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DE SÉCURITÉ SANITAIRE
DES ALIMENTS

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OPINION

of the French Food Safety Agency on a draft order regarding the use of taurine and D-glucurono-gamma-lactone in non-alcoholic beverages

THE DIRECTOR GENERAL

Review of the request:

On Friday, 29 May 2009 the Directorate General for Competition, Consumer Affairs and Fraud Control (DGCCRF) requested that the French Food Safety Agency (AFSSA) assess a draft order regarding the use of taurine and D-glucurono-gamma-lactone in non-alcoholic beverages.

This draft order states that:

1. the addition of taurine and D-glucurono-gamma-lactone to non-alcoholic beverages shall be authorised under the following conditions:

- when taurine is added to a non-alcoholic beverage, the total amount of taurine in that non-alcoholic beverage shall not exceed 4000 mg per litre;
- when D-glucurono-gamma-lactone is added to a non-alcoholic beverage, the total amount of D-glucurono-gamma-lactone in that non-alcoholic beverage shall not exceed 2400 mg per litre;

2. the labelling for drinks containing taurine and D-glucurono-gamma-lactone, alone or in combination, shall bear the words:

“Consume in moderation”

“Not recommended for children and pregnant women”

After consulting the Scientific panel on ‘Human nutrition’, on 9 July and 24 September 2009, AFSSA is issuing the following Opinion:

Context of the request:

The request letter states that Article 4 of Decree no. 2006-1264 on vitamins, mineral substances and other substances used in manufacturing foodstuffs stipulates that an Order must name the substances that have been authorised for use in the foodstuffs in accordance with Articles 2 and 3 of the above-mentioned decree.

The request also falls within the scope of Regulation 1925/2006 on the addition of vitamins, minerals and certain other substances to foodstuffs.

The fortification levels proposed for the addition of taurine and D-glucurono-gamma-lactone to non-alcoholic beverages are identical to those found in what are referred to as ‘energy’ drinks, previously assessed by AFSSA. Note that the term ‘energy’ drinks does not refer to any regulatory definition and does not correspond to any physiological reality.

27-31, avenue
du Général Leclerc
94701

Maisons-Alfort cedex
Tel 01 49 77 13 50
Fax 01 49 77 26 13
www.afssa.fr

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Background

➤ On the national level

In 1996, the French High Council for Public Hygiene (CSHPF) delivered an unfavourable Opinion on the sale of 'energy' drinks containing taurine (4000 mg/L) and D-glucurono-gamma-lactone (2400 mg/L). Since then, AFSSA has examined several studies conducted by the petitioner on the safety of taurine and D-glucurono-gamma-lactone in these beverages. Considering that the safety in use of these substances had not been demonstrated on the basis of the studies conducted, AFSSA had emphasised the need for further studies, in order to confirm or exclude suspected renal toxicity of D-glucurono-gamma-lactone and adverse neurobehavioural effects of taurine. Moreover, AFSSA highlighted the fact that doses of taurine and D-glucurono-gamma-lactone in 'energy' drinks are significantly higher compared to common dietary intake levels (AFSSA, 2003, 2006a, 2006b).

➤ In Europe

The Scientific Committee on Food (SCF) made similar observations about these same beverages twice, in 1999 and 2003, concluding each time that it was impossible to ensure with certainty that the taurine and D-glucurono-gamma-lactone levels in these products did not carry any health risk, and recommending that additional toxicology studies be conducted to establish the maximum daily consumption for these substances (SCF, 2003).

Based on new data provided by the petitioner, the European Food Safety Authority (EFSA) issued an Opinion on 15 January 2009 concluding that "the exposure to taurine and D-glucurono-gamma-lactone at the levels currently used in 'energy' drinks is not of safety concern" (EFSA, 2009).

Regarding the toxicological data

➤ Taurine

The objective of the 13-week study of subacute toxicity in rats described in the EFSA Opinion was to assess the potential neurotoxic effect of taurine administered either orally or by gavage at doses of 600 and 1000 mg/kg bw/day, or *ad libitum* in doses of 1000 and 1500 mg/kg bw/day.

According to the EFSA Opinion, no neurobehavioural effects were observed; EFSA established a NOAEL¹ of 1000 mg of taurine/kg bw/day (EFSA, 2009).

➤ D-glucurono-gamma-lactone

The objective of the 13-week study of subacute toxicity carried out by oral route in rats, described in the EFSA Opinion, was to assess the potential effect of D-glucurono-gamma-lactone on kidney function. The substance was administered either by force-feeding or *ad libitum* (in drinking water) at doses of 0, 300, 600 and 1000 mg/kg bw/day.

According to the EFSA Opinion, no histological renal changes were observed; EFSA established a NOAEL of 1000 mg/kg bw/day in rats for D-glucurono-gamma-lactone (EFSA, 2009).

¹ No-observed-adverse-effect-level

Regarding the risks associated with interactions between substances

In 2006, AFSSA pointed out that an increase in systolic ejection volume in response to stress was observed after the consumption of 'energy' drinks during the post-exercise recovery period (AFSSA, 2006). This phenomenon could result from a synergistic effect of taurine and caffeine (Sung *et al*, 1990; Baum *et al*, 2001).

