Vitenskapskomiteen for mattrygghet
Norwegian Scientific Committee for Food Safety

New information on ingredients in so-called ”energy drinks”

Opinion of the Panel on Food Additives, Flavourings, Processing Aids, Materials in Contact with Food and Cosmetics of the Norwegian Scientific Committee for Food Safety

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SUMMARY

The term "energy drinks" is a commercial designation for a category of beverages that contains caffeine and various combinations of substances, such as carbohydrates, vitamins, taurine and D-glucurono-γ-lactone. The intake of different constituents found in the "energy drink" Red Bull and similar products were evaluated by the Norwegian Scientific Committee for Food Safety (VKM) in 2005. The evaluation by VKM was based on the SCF opinions on "energy drinks" from 1999 and 2003, safety-in-use documentation from Red Bull GmbH as well as novel available literature on the subject. In 2009, EFSA (Panel on Food Additives and Nutrient Sources added to Food, ANS) published a revised scientific opinion evaluating the safety-in-use of taurine and D-glucurono-γ-lactone as separate constituents of "energy drinks" based on new studies provided by Red Bull GmbH and other new studies. After establishing no observed adverse effect levels (NOAELs) for taurine and D-glucurono-γ-lactone, the ANS Panel concluded that actual exposure to these two constituents at the levels presently used in "energy drinks" is not of safety concern. However, the ANS Panel emphasised that they did not evaluate the safety of "energy drinks" as such.

The Norwegian Food Safety Authority has asked VKM to examine, on the basis of the EFSA 2009 opinion, whether the conclusions of the VKM opinion from 2005 need to be revised, particularly in view of the new information presented on taurine and D-glucurono-γ-lactone. In addition, VKM is asked to take into consideration new information from a 2008 risk assessment of caffeine among children and adolescents in the Nordic countries.

According to the terms of reference of the present opinion, the VKM Panel on Food Additives, Flavourings, Processing Aids, Materials in Contact with Food and Cosmetics (Panel 4) was requested to answer the following questions:

1) How will the new information on taurine and D-glucurono-γ-lactone and the conclusions presented in the new opinion from EFSA influence the conclusions of the VKM opinion from 2005, which concerned "energy drinks" as such?

In 2005, VKM concluded that no NOAEL for taurine could be determined. Due to lack of data no statement was given in the VKM 2005 opinion on whether the intake of taurine or D-glucurono-γ-lactone from"energy drinks" could pose a risk to human health. Based on new studies presenting NOAELs for taurine and D-glucurono-γ-lactone, both of 1000 mg/kg bw/day, the EFSA ANS Panel concludes that exposure to taurine and D-glucurono-γ-lactone as individual ingredients at the levels presently used in "energy drinks", and at the intake levels presented are of no safety concern. The VKM Panel 4 endorses this conclusion and considers it as valid also for Norway.

In the opinion from 2005, VKM concluded that there was too limited knowledge on combined effects of components in "energy drinks", especially of caffeine and taurine to exclude negative health effects related to intake of such drinks. New data presented in the EFSA 2009 opinion demonstrates that a possible stimulatory effect from taurine on the central nervous system (CNS) is considered improbable. In addition, new data show that additive effects between taurine and caffeine on diuretic effects are unlikely. Other interactions were not investigated. However, potential combined effects of taurine and caffeine on the cardiovascular system, e.g. for susceptible individuals cannot be ruled out, since this is not properly investigated. The VKM Panel 4 agrees with the SCF opinion from 2003 that there is

no *a priori* reason to expect combined effects of D-glucurono-γ-lactone and caffeine or taurine.

In their recent opinion from 2009, EFSA emphasised that they did not evaluate the safety of "energy drinks" as such. It should be noted that several new cases of possible adverse effects of "energy drinks" in combination with alcohol or exercise have been reported since the VKM opinion from 2005. However, it is not possible to determine whether the reported effects are causally related to the "energy drink" or to simultaneous exposure to alcohol or exercise. In some cases narcotic drugs may have been involved.

2) Has the risk of adverse health effects due to caffeine intake among different consumer groups in Norway changed since the last evaluation? If so, do these changes influence the conclusions in the VKM opinion on "energy drinks" from 2005?

New intake scenarios based on exposure to the main caffeine-containing food groups, and with an additional exposure to caffeine from "energy drinks" have now been conducted for the age groups children, adolescents and adults. The new intake estimates of caffeine show that the caffeine intake in the different age groups in the Norwegian population has not changed considerably since the last risk assessment from VKM in 2005. The VKM Panel 4 noted that in general there is a large inter-individual variation in the tolerance to caffeine.

The estimated consumption of "energy drinks" will have a major impact on the total caffeine intake in children and will contribute to an increased incidence of exceeding the lowest observed adverse effect level (LOAEL) for anxiety. Such effects of caffeine are unwanted in children below 12 years. The VKM Panel 4 considers the estimated consumption of "energy drinks", and the increased intake of caffeine as described in this opinion to be of concern for children.

Adolescents are developmentally in-between children and adults, and they might have the same potential consumption of "energy drinks" as adults, while the consumption of coffee is still very low. On the other hand it is assumed that adolescents who have a considerable intake of caffeine from soft drinks might develop some tolerance to caffeine. Potential adverse effects of "energy drink" consumption can not be ruled out for adolescents with no or low tolerance for caffeine. The risk of adverse effects to caffeine from "energy drinks" is highest for adolescents aged 13-15 years old, where the consumption of coffee is low and the tolerance development to caffeine is expected to be lower than for adults. The highest risk is anticipated to be connected to acute consumption of "energy drinks".

For adults, the caffeine intake from soft drinks, coffee, tea and chocolate is considerably lower than the LOAEL for anxiety even when the additional high chronic or acute intake of "energy drinks" is included. The VKM Panel 4 regards this increase in caffeine intake of no safety concern for adults.

The half-life of caffeine is doubled or tripled during pregnancy due to hormonal changes. The VKM Panel 4 therefore maintains the recommendations given in the VKM opinion from 2005, that the intake of caffeine in pregnant women should not exceed 100 - 200 mg/day.

NORSK SAMMENDRAG

Begrepet "energidrikker" er en kommersiell betegnelse på en kategori drikkevarer som inneholder koffein og ulike kombinasjoner av flere andre bioaktive komponenter, slik som for eksempel karbohydrater, vitaminer, taurin og glukuronolakton. Vitenskapskomiteen for mattrygghet (VKM) risikovurderte i 2005 inntaket av ingrediensene i "energidrikken" Red Bull og lignende produkter. VKMs risikovurdering var basert på vurderinger fra EU Scientific Committee for Food (SCF) i 1999 og 2003, dokumentasjon fra Red Bull GmbH og ny tilgjengelig relatert til problemstillingen. I 2009 publiserte EFSAs Panel on Food Additives and Nutrient Sources added to Food (ANS) en ny uttalelse der de har vurdert bruken av taurin og glukuronolakton som separate bestanddeler i "energidrikker". Den nye vurderingen fra EFSA er basert på nye studier fremskaffet av Red Bull GmbH og annen ny litteratur, som har gjort det mulig å fastsette nulleffektsdoser (NOAEL) for taurin og glukuronolakton fra dyreforsøk. Med bakgrunn i denne nye kunnskapen konkluderte EFSA med at et jevnlig konsum av "energidrikker" ikke vil medføre et bekymringsverdig inntak av de to stoffene. De understreket imidlertid at de ikke har vurdert "energidrikker" som sådan, men to mye brukte ingredienser i slike produkter.

