Bundesinstitut für Risikobewertung

Comments from the Federal Institute for Risk Assessment (BfR), Germany on EFSA's draft scientific opinion on the safety of caffeine

First draft

Abstract, line 15
„Other common constituents of “energy drinks” (i.e. taurine, D-glucurono-γ-15 lactone) or alcohol are unlikely to adversely interact with caffeine.”

BfR cannot follow this conclusion. An explanation is given in the comments for the body text.

Page 3, line 95
Specific subgroups like pregnant women, lactating women, etc.

BfR suggest considering also caffeine sensitive persons as a specific risk group, e.g. persons with predispositions to serious ventricular arrhythmias or persons with asymptomatic channelopathies.

3. Dietary Intake
3.3.2. Caffeine intake from “energy drinks” on a “single session” estimated from the EFSA report on “energy drinks”
Page 22, line 783
“In this survey, 51, 25, 11, 6 and 7 % of “energy drink consumers” declared to consume 1, 2, 3, 4 and ≥ 5 cans of “energy drinks” within a “single session”.

BfR recommends that the report “Event-Related Survey of High Consumers of Energy Drinks” from BfR should also be considered (http://www.bfr.bund.de/de/bfr_wissenschaft_2013.html).
The objective of this survey was a compilation of data for risk assessment of energy drinks considering an excessive consumption of products containing a relative high proportion of caffeine. The study participants were interviewed during specific consumption situations as dance, concerts, sport events and LAN-parties.
From BfR perspective a higher risk for adverse effects from energy drink consumption may apply especially to these high consumers and in particular in combination with intensive physical activity and alcohol.
BfR suggests discussing also the health risk in respect to the consumption of such high caffeine amounts (95th percentile; ≥ 5 cans of “energy drinks”). The EFSA opinion focuses mainly on the prevalence of adults or adolescents, which consume more than 200 mg caffeine on a single session of “energy drinks”.

4. Hazard Identification

4.3. Adverse effects of caffeine: methodological considerations

Page 27, line 1041

“The Panel also considers that, although case reports of adverse events following consumption of caffeine-containing foods or beverages are useful to identify health concerns for further investigation, they generally provide insufficient information to conclude on a factor or combination of factors which trigger the adverse event and/or the doses of caffeine which could be considered as safe/unsafe for the general healthy population.”

See also summary, page 3, line73
“Case reports of adverse events have not been considered for the scientific assessment.”

BfR refers to the terms of reference as provided by the commission:

- Review the existing scientific data on the potential link between caffeine intakes, from all sources, and possible adverse health effects in the general population and as appropriate, in specific subgroups of the population, including but not limited to, individuals performing physical activity of various intensities, women of childbearing age, pregnant women, breastfeeding women, children and adolescents;

……..

- Advise whether, and the extent to which, the consumption of caffeine together with other food constituents, such as alcohol or substances found in energy drinks, could present a risk to health and for which additional or different recommendations should be provided. Advice should focus inter alia on: 1) a daily intake of caffeine when combined with other food constituents and 2) a recommended interval between caffeine and other food constituents’ consumption to prevent possible interactions.

BfR is of the opinion that a “review of the scientific data…”

- should comprise also details on the entirety of case reports in which energy drink consumption has been associated with adverse effects and should especially focus on findings on likely and very likely causal relationships on this as elaborated on the basis of the French nutrivigilance system.
- should address possible adverse effects in “specific subgroups of the population” with certain known or unknown diseases, such as asymptomatic channelopathies or epilepsy, which are assumed to be associated with higher risks for certain adverse effects of energy drinks (ANSES, 2013).

Regarding energy drinks, case reports refer not only to single but to series of observations as reports from poisoning centers show.

In view of the BfR an “Advise whether….the consumption of caffeine together with other food constituents, such as alcohol or substances found in energy drinks, could present a risk to health” should take into account realistic situations of high exposure on certain events as described in the BfR report “Event-Related Survey of High Consumers of Energy Drinks” and include risk assessments referring to these conditions. In case this is not possible due to lack of study data this should also be addressed.

4.4.1.1. Blood pressure, endothelial function and arterial compliance
Page 31, line 1214 and page 32 line 1235

The “unpublished study (Bischoff, 2013)“ is published meanwhile. Please see the link http://download.ble.de/09HS022/09HS022_AB.pdf
It is also actually under the review process in an international scientific journal.

