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

SUPPORTING DOCUMENT 2

NUTRITION ASSESSMENT

APPLICATION A1041 – FOOD DERIVED FROM STEARIDONIC ACID SOYBEAN LINE MON87769

Nutritional implications of the increase in the SDA content and the *trans* fatty acid profile of SDA soybean oil

Contents

Glossary

ALA	α-linolenic acid
BCSO	Black currant seed oil
DHA	Docosahexaenoic acid
DLA	Dihomo- γ-linolenic acid
DPA	Docosapentaenoic acid
DSA	Docosatetraenoic acid
EPA	Eicosapentaenoic acid
ETA	Eicosatetraenoic acid
GLA	γ-linolenic acid
ITT	Intention to treat
PBMCs	Peripheral blood mononuclear cells
PP	Per protocol
PUFA	Polyunsaturated fatty acid
RCT	Randomised, double-blind, placebo-controlled trial
SBO	Soybean oil
SD	Standard deviation
SDA	Stearidonic acid
SDT	Suggested Dietary Target
TFA	*Trans* fatty acid
Trans-ALA	*Trans*-α-linolenic acid
Trans-SDA	*Trans*-stearidonic acid

1. Introduction

This report addresses the nutritional implications of the intentional change to increase the stearidonic acid (SDA) content of edible oil derived from the genetically modified soybean (MON87769) and the consequential increase in the *trans* fatty acid content of this oil. Throughout this report the genetically modified soybean oil is referred to as 'SDA soybean oil' or 'SDA SBO'.

1.1 SDA soybean oil as a potential source of dietary omega-3s

The Applicant claims that SDA soybean oil

> "....is a sustainable alternate source of an omega-3 fatty acid to help meet the need for increased dietary intake of long chain omega-3 fatty acids".

In recent years, increased intakes of long chain omega-3 polyunsaturated fatty acids (PUFAs, omega-3 acids with at least 20 carbon atoms) have been recommended by several national authorities. In 2006, the National Health and Medical Research Council (NHMRC) and the New Zealand Ministry of Health (NZMoH) recommended for the first time that Australians and New Zealanders over the age of 14 consume a Suggested Dietary Target (SDT[1]) of long chain omega-3 PUFAs of 610 mg/day for men and 430 mg/day for women. The purpose of this recommendation was to reduce the risk of chronic disease (NHMRC and NZMoH, 2006). These recommendations can be achieved by consuming at least two fish meals per week (preferably oily fish) which is equivalent to about 430-570 mg/day (NHMRC and NZMoH, 2006).

In November 2008, the Heart Foundation of Australia updated its recommendations in relation to the intake of fish, fish oils and omega-3 PUFAs (Heart Foundation, 2008). They recommended that all Australians should consume about 500 mg/day of eicosapentaenoic acid (EPA) and docosahexaenoic acid (DHA) combined, as well as consuming at least 2 g/day of α-linolenic acid (ALA) to lower the risk of coronary heart disease. For those already with coronary heart disease, the recommendations for EPA and DHA combined are 1,000 mg/day.

Despite these recommendations, it is well accepted that changing dietary preferences in favour of increasing seafood consumption is difficult. As well, there are increasing concerns about the sustainability of fish stocks. In response, researchers are investigating whether plants could be used as sources of long chain omega-3 PUFAs.

1.2 SDA and TFA composition of SDA soybean oil

Table 1 highlights the primary changes in fatty acid composition between conventional soybean oil (SBO) and SDA SBO that are discussed in this report[2]. In terms of changes in the SDA content, the mean concentration is not detectable in conventional SBO and increases to approximately 23% of the total fatty acid content in SDA SBO. The increased proportion of SDA and ALA (9.2 to 11.2% in seed), lead to an increase in the trans-isomers of these fatty acids. Compared with conventional SBO, the fatty acid *trans*-α-linolenic acid (trans-ALA) was significantly higher in SDA SBO ($p<0.001$). From a commercial perspective, however, the Applicant notes that this is "within the 99% tolerance level" of

[1] An SDT is 'a daily average intake from food and beverages for certain nutrients that may help in prevention of chronic disease' (NHMRC and NZMoH, 2006).
[2] The Safety Assessment Report for this Application provides greater detail of the differences in