Med utgangspunkt i de nye opplysningene som framkommer om ingrediensene taurin og glukuronolakton i vurderingen fra EFSA, har Mattilsynet bedt VKM om å vurdere hvorvidt konklusjonene i VKMs risikovurdering av "energidrikker" fra 2005 må oppdateres. I tillegg er VKM bedt om å ta i betraktning ny informasjon om koffein beskrevet i en nordisk risikovurdering av koffeininntaket hos barn og ungdom fra 2008.

I oppdragsteksten fra Mattilsynet ble VKMs faggruppe for tilsetningsstoffer, aroma, matemballasje og kosmetikk (Faggruppe 4) bedt om å besvare følgende spørsmål:

1) Hvordan påvirker konklusjonene i EFSAs nye vurdering av taurin og glukuronolakton konklusjonene i VKMs risikovurdering fra 2005 der man blant annet vurderte alle ingrediensene i drikken som sådan i forhold til hverandre?

VKM konkluderte i 2005 med at det ikke kunne fastsettes noen nulleffektsdose for taurin. VKMs vurdering omtaler ikke i hvilken grad inntak av taurin eller glukuronolakton fra "energidrikker" kan utgjøre en helserisiko ettersom det ikke fantes tilstrekkelige data til å avgjøre dette. Nye studier har gjort det mulig å fastsette nulleffektsdoser for taurin og glukuronolakton, begge på 1000 mg/kg kroppsvekt/dag. Basert på disse studiene konkluderer EFSAs ANS panel med at eksponering for taurin og glukuronolakton, som individuelle ingredienser i de konsentrasjoner som normalt brukes i "energidrikker", og ved de inntaksnivåene som er presentert, ikke utgjør noen helserisiko. VKMs Faggruppe 4 slutter seg til denne konklusjonen og vurderer den som gjeldende også for norske inntaksnivåer av de to stoffene.

VKM konkluderte i sin vurdering fra 2005 med at kunnskapen om eventuelle kombinasjonseffekter av ingrediensene i "energidrikker" var begrenset. Spesielt ble det trukket fram at man vet for lite om interaksjoner mellom taurin og koffein til å kunne utelukke negative helseeffekter relatert til denne typen drikker. Nye data som omtales i EFSAs vurdering fra 2009 viser at mulig stimulerende effekt av taurin på sentralnervesystemet (CNS) nå vurderes som usannsynlig. Både taurin og koffein kan føre til tap av vann og natrium fra kroppen (økt urinutskillelse, diuretisk effekt) og ettersom virkningsmekanismen for de to stoffene er forskjellig, har det vært diskutert om de kan ha en additiv effekt. Nye data tilsier imidlertid at en slik additiv effekt mellom taurin og koffein er lite trolig. Andre kombinasjonseffekter ble ikke undersøkt. Det er imidlertid verdt å merke seg at mulige kombinasjonseffekter av taurin og koffein på hjerte- og karsystemet ikke kan utelukkes, særlig for spesielt følsomme individer, men dette har ikke blitt

tilstrekkelig undersøkt. VKMs Faggruppe 4 støtter konklusjonen i EU SCF sin vurdering fra 2003 om at det ikke er noen *a priori* grunn til å forvente kombinasjonseffekter av glukuronolakton og koffein eller taurin.

EFSA understreker i sin nye vurdering av taurin og glukuronolakton at de ikke har vurdert "energidrikker" som sådan. Flere nye tilfeller av mulige negative helseeffekter i forbindelse med konsum av "energidrikker" i kombinasjon med alkohol og/eller fysisk aktivitet er rapportert i etterkant av VKMs vurdering fra 2005. Det er imidlertid ikke mulig å fastslå om det er noen årsakssammenheng mellom de rapporterte effektene og et konsum av "energidrikker", eller til en samtidig eksponering for alkohol og/eller fysisk aktivitet. I enkelte tilfeller kan også narkotiske stoffer være innblandet.

2) Er det framkommet endringer i risikobildet ved inntak av koffein blant ulike brukergrupper i Norge siden gjennomføring av forrige risikovurdering, og eventuelt hvilke? Hvilken betydning vil disse eventuelle endringene ha å si i forhold til konklusjonene fra risikovurderingen fra 2005.

I denne oppdaterte vurderingen fra VKMs Faggruppe 4 er det gjennomført nye beregninger av inntaksscenarioer for aldersgruppene barn, tenåringer og voksne. Beregningene er basert på eksponering for de viktigste koffeinholdige matvaregruppene, og dessuten et tilleggsbidrag av koffein fra "energidrikker". De nye inntaksberegningene viser at koffeininntaket i de ulike aldersgruppene ikke har endret seg vesentlig siden forrige risikovurdering fra VKM i 2005. Faggruppen bemerker at det generelt er store individuelle forskjeller i toleransen for koffein hos mennesker.

Det estimerte tilleggskonsumet av "energidrikker" vil ha stor innflytelse på det totale koffeininntaket hos barn, noe som bidrar til at terskelnivået (LOAEL) for engstelse og anspenthet overskrides. Slike effekter av koffein er ikke ønskelig hos barn under 12 år. VKMs Faggruppe 4 mener at det estimerte konsumet av "energidrikker", og det økte inntaket av koffein som beskrives i denne risikovurderingen er av bekymring for barn.

Tenåringer er utviklingsmessig i en mellomfase mellom barn og voksne, og de kan potensielt ha et tilsvarende konsum av "energidrikker" som voksne, mens de fortsatt drikker veldig lite kaffe. Det antas imidlertid at tenåringer med et betydelig inntak av koffein fra brus kan utvikle toleranse for koffein (kroppen innstiller seg til et visst koffeininntak). Det kan ikke utelukkes at tenåringer med lav toleranse for koffein kan oppleve mulige negative helseeffekter som følge av et konsum av "energidrikker". Risikoen for negative helseeffekter av koffein fra "energidrikker" vil være størst hos tenåringer i alderen 13-15 år, ettersom denne aldersgruppen fortsatt drikker lite kaffe og derfor forventes å tåle mindre koffein enn voksne. Det antas at det er størst risiko forbundet med et akutt konsum av "energidrikker".

Koffeininntaket fra brus, kaffe, te og sjokolade hos voksne ligger betydelig lavere enn terskelnivået for engstelse og anspenthet, selv når tilleggsbidraget fra et høyt kronisk eller akutt inntak av "energidrikker" inkluderes. Faggruppen anser at dette tilleggsbidraget av koffein fra "energidrikker" ikke er av bekymring for voksne.

Halveringstiden for koffein i kroppen dobles til tredobles under graviditet på grunn av hormonelle endringer. Faggruppen opprettholder derfor anbefalingene fra VKMs risikovurdering i 2005 om at gravide og ammende ikke bør ha et inntak som overstiger 100 - 200 mg koffein/dag.