4.4.1.3. Cardiovascular disease risk
Page 36, line 1467

“The Panel notes that these three case-crossover studies suggest an increased risk of acute cardiovascular events in the hour following consumption of caffeinated coffee, particularly in subjects with low habitual coffee intake. Although not formally tested, co-consumption of caffeine and alcohol does not appear to modify the risk.”

See also abstract, page 1, line 15
„Other common constituents of “energy drinks” (i.e. taurine, D-glucurono-γ-15 lactone) or alcohol are unlikely to adversely interact with caffeine.”

See also Summary, page 3, line 86
“Other common constituents of “energy drinks” (i.e. taurine, D-glucurono-γ-lactone) or alcohol are unlikely to adversely interact with caffeine.”
BfR cannot follow the conclusion, that co-consumption of caffeine and alcohol does not appear to modify the risk.
The three case-crossover studies (Selb Semerl et al., 2004; Mostofsky et al., 2010a; Mostofsky et al. 2010b) analyse the temporal association between caffeine exposure and stroke/sudden cardiac death and between alcohol exposure and stroke/sudden cardiac death. In the Selb Semerl-study no information is given about a co-consumption of alcohol and caffeine. In the two Mostofsky publications, which are based on the same multicenter case-crossover study, it is indicated that only one person drank alcohol as well as coffee one hour prior to stroke. In these two studies it is not discussed if this co-consumption results in more or less adverse effects for this person.
From BfR perspective it cannot be concluded on an interaction or on no interaction between caffeine and alcohol on the basis of these three studies.

4.4.1.4. Conclusion on the cardiovascular system
Page 37, line 1488
“Consumption of alcohol in combination with caffeine does not appear to modify the CVD risk.”

BfR cannot follow the conclusion; see explanation before.

In general the risks for patients suffering from known or unknown asymptomatic channelopathies should be addressed in this chapter.

4.5.2.5 Atrial fibrillation
Page 52, line 2217

“The Panel notes that habitual caffeine consumption from all sources up to about 1 000 mg per day was not significantly associated with an increased risk of stroke in these two meta-analyses.”

Please check if the Panel really refers to “stroke” in this sentence.

5. Dose Response Assessment and derivation of intake levels of no concern
Page 61, line 2647

“The Panel considers that other common constituents of “energy drinks” (i.e. taurine, D-glucurono-γ- lactone) or alcohol are unlikely to adversely interact with caffeine in relation to these outcomes at the dose levels reported in the studies reviewed.”

To avoid misinterpretation the dose levels and endpoints, which were considered in evaluating the possible interactions of caffeine with alcohol or taurine, should be specified in this conclusion, also in other parts of the opinion, e.g. the abstract.

6. Characterisation of the risk
Page 63

In view of BfR an analysis of reported cases on adverse effects, especially those with severe outcome and reported likely or very likely causality should be included in this chapter, considering consumed doses, exposure conditions and state of health (e.g. existing cardiovascular diseases).

7. Conclusions
Page 64 – 65

See also summary, page 3-4.

Only certain subgroups such as pregnant women, lactating women, etc. are addressed. With regard to the terms of reference, BfR recommendss to consider also other “specific subgroups of the population”, e.g. those with certain known or unknown diseases such as asymptomatic channelopathies or epilepsy, which are assumed to be associated with higher risks for certain adverse effects of energy drinks (ANSES, 2013).

Furthermore BfR advises to also address possible risks associated with known realistic high consumption patterns of energy drinks.

References:

ANSES (Agence nationale de sécurité sanitaire de l'alimentation), 2013. Opinion of the French Agency for Food, Environmental and Occupational Health & Safety on the assessment of risks concerning the consumption of so-called “energy drinks”. Opinion Request no. 2012-SA-0212, 108 pp.

New Human Data on the Assessment of Energy Drinks
BfR Information No. 016/2008, 13 March 2008
http://www.bfr.bund.de/cm/349/new_human_data_on_the_assessment_of_energy_drinks.pdf

Bischoff, 2013;
Abschlussbericht zum Forschungsvorhaben
„Humanstudie zur Wirkung von Koffein und Taurin aus
Energy Drinks auf Parameter des Herz-Kreislauf-Systems
http://download.ble.de/09HS022/09HS022_AB.pdf

BfR-Wissenschaft 06/2013; Anlassbezogene Befragung von Hochverzehrern von Energy-Drinks
ISBN: 978-3-943963-02-1; ISSN: 1614-3841
http://www.bfr.bund.de/de/bfr_wissenschaft_2013.html