

Supporting Document 1

Safety assessment (Approval) – Application A1039

Low THC Hemp as a Food

Executive Summary

The FSANZ approach to the safety assessment of this Application is to provide an update of the previous safety and nutrition assessments for Application A360.

For the assessment of Application A360, FSANZ conducted a thorough risk assessment which established a tolerable daily intake (TDI) of 6 micrograms of delta-9-tetrahydrocannabinol (THC) per kilogram of bodyweight (6 µg THC per kg bw).

For the present Application, additional THC studies, which were identified in a recent review, were considered, in order to establish whether new data indicate a need to change the TDI. The updated safety assessment concludes that the TDI of 6 µg THC per kg bw remains valid and that the maximum limits for THC content of hemp foods are appropriate.

The safety assessment for this Application included an update on the dietary modelling conducted for Application A360. The updated dietary modelling included food consumption data from the recent national children's surveys in Australia and New Zealand, which were not available at the time of the Application A360 assessment. The chronic dietary exposure assessment indicates that potential dietary exposures to THC are below the TDI of 6 µg/kg bw for all age groups for the Australian and New Zealand populations.

The nutrition assessment for this Application reinforces the outcome of the Application A360 nutrition assessment, and concludes that low THC hemp in food products may provide a useful alternative dietary source of many nutrients and polyunsaturated fatty acids, particularly omega-3 fatty acids. Only small quantities of whole hempseed or hempseed oil need be consumed to meet the adult Adequate Intake for alpha-linolenic acid (an essential omega-3 fatty acid).

Abbreviations

Time		Weight	
h	Hour	bw	Bodyweight
d	Day	kg	Kilogram
		ng	Nanogram
		µg	Microgram
		mg	Milligram
		g	Gram
Dosing			
mg/kg bw	mg/kg bodyweight		
µg/kg bw	µg/kg bodyweight		

Chemistry	
ALA	<i>Alpha</i> -Linolenic Acid
DHA	Docosahexaenoic Acid
EPA	Eicosapentaenoic Acid
GLA	<i>Gamma</i> -Linolenic Acid
LA	Linolenic Acid
SAA	Sulphur containing Amino Acids
SDA	Stearidonic acid
THC	Delta-9-tetrahydrocannabinol
PUFAs	Poly Unsaturated Fatty Acids
Terminology	
AI	Adequate Intakes
AUS	Australia
C _{max}	Maximum Concentration
CNS	Central Nervous System
DEA	Dietary Exposure Assessment
DIAMOND	Dietary Modelling of Nutritional Data
IEFS	Institute of European Food Studies
LOEL	Lowest Observed Effect Level

ML	Maximum Levels
MS	Multiple Sclerosis
n	Number
NCS	Australian National Children's Nutrition and Physical Activity Survey
NNS	Australian National Nutrition Survey
NOAEL	No Observed Adverse Effect Level
NOEL	No Observed Effect Level
NRV	Nutritional Reference Value
NZ	New Zealand
NZCS	New Zealand Children's Nutrition Survey
NZS	New Zealand Adult Nutrition Survey
<i>p</i>	Probability
PDCAAS	Protein digestibility corrected amino acid score
TDI	Tolerable Daily Intake
WHO	World Health Organization

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1.

1. Hazard Assessment

1.1 Background

1.1.1 Previous assessment of THC in foods by FSANZ

FSANZ has previously evaluated the safety of THC in foods in relation to Application A360 – Use of industrial hemp as a novel food (completed in 2002). This evaluation concluded that on the basis of the data available, there is no evidence of adverse health effects in humans at low levels of THC exposure and a tolerable daily intake of 6 µg/kg bw can be established. If the products from low THC hemp plants are used as food, the level of THC in the final products should be such that the dietary intake of THC is no greater than 6 µg/kg bw.

1.1.2 Scope of the hazard assessment

The scope of this hazard assessment is to evaluate relevant data published after FSANZ's most recent (2002) evaluation.

1.2 Tolerable daily intake of THC

For the assessment of Application A360, FSANZ conducted a risk assessment which concluded that, while the bulk of the human data on the toxicity of THC is derived from inhalation of cannabis rather than consumption of THC as a component of food, there were adequate human data to assess the toxicity of THC following oral administration and establish a tolerable daily intake (TDI). It was concluded that following oral administration the most sensitive adverse effects observed in humans appear to be related to skill performance (e.g. hand-eye coordination and reaction time) and cognitive tasks (e.g. performance on arithmetic tasks). The TDI was derived from the results of a human study in which the effect of oral THC on skill performance, cognitive function and mood was examined at dose levels of 0, 5, 10, 15 and 20 mg/person (Chesher et al. 1990). Doses could not be expressed as mg/kg bodyweight (bw) because no information on mean group bodyweights was provided in the published report. THC, dissolved in sesame oil and taken as capsules, was administered orally to groups of university students (n = 16/group with variable ratios of males:females in each group). The subjects consumed a light breakfast prior to ingesting the capsules. The performance measures included standing steadiness, hand-eye coordination, reaction time tests and an arithmetic test. Degree of intoxication was self-reported on a scale of 0 to 5. The subjects completed the test battery at 1.3, 2.3, 3.3 and 4.3 h after swallowing the capsules. The results indicated an approximately linear dose-response relationship between THC intake and a composite measure of performance decrement at the first three time-points. On the self-reporting intoxication scale, the lowest dose level (5 mg/person) was not distinguishable from placebo, although there was a dose-related effect reported at the other dose levels. The safety assessment concluded that a slight but reversible effect on skill performance may occur at an oral dose of 5 mg/person. By using the highest bodyweight individual in the study (84 kg) the threshold effect dose (5 mg/person) was conservatively calculated to be 60 µg/kg bw. In order to take account of the possible variability in response in the human population, an uncertainty factor of 10 was applied to derive an overall TDI of 6 µg/kg bw. The use of an acute human study to establish a TDI is considered appropriate because of the known development of tolerance to THC following regular exposure. Thus, it is plausible that effects on skill performance and cognitive function may be observable after a single dose of THC but not apparent when the same dose is received daily over an extended period.

In relation to psychotropic effects, the safety assessment for Application A360 concluded that the studies available indicated that the more sensitive individuals require a minimum oral dose of 10 mg THC to experience a psychotropic effect, while the majority of individuals require an oral dose of 15-20 mg to experience a psychotropic effect. Thus, the lowest psychotropic effect level is around 140 µg/kg bw for a 70 kg person (i.e. approximately 20-fold greater than the TDI).