CONTENTS

CONTRIBUTORS

Persons working for VKM, either as appointed members of the Committee or as *ad hoc* experts, do this by virtue of their scientific expertise, not as representatives for their employers. The Civil Services Act instructions on legal competence apply for all work prepared by VKM.

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BACKGROUND

The intake of different constituents found in the ”energy drink” Red Bull and similar products were evaluated by the Norwegian Scientific Committee for Food Safety (VKM) in 2005 (VKM, 2005). The evaluation by VKM was based on the SCF opinions on “energy drinks” from 1999 and 2003 (SCF, 1999; 2003), safety-in-use documentation from Red Bull GmbH as well as novel available published data on the subject. The term so-called “energy drinks” was then used to encompass a category of beverages that have appeared on the European market the last decade, which contain caffeine and various combinations of substances, such as carbohydrates, vitamins, taurine and D-glucurono-γ-lactone. It should be noted that the term “energy drinks” is a commercial designation, and whether the claim that these drinks provide energy in the conventional nutritional sense is scientifically justified, were not further discussed (SCF, 1999; VKM, 2005). These considerations are also valid for this opinion from VKM Panel 4.

In 2009, EFSA (Panel on Food Additives and Nutrient Sources added to Food, ANS) published a revised scientific opinion evaluating the safety-in-use of taurine and D-glucurono-γ-lactone as separate constituents of “energy drinks” based on new studies provided by Red Bull GmbH and other new studies. After establishing no observed adverse effect levels (NOAELs) for taurine and D-glucurono-γ-lactone, the ANS Panel concluded that actual exposure to these two constituents at the levels presently used in “energy drinks” is not of safety concern. However, the ANS Panel emphasised that they did not evaluate the safety of “energy drinks” as such (EFSA, 2009).

The Norwegian Food Safety Authority has asked VKM to examine, on the basis of the EFSA 2009 opinion, whether the conclusions of the VKM opinion from 2005 need to be revised, particularly in view of the new information presented on taurine and D-glucurono-γ-lactone. In addition, VKM is asked to take into consideration new information from a 2008 risk assessment of caffeine among children and adolescents in the Nordic countries.

TERMS OF REFERENCE

1 How will the new information on taurine and D-glucurono-γ-lactone and the conclusions presented in the new opinion from EFSA influence the conclusions of the VKM opinion from 2005, which concerned “energy drinks” as such?

2 Has the risk of adverse health effects due to caffeine intake among different consumer groups in Norway changed since the last evaluation? If so, do these changes influence the conclusions in the VKM opinion on “energy drinks” from 2005?

EVALUATION

Introduction

The present opinion is based on the recent EFSA report "*The use of taurine and D-glucurono-γ-lactone as constituents of the so-called "energy" drinks* (EFSA, 2009), and the report *"Risk assessment of caffeine among children and adolescents in the Nordic countries"* from the Nordic Council of Ministers (NCM, 2008). Only studies included in the EFSA opinion submitted after publication of the VKM opinion "*Risikovurdering av "energidrikker" med koffein, taurin, glukuronolakton, inositol og vitaminer*" from 2005 were discussed and considered for the two ingredients taurine and D-glucurono-γ-lactone. The caffeine exposure in children and adolescents was evaluated in light of the findings and the identified NOEL and LO(A)ELs (no/lowest observed (adverse) effect level) for tolerance development, anxiety and sleep disturbance described in the Nordic report. A LOAEL for anxiety described in Nawrot *et al.*, (2003) was used for adults. Relevant literature on caffeine-containing "energy drinks" published later than the VKM opinion from 2005 was also taken into consideration (BfR, 2008; Reissig *et al.*, 2009).

Comments related to combined effects of the ingredients caffeine, taurine and D-glucurono-γ-lactone in "energy drinks" and combined effects of alcohol, exercise and "energy drinks" are mainly based on what is described in the EFSA opinion on taurine and D-glucurono-γ-lactone. A few other available studies on the subject are also included and given some attention in this opinion (Miller, 2008; Reissig *et al.*, 2009, Wiklund *et al.*, 2009).

"Energy drinks" with a higher content of the ingredients taurine, D-glucurono-γ-lactone and caffeine than in the product Red Bull are not addressed in this opinion. Neither are any new data or information on niacin, vitamin B6 or vitamin B12 considered.

Regulation

Current regulation of caffeine in foodstuffs in Norway

The European Union (EU) regulation of caffeine in foodstuffs is not harmonised. In Norway, caffeine is classified as a pharmaceutical based on its pharmacological properties and it is included in the list of pharmaceuticals administered by the Norwegian Medicines Agency.

The Norwegian Medicines Agency has, however, recently changed their interpretation of the regulation of pharmaceuticals as regards classification of products containing pharmaceutical substances. Classification of products containing caffeine will now depend on an overall evaluation by the Norwegian Medicines Agency where criteria's such as the content of caffeine, the nature and the marketing of the products will be considered.

Thus, marketing of products containing caffeine and which are not classified as pharmaceutical products have to comply with the Norwegian Food Law. The "energy drink" Red Bull has been classified as a pharmaceutical product and therefore banned for sale in Norway up to the autumn 2008, when the Norwegian Ministry of Health and Care Services made it clear that, despite of its content of caffeine, Red Bull should no longer be classified as

a pharmaceutical product. The product should rather be regulated under the Food Law. The Ministry forwarded the application from Red Bull GmbH to the Norwegian Food Safety Authority for appraisal. After reducing the content of vitamin B6 according to Norwegian legislation, permission to market this specific variant of Red bull is now given to Red Bull GmbH. The permission is product- and producer specific, and other "energy drinks" still require to be applied for before being placed on the market. The use of caffeine for flavouring purposes in aromatic drinks, are however generally allowed in amounts up to 150 mg/litre.

The Norwegian Food Safety Authority anticipates that a possible consequence of the change in the domestic classification of pharmaceuticals could lead to an increase in caffeine-containing products on the Norwegian market.

How will the new information on taurine and D-glucurono-γ-lactone and the conclusions presented in the new opinion form EFSA influence the conclusions of the VKM opinion from 2005, which concerned "energy drinks" as such?

The VKM opinion "*Risikovurdering av "energidrikker" med koffein, taurin, glukuronolakton, inositol og vitaminer*" from 2005 referred to three reports from EUs Scientific Committee on Food (SCF) (*Opinion on Caffeine, Taurine and D-glucurono- γ-lactone as constituents of so-called "energy"drinks* (SCF, 1999); *Opinion of the Scientific Committee on Food on Additional information on "energy" drinks* (SCF, 2003) and *Report of the Scientific Committee on Caffeine* (SCF, 1983)) and relevant studies published from March 2003. Available national data on intake, and the consideration of possible specific Norwegian conditions that could lead to different conclusions than the EU opinions was also included in the 2005 VKM assessment.

Taurine

VKM 2005: According to the SCF 2003 Opinion, there was not sufficient data to set a Tolerable Upper Intake Level (UL) for taurine. As described, studies in rats demonstrated behavioural effects at various doses of taurine. No NOAEL had been determined since none of the administered doses were without effect.

