FOOD STANDARDS Australia New Zealand
Te Mana Kounga Kai – Ahitereiria me Aotearoa

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Supporting document 1

Risk and technical assessment – Urgent Proposal P1054

Pure and highly concentrated caffeine products

Executive summary

Caffeine has the technological function as a flavouring in many countries, including in Australia and New Zealand. In the Code, it is permitted to be added as a flavouring to cola type drinks. If used as a stimulant (not a food additive), it can be added to formulated caffeinated beverages to enhance mental performance. Regardless of the purpose of adding caffeine to food it is appropriate that it complies with a relevant specification in Schedule 3. One of the primary sources of specifications in Schedule 3 is the Food Chemicals Codex which contains a specification for caffeine.

FSANZ's risk assessment confirmed that there is an immediate and acute risk posed by the sale of pure or highly purified forms of caffeine to consumers. Ingestion of small amounts of these substances can result in severe health effects, including death.

For powders and other solid products containing caffeine, FSANZ has identified that less than or equal to 5% caffeine is not considered to pose an unacceptably high risk to consumers. A caffeine concentration of 5% is slightly higher than the levels of caffeine typically found in instant coffee, and a heaped tablespoon of such a powder would contain approximately 825 mg caffeine, a dose which would be unlikely to cause severe health effects in healthy adults.

Accidental ingestion of liquid containing high concentrations of caffeine may occur more easily than with bulk powder products. FSANZ considers that for concentrated solutions of this type, a maximum level of 1% w/v caffeine is required to protect public health and safety. This value is based on the practical consideration that in order to dispense 100 mg caffeine, 10 mL of solution would be required.

The Risk Assessment therefore concluded that the maximum concentration of caffeine in powders or other solids should not exceed 5% w/w, and that the maximum concentration of caffeine in liquids should not exceed 1% w/v.

Table of contents

1 Introduction

1.1 Objectives of the assessment

The objectives of this risk and technical assessment for this Proposal were to:

- Prepare a food technology assessment regarding caffeine
- Prepare a risk assessment, to determine:
    - The answer to the question: do pure and highly caffeinated food products (sold at retail, direct to consumers) pose a serious adverse health threat to consumers?
        - If the answer to that question is yes, what concentration of caffeine in a powder or liquid concentrate is unlikely to be associated with serious adverse health effects in healthy adults?
        - In relation to any concentration limits established above, is it the same for children, pregnant or lactating women, subpopulations sensitive to caffeine, and/or persons with medical conditions?

2 Food technology assessment

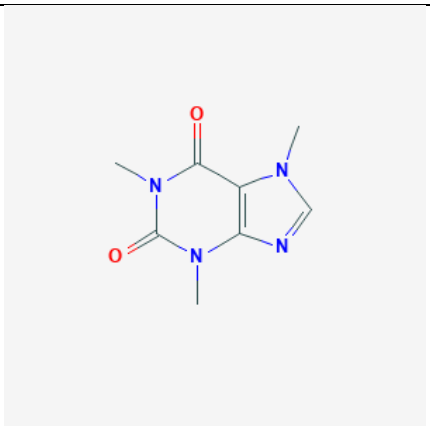
2.1 Assessment of the caffeine permissions in the Code

2.1.1 Chemical and physical properties of caffeine

Caffeine is a stable alkaloid that is found in various plants such as coffee and cocoa beans, tea leaves, guarana berries and kola nut having a long history of human consumption as a component of such foods. As a pure extracted substance it is also permitted to be added as a flavouring substance (see section 2.1.2 below) in cola type drinks and as a stimulant in formulated caffeinated beverages (see section 2.1.3 below). The chemical and physical properties of the substance are summarised in Table 1 (Food Chemicals Codex 2018, PubChem 2020).

Table 1 Chemical and physical properties of caffeine

Common name	caffeine
Chemical name	1,3,7-Trimethylxanthine
Alternative names	Guaranine Methyltheobromine Thein(e)
IUPAC name	1,3,7-trimethylpurine-2,6-dione
Molecular formula (anhydrous)	$C_8H_{10}N_4O_2$
Molecular weight (anhydrous)	194.19 g mol^{-1}
CAS number (anhydrous)	58-08-2

Chemical structure	
Description	White powder or white glistening needles, odourless, with a bitter taste
Melting point (°C)(dried, 80°C 4 hrs)	235-238

2.1.2 Caffeine as a flavouring food additive

Caffeine has been permitted and used as a flavouring substance in cola type drinks throughout the world for many years.