The risk assessment also considered data on reproductive and developmental toxicity, genotoxicity and carcinogenicity. Reproductive and developmental toxicity studies in animals gave effects only at higher doses of THC and it was concluded that the findings are unlikely to be relevant to low-dose human exposure. *In vitro* genotoxicity data indicated that THC is not mutagenic. Evidence regarding the possible induction of chromosome aberrations was considered to be inconclusive. However, two-year oral gavage studies in mice and rats gave no evidence that THC was carcinogenic. Based on these findings it was considered appropriate to base the TDI on the most sensitive known endpoint, namely skill performance in humans.

The previous risk assessment considered published data up to and including 1998. For the present Application, oral THC studies identified in a recent review were considered (Zuurman et al. 2009), along with any relevant studies published subsequently up to December 2010, in order to establish whether new data indicate a need to change the TDI.

Zuurman et al. (2009) reviewed published studies relevant to biomarkers for the effects of cannabis and THC exposure in healthy volunteers. Oral, intrapulmonary and intravenous routes of exposure were considered. Studies with <10 subjects were not included. The literature search conducted for the review yielded 165 different studies on cannabis and THC that met the specified criteria, published between 1966 and November 2007. There were only 10 cited studies published post-1998 that included data on oral THC administration, however the lowest THC doses tested in these studies were all greater than the low dose of 5 mg/person tested by Chesher et al. (1990). For example, two studies used single dose levels of 10 mg/person (Ploner et al. 2002) or 20 mg/person (Hart et al. 2002) while four studies used oral THC dose levels of 7.5 and 15 mg/person (Kirk and de Wit 1999; Wachtel and de Wit 2000; Curran et al. 2002; McDonald et al. 2003). Because the doses used in these 10 studies were higher than the dose of 5 mg/person from which the TDI was derived, any findings in these studies cannot be used to justify a lower TDI for THC.

The review by Zuurman et al. did not aim to specifically establish a threshold dose for effects observed after oral administration, however one of the major conclusions of the review was that the subjective reporting of feeling 'high' appeared to be the most sensitive CNS biomarker for the effects of THC. This is in contrast to the Chesher study which reported slightly decreased skill performance at 5 mg/person but no self-reported feeling of intoxication at this dose. It is possible that the reported decreased skill performance at 5 mg/person may be an artefact of the statistical analysis used in the Chesher study. This possibility is supported by the analysis of the data collected at the 3rd time-point (3.3 h post-dose) which indicated that skill performance following the 10 mg/person dose was slightly less impaired relative to the 5 mg/person dose. In addition, Chesher et al. reported a statistically significant ($p < 0.05$) trend of performance decrement with increasing THC dose, however the paper did not state whether the performance decrement reported at the dose of 5 mg/person was statistically significant. Since a dose of 5 mg/person was associated with no subjective feeling of intoxication, and any association with decreased skill performance is questionable, it is considered that this dose level represents a no observed adverse effect level (NOAEL) in this study. This conclusion is consistent with recent studies which measured plasma/serum concentrations of THC following cannabis smoking and oral administration of THC.

In a study on smoked cannabis it was concluded that the threshold of impairment of skill performance is associated with a serum THC concentration of 2 ng/mL (Ramakers et al. 2006). This compares to the results of an oral study in which the mean C_{max} for THC after a dose of 14.8 mg/person administered to 6 subjects was 1.2 ng/mL (Goodwin et al. 2006). Furthermore, a 10-year study of 3400 driving fatalities in three Australian states found that there was no increased risk of car accidents at THC blood concentrations of ≤ 5 ng/mL (Drummer et al. 2004; reviewed in Sewell et al. 2009).

Several studies investigating the effects of oral THC in humans have been published subsequent to the literature search conducted by Zuurman et al. (2009), however only one study was located which employed dose levels of 5 mg/person or lower. This was a small double-blind study investigating the tolerability and effects of oral THC in a group of adolescents with marijuana use disorders (Gray et al. 2008). Eight participants (ages 16–21 years), smoking an average of ~5 days/week and 2.5 “joints”/day, completed this four-session study, during which they received one of four oral THC doses (0, 2.5, 5, 10 mg/person) each session. The participants were instructed to abstain from marijuana use 24 hours prior to each oral dose. Physiological (blood pressure, heart rate), psychomotor, and subjective measures (mood, experience of a drug effect) were assessed at baseline and at three time-points after THC administration (+60, +120, and +180 min). Psychomotor performance was evaluated using a computerised task designed to assess visual-spatial processing.

Oral THC had no effect on psychomotor performance, heart rate or blood pressure. Oral doses of 2.5 and 5 mg/person had no statistically significant effect on subjective rating of a drug effect while the 10 mg/person dose significantly increased subjective ratings of “good drug effect” and feeling “high” as compared to placebo ($p < 0.05$), while producing no significant effects on ratings of “bad drug effect.” However, two participants reported “good drug effect” and feeling “high” when they received placebo indicating that these subjective measures are not generally reliable at the relatively low oral doses used in this study. In addition, the 5 mg/person dose resulted in statistically significant ratings of decreased irritability and decreased tiredness relative to placebo while the doses of 2.5 and 10 mg/person had no reported effect on these subjective measures. It is concluded that none of the oral THC dose levels tested in this study were associated with adverse effects.

The Zuurman review did not consider publications that reported the results of clinical trials with oral THC. Extensive data on the clinical use of oral THC have been published in the past 10 years, in particular for the treatment of spasticity and other symptoms related to multiple sclerosis (MS). When used as a therapeutic agent, oral THC has shown a favourable safety profile even at relatively high doses. For example, a study in MS patients receiving a maximum oral dose of 25 mg THC daily for up to 12 months reported that minor adverse events were evident in 361 patients: 109 receiving THC, 125 receiving cannabis extract and 127 on placebo (Zajicek et al. 2005). It was stated that most of the 74 serious adverse events reported (24 THC, 27 cannabis extract, 23 placebo) were as expected in the patient population participating in the trial. Thus, oral THC was indistinguishable from placebo with regard to the incidence of adverse events.