EFSA 2009: No new data on intake of "energy drinks" was presented. Therefore, the mean chronic consumption of 0.5 (250 ml/can) and the high (95^{th} percentile of regular users) chronic consumption of 1.4 cans per person per day, established by SCF 2003, were used to estimate human exposure. These values result in a daily mean and high chronic exposure of 500 mg taurine (8.3 mg/kg bw/day for a 60 kg person) and 1400 mg taurine (1400 mg/kg bw/day for a 60 kg person), respectively.

A new study on absorption, tissue distribution, metabolism and elimination performed in rats given taurine orally was provided by the petitioner (Sved *et al.*, 2007). It showed that taurine was rapidly absorbed, distributed to tissues and excreted unchanged in the urine. Elimination of radioactivity from intracellular pools was slow and pre-treatment with unlabeled taurine for

14 days did not affect the result. Total amount of taurine in the brain did not increase after 14 days of daily treatment of taurine. The petitioner claimed that this data excludes the possibility that oral exposure to taurine may exhibit acute central pharmacological effects mediated by an action on the central nervous system (CNS).

A new 13-week study with focus on neurotoxicity performed in male and female rats according to FDA and OECD GLP guidelines was provided by the petitioner (cited in EFSA, 2009). Taurine was administered to the rats either by gavage or in drinking water in doses of 600 - 1500 mg/kg bw/day. Locomotor activity and functional observational battery (FOB) parameters were unaffected by taurine administration. No other effects were observed (deaths, clinical or microscopic findings and effects on body weights). This confirms the NOAEL from the earlier study of 1000 mg/kg bw/day, and provides evidence of a NOAEL of 1500 mg/kg bw/day for behavioural effects. A NOAEL of 1000 mg/kg bw/day is 120-fold higher than the estimated mean and a 43-fold higher than the estimated high chronic exposure to taurine from "energy drinks" only.

Based on the new studies submitted by the petitioner, and given that taurine is a natural body constituent, the EFSA ANS Panel concluded that exposure to taurine as an individual ingredient at the levels presently used in "energy drinks" and at the intake levels established by SCF in 2003 is of no safety concern.

Comments from VKM Panel 4
New studies on neurotoxicity in rats have been provided and a NOAEL for taurine of 1000 mg/kg bw/day was established. Based on this, the EFSA ANS Panel concludes that exposure to taurine as individual ingredient at the levels presently used in "energy drinks" and at intake levels presented in the EFSA opinion, is of no safety concern. The VKM Panel 4 endorses this conclusion and considers it as valid also for Norway.

D-glucurono-γ-lactone

VKM 2005: Little research had been done to study effects of D-glucurono-γ-lactone in humans up to 2005. Some animal data was available that showed unclear effects on the kidney (SCF, 2003), but the human metabolism of D-glucurono-γ-lactone differs from the metabolism in the species of animals used in those studies.

EFSA 2009: No new data on intake of "energy drinks" was presented. Therefore, the mean chronic consumption of 0.5 cans and the high chronic consumption of 1.4 cans per person per day, established by SCF 2003, were used to estimate human exposure. These values result in a daily mean and high chronic exposure to D-glucurono-γ-lactone of 300 mg (5.0 mg D-glucurono-γ-lactone/kg bw/day for a 60 kg person) and 840 mg D-glucurono-γ-lactone (14 mg D-glucurono-γ-lactone/kg bw/day for a 60 kg person), respectively.

The rat has previously been questioned as an appropriate model for testing D-glucurono-γ-lactone due to their ability to synthesise vitamin C endogenously from glucuronic acid. Humans and guinea pig do not possess this metabolic pathway. The petitioner claimed that this is a minor pathway in rats and thus of limited relevance to the safety assessment of exogenous D-glucurono-γ-lactone. This is supported by recent literature data which demonstrate that D-glucurono-γ-lactone is predominantly metabolised in rats via the pentose

pathway and the flux through the pathway synthesising vitamin C is relatively small (cited in EFSA, 2009).

Data from a new 13-week oral (gavage and drinking water) toxicity study of D-glucurono-γ-lactone in rats with specific focus on kidney has been provided (cited in EFSA, 2009*)*. The study has been performed according to FDA and OECD GLP principles. Dose levels were 0 – 1000 mg/kg bw/day. No test article-related toxic effects were observed in the kidneys. The study supports a NOAEL of 1000 mg/kg bw/day D-glucurono-γ-lactone orally administered in rats. A NOAEL of 1000 mg/kg bw/day is 200-fold higher than the estimated mean and 71-fold higher than the estimated high chronic exposure to D-glucurono-γ-lactone from "energy drinks" only.

Based on the new study provided by the petitioner, and given that D-glucurono-γ-lactone is a natural body constituent, the EFSA ANS Panel concluded that exposure to D-glucurono-γ-lactone as individual ingredient at the levels presently used in "energy drinks" and at the intake levels established by SCF in 2003 is of no safety concern.

Comments from VKM Panel 4
Due to lack of data no statement was given in the VKM 2005 opinion on whether the intake of D-glucurono-γ-lactone from drinking "energy drinks" could pose a risk to human health. A new study in rats with specific focus on kidney has been provided and a NOAEL for D-glucurono-γ-lactone of 1000 mg/kg bw/day was established. Based on this, the EFSA ANS Panel concludes that exposure to D-glucurono-γ-lactone as individual ingredient at the levels presently used in "energy drinks" and at intake levels presented in the EFSA opinion, is of no safety concern. The VKM Panel 4 endorses this conclusion and considers it as valid also for Norway.

Caffeine

VKM 2005: VKM concluded in their opinion from 2005 that "energy drinks" could represent a significant source of caffeine for children and young adults provided their relatively high intake of soft drinks was substituted with "energy drinks".

EFSA 2009: The safety of caffeine as an individual ingredient of "energy drinks" has not been evaluated by EFSA.

Comments from VKM Panel 4
The exposure to caffeine among different consumer groups is presented in the section which answers question number 2 in the terms of reference (see page 15). Any new information that influences the conclusions in the VKM opinion on "energy drinks" from 2005 will be further described there.

Combined effects of caffeine, taurine and D-glucurono-γ-lactone

VKM 2005: In the SCF 2003 opinion referred to by VKM, potential interactions between caffeine and taurine are discussed. Based on theoretical knowledge, it is argued that there are reasons to believe that taurine would reduce the effect of caffeine on various receptors in the central nervous system. Another concern is that both taurine and caffeine have diuretic effect.

The mechanisms of action are different, it was therefore suggested that the combined effect could be additive. According to the SCF 2003 opinion, it was considered unlikely that D-glucurono-γ-lactone would have any interaction with taurine and caffeine. In their 2005 opinion, however, VKM pointed to the lack of studies where NOAELs were demonstrated and as a consequence, no ADI or upper tolerable level for caffeine, taurine or D-glucurono-γ-lactone had been determined. Furthermore, there were no studies available in order to determine a safe intake level for the combination of components in Red Bull and comparable "energy drinks". VKM concluded that the possibility of health risk after consumption of "energy drinks" could not be ruled out.

EFSA 2009: In the SCF opinion from 2003 it was concluded that the possible stimulatory effects from taurine and caffeine at the level of CNS could not be ruled out. The new study on absorption, tissue distribution, metabolism and elimination performed in rats, which were provided, showed that oral intake of taurine did not increase the level of taurine in the brain (Sved *et al.*, 2007). This was supported by the EFSA ANS Panel.