There is the only one permission for the use of caffeine as a food additive within the Code. The Code permits the use of caffeine in cola type drinks (S15—5, food class 14.1.3.0.2) at a maximum permitted level (MPL) of 145 mg/kg as listed in the table to section 5 of Schedule 15. Caffeine is performing the technological purpose of a flavouring when added to cola type drinks and is considered a food additive in this instance. Substances used as a food additive (defined by section 1.1.2—11 of the Code) must perform one or more of the technological purposes listed in S14. Flavouring is one of those technological purposes. There are no other technological purposes listed in Schedule 14 that apply to the additional of caffeine to cola type drinks.

The entry for *Permitted flavouring substances in tables to section 2 of Schedule 16, S16—2, specifically excludes caffeine. Therefore food additive permissions in the table to S15—5 for food classes that refer to ‘Additives permitted at GMP’, those food additives listed in the tables to S16—2, explicitly does NOT include a permission for caffeine.

The definition of ‘permitted flavouring substance’ in Standard 1.1.2 means a substance that is listed in one of four publications. The first of these is the Flavour and Extract Manufacturers Association of the United States (FEMA) Generally Recognized as Safe (GRAS) list. Caffeine is listed in the FEMA GRAS list with the FEMA number 2224. In FEMA’s original GRAS determination in 1965 (being the first list of GRAS flavourings, titled III GRAS substances) it indicated that the average of the maximum use levels of companies to be 120 mg/kg (L) in beverages, but not used in other food categories.

International permissions

The U.S. Code of Federal Regulations (CFR) enforced by the US Food and Drug Administration (US FDA) has a specific permission for caffeine as a GRAS substance that can be added to cola-type beverages at a level up to 0.02% (200 mg/kg(L)) (USFDA 2020)). It is understood that this GRAS permission is given for its use as a flavouring substance but it is not explicitly stated as such. It is noted that the US Food Chemicals Codex specification for caffeine lists its function as a flavouring agent.

Europe also considers caffeine as a flavouring substance as detailed in the European Commission list of flavouring substances search page (European Commission 2020). The EC flavouring number is 16.016. The EU regulation 2018/1482 (European Commission 2018) relates to specific permissions for caffeine addition to food. This contains a maximum level of 150 mg/kg for the food category 14.1 (non-alcoholic beverages). There are other permissions for the use of caffeine as a flavouring in other food categories (with their maximum limits in parentheses) being: dairy products and analogues (70 mg/kg), edible ices (70 mg/kg) and confectionery (100 mg/kg). Caffeine is also a flavouring with the Council of Europe, with flavouring number 11741.

The levels of use of caffeine as a flavouring in cola type drinks is therefore similar in Australia and New Zealand, with a MPL of 145 mg/kg compared to 200 mg/kg in the US and 150 mg/kg in Europe.

2.1.3 Caffeine as a stimulant

Caffeine is also one of the most commonly consumed stimulants, affecting the central nervous system. One of the most well-known mechanisms of its function as a stimulant is blocking the action of adenosine, preventing the onset of drowsiness induced by adenosine. There is also evidence and claims in the literature that caffeine consumption can improve reaction time, concentration and motor coordination. As well there is literature that caffeine consumption can improve mental performance as well as physical performance such as sprint and endurance performance and with reduced perceived exertion.

The Australia New Zealand Food Authority (ANZFA), the forerunner of FSANZ, established Standard 2.6.4 – Formulated caffeinated beverages as an outcome of application A394 in 2001 (ANZFA 2001). The definition of formulated caffeinated beverage in the Standard refers to ‘the purpose of enhancing mental performance’ without any mention of physical performance. The assessment reports for A394 noted this was to distinguish these products from sports and electrolyte beverages whose purpose is related to physical performance. The reference to enhancing mental performance was directly focused on the addition of caffeine as the only essential ingredient for these products.

2.1.4 Caffeine specification

All permitted food additives are required to meet requirements of identity and purity to ensure that they are safe to be added to food due to the identity and purity requirements of section 1.1.1—15.

The permission for caffeine addition for formulated caffeinated beverages where caffeine does not have the technological purpose of a food additive, that is, it is not being considered as a flavouring substance, but as a stimulant is not explicitly addressed in section 1.1.1—15. Regardless, it is appropriate that caffeine added to formulated caffeinated beverages needs to meet an appropriate purity specification.

Food Chemicals Codex is a primary source of specifications for substances in Schedule 3, being paragraph S3—2(1)(c), which has a specification for caffeine.

2.2 Food technology conclusion

Caffeine has the technological function as a flavouring in many countries, including in Australia and New Zealand. Flavouring is one of the technological functions of food additives in the Code. However, it does not have general permissions as a flavouring, only for addition to cola type drinks. The permitted levels of use of caffeine in cola types drinks in Australia

and New Zealand is similar to those in the US and Europe.

Caffeine can also have the technological function as a stimulant, which is not a function of a food additive. It has permission in the Code to be added as a stimulant to formulated caffeinated beverages specifically to enhance mental performance.