Published human data on the potential adverse effects of chronic oral exposure to THC are lacking. However, with regard to chronic exposure to THC from smoking cannabis, a recent review concluded that case-control studies suggest that some adverse health outcomes may be elevated among heavy cannabis users, namely, fatal motor vehicle accidents, and possibly respiratory and brain cancers (Calabria et al. 2010). It was also concluded that there was insufficient evidence to assess whether the all-cause mortality rate is elevated among cannabis users in the general population. THC per se has not been shown to possess genotoxic or carcinogenic potential and any association with respiratory and brain cancers may be explained by exposure to other chemicals in cannabis smoke.

EFSA Opinion

In March 2011, the European Food Safety Authority published a scientific opinion on the safety of hemp for use as animal feed (EFSA 2011). EFSA derived a Provisional Maximum Tolerable Daily Intake (PMTDI) of 0.4 µg THC per kg bw. EFSA stated that the PMTDI was derived from studies in humans which identified psychotropic effects at a dose of 0.04 mg THC per kg bw. FSANZ has reviewed the studies which underpin this health based guidance value and found that they include psychotropic effects following inhalational exposure and the clinical benefit following oral administration of THC in terminally ill patients. In view of the uncertainty which these studies impart on the EFSA health based guidance value FSANZ will apply the TDI it had established.

1.3 Allergenicity of hemp foods

No papers were located in the published scientific literature reporting allergies to hemp foods. There are several reports of allergic reactions arising from exposure to Cannabis plant material by routes that are not relevant to oral exposure such as from skin contact with cannabis leaves or inhalational exposure of Cannabis seeds (e.g. Vidal et al. 1991).

1.4 Conclusion

Consideration of data published subsequent to the assessment of Application A360 indicates that the TDI of 6 µg THC per kg bw remains valid. Hemp foods are not known to be allergenic.

2. Nutrition Assessment

2.1 Previous nutrition assessment – 2002

In 2002, FSANZ previously assessed low THC hempseed and hempseed oil in application A360 - *Use of industrial hemp as a novel food*. The previous nutrition assessment considered the fatty acid profile to assess hemp as a source of polyunsaturated fatty acids in the human diet. The assessment reported that approximately 80% of hempseed's fatty acid profile is polyunsaturated, notably the essential fatty acids, alpha-linolenic acid (ALA, omega-3) and linoleic acid (LA, omega-6) in a favourable omega-6 to omega-3 ratio of approximately 3:1. Hempseed and hempseed oil were identified as an alternative to both linseed and soy bean products because of their favourable nutrient profile, particularly the essential fatty acid content. The assessment also concluded that industrial hemp in food products could provide an alternative for individuals to increase their intake of unsaturated fatty acids and consume a more appropriate omega 6:omega 3 polyunsaturated fatty acid ratio through a food product rather than a supplement.

2.2 Scope of and approach to the updated nutrition assessment

This nutrition assessment does not examine all the nutrient components of hempseed and hempseed oil. The assessment focuses on the protein content and quality of these products and expands the previous nutrition assessment of the fatty acid profile by including data published since FSANZ's 2002 assessment. The assessment does not include a consideration of potential beneficial health effects.

The approach taken was to conduct a literature search in the following bibliographic databases: Food Science and Technology Abstracts and Food Science Source and Science Direct to identify published literature on the nutrient composition of hempseed and hempseed oil. A small number of papers (five) and studies examining the nutrient composition of low THC hempseed and hempseed oil were identified (Callaway and Pate 2009, House et al. 2010, Schwab et al. 2006, Tang et al. 2006, Wang et al. 2008).

2.3 Key risk assessment questions

For the nutrition assessment of low THC hempseed and hempseed oil the following questions were posed:

- a) How does the nutrient content of hempseed/hempseed oil compare with similar foods?
- b) What is the potential contribution of hempseed/hempseed oil to omega-3 and omega-6 fatty acid intakes?

2.4 Nutrient composition of low THC hempseed and hempseed oil as a food

Whole, low THC hempseed is a nutritious food containing sizable amounts of protein, polyunsaturated fats and dietary fibre (Callaway and Pate 2009) as well as micronutrients such as thiamin, vitamin E, phosphorus, potassium, magnesium, calcium, iron and zinc (Rodriguez-Leyva and Pierce, 2010). Hempseed oil contains the second highest amount of omega-3 fatty acids of all commonly available plant-based oils (Callaway 2004; FSANZ 2011).

2.4.1 Protein content of hempseed

Whole hempseed contains approximately 20-25% protein (Leizer et al. 2000). The main proteins in hempseed, albumin and edestin, are both rich in the essential amino acids (Wang et al. 2008). Table 1 provides a comparison of the total protein content of hempseed with egg, soy flour, and other nuts and seeds. Although hempseed (whole, hulled and meal) has a higher amount of protein than egg, the traditional animal reference protein, whole hempseed is comparable to other seed and nut protein sources. The protein content of hulled hempseed and hempseed meal is similar to that in an equivalent quantity of cooked beef that has been trimmed of fat (about 30-32 g/100 g). The protein content of hempseed is second only to soy flour, and higher than whole soy bean.

Table 1: Protein content of hempseed¹ and selected foods² (g/100 g edible portion)

Food name	Protein ¹
Soy flour, low fat	46.5
Hempseed, meal, defatted	33.5
Hempseed, whole, raw	24.8
Hempseed, hulled, raw	33.0
Peanut, with skin, raw	24.7
Pumpkin, seed, hulled & dried	24.4
Sunflower, seed	26.8

Food name	Protein ¹
Sesame, seed, white	22.2
Almond, with skin	19.5
Flaxseed	18.3
Soy bean, dried, soaked, boiled, drained	13.5
Egg, chicken, whole, raw	12.7
Tofu (soy bean curd), firm, as purchased	12.0
Egg white, boiled	11.6
Egg white, raw	11.2

¹ Data for whole hempseed and hempseed meal sourced from Callaway (2004) and data for hulled hempseed sourced from Callaway and Pate (2009).

² Data for all other foods sourced from NUTTAB 2010 (FSANZ 2011)

2.4.2 Protein quality of hempseed and hempseed products

The protein quality of hempseed, egg white and soy bean is shown in Table 2 using the method of the protein digestibility corrected amino acid score (PDCAAS) described by WHO (WHO 2007). This method estimates the relative utilisation of food proteins based on a calculation using the digestibility of a protein and its essential amino acid profile. The amino acid score describes the content of essential amino acids in a protein compared with the amino acid requirement pattern (for protein synthesis). The digestibility of a protein source is an estimate of the proportion of a food protein which is absorbed compared with the total consumed (accounting for faecal, urinary and other metabolic nitrogen losses). The purpose of the PDCAAS is to enable comparison of the relative quality of food protein sources (individually or mixed) (WHO 2007).