New human data have been published on the possible additive effect of taurine and caffeine on diuretic effects (Riesenhuber *et al.*, 2006). The results demonstrated that the diuretic potential and natriuretic effects of the tested combinations were largely mediated by caffeine and that there were no additive effects of taurine and caffeine. Other interactions were not investigated.

In a recent study, possible cardiovascular effects of the combined exposure to caffeine and taurine were investigated in healthy volunteers with low blood pressure (Steinke *et al.,* 2007). The study showed an increase in heart rate and systolic blood pressure, but it was not designed to show whether the effects were due to taurine, caffeine or the combination. Until further findings are presented, the researchers recommend that patients with high blood pressure or cardiac diseases and corresponding medication should refrain from consuming "energy drinks" because of a possible health risk.

No new data is presented on combined effects of D-glucurono-γ-lactone and caffeine or taurine. The EFSA ANS Panel refers to the SCF Opinion from 2003 and concludes that it is unlikely that D-glucurono-γ-lactone would have any interaction with caffeine or taurine.

Comments from VKM Panel 4

In the 2005 opinion, VKM supported earlier opinions from SCF and concluded that there was too limited knowledge on combined effects of components in "energy drinks", especially of caffeine and taurine to exclude negative health effects related to intake of such drinks. New data demonstrates that oral intake of taurine does not result in increased concentrations of taurine in the central nervous system (CNS). Therefore a possible stimulatory effect from taurine on the CNS is considered improbable. In addition new data shows that additive effects between taurine and caffeine on diuretic effects are unlikely. Other interactions were not investigated. However, potential combined effects of taurine and caffeine on the cardiovascular system, e.g. for susceptible individuals, cannot be ruled out since this is not properly investigated. The VKM Panel 4 agrees with the SCF opinion from 2003 that there is no *a priori* reason to expect combined effects of D-glucurono-γ-lactone and caffeine or taurine.

Notably, EFSA 2009 emphasised that they did not evaluate the safety of "energy drinks" as such. Evaluating the safety of all the ingredients and their possible interactions will require more scientific information.

Combined effects of alcohol, exercise and "energy drinks"

VKM 2005: It is known that adolescents may use "energy drinks" to obtain physiological effects, some times in combination with alcohol and/or physical activity. The VKM opinion from 2005 refers to some studies on the combined exposure to "energy drinks" and alcohol, presenting no consistent findings.

EFSA 2009: New human data on the assessment of "energy drinks" have been compiled in a recent opinion from Bundesinstitut für Risikobewertung (BfR) in 2008 referring to several new cases of possible adverse effects of "energy drinks". In these cases "energy drinks" had either been consumed in very high amounts, in combination with physical exercise or more frequently together with alcohol (BfR, 2008). The SCF opinion from 2003 also took into account that drugs, such as ecstasy and amphetamine may have been involved. The effects mentioned includes tremors, seizures, drowsiness, muscle weakness, dizziness, nervousness, tachycardia, palpitations, nausea, vomiting, headache, bronchospasm, hyperventilation and also myocardial infarction and sudden unexplained death, possibly resulting from cardiac dysrhytmia. The SCF concluded that: "The co-consumption of alcohol and/or drugs noted in most of the case reports makes interpretation particularly difficult. There is no confirmation of any causal relationship between the reported effects and the consumption of "energy drinks". With regard to some actual reports the EFSA ANS Panel considered that it is possible that the effects could be due to high caffeine intake while the causal relationship with taurine intake is lacking scientific evidence.

Comments from VKM Panel 4
Several new cases of possible adverse effects of "energy drinks" in combination with alcohol or exercise have been reported since the VKM opinion from 2005, e.g. a small preliminary Swedish study indicated that combining intake of "energy drinks" and alcohol with physical exertion gave rise to a temporary reduction in heart rhythm variability among the 10 subjects included (Wiklund *et al.*, 2009).

It is not possible to determine whether the reported effects in relation to the "energy drinks" are causally related to the "energy drink" or to simultaneous exposure to alcohol or exercise. In some cases narcotic drugs may have been involved (Reissig *et al.*, 2009). The EFSA ANS Panel suggested that the reported effects could be due to the well known caffeine effects, not involving taurine, but does not further discuss the implications of this.

Marketing of "energy drinks" is targeted primarily towards young males and the consumption of these drinks was associated with self-reported measure of masculinity and risk taking behaviour in students in the USA (Miller, 2008). Caffeine intake has in some studies been associated with narcotic drug use (cited in NCM, 2008; Reissig *et al.*, 2009).

It is also worth noting that the term "energy drink" does not refer to the energy (calorie) content of the product. Therefore, there may be a risk of confusing "energy drinks" with carbohydrate-containing sports beverages used for supplying caloric energy and water during exercise.

Has the risk of adverse health effects due to caffeine intake among different consumer groups in Norway changed since the last evaluation? If so, do these changes influence the conclusions in the VKM opinion on "energy drinks" from 2005?

Hazard identification and characterisation of caffeine

The Nordic Council of Ministers has recently published a risk assessment of caffeine among children and adolescents in the Nordic countries (NCM, 2008). The short section on the hazard identification and characterisation of caffeine given in this opinion is based on the information on caffeine's pharmacology, kinetics and toxicity presented in the Nordic report. Special emphasis is put on adverse effects of caffeine on the central nervous system, because much of the concern regarding caffeine exposure to children and adolescents is related to this.

The main molecular mechanism of action of caffeine is its inhibitory effect on the adenosine receptors, which are found in many tissues including the brain. Caffeine can induce tolerance and upon withdrawal unpleasant symptoms such as headache, reduced awareness and other symptoms may be experienced. A major difference between children and adults is the caffeine clearance from the body. In the foetus and up to about one year of age the clearance is extremely slow, whereas from about one year and up to about 12 years of age caffeine clearance is slightly higher than in adults. The half-life of caffeine is doubled or tripled during pregnancy due to hormonal changes that take place in the body of the pregnant women. The prolonged half-life of caffeine results in accumulation of caffeine in the body, and is expected to significantly increase the tissue concentration of caffeine. Negative health effects from caffeine may therefore occur at much lover coffee consumption (Andersson *et al.*, 2005).

The estimated lethal dose of caffeine is approximately 140 - 170 mg/kg bw (corresponding to approximately 60 - 100 cups of coffee). Toxic and fatal reactions have been associated with blood concentrations in excess of 15 and 80 mg/l respectively (Moffat, 2004). Lethal exposures are rare but some recent cases have been reported (Holmgren, 2004, Kerrigan and Lindsey, 2005). The lethal dose in children varies from case to case. For a 5-year-old girl, a dosage of 3 g caffeine was fatal.