More recently, a study showed that consuming two cans of 'energy' drinks led to a rise in blood pressure in the short and medium term and an increase in heart rate of approximately 10% (Steinke *et al*, 2009). Another study showed that caffeine and taurine intake, at respective concentrations of 100 mg and 1000 mg, also led to increased blood pressure and changes in heart rate (Bichler *et al*, 2006).

Although the literature suggests that caffeine and taurine can alter cardiovascular parameters independently, the unproven taurine/caffeine interaction is still suspected.

Furthermore, AFSSA and the BfR² call attention to:

- the probable interaction of the caffeine-*D*-glucurono- γ -lactone combination with concomitant alcohol consumption; and
- the risks associated with the combination of consuming 'energy' drinks and engaging in intense physical activity (AFSSA, 2006; BfR, 2008).

Regarding the nutritional data

➤ **Natural sources of taurine and *D*-glucurono- γ -lactone**

- *Taurine*

Taurine is provided in the diet by animal products such as meat, fish, and seafood, at concentrations ranging between 40 and 500 mg/100 g. It is also found in milk and dairy products (1 to 4 mg/100 g). The usual dietary intake is about 100 mg/day in the general population, rarely exceeding 180 mg/day, but is very low in lacto-ovo vegetarians (17 mg/day) (AFSSA, 2007). In its latest Opinion, EFSA listed several studies reporting consumption levels ranging from 9 to 400 mg/day (EFSA, 2009).

- *D*-glucurono- γ -lactone

D-glucuronolactone may be supplied by various natural dietary sources at levels of 1 to 2 mg/day (SFC, 2003).

➤ **Nutritional value**

Taurine and *D*-glucurono- γ -lactone are produced by endogenous synthesis in humans. In the healthy adult, there is no evidence of an inadequate intake of taurine and *D*-glucurono- γ -lactone.

Regarding the exposure data

➤ **In Europe**

Based on a review of data recorded in an Austrian survey, the 2003 SCF report indicated an average chronic daily consumption of 'energy' drinks of 0.5 cans, or 125 mL, corresponding to a mean daily exposure of 500 mg of taurine (8.3 mg/kg bw/day for a 60 kg person) and 300 mg of *D*-glucurono- γ -lactone (5 mg/kg bw/day for a 60 kg person). Regarding the consumption of 'energy' drinks at the 95th percentile of regular consumers, this was estimated at 1.4 cans per day, or 360 mL, corresponding to a mean daily exposure to taurine and *D*-glucurono- γ -lactone for a 60 kg person of 1400 mg (23.3 mg/kg bw/day) and 840 mg (14 mg/kg bw/day) respectively (Table 1). Occasional consumption of up to 750 mL/day, or three cans daily was also indicated. Consumption of up to eight to 12 cans per day was also reported in some extreme consumers (SCF, 2003).

² Federal Institute for Risk Assessment - Germany

On the basis of these consumption levels, EFSA estimated that chronic exposure to taurine at the 95th percentile from 'energy' drinks, and mean consumption, were respectively 43 and 120 times lower than the NOAEL for taurine, established at 1000 mg/kg bw/day, calculated for a 60 kg adult. The estimate of chronic exposure at the 95th percentile to D-glucurono-gamma-lactone from these 'energy' drinks, and mean consumption, were respectively 71 and 200 times lower than the NOAEL for D-glucurono-gamma-lactone, established at 1000 mg/kg bw/day by EFSA, calculated for a 60 kg adult (EFSA, 2009).

➤ **On the national level**

- *Consumption of 'energy' drinks*

To date, there are no data that make it possible to estimate the intake level of 'energy' drinks in representative samples of the French population.

Therefore, the data on purchases of 'energy' drinks (TNS Worldpanel, 2008) were used to obtain preliminary information on consumption of this type of beverage. During a six-month observation period, purchases of these beverages involved 6% of households and the volume purchased on each occasion was around one litre. The estimated consumption based on purchasing data showed low mean levels: 52% of consumers drink less than 3.2 mL/day and 13% drink more than 15.8 mL/day. The consumption of 'energy' drinks most likely pertains to only a part of the population, adolescents and young adults in particular. Nevertheless, the results of this study should be viewed with caution, given the limited number of buyers, the short duration of the study and its limitation to home consumption (excluding sales in bars and discos).

Furthermore, it would be useful to have information on the higher levels of 'energy' drink consumption, specifically in adolescents and young adults.

- *Possible consequences of applying a draft order: the addition of taurine and D-glucurono-gamma-lactone to non-alcoholic beverages at the respective levels of 4000 mg/L and 2400 mg/L*

The dietary intake data come from the National Individual Survey on Food Consumption (INCA-2) study conducted in 2006-2007 on 4,079 individuals. According to the nomenclature used in the INCA-2 study, the 'non-alcoholic beverages' (BRSA) group includes 60 beverages divided into five sub-groups: fruit juices, cordials, fruit drinks, soft drinks and colas, and other cold drinks.