House et al. (2010) analysed thirty samples of commercial whole hempseed, hulled hempseed, and hempseed meal, and determined protein quality using PDCAAS. The analysis showed that lysine was the limiting amino acid for all the hemp protein sources analysed. The analysis also showed that removal of the hull fraction improves the digestibility of the protein and the corresponding PDCAAS; this is most likely due to the removal of significant fibre components. Results from *in-vitro* digestibility studies suggest that the protein isolates from hempseed are more easily digestible than soy protein isolates (Tang et al. 2006, Wang et al. 2008)

FSANZ estimates of the PDCAAS relative to adult requirements for egg white, soy bean and hempseed, indicate that lysine makes the lowest relative contribution to adult essential amino acid requirements (Table 2). Estimates also show that lysine is the limiting amino acid (below 1.00) for hempseed, which agrees with the findings of House et al. (2010) above. Estimates of PDCAAS were also done for other population age groups: infants, pre-school children, and older children (data not shown). Lysine in hempseed was the most limiting amino acid for these population groups as well.

Table 2: Protein Digestibility Corrected Amino Acid Score (PDCAAS) for hempseed, egg white and soy bean relative to adult requirements

Food	Digestibility	PDCAAS relative to adult requirements ³			
		Lysine	SAA ⁴	Threonine	Tryptophan
Egg white ¹	0.97	1.23	2.58	1.88	2.49
Soy bean ¹	0.86	1.03	1.31	1.58	1.84
Hempseed, whole ²	0.85	0.68	1.57	1.56	1.36
Hempseed, hulled ²	0.95	0.74	1.91	1.46	1.67
Hempseed, meal ²	0.87	0.62	1.63	1.25	1.38

¹ Digestibility data for egg and soy flour sourced from WHO (2007). Protein and amino acid data for egg white and soy flour sourced from Callaway (2004).

² All data for hempseed sourced from House et al. (2010).

³ PDCAAS estimates were calculated by FSANZ using the method described by WHO (2007).

⁴ SAA is an acronym for the sulphur-containing amino acids, cysteine and methionine.

2.4.3 Fatty acid profile of hempseed and hempseed oil

Over 80% of fatty acids in hempseed oil are polyunsaturated comprising mostly linoleic acid (LA; 18:2 omega-6) and alpha-linolenic acid (ALA; 18:3 omega-3) (Callaway 2004). LA is a structural component of cell membranes and is important in cell signalling as well as being a precursor for the long chain fatty acid arachidonic acid (20:4, omega-6), and eicosanoid production. ALA is less common in the diet than LA and is the precursor for EPA (20:5, omega-3) which in turn is metabolised to DHA (22:6, omega 3) (NHMRC and NZMoH 2006).

Other derivatives of LA also present in hempseed oil are gamma-linoleic acid (GLA, 18:3 omega-6) and stearidonic acid (SDA, 18:4 omega-3) at approximately 4% and 2%, respectively (Callaway 2004). The presence of both GLA and SDA in vegetable oil is unusual and these concentrations are higher than many other oils (Schwab et al. 2006, Calloway and Pate 2009).

Table 3 provides the fatty acid profile of hempseed and other plant-based oils in descending order of ALA content. Hempseed oil is comparable to soy bean oil and sunflower oil in LA content; however it is higher than most other plant-based oils in ALA content, being second only to flaxseed oil.

Table 4 (presented in descending order of ALA content) shows that, in comparison with whole seeds, nuts and soy bean, whole raw hempseed has comparable LA content to pumpkin seed while being lower than walnut and sunflower seed. Whole raw hempseed is much higher in ALA content than most nuts and seeds, being second only to flaxseed (NHMRC and NZMoH 2006). No published data were available for the fatty acid content of hulled hempseed.

Table 3: Fatty acid composition of hempseed oil and comparable oils (g/100 g)

Oil ¹	Saturated fatty acids, total	Monounsaturated fatty acids, total	Polyunsaturated fatty acids		
			Total	LA	ALA
Flaxseed, oil	8.5	17.8	68.7	14.2	54.6
Hempseed, oil ²	6.7	8.6	80.3 ³	53.5	21.0

Oil ¹	Saturated fatty acids, total	Monounsaturated fatty acids, total	Polyunsaturated fatty acids		
			Total	LA	ALA
Canola, oil	6.9	59.5	28.5	18.5	10.0
Soy bean, oil	14.7	18.5	62.3	55.2	7.2
Olive, oil	16.0	69.9	9.5	8.8	0.7
Sunflower seed, oil	10.7	25.1	59.8	59.5	0.3
Peanut, oil	18.1	43.9	33.6	33.3	0.3

1 The data source for all oils is AUSNUT 2007 (FSANZ 2011), except hempseed oil (Callaway, 2004).

2 Derived from Callaway, 2004 by applying 0.956 lipid conversion factor representing the proportion of total fatty acids in total fat.

3 Includes 1.9 g/100 g GLA and 3.8 g/100 g SDA.

Table 4: Fatty acid composition of whole raw hempseed, comparable seeds and nuts, and soy bean (g/100 g)

Food name ¹	Fat, total	Saturated fatty acids, total	Mono-unsaturated fatty acids, total	Polyunsaturated fatty acids		
				Total	LA	ALA
Flaxseed	42.2	3.6	7.5	29.0	6.0	23.0
Hempseed, whole, raw	35.5	2.4	3.1	28.5 ²	19.0	7.5
Walnut, raw	69.2	4.4	12.1	49.6	43.3	6.3
Soy bean, dried	20.2	2.9	3.1	12.5	11.0	1.6
Soy bean, dried, soaked, boiled, drained	7.7	1.1	1.2	4.8	4.2	0.6
Pumpkin seed, hulled, dried	45.6	8.4	14.1	20.8	20.6	0.2
Hazelnut, raw	61.4	2.7	48.8	7.2	7.0	0.1
Sunflower seed	51.0	4.3	9.9	34.5	34.5	0.0
Peanut, with skin, raw	47.1	7.1	23.1	14.9	15.0	0.0

1 The data source for all foods is NUTTAB 2010 except flaxseed which is from AUSNUT 2007 (FSANZ 2011) and hempseed which is derived from hempseed oil (Callaway, 2004). The fatty acid composition of hulled hempseed was not provided.