High exposures to caffeine in adults may induce adverse effects like nervousness, anxiety, restlessness, insomnia, tremors and hyperesthesia. However, the doses of caffeine associated with severe neurotoxicity appear to be far above those commonly consumed. For example, the literature suggest that caffeine can produce anxiety at the doses of 17 mg/kg bw and above (Nawrot *et al.*, 2003). Very few data on adverse effects of caffeine in children are available. In children, anxiety seems to be induced at a dose from 2.5 mg/kg bw (Bernstein, 1994). Like adults, children probably derive little or no benefit from habitual caffeine intake, although negative effects associated with overnight caffeine withdrawal are avoided or rapidly reversed by subsequent caffeine intake. A lowest observed effect level (LOEL) for tolerance development with withdrawal symptoms were observed in children at the doses 1.0 – 1.25 mg/kg bw (Bernstein, 2002; Heatherley, 2006). The VKM Panel 4 noted that in general there is a large inter-individual variation in the tolerance to caffeine and adverse effects (NCM, 2008).

In adults, doses less than 100 mg (1.4 mg/kg bw) seem to have no effect on sleep disturbance in non-habitual coffee consumers (Nehlig, 1992). Although it is well known that children consuming caffeine show sleep disturbances, quantitative data on sleep disturbances in children are insufficient to conclude on doses. Turley and Gerst (2006) showed a significantly lower heart rate and higher blood pressure in both young girls and boys. Moderate doses of caffeine (5 mg/kg bw) did not affect metabolism in young children at low-moderate intensities of exercise. One study indicates that children and adolescents with a high (1.5L) daily consumption of caffeine in the form of cola drinks may develop caffeine-induced headache (Hering-Hanit and Gadoth, 2003).

Exposure assessment of caffeine

In the opinion on "energy drinks" from VKM in 2005, the exposure to caffeine in children, adolescents and adults was estimated. With exception of soft drinks, the exposure calculations in this updated opinion is based on the same content of caffeine in the different food groups included in the dietary surveys. New intake scenarios based on exposure to the main caffeine-containing food groups, and with an additional exposure to caffeine from "energy drinks" have now been conducted for the age groups children, adolescents and adults. For a more detailed description of the exposure calculations see Appendix.

The main food sources for caffeine intake are soft drinks, coffee, tea and chocolate products. Several food items contain caffeine from natural sources, such as cacao beans, tea, coffee and guarana. In soft drinks, caffeine is added as flavouring with maximum levels of 150 mg/litre (see page 9-10). In Denmark it was reported that very few children drink coffee before the age of 13 years. The drinking of coffee then gradually increases from the age of 15 years. In the same study it was shown that some young children (6-7 years old) consumed tea, and that the level is slightly increasing in adolescents (NCM, 2008). In Norway, children have nearly as high consumption of soft drinks as adults, while 13-year-old children have a higher consumption of soft drinks than adults (VKM, 2007).

Children and adolescents

The caffeine intake from other sources than "energy drinks" was estimated for children (4 years old) and adolescents (13 years old) (see Tables 1 and 2). The intake estimates include caffeine consumers only and are presented in mg/kg bw/day. It should be noted that only consumers that have reported their body weight are included in the estimates. This amounts to 298 of a total of 391 children and 861 of a total of 1005 adolescents represented in the dietary surveys (Pollestad *et al.*, 2002; Øverby and Andersen, 2002).

Table 1. *Intake of caffeine from different sources in Norwegian children (4 years old). The numbers include consumers only.*

Type of drink/food	N[a] (%)	Mean[b] (mg/kg bw/day)	95 percentile[b] (mg/kg bw/day)
Soft drinks*	204 (68)	0.7	1.7
Coffee	2 (0.7)	0.9	1.4
Tea	22 (7)	1.0	2.1
Chocolate products	203 (68)	0.2	0.5
Total	260 (87)	0.8	1.9

**Assuming that all soft drinks are cola drinks and includes light soft drinks*
[a] *Only children (N=298) who have reported their body weight in the dietary survey are included in the estimates*
[b] *The mean body weight for the 4-year-old children in the survey was 18 ± 2.5 kg*

Table 2. *Intake of caffeine from different sources in Norwegian adolescents (13 years old). The numbers include consumers only.*

Type of drink/food	N[a] (%)	Mean[b] (mg/kg bw/day)	95 percentile[b] (mg/kg bw/day)
Soft drinks*	784 (91)	1.0	2.3
Coffee	10 (1.2)	0.2	0.4
Tea	138 (16)	0.5	1.4
Chocolate products	485 (56)	0.2	0.5
Total	821 (95)	1.1	2.7

**Assuming that all soft drinks are cola drinks and includes light soft drinks*
[a] *Only adolescents (N=861) who have reported their body weight in the dietary survey are included in the estimates*
[b] *The mean body weight for the 13-year-old adolescents in the survey was 49.4 ± 9.4 kg*

The consumption data on "energy drinks" is taken from the recent EFSA opinion "*The use of taurine and D-glucurono-γ-lactone as constituents of the so-called "energy" drinks*" (SCF, 2003; EFSA, 2009). Adolescents are developmentally in-between children and adults, and they might have the same potential consumption of "energy drinks" as adults. The VKM Panel 4 therefore assumes that adolescents have the same consumption of "energy drinks" as adults. In the EFSA opinion the high chronic consumption (95th percentile) was estimated to be 1.4 cans/person/day, where a can of "energy drink" contains 250 ml. If consumption by children would be 2.5 times lower than adults and adolescents, the high chronic consumption of "energy drinks" would be 0.56 cans/person/day. The acute consumption of "energy drinks" for adults/adolescents were estimated to 3 cans/day, being higher than the 90th percentile in an Austrian survey and being the average reported in an Irish survey for most numbers of cans consumed in a single session (cited in EFSA 2009 and SCF 1999). High consumers (95 percentile) of soft drinks among 4-year-old children consume 200 ml/day (NCM, 2008). A reasonable assumption would be that the acute consumption of "energy drinks" for children at this age would be 1 can/day. The content of caffeine is reported to be 0.03% on the label of Red Bull, which corresponds to 75 mg caffeine in a 250 ml can of Red Bull. The intake of caffeine from "energy drinks" for the children and adolescents is shown in Table 3.

Table 3. *Estimated intake of caffeine from "energy drinks" in Norwegian children (4 years old) and adolescent (13 years old).*

Age group	Consumption	"Energy drinks" (cans/day)	Intake (mg/day)	Intake* (mg/kg bw day)
Children	High chronic	0.56	42	2.3
Children	Acute	1	75	4.2
Adolescent	High chronic	1.4	105	2.1
Adolescent	Acute	3	225	4.5

**The mean body weight used for children and adolescents in the survey was 18 ± 2.5 kg and 49.4 ± 9.4 kg respectively.*

If we assume, in a worst case situation, that 100% of all consumed soft drinks are cola drinks and that the persons consuming "energy drinks" also have a high consumption (95th percentile) of soft drinks, tea, coffee and chocolate products, the intake of caffeine for children will be 4.2 and 6.1 mg/kg bw/day for high chronic and acute consumption of "energy drinks", respectively. The adolescents will have an estimated caffeine intake of 4.8 and 7.2 mg/kg bw/day for high chronic and acute consumption of "energy drinks", respectively.

Adults

The caffeine intake from other sources than "energy drinks" was estimated for adults (16-79 years old) (see Table 4). The intake estimates include caffeine consumers only and are presented in mg/kg bw/day. It should be noted that only consumers that have reported their body weight are included in the estimates. This amounts to 2582 of a total of 2672 adults represented in the dietary survey (Johansson and Solvoll, 1999).