To measure the impact on exposure levels of extending the addition of taurine and D-glucurono-gamma-lactone to other beverages, two scenarios were considered:

- fortification of all non-alcoholic beverages, i.e., the five sub-groups, with taurine and D-glucurono-gamma-lactone; and
- possible fortification of just soft drinks and colas, the subgroup considered closest to the 'energy' drinks on the market, with taurine and D-glucurono-gamma-lactone.

An estimate of the intake of these substances was drawn from consumption data for the aggregate of BRSA, and soft drinks and colas in adults from 18 to 79 years of age using the maximum amounts proposed by the draft order, namely 4000 mg/L for taurine and 2400 mg/L for D-glucurono-gamma-lactone (Table 1). Assuming maximal fortification of all BRSA, the intake level would be approximately 50% higher than was estimated in the Austrian survey carried out in regular high consumers of 'energy' drinks (526 mL/day versus 360 mL/day) (Table 1).

Taurine and D-glucurono-gamma-lactone exposures estimated at the 95th percentile of soft drink and cola consumption are respectively 44 times and 73 times lower than the NOAELs for taurine and D-glucurono-gamma-lactone, both fixed by EFSA at 1000 mg/kg bw/day, calculated for a 60 kg adult. These exposure margins are very close to those calculated by EFSA based on the exclusive consumption of ‘energy’ drinks.

However, broadening the fortifiable vectors, namely enriching all BRSAs with taurine and D-glucurono-gamma-lactone, leads to a decrease in the exposure margin. Exposure to taurine and D-glucurono-gamma-lactone estimated at the 95th percentile of the aggregate of non-alcoholic beverage consumption, including soft drinks and colas, is respectively 29 times and 48 times lower than the NOAELs for taurine and D-glucurono-gamma-lactone, both fixed by EFSA at 1000 mg/kg bw/day, calculated for a 60 kg adult.

Exposure to taurine and to D-glucurono-gamma-lactone for an average consumption of all non-alcoholic beverages, including soft drinks and colas, is respectively five and 150 times higher than natural intake from food.

For very high consumers, i.e., those consuming 10 cans per day of beverages fortified with these substances (observed in the Austrian survey), exposure to taurine and to D-glucurono-gamma-lactone would be respectively six times and 10 times lower than the NOAELs for taurine and D-glucurono-gamma-lactone, both established by EFSA at 1000 mg/kg bw/day, calculated for a 60 kg adult.

Consumption references	Types of beverages		Consumption (mL/day)	Taurine intake (in mg/kg bw/day)**	D-glucurono-gamma-lactone intake (in mg/kg bw/day)**
Austrian data	Energy drinks	Mean	125	8.3	5
		95 th percentile	360	23.3	14
INCA 2 data	Soft drinks and colas group	Mean	54.2	3.6	2.2
		95 th percentile	342.9	22.9	13.7
	BRSAs*	Mean	139.8	9.3	5.6
		95 th percentile	525.7	35	21

Table 1: Data on exposure to taurine and D-glucurono-gamma-lactone through beverages

* Aggregate of non-alcoholic beverages including soft drinks and colas, fruit juices, cordials, fruit drinks, and other cold drinks

** Calculated with respective taurine and D-glucurono-gamma-lactone levels of 4000 mg/L and 2400 mg/L for a 60 kg adult

Conclusion

AFSSA emphasises that fortifying non-alcoholic beverages with taurine and D-glucurono-gamma-lactone has no nutritional value. Expanding dietary vectors fortified with taurine and D-glucurono-gamma-lactone, at respective doses of 4000 mg/L and 2400 mg/L, from ‘energy’ drinks to the entire group of non-alcoholic beverages is likely to significantly increase exposure when compared to a standard diet.

If taurine and D-glucurono-gamma-lactone were present in all non-alcoholic beverages at the maximum levels proposed by the draft order:

- exposure to these substances, in France, calculated on the basis of mean consumption (139 mL) and at the 95th percentile (525 mL), would be respectively 107 and 29 times lower for taurine, and 179 and 48 times lower for D-glucurono-gamma-lactone than the NOAELs proposed by EFSA. These exposure margins could be regarded as acceptable since they are based on an NOAEL (itself corresponding to the maximal dose tested in the study) and not an LOAEL [lowest-observed-adverse-effect-level]. However, this margin is lower than the margin calculated by EFSA for the consumption of 'energy' drinks alone;
- for very high consumers (10 cans of 250 mL), exposure to taurine and to D-glucurono-gamma-lactone would be respectively six and 10 times lower than the NOAELs proposed by EFSA, thus leading to a much lower exposure margin than was obtained at the 95th percentile of consumption of all non-alcoholic beverages.

Moreover, AFSSA points out that cumulative intake, through dietary supplements and fortified foods other than beverages, would lead to increased exposure to these substances.

Considering all these factors, the acquisition of experimental data on higher doses of taurine and D-glucurono-gamma-lactone than those currently available would serve to confirm these exposure margins.

In general, AFSSA reiterates that the fortification of foods must be systematically assessed in terms of overall diet, taking into account the variety and multiplicity of the vectors likely to be used.

The Director General

Marc MORTUREUX

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Key words:

Substance, fortification, beverage, exposure