2 Includes 0.7 g/100 g GLA and 1.3 g/100 g SDA.

2.5 Potential contribution of hempseed and hempseed oil to omega-3 and omega-6 fatty acid intakes

The most recent revision of the Nutrient Reference Values¹ for Australia and New Zealand include Adequate Intakes (AIs²) for the essential fatty acids: LA (men 13 g/day; women 8 g/day) and ALA (men 1.3 g/day; women 0.8 g/day.)

Table 5 shows the contribution of 20 g of whole hempseed or hempseed oil to essential fatty acid AIs for men and women. The data indicate that 20 g of hempseed oil (about one tablespoon) could contribute as much as five times the AI for women and three times the AI for men. Thus, the AI for ALA could be achieved by consuming about 11–17 g raw hempseed or 4–6 g hempseed oil for women and men, respectively.

Used in the diet as an alternative or an addition to other seed or nut oils, or as a whole food in place of soy bean or commonly available nuts and seeds, hempseed and hempseed oil could provide a useful dietary source of the essential fatty acids LA and particularly ALA.

Table 5: Potential contribution of 20 g hempseed and hempseed oil to LA and ALA Adequate Intakes

	LA			ALA		
	(g/20 g)	% AI men	% AI women	(g/20 g)	% AI men	% AI women
Hempseed, whole, raw ¹	3.8	29	47	1.5	115	187
Hempseed, oil ²	10.7	82	133	4.2	323	525

¹ The fatty acid composition for hempseed is derived from hempseed oil published in Callaway (2004).

² The data source for hempseed oil is Callaway (2004).

2.6 Conclusion

Low THC hempseed contains a substantial amount of good quality protein, as well as many vitamins and minerals, similar to the nutritional profile of many nuts and seeds. Hempseed and hempseed oil are also potential dietary sources of polyunsaturated fatty acids, particularly omega-3 fatty acids. Only a small quantity of whole hempseed or hempseed oil needs to be consumed to meet the adult AI for ALA.

3. Dietary Exposure Assessment

3.1 Background

A chronic Dietary Exposure Assessment (DEA) was undertaken for Application A360. For the purposes of assessing the current Application, this earlier DEA was updated to incorporate dietary exposure estimates based on the dietary survey data for both the Australian and New Zealand populations that has since become available.

¹ Nutrient Reference Values (NRVs) indicate the daily amount of essential nutrients required for good health, as well as a safe intake of nutrients.

² AIs are used when a Recommended Dietary Intake cannot be determined. They refer to the “average daily nutrient intake level based on observed or experimentally determined approximations or estimates of nutrient intake by a group (or groups) of apparently healthy people that are assumed to be adequate (NHMRC and NZMoH 2006 p. 1). In the case of LA and ALA they are based on the “highest median intakes of any of the gender-related age groups taken from an analysis of the National Nutrition Survey of Australia of 1995” (NHMRC and NZMoH, 2006 p. 37).

A chronic DEA was undertaken for Application A360 to ensure that the proposed maximum permitted levels of THC within foods containing low THC hemp would not lead to dietary exposures greater than 6 µg/kg bw, the tolerable daily intake (TDI) for the human population (see Section 2 – Hazard Assessment).

Dietary modelling integrates food consumption data with food chemical concentration data to estimate dietary exposure:

$$\text{Dietary exposure} = \text{food chemical concentration} \times \text{food consumption}$$

A brief explanation of how dietary exposure assessments are conducted at FSANZ is provided in Appendix 1.

3.2 Food consumption data

The food consumption data used for the dietary modelling were derived from the four most recent national nutrition surveys (NNSs) conducted in Australia and New Zealand:

- 1995 National Nutrition Survey of Australia (1995 NNS), surveying 13858 people aged 2 years and over. This survey used one 24-hour recall for all respondents and a second 24-hour recall for approximately 10% of respondents.
- 1997 New Zealand NNS (1997 NZS), surveying 4636 people aged 15 years and over. The survey used one 24-hour recall for all respondents and a second 24-hr recall for approximately 15% of respondents.
- 2002 New Zealand Children's Nutrition Survey (2002 NZCS), surveying 3275 people aged 5-14 years. The survey used one 24-hour recall for all respondents and a second 24-hr recall for approximately 15% of respondents.
- 2007 Australian National Children's Nutrition and Physical Activity Survey (2007 NCS), surveying 4487 people aged 2-16 years. The survey used two 24-hr recalls for all respondents.

DIAMOND, FSANZ's custom built dietary modelling program, provides access to the individual dietary records from each NNSs, which included records of individual body weights. The use of DIAMOND to access individual dietary records gives more information about the distribution of the individual dietary exposure estimates than is possible using point estimates of population food consumption.

Further information on the national nutrition surveys and some of the limitations associated with using consumption data derived from these surveys is set out in Appendix 1.

3.3 Food chemical concentration data

As little information is available on actual concentrations of THC in foods, and in order to minimise the risk to public health and safety, maximum levels (MLs) of THC in certain commodities were calculated. These MLs were then used in the dietary modelling.

3.3.1 Calculation of MLs

Proposed MLs for various commodities likely to contain low THC hemp were derived by estimating a maximum concentration of THC in each commodity that would not result in consumers exceeding the TDI for THC, assuming consumption at the 95th percentile³ level. The highest 95th percentile consumption figure from the 1995 NNS of individual foods in each commodity group was taken; for example, the 95th percentile consumption of olive oil was the highest of all potential salad oils considered. The maximum concentration of THC for each commodity group that would not result in exposure above the TDI was estimated, assuming a high level of food consumption. These calculations assume that the entire commodity contains THC and that it is the only product consumed. An exception was made for wheat flour, where it was considered unrealistic to assume that 100% of the commodity contained low THC hemp; therefore 10% of the 95th percentile consumption of wheat flour was used. The equation used for these calculations is as follows:

$$\text{Maximum THC concentration (mg/kg)} = \frac{\text{TDI (mg/d)}}{\text{Consumption (kg)}}$$

The consumption figures used in the calculations and the results are shown in Table 6.