Table 4. *Intake of caffeine from different sources in Norwegian adults. The numbers include consumers only.*

Type of drink/food	N[a] (%)	Mean[b] (mg/kg bw day)	95 percentile[b] (mg/kg bw day)
Soft drinks*	1731 (67)	0.6	2.1
Coffee	2129 (82)	2.3	6.5
Tea	1803 (70)	0.9	3.2
Chocolate products	576 (22)	0.2	0.3
Total	2553 (99)	3.0	7.4

**Assuming that all soft drinks are cola drinks and includes light soft drinks*

[a] *Only adults (N=2582) which have reported their body weight in the dietary survey are included in the estimate*

[b] *The mean body weight for adults in the survey was 74 kg*

In adults, the high chronic consumption (95th percentile) was estimated to be 1.4 cans/person/day, where a can of "energy drink" contains 250 ml. The acute consumption of "energy drinks" for adults/adolescents was estimated to 3 cans/day (cited in EFSA 2009 and SCF 1999). The intake of caffeine from high chronic and acute consumption of "energy drinks" in adults is presented in Table 5.

Table 5. *Estimated intake of caffeine from "energy drinks" in Norwegian adults.*

Age group	Consumption	"Energy drinks" (cans/day)	Intake (mg/day)	Intake* (mg/kg bw day)
Adults	High chronic	1.4	105	1.75
Adults	Acute	3	225	3.75

** The mean body weight for adults in the survey was 74 kg*

If we assume, in a worst case situation, that 100% of all soft drinks consumed are cola drinks and that the persons consuming "energy drinks" also have a high consumption (95th percentile) of soft drinks, tea, coffee and chocolate products, the intake of caffeine for adults will be 9.2 and 11.2 mg/kg bw/day for high chronic and acute consumption of "energy drinks", respectively.

Risk characterisation

A risk assessment of caffeine among children and adolescents in the Nordic countries were published in 2008 (NCM, 2008). In the report a brief review of pharmacological and toxicological actions of caffeine in humans was described. In this opinion from VKM Panel 4, the LO(A)ELs identified in the Nordic report will be used in the risk characterisation for children and adolescents, while the LOAEL from Nawrot *et al*. 2003 will be used for adults. For children there were identified a LOAEL of 2.5 mg/kg bw for anxiety. A LOAEL of 1.4 mg/kg bw were identified for sleep disturbance in adults who are non-habitual coffee consumers. This LOAEL is used for adolescents who have a low coffee consumption. For adults having a normal coffee consumption a LOAEL of 17 mg/kg bw were identified for anxiety (Nawrot *et al.*, 2003).

Children

The caffeine intake for children, based on the high caffeine (95th percentile) intake from other sources and the additional caffeine intake from "energy drinks", is compared with the LOAEL of 2.5 mg/kg bw for anxiety. The children have an estimated caffeine intake of 4.2 and 6.1 mg/kg bw/day for high chronic and acute consumption of "energy drinks", respectively. The estimated daily intake of caffeine for children with high chronic consumption of "energy drinks" is approximately 1.7-fold higher than the LOAEL for anxiety. For children with an acute consumption of "energy drinks" the caffeine intake is 2.5-fold higher than the LOAEL for anxiety. The caffeine intake is below this LOAEL for high consumers of other sources of caffeine not consuming "energy drinks".

The estimated consumption of "energy drinks" will have a major impact on the total caffeine intake in children and will contribute to an increased incidence of exceeding the LOAEL for anxiety for caffeine in children. Such effects of caffeine are unwanted in children below 12 years. The Panel considers the estimated consumption of "energy drinks", and the increased intake of caffeine as described in this opinion to be of concern for children.

Adolescents

The caffeine intake for adolescents, based on the high caffeine (95th percentile) intake from other sources and the additional caffeine intake from "energy drinks", is compared with the LOAEL of 1.4 mg/kg bw for sleep disturbance. The adolescents have an estimated caffeine

intake of 4.8 and 7.2 mg/kg bw/day for high chronic and acute consumption of "energy drinks", respectively. The estimated daily intake of caffeine for adolescents with high chronic consumption of "energy drinks" is approximately 3.4-fold higher than the LOAEL for sleep disturbance. For adolescents with an acute consumption of "energy drinks" the caffeine intake is 5.1-fold higher than the LOAEL for sleep disturbance.

Adolescents are developmentally in-between children and adults, and they might have the same potential consumption of "energy drinks" as adults, while the consumption of coffee is still very low. On the other hand it is assumed that the adolescents might have a considerable intake of caffeine from soft drinks, and that some tolerance development to caffeine from soft drinks might be expected. Consumption of coffee is accepted in the Norwegian society. This also implies a general acceptance for tolerance development to caffeine in adults, and also to a certain degree in adolescents who starts to drink coffee. High chronic intake of "energy drinks" may induce the same tolerance to caffeine as consumption of coffee. Potential adverse effects of "energy drink" consumption can not be ruled out for adolescents who have low tolerance for caffeine from other sources. The risk of adverse effects to caffeine from "energy drinks" is highest for adolescents aged 13-15 years old, where the consumption of coffee is low and the tolerance development to caffeine is expected to be lower than for adults. The highest risk is anticipated to be connected to acute consumption of energy drinks.

Adults

The caffeine intake for adults, based on the high caffeine (95^{th} percentile) intake from other sources and the additional caffeine intake from "energy drinks", is compared with the LOAEL of 17 mg/kg bw for anxiety. The adults have an estimated caffeine intake of 9.2 and 11.2 mg/kg bw/day for high chronic and acute consumption of "energy drinks", respectively. The estimated intake of caffeine for adults is below the LOAEL for anxiety both for high chronic and acute consumption of "energy drinks".

In adults, there is a general acceptance for caffeine intake and an associated tolerance development. The anticipated "energy drinks" consumption gives caffeine intake below the levels estimated for coffee and gives a total caffeine intake below the level that results in anxiety. The VKM Panel 4 regards this increase in caffeine intake of no safety concern for adults.

The half-life of caffeine is doubled or tripled during pregnancy due to hormonal changes. Pregnant women should therefore be careful with the intake of caffeine. The VKM Panel 4 maintains the recommendations given in the VKM opinion from 2005 that the intake of caffeine in pregnant women should not exceed 100-200 mg/day.

CONCLUSIONS AND RECOMMENDATIONS

Question 1: How will the new information on taurine and D-glucurono-γ-lactone and the conclusions presented in the new opinion from EFSA influence the conclusions of the VKM opinion from 2005, which concerned "energy drinks" as such?

- New studies have established a NOAEL for taurine of 1000 mg/kg bw/day. Based on this, the EFSA concludes that exposure to taurine as an individual ingredient at the levels presently used in "energy drinks" and at intake levels presented in the EFSA opinion, is of no safety concern. The VKM Panel 4 endorses this conclusion and considers it as valid also for Norway.

- New studies have established a NOAEL for D-glucurono-γ-lactone of 1000 mg/kg bw/day. Based on this, the EFSA concludes that exposure to D-glucurono-γ-lactone as an individual ingredient at the levels presently used in "energy drinks" and at intake levels presented in the EFSA opinion, is of no safety concern. The VKM Panel 4 endorses this conclusion and considers it as valid also for Norway.

