverage-food-detail.jsp?id=1439&type=drink (last accessed May 30, 2013).

[15] CARIBOU COFFEE CO., *Coffee of the Day*, *available at* http://www.cariboucoffee.com/page/1/beverage-food-detail.jsp?id=1436&type=drink (last accessed May 30, 2013).

Table 1 shows, numerous foods and beverages contain caffeine at levels comparable to or greater than those in energy drinks. These foods have a long history of safe consumption in the U.S. and globally by persons of all age groups. It is therefore clear that energy drinks do not introduce new or alarming levels of caffeine into the food supply, as has been suggested by the Authors of the Arria Letter. Further, while the Arria Letter states that "many energy drinks and related products containing added caffeine exceed the caffeine concentration of even the most highly caffeinated coffee,"[16] the data in Table 1 regarding caffeine content of coffee make clear that this statement is not correct.

The Authors of the Arria Letter suggest a distinction between "naturally occurring" caffeine and "added" caffeine, implying somehow that "added" caffeine is more problematic.[17] There is no scientific basis for this assertion. The body identifies and processes added caffeine, from any source, in the same way that it processes caffeine that may be naturally occurring in foods and beverages.[18] We also note that many energy drinks incorporate "naturally occurring" caffeine, including from green tea and coffee. Significantly, manufacturers who add caffeine to their products can control the amount to a far greater extent than producers or marketers of food in which caffeine is naturally occurring such as tea or coffee. An energy drink manufacturer can ensure with a high degree of precision and accuracy that its products contain the amount of caffeine declared on their labels. By contrast, the caffeine content of coffee products varies widely due to many factors, such as brewing method, origin of the bean, degree of roasting, and other attributes. Indeed, one well-cited study found that the caffeine content of one specific coffee (Starbucks Breakfast Blend) at a single coffee shop varied by hundreds of milligrams (from 259 to 564 mg in a 16 fl. oz cup) over the course of six consecutive days.[19]

The Authors also distinguish energy drinks from coffee by saying that "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."[20] No data are offered to support these statements, which are selective characterizations that fail to account for the fact that many, if not most, consumers sweeten their coffee and add milk and drink it quickly enough to avoid it becoming cold. Perhaps even more relevant in the context of the Authors' focus on children and adolescents, these statements do not

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[16] Arria Letter, at 2.
[17] *Id.*
[18] One of the Authors, Dr. Roland Griffiths, recently stated that "caffeine is caffeine," (quoted in Hill, M., *Energy Drinks Go Natural as Market Buzzes Along*, USA TODAY, July 6, 2013, *available at* http://www.usatoday.com/story/money/business/2013/07/06/energy-drinks-go-natural/2479993/ (last accessed July 10, 2013)).
[19] McCusker, R.R. et al., *Caffeine Content of Specialty Coffees*, 27 J. ANALYTICAL TOXICOLOGY 520 (2003).
[20] Arria Letter, at 2.

account for cold or iced coffee beverages, which are typically sweetened and are quite popular among younger consumers. Moreover, the Authors fail to account for the difference in caffeine content between coffee and energy drinks. As noted, a medium 16 fluid ounce premium coffee contains twice the amount of caffeine found in a 16 fluid ounce serving of energy drinks, negating any discrepancy that might arise from differences in the rate of consumption. In any case, the human body absorbs, distributes, metabolizes, and excretes caffeine in the same exact manner regardless of whether it is delivered to the stomach cold or hot.

Even if the purported differences asserted by the Authors are correct, there is no scientific evidence provided or available that establishes that sipping coffee or drinking an energy drink changes caffeine absorption from the gut in a meaningful manner, or that different manners of ingesting caffeine-containing beverages alter the metabolism of caffeine in the body. Given the pharmacokinetic parameters of caffeine, oral administration of equal doses over a short window (five minutes, for example) as opposed to an extended window (30 minutes, for example) would have a negligible effect on serum levels.[21]

Using available data and simple clinical pharmacokinetic models, it is possible to evaluate the absorption of caffeine with different input times. When an evaluation of concentrations achieved (instantaneous intravenous administration versus 5 minute ingestion time versus 30 minute ingestion time) after a 240 mg dose of caffeine is given, using the following accepted pharmacokinetic assumptions and models, only nominal differences in concentration are revealed. In each of these three cases peak concentrations of approximately 4-4.3 mg/L would be achieved and concentrations of 1.6-1.8 mg/L would be expected eight hours after the dose.

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[21] Arnaud, M., *Pharmacokinetics And Metabolism Of Natural Methylxanthines In Animal And Man*, METHYLXANTHINES, HANDBOOK OF EXPERIMENTAL PHARMACOLOGY 200, at 33-91 (B. Fredholm ed., 2011)). *See also* Liguori A. et al., *Absorption and Subjective Effects of Caffeine from Coffee, Cola and Capsules*, 58 PHARMACOLOGY BIOCHEMISTRY AND BEHAVIOR 721 (1997) (finding that peak caffeine absorption, time to peak absorption, and subjective effects do not appear to be influenced by a cold cola vehicle versus hot coffee or capsule vehicles).

- Subject wt= 80 kg
- S= salt fraction= 1
- F= bioavailability= 1 or 100%
- D= 240 mg
- V_d= 0.7 L/kg= 56L
- Absorption time= 0.75 hr
- Cl= 0.078L/kg/hr= 6.24L/hr
- K_e= Cl/Vd= 0.11 hr^{-1}
- A non-steady state short infusion model.[22]

When taken together, these three scenarios (intravenous administration, 5 minute, and 30 minute, oral administration) demonstrate that, given the absorption pattern of caffeine, the duration of administration is not clinically significant. The model used above does have limitations but generally demonstrates that rate of input is not a major factor in determining peak serum concentrations. This is because caffeine is well absorbed within about 45 minutes, and has a half-life of about 5 hours.[23] This means that not very much of the compound is eliminated during the absorption time.

The major factor governing an overdose/toxicity of caffeine is the total dose. A fatal acute dose of caffeine in adult humans is estimated to be between 10 and 20 g.[24] Subjects consuming caffeine-containing beverages tend to self-regulate the amount they consume, often based on previous experience.[25] Fatal caffeine overdose via beverages is very difficult if not impossible to achieve because the volume of fluid required to provide a toxic dose of caffeine is dose limiting (for example, 100 cups (8 fluid oz.) of coffee, 62 servings (16 fluid

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[22] *See* Carillo J.A., and Benitez, J., *Clinically Significant Pharmacokinetic Interactions Between Dietary Caffeine and Medications*. 39 CLIN. PHARMACOKINET. 127-153 (Aug. 2000); Heckman, M.A. et al., *Caffeine (1, 3, 7-trimethylxanthine) in Foods: A Comprehensive Review on Consumption, Functionality, Safety, and Regulatory Matters,* 75 JOURNAL OF FOOD SCIENCE R77-R87 (Apr. 2010); Juliano, L.M. et al., *The Pharmacology of Caffeine, in* PRINCIPLES OF ADDICTION MEDICINE (4th ed. 2009); Winter, M.E., BASIC CLINICAL PHARMACOKINETICS (5th ed. 2010); IOM, *Caffeine for the Sustainment of Mental Task, Performance: Formulations for Military Operations* (2001) (hereinafter *"IOM Report on Caffeine"*); Arnaud, *supra* note 21.

[23] Blanchard, J. and Sawers, S.J.A., *Comparative Pharmacokinetics of Caffeine in Young and Elderly Men*, 11 J. PHARMACOKIN. BIOPHARM. 109-126 (1983).

[24] *IOM Report on Caffeine*, *supra* note 22 at 56.

[25] Kaplan, G.B.et al., *Dose-dependent pharmacokinetics and psychomotor effects of caffeine in humans*, 37 J CLIN. PHARMCOL. 693-703 (1997).

oz.) of a typical energy drink). Conversely, toxic doses are more readily achieved with consumption of caffeine tablets.

In sum, the foregoing data and information document that mainstream energy drinks are not "high" in caffeine relative to other common caffeine-containing beverages and foods, and there is no genuine difference in how the human body absorbs caffeine from coffee or other foods or from energy drinks.