Table 6: Calculations for derivation of proposed MLs for THC in various food groups

Commodity	Source of consumption figures (1995 NNS)	Age (years)	95 th Percentile Food Consumption (kg/day)	Resulting maximum THC concentration (mg/kg)
Hemp oils	Olive oil	2 – 12	0.016	10.22
		20 and above	0.028	16.07
Hempseed	Mustard seed	2 – 12	0.007	24.56
		20 and above	0.013	33.58
Hemp tea, brewed	Black tea, brewed	2 – 12	0.615	0.27
		20 and above	1.776	0.25
Hemp-based beverage	Mammalian milk	2 – 12	1.461	0.12
		20 and above	1.558	0.29
Hemp flour	10% Wheat flour	2 – 12	0.021	8.1
		20 and above	0.024	18.5

Note: The TDI in mg/d for adults aged 20 years and above is 0.45 mg/d (based on a mean body weight of 75 kg and TDI of 6 µg/kg bw), and for children aged 2-12 years is 0.168 mg/d (mean body weight of 28 kg).

³ FSANZ previously routinely used 95th percentile dietary exposure estimates to represent the high consumer of the food chemical of interest. Following international peer review of its dietary modelling procedures FSANZ has since adopted a policy that a high consumer's chronic dietary exposure is best represented by the 90th percentile of exposure. Estimated dietary exposure to THC is reported at the mean and 90th percentile for all population groups later in this report. For further information on the use of the 90th percentile for dietary exposure assessments, refer to the FSANZ information paper: Protecting 'high consumers' at: <http://www.foodstandards.gov.au/scienceandeducation/scienceinfsanz/dietaryexposureassessmentsatfsanz/protectinghighconsum4441.cfm>

It is noted that the use of 95th percentile food consumption amounts for individual proxy foods to calculate MLs is more conservative than the 90th percentile from a dietary risk perspective.

Proposed MLs have been derived from the worst case scenario presented in Table 6, usually from the maximum concentration for children aged 2-12 years old, by use of the convention of rounding down to the nearest 1, 2, 5 or 10 mg/kg figure.

From the above table, the proposed ML for hemp oil is 10 mg/kg; the proposed ML for hempseed alone would be 20 mg/kg.

As hemp flour is a product of hempseed and is the major food derived from hemp, the data from hemp flour were used and the nearest whole number of 8 mg/kg was rounded down to 5 mg/kg, and applied to both hempseed and hemp flour.

For hemp-based beverages, although the maximum concentration would be 0.1 mg/kg, it was concluded that 0.2 mg/kg would be appropriate because it is very unlikely that hemp-based beverages would replace all mammalian milk consumption. In other countries, hemp-based beverages are sold in smaller containers, up to one litre in volume, and it is considered unlikely that it would be consumed in the large quantities that have been reported in the 1995 NNS for milk (1.4-1.6L).

Proposed MLs were derived using Australian food consumption data only. It was assumed that the consumption of the food groups in New Zealand were similar.

In summary, the proposed MLs are as follows:

- Hempseed and hemp flour 5 mg/kg
- Hemp oil 10 mg/kg
- Hemp-based non-dairy beverages 0.2 mg/kg
- Other foods 0.2 mg/kg

3.4 THC dietary exposure estimate

To assess if exposure to a diet containing THC at the proposed MLs posed a public health and safety risk, a chronic dietary exposure estimate was undertaken using those proposed MLs. Foods likely to contain low THC hemp that were considered for inclusion in the modelling were as follows:

Hempseeds can be used to make muesli bars and baked goods, as well as being eaten by themselves. Hempseeds were not a part of the Australian or New Zealand diet when the NNSs were conducted, and therefore consumption data from the 1995, 1997, 2002 and 2007 NNSs for seeds that could be used similarly to hempseeds were included in the modelling (poppy seeds, sesame seeds, sunflower seeds and mustard seeds). A THC level of 5 mg/kg in hempseeds was used.

Hemp oil is a product that would be mainly used as a salad oil. An approach similar to that used for hempseeds was used for hemp oil, where oils with similar uses were included in the modelling. The oils modelled were rapeseed oil, soy bean oil, cotton seed oil, safflower oil, sesame seed oil, sunflower seed oil and olive oil. A THC level of 10 mg/kg in hemp oil was used.

Hemp flour can be made in one of two ways. Whole hempseeds can be ground into flour, whereby the flour would have a similar THC concentration as the hempseed (assuming no destruction of the THC due to processing). Alternatively, the husk can be removed from the seed, and the hulled seed can be ground into flour. The THC concentration would be lower using this process. In the model, a THC level of 5 mg/kg in flour, which is the same as the proposed ML for seed, was used.

Hemp based non-dairy milk is made from soaking hempseeds in liquid. A THC level of 0.2 mg/kg was used for this beverage.

Other hemp containing food groups were identified, as they were either available overseas as a hemp product, or likely to be produced containing hemp (Grotenhermen, Jarus & Lohmeyer 1998). For example, hemp tofu is another product made from low THC hemp. Also, hemp tea is made from soaking hemp leaves in liquid. Although the above calculation suggests an ML of 0.2 mg/kg is suitable for hemp-based tea as consumed, no information was available to propose an ML for dried hemp leaves used for preparation of hemp-based tea. As these foods are minor uses for hemp, their contribution to the total diet would be minimal. Their inclusion in the modelling would have very little impact on estimated dietary exposures to THC.

Another product that may contain low THC hemp is beer. This product was not included in the dietary modelling for THC because the process that is involved in the brewing of beer is believed to destroy the THC.

Table 7 contains the THC concentrations for the various commodities used in the modelling.

Table 7: THC Concentrations used in dietary modelling for various food groups

Food	Proposed ML (mg/kg)
Flour	5
Hemp-based non-dairy milk	0.2
Seeds	5
Oils	10

It was not considered realistic to assume 100% of commodities in the chronic dietary exposure model are hemp products exclusively, for the following reasons:

- hemp flour needs to be mixed with other flour for baking. Consumers would not bake all products containing flour with hemp flour (i.e. cakes, bread, pasta etc.);
- it would be difficult to consume hempseeds exclusively as part of a bar for example. Muesli bars can contain around 3-10 % of hempseeds; and
- hemp-based non-dairy milk is a very sweet product, a property that could make it difficult to consume in the same quantity as cow's milk.