- EFSA concluded that additive effects between taurine and caffeine on diuretic effects are unlikely. Other interactions between taurine and caffeine were not investigated. However, it should be noted that potential combined effects of taurine and caffeine on the cardiovascular system, e.g. for susceptible individuals, cannot be ruled out since this is not properly investigated. The VKM Panel 4 agrees with the SCF opinion from 2003 that there is no *a priori* reason to expect combined effects of D-glucurono-γ-lactone and caffeine or taurine.

- EFSA did not evaluate the safety of "energy drinks" as such. It should be noted that several new cases of possible adverse effects of "energy drinks" in combination with alcohol or exercise have been reported since the VKM opinion in 2005. It is not possible to determine whether the reported effects in relation to the "energy drinks" are causally related to the "energy drink" or to simultaneous exposure to alcohol or exercise. In some cases narcotic drugs may also have been involved.

Question 2: Has the health risk of caffeine among different consumer groups in Norway changed since the last evaluation? If so, do these changes influence the conclusions in the VKM opinion on "energy drinks" from 2005?

New intake scenarios based on exposure to the main caffeine-containing food groups, and with an additional exposure to caffeine from "energy drinks" have now been conducted for the age groups children, adolescents and adults. With exception of soft drinks, the exposure calculations in this updated opinion is based on the same content of caffeine in the different food groups included in the dietary surveys as in 2005. For a more detailed description of the exposure calculations see Appendix.

The new intake estimates of caffeine for children, adolescents and adults show that the caffeine intake in the different age groups in the Norwegian population has not changed considerably since the last risk assessment from VKM in 2005. The VKM Panel 4 noted that in general there is a large inter-individual variation in the tolerance to caffeine.

- The caffeine intake for high consumers of soft drinks, tea and chocolate among children approaches the LOAEL for anxiety. In addition, the estimated consumption of "energy drinks" will have a major impact on the total caffeine intake in children and will contribute to an increased incidence of exceeding the LOAEL for anxiety. Such effects of caffeine are unwanted in children below 12 years. The VKM Panel 4 considers the estimated consumption of "energy drinks", and the increased intake of caffeine as described in this opinion to be of concern for children.

- Adolescents are developmentally in-between children and adults, and they might have the same potential consumption of "energy drinks" as adults, while the consumption of coffee is still very low. On the other hand, it is assumed that adolescents might have a considerable intake of caffeine from soft drinks, and that some tolerance development to caffeine from soft drinks might be expected. Potential adverse effects of "energy drink" consumption can not be ruled out for adolescents with no or low tolerance for caffeine. The risk of adverse effects of caffeine from "energy drinks" is highest for adolescents aged 13-15 years old, where the consumption of coffee is low and the tolerance development to caffeine is expected to be lower than for adults. The highest risk is anticipated to be connected to acute consumption of "energy drinks".

- For adults, the caffeine intake from soft drinks, coffee, tea and chocolate is considerably lower than the LOAEL for anxiety even when the additional high chronic or acute intake of "energy drinks" is included. The VKM Panel 4 regards this increase in caffeine intake of no safety concern for adults.

- The half-life of caffeine is doubled or tripled during pregnancy due to hormonal changes. Pregnant women should therefore be careful with the caffeine intake. The VKM Panel 4 maintains the recommendations given in the VKM opinion from 2005, that the intake of caffeine in pregnant women should not exceed 100-200 mg/day.

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APPENDIX

Data on food consumption in Norway are available at three different levels; the national food supply, household surveys and dietary surveys. In the present opinion, the exposure assessment for caffeine has been based on data from national representative dietary surveys. In this type of surveys, information about food consumption among individuals is collected using various dietary assessment methods. Presently, there is no method available without shortcomings to measure food exposure. Therefore, evaluation of the dietary assessment tools should be performed, and results from these evaluation studies should be kept in mind in interpretation of results from the surveys. The following national representative dietary surveys have been used in this opinion:

4-year-old children: Ungkost 2000 (Pollestad *et al.*, 2002). Ungkost 2000 is based on a 4-day food consumption registration (391 children), where portions should be assigned according to an illustrative book with different food portion sizes. The intake estimates in this opinion include only the children that have reported their body weight (298 children).

13-year-old children: Ungkost 2000 (Øverby and Andersen, 2002). Ungkost 2000 is based on a 4-day food consumption registration (1005 adolescents), where portions should be assigned according to an illustrative book with different food portion sizes. The intake estimates in this opinion include only the adolescents that have reported their body weight (861 adolescents).

Adults: Norkost 1997 (Johansson and Solvoll, 1999). Norkost is based on a quantitative frequency questionnaire that was answered by 1291 males and 1381 females aged 16-79 years. The intake estimates in this opinion include only the adults that have reported their body weight (2582 adults).

Information on the content of caffeine in the different food items which are included in the exposure calculations are based on data from the literature. The content of caffeine in different foods will vary depending on which plant species and processing methods that are used and also between different brands. With exception of soft drinks, the exposure is based on the same data on caffeine content as was used in the VKM opinion on “energy drinks” from 2005 (VKM, 2005). The exposure to soft drinks is based on a content of 130 mg caffeine/litre in cola drinks according to information from the Coca Cola Company Norway in October 2005 (NCM, 2008).

It should be noted that since the dietary surveys did not specify whether the soft drinks contained caffeine or not, the assumption that all soft drinks are cola drinks has been made. Both soft drinks with sugar and intense sweeteners (light soft drinks) are included in the exposure estimations. Exposure to caffeine from pharmaceutical products and dietary supplements is not included. An overview of the caffeine content in different foods and beverages used in the exposure calculations in this opinion is shown in Table 6.

Table 6. Caffeine content in different foods and beverages (mg/litre) used in the exposure calculations. Data from Coca Cola Company Norway (October 2005)[1]. "Food Surveillance Information Sheet No. 144" (March 1998), MAFF, London[2], Norwegian Coffee Association (www.kaffe.no)[3], The Coffee Science Information Centre (http://www.cosic.org/caffeine/whatisit)[4].

Food items	mg/caffeine/litre
Soft drinks[1]*	**130**
Filtered coffee[2]	105-215 (mean value **180**)
Instant coffee[3]	**400**
Brewed coffee[4]	267-1200 (mean value **650**)
Tea[3]	**267**
Chocolate drinks[2]	5.5-41 (mean value **23**)
Cocoa drinks[4#]	13-133 (**27**)
Milk chocolate[4]	33-500 (**200**)
Dark chocolate[4]	167-1167 (**667**)
Plain chocolate[4]	**867**

** Assuming that all soft drinks are cola drinks and includes light soft drinks*

[#] Data based on consumption of cocoa powder. The content of caffeine in cocoa powder is estimated from a content of 27 mg caffeine/litre in chocolate drinks. It is assumed that 4 tablespoons cocoa powder (6 g) is used per litre of chocolate drink, i.e. 24 g cocoa powder/litre. This calculation results in a content of 1.1 mg caffeine pr g cocoa powder (27 mg caffeine per 1000 g chocolate drink/24 g cocoa powder).