II. Consumption Data Confirm that Children and Adolescents Are Not Frequent Consumers of Energy Drinks and that Overall Consumption of Caffeine Has Not Markedly Increased

The Arria Letter includes several very general statements on energy drink consumption in adolescents (persons aged 12 - 17). For example, it states "65% of energy drink consumers are 13-to 35-year-olds,"[26] yet the Arria Letter does not further identify which age groups within that very broad age range are the frequent and infrequent consumers of energy drinks. Nor does it identify how many energy drinks were consumed by a specific age group during any particular time period. The Arria Letter includes several additional statements related to adolescent consumption of energy drinks: (1) "More recent reports show that 30 to 50% of adolescents and young adults consume energy drinks"; (2) "35% of eighth graders and 29% of both tenth and twelfth graders consumed an energy drink during the past year"; and (3) "18% of eighth graders reported using one or more energy drinks every day."[27]

These statements do not support the allegations of the Authors that adolescents are regular consumers of high amounts of energy drinks. On the contrary, the fact that 30 to 50% of adolescents "consume" energy drinks is vague and could mean a consumption of only one energy drink during the period of time in question. Similarly, the second statement shows only that over the course of one year 35% of eighth graders and 29% of tenth and twelfth graders consumed at least one energy drink. (Indeed, it does not specify whether "consume" means drink an entire can, or merely taste or sample.) The third stands at odds with most other consumer research on energy drink consumption, including that conducted or commissioned by government bodies. In any case, government data show that consumption of energy drinks by younger consumers has not increased those consumers' overall caffeine intake. Therefore, the amount of energy drinks consumed by younger people is not a cause for alarm.

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[26] Arria Letter, at 1.
[27] *Id.* at 1-2.

U.S. caffeine consumption data obtained from the United States Department of Agriculture ("USDA") National Health and Nutrition Examination ("NHANES") surveys show that caffeine consumption in the U.S. has remained essentially stable over the past decade. The NHANES survey results from 2001-2010 show caffeine intake has remained steady, despite the introduction of energy drinks and caffeinated waters during that time. Moreover, in direct contrast to the Authors' conclusions, the survey data indicate that the level of caffeine consumption for children *decreased* between 2001 - 2010, despite the availability of energy drinks (Table 2).

Table 2. Caffeine Intakes From Beverages and Foods (NHANES 2001 - 2010)*

Age (years)	Caffeine (mg)/person			
	2001-2002[1]	2005-2006[2]	2007-2008[3]	2009-2010[4]
Males				
2-5	15.2	8.4 ± 0.72	7.8 ± 0.80	6.0 ± 0.70
6-11	26.1	19.72.74	29.9± 3.59	18.21.78
12-19	74.3	69.5 ± 6.70	73.6± 10.18	66.3 ± 11.12
20-29	151.9	133.4 ±14.46	139.6± 14.39	124.0 ±13.82
30-39	215.0	211± 12.21	187.8 ±18.29	187.9 ± 18.79
40-49	240.1	263.6 ±14.78	259.6 ±20.99	253.3 ± 22.34
50-59	243.0	295.6± 26.51	273.4 ±22.40	282.0 ± 19.41
60-69	203.8	228.0± 16.17	228.3 ±17.81	220.5 ± 15.75
70 and over	160.1	156.9 ±12.81	162.7 ± 8.23	174.8 ± 15.93
20 and over	207.7	216.1 ± 8.23	211.0 ±10.78	208.6 ± 10.70
Females				
2-5	12.3	6.9 ± 0.90	8.9 ± 1.63	5.7 ± 0.56
6-11	23.0	170 ± 1.26	19.0± 3.29	16.1 ± 0.99
12-19	49.1	46 6 ± 4.18	60.4 ± 4.40	48.4 ± 4.28
20-29	91.4	82.2 ± 8.14	105.8 ±13.35	107.6 ± 7.62
30-39	168.9	165.2 ± 19.3	153.5 ±15.04	155.8 ± 12.22
40-49	190.0	219.8 ±10.24	194.4 ±11.96	168.8 ± 12.22
50-59	190.6	225.3 ±15.33	207.2 ±32.17	186.1 ± 15.95
60-69	153.0	163.7 ±19.05	180.7 ±17.96	166.8 ± 14.61
70 and over	118.5	120.8 ± 7.61	139.1 ±10.39	121.9 ± 11.93
20 and over	153.4	165.3 ± 4.91	163.8 ± 8.51	152.2 ± 7.79
Males and females				
2 and over	142.1	149.8 ± 5.27	148.8 ± 7.44	142.2 ± 6.33

* Data are reported as mean error *per* individual (*per capita*) by gender and age in United States people 2 years and over (excluding breast-fed children) unless indicated otherwise.

[1] No standard errors were reported. Does not include separate food codes for energy drinks.

[2] Includes separate food codes for one brand of energy drinks and a general food code for "Energy Drink."

[3] Includes separate food codes for ten different brands of energy drinks and a general food code for "Energy Drink."

[4] Includes separate food codes for ten different brands of energy drinks and a general food code for "Energy Drink."

In addition, the results of a study commissioned by FDA ("the Somogyi study") confirm the NHANES consumption data, showing that caffeine consumption in the U.S. has remained "relatively stable at approximately 300 milligrams per person per day (mg/p/d), despite the entry of 'energy drinks' into the market place."[28] The study results also confirm that U.S. consumers have not significantly modified their caffeine consumption patterns since the appearance of energy drinks on the market: "In response to the emergence of energy drinks as a new class of caffeinated products, FDA completed an updated assessment of the amount of caffeine that people in the United States ingest from all sources. The results show that, even when the consumption of energy drinks is considered, most of the caffeine consumed comes from what is naturally present in coffee and tea."[29]

Based on data from U.S. government sources, it is clear that adolescents do not consume high amounts of caffeine. The Somogyi study reported that "teens and young adults (14-21 years of age) consume, at the mean, approximately one-third (or about 100 mg/p/d) the amount of caffeine as adults, and that their caffeine consumption is mainly from coffee, soft drinks, and tea."[30] Adolescent caffeine consumption also has remained relatively stable since 2001.[31] FDA has therefore concluded that "'energy drinks contribute a small portion of the caffeine consumed, even for teens."[32]

Moreover, only a small percentage of adolescents regularly consume energy drinks. The Somogyi study cited a recent, nationwide survey of 2,000 nationally representative households, which concluded that 0.9% of 14-21 year old individuals are "regular energy drinkers."[33] Because the survey might have under-reported energy drinking for young persons, Somogyi assumed that 2% of the entire population older than 10 are "regular consumers" of energy drinks, though "regular consumers" was not defined. Somogyi noted that "[r]eliable consumption data for habitual energy drinkers are unavailable" for any age

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[28] Letter from Michele Mital, Acting Associate Commissioner for Legislation, FDA, to the Honorable Richard J. Durbin, United States Senate at 4 (Nov. 21, 2012) (hereinafter "FDA November 2012 letter"), *citing* Somogyi, L., *Caffeine Intake By The U.S.. Population* (September 2009, rev'd Aug. 2010) *available at* http://www.fda.gov/downloads/AboutFDA/CentersOffices/OfficeofFoods/CFSAN/CFSANFOIAElectronicReadingRoom/UCM333191.pdf (last accessed July 9, 2013).

[29] Letter from Jeanne Ireland, Assistant Commissioner for Legislation, FDA, to the Honorable Richard J. Durbin, United States Senate (Aug. 10, 2012) (hereinafter "FDA August 2012 letter").

[30] FDA November 2012 letter, *supra* note 28, at 4, *citing* Somogyi.

[31] Somogyi, *supra* note 28, at 48, Table 26.

[32] FDA November 2012 letter, *supra* note 28, at 4.

[33] Somogyi, *supra* note 28, at 61.

group.[34] The study assumed that the 2% of the general population estimated to consume energy drinks consume about 1.55 - 16 fluid oz. servings per day.[35] This amount would yield caffeine exposures that are well within those accepted as safe in the published scientific literature and statements of governmental and other authoritative bodies, as discussed herein.