Regardless of the purpose of adding caffeine to food it is appropriate that it complies with a relevant specification in Schedule 3. One of the primary sources of specifications in Schedule 3 is the Food Chemicals Codex which contains a specification for caffeine.

3. Risk Assessment

3.1 Previous FSANZ assessments

A FSANZ Expert Working Group analysed the available literature on caffeine in 2000. The Expert Working Group noted that a no effect level for caffeine in humans has not been established, and concluded that there was evidence of increased anxiety levels in both adults and children at doses of about 3 mg of caffeine per kilogram of bodyweight per day (ANZFA 2000). This level equates to a caffeine dose of 95 mg per day (approximately two cans of cola) in children and about 210 mg per day (approximately three cups of instant coffee) for adults.

3.2 Assessments by other regulatory agencies

The European Food Safety Authority (EFSA) concluded in 2015 that a total caffeine intake of 400 mg/day (5.7 mg/kg bodyweight/day) is safe for most adults. EFSA recommends that pregnant women should not consume more than 200 mg/day, or approximately 3 mg/kg bw/day, on the basis of a risk of adverse effects on foetal growth and on birthweight at higher levels of maternal consumption. EFSA concluded that there is insufficient information to determine safe levels of caffeine for children or adolescents, but that the acute intake of no concern to adults (3 mg/kg bw/day) may be used to derive acute and daily caffeine consumption values for those groups (EFSA 2015).

The United States Food and Drug Administration(US FDA) (USFDA 2018a, USFDA 2018b) also considers that 400 mg/day of caffeine is not associated with adverse effects. The US agency warns that some medical conditions, and some medications, may increase individual sensitivity to caffeine, and advises pregnant and breastfeeding women to seek the advice of their healthcare provider. The US FDA has not set a level of caffeine for children, but noted that the American Academy of Paediatrics discourages the consumption of caffeine by children and adolescents. The US FDA estimated that severe adverse effects, such as seizures, may occur with rapid consumption of 1 200 mg caffeine or more.

The US FDA has identified products consisting of or containing only pure or highly concentrated caffeine as ‘a significant public health threat’, after the US FDA linked at least two recent deaths in the United States to such products. In response, the US FDA issued guidance stating that it considers certain types of these products to be adulterated and, therefore, prohibited under US food law because they present a significant or unreasonable risk of illness or injury.

3.3 Assessment of the acute health risk posed by the sale of pure and highly concentrated caffeine food products or caffeine analogues

The effects of acute caffeine intake on healthy non-pregnant adults, at doses from 20 mg to 10 000 mg, are shown in Table 2.

Table 2 Acute effects of caffeine in adults

Acute dose (mg)	Effects/Comments
>20 mg	Self-reported positive effects on mood[a]
60	Measurable decrease in reaction time[a]
80–95	Single cup of coffee[a,b]
100	May delay sleep and reduce sleep duration[a, c]
140	Minor increase in diastolic pressure[a]
200	Up to this level not associated with safety concerns[c]
200–250	Effects including an increase in blood pressure and plasma catecholamines. Reduction in myocardial blood flow when exercising[c]
280	Reduction in perceived exertion during exercise[c]
400-500	Increase in anxiety in psychologically normal subjects[c]
>500	Rate of clearance of caffeine is decreased[b]
1200	Tachycardia, ventricular arrhythmia, seizures[a,b]
3 000	Lowest lethal dose identified by FSANZ[a]
5 000–10 000	Life-threatening dose[a]

[a]ANZFA (2000); [b]US FDA (2018b); [c]EFSA (2015)

Intake of caffeine of up to 210 mg (approximately 3 mg/kg bodyweight/day) is not associated with safety concerns in healthy adults. Above that dose, caffeine intake is generally associated with an increase in blood pressure, plasma catecholamines and increased anxiety. At or above 1 200 mg more serious effects such as tachycardia, ventricular arrhythmia or seizures may develop and urgent medical attention may be required. Death has been reported at a dose of 3 000 mg, however it is more commonly associated with doses of around 5 000 to 10 000 mg caffeine.

Subpopulations particularly sensitive to effects of caffeine, as identified by EFSA and the US FDA, include pregnant women, lactating women, people with hypertension, people with impaired myocardial perfusion, people with certain mood disorders such as anxiety, and people who are taking *p*-synephrine.

3.3.1 Pure caffeine powder

FSANZ's assessment is that pure and highly concentrated caffeine food products are a high risk and pose a significant health concern. Ingestion of a 5 mL teaspoon of pure caffeine powder (approximately 3 000 mg caffeine) will result in severe health effects and could be fatal to some individuals. The risk of serious health effects is compounded by the fact that

these products can require fine scales (most kitchen scales measure in grams, not milligrams) to weigh an appropriate dose.