Ten per cent of the food products (except hemp-based non-dairy milk, see below) have been identified as potentially containing hemp (Grotenhermen, Jarus & Lohmeyer 1998). Therefore, an adjustment factor of 10% was used in the model to represent the amount of the mainstream commodity (oils, seed, and flour) that would be likely to be replaced by hemp containing products. From the 1995 NNS it was estimated that approximately 3% of milk consumers drink soy beverages. In estimating the dietary exposure to THC it was assumed that consumption of hemp-based beverages would be similar to that of soy beverages. There is little information on soy beverage consumption for the 1995 Australian and 1997 New Zealand NNSs so mammalian milk consumption was used with a 3% adjustment factor for these surveys. Soy and rice beverages were used to estimate THC exposure from hemp-based beverages for the 2002 and 2007 New Zealand and Australian Children's surveys with a 10% adjustment factor.

Modelling to estimate THC exposure was conducted for specific age groups using data derived from the most recent Australian and New Zealand NNSs:

- 1995 NNS – Used to estimate THC exposure for Australians aged 2 years and above and 17 years and above.
- 1997 NZS – Used to estimate THC exposure for New Zealanders aged 15 years and above and 15-19 years.
- 2002 NZCS – Used to estimate THC exposure for New Zealanders aged 5-14 years.
- 2007 NCS - Used to estimate THC exposure for Australians aged 2-12 years and 13-16 years.

The Australian and New Zealand populations were broken down into age groups to better characterise the risk associated with THC consumption in younger people including children and adolescents. Children are more vulnerable to exceeding a TDI due to their large food consumption compared to their small body weight. Adolescents can also eat large quantities of foods per kilogram of body weight. A breakdown of population sample details can be found in Table 8.

Table 8: Population sample details for THC dietary modelling for Australia and New Zealand

Population	Group Description	Number of Respondents	Number of Consumers	Consumers as a % all Respondents	Mean body Weight (kg)
Australia	2 years & above*	13858	13818	99.7	67
	2 – 12 years°	3268	3268	100	29
	13 – 16 years°	1219	1219	100	61
	17+ years*	11129	11090	99.6	74
New Zealand	15 years & above^	4636	4620	99.7	71
	5 - 14 years▫	3275	3269	99.8	40
	15 - 19 years^	297	296	99.7	65
	20+ years^	4339	4324	99.7	71

* 1995 NNS, ° 2007NCS, ^ 1997 NZS, ▫ 2002NZCS

3.4.1 Results

Dietary exposure estimates for mean and 90th percentile THC consumers are displayed below in Table 9 as µg THC/kg bw/day and as a percentage of the TDI.

Table 9: Estimated chronic dietary exposures to THC for potential consumers of foods containing hemp and various age groups for Australia and New Zealand

Population	Group Description	Mean exposure µg/kg bw/day (% TDI)	90 th %tile exposure µg/kg bw/day (% TDI)
Australia	2 years and above*	1.0 (16.3)	2.0 (33.2)
	2 - 12 years [°]	1.9 (32.0)	3.4 (55.9)
	13 - 16 years [°]	1.2 (19.5)	2.1 (34.4)
	17 years and above*	0.8 (12.6)	1.4 (23.7)
New Zealand	15 years and above [^]	0.8 (14.0)	1.6 (26.2)
	5 - 14 years [▣]	1.9 (31.8)	3.5 (58.8)
	15 - 19 years [^]	1.2 (19.5)	2.3 (37.6)
	20+ years [^]	0.8 (13.6)	1.5 (25.3)

* 1995 NNS, ° 2007NCS, ^ 1997 NZS, ▣ 2002NZCS

3.4.2 Discussion

The results, shown in Table 9, illustrate that it is likely that no consumers in Australia or New Zealand, for the total population, or in sub population groups, for both mean consumers, and consumers of THC at the 90th percentile, are at risk of exceeding the TDI for THC, using the proposed MLs. The major contributors to THC exposures for both Australian consumers aged 2 years and above and New Zealand consumers aged 15 years and over were hemp flour (89%) and hemp-based non-dairy beverage (7%).

It should be noted that dietary exposures are likely to be overestimated, due to a number of reasons:

- there is the conservative assumption that 10% (3% for milk for the 1995 and 2007 NNS) of all foods consumed from the food groups will contain hemp;
- the models assume that all of the 10% (3% for hemp-based beverages modelled using 1995 Australian and 1997 New Zealand NNSs) contains the THC at the proposed maximum levels. The actual THC levels resulting in the food should be lower than the ML; and
- 24-hour recall food consumption data tends to overestimate habitual consumption of a given commodity, leading to higher estimates of potential dietary exposure than would be the case over a long period of time.

3.5 Conclusion

Proposed MLs for various commodities containing low THC hemp were derived by estimating a maximum concentration of THC in the commodity that would not result in consumers exceeding the TDI for THC at a high level of consumption of that commodity (95th percentile level). The proposed MLs were then used for the dietary exposure assessment to ensure that they would not lead to a total chronic dietary exposure greater than the TDI.

The dietary exposure assessment indicates that potential chronic dietary exposures to THC are below the TDI of 6 µg/kg bw for all age groups for the Australian and New Zealand populations. The exposures obtained are likely to be an overestimate because THC levels were assumed to be at the proposed ML and it is unlikely that the proportion of foods containing hemp in each food category would be as high as that assumed (10% for all foods groups considered except mammalian milk at 3%).

4. Conclusions

The conclusions from this updated risk assessment are consistent with those for the A360 application.

The TDI of 6 µg THC per kg bw remains valid and the proposed maximum limits for THC content of hemp foods are appropriate.

The potential dietary exposures to THC are below the TDI of 6 µg/kg bw for all age groups for the Australian and New Zealand populations.

Low THC hemp in food products may provide a useful alternative dietary source of many nutrients and polyunsaturated fatty acids, particularly omega-3 fatty acids.

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Appendix 1 – Dietary exposure assessments at FSANZ

A dietary exposure assessment is the process of estimating how much of a food chemical a population, or population sub group, consumes. Dietary exposure to (or intake of) food chemicals is estimated by combining food consumption data with food chemical concentration data. The process of doing this is called 'dietary modelling'.

$$\text{Dietary exposure} = \text{food chemical concentration} \times \text{food consumption}$$

FSANZ's approach to dietary modelling is based on internationally accepted procedures for estimating dietary exposure to food chemicals. Different dietary modelling approaches may be used depending on the assessment, the type of food chemical, the data available and the risk assessment questions to be answered. In the majority of assessments FSANZ uses the food consumption data from each person in the national nutrition surveys to estimate their individual dietary exposure. Population summary statistics such as the mean exposure or a high percentile exposure are derived from each individual person's exposure.