The Somogyi and NHANES findings were echoed in a large survey (over 37,000 participants) of the caffeine intake from beverages throughout the U.S. conducted between 2010 and 2011 by researchers at Penn State University on behalf of ILSI. These researchers again found that Americans consume the bulk of their caffeine from coffee and soft drinks, and not from energy drinks. Specifically with respect to energy drinks, the researchers determined that "[t]he percentage of energy drink users was low (<u>≤10%</u>) and these beverages were minor contributors to overall caffeine intakes in <u>all</u> age groups."[36] The researchers found that only 4% of caffeine consumers reported consuming energy drinks, and that even teenagers (ages 13 to 17) in the 90th percentile of caffeine consumption ingest their caffeine from coffee at a far greater level than they do from energy drinks - 132.9 milligrams/day from energy drinks v. 223.7 milligrams/day from coffee.[37]

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[34] *Id.* at 2. In contrast, the Authors cite one of their own articles to suggest that 30% to 50% of adolescents and young adults consume energy drinks. Seifert, S. et al., *Health Effects of Energy Drinks on Children, Adolescents, and Young Adults*, 127 PEDIATRICS 511 (2011). The levels of consumption cited in that 2011 Seifert report do not provide any insight, however, into regular energy drink consumption. One 2007 source cited by the 2011 Seifert report found that 28% to 34% of teens and young adults reported "regularly consuming" energy drinks but did not define "regular consumption." Another source cited by the 2011 Seifert report, a German study published in 1996, referred to consumption "regularly but at a rate of < 1 can per week." The German study also found that 53% of adolescents had "tasted" energy drinks, 24% drank <1 8 oz. can per week, and 3% drank 1 to 7 such cans per week. In fact, the German study concluded that all young people in Germany knew about energy drinks but that they actually consume them moderately, and that they prefer cola drinks. Viell, B. et al., *New Caffeinated Beverages: A Pilot Survey Of Familiarity And Consumption By Adolescents In North-Rhine Westphalia And Berlin And Considerations Of Consumer Protection* [in German], 35 Z. ERNÄHRUNGSWISS 378-386 (1996). While Seifert asserts that "[m]ost children in the study consumed energy drinks in moderation but a small group consumed extreme amounts," that "small group" appears to have been comprised of just three out of 1265 survey participants who said they consumed 32 oz. of energy drinks a day, for a total of 320 mg of caffeine, which is not "extreme amounts." In sum, data referenced in the 2011 Seifert report provide little insight into current patterns of energy drink consumption in the U.S., and are far less relevant than the recent U.S. consumption figures recorded in the study commissioned by the FDA.

[35] Somogyi, *supra* note 28, at 61.

[36] Mitchell, et al., *supra* note 4.

[37] *Id.*

Finally, these data are consistent with a survey conducted in Québec, Canada, in 2011, which evaluated 10,000 teens between the ages of 12 to 17 years, and found that 93% of teens rarely or never consumed energy drinks while only 1% consumed them daily.[38] The table below (Table 3) summarizes the results from this survey.

Table 3. Frequency of Energy Drink Consumption by Quebec Teens

Frequency	Percent
Daily	**1%**
3 to 4 times/week	**1%**
1-2 times/week	**5%**
Rarely	**28%**
Never	**65%**

Similarly, a survey of more than 60,000 teens, 13 to 17 years of age in Québec found that 82.8% of teens rarely or never consumed energy drinks, and only 1.5% consumed them daily.[39]

[38] *Enquête Québécoise sur le Marketing de la Malbouffe: 10,000 Jeunes se Prononcent!* Ste- Thérèse, Québec: Réseau du sport étudiant du Québec (RSEQ) (2011). *available at* http://ll.rseq.ca/download/attachments/15958040/Rapport+d'enquete-FRA-1-page.pdf?version=1&modificationDate=132812270990 (last accessed July 9, 2013).

[39] Institut de la Statustique du Québec, *Tableau A3.2: Fréquence de consommation habituelle de certaines boissons sucrées, élèves du secondaire, Québec, 2010-2011*, in L'ENQUÊTE QUÉBÉCOISE SUR LA SANTÉ DES JEUNES DU SECONDAIRE 2010-2011: TOME 1: LE VISAGE DES JEUNES D'AUJOURD'HUI: LEUR SANTÉ PHYSIQUE ET LEURS HABITUDES DE VIE. (2012) *available at* http://www.stat.gouv.qc.ca/publications/sante/eqsjs.htm (last accessed July 9, 2013)

III. Children and Adolescents Are Not at Unique Risk for Health Effects from Energy Drinks or Caffeine Consumption

The bulk of the Arria Letter discusses the alleged "health complications associated with the consumption of energy drinks"[40] by children and adolescents, including the alleged relationship between energy drinks/caffeine and fatalities and injuries, emergency room ("ER") visits, cardiovascular complications, seizures, behaviors, and childhood obesity.

As detailed below, the bulk of the scientific literature does not provide a "robust correlation" between caffeine levels in energy drinks and adverse health effects, nor does it show that children are uniquely susceptible to caffeine effects. To the contrary, as detailed below, the weight of the published, peer-reviewed scientific and medical literature supports the conclusion that consumption of mainstream energy drinks is not associated with such health risks.

It should be noted that 19 of the 66 articles cited in the Arria Letter were written by the Letter's Authors, and that these articles form the basis for the Authors' conclusions regarding the adverse effects of energy drink consumption. Two of these studies have not been published or peer-reviewed.[41] Nevertheless, in the Letter, the Authors self-proclaim their studies as part of the "best available scientific evidence."[42] The Authors fail to discuss in the Letter any of the limitations of their studies, and, as explained in more detail below, most of the conclusions in their studies are refuted by, or in conflict with, the majority of the published peer-reviewed scientific medical literature.

In support of their conclusion that energy drinks should not be consumed by adolescents, the Authors reference statements in a review article by the American Academy of Pediatrics' ("AAP") Committee on Nutrition and the Council of Sports Medicine and Fitness, which states that "caffeine and other stimulant substances contained in energy drinks have no place in the diet of children and adolescents" and "are not appropriate for children and adolescents and should never be consumed."[43] The statement in the AAP Committee article that "caffeine and other stimulant substances contained in energy drinks have no place in

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[40] Arria Letter, at 3.

[41] *See* Seifert, S. et al., *Energy Drink Exposures In The American Association Of Poison Control Centers (AAPCC) National Poison Data System (NPDS) Database*, Paper presented at Annual Meeting of the North American Congress of Clinical Toxicology, Las Vegas, Nev. (2012); Higgins, J. and Babu, K., *Caffeine Reduces Myocardial Blood Flow During Exercise*, AM. J. MED. (in press).

[42] Arria Letter, at 1.

[43] AAP Committee on Nutrition and the Council on Sports Medicine and Fitness, *Sports Drinks and Energy Drinks for Children and Adolescents: Are They Appropriate?* 127 PEDIATRICS 1182, 1185 (2011) (hereinafter "PEDIATRICS 2011").

the diet of children and adolescents," cites to a 2007 IOM report on nutrition standards for foods in schools in support.[44] That 2007 IOM report concluded that "[a]lthough there may be some benefits associated with caffeine consumption among adults," the IOM Committee on Nutrition Standards for Foods in Schools did not support offering caffeinated beverages in schools because of the potential for effects such as physical dependency and withdrawal.[45] This recommendation related to all caffeinated beverages except those with trace amounts of naturally occurring caffeine substances. That is, this recommendation applied to coffee, tea, and caffeinated sodas, as well as energy drinks. Further, the potential effects described, such as physical dependence and withdrawal, were not unique effects on children and adolescents but were the same as those experienced by adults. Thus, this citation does not establish any unique health effects of caffeine on youth.

The second statement is not associated with a particular citation, but is reflective of an overall cautious tone, which perhaps is not inappropriate for the AAP Committee but which does not reflect evidence of a different effect of caffeine on children and adolescents. Notably, the authors of that article acknowledge that caffeine has been shown to enhance physical performance in adults by increasing aerobic endurance and strength, improving reaction time, and delaying fatigue, though they state that these effects have not been studied in children and adolescents.[46] They note a number of effects of caffeine that have been addressed herein, such as increases in blood pressure, increases in attentiveness, withdrawal effects and sleep disturbances, but these effects are neither unique to children nor documented to pose genuine health risks. The AAP Committee article states that caffeine is "known also to play a role in triggering arrhythmias," but cites for this proposition only an experimental study in dogs with a review of the literature,[47] which stands at odds with the comprehensive analyses discussed above refuting the alleged association of caffeine and arrhythmias.

The AAP Committee discourages dietary intake of caffeine by children – from all sources, not just energy drinks –"[b]ecause of the potentially harmful adverse effects and developmental effects of caffeine."[48] Such potential developmental effects are the only effects alleged to be particular to children, but the apparent source cited in support for these effects is equally cautious and speculative. That source, Nawrot, et al., noted behavioral effects of caffeine in children and adolescents comparable to those discussed below, as well as reports of

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[44] IOM, *Nutrition Standards For Foods In Schools: Leading The Way Toward Healthier Youth* (2007).
[45] *Id.* at 134.
[46] PEDIATRICS 2011, *supra* note 43, at 1185.
[47] *Id.*, citing Mehta, A. et al., *Caffeine and cardiac arrhythmias: an experimental study in dogs with review of the literature,* 52 ACTA CARDIOL. 273-283 (1997).
[48] PEDIATRICS 2011, *supra* note 43, at 1185.

beneficial effects such as improvements in attention.[49] Nawrot concludes, "Owing to these findings [of behavioral effects], as well as the fact that the nervous system in children is continually developing and the lack of available information on the longer-term effects of caffeine in this population, a cautious approach is warranted."[50] Thus, the reference to potential developmental effects is a cautionary one and not grounded in evidence of such an effect or evidence of an impact of caffeine on children that is qualitatively different from that on adults.

Finally, the authors of the AAP Committee article express concern about "large and varied amounts of caffeine" in energy drinks stating that the "total amount of caffeine contained in some cans or bottles of energy drinks can exceed 500 mg (equivalent to 14 cans of common caffeinated soft drinks)."[51] As noted in Table 2, above, reflecting approximately 95% of the energy drink category, virtually all energy drinks have less than half this amount. Thus, it appears the view of these authors may have been skewed by a misperception of the caffeine content of typical energy drinks.

Similarly, the Authors selectively quote from or interpret the study by Kaplan, Greenblatt, Ehrenberg et al.[52] The Authors cite the Kaplan study for the proposition that metabolism of caffeine at high doses (500 mg) was non-linear as compared to a 250 mg dose. While the understanding that caffeine does not follow linear kinetics as concentration changes has been documented since at least 1990,[53] this very property of non-linearity kinetics may have some impact on the self-regulating nature of caffeine (notably, this property does not directly have an impact on the known human fatal dose of caffeine of 10,000 mg to 20,000 mg). The Authors fail to note that the referenced paper cites cognitive and performance improvement at the 250 mg dose with some unpleasant effects at the higher dose. Importantly, the authors of the cited study conclude that "the unfavorable and somatic effects, as well as performance disruption, from high doses of caffeine may intrinsically limit the doses of caffeine used in the general population."[54] In reality, the Kaplan study tells us what we already know. Caffeine in low to intermediate doses produces favorable effects while higher doses tend to be perceived unfavorably and are not associated with consistent

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[49] Nawrot P. et al. *Effects of caffeine on human health,* 20 FOOD ADDIT. AND CONTAM. 1-30 (2003).
[50] *Id.* at 23.
[51] PEDIATRICS 2011, *supra* note 43, at 1185.
[52] *See* Arria Letter, at 3 (citing Kaplan, et al., *supra* note 25)).
[53] *See* Denaro, C.P. et al., *Dose-dependency of Caffeine Metabolism with Repeated Dosing,* 48 CLINICAL PHARMACOLOGY AND THERAPEUTICS 277 (1990); Cheng, W. et al., *Dose Dependent Pharmacokinetics of Caffeine in Humans: Relevance as a Test of Quantitative Liver Function,* 47 CLINICAL PHARMACOLOGY AND THERAPEUTICS 516 (1990).
[54] Kaplan, et al., *supra* note 25.

enhancement of performance which, in turn, results in self-regulation of intake. None of these latter conclusions are acknowledged by the Authors.

The Arria Letter also asserts that the accumulation of caffeine metabolites could compound the "negative effects of caffeine at high blood levels."[55] This would only be the case in situations of overt caffeine overdose (for example, purposeful caffeine tablet overdose). Caffeine is known not to accumulate in any body tissues.[56] Additionally, under normal metabolic conditions, accumulation of metabolites is not something that has been demonstrated as the three primary metabolites paraxanthine, theobromine, and theophylline are themselves metabolized and excreted via multiple pathways.[57] The Arria Letter also describes the metabolites as stimulants themselves.[58] With normal caffeine ingestion, the metabolites are present at small levels, do not accumulate, and while they may have stimulant properties similar to caffeine they are not the source of the primary stimulant effect of caffeine-containing beverages.

While selectively quoting from a limited set of articles, the Authors fail to reference any of the authoritative publications confirming the safety of energy drinks and of caffeine at levels delivered by energy drinks for adolescent as well as adult consumers. For example, energy drinks have been reviewed by European food safety authorities on three occasions spanning a decade, and have been found to be safe, including for young consumers. In a 1999 opinion, the European Commission Scientific Committee on Food ("SCF") expressed no safety concerns with consumption of energy drinks formulated with a caffeine content comparable to that in mainstream energy drinks.[59] SCF also addressed consumption of energy drinks by children and reported no safety concerns from the exposure of young people to the caffeine in these products. SCF revisited energy drinks again in 2003 and estimated mean chronic, high chronic, and acute consumption of energy drinks by regular consumers of such drinks to be 125, 350, and 750 ml/day, respectively, concluding that its 1999 opinion on the safety of caffeine and energy drinks remained unchanged.[60] In 2009, the European Food Safety Authority ("EFSA"), SCF's successor entity, evaluated new data on

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[55] Arria Letter, at 3.
[56] Carillo, *supra* note 22.
[57] Juliano et al., *supra* note 22.
[58] Arria Letter, at 3.
[59] SCF, *Opinion On Caffeine, Taurine, And D-Glucurono-γ-Lactone As Constituents Of So-Called "Energy" Drinks* (1999), *available at* http://ec.europa.eu/food/fs/sc/scf/out22_en.html (last accessed May 30, 2013).
[60] SCF, *Opinion of the Scientific Committee on Food on Additional Information on "Energy" Drinks*, at 2-3, 12 (2003), *available at* http://ec.europa.eu/food/fs/sc/scf/out169_en.pdf (last accessed July 9, 2013).

taurine and glucuronolactone in caffeinated energy drinks and did not identify any safety concerns.[61]

Contrary to the Authors' assertions, the vast body of scientific and medical literature has conclusively established the safety of caffeine. Regulatory authorities in the U.S., Canada, Australia/New Zealand and Europe have reviewed this literature and have concluded that the level of caffeine in mainstream energy drinks is safe. Caffeine is one of the most widely studied ingredients in the food supply and has been the subject of clinical and other research for decades. Consequently, there are hundreds of peer-reviewed, published studies confirming the safety, function, and pharmacology of caffeine. Included below are examples of the body of evidence on the safety of caffeine as determined by scientists and governmental or other authoritative bodies.

A. Caffeine Effects are a Function of Body Weight, Not Age

The substantial body of scientific and medical literature demonstrates that: (1) children and adolescents experience no particular or unique safety effects from caffeine; (2) dose response is always a function of body weight (mg/kg), not age; and (3) any behavioral or other effects adolescents may experience from caffeine are the same as those experienced by adults.[62] For these reasons, many of the analyses in the scientific literature refer to safe levels of caffeine in terms of mg/kg body weight per day, either in addition to, or instead of, an absolute amount.

Perhaps most notably, FDA has approved caffeine as safe for use in over-the-counter ("OTC") drug products at levels up to 200 mg caffeine every 3 to 4 hours for consumers aged 12 and older.[63] The agency made no distinction between adolescents and adults and concluded that these acute and repeated caffeine consumption levels were safe for both age groups. These levels of caffeine are comparable to, or higher than, those found in mainstream energy drinks. FDA's conclusions in this monograph (which went through a 1975 proposed rule, 1978 tentative final order, and 1988 final rule, all published in the *Federal Register* allowing for public comment) establish that caffeine at the levels present in mainstream energy drinks are safe for adolescents as well as adults.

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[61] EFSA, *The Use Of Taurine And D-Glucurono-γ-lactone As Constituents Of The So-Called "Energy" Drinks*, 935 THE EFSA JOURNAL 1, 23 (2009).

[62] Leviton, A., *Behavioral Correlates Of Caffeine Consumption By Children*, 31 CLIN. PEDIATR. 742, 743, (1992). *See also* Arnaud, *supra* note 21, at 35-36.

[63] *See* 21 C.F.R. § 340.50. FDA's approved OTC monograph for stimulant drug products includes the following directions for use: "Adults and children 12 years of age and over: Oral dosage is 100 to 200 milligrams not more often than every 3 to 4 hours." *Id.* at § 350.50(d). FDA noted that caffeine from other sources should be taken into account. *Id.* at § 350.50(c)(1).

The following examples from the published, peer-reviewed scientific and medical literature also demonstrate that caffeine metabolism and caffeine effects are dependent on body weight, not age.

As long as two decades ago, Dr. Alan Leviton, of Harvard Medical School and Children's Hospital in Boston, Massachusetts, presented a paper at the Annual Meeting of the American Academy of Pediatrics ("AAP") which documented that after infancy, neither caffeine's absorption, its excretion, nor its half-life are age-dependent and that "[c]affeine, at levels consumed by most children, does not appear to produce adverse effects."[64]

Articles reviewing the relative caffeine amounts in particular bodily fluids or tissues reflected no appreciable differences in children's and adults' caffeine pharmacokinetics.[65] For example, "[a] mean distribution volume of 0.7 L/kg (0.5–0.8 L/kg) was found in newborn infants, adult subjects, or aged subjects. The pharmacokinetics of caffeine in healthy young men aged 20.5 ± 2.0 years and in healthy elderly men aged 71.2 ± 3.9 years showed that Tmax, Cmax, and caffeine bioavailability were essentially identical."[66] Therefore, as in adults, the amounts of caffeine that distribute to a child's or adolescent's tissues appear to be a result of the individual's caffeine intake in relation to his or her weight, rather than of any differences in the rate and extent of children's and adults' caffeine metabolism.

The foregoing discussion confirms there are no scientific grounds for safety concerns about consumption of caffeine or energy drinks simply based upon the consumer's chronological age, as caffeine effects are a function of body weight. For example, the term "teenagers" captures 13- to 19-year-olds, yet a 13-year-old typically weighs considerably less than a 19-year-old. Recent data (2007-2010) reported by the Centers for Disease Control and Prevention (CDC) reveal that for adolescent males, mean weight ranges from 59.2 kg for 13-year-olds to 79.5 kg for 19-year-olds.[67] For adolescent females, mean weight ranges from 56.8 kg for 13-year-olds to 68.0 kg for 19-year-olds.[68] These data reveal that even the youngest teenagers are, on average, not particularly small.

The Authors also make the argument that the safety of caffeine should take into consideration "individuals having varying sensitivities to caffeine" rather than on "healthy"

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[64] Leviton, *supra* note 62 at 743, 748;*see also* Arnaud *supra* note 21 at 35-36.
[65] Arnaud, *supra* note21, at 36-37.
[66] *Id.* at 45.
[67] Centers for Disease Control and Prevention, *Anthropometric Reference Data For Children And Adults: United States, 2007-2010*, 11 VITAL HEALTH STAT. 1, 7-9 (2012).
[68] *Id.*

individuals.[69] Mainstream energy drinks are prominently labeled as not recommended for people sensitive to caffeine. This is consistent with the FDA regulatory approach to food ingredients for sensitive subpopulations, which requires disclosure of ingredients rather than limitations on their use simply because a small portion of the population may have a special sensitivity. For example, peanuts and eggs are not deemed harmful even though allergic consumers may have serious or even life-threatening reactions to these ingredients in a food. Rather, FDA requires that the presence of these ingredients be declared on the product label, even if they are only used in a flavoring or otherwise at very low levels.[70] The agency takes the same approach to added sulfiting agents, which also may cause serious harm to those with sulfite sensitivities. These ingredients are not deemed unsafe but rather must be declared where present over 10 ppm, even if used only as incidental additives.[71] Thus, the safety of caffeine is not undermined by the fact that some consumers may be differentially affected by the ingredient. Rather, such sensitivities are managed through labeling, which enables caffeine-sensitive individuals to manage their caffeine consumption. American Beverage Association member companies voluntarily declare the caffeine content from all sources on the label of their energy drinks.

B. Alleged Fatalities and Injuries

The Authors assert, as a preface to a discussion of alleged fatalities and injuries associated with energy drinks, that the absence of a systematic system to ascertain the prevalence of possible adverse events related to energy drinks properly leads to the conclusion that the available data understate the actual occurrence of adverse events. It is just as plausible that the existing data overstate the occurrence of adverse events reasonably attributed to energy drinks. When one considers the fact that nearly 90% of North Americans consume caffeine with regularity,[72] the notion that a small number of deaths in people consuming caffeine-containing beverages must have been caused by those beverages is non-defensible on its face. The overwhelming body of knowledge regarding caffeine clearly demonstrates that its use is at best a healthy activity, and at worst neutral. Additionally, specific to energy drinks, there are no data nor is there a plausible suggested mechanism by which any of the commonly utilized additives and additional ingredients would cause any form of toxicity.[73]

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[69] *See* Arria Letter, at 3 (stating that caffeine safety standards should not be based on "healthy" individuals because doing so "does not take into consideration that individuals have varying sensitivities to caffeine.").
[70] *See* 21 U.S.C. § 343(w).
[71] *See* 21 C.F.R. § 101.100(a)(4).
[72] Mitchell, *supra* note 4.
[73] The most current reviews of taurine and glucoronlactone have concluded that they are safe in the amounts commonly encountered in energy drinks.

The relatively small number of adverse events reported to FDA in connection with energy drinks marketed as supplements do not establish any causal relationship (as FDA acknowledges). Notably, with regard to reports submitted to the FDA through its voluntary Adverse Event Reporting System ("CAERS"), the data from these reports cannot be used to calculate the actual incidence of an adverse event or any causal relationships between the reports and the products due to stated limitations. FDA acknowledges that individual adverse event reports about a particular product and the total number of adverse event reports for that product in CAERS only reflect information as reported, and do not represent any conclusion by FDA about whether the product actually caused the adverse events. CAERS records what the person/entity submitting the report believes to be the cause of the adverse event. Reports to FDA do not necessarily include all relevant data, such as whether an individual also suffered from other medical conditions (such as cardiac disease) or took other supplements or medication at the same time. Reports often do not contain enough detail to properly evaluate an event and may not include accurate or complete contact information for FDA to seek further information about the event, or complainants may choose not to participate in the follow-up investigation. Additionally, duplicate reports may exist in CAERS for the same adverse event because multiple people (such as an injured consumer and a health care provider) may have submitted reports.

In support of their conclusion that energy drinks are the cause of fatalities and injuries, especially in children, the Authors reference several adverse event reports ("AERs") submitted to FDA that cite energy drinks.[74] FDA has repeatedly emphasized that AERs associated with a consumer product are not reports by FDA and do not establish any cause or link between a product and the reported event.[75] In a recent interview, you stressed that AERs related to energy drinks do not suggest a causal effect: "Frankly, many of the reports, when examined with a real look at the science and the potential for a causal relationship, are not very compelling."[76] FDA has long been aware of the AERs for energy drinks and has stated that the available evidence reveals no new previously unknown risks associated with caffeine consumption.[77] In addition, the Authors concede that FDA did not disclose the ages

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[74] Arria Letter, at 3-4.