3.3.2 Products containing a high level of caffeine

Bulk powder products containing caffeine

Powders and other solid products containing less than or equal to 5% caffeine are not considered to pose an unacceptably high risk to consumers. A caffeine concentration of 5% i.e. 5 000 mg/100 g is slightly higher than the levels of caffeine typically found in coffee (Table 2), and not likely to pose significant additional acute health risks to those associated with traditional coffee products.

Ingestion of a single serving of a heaped tablespoon of a caffeine powder containing 5% caffeine would be likely to deliver approximately 825 mg caffeine.[1] Acute doses in this range would be unlikely to cause severe health effects in healthy adults, although they could be expected to be associated with unpleasant effects such as anxiety.

The same doses may be hazardous to sensitive subpopulations such as children and pregnant women. For example, in children an acute dose of 825 mg caffeine would result in a higher exposure on a mg/kg bw basis than an adult because children typically have lower body weights. However it needs to be recognised that a similar level of risk exists, and is accepted, for naturally caffeine-containing products such as coffee which are kept in the home. As such, a level of 5% caffeine in bulk powder products is considered acceptable.

FSANZ advises that children should not consume more than 3 mg/kg bodyweight of caffeine in a single serving (ANZFA 2000).

Liquid caffeine concentrate products

Concentrated caffeine solutions, used to make energy drinks by consumers, are of high risk and pose a significant health concern. Accidental ingestion of liquid products may occur more easily than bulk powder products.

FSANZ considers that for concentrated solutions of this type, a maximum concentration of 1% w/v caffeine is required to protect public health and safety. This value is based on the calculation that in order to measure 100 mg caffeine, 10 mL of solution would be required. Accurate measurement of 10 mL is considered to be reasonably achievable in a home situation.

Individually packaged portion-controlled caffeine products

Individually packaged caffeine products are expected to pose lower risk to consumers, as compared to bulk powders and liquid concentrates, because total caffeine exposure is likely to be limited by the portion-controlling packaging.

[1] Assuming a poured bulk density of powdered caffeine of 0.55 g/mL (https://www.fda.gov/inspections-compliance-enforcement-and-criminal-investigations/warning-letters/smartpowders-08272015) a 15 mL tablespoon (NZ) would have a mass of 8.25 g. A heaped tablespoon might be expected to have a mass of approximately 16.5 g. If caffeine was extended with other powdered material of similar density, a heaped tablespoon of a powder containing 5% caffeine would deliver approximately 825 mg caffeine.

Caffeine content of chewable sports supplements identified by FSANZ ranges from 0.085 to 0.25% w/w, and the highest single dose located is 100 mg. Gels appeared to range from 0.08-0.4% w/w caffeine, with the highest single dose 160 mg caffeine. Chewables and gels therefore do not pose a risk to health when presented for sale in portion-controlled serves per package.

3.3.3 Caffeine analogues

FSANZ is aware that a number of analogues or derivatives of caffeine exist naturally or can be chemically synthesised (Bello et al. (2019); Daly et al. (1986); Murbach et al. (2019); Muller and Jacobson (2011)). FSANZ will further consider the potential health impacts of sports foods containing caffeine and caffeine analogues or derivatives, both those that occur naturally or that may be chemically synthesised, as a part of the review of Standard 2.9.4 – Formulated Supplementary Sports Foods (P1010).

3.4 Risk assessment conclusion

FSANZ's risk assessment confirmed that there is an immediate and acute risk posed by the sale of pure or highly purified forms of caffeine to consumers. Ingestion of small amounts of these substances can result in severe health effects, including death.

FSANZ's risk assessment considered the adverse effects of high doses of caffeine; the existing exposure of consumers to caffeine through coffee and other caffeine-containing foods; and the volumes that are likely to be reasonably easy for consumers to measure.

For powders and other solid products containing caffeine, FSANZ has identified that less than or equal to 5% caffeine is not considered to pose an unacceptably high risk to consumers. A caffeine concentration of 5% is slightly higher than the levels of caffeine typically found in instant coffee, and a heaped tablespoon of such a powder would contain approximately 825 mg caffeine, a dose which would be unlikely to cause severe health effects in healthy adults.

Accidental ingestion of liquid containing high concentrations of caffeine may occur more easily than with bulk powder products. FSANZ considers that for concentrated solutions of this type, a maximum concentration of 1% w/v caffeine is required to protect public health and safety. This value is based on the practical consideration that in order to dispense 100 mg caffeine, 10 mL of solution would be required.

The Risk Assessment therefore concluded that the maximum concentration of caffeine in powders or other solids should not exceed 5% w/w, and that the maximum concentration of caffeine in liquids should not exceed 1% w/v.

4 References

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