An overview of how dietary exposure assessments are conducted and their place in the FSANZ Risk Analysis Process is provided on the FSANZ website at:

<http://www.foodstandards.gov.au/scienceandeducation/scienceinfsanz/dietaryexposureassessmentsatfsanz/dietaryexposureandin4438.cfm>

FSANZ has developed a custom built computer program 'DIAMOND' to calculate dietary exposures. More information on DIAMOND is available on the FSANZ website at:

<http://www.foodstandards.gov.au/scienceandeducation/scienceinfsanz/dietaryexposureassessmentsatfsanz/fsanzdietaryexposure4439.cfm>

Further detailed information on the principles and practices of conducting dietary exposure assessments at FSANZ is provided in *Principles and Practices of Dietary Exposure Assessment for Food Regulatory Purposes* (FSANZ, 2009), available at:

<http://www.foodstandards.gov.au/srcfiles/Principles%20&%20practices%20exposure%20assessment%202009.pdf>

1 Food consumption data used

The most recent food consumption data available were used to estimate exposures to THC for the Australian and New Zealand populations. The national nutrition survey (NNS) data used for these assessments were:

- The 2007 Australian National Children's Nutrition and Physical Activity Survey (also known as 'Kids Eat Kids Play') (2007 AusNNS)
- The 1995 Australian National Nutrition Survey (1995 AusNNS)
- The 1997 New Zealand National Nutrition Survey (1997 NZNNS)
- The 2002 New Zealand National Nutrition Survey (2002 NZNNS)

The design of each of these surveys varies somewhat and key attributes of each are set out below.

1.1 2007 Australian Children's Nutrition & Physical Activity Survey (2007 AusNNS)

The 2007 AusNNS collected data on nutrition and physical activity for 4,487 children aged 2-16 years across Australia. The survey was conducted over a seven month time period, from February to August 2007.

In contrast to other national nutrition surveys used to date by FSANZ (the 1995 Australian and 1997 New Zealand surveys), in the 2007 AusNNS each respondent completed two 24-hour recalls on non-consecutive days. The availability of two days of food consumption data provides a more realistic estimate of long term consumption of infrequently consumed foods, because it takes account of those who may eat a food on one day of the survey but not on the other. Using one 24-hour recall may capture an unusual eating occasion for an individual that does not describe how they normally eat.

In this assessment, exposure to THC was estimated from each consumer's average exposures from foods containing THC across Day 1 and Day 2. The results of the 2007 AusNNS were weighted to represent the overall population of Australian children because stratified sampling with non-proportional samples was used.

1.2 1995 Australian National Nutrition Survey (1995 AusNNS)

The 1995 AusNNS provides comprehensive information on dietary patterns of a sample of 13,858 Australians aged from 2 years and above (McLennan & Podger 1998). It is the most recent NNS for Australians aged 17 years and above. The survey used a 24-hour recall method for all respondents, with 10% of respondents also completing a second 24-hour recall on a second, non-consecutive day. The data were collected over a 13 month period. Food frequency data are available for a subset of the national sample (respondents aged 12 years and above) as are responses to a series of short dietary questions about food habits. These data are used unweighted in DIAMOND.

1.3 1997 New Zealand National Nutrition Survey (1997 NZNNS)

The 1997 NZNNS provides comprehensive information on the dietary patterns of a sample of 4,636 respondents aged from 15 years and above. The survey was conducted on a stratified sample over a 12 month period. The survey used a 24-hour recall methodology with 15% of respondents also completing a second 24-hour recall with an additional food frequency questionnaire and questions on food consumption patterns. These data are used unweighted in DIAMOND.

1.4 2002 New Zealand National Nutrition Survey (2002 NZNNS)

The 2002 New Zealand Children's National Nutrition Survey provides comprehensive information on the dietary patterns of a nationally representative sample of 3,275 New Zealand children aged 5-14 years, including sufficient numbers of children in the Māori and Pacific groups to enable ethnic-specific analyses. The survey was conducted using a 24-hour recall methodology and collected data on dietary supplements as well as foods and beverages. A repeat 24-hour diet recall was obtained from a subsample, which enabled the statistical adjustment of the data to present the 'usual' intake distribution for nutrients by subgroup.

Further information on how the Australian National Nutrition Surveys are used to conduct dietary exposure assessments is available on the FSANZ website at:
<http://www.foodstandards.gov.au/scienceandeducation/scienceinfsanz/dietaryexposureassessmentsatfsanz/foodconsumptiondatau4440.cfm>

Further information on the New Zealand National Nutrition Surveys is available from the New Zealand Ministry of Health website at:
<http://www.moh.govt.nz/moh.nsf/indexmh/dataandstatistics-subjects-nutrition>

2 Limitations of dietary exposure assessments

Dietary exposure assessments based on the most recently available food consumption data provide the best estimate of actual consumption of a food and the resulting estimated dietary exposure for the Australian New Zealand populations. However, it should be noted that NNS data do have limitations. Further details of the limitations relating to dietary exposure assessments undertaken by FSANZ are set out in the FSANZ document, *Principles and Practices of Dietary Exposure Assessment for Food Regulatory Purposes* (FSANZ 2009a).

In particular, it should be noted that the range of food consumption figures reported in 24-hour and two day recall surveys will tend to be far greater than that reported in 7-day surveys which report on dietary patterns averaged over a greater period of time. For staple foods that are frequently consumed, there may be little difference between the range of consumption reported over 24 hours and that averaged over a longer time period. However, for occasionally consumed foods the amount of food reported as consumed from single or two day 24-hour recall data will be much greater than that from surveys that reported over a longer period of time. A collaborative study undertaken by the Institute of European Food Studies (IEFS 1998) to assess the influence of survey duration on reported food consumption shows very clearly that as the duration of the surveys increases, the number of consumers of each food item increases but mean consumption for consumers only (eaters) decreases when averaged over the number of days in the survey. However, for staple foods, such as bread, the change is much less marked than that for occasionally consumed foods, such as pizza. The amount of food consumed by all respondents does not change over time.