[75] FDA, *Energy "Drinks" And Supplements: Investigations Of Adverse Event Reports* (Nov. 16, 2012), *available at* http://www.fda.gov/Food/NewsEvents/ucm328536.htm (last accessed May 30, 2013). In a statement that accompanied FDA's November 16, 2012 release of AERs pertaining to energy drinks, FDA explained, "[t]he existence of an adverse event report does not necessarily mean that the product identified in the report actually caused the adverse event. FDA assesses the relationship, if any, between a product or ingredient and the reported adverse event."

[76] Choi, C. and Jalonick, M., *Monster Hits Back at Lawsuit Over Teenager's Death*, YAHOO! NEWS (Mar. 4, 2013), *available at* http://news.yahoo.com/monster-hits-back-lawsuit-over-160836281.html (last accessed May 30, 2013).

[77] FDA August 2012 letter, *supra* note 29, at 2-3.

of the consumers identified in the AERs allegedly associated with energy drinks, so these AERs provide no support for the Authors' argument that energy drinks are particularly harmful to young consumers.

The Authors identify the case of 14-year old Anais Fournier who died of a cardiac arrhythmia to try and establish a link between energy drinks and the fatality.[78] According to published news reports, Ms. Fournier's medical records establish she had a known, pre-existing heart condition, for which she was taking medication. It is alleged that Ms. Fournier consumed two 24-ounce cans of Monster Energy drink 24 hours apart. She drank the first can without incident. According to the body of scientific and medical literature on normal caffeine metabolism, the caffeine from the first beverage would have completely dissipated by the time she drank the second beverage 24 hours later. While the death of Ms. Fournier is a tragedy, there is simply no scientific or medical basis upon which to conclude that the levels of caffeine in mainstream energy drinks are unsafe when consumed in accordance with the labels of those products.

The Authors also reference an unpublished paper, co-authored by one of the Authors, in support of the conclusion that there has been a greater incidence of accidental ingestion of caffeine from energy drinks than other forms of caffeine in children under 6 years of age.[79] All mainstream energy drinks bear a label statement "not intended/recommended for children." The accidental ingestion of substances to which children should not be exposed provides no basis for concluding that the substances themselves are unsafe for their intended use.

C. Emergency Room Visits

The Authors cite to the oft-mischaracterized report on so-called energy drink-related ER visits (the Drug Abuse Warning Network ("DAWN") report)[80] in an attempt to establish an increase in energy drink-related ER visits. The DAWN report, however, has many limitations, and therefore does not establish a causal relationship between energy drink consumption and ER visits.

For example, the report did not track the energy drink brands consumed or provide estimates of amounts of caffeine consumption. The report is based on ER visits involving use of drugs, where drugs are defined as alcohol, cocaine, heroin, marijuana, pharmaceuticals,

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[78] Arria Letter, at 3-4.
[79] *Id.* at 4.
[80] *See* Substance and Abuse Mental Health. Servs. Admin., Ctr. for Behavioral Health. Statistics and Quality, *The DAWN Report Update on Emergency Department Visits Involving Energy Drinks* (Jan 10, 2013).

nutritional supplements, vitamins, and caffeine products, though DAWN does not track ER visits related to caffeine consumption from coffee. In more than half of the visits in which energy drinks were reportedly consumed by 18- to 25-year olds, the subjects also reported using alcohol and other drugs (and this figure is likely an underestimate given that alcohol and drug use was self-reported and thus likely underreported). The DAWN report did not provide patient outcomes. Where energy drink consumption was reported, the report did not include the amount of energy drink consumed or the amount of other sources of caffeine consumed. The DAWN report, therefore, does not contain sufficient information to determine the nature of patients' complaints, the amount of caffeine consumed from all sources (including coffee, sodas, etc.), or whether there was any causal connection between the complaints and the consumption of energy drinks. Moreover, the report concludes that while ER visits doubled, "visits among adolescents aged 12 - 17 remained stable."[81]

Moreover, the doubling of energy drink-related emergency room visits reported in the DAWN report must be viewed in context. The 20,000 reported ER visits is a tiny percentage of the total number of ER visits in the time period covered by the DAWN Report (an estimated 136 million). Most of the ER visits did not require further treatment because they were not serious. Finally, during the period covered by the DAWN Report, there were greater increases in ER visits for adverse events related to topical hydrogen peroxide and oral nutritional supplements than for energy drinks.[82]

In contrast to the implications of the DAWN report, the International Society of Sports Nutrition's ("ISSN's") 2013 position statement on energy drinks, which is based on a thorough review of the scientific literature and 224 medical and clinical studies, states, "the rate of adverse events [associated with energy drinks] appears low in the population of consumers" and the current evidence "suggests that consumption of energy drinks and energy shots are safe in healthy populations and similar to ingesting other foods and beverages containing caffeine."[83]

D. Cardiovascular Effects

The Authors discuss several adverse cardiac effects in children associated with "consumption of highly caffeinated energy drinks," such as elevated blood pressure, altered heart rates, and severe cardiac events, yet none of the studies they cite to that reportedly demonstrate

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[81] *Id.* at 3.

[82] Pinney Associates Report Prepared for the American Beverage Association, *Emergency Department Visits Involving Energy Drinks and Limitations of the Drug Abuse Warning Network (DAWN),* at 5 (Jul. 25, 2013) (attached).

[83] Campbell, B. et al., *International Society of Sports Nutrition Position Stand: Energy Drinks*, 10 J. INT. SOC. SPORTS NUTR. 1, 10 (2013).

adverse cardiac effects of energy drinks were conducted in children. Rather, the bulk of the articles they cite studied caffeine consumption in adults (including young adults) or adolescents. In addition, the Authors concede that adverse cardiac effects related to caffeine are more significant for "those with underlying cardiovascular diseases." Significantly, the Authors do not define the amount of caffeine that makes a "highly caffeinated" energy drink, so it is unclear what level of caffeine would result in the cardiac effects identified by the Authors. Because mainstream energy drinks are not "highly caffeinated" as explained above, the conclusions of the Authors regarding high levels of caffeine and cardiac effects do not apply to them.

It should be noted that in support of their conclusions of caffeine-related adverse cardiac effects, the Authors cite only eight studies, five of which were authored by the Authors, including one paper that is not a published peer-reviewed article. This latter unpublished paper is used by the Authors in support of their conclusion that consumption of energy drinks before or during exercise "might be linked" to an increased risk for myocardial ischemia. The Authors do not provide details of the study, including the type of study or the type of energy drink consumed. Given the absence of study information and the paper's lack of publication, lack of peer review, and its feeble conclusion that caffeine consumption "might be linked" to cardiac effects, the paper is not sufficiently rigorous to support an association between energy drinks and adverse cardiac effects.

In contrast, several substantial reviews of the scientific literature on caffeine and cardiac effects conducted by highly reputable governmental and other authoritative organizations find no scientifically valid relationship between consumption of up to 500 to 600 mg caffeine per day and heart disease or cardiac arrhythmias, nor does the evidence document significant or long-term effects on blood pressure. Literature reviews conducted by scientific experts reach the same conclusion. The following are a sample of published peer-reviewed scientific studies that refute the few studies cited by the Authors, and establish that the bulk of the published scientific literature confirms that caffeine consumption at levels similar to those in mainstream energy drinks does not result in adverse cardiac effects.

