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Energy Drinks: An Assessment of the Potential Health Risks in the Canadian Context

Regular Paper

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Abstract The purpose of this document is to develop a health risk assessment on energy drinks, based on health hazard and exposure assessments when consumed as a food in Canada. In this document, a typical energy drink is exemplified by the product known as Red Bull™, where a single can serving of 250 ml contains 80 mg of caffeine, 1000 mg of taurine, 600 mg of glucuronolactone and several B vitamins.

Health hazard data on energy drinks were found to be limited and therefore the hazard assessment was based on individual ingredients. Caffeine was identified as the ingredient with the greatest potential for intakes of possible health concern. On this basis, excess consumption of energy drinks would be expected to result in health consequences similar to those from excess exposure to caffeine. The more mild and transient health consequences could include anxiety, headache and insomnia and these health consequences can become chronic conditions. More severe health consequences may include irregular heartbeat, heart attack and, very rarely, death. Currently, the potential for taurine and glucuronolactone to interact with caffeine is unknown and therefore they may or may not exacerbate the effects of caffeine. In addition, the health effects of excessive intake of taurine and glucuronolactone are also unknown. The health hazard assessment concluded that the general adult population could safely consume 2 servings of a typical energy drink per day, with no health consequences. This conclusion was based on the safety of the non-caffeine ingredients of energy drinks at this level of consumption, and the fact that caffeine from other dietary sources in addition to that in 2 servings of energy drinks would not pose a health hazard to the general adult population. The consumption of energy drinks by subpopulations, such as children, adolescents, and pregnant women, should be limited to their respective recommended maximum daily intakes of caffeine, as recommended by Health Canada.

Using exposure modelling, the potential health risk posed by energy drink consumption was examined. However, no Canadian intake data for energy drinks were available. Therefore, for the purpose of modelling intake, it was assumed that energy drinks are consumed in a manner similar to that of caffeinated carbonated soft drinks. In the worst case modelling exposure scenario, energy drinks were substituted for caffeinated carbonated soft drinks on a volume basis.

The energy drink caffeine concentration was set to 320 ppm (80 mg of caffeine/250 ml serving) for modelling purposes. In the most conservative scenario, all caffeinated carbonated soft drinks were replaced by a typical energy drink for consumers who drink these beverages (eaters only). The results of this conservative estimate showed that slightly less than 30% of male and female adults, about 15% of pregnant woman and more than 50% of the children and adolescents, amongst consumers who drank caffeinated carbonated soft drinks, were above Health Canada's recommended maximum daily caffeine intake.

This extreme scenario only applies to that subset of the population that consumes caffeinated carbonated soft drinks, which does not exceed 8% of young children (1-8 years old), 22% of older children (9-14 years old), 32% of adolescents, 20% of the adult population and 13% of pregnant females.

In critically reviewing the outcomes of this exposure modelling, it appeared that the corresponding health concerns for children and adults would be limited to remote, based on this scenario, in view of the parental control that should exist and would limit access of these products to children, as well as the ability of adults and pregnant women to monitor their own caffeine intake.

This hypothetical scenario and its outcomes could not be as easily excluded for adolescents, given that energy drinks tend to be marketed to this subset of the population, which is less likely to adhere to consumption recommendations than adults. The existence of larger volume containers (e.g., 710 ml) increases the likelihood of exceeding caffeine recommended intakes in one consumption setting.

Specific risk management measures to address potentially high caffeine levels in larger volume energy drink products would therefore be desirable.

It is acknowledged that various data gaps would need to be addressed to improve the exposure assessment and the overall risk characterization. In particular, data related to the evolving consumption patterns of these products by the various subsets of the population, in Canada, needs to be gathered.

Health Canada's proposed risk management approach for energy drinks, announced in October 2011 and updated in 2012, limits the concentration and total amount of caffeine in these products and requires that caffeine and nutrition information be displayed on product labels. These measures support the mitigation of risks related to overconsumption of caffeine from this type of product that are within the possible areas of intervention available to a federal food regulator. A more concerted approach (e.g., education, awareness and regulation) and more research would be needed to ascertain the effectiveness of the various measures taken by regulators and other stakeholders.

Keywords Energy drink, Caffeine, Taurine, Glucuronolactone, Inositol, B vitamin

Disclaimer:

This document was developed as a review of the scientific information available pertaining to the safety of ingredients that may be part of the composition of the beverages known as Caffeinated Energy Drinks (Energy Drinks). The document was developed during a period spanning from 2010 to late 2011. A number of references and new studies have been made available since then and are not referenced in the present document. An update of the present Health Risk Assessment is envisaged in 2014-15, upon review of information currently being collected by Health Canada's Food Directorate since the regulatory decision made in October 2011, to regulate Energy Drinks as beverages (i.e. food) as opposed to their former classification as Natural Health Products.

1. Introduction

1.1 Purpose

The purpose of this document is to provide a health risk assessment of energy drink products based on their consumption as beverages in Canada. The document attempts to provide a scientific analysis based on the information available to date, which could then be used to support the development of suitable risk management measures for these products when consumed as foods.

2. Defining a typical energy drink

2.1 Defining products known as energy drinks

For the purpose of this document, a typical energy drink is characterised by the ingredients and ingredient levels shown in Table 1. Ingredients include caffeine, taurine, glucuronolactone, inositol and a variety of B vitamins. The basis for this characterisation is the formulation of the most commonly sold products of this category of beverages, such as the product known as Red Bull™, which was the first energy drink approved for the market in Canada. Based on 2009 market data of the global marketing research firm ACNielsen, Red Bull™ comprised approximately 37% of the sales of energy drinks in Canada and, as such, had the largest market share. This is consistent with a more recent report (AAFC, 2011) that states that Red Bull™ constitutes 43% of the sales of energy drinks in North America.

Although Health Canada does not have a definition or standard for products known as energy drinks, other food regulators have reached a decision on this aspect of these products. For example, Australia and New Zealand categorizes energy drinks as 'formulated caffeinated beverages' which are defined under the *Australia New Zealand Food Standards Code* as "a non-alcoholic water-based flavoured beverage which contains caffeine and

may contain carbohydrates, amino acids, vitamins and other substances, including other foods, for the purpose of enhancing mental performance".

In Europe, the Ireland Food Safety Promotion Board (FSPB) established a committee consisting of external experts to research the health effects of 'stimulant drinks' (energy drinks). The committee noted in its final report that there is no agreed definition in the regulatory framework for products referred to as energy drinks or 'stimulant drinks'. For the purposes of the report, the term 'stimulant drinks' was adopted. The committee defined stimulant drinks as "beverages, which typically contain caffeine, taurine and vitamin(s), and may contain an energy source (e.g. carbohydrate), and/or other substance(s), marketed for the specific purpose of providing real or perceived enhanced physiological and/or performance effects" (FSPB, 2003).

2.2 Major components of energy drink products

During the preparation of this manuscript, energy drinks were marketed in Canada under the Natural Health Products (NHP) Regulations. At the time, it was estimated that over 300 energy drink product submissions were before Health Canada for consideration as NHPs. Only twelve were assessed and received a license. Approximately half of the 300 product submissions were either refused a license or withdrawn by the petitioner. A number of products were also on the Canadian market under the provisions of the Unprocessed Product Licensing Regulations. Table 1 below lists the major ingredients and levels typically found in the products that were in the queue for consideration to be licensed as an NHP. For comparison purposes, Table 1 also provides the levels of major ingredients that are typically found in a standard energy drink product.

Substance	Formulation of products known as Energy Drinks that have been either licensed or in queue with Health Canada for consideration as NHPs. (mg per serving*)	Typical energy drink (mg per 250 ml serving)
Caffeine	50 – 200	80
Taurine	10 – 2000	1000
Glucuronolactone	600 – 1200	600
niacin	10 – 40	18[a]
vitamin B6	5 – 10	2
vitamin B12	0.002 - 0.2	0.001
pantothenic acid	5 – 10	6
thiamine	0.5 - 5	2
riboflavin	0.5 - 5	1.65
Inositol	50-200	50

* Serving size is typically 250-473 ml.

[a] Energy drinks contain niacin either in the form of nicotinamide or nicotinic acid. Red Bull™ contains nicotinamide.

Table 1. Amounts of major ingredients in energy drinks

Of the energy drink products that were in the NHP submission queue, approximately 13% fell within the 'typical description' for energy drinks. Based on market share data from ACNielsen (2009), Red Bull™ was ranked the highest, comprising approximately 37% of the market. Energy drinks such as Monster™ and Rockstar™, which contain levels of ingredients higher than the standard and/or contain other ingredients that are not part of the standard, were ranked next but well below Red Bull™ with 5.5% and 4.4% of the market respectively. This market share data has been evolving over the years and may not be reflective of the current market situation.

A wide range of energy drink products is available internationally and in the Canadian marketplace. Ingredients and ingredient levels vary from product to product. While the major ingredients typically found in energy drinks in Canada are listed in Table 1, many other ingredients can be found in these products, particularly various herbs and extracts such as ginseng, ginkgo biloba and green tea extract.

2.3 Energy drink market growth in Canada

According to a 2008 report on the Canadian energy drink market published by Agriculture and Agri-Food Canada (AAFC), in 2006 the "functional beverage category" was valued at 7% of the total soft drink market. Energy drinks are included in the functional beverage category along with sport and nutraceutical drinks. Energy drinks accounted for 65% of the functional beverage sector and 4.6% of the value of the soft drink market. In a more recent report by AAFC (2011), it was noted that there are more than 210 different energy drink brands in North America. It also reported that the energy drink market grew 60.2% from 2007 to 2010 and 5.1% from 2009 to 2010.

3. Health Effects of Energy Drinks

3.1 Introduction

The research on energy drinks is largely limited to a small number of clinical studies (about 12 studies) and case reports. The clinical studies tended to have small numbers of participants (less than 100 subjects) and focused on very specific health effects. These studies mostly examined the effect of energy drink consumption on behaviour and physical activity; therefore, the parameters examined were limited and not necessarily significant from a health and safety perspective. Other studies assessed the consequences of consuming the combination of energy drinks and alcohol.

3.2 Health effects of energy drinks

3.2.1 Acute physiological effects of energy drinks

There is concern that some individuals, who may have increased sensitivity to the ingredients in energy drinks,

may have an acute physiological response, specifically an increase in heart rate and blood pressure. Table 2 summarizes the limited studies on the acute physiological effects of energy drinks. Rashti et al. (2009) investigated 10 healthy women, mean age 20 years. Subjects consumed 140 ml of an energy drink or a placebo. Average systolic blood pressure[1] was significantly higher for the energy drink group compared to placebo. No differences were seen in heart rate, diastolic blood pressure or profile of mood states at any time point. American Heart Association (2007) reported on a study concerning the cardiovascular effects of energy drinks. Fifteen subjects (8 women, 7 men, mean age 26 years) were given 500 ml of an energy drink. The researchers noted an increase in systolic blood pressure and an increase in heart rate in the four hours after consumption of the beverage (cited in BfR 2008). However, across the various studies, changes in blood pressure did not reach hypertensive levels with the consumption of energy drinks. These effects were similar to the effects on blood pressure demonstrated with the consumption of coffee (Riksen et al. 2009).

3.2.2 Behavioural/performance effects of energy drinks

A limited number of studies have assessed the behavioural effects following consumption of energy drinks containing both glucose and caffeine, along with other potentially active agents (see Table 3 below). These studies have identified improvements in performance of attention and/or reaction time tasks and various indices of alertness. For example, Alford et al. (2001) examined the effects of Red Bull Energy Drink over 3 studies in 36 volunteers. Significant improvements in mental performance including choice reaction time, concentration and memory were observed with Red Bull compared to the control drinks. Scholey and Kennedy (2004) investigated the effects of glucose alone, caffeine alone, ginseng and ginkgo at flavouring levels, an energy drink or a placebo in 20 students. Compared to placebo, the energy drink resulted in significantly improved performance on secondary memory and speed of attention factors. Some of the studies attributed the demonstrated effects to the combination of ingredients in energy drinks, rather than caffeine only (Alford et al. 2001; Reyner & Horne 2002; Scholey & Kennedy 2004).

3.2.3 Calories

Except for sugar-free versions, energy drinks, like many beverages, contain sugars in the form of sucrose, glucose, and/or high-fructose corn syrup. The sugar content varies among energy drinks but ranges from 21 to 34 grams per 237 ml can (Clauson et al. 2008). This sugar content is similar to that of carbonated caffeinated soft drinks. It constitutes the vast majority of calories in these products. A 250 ml serving of a typical energy drink contains 110 calories, which is similar to the 86-130 calories in the same volume of a carbonated caffeinated soft drink (USDA Nutrient Database, 2011).

3.3 Health Effects of Energy Drinks and Sports Activity

Energy drinks are frequently marketed to individuals interested in athletics and an active lifestyle. The main ingredients in energy drinks purported to enhance sport performance are caffeine and carbohydrates. The term "energy drink" itself implies that its consumption might enhance physical activity.

Energy drinks should not be confused with 'sports drinks'. Sports drinks are typically a mixture of carbohydrates and electrolytes formulated to enhance athletic performance and prevent dehydration, and, unlike energy drinks, they do not contain caffeine. Conversely, energy drinks contain caffeine which is a stimulant and therefore they are not considered suitable to re-establish normal body function after exercise (e.g. normal heart rate).

The effects of energy drinks on exercise have been investigated in a small number of studies (see Table 4 below). Studies investigating the use of energy drinks have generally found an improvement in endurance performance. Ivy et al. (2009) found that the consumption of 500 ml of a Red Bull energy drink 40 minutes before a simulated cycling time trial in 12 trained cyclists significantly improved endurance performance compared to a non-caffeinated, sugar-free placebo. Forbes et al. (2007) found that the consumption of Red Bull energy drink significantly increased upper body muscle endurance but had no effect on anaerobic peak or average power during repeated Wingate cycling tests in healthy young adults, when compared to a non-caffeinated, isoenergetic, control beverage. Lockwood et al. (2009) found that pre-workout energy drink consumption, significantly improved some physiological adaptations to combined aerobic and resistance training, when compared to a non-caffeinated, sugar-free control drink. Lastly, a study investigating the use of a sugar-free energy drink (Red Bull) found that there was no difference in run time-to-exhaustion or perceived exertion in young adults when compared to non-caffeinated sugar-free placebo (Candow et al. 2009). Overall the studies' result suggest that the consumption of energy drinks may enhance physical ability but it is not clear whether the effect is due to the presence of caffeine, sugar or both of these constituents in the energy drink.

[1] During each heartbeat, blood pressure varies between a maximum (systolic) and a minimum (diastolic) pressure.

Study Design	Test Material (composition) [1]	Methods	Results	Reference
Double-blind, placebo-controlled	Red Bull Energy Drink (32 mg/dL caffeine, 240 mg/dL glucuronolactone, 400 mg/dl taurine) Low Calorie Red Bull Energy Drink (32 mg/dL caffeine, 240 mg/dL glucuronolactone, 400 mg/dl taurine) High Calorie Placebo (carbonated water, tap water and dextrose) Low Calorie Placebo (carbonated water, tap water and dextrose) NB: Banana flavouring and green colouring were added to all test materials	Study 1: 69 subjects (48 women, 21 males, mean age 20 y) consumed 250 ml Red Bull™, Low Calorie Red Bull™, high calorie placebo, or low calorie placebo. Study 2: 21 subjects (9 men, 12 women, mean age 22 y) consumed 250 ml Red Bull™ pre and post cold pressor test.	Study 1: No changes noted in overall cardiovascular function or blood glucose over 2 hour test period. Study 2: A significant increase in diastolic blood pressure in the males immediately after submersion of the hand in cold water (5º C). No significant change noted in females.	Ragsdale et al. 2010
Randomized, double-blind, cross-over, placebo-controlled	Meltdown RTD (140 ml contains: 230 mg caffeine, unknown amounts of methyltetradecythioacetic acid, yerba mate extract, methyl-synephrine, methylphenylethylene, 11-hydroxy yohimbine, yohimbine HCL, alpha-yohimbiine, and methyl-hordenine HCl) Placebo (described as similar in appearance and taste to Meltdown RTD but only contained inert substances)	10 subjects (mean age 20 y) received 140 ml of Meltdown RTD energy drink or a placebo.	Mean systolic blood pressure was significantly higher for the energy drink group compared to placebo. No differences noted in heart rate, diastolic blood pressure, or profile of mood states.	Rashti et al. 2009
Prospective	Unspecified energy drink (250 ml contains: 1000 mg taurine, 100 mg caffeine, unstated amounts of vitamins B5, B6, B12, glucuronolactone, niacinamide)	15 subjects (7 men, 8 women, mean age 26 y) consumed 500 ml (2 cans) of an energy drink daily for the next 5 days.	Within 4 hours of energy drink consumption, mean systolic blood pressure and heart rate significantly increased. Diastolic blood pressure significantly increased within 2 hours of energy drink consumption.	Steinke et al. 2009
Placebo-controlled	Unspecified energy drink (250 ml contains: 1000 mg taurine, 80 mg caffeine, 600 mg glucuronolcatone, unstated amounts of vitamins B2, B5, B6 and B12, sugar-free sweetener and thickeners) Placebo (carbonated water)	50 subjects (34 men, 16 women, mean age 22 y) consumed either a 250 ml sugar-free energy drink or 250 ml of carbonated water (control)	Compared with baseline values, there was a significant increase in platelet aggregation following energy drink consumption; no change was observed with control. Mean arterial pressure significantly increased following energy drink consumption compared with control.	Worthley et al. 2010

[1] Test material composition is listed as it is described in the published report.

Table 2. Studies investigating the acute physiological effects of energy drinks

Study Design	Test material (composition)[1]	Methods	Results	Reference
Randomized, double-blind	Red Bull Energy Drink (250 ml contains: carbonated water, 21.5 g sucrose, 5.25 glucose, 1000 mg taurine, 600 mg glucuronolactone, 80 mg caffeine, 50 mg inositiol, unstated amounts of niacin, panthenol, B6, B12, riboflavin, flavours, colours) Carbonated water Dummy energy drink (unstated amounts of low calorie quinine flavoured carbonated water with lime, apple and blackcurrant concentrates)	36 subjects (19 men, 17 women, age range 18-30 y) in 3 studies received no drink, 250 ml of carbonated water, Red Bull energy drink, or "dummy" energy drink.	Compared to control drinks, Red Bull energy drink significantly improved mental performance including choice reaction time, concentration, and memory.	Alford et al. 2001
Double-blind	Red Bull Energy Drink (250 ml contains: 21 g sucrose, 5 g glucose, 1 g taurine, 600 mg glucuronolactone, 80 mg caffeine, 50 mg inositol, and unstated amounts of vitamin B complex) Placebo (250 ml contains: 21 g sucrose, 5 g glucose, 50 mg inositol, and unstated amounts of vitamin B complex)	11 subjects (male and female, mean age 24 y) received 500 ml of an energy drink or a control drink prior to car simulator test. Control drink consisted of identical drink minus the caffeine, taurine and glucuronolactone.	The energy drink significantly reduced lane drifting and improved reaction time, particularly for the 1st hour.	Horne & Reyner 2001
Double-blind	Red Bull Energy Drink (250 ml contains: 21 g sucrose, 5 g glucose, 1 g taurine, 600 mg glucuronolactone, 80 mg caffeine, 50 mg inositol, and unstated amounts of vitamin B complex) Placebo (250 ml contains: 21 g sucrose, 5 g glucose, 50 mg inositol, and unstated amounts of vitamin B complex)	12 subjects (7 men, 5 women, mean age 24 y) received 250 ml of Red Bull energy drink or a control drink prior to car simulator test. Control drink consisted of identical drink minus the caffeine, taurine and glucuronolactone.	Compared with the control, the energy drink significantly reduced sleep-related driving incidents and subjective sleepiness for the 1st 90 minutes of the drive.	Reyner & Horne 2002
Randomized, double-blind, 5 way cross-over, placebo-controlled	Placebo (250 ml contains: water with flavour and sweeteners), Drink 1 (250 ml contains: water with flavour, sweeteners and 75 mg caffeine Drink 2 (250 ml: water with flavour, sweeteners and 37.5 g glucose) Drink 3 (250 ml contains: water with flavour, sweeteners, 12.5 mg ginseng extract, 2 mg ginkgo biloba extract) Unspecified energy drink (250 ml contains: water with flavour, sweeteners, 75 mg caffeine, 37.5 g glucose, 12.5 mg ginseng extract, 2 mg ginkgo biloba extract)	20 subjects (14 women, 6 men, mean age 21 y) received 1 of 5 drinks: placebo, drink 1, drink 2, drink 3 or an energy drink for a total of 6 study days, each 7 days apart.	Compared with placebo, the energy drink resulted in significantly improved performance on secondary memory and speed of attention factors.	Scholey & Kennedy 2004

Double-blind, 2 way cross-over, placebo-controlled	Unspecified energy drink (250 ml contains: 80 mg caffeine, 1000 mg taurine, 600 mg glucuronolactone, 5.25 mg glucose, 21. 5 mg sucrose, 50 mg inositol, 20 mg niacin, 5 mg vitamin B6, 5 mg vitamin B5, 1.5 mg vitamin B2, and 0.005 mg vitamin B12) Sugar-free placebo (250 ml contains: 1000 mg taurine, 600 mg glucuronolactone,5.25 mg glucose 50 mg inositol, 20 mg niacin, 5 mg vitamin B6, 5 mg vitamin B5, 1.5 mg vitamin B2, and 0.005 mg vitamin B12) Placebo (250 ml contains: 22.5 mg caffeine, 1000 mg taurine, 600 mg glucuronolactone, 6.5 mg glucose, 21.5 mg sucrose, 50 mg inositol, 20 mg niacin, 5 mg vitamin B6, 5 mg vitamin B5, 1.5 mg vitamin B2, and 0.005 mg vitamin B12)	42 subjects (age 18-24 y) consumed 250 ml of an energy drink or a placebo, either a sugar-free placebo or a placebo with additional glucose.	The energy drink improved attention and verbal reasoning compared to the sugar-free and the additional sugar-containing placebos.	Warburton et al. 2001

[1] Test material composition is listed as it is described in the published report.

Table 3. Studies investigating behavioural/performance effects of energy drinks

Study Design	Test material (composition) [1]	Methods	Results	Reference
Randomized, double-blind, cross-over, placebo-controlled	Sugar-free Red Bull Energy Drink (2 mg/kg caffeine; ~146 mg caffeine) Placebo (decaffeinated, sugar-free, lemon-lime flavoured soft drink, tonic water, and lime juice)	17 subjects (9 men, 8 women, mean age 21 y) received either sugar-free Red Bull energy drink or decaffeinated, sugar-free placebo on 3 days of testing, during which they performed physical activity.	No significant difference in run time-to-exhaustion, perceived exertion or calcium lactate between groups.	Candow et al. 2009
Randomized, double-blind, cross-over, placebo-controlled	Red Bull Energy Drink (2 mg/kg caffeine; ~146 mg caffeine) Placebo (isoenergetic, isovolumetric, non caffeinated)	15 subjects (11 men, 4 women, mean age 21 y) received Red Bull Energy Drink (2 mg/kg caffeine) or non-caffeinated placebo separated by 7 days. Muscle endurance assessed by the maximum number of repetitions over 3 sets. Three Wingate cycling tests were used to assess peak and average power output.	Red Bull Energy Drink significantly increased upper body muscle endurance but had no effect on anaerobic peak or average power.	Forbes et al. 2007
Randomized, double-blind, cross-over, placebo controlled	Red Bull Energy Drink (500 ml contains: 2 g taurine, 1.2 g glucuronolactone, 160 mg caffeine, 54 g carbohydrate, 40 mg niacin, 10 mg pantothenic acid, 10 mg vitamin B6, 10 ug vitamin B12) Placebo (500 ml contains: flavoured drink)	12 trained cyclists (6 men, 6 women, mean age 27 y) consumed 500 ml of either placebo or Red Bull Energy Drink 40 minutes before simulated cycling time trial.	Performance significantly improved with energy drink compared to placebo but no difference in rating of perceived exertion between treatments.	Ivy et al. 2009

Randomized, double-blind, placebo-controlled	Unspecified energy drink (12 fl oz contains: carbonated water, citric acid, natural flavours (lemon-lime), sucralose, 60 mg vitamin C, 1.7 mg riboflavin, 20 mg niacin, 2 mg vitamin B6, 6 ug vitamin B12, 300 ug biotin, 10 mg pantothenic acid, 50 mg calcium, 50 ug chromium, 6 mg sodium, 1810 mg combined taurine, guarana extract, greentea leaf extract, caffeine, glucuronolactone, ginger extract (total 200 mg caffeine)) Placebo (12 fl oz contains: carbonated water, citric acid, natural flavours (lemon-lime), sucralose)	38 subjects (male, 18 -45 years old) received energy drink + exercise, energy drink, placebo, or placebo + exercise for 10 weeks (1 drink per day)	Significantly greater decreases in fat mass and percentage body fat, as well as power output at ventilatory threshold were observed in energy drink + exercise compared to placebo + exercise.	Lockwood et al. 2009

[1] Test material composition is listed as it is described in the published report.

Table 4. Studies investigating energy drinks and exercise

3.4 Energy Drinks and Alcohol

Due to concerns with the combination of energy drinks and alcohol, Health Canada has recommended since 2004, the date of licensing of the first Energy Drinks as NHPs, that these products should not be mixed with alcohol (Health Canada: It's Your Health 2010). Nonetheless, the ingestion of energy drinks with alcohol has become increasingly popular (Health Canada: It's Your Health 2010). A survey of 496 American college students examined the frequency of energy drink use for six "situations": insufficient sleep, to increase energy, while studying, driving long periods of time, drinking with alcohol, and to treat hangover. The majority of users consumed one energy drink to treat most situations (namely, hangover, insufficient sleep, increase energy, driving a car for a long period of time) although using three or more to drink with alcohol while partying was a common practice (49%) (Malinauskas et al. 2007). In a survey of 4271 American college students, 24% (697 students) reported consuming energy drinks with alcohol (O'Brien et al. 2008). A summary of studies investigating the use of energy drinks and alcohol can be found in Table 5 below.

Basic physiology suggests that the carbonation of the energy drink permits a quicker absorption of alcohol while the caffeine of the energy drink may mask the drowsiness associated with alcohol intake. Although there is little direct evidence for it, when mixing energy drinks and alcohol, users may not feel the symptoms of alcohol intoxication which may increase the potential for alcohol-related injury (Ferreira et al., 2006)[2]. A survey of American college students by O'Brien et al. (2008) found that in comparison to those who consumed alcohol alone, students who consumed alcohol mixed with energy drinks had a significantly higher prevalence of alcohol-related consequences, including: being taken advantage of, or taking advantage of another student sexually, riding in an automobile with a driver under the influence of alcohol, or being hurt or injured. In addition, mixing energy drinks with alcohol was associated with increased heavy episodic drinking and episodes of weekly drunkenness. Thombs et al. (2010) conducted a field study in a U.S. bar district, interviewing 802 randomly selected and self-selected participants and found that those who mixed energy drinks with alcohol were at a 3-fold risk of leaving a bar highly intoxicated as well as a 4-fold risk of intending to drive upon leaving the bar district, compared to those who did not mix alcohol with energy drinks.

In Germany, the Federal Institute for Risk Assessment (BfR) recommends that "adverse effects cannot be ruled out when larger amounts of these beverages are consumed in conjunction with intensive physical activity or with the intake of alcohol beverages". The BfR looked at case reports from their Swedish regulatory counterpart, the National Food Administration. Information obtained from the Swedish literature search is described in Table 6 below.

[2] While this manuscript was in preparation, a study was published which suggested that energy drinks did not mask the effect of alcohol (Alford et al., 2012). As well, a statement was published by the Committee on Toxicity(UK) 2012, which concluded that the limited currently available evidence does not support a harmful interaction between alcohol and caffeine.

Study Design	Test material [1]	Methods	Results	Study
Randomized, double-blind, placebo-controlled	Green Monster (16 oz contains: 160 mg caffeine, 52 g sugar, 2000 mg taurine, 400 mg ginseng, unstated amount of guarana) Alcoholic, caffeinated beverage (16 oz contains : 6% alcohol, 87 mg caffeine, 47 g sugar, unstated amounts of taurine, ginseng and guarana) Non-alcoholic, non-caffeinated beverage (16 oz contains : 5 g sugar)	27 female subjects (mean age: 22 years) consumed Green Monster energy drink alone (1 drink), with alcohol, or a non-alcoholic, non-caffeinated control.	Energy drink plus alcohol significantly lowered post-test performance on a global score of neuropsychological status, specifically visuospatial/ constructional and language performance scores.	Curry and Stasio 2009
Randomized, double-blind	Red Bull energy drink (250 ml/can)	26 male subjects (mean age 23 y) received Red Bull Energy drink (1 can) plus vodka (0.6 g/kg or 1 g/kg) or alcohol alone or energy drink alone.	When compared to the ingestion of alcohol alone, the ingestion of alcohol + energy drink significantly reduced subjects' perception of headache, weakness, dry mouth, and impairment of motor coordination.	Ferreira et al. 2006
Survey and field test	Unspecified energy drinks	496 US college students completed questionnaires	The majority of users reported consuming energy drinks for insufficient sleep (67%), to increase energy (65%), and to drink alcohol while partying (54%). Common practice to drink 3 or more energy drinks with alcohol (49%). Weekly jolt and crash episodes were experienced by 29% of the users, 22% reported ever having headaches, and 19% heart palpitations from consuming energy drinks.	Malinauskas et al. 2007
Web-based random sample survey	Unspecified energy drinks	Survey was conducted in 4271 college students from 10 universities in North Carolina	697 students (24%) reported consuming alcohol with energy drinks. Students who were male, white, intramural athletes, fraternity or sorority members or pledges, and younger were significantly more likely to consume alcohol with energy drinks. Consumption of energy drinks with alcohol was associated with significantly increased heavy episodic drinking, and twice as many episodes of weekly drunkenness. Students consuming alcohol with energy drinks also had significantly higher prevalence of alcohol-related consequences.	O'Brien et al. 2008
Questionnaire	Unspecified energy drinks	450 college students filled out the questionnaire	56.9% students declared using energy drinks. 48.4% of users frequently associated energy drinks with alcohol.	Oteri et al. 2007
Randomized, field interview	Unspecified energy drinks	802 patrons from 7 bars over 4 consecutive nights. Every 3rd patron exiting bar was approached.	3-fold increased risk of leaving a bar highly intoxicated and 4-fold increased risk of intending to drive upon leaving the bar district, compared to patrons who did not mix energy drinks with alcohol.	Thombs et al. 2010

[1] Test material composition is listed as it is described in the published report.

Table 5. Studies investigating the energy drinks consumed with alcohol

Subject	Product	Effects	Outcome
Female 19 y	6 drinks made from Red Bull and vodka	Hemorrhagic pulmonary edema	Death; clear cause not established
Female 31 y	Drank Red Bull plus vodka	Loss of responsiveness, collapse, ventricular fibrillation	Death; clear cause not established
Male 20 y	Drank Red Bull plus vodka	Acute seizures, epilepsy as child but no further attacks since 8 y	Unknown, clear cause not established

Table 6. Swedish case reports investigating energy drinks mixed with alcoholic beverages

In addition to alcohol consumption, energy drinks may be used along with prescription medication and recreational drugs. Diamond et al. (2000) demonstrated that caffeine can enhance the effect of certain analgesics, including ibuprofen. Staib et al. (1987) advised that caffeine intake should be reduced in individuals prescribed certain antibiotics as they may inhibit the elimination of caffeine from the body. Studies conducted in humans show that caffeine produces subjective and behavioural effects that are similar to those of typical psychomotor stimulant drugs that are known to be dopaminergically mediated (e.g., amphetamines, cocaine). Caffeine, like amphetamine and cocaine, enhances feelings of well-being, motivation for work, energy, and concentration, delays sleep, and enhances vigilance performance on psychomotor tasks (Garrett & Griffiths 1997).

Overall, the evidence does not conclusively indicate a harmful toxicological interaction between energy drinks and alcohol. However, the data are limited and there is substantial uncertainty. It was noted that adverse events associated with energy drink and alcohol co-consumption happened most frequently with young adults. This affected subpopulation is relatively inexperienced as alcohol consumers and relatively susceptible to peer pressure. The advice to recommend not to mix energy drinks and alcohol could therefore be argued to be a prudent safety measure.[3]

3.5 Canadian adverse reaction reports

Health Canada's Marketed Health Products Directorate (MHPD) conducted a search of the Canada Vigilance Adverse Reaction Database[4] from January 01, 1965 to July 20, 2010 and found 61 adverse reactions associated with the consumption of energy drinks.[5] Thirty-two of these reactions are considered "serious", 15 of which involved the cardiac system (arrhythmia, increased heart rate, palpitations and chest pain). Six of these 15 cardiac events occurred in individuals aged 13-17 years. Based on these reports, analysis of available scientific literature, MHPD detected a safety signal[6] indicating an association between adverse cardiac events and the consumption of energy drinks. Almost all of the reports are in healthy young individuals without concurrent disease or medications. Therefore, alternative causes such as underlying disease or drug interaction were not apparent. Four (4) adverse cardiac reactions were assessed to be of probable causality and 8 were assessed to be of possible causality, using the WHO causality assessment algorithm[6]. Three adverse reactions, including the 2 deaths that were associated with energy drinks, could not be assessed because of lack of information. The incidence of cardiac events in the healthy young population is rare and not well characterized in the scientific literature. In addition, the absence of observational and clinical trial data on energy drink use prevents a comparison between reactions associated with these products and the background incidence of cardiac events.

Reported adverse reactions rates are known to be under reported, particularly for NHPs. Both consumers and healthcare practitioners, generally regard NHPs as safe and are usually unaware that adverse reactions can occur with these products and that they can be reported to Health Canada. Even though energy drinks have been regulated as NHPs (therefore health products, subject to adverse reaction reporting) from 2004 to 2011; they may not have been recognized as such, given the way they have been made available (grocery stores next to other beverages, convenience stores, gas stations). Being perceived as beverages (i.e. food) did not support consistent adverse reaction reporting associated with these products.

While these adverse reactions are important to note, they are to be put into perspective, considering the comparatively small number of reported adverse reactions in view of the number of product units sold (around 91 million units in Canada per year, according to 2009 ACNielsen data). This comparison is an over-simplification. It would be better to compare the number of adverse effects to the number of

[3] While this manuscript was in preparation, the UK Committee on Toxicity of Chemicals in Food, Consumer Products and the Environment published a statement on the interaction of caffeine and alcohol (2012). The Committee concluded that the overall current evidence does not support a harmful interaction between caffeine and alcohol. However, it states that there is substantial uncertainty in this conclusion.

[4] The number of adverse reports in the Canada Vigilance Adverse Reaction Database should not be used as a basis for determining the incidence of a reaction or for estimating risk of a particular product, as neither the total number of reactions occurring, nor the number of patients exposed to the health product, is known.

[5] The first authorized energy drink was Red Bull in 2004.

[6] A signal is reported information on a possible causal relationship between an adverse event and a drug, the relationship being unknown or incompletely documented previously (World Health Organization 1991).

consumers of energy drinks, but at this time, Canadian consumption data are not available. Nonetheless, it can be said that the number of adverse reactions reported to Health Canada is relatively small compared to general consumption.

3.6 Summary

Energy drinks, like other beverages containing added sugars, are often associated with a high caloric intake. These drinks are not to be considered "sports drinks" as they contain at least one ingredient that is a stimulant (caffeine). Despite some study results suggesting that energy drink consumption prior to exercise may have some performance benefits, there are concerns, as caffeine may delay the return to a resting heart rate. Limited study results have shown increases in systolic blood pressure and heart rate associated with moderate intakes of energy drinks (2 servings). However, across the various studies, transitory changes in blood pressure did not reach hypersensitive levels with consumption of energy drinks. These effects were deemed to be similar to the effects on blood pressure demonstrated in conjunction with caffeine intake (Riksen et al., 2009).

Surveys also suggest that in social settings (e.g., bars, parties) moderate or high consumption of energy drinks with alcohol is not uncommon, and could lead to risky behaviour since energy drinks may mask the effects of alcohol. There have been adverse reactions associated with the consumption of energy drinks, whether alone or in combination with other physiologically active substances, in Canada. Only 4 of the 15 reported cardiac adverse reactions were assessed as having a probable causality. The significance of these reported adverse reactions is to be discussed in the context of their limited number versus the number of energy drink units consumed and the absence of observational and clinical trial data, which prevents a comparison between reactions associated with these products and the "background" incidence of cardiac events.

There were insufficient toxicological data to characterize the health hazard associated with energy drinks as a single product. As a consequence, the major individual ingredients were assessed for hazard identification and hazard characterization, and this was considered a means to gain insight into the hazard characterization of energy drinks.

4. Assessment of Individual Ingredients of Energy Drinks

4.1 Introduction

In other jurisdictions, the approach used for assessments on energy drinks considered the nutritional and toxicological aspects of the individual ingredients in these products. This approach was taken because the published literature on energy drinks was limited to a few clinical studies and case reports. No relevant preclinical (animal) studies have been conducted. One study did administer an energy drink to mice for up to 13 weeks but the work was not considered to be useful in the safety assessment, since the amount consumed did not constitute a very high dose of the energy drink (cited in EFSA 2009). In contrast, there is a good biological understanding and a broad toxicological database for many of the individual ingredients that constitute energy drinks. Therefore, this approach was also used in this hazard characterization.

Energy drinks can be generally characterised as containing the following ingredients: caffeine, taurine, glucuronolactone, inositol and a variety of B vitamins, including thiamine, niacin, vitamin B6, vitamin B12, pantothenic acid and riboflavin (as mentioned in Table 1). The dietary sources, nutritional aspects and toxicity of these ingredients are reviewed below.

4.2 Caffeine

Caffeine is consumed as a natural constituent of coffee, tea, chocolate and other natural sources, such as guarana and yerba mate. It is also used as a food additive and is present in certain carbonated soft drinks. It is also present in some therapeutic products, such as cold remedies and allergy medicines. In Canada, it is estimated that male and female adults have a respective mean intake of 281 and 230 mg of caffeine per day (Canadian Community Health Survey, 2004). These amounts are about three times the 80 mg of caffeine present in a single 250 ml serving of a typical energy drink.

When a single serving of a caffeinated beverage containing 40-120 mg of caffeine[7] is consumed the main biological effect of caffeine is that it acts as a stimulant and promotes alertness, enhances cognitive performance, relieves fatigue and promotes physical endurance (Doherty and Smith, 2004; Lorist and Tops, 2003; Astorino and Robertson, 2010) A single serving can also cause transient adverse effects, such as insomnia, headaches and nervousness in caffeine-sensitive individuals (Nawrot et al. 2003; Higdon and Frei, 2006).

In an extensive review of the literature, Health Canada assessed more than 300 studies that examined the potential health effects of caffeine (Nawrot et al. 2003). It was concluded that a healthy adult could tolerate a maximum intake of 400 mg of caffeine per day (equivalent to 6 mg/kg bw/day for a 65 kg adult). This amount of caffeine was not associated with adverse effects such as general toxicity, cardiovascular effects, effects on bone status, changes in

[7] Generally, a serving of tea or cola can contain around 40 mg of caffeine while coffee, depending on the type and brewing method, can contain around 120 mg caffeine and higher.

behaviour, effects on male fertility or increased incidence of cancer development.

Further, the assessment concluded that reproductive-aged women could tolerate a maximum intake of up to 300 mg caffeine per day (equivalent to 4.6 mg/kg bw/day for a 65 kg adult), based on reproductive considerations (spontaneous abortion, retarded fetal growth). Finally children, aged 4 to 12 years, were considered to tolerate a maximum of 45 to 85 mg of caffeine per day (equivalent to 2.5 mg/kg bw/day for a child weighing 18 to 34 kg), based on transient mild behaviour changes.

There were insufficient data to recommend a daily maximum intake of caffeine for adolescents, aged 13 to 18 years. However, the adult recommendation could be considered inappropriate since many adolescents may have a lighter body weight than the average adult. More importantly, adolescents are less developed than adults and their growing bodies may be more susceptible to adverse effects of caffeine. One author has suggested that caffeine may adversely affect the growing adolescent brain (Temple 2009). Alternatively, adolescents may be less habituated to consuming caffeine and therefore may be more susceptible. In any case, there is substantial uncertainty as to whether the adult recommendation should be applied. As a precaution, it would be prudent to recommend that an adolescent have a daily intake of caffeine no greater than the amount calculated from the dose used to determine the recommended maximal intake for children (2.5 mg/kg bw/day) and the individual adolescent body weight (estimated range of adolescent body weights: 40-70 kg). This dose would suggest that adolescents could consume 100 to 175 mg of caffeine daily, depending on the individual body weight of the adolescent.

It should be noted that all of these recommended maximum intakes of caffeine are considered a daily amount that would be the result of cumulative consumption throughout the day. The ingestion of the daily maximum intake in a brief period of time, that is 1-2 hours, may cause adverse reactions, such as insomnia, headache, stomach ache, nervousness, nausea or more serious reactions. For example, studies have shown that a single ingestion of more than 250 mg of caffeine by a healthy adult can also cause an increase in blood pressure (Maughan and Griffin, 2003) while more than 450 mg of caffeine may result in tachycardia (Nawrot et al. 2003).

4.3 Taurine

Taurine is an amino acid that is naturally present in the diet. Specifically, it is found in meat and seafood. Estimates of human daily intake of taurine range from 40 mg to 400 mg (Hayes and Trautwein 1994). These dietary levels of taurine are relatively low compared with the 1000 mg of taurine present in a single serving of a typical energy drink.

Taurine is also synthesized in the liver from the amino acid cysteine, as well as from other sulphur compounds. It has a role in several biological processes, including the formation of bile salt, cell membrane stability, the modulation of calcium flow and neuronal excitability (FSPB 2002). Taurine is considered essential for the normal development of infants and consequently it is a standard ingredient in infant formula, such that newborns ingest about 280 mg daily (equivalent to a dose of 17 mg/kg bw/day).

Taurine is one of the most abundant amino acids in the human body. It is present in relatively high amounts in skeletal and cardiac muscle (Timbrell et al., 1995) and evidence in experimental animals suggests that it is essential to normal muscle maintenance and function (Warskulat et al., 2007). Limited literature has suggested that taurine supplements may have a beneficial effect in persons with congestive heart failure, hypertension, diabetes and skeletal muscle disorders (references cited in Bouknooghe et al., 2006; Shao and Hathcock, 2008).

Human studies suggest that taurine is readily absorbed from consumed food and that plasma level of taurine peak within an hour after ingestion (SCF 2003). This observation is consistent with the findings of a study where rats received taurine as a single oral dose of 300 mg/kg bw. It was observed that the exogenous taurine is quickly absorbed into the body, equilibrates with endogenous pools of taurine and that excess amounts are rapidly eliminated by the kidneys. The study also showed that a 14-day repeat treatment with taurine did not change the fate of the last single oral dose (Sved et al. 2007), which suggests that the body can metabolically handle relatively large amounts of taurine daily.

The acute oral toxicity of taurine is considered relatively low, such that no adverse effects have been observed following a single administration in rats up to 7000 mg/kg bw or in humans up to 150 mg/kg bw (equal to 10,500 mg for a 70 kg adult).

In short-term studies with human subjects, the ingestion of up to 6000 mg per day for 42 days and 1500 mg per day for 90 days showed no evidence of adverse effects (SCF 2003). In a 90-day study in rats, taurine was administered by gavage to groups of animals (20 animals/sex/dose) at doses of 0, 300, 600 or 1000 mg/kg bw/day. No taurine-related changes of standard toxicological parameters were observed. The exception was a dose-related behavioural change (increased activity, self-injury) that was observed in all three treated

groups and in both sexes of the test animal (SCF 2003). Subsequently, a second 90-day study was conducted, where taurine was administered by gavage to groups of rats (20 animals/sex/dose) at doses of 0, 600 or 1000 mg/kg bw/day, and another set of rats (20 animals/sex/dose) received taurine in drinking water at doses of 0, 1000 or 1500 mg/kg bw/day. In addition to standard toxicological parameters, a functional observational battery and locomotor activity data were collected at 0, 6 and 12 weeks of the study and conducted in a blind manner (the previous 90-day study's findings were argued by the study's author to be biased since they were not blinded). The results indicated that there were no taurine-related deaths, clinical toxicities, body weight changes, food or water consumption differences, or macroscopic changes. The functional observational battery and locomotor activity data did not show any taurine-related effect. There were no adverse behavioural effects observed in this second study. A NOAEL for taurine was established at the level of 1000 mg/kg bw/day, based on the highest dose tested in the first 90-day study, which included a histopathological assessment (EFSA 2009).

A developmental toxicity study in mice showed that when orally administered at a dose of 4000 mg/kg bw/day on days 7 to 14 of gestation, taurine was not a teratogen, that is, it did not cause birth defects (Takahashi et al. 1972).

In the additional studies conducted, taurine has not shown any mutagenic or genotoxic potential in bacterial or mammalian cell in vitro assay systems (S.A. Laidlaw et al. 1989; R. Cossi et al. 1995).

There are no long-term toxicity or carcinogenicity studies conducted to assess the carcinogenic potential of taurine; however, there is no indication that taurine is a carcinogen based on short-term toxicity studies.

In over thirty studies with adult, child and infant subjects, the use of taurine has not demonstrated any safety concerns. Most of these studies involved the ingestion of taurine on a daily basis with doses in the range of 3000 to 6000 mg for periods of up to one month or longer without any apparent adverse health effects (EFSA 2009).

One double-blind study in human volunteers (14 subjects) showed that a combination of caffeine and taurine, at levels present in a typical energy drink, had no effect on short-term memory, as indicated by an abbreviated version of a standard test for short-term memory. However, this combination did induce a decrease in heart rate and an increase in mean arterial blood pressure. This finding is unexpected since caffeine generally stimulates heart rate. Further investigation into the combination of these two substances is warranted (Bichler et al., 2006).

4.4 D-Glucurono-γ-lactone

D-Glucurono-γ-lactone (glucuronolactone) is the γ-lactone of glucuronic acid. It is a normal human metabolite and formed from glucose and glucuronic acid. It seems to be found naturally in only a small number of foods such as wine and plant gums (e.g. guar gum, gum Arabic). An estimate of the mean daily intake is 1.2 mg/day and a high daily intake is suggested to be 2.3 mg/day (SCF 1999). These intake values are very small when compared to the intake of glucuronolactone of 600 mg from the consumption of a single serving of a typical energy drink. It is claimed that glucuronolactone is a quick energy source and may assist in the detoxification of xenobiotics (SCF 1999).

Human and rat studies show that when ingested, glucuronolactone is rapidly absorbed, metabolised and excreted as glucaric acid, xylitol and L-xylulose. These compounds are not considered to be toxicologically significant (ANZFA 2001). In contrast to humans, mice and rats have an additional metabolic pathway that allows them to use glucuronic acid to synthesize vitamin C. Rodents can also use exogenous glucuronolactone to yield glucuronic acid and then generate vitamin C. This additional pathway in the rodent created some uncertainty with respect to the appropriateness of rodents as a model for humans (SCF 1999). However, further examination of the issue has determined that the rodent metabolic pathway is relatively minor in the animal's handling of glucuronolactone, which suggests that toxicological results from rodents are relevant to the human situation (SCF 2003.

The acute oral toxicity of glucuronolactone is very low, such that in mice the oral LD_{50} is greater than 20000 mg/kg bw and in rats it is approximately 11000 mg/kg bw. The short-term oral toxicity of glucuronolactone was assessed in a study where groups of rats (20 animals/sex/dose) were administered a single daily gavage dose of 0, 300, 600 or 1000 mg/kg bw, for up to 90 days (SCF 2003). The results showed no treatment-related deaths, no significant difference in body weights, food consumption, hematological or clinical chemistry parameters. Urinalysis showed that males treated with 1000 mg/kg bw group had urine with a lower pH than the control group, and males in the 600 and 1000 mg/kg groups had a lower specific gravity than the control group. Results from histopathological examination showed vacuolisation and inflammatory changes localised to the papilla of the kidney in females such that at doses of 0, 300, 600 and 1000 mg/kg bw/day, the incidences were respectively 11/20, 9/20, 11/20 and 11/20. The incidence of effect was not dose-related but reviewers of the study noted that the severity of this kidney lesion showed an increase with dose. At doses of 0, 300, 600 and 1000 mg/kg bw/day, the incidences of a grade 2 lesion

(mild severity) were respectively 1/20, 1/20, 5/20 and 8/20. The reviewers concluded that the NOAEL for the study was 300 mg/kg bw/day.

In a second 90-day study in rats, the toxicity of glucuronolactone was assessed with specific focus on the kidneys (SCF 2009). The previous gavage study was repeated with an additional four sets of animals (20 animals/sex/dose) that received glucuronolactone in drinking water; with both routes of administration animals received nominal doses of 0, 300, 600 or 1000 mg/kg bw for 90 days. There were no treatment-related deaths, no effects on clinical observations, food or water consumption, body weights, clinical parameters, organ weights or clinical chemistry parameters related to renal function. Urinalysis demonstrated no treatment-related effects and no differences between the gavage and drinking water groups. Lastly there were no test material-related gross or microscopic findings. This included the kidneys which showed typical amounts of background lesions for this strain of rat. There was no test material-related vacuolisation of the cells lining the collecting tubules of the kidney. This suggests that the kidney lesions observed in the first study were not significant, since the drinking water administered in the second study was more relevant to the human situation. The NOAEL for the study was set at 1000 mg/kg bw/day, the highest dose tested.

Reproductive and developmental toxicity studies for glucuronolactone were not available but were not considered necessary to conduct, as part of the safety evaluation since glucuronolactone in the body hydrolyses to glucuronic acid, which is an endogenous metabolite in humans and present in normal human diets (EFSA 2009).

Glucuronolactone was shown not to be mutagenic in a bacterial reverse mutation system (Kuroda et al. 1986).

One study (Ahrens et al. 1987) assessed the long-term toxicity of glucuronolactone. Groups of 25 male rats were administered orally 0 mg (water), 125 mg of glucuronic acid, 250 mg of glucuronic acid or 125 mg of glucuronolactone per day from the age of about 1 year to death (about 3 years of age). The daily amount of glucuronolactone was equivalent to about 250 mg/kg bw/day. There were no significant differences between the treatment groups with respect to cause of death, body weights at death or autopsy findings. The carcinogenic potential of glucuronolactone was not assessed in this or any other study, however, there is no indication that glucuronolactone is a carcinogen, based on short-term toxicity studies and its role in normal human metabolism.

It has been reported that glucuronolactone has been used at doses of 1 to 3 g/day (1000 to 3000 mg/day) in long-term therapy for carriers of the typhoid organism because of its ability to inhibit viral and bacterial β-glucuronidase. Its use was not observed to cause any adverse effects (Kohler and Schmid 1980).

4.5 Inositol

Myoinositol (inositol) is a constituent of phosphatidylinositol, a phospholipid, which plays an essential role in growth, metabolism regulation and signal transduction. Inositol is a normal component of human tissue and can be synthesized in some tissues. It is a normal part of food derived from plants in the form of phytate and from animals in the form of free and phosphorylated inositol and as inositol phospholipid. It is estimated that adults ingest about 500 to 1000 mg of inositol daily. This amount is relatively large compared to the 50 mg of inositol present in a single serving of a typical energy drink, as described in Table 1. Potential benefits of inositol may include decreased cholesterol levels and thus a lowered risk of cardiovascular disease (ANZFA 2001).

The toxicity associated with inositol is very low. In mice the oral LD_{50} is reported to be 10000 mg/kg bw. There are no reproductive or developmental toxicity studies or genotoxicity studies that assessed inositol. Although inositol was not tested as a carcinogen, several studies assessed its ability to prevent cancer development in mouse models. The results showed that a 3% level in the diet (equivalent to a dose of 6000 mg/kg bw/day) did not increase cancer formation (Estensen and Wattenberg 1993).

In humans, inositol has been used as an experimental therapy for depression, panic disorder, and obsessive compulsive disorder. There is a report of people consuming up to 20,000 mg of inositol daily for 2 weeks (Arendrup et al. 1989). Another report cites the administration of 18 g of inositol daily for 6 weeks (Koponen et al. 1997). In these reports and several others, no adverse effects were observed (Colondy and Hoffman 1998).

4.6 B Vitamins

Most energy drinks contain added B vitamins including thiamine, riboflavin, niacin, vitamin B6, vitamin B12, and pantothenic acid.

4.6.1 Thiamine (Vitamin B1)

Thiamine is widely found in foods, including meat, legumes, and whole or enriched grain products. The Recommended Dietary Allowance (RDA)[8] for thiamine for adult males is 1.2 mg/day and for adult females, 1.1

[8] The Dietary Reference Intakes (DRIs) are nutrient reference values that replace the 1990 Recommended Nutrient Intakes (RNIs) in Canada and the 1989 Recommended Dietary Allowances in the United States (Health Canada, http://www.hc-sc.gc.ca/fn-an/nutrition/reference/dri_using-util_anref-eng.php). The DRIs include Recommended Dietary Allowance (RDA) and Adequate Intake (AI).

mg/day (IOM 1998). Based on data from the Canadian Community Health Survey (CCHS) (2004), the 95th percentile of dietary intake indicates that adults consume up to 4 mg of thiamine per day. The formulation of a typical energy drink product as described in Table 1 does not contain thiamine; however, other energy drinks may contain up to 5 mg of thiamine per serving.

The US Institute of Medicine (IOM) was not able to set a tolerable upper intake level (UL) for thiamine due to the lack of data on adverse effects (IOM 1998). In addition, the European Commission concluded that while it is not possible to derive a UL for thiamine, current levels of intake from all sources do not represent a health risk for the general population (European Commission 2001). However, the Australia New Zealand Food Authority (ANZFA) set a maximum limit for thiamine of 20 mg/250 ml in formulated caffeinated beverages as a conservative limit that was based on a maximum one-day quantity of 40 mg thiamine (ANZFA 2001).

Orally ingested thiamine has a long history of use as a supplement without reported adverse effects. There are no reports of adverse effects of oral thiamine, even at dosages of several hundred milligrams per day (European Commission 2001). A Canadian evaluation of micronutrient safety classified thiamine as a nutrient with no known adverse effects (Program on Food Safety 1996).

4.6.2 Riboflavin (Vitamin B2)

Riboflavin is found in a wide variety of foods but milk and milk products are thought to contribute the majority of dietary riboflavin. Eggs, meat, and legumes also provide riboflavin in significant quantities (Groff & Gropper 2000). The RDA for riboflavin for adult males is 1.3 mg/day and for adult females, 1.1 mg/day (IOM 1998). Based on data from CCHS (2004), the 95th percentile of dietary intake indicates that adults consume up to 4.5 mg of riboflavin per day. The typical energy drink product formulation, as described in Table 1, contains 1.65 mg of riboflavin per 250 ml serving while other energy drinks may contain up to 5 mg of riboflavin per serving.

IOM was not able to set a UL for riboflavin due to the lack of data on adverse effects (IOM 1998). In addition, the European Commission concluded that while it is not possible to derive a UL for riboflavin, current levels of intake from all sources do not represent a risk to human health (European Commission 2000). However, ANZFA set a maximum limit for riboflavin of 20 mg/day in formulated caffeinated beverages based on the composition of Red Bull and knowledge of regular consumption of 500 ml per day of this product (ANZFA 2001).

The toxicity of riboflavin is considered to be extremely low due in part to ready excretion of excess amounts (ANZFA 2001). Available sub-chronic data from human studies and pharmacokinetic studies do not show reported effects on oral toxicity of riboflavin. Apart from a few minor gastrointestinal disorders, which are not clearly related to riboflavin intake, it is free from serious side effects (European Commission 2000).[9,10]

4.6.3 Niacin (Vitamin B3)

Niacin is the term used to describe vitamin B3; nicotinic acid and nicotinamide are two different forms of niacin. The best dietary sources of niacin include tuna, beef, other meats, and cereal grains (Groff & Gropper 2000). The RDA for niacin for adult males is 16 mg/day and for adult females, 14 mg/day (IOM 1998). Based on data from CCHS (2004), the 95th percentile of dietary intake indicates that adults consume up to 76.7 mg of niacin per day. The typical energy drink, as defined in Table 1, contains 18 mg of niacin per 250 ml serving while other energy drinks may contain up to 40 mg of niacin per serving. The niacin in these products is generally present in the form of nicotinamide and is most likely added due to its role in energy metabolism.

The Institute of Medicine (IOM) in the United States (1998) set a UL of 35 mg/day for niacin based on the adverse effect of flushing[11]. Flushing is first observed after excess niacin intake and is generally observed at lower doses than are other effects. Flushing that results in patients deciding to change the pattern of niacin intake (i.e., reduce the amount taken at a time or withdraw from treatment) was selected as the most appropriate endpoint on which to base a UL. Although nicotinamide appears not to be associated with flushing effects, a UL for nicotinic acid that is based on flushing is considered protective against potential adverse effects of nicotinamide (IOM 1998).

Other jurisdictions have set ULs for both nicotinic acid and nicotinamide. However, as nicotinamide is typically found in energy drinks, only the ULs relating to this form of niacin are discussed. The European Commission set a UL of 900 mg/day (12.5 mg/kg bw/day) for nicotinamide based on a NOAEL of 25 mg/kg bw/d, derived from studies in subjects with or at risk of diabetes. (European Commission, 2002).

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[9] While this manuscript was in preparation, Health Canada published the document Category Specific Guidance for Temporary Marketing Authorization: Caffeinated Energy Drinks (March 2012). A daily maximum level of 5 mg/day was set for the addition of thiamine to energy drinks.

[11] Health Canada's Category Specific Guidance for Temporary Marketing Authorization: Caffeinated Energy Drinks (March 2012) set a daily maximum level of 27 mg/day for the addition of riboflavin to energy drinks.

[11] Flushing refers to a transitory sensation of extreme heat.

The Expert Group on Vitamins and Minerals (Food Standards Agency 2003) set a guidance level of 560 mg/day for nicotinamide as the limited data on the occurrence of nicotinamide toxicity indicates that it is quite low.

ANZFA set a maximum limit for niacin of 40 mg/day (2 cans of 20 mg/250 ml) in formulated caffeinated beverages based on their assessment (ANZFA 2001).[12]

There is no evidence of adverse effects from the consumption of normal levels of niacin in foods. Adverse effects have been observed with intakes of nicotinamide greater than 3000 mg/day compared with intakes of nicotinic acid of 1500 mg/day (ANZFA 2001). Adverse effects can be observed following high intakes of nicotinic acid, which may be achieved through consumption of pharmacological preparations or dietary supplemental products. Adverse effects associated with the use of nicotinic acid as a drug, especially in doses of 1 g or more per day include:

- Possible injury to the liver, as indicated by elevated serum levels of enzymes of hepatic origin (e.g., transaminases) and by obstruction of normal bile flow from the liver to the small intestine;
- Development of dermatological problems such as itching; and
- Elevation of plasma glucose levels (Groff and Gropper 2000).

4.6.4 Pyridoxine (Vitamin B6)

Excellent sources of vitamin B6 in commonly consumed foods are bananas, navy beans, and walnuts (Groff & Gropper 2000). The RDA for vitamin B6 for adult males is 1.3-1.7 mg/day and for adult females, 1.3-1.5 mg/day (IOM 1998). Based on data from CCHS (2004), the 95th percentile of dietary intake indicates that adults consume up to 4.5 mg of vitamin B6 per day. The typical energy drink, as described in Table 1, contains 2 mg of vitamin B6 per 250 ml serving while other energy drinks may contain up to 10 mg of vitamin B6 per serving.

IOM set a UL for vitamin B6 of 100 mg/day based on a NOAEL of 200 mg/day and applying an uncertainty factor of 2 to account for the limitations in data (IOM 1998). The European Commission set a UL of 25 mg/day for vitamin B6 (European Commission 2000) by taking the average intakes of vitamin B6 (100 mg) from the study by Dalton and Dalton (1987) and applying an uncertainty factor of 4 to account for long-term intake.

ANZFA set a maximum limit for vitamin B6 of 10 mg/day in formulated caffeinated beverages based on history of use, rather than the U.S. UL (ANZFA 2001).

There are no safety concerns in relation to vitamin B6 intake from food sources. However, adverse neurological effects have been detected in humans after very high doses (>500 mg/day, equivalent to approximately 8 mg/kg/day)[13]. Minor neurological symptoms may be apparent at doses of 100 mg/day or more if consumed for long periods. There are no subgroups that are known to be unusually susceptible to the adverse effects of vitamin B6 (European Commission 2000).

4.6.5 Cobalamin (Vitamin B12)

The only dietary sources of vitamin B12 for humans are from animal products, which have derived their cobalamins from microorganisms. The best sources of cobalamins are meat and meat products, poultry and eggs. The RDA for vitamin B12 for adult males and females is 2.4 mcg/day (micrograms/day) (IOM 1998). Based on data from CCHS (2004), the 95th percentile of dietary intake indicates that adults consume up to 6 mcg of vitamin B12 per day. The typical amount used for energy drinks, as described in Table 1, contains 1 mcg of vitamin B12 per 250 ml serving while other energy drinks may contain up to 20 mcg of vitamin B12 per serving.

IOM was not able to set a UL for vitamin B12 due to the lack of data on adverse effects (IOM 1998). Similarly, the European Commission concluded that it is not possible to derive a UL for vitamin B12 as there are no clearly defined adverse effects produced from this vitamin (European Commission 2000). ANZFA set a maximum limit for vitamin B12 of 10 mcg/day in formulated caffeinated beverages based on history of use (ANZFA 2001).

No adverse effects have been associated with excess vitamin B12 intake from food or supplements in healthy individuals (European Commission 2000). [14]

4.6.6 Pantothenic acid (Vitamin B5)

Meats (especially liver), egg yolk, legumes, and whole grain cereals are good sources of pantothenic acid. The adequate intake (AI) for pantothenic acid for adult males and females is 5 mg/day (IOM 1998). CCHS (2004) did not have any dietary intake data on pantothenic acid; however, another source indicates that average intakes of adults range between 3-12 mg/d (European Commission 2002). The typical energy drink, as defined in Table 1,

[12] Health Canada's Category Specific Guidance for Temporary Marketing Authorization: Caffeinated Energy Drinks (March 2012) set a daily maximum level of 450 mg/day for the addition of nicotinamide to energy drinks.

[13] At doses less than 500 mg/day, the adverse effects were reversible.

[14] Health Canada's Category Specific Guidance for Temporary Marketing Authorization: Caffeinated Energy Drinks (March 2012) set a daily maximum level of 25 mcg/day for the addition of vitamin B12 to energy drinks.

contains 6 mg of pantothenic acid per 250 ml serving while other energy drinks may contain up to 10 mg of pantothenic acid per serving.

IOM was not able to set a UL for pantothenic acid due to the lack of data on adverse effects (IOM 1998). In addition, the European Commission concluded that while it is not possible to derive a UL for pantothenic acid, current levels of intake from all sources do not represent a health risk for the general population (European Commission 2000). ANZFA set a maximum limit of 10 mg/day for pantothenic acid in formulated caffeinated beverages based on the composition of the reference product known as Red Bull™ and knowledge of regular consumption of 500 mL per day of this product (ANZFA 2001).

There are no reports of pantothenic acid or panthenol toxicity in humans. Minor gastrointestinal effects such as occasional diarrhea and water retention occurred only at very high intakes (10-20 g/day) (European Commission 2002).[15]

4.7 Summary

Health hazard data on energy drinks are extremely limited and therefore the hazard assessment was based on individual ingredients. Caffeine was identified as the ingredient in energy drinks having the greatest potential for intakes of health concern. Assuming no additional caffeine from the diet, it was determined that no more than 5 servings per day of a typical energy drink should be consumed by the general adult population. At this level of consumption, the levels of taurine and glucuronolactone in a typical energy drink are not expected to pose a health hazard in the short term. Although there are limited hazard data on energy drinks as formulated in the published literature, actual use of energy drinks has been associated with some adverse reactions. However, due to the absence of long-term safety data on high levels of consumption of taurine and glucuronolactone, the potential interaction of these substances with caffeine, and for most consumers, the known addition of caffeine from other dietary sources, it was concluded that the long-term consumption of 5 servings of energy drinks per day could not be considered to represent no health concern for the general adult population.

Also, the evidence examined suggests that most of the B vitamins and other constituents of a typical energy drink would not pose a health hazard in the short term, but long-term safety data were not available for this level of consumption.

The health hazard assessment concluded that the general adult population could consume 2 servings of a typical energy drink per day with no expected negative health consequences. This conclusion was based on the safety of the non-caffeine ingredients of energy drinks (i.e. taurine, glucuronolactone, inositol and B vitamins) at this level of consumption, and the fact that caffeine from other dietary sources in addition to that in 2 servings of energy drinks would not pose a health risk to the general adult population.

More specifically, the respective mean daily intakes of caffeine from all dietary sources for adult Canadian males and females are 281 and 230 mg. With body weights of 80 and 65 kg, theses intakes are equivalent to a daily dose of 3.5 and 3.1 mg/kg bw, respectively (Statistics Canada, Canadian Community Health Survey, 2004). The consumption of two servings of a typical energy drink containing 80 mg of caffeine per serving would result in the addition of 160 mg caffeine to the diet. In males, this would result in a daily dose of 5.5 mg/kg bw and in females, a daily dose of 6.0 mg/kg bw.[16] Health Canada's recommended maximum daily intake of caffeine for adults is 6.5 mg/kg bw or about 400 mg for an adult weighing 65 kg (Nawrot et al., 2003). Given that the addition of two servings of a typical energy drink to the diet would not exceed the recommended maximum daily intake of caffeine, it can be concluded that this level of consumption would not pose an additional health hazard based on the caffeine content of these products.

The consumption of energy drinks by subpopulations, such as children and pregnant and breastfeeding women, is not generally recommended. Based on caffeine content, consumption of such drinks by any group should be limited to their recommended maximum daily intake of caffeine. Excess consumption of energy drinks would be expected to result in health consequences similar to those from excess exposure to caffeine.

5. Surveys and Studies on Energy Drink Consumption Levels and Patterns

5.1 Introduction

A limited number of qualitative and quantitative surveys and studies on energy drink consumption have been carried out in other jurisdictions since the late 1990's. Data on levels of intake as well as patterns of consumption were collected for various age groups as described in the survey and study summaries below.

[15] Health Canada's Category Specific Guidance for Temporary Marketing Authorization: Caffeinated Energy Drinks (March 2012) set a daily maximum level of 50 mg/day for the addition of pantothenic acid to energy drinks.

[16] In males, this would result in a daily dose of 5.5 mg/kg bw (= 441 mg of caffeine/ 80 kg bw = 281 mg of caffeine + 160 mg from 2 servings of energy drinks / 80 kg bw) and in females in a daily dose of 6.0 mg/kg bw (= 390 mg of caffeine / 65 kg bw = 230 mg of caffeine + 160 mg from 2 servings of energy drinks / 65 kg bw).

5.2 International survey data

Data from the European Commission (EC 1999) indicated that 9% of the population could be described as 'regular consumers' of energy drinks, with intake by these consumers likely to be in the order of 500 ml per day (2 x 250 ml cans).[17]

An Australian survey assessed the incidence of consumption of energy drinks within a two-week period in 1999. However, this study did not record quantities consumed or frequency of consumption. The results from this survey are given in Table 7.

Sample	% Consumers
141	27% males aged 8-12 years 12% females aged 8-12 years
240	24% males aged 12- 18 years 20% females aged 12- 18 years

Table 7. Energy drink consumption in Australia in a Two Week Period during 1999

New Zealand data are available from the Panorama survey of 12 000 respondents aged 10 years and over, conducted by ACNielsen in 1999. Two hundred and sixty-four (264) individuals aged 10 to 14 years were interviewed regarding their consumption of energy drinks, and the resultant data for the 64 (24%) who reported drinking them are presented in Table 8.

Consumption rate	No. consumers	Percentage 10-14 year olds
At least once per day	6	2
Once a week	21	8
At least once a month	37	4

Table 8. Energy drink consumption in New Zealand by 10 to 14 year olds

In 2001, Red Bull Gmbh conducted a survey of energy drink consumption in Austria. The survey was conducted on 8500 Austrians aged 15 years and over. Forty-two percent of the sample consumed energy drinks at least occasionally and 12% were regular users which were defined as those who consumed at least one energy drink per week. For the surveyed population, mean chronic consumption, chronic consumption at the 95th percentile, and acute consumption at the 90th percentile were approximately 0.47 cans per day, 1.4 cans per day and 2.6 cans per day, respectively (1 can = 250 mL).

A market research survey of 1260 people aged 11-35 years was conducted in Northern Ireland and the Republic of Ireland in 2001. The results of the survey were similar to those obtained in the Austrian survey. In Northern Ireland and Republic of Ireland respectively, 51% percent and 37% of participants reported 'ever' consuming energy drinks and 10% and 11% reported consuming energy drinks frequently. Among 'ever' consumers, average consumption was 3 (250mL) cans/week and for the 95th percentile consumers, it was 8 cans/week. The most number of cans consumed in a single session among 'ever' consumers averaged approximately 3 cans, rising to 8 cans among the highest consumers; the comparable figure for 11-14 year-olds was approximately 2 cans.

In the Ireland survey, energy drink consumption was strongly related to alcohol consumption. Among those who ever consumed energy drinks, 84% of all respondents had consumed the drink with alcohol, while 56% reported consuming the drinks with alcohol regularly.

O'Dea (2003) conducted a study to obtain qualitative data about the type of nutritional supplements and drinks consumed by adolescents in Australia. Semi-structured focus group interviews were conducted among 78 participants aged 11-18 years. Participants reported consuming sport drinks, a number of nutritional supplements and energy drinks. Results of the study indicated that adolescents appear to be incorrectly attributing the 'creation' of energy to these supplements when the actual effect is a stimulant effect caused by caffeine, and other stimulants in products such as energy drinks. The author noted that many of the misguided 'energy creation' beliefs may be attributed to information provided to consumers in advertising and marketing of these products. According to the author, the adolescents in the study had deliberately sought an 'energy boost', and had received it in the form of a stimulant effect from the caffeine-containing supplements and drinks.

Malinauskas et al. (2007) conducted a survey of energy drink consumption patterns among United States college students wherein consumption patterns of 496 randomly surveyed college students were assessed. Fifty one percent of those surveyed reported consuming greater than one energy drink each month in an average month for the semester. The majority of users consumed energy drinks for insufficient sleep (67%), to increase energy (65%), and to drink with alcohol while partying (54%). The majority of users consumed one energy drink in most situations, although consuming three or more with alcohol while partying was a common practice (49%). For the majority of students (73-86%), energy drinks were consumed 1-4 days in a month. Five to 12% of students consumed energy drinks eleven or more days a month.

[17] While this manuscript was in preparation, the European Food Safety Authority (EFSA) released a study, Gathering consumption data on specific consumer groups of energy drinks. (Zucconi et al., 2013), detailing the consumption of energy drinks by Europeans.

5.3 Canadian survey data

Based on the most recent Canadian Community Health Survey (CCHS), 2004, a determination of daily exposure levels is not possible due to the limited reporting of energy drink consumption in that survey.

ACNielsen carried out surveys from 2006-2009 to provide national sales and consumer purchase and demographic data for Natural Health Products (NHPs) of interest. While the ACNielsen data offer an indication of the relative size, strength and demand for energy drinks in Canada, the data do not provide sufficient information to determine daily consumption levels of energy drinks by Canadians.

5.4 Summary

The Canadian and international consumption data for energy drinks are considered very limited. In addition, international data that are available from early 2000 may not reflect current energy drink consumption patterns in Canada as these products have become much more pervasive in the Canadian marketplace in recent years.

6. Modelling Exposure Scenario

The health risk assessment of the ingredients in a typical energy drink determined that caffeine has the greatest potential to present a hazard. A single 250 ml serving of a typical energy drink contains 80 mg of caffeine. Although this amount is half the 160 mg of caffeine that a single 250 ml serving of coffee can contain, it is double the 40 mg present in a 355 ml serving of a caffeinated carbonated soft drink (CSD). In any case, the amount of caffeine in a typical energy drink can make a significant contribution to the total dietary caffeine intake.

In order to determine the total dietary intake of caffeine, Health Canada accessed data on the consumption of a wide variety of foods, including foods containing caffeine, by various age groups (Statistics Canada, Canadian Community Health Survey Cycle 2.2., 2004). Using food intake data from this survey, caffeine consumption was determined from all food sources, including coffee, tea and soft drinks. However, intake data specific to energy drinks were not available because there was an insufficient number of respondents who reported energy drink consumption in the 2004 survey. In the absence of intake data specific to energy drinks, the patterns of potential exposure to components of energy drinks can be determined from intake data for a food for which consumption can be assumed to be similar to that of energy drinks. In the following exposure assessment patterns, intake data for caffeinated carbonated soft drinks were used as surrogate data for energy drinks in order to generate possible patterns of an exposure model that includes energy drinks.

Age in years (gender)	Median intake for All persons (consumers and non-consumers of CSDs) (mg/kg bw/day)	Median intakes for All persons (consumers and non-consumers of CSDs) if EDs substituted for CSDs by volume (mg/kg bw/day) [1]	Median intake for consumers of CSDs (mg/kg bw/day)	Median intakes for consumers of CSDs if EDs substituted for CSDs by volume (mg/kg bw/day) [1]
2-3	0.06	0.06	0.98	2.62
4-5	0.13	0.13	1.18	3.19
6-8	0.14	0.14	1.35	3.41
9-11 (male)	0.15	0.15	1.19	2.94
9-11 (female)	0.14	0.14	0.97	2.46
12-14 (male)	0.18	0.18	1.05	2.81
12-14 (female)	0.15	0.15	0.86	2.65
15-16 (male)	0.37	0.47	1.00	2.57
15-16 (female)	0.17	0.17	1.08	2.89
17-19 (male)	0.55	1.26	1.17	2.55
17-19 (female)	0.62	0.95	0.98	2.75
20+ (male)	2.23	2.66	2.67	4.19
20+ (female)	2.21	2.46	2.70	4.07
Pregnant	0.48	0.53	1.19	2.18

[1] Caffeinated carbonated soft drinks were substituted with energy drinks on a volume basis. The caffeine concentration of caffeinated carbonated soft drinks ranged from 73 to 140 ppm and of energy drinks was 320 ppm.

Table 9. Exposure modelling of *total dietary* caffeine intake for (1) All persons (consumers and non-consumers of caffeinated carbonated soft drinks (CSDs)), (2) All persons, if all CSDs are replaced by typical energy drinks (EDs), (3) Consumers of CSDs, (4) Consumers of CSDs if all CSD consumption is replaced by typical energy drinks

The absence of consumption modelling for energy drinks is acknowledged. Therefore, the model below would be more a representation of a worst case scenario, as opposed to a description of an expected consumption pattern. Other factors such as taste, cost and the time between servings (binging) may ultimately influence the least conservative and the worst case models for energy drink consumption.

Age in years (gender)	RMDI [1] (mg/kg bw/day)	Median intake for All persons for CSDs (mg/kg bw/day)	% of All persons exceeding RMDI	Median intakes for All persons if CSDs substituted with EDs (mg/kg bw/day) [2]	% of All person exceeding RMDI if CSDs substituted with EDs
2-3	2.5	0.06	2.3	0.06	4.9
4-5		0.13	3.5	0.13	7.8
6-8		0.14	3.1	0.14	8.2
9-11 (male)		0.15	3.8	0.15	13.2
9-11 (female)		0.14	2.9	0.14	9.1
12-14 (male)		0.18	3.4	0.18	17.2
12-14 (female)		0.15	2.4	0.15	21.9
15-16 (male)		0.37	6.7	0.47	21.5
15-16 (female)		0.17	10.3	0.17	20.8
17-19 (male)		0.55	14.6	1.26	30.9
17-19 (female)		0.62	17.8	0.95	27.6
20+ (male)	6.0	2.23	14.3	2.66	17.5
20+ (female)		2.21	13.0	2.46	15.2
Pregnant	4.6	0.48	4.7	0.53	5.4

[1] RMDI is the recommended maximum daily intake.

[2] Caffeinated carbonated soft drinks were substituted with energy drinks on a volume basis. The caffeine concentration of caffeinated carbonated soft drinks ranged from 73 to 140 ppm and of energy drinks was 320 ppm.

[3] Figures in **bold** equal or exceed the RMDI for caffeine intake for that age group.

Table 10. Potential Health Risk for (1) All persons (consumers and non-consumers of caffeinated carbonated soft drinks (CSDs), (2) All persons if all CSD consumption is replaced by typical energy drinks (EDs)

Table 9 shows exposure to caffeine for all persons and for consumers of caffeinated carbonated soft drinks in various age groups, expressed as mg/kg bw/day. Median caffeine intake from all dietary sources is depicted for consumers of soft drinks containing caffeine at "current market use" levels. Table 9 also shows the median dose of caffeine from all dietary sources for all persons and consumers of caffeinated carbonated soft drinks, if energy drinks were substituted for caffeinated carbonated soft drinks on a volume basis ("substituted by volume"). This is not to be construed as an estimate of exposure in the true population since energy drink consumption is likely to be less on a volumetric scale than caffeinated carbonated soft drinks.

Age in years (gender)	RMDI [1] (mg/kg bw/day)	Median intake for consumers of CSDs (mg/kg bw/day)	% of CSD consumers exceeding RMDI	Median intakes for CSD consumers if CSDs substituted with EDs (mg/kg bw/day) [2]	% exceeding RMDI if CSDs substituted with EDs
2-3	2.5	0.98	3.3	**2.62** [3]	56.8
4-5		1.18	8.3	**3.19**	68.9
6-8		1.35	13.5	**3.41**	62.9
9-11 (male)		1.19	14.0	**2.94**	61.3
9-11 (female)		0.97	7.3	**2.46**	46.7
12-14 (male)		1.05	8.2	**2.81**	59.3
12-14 (female)		0.86	6.7	**2.65**	55.7
15-16 (male)		1.00	12.6	**2.57**	52.0
15-16 (female)		1.08	20.4	**2.89**	60.6
17-19 (male)		1.17	19.6	**2.55**	59.0
17-19 (female)		0.98	17.3	**2.75**	54.1
20+ (male)	6.0	2.67	16.2	4.19	29.4
20+ (female)		2.70	15.5	4.07	28.1
Pregnant	4.6	1.19	9.7	2.18	14.9

[1] Recommended Maximum Daily Intake. Adolescents are conservatively assumed to have a RMDI equal to children.

[2] Caffeinated carbonated soft drinks were substituted with energy drinks on a volume basis. The caffeine concentration of caffeinated carbonated soft drinks ranged from 73 to 140 ppm and of energy drinks was 320 ppm.

[3] Figures in **bold** equal or exceed the RMDI for caffeine intake for that age group.

Table 11. Potential Health Risk for (1) Consumers of caffeinated carbonated soft drinks (CSDs), (2) Consumers of CSDs if all caffeinated carbonated soft drink consumption is replaced by typical energy drinks (EDs)

7. Potential Health Risk

The potential health risk posed by the caffeine in energy drinks can be characterized by considering the hazard due to caffeine and the potential exposure to all sources of dietary caffeine, including energy drinks, within an age group or subgroup of the population.

Health Canada used scientific data on the health hazard posed by caffeine to establish recommended maximum daily intake (RMDI) values for children (2.5 mg/kg bw/day), adults (6.0 mg/kg bw/day) and women of reproductive age (4.6 mg/kg bw/day). There are

insufficient data to determine a separate RMDI for adolescents. As a precautionary approach, adolescents can be considered to be as sensitive as children to caffeine, in which case, the RMDI for children can be conservatively applied to adolescents.

The results of exposure modelling indicate that the median total dietary caffeine intake by all consumers (Table 10) and by consumers of caffeinated carbonated soft drinks (Table 11) do not exceed the RMDI in any of the age groups. The situation for median intake remains essentially unchanged for all persons when energy drinks are substituted for caffeinated carbonated soft drinks, that is no age group exceeds its RMDI (Table 10). In contrast, when energy drinks are substituted for caffeinated carbonated soft drinks, the median total dietary caffeine intake by CSD consumers in every population group of children and adolescents meets or exceeds its RMDI, while those of adults and pregnant women do not (Table 11). The results also show that the percentage of consumers in each population group who exceed their RMDI increases dramatically when energy drinks are substituted for caffeinated carbonated soft drinks both for all persons (Table 10) and CSD consumers (Table 11). For example, the greatest increase (from 3% to 57%) in the percentage of CSD consumers who exceed their RMDI is observed in 2- to 3-year-olds (although it is considered that this scenario would be highly unlikely, given that this age group would normally not be given energy drinks to consume) (Table 11).

Using the data from Tables 10 and 11, a comparison for exposure modelling purposes is made in Table 12 of the percentage of all persons and consumers of CSDs who exceed their RMDI for caffeine under two scenarios. The first scenario assumes current market use, while the second assumes that all CSDs were replaced with energy drinks. Since only a portion of any given population group consumes CSDs, the percent of CSD consumers that exceeds the RMDI for that population group can be much greater than the percentage of all persons that exceed the RMDI. For example, among 2- to 3-year-olds, only 6% consume CSDs. Replacing CSDs with energy drinks in this age group brings the percentage of consumer who exceed the RMDI to 57 % compared to only 5% of all persons who do so.

The previous section presented a worst case exposure scenario in which the consumption of energy drinks was patterned after that of caffeinated carbonated soft drinks and resulted in more than 50% of children and adolescents, about 30% of adults and 15% of pregnant females exceeding their respective recommended maximum daily intake (RMDI) for caffeine. It is important to assess how realistic this worst case exposure scenario is.

		All persons (consumers and non-consumers of CSDs)		**Consumers of CSDs**	
Age in years (gender)	Percent consuming CSDs[1]	% All persons, including CSD consumers, exceeding RMDI[2]	% exceeding if CSDs substituted with EDs by volume	% CSD consumers whose total dietary caffeine intake exceeds the RMDI	% exceeding if CSDs substituted with EDs by volume
2-3	6%	2.3	4.9	3.3	56.8
4-5	7%	3.5	7.8	8.3	68.9
6-8	12%	3.1	8.2	13.5	62.9
9-11 (male)	19%	3.8	13.2	14.0	61.3
9-11 (female)	16%	2.9	9.1	7.3	46.7
12-14 (male)	29%	3.4	17.2	8.2	59.3
12-14 (female)	22%	2.4	21.9	6.7	55.7
15-16 (male)	36%	6.7	21.5	12.6	52.0
15-16 (female)	25%	10.3	20.8	20.4	60.6
17-19 (male)	40%	14.6	30.9	19.6	59.0
17-19 (female)	27%	17.8	27.6	17.3	54.1
20+ (male)	24%	14.3	17.5	16.2	29.4
20+ (female)	16%	13.0	15.2	15.5	28.1
Pregnant	18%	4.7	5.4	9.7	14.9

[1] Data from The Canadian Community Health Survey B Cycle 2.2 on Nutrition, Statistics Canada, 2004.

[2] RMDI is the recommended maximum daily intake. The value for children, adults and pregnant females are 2.5, 6.0 and 4.6 mg/kg bw/day, respectively. Adolescents are conservatively assumed to have a RMDI equal to children.

Table 12. A comparison of percent of total dietary caffeine intakes that exceed the caffeine RMDI between (1) consumers of caffeinated carbonated soft drinks (CSDs), with or without energy drink substitution; and (2) "all persons" (consumers and non-consumers of CSDs), with or without energy drink substitution.

It may be reasonably argued that the diet of children (2-11 years old) is monitored and that parents, knowing the potential of adverse effects of excessive caffeine, are unlikely to permit these beverages in their children's diet. Further, young children (2-8 years old) do not readily have the ability to purchase these products, which are therefore much less likely to be part of their diet. The percentage of children exceeding the RMDI for caffeine from the consumption of energy drinks is therefore very

unlikely to be in the range of 48 to 69% as indicated in Table 11 and 12, which is based on the scenario that energy drinks would replace caffeinated carbonated soft drinks for this age group.

It can also be argued that adults (20 years and older) are capable of monitoring their own caffeine intake and would recognize the acute adverse events associated with excess caffeine intake and then moderate their consumption accordingly. Excess energy drink consumption would result in similar effects as excess coffee consumption (a typical energy drink contains 80 mg of caffeine per 250 ml compared to cup of coffee with 76-180 mg of caffeine per 237 ml). Similarly pregnant women are capable of monitoring their own caffeine intake. For these reasons, it is unlikely that the worst case exposure scenario would apply to these groups within the general population.

Adolescents (12-19 years old) present a more complicated situation. In the absence of adequate safety data to establish a RMDI of caffeine for adolescents, Health Canada followed a precautionary approach and applied the maximum daily dose recommended for children (2.5 mg/kg bw/day) to adolescents. The application of the children's RMDI to adolescents is likely very conservative. There is no compelling safety reason to suggest that 19-year-old adolescents can only consume 2.5 mg/kg bw/day of caffeine whereas adults (20 years and older) can consume 6 mg/kg bw/day. It is more likely that adolescents could increase their maximum daily intake of caffeine from 2.5 to 6 mg/kg bw/day as they mature without appreciable health risks. Nevertheless, in the absence of data to allow the establishment of a specific RMDI for adolescents, it was considered prudent to set the maximum recommended daily intake of caffeine by adolescents closer to that recommended for children than that recommended for adults.

In the worst case exposure scenario, described in the previous section, the percentage of adolescents who exceeded their RMDI ranged from 47% to 61% of caffeinated carbonated soft drinks consumers, depending on age and gender (Table 12). As suggested in the paragraph above, it is likely most adolescents can tolerate greater amounts of caffeine than their RMDI. As shown in Table 11, the median intakes of caffeine by subgroups of adolescents are less than 3.0 mg/kg bw/day, and therefore only slightly greater than the RMDI of 2.5 mg/kg bw/day.

The intake in excess of the RMDI is similar to what an adolescent (12-19 years old) who drank a cup of strong coffee (180 mg of caffeine/237 ml) would be exposed to. For example, the caffeine intake from a single cup of coffee would result in a dose of 3.14 and 2.8 mg/kg bw/day for an adolescent female (about 57 kg bw) and male (about 64 kg bw) respectively. Since these caffeine intakes are very close to the conservative recommended maximum daily intake of 2.5 mg/kg bw/day, they would be unlikely to pose a health hazard.

One or two servings of a typical energy drink (80 mg of caffeine/serving) would therefore be unlikely to pose an acute health hazard based on caffeine content. However, it is known that some very young (12-14 year) adolescent males (about 56 kg bw) and females (about 52 kg bw) will consume a large volume of carbonated soft drink in a single episode, about 760 ml and 519 ml, respectively (Canadian Community Health Survey 2.2, 2004). This is further corroborated by the prevalence of larger volumes of energy drink cans, in comparison to other soft drink cans (710 ml cans versus 355 ml cans). If this pattern of consumption is applied to energy drinks, then there could be very young adolescents who drink two containers of a 250 ml energy drink, or one container of a 473 ml energy drink, and young adolescent males who could drink a full 710 ml energy drink in a single episode. Given the amount of caffeine in typical and some non-typical energy drinks, these adolescents could have excessive caffeine intake, especially when consuming large format energy drinks.

Given that marketing for energy drinks tend to target some subsets of adolescents, that they are capable of purchasing these products (unlike children), and are less familiar with adverse effects of excessive caffeine (unlike adults), it is reasonable to conclude that the caffeine present in energy drinks could pose a health risk for adolescents.

7.1 Summary

Based on the hazard characterisation of each of the ingredients in a typical energy drink, as defined in Table 1, it was determined that the exposure assessment should focus on caffeine. However, limited information is available to date on actual consumption of energy drink products in Canada. Research is being considered to fill consumption data gaps and to provide further insights into whether the label instructions related to consumption advice on energy drinks are effective (i.e. are followed).

In the absence of critical consumption data, exposure modelling was conducted by substituting, on a volume basis, energy drinks for caffeinated carbonated soft drinks, for which there is intake data. This approach conservatively assumes that energy drinks are consumed in a manner similar to that for caffeinated carbonated soft drinks, and that energy drink label instructions are not followed. It also assumes that a volume basis of substitution is a more likely than a serving basis of substitution.

The results of the exposure assessment that considered a worst case scenario determined that of the consumers

who replace caffeinated carbonated soft drinks with energy drinks, more than 50% of children and adolescents, about 30% of adults and 15% of pregnant females would exceed their respective recommended maximum daily intakes of caffeine and therefore may be susceptible to the adverse effects associated with excess caffeine consumption. Consumers of caffeinated carbonated soft drinks represent roughly 8% of young children (1- 8 years old), 22% of older children (9-14 years old), 32% of adolescents, 20% of the adult population and 13% of pregnant females.

The amount of caffeine in energy drinks would pose a health concern if consumed by children (2-11 years old). However, parents are likely to be aware that excessive caffeine can be harmful and would keep energy drinks out of their children's diets. Energy drinks are therefore not a health concern for this age group.

Adults (20 years and older) and pregnant women are capable of monitoring their own caffeine intake. They would recognize acute adverse events associated with excess intake and moderate their consumption accordingly.

The situation of adolescents (12-18 years old) is more complex. Because of inadequate safety data currently available, Health Canada conservatively applied the RMDI for children (2.5 mg/kg bw/day) to this age group using a worst case scenario (patterning energy drink use on caffeinated carbonated soft drink consumption) to determine potential health risk. The percentage of adolescents who exceeded their RMDI ranged from 47% to 61% of caffeinated carbonated soft drinks consumers. But, at less than 3.0 mg/kg bw/day, median intakes were only slightly greater than the RMDI and likely to be tolerated. The caffeine content of one or two servings of a typical energy drink (80 mg caffeine/serving) would be unlikely to pose an acute health hazard.

However, some young adolescents (12-14 year) consume large volumes of caffeinated carbonated soft drinks (up to 760 ml) in a single episode. Applying this pattern of consumption to energy drinks could result in excessive caffeine intake by a proportion of young adolescents.

In conclusion, the modelling exposure scenario as applied to children and adults is unlikely to represent a realistic health risk. However, for adolescents the likelihood of a health risk is greater, which may reflect the conservative assumptions made about this subpopulation.

8. Overall Summary and Conclusions

The purpose of this document is to provide a health risk assessment of energy drink products when they are consumed as foods in Canada.

In this document a typical energy drink formulation was defined by its ingredients and serving size, where a single can serving of 250 ml contains 80 mg of caffeine, 1000 mg of taurine, 600 mg of glucuronolactone and several B vitamins.

The literature on health effects of energy drinks is limited to less than a dozen studies, each with a small number of subjects (N< 50 subjects/study). These studies demonstrate that consuming 1-2 servings of a typical energy drink formulation will temporarily increase alertness and attentiveness, as well as temporarily increase blood pressure and heart rate, in a manner similar to other caffeinated beverages.

Studies that examine energy drink use prior to exercise showed that it may enhance physical endurance. In contrast, the consumption of an energy drink after exercise may result in a delay of the return to a resting heart rate.

Studies also suggest that the combined consumption of energy drinks and alcohol may pose a health risk. The potential consequence is that a person consuming an energy drink with alcohol may become intoxicated more quickly and may be less aware of their physical impairment, which may lead to risky behaviour, such as excessive alcohol consumption. At present, clear evidence supporting this suggestion is lacking but it merits further investigation.

It was concluded that the published information available on energy drinks was insufficient to characterize the hazard that this product as a whole may pose. For this reason, a review of each of the major ingredients contained in a typical energy drink was conducted, i.e., the potential health effects of caffeine, taurine, glucuronolactone, inositol and the B vitamins were assessed. In doing so, and in contrast with previously published information, the adverse reaction data related to each of the ingredients in the formulation that were presented in this document attempted to reflect to the extent possible "the real world use" of the products as formulated, in various user populations.

With respect to caffeine, an earlier review conducted by Health Canada's Food Directorate concluded that a healthy adult could tolerate a maximum intake of 400 mg caffeine per day, which could be equivalent to 5 servings of a typical energy drink per day. This amount of caffeine was not associated with adverse effects such as general toxicity, cardiovascular effects, effects on bone status, changes in behaviour, effects on male fertility or increased incidence of cancer development. Further, the study concluded that reproductive-aged women could tolerate a maximum intake of 300 mg caffeine per day, based on reproductive considerations. It was also concluded that children, aged 4

to 12 years, could tolerate a maximum of 45 to 85 mg of caffeine per day, based on transient mild behaviour changes. Concerning adolescents, aged 13 to 18 years, there were insufficient data to determine a daily maximum intake of caffeine. However, the adult recommended maximum daily intake was considered inappropriate since many adolescents have a lower body weight than the average adult, but more importantly the growing adolescent was considered to be more sensitive to caffeine. Due to this uncertainty, it was more recently concluded that, as a precaution, adolescents should consume a dose no greater than that for children (2.5 mg/kg bw/day). At this dose, adolescents could consume 100 to 175 mg of caffeine daily, depending on the individual body weight (estimated to range from 40–70 kg). Lighter-weight adolescents (40 kg bw) would meet the suggested maximum intake of caffeine with slightly more than a single serving of a typical energy drink, whereas heavier teens (70 kg) could consume 2 servings per day in the absence of other sources of dietary caffeine.

Taurine, glucuronolactone and inositol were considered to be normal constituents of the diet and easily handled by ordinary metabolic processes. While generally considered to be of very low or low toxicity, there was some uncertainty about the safety of the levels of these substances in a typical energy drink, since the levels of some greatly exceeded the amount consumed through a normal diet. For example, a high dietary intake of taurine is estimated to be 400 mg/adult/day, whereas the intake from 5 servings of a typical energy drink would provide 5000 mg/adult /day. Glucuronolactone has an estimated daily dietary intake of 2.3 mg/adult/day, compared to the 3000 mg/adult/day intake from 5 servings of a typical energy drink. Based on a review of 90-day feeding studies in laboratory animals, knowledge of the metabolism of these two substances and information about their experimental therapeutic use, it was concluded that no hazard was demonstrated at the level of 5 servings per day in the short-term; however, long-term use in the diet posed an uncertainty. Further, there was uncertainty about the possible interaction of taurine with caffeine on the nervous system.

Concerning the B vitamins, it was concluded that the consumption of 5 servings of a typical energy drink per day would not exceed the tolerable upper limit of most of these vitamins and they would be unlikely to pose a health risk in the short term. There is uncertainty in the safety of life-long consumption at this level since the rest of the diet would also contribute to the total intake of these substances, which could lead to excessive intake and potential adverse health effects. Niacin, which can be present as nicotinamide or nicotinic acid, was a unique case. When present as nicotinic acid, the amount in 1 serving of a typical energy drink (20 mg) was not greater than the tolerable upper limit for niacin (35 mg/adult/day) and is unlikely to pose a health concern. However, the consumption of 2 servings per day could potentially result in flushing. In contrast, when niacin is present as nicotinamide, there are no health concerns at the consumption level of 5 servings per day, since some jurisdictions have tolerable upper limits of nicotinamide up to 900 mg/adult/day.

Based on caffeine content alone, it could be suggested that a healthy adult could consume up to 5 servings of a typical energy drink per day in the absence of any other dietary source of caffeine. A typical energy drink contains 80 mg of caffeine and 5 servings would be equal to 400 mg, the maximum daily intake of caffeine for an adult. Five servings per day would be equal to 5000 mg of taurine, 3000 mg of glucuronolactone and 300 mg of inositol. Considered individually, these ingredients consumed at these levels would not be expected to cause adverse effects in the short-term, based on animal studies. However, long-term studies on taurine and glucuronolactone have not been conducted. In the absence of such studies, a better understanding of the human metabolism and physiological impact of these high doses would be required to increase confidence in the conclusion that those levels would not likely cause adverse effects.

In conclusion, consuming 5 servings per day for an adult, where a serving is represented by 250 ml of the typical energy drink product formulation, cannot be recommended based on possible exposure to other dietary sources of caffeine, uncertainties about the long-term effects of some ingredients, the potential interaction between ingredients and the impact of chronic consumption of high levels of certain B vitamins (see table in Appendix I).

Despite the uncertainties about possible interactions between some of the ingredients, 2 servings of a typical energy drink per day would not be expected to pose a health risk for the general adult population. This conclusion was based on the safety of the non-caffeine ingredients of energy drinks at this level of consumption and the fact that caffeine from other dietary sources in addition to that in 2 servings of energy drinks would not exceed Health Canada's recommended maximum daily intake of caffeine for the general adult population. The consumption of energy drinks by other sub-groups would need to be limited based on the respective recommended maximum daily intake of caffeine. However, it can be noted that current caffeinated energy drink product labels do not recommend consumption by children, pregnant or breastfeeding women, or caffeine-sensitive persons.

This assessment would also apply to other energy drinks, described in this report, which contain major ingredients at levels greater than those in the typical formulation of

energy drink products. These products may be consumed by adults at a level equivalent to 2 servings of a typical energy drink. However, there is uncertainty about the safety of consuming greater amounts of these other formulations**.** It was also noted that several products contain other bioactive ingredients such as nutrients (e.g. folic acid) or other herbal or natural extracts (e.g. ginkgo biloba). These other formulations would need to be reviewed on a case-by-case basis.

Exposure data to energy drinks in Canada are limited, in that consumption information is not reliable based on Canadian survey data. In the absence of estimates of real consumption data, the health risk posed by energy drinks due to the caffeine content was estimated by modelling exposure using caffeinated soft drink consumption data as a surrogate for energy drink consumption.

In a worst case modelling exposure scenario, energy drinks were substituted for caffeinated carbonated soft drinks on a volume basis and the energy drink caffeine concentration set to 320 ppm for modelling purposes. The results showed that of the consumers who drink caffeinated carbonated soft drinks, more than 50% of the children and adolescents would be above the recommended maximum daily caffeine intake if all carbonated soft drinks were replaced by a typical energy drink. Further, slightly less than 30% of male and female adults and about 15% of pregnant females would exceed the Health Canada's recommended maximum daily intake for caffeine. Consumers of caffeinated carbonated soft drinks are however only a subset of the population and represent roughly 8% of young children (1- 8 years old), 22% of older children (9-14 years old), 32% of adolescents, 20% of the adult population and 13% of pregnant females.

Although the intake modeling showed that children (2-11 years old) would exceed Health Canada's recommended levels for caffeine, the corresponding health concern is limited, given, that children are less likely to obtain these products on their own and that parents are expected to keep energy drinks out of their children's diets. It was also concluded that adults (20 years and older) and pregnant women are capable of monitoring their own caffeine intake. They would also be more likely to recognize acute adverse events associated with excess intake and moderate their consumption accordingly.

Applying these hypothetical consumption patterns of energy drinks to adolescents has identified a potential to exceed the recommended caffeine intake by a significant proportion of young adolescents. These scenarios could not be excluded, given that energy drinks tend to be marketed to adolescents who (unlike children) are capable of accessing these products, including the larger volumes, but may be less likely than adults to adhere to consumption recommendations. Attention may therefore be warranted as to the levels of caffeine present in energy drink products made available for sale in a large volume container (710 ml), which are becoming prevalent and likely to be consumed by this subset of the population.

Specific risk management measure to address potentially high caffeine levels in larger volume energy drink products would help mitigate some risks associated with exceeding Health Canada's maximum recommended caffeine intake in one consumption setting.

Health Canada's proposed risk management approach for energy drinks announced in October 2011 (http://hc-sc.gc.ca/ahc-asc/media/nr-cp/_2011/2011-132-eng.php) and updated in 2012 (http://hc-sc.gc.ca/fn-an/legislation/guide-ld/guidance-caf-drink-boiss-tma-amt-eng.php) helps address a number of these concerns, through setting caffeine concentration limits, total caffeine amount limits, and maximum levels of vitamins, minerals and other formulation constituents. Caffeine and other nutrition labelling requirements were also imposed. These measures contribute to mitigating some of the risks related to the consumption / overconsumption of energy drink products in those areas where intervention is possible by a federal food regulator within the Canadian food regulatory system.

Given the behavioural aspects related to some of the potential risks - co-consumption with alcohol, over exposure to caffeine due to excessive and uninformed consumption – it is acknowledged that other areas of intervention, such as responsible marketing and advertising, as well as education and awareness, would be required in a concerted fashion.

More research and surveillance would be required to ascertain the effectiveness of the various facets of the proposed risk management approach.

Various data gaps have been noted in this assessment, in particular:

-Data that support the hazard characterisation in particular as they pertain to possible interaction of the effects of the various active ingredients in energy drink product formulation (e.g. the combined effect of taurine and caffeine at high consumption levels)

- Data that support an improved characterisation of energy drink consumption patterns in Canada by various population subsets (e.g. older children and adolescents).

Efforts are currently underway to initiate research activities enabling some aspects of the data collection. This assessment will therefore be updated upon availability of new Canadian data and taking into account any new findings on the safety of energy drinks domestically and internationally.

9. Appendix 1

Ingredient	Required daily intake	Daily dietary intake	Amount per serving	Amount per 2 servings	Amount per 5 servings	Upper tolerable limit (UL)/Maximum recommended intake (MRI)/Maximum Limit (ML)	Other safety data
Caffeine	Not applicable	160 mg	80 mg	160 mg	400 mg	400 mg = MRI	
Taurine	Not applicable	40 – 400 mg	1000 mg	2000 mg	5000 mg	Not established	6000 mg/day = NOAEL in 42 day human study 1000 mg/kg bw/day = NOAEL in 90-day rat study
Glucuronolactone	Not applicable	1.2- 2.4 mg	600 mg	1200 mg	3000 mg	Not established	3000 mg/day = NOAEL as experimental therapy in human 1000 mg/kg bw/day= NOAEL in 90-day rat study
Inositol	Not applicable	500-1000 mg	50 mg	100 mg	250 mg	Not established	18000 mg/day = NOAEL in 42 day therapy in human study 6000 mg/kg bw/day = NOAEL in 24 week mouse study
Thiamine	1.1-1.2 mg	4 mg	5 mg	10 mg	25 mg	40 mg = ML	Little danger of thiamine toxicity associated with oral intake of large amounts (500 mg daily for 1 month)
Riboflavin	1.1-1.3 mg	4.5 mg	1.65 mg	3.30 mg	8.25 mg	20 mg = UL	50 mg/kg bw/day = NOAEL in 13 week feeding study in rats. No published data with toxic effects in humans.
Niacin (as nicotinamide)	16 mg	77 mg	18 mg	36 mg	90 mg	900 mg = UL	3-9 g/day nicotinamide for several days resulted in nausea in single subject and hepatitis in another subject.
Vitamin B6	1.3-1.7 mg	0.9-4.5 mg	2 mg	4 mg	10 mg	Not established	100 -500 mg causes neurological symptoms
Vitamin B12	2.4 mcg	2-6 mcg	1 mcg	2 mcg	5 mcg	20 mcg = ML	Oral and parenteral supplementation with dosages between 1-5 mg every 2 weeks or month have been given for up to at least 5 years, in patients with compromised vitamin B12 absorption, without any identified adverse effects.
Pantothenic Acid	5 mg	3-12 mg	6 mg	12 mg	30 mg	20 mg = ML	10000 mg causes gastrointestinal effects in humans
Notes: MLs for thiamine, vitamin B12 and pantothenic acid were specifically assigned to energy drinks by NHPD. These figures are not ULs or MLs for these B vitamins for the total diet. UL for niacin was determined by the European Community.							

Table A1. Summary of Safety Assessments of the Ingredients in a Typical Energy Drink

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