In perhaps the best clinical study of its kind, the Framingham Study (a landmark longitudinal study initiated in 1948 to identify cardiovascular risk factors) examined whether there was any relationship between various dietary factors, including caffeine, and the incidence of atrial fibrillation, the most commonly encountered cardiac arrhythmia in clinical practice.[84] The Framingham Study included 4526 individuals who had undergone 9640 clinical examinations and were prospectively followed for four years. A multivariate analysis was

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[84] Shen, J. *et al.*, *Dietary Factors and Incident Atrial Fibrillation: the Framingham Heart Study*, 93 AM. J. CLIN. NUTRITION 261, 261 (2011).

performed to account for nine important confounding factors including age, gender, and body-mass index. Individuals were divided into four quartiles based on daily caffeine intake. Compared to individuals with the lowest daily caffeine intake (median 23 mg/day, range 0 to 82 mg/day), the individuals with the highest daily caffeine intake (median 452 mg/day, range 366 to 1203 mg/day) were at no higher risk for atrial fibrillation (hazard ratio: 0.98, 95% confidence interval: 0.70 – 1.39).[85] The authors concluded that consumption of caffeine "was not significantly associated with [atrial fibrillation] risk.[86]

- The 2001 IOM study of caffeine for the military concluded: "The preponderance of evidence indicates that the use of caffeine by the military would not place personnel at increased risk of cardiovascular disease."[87] That report stated further that, "[d]espite numerous studies attempting to show a relationship between caffeine and serum lipoproteins, blood pressure, cardiac arrhythmias, and risk of coronary heart disease, results have failed to show a consistent adverse effect of ingestion of moderate amounts of caffeine."[88]

- The Organisation for Economic Co-operation and Development ("OECD") reported in 2002: "Though consumption of caffeine (eight cups of regular coffee corresponding to 500 mg caffeine per day) may exhibit acute increases in blood pressure, the long-term effects appear to be minimal. After one to four days of regular consumption a tolerance develops, with blood pressure returning to previous levels."[89]

- The 2002 OECD report also concludes that although studies before the mid-1970s suggested an association between consumption of more than six cups of coffee and coronary heart disease, retrospective and prospective studies conducted since then have consistently failed to demonstrate an association between caffeine and heart disease.[90] It also cites repeated dose toxicity rodent studies of caffeine that showed the average No Observable Adverse Effect Levels

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[85] *Id.* at 264.
[86] *Id.* at 261, 265.
[87] *IOM Report on Caffeine*, *supra* note 22, at 59.
[88] *Id.* at 51.
[89] United Nations Environment Programme, Organisation for Economic Co-Operation and Development, *Screening Information Dataset: Cafeine, available at* http://www.chem.unep.ch/irptc/sids/OECDSIDS/CAFEINE.pdf (last accessed July 11, 2013).
[90] *Id.* at 15.

("NOAELs") were 160 mg for each kilogram of body weight of the rat per day, and 170 mg/kg bw/day (highest dose tested) in mice.[91]

- A thorough review of the scientific literature on caffeine consumption examining the supposed causal connection between caffeine and heart disease concludes that the body of relevant scientific literature fails to show that the consumption of caffeine in moderate quantities results in an increased risk of coronary heart disease or arrhythmias. In particular, the review notes that more recent and better-conducted research undermines earlier erroneous assumptions that caffeine consumption has a significant, long-term impact on cardiovascular health.[92]

- A 2011 review concludes that human studies examining the effect of caffeine on cardiovascular endpoints are consistent in finding minimal to no effect of caffeine on coronary artery disease or stroke, and that large human studies generally reveal no association between caffeine and arrhythmias.[93]

- A 2010 article on a prospective study of caffeine consumption by women concluded that increased consumption was not associated with an increased risk of atrial fibrillation.[94] In follow-up observations, participants in the study comprising the highest quintile of caffeine consumption were found to have a similar risk of developing atrial fibrillation as their counterparts in the lowest quintile of caffeine consumption.[95] The researchers discovered that women in the third quintile of caffeine consumption were found to have a lower risk of incident atrial fibrillation, suggesting that the consumption of small to moderate amounts of caffeine may even be beneficial, as it may have a "small but significant protective effect on the occurrence of [atrial fibrillation]."[96]

- A 2011 review of eleven prospective studies was performed to examine the effect of caffeine on arrhythmia. The Danish Diet, Cancer and Health study (47,949 subjects followed for an average of 5.7 years), the Women's Health Study (33,638

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[91] *Id.* at 24.
[92] Chou, T. and Benowitz, N., *Caffeine And Coffee: Effects On Health And Cardiovascular Disease*, 109 COMP. BIOCHEM. PHYSIOL. 173, 185-186 (1994).
[93] Pelchovitz, D. and Goldberger, J., *Caffeine And Cardiac Arrhythmias: A Review Of The Evidence*, 124 AM. J. MED. 284, 285 (2011).
[94] Conen, D. et al., *Caffeine Consumption And Incident Atrial Fibrillation In Women*, 92 AM. J. CLIN. NUTR. 509, 512 (2010).
[95] *Id.* at 512-13.
[96] *Id.* at 513.

women followed for an average of 14.4 years), and some smaller-scale studies in healthy men or men with heart disease or known arrhythmias showed no effect of up to 450 mg/day caffeine on heart rhythm. The review concludes that in most patients (even those with known or suspected arrhythmia), moderate doses of caffeine are well tolerated.[97]

- A meta-analysis of eleven prospective, longitudinal cohort studies shows no increased risk of coronary heart disease associated with consumption of < 6 cups of coffee per day.[98] Based on an average of 133 mg caffeine per cup of coffee, six cups of coffee would result in a dose of 798 mg/day caffeine (approximately 11.4 mg/kg bw/day).

- A prospective study involving 85,747 women over a time course of ten years indicates no association between consumption of 4-5 or > 6 cups of coffee per day (approximately 532-665 mg or 798 mg/day caffeine, respectively) and risk of coronary heart disease in women.[99]

- Recent review articles show that although some case control (retrospective) studies have shown increased risk of myocardial infarction in individuals consuming > 4 cups of coffee/day, the more reliable prospective studies with a follow-up period of 3-44 years have shown that consumption of > 4 cups of coffee/day (approximately 532 mg caffeine) is not associated with increased risk of acute myocardial events and cardiovascular mortality.[100]

E. Seizures

In support of their conclusion that seizures have been "attributed to energy drink consumption," the Authors cite a handful of individual case reports.[101] The Authors do not cite any human clinical studies or animal studies. The case reports cited by the Authors have significant limitations and do not establish any causal link between seizures and consumption of energy drinks. For example, most of the patients had a past history of

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[97] Pelchovitz et al., *supra* note 93.
[98] Myers, M. and Basinski, A., *Coffee And Coronary Heart Disease*, 152 ARCH INTERN. MED. 1767 (1992).
[99] Willett, W. et al., *Coffee Consumption And Coronary Heart Disease in Women: A Ten-Year Follow-Up*, 275 JAMA 458 (1996).
[100] Riksen, N., et al., *The Cardiovascular Effects of Methylxanthines*, 200 HANDB. EXP. PHARMACOL. 413 (2011); Sofi, F. et al., *Coffee Consumption And Risk Of Coronary Heart Disease: A Meta-Analysis*, 17 NUTR. METAB. CARDIOVAS. 209 (2007).
[101] *See* Arria Letter, at 5.

seizures, had consumed other high caffeine sources such as diet pills, had a past history of stroke, or had neurological or other disorders. [102]

In contrast to the anecdotal reports cited by the Authors, the largest and best study on this subject found that moderate-to-high intake of caffeine was not associated with risk of seizures or epilepsy.[103] For its analysis of caffeine, the Nurses' Health Study followed 105,941 study participants for a total of 1,440,850 person-years of follow up. A multivariate analysis was performed to take into account important potential confounding factors. Compared to individuals with a long-term average caffeine intake of < 200 mg/day, individuals with a long-term average caffeine intake of ≥ 400 mg/day did not have a greater risk of seizures or epilepsy (seizure relative risk: 0.77, 95% confidence interval: 0.41-1.47; epilepsy relative risk: 0.97, 95% confidence interval: 0.57-1.67). In addition, there was no linear relationship between increasing caffeine intake and seizure or epilepsy risk (seizure relative risk: 0.95, 95% confidence interval: 0.80-1.11, p = 0.5; epilepsy relative risk: 0.97, 95% confidence interval: 0.85-1.11, p = 0.6).[104]

F. Childhood Obesity

The Authors state that energy drinks "have been shown to contribute to youth obesity due to their high calorie and sugar content[,]" and they cite to an AAP report to conclude that "the consumption of excessive carbohydrate calories from energy drinks increases risk for pediatric overweight."[105] It is common knowledge that "excessive" consumption of calories from any food or beverage without concomitant energy expenditure increases the risk of obesity for any person and that "excessive" consumption of sugary foods should be avoided. Some energy drinks have no sugar or are low in sugar. There are no published data that specifically associate energy drink consumption and obesity.

G. Behavioral Effects

The Authors conclude that caffeine consumption is associated with several negative behavioral effects in "youth."[106] The science, however, establishes that caffeine effects on

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[102] *See, e.g.,* Iyadurai, S. and Chung, S., *New-Onset Seizures In Adults: Possible Association With Consumption Of Popular Energy Drinks*, 10 EPILEPSY BEHAV. 504-508 (2007); Trabulo, D.et al., *Caffeinated Energy Drink Intoxication*, 28 BMJ CASE REP. 712-714 (2011).

[103] Dworetzky, B. et al., *A Prospective Study of Smoking, Caffeine, and Alcohol as Risk Factors for Seizures or Epilepsy in Young Adult Women: Data from the Nurses' Health Study II*, 51 EPILEPSIA 198 (2009).

[104] *Id.*

[105] Arria Letter, at 5.

[106] Arria Letter, at 5.

behavior are dependent upon the amount of caffeine a person normally consumes, and are not unique for young consumers. This body of evidence includes the work of Judith L. Rapoport, M.D., Chief, Child Psychiatry Branch, and colleagues at the National Institute of Mental Health, National Institutes of Health. As early as 1984, their review of the literature led to the conclusion that "[t]here is no clear behavioral toxicity from caffeine in normal children. Those self-selecting high caffeine diets generally do not seem to get negative effects."[107] An earlier study by Rapoport even found no negative outcomes when 19 children were given 3 mg/kg or 10 mg/kg caffeine (500 mg for a 110-pound child).[108] Rapoport and another NIH colleague reviewed the literature again in 2002, and described the results of seven studies performed with hyperactive children and eight with normal children.[109] The authors concluded that "[t]he effects of caffeine in children seem to be modest and generally innocuous."[110] Notably, the authors reported that the administration to children habituated to caffeine of 10 mg/kg bw/day produced no significant behavioral effects.[111] The review concludes that in children (as with adults), the amount of caffeine a person normally consumes is very important in determining their behavioral response to caffeine. The behavioral effects that were observed in children not habituated to caffeine were the same as those observed in adults, thereby indicating no unique effects on children. Similar conclusions have been reached by medical researchers studying the effects of caffeine on a wide range of children.[112]

H. Combining Energy Drinks with Alcohol

The authors state that "energy drinks also pose unique dangers when combined with alcohol."[113] FDA has previously acted to remove from the market alcoholic beverages that

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[107] Rapoport, J. and Kruesi, M., *Behavior And Nutrition: A Mini Review*, 51 J. DENT. CHILD. 451 (1984); *see also* Rapoport, J. et al., *Behavioral Effects Of Caffeine In Children*, 41 ARCH. GEN. PSYCHIATRY 1073 (1984); Zahn, T. and Rapoport, J., *Acute Autonomic Nervous System Effects Of Caffeine In Prepubertal Boys*, 91 PSYCHOPHARMACOLOGY (BERL.) 40 (1987).

[108] Rapoport, J. et al., *Behavioral And Autonomic Effects Of Caffeine In Normal Boys*, 3 DEV. PHARMACOL. THER. 74 (1981).

[109] Castellanos, F. and Rapoport, J., *Effects Of Caffeine On Development And Behavior In Infancy And Childhood: A Review Of The Published Literature*, 40 FOOD CHEM. TOXICOL. 1235 (2002).

[110] *Id.* at 1242.

[111] *Id.* at 1241.

[112] *See, e.g.*, Bernstein, G. et al., *Caffeine Effects On Learning, Performance, And Anxiety In Normal School-Age Children*, 33 J. AM. ACAD. CHILD ADOLESC. PSYCHIATRY 407 (1994); Barr, H. and Streissguth, A., *Caffeine Use During Pregnancy And Child Outcome: A 7-Year Prospective Study*, 13 NEUROTOXICOL. TERATOL. 441 (1991); Baer, R., *Effects Of Caffeine On Classroom Behavior, Sustained Attention, And A Memory Task In Preschool Children*, 20 J. APPL. BEHAV. ANAL. 225 (1987); Elkins, R., et al., *Acute Effects Of Caffeine In Normal Prepubertal Boys*, 138 AM. J. PSYCHIATRY 178 (1981).

[113] Arria Letter, at 5.

contained caffeine on the grounds that the use of caffeine in an alcoholic beverage has not been shown to be generally recognized as safe.[114] The fact that some users of a product such as an energy drink may choose to combine it with alcohol is not pertinent to consideration of the legal status of the product or the GRAS status of caffeine. Alcohol is routinely combined by consumers with many liquid refreshments without their regulatory status being questioned. Energy drinks should be treated similarly.[115]

IV. Conclusion

The totality of the scientific data and information on caffeine in beverages, including the long history of safe use worldwide, demonstrates fully that caffeine at the levels found in mainstream energy drinks is safe under the intended conditions of use. Those extensive data amply support the conclusion that caffeine is generally recognized as safe when used in mainstream energy drinks.

The scientific and medical literature clearly refutes the Authors' ultimate conclusion 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 plainly and thoroughly set forth above, scientists, medical professionals, and regulators generally agree that caffeine effects are a function of body weight, not age, and that caffeine levels such as those delivered by most energy drinks present no safety issues for children or adults alike. The Arria Letter is founded on speculation that is simply not borne out by the data.

FDA has made clear, and courts have confirmed, that the consensus of expert opinion needed to establish GRAS status does not require unanimity among qualified experts,[116] and

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[114] FDA Warning Letter to Phusion Projects, Inc. (November 17, 2010), *available at* http://www.fda.gov/iceci/enforcementactions/warningletters/ucm234023.htm (last accessed July 12, 2013).

[115] The Authors assert without qualification that caffeine and alcoholic beverages are harmful. The most comprehensive assessment of this issue was undertaken by the United Kingdom Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment, which was asked by the UK Food Standards Agency "to comment on concerns that caffeine in energy drinks may interact with alcohol in causing adverse behavioural or toxic effects." The Committee concluded that "the current balance of evidence does not support a harmful toxicological or behavioural interaction between caffeine and alcohol." The Committee did acknowledge that its conclusion should be reviewed if "important new evidence emerges." UK Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment, *COT Statement on the Interaction of Caffeine and Alcohol and their Combined Effects on Health and Behaviour* (December 2012), *available at* http://cot.food.gov.uk/pdfs/cotstatementcaffalco201204.pdf (last accessed July 12, 2013).

[116] FDA Proposed Rule, *Substances Generally Recognized as Safe*, 62 Fed. Reg. 18938, 18939 (April 17, 1997) ("Unanimity among experts regarding safety of a substance is not required.") (citing *United*

that "mere conflict among experts is not enough to preclude a finding of general recognition."[117] The conclusions of the Authors and selective citations in their Letter–including frequent citations to their own, sometimes unpublished, work–do not undermine the GRAS status of caffeine for use in mainstream energy drinks. Rather, the weight of the scientific and medical literature, including that by governmental and other authoritative bodies, establishes the safety and GRAS status of caffeine as used in mainstream energy drinks.

Sincerely yours,

Richard H. Adamson

Richard H. Adamson, Ph.D.
For the American Beverage Association

cc: Michael R. Taylor
Michael M. Landa

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*States v. Articles of Drug * * * 5,906 boxes*, 745 F.2d 105, 119 n. 22 (1st Cir. 1984); *United States v. An Article of Drug * * * 4,680 Pails*, 725 F.2d 976, 990 (5th Cir. 1984); United States v. Articles of Food and Drug * * * *Coli-Trol 80*, 518 F.2d 743, 745 (5th Cir. 1975); *Promise Toothpaste*, 624 F.Supp. 776, 782 (N.D. Ill. 1985)).

[117] 62 Fed. Reg. at 18939 (citing *Coli-Trol 80*, *supra* note 116, at 745 (5th Cir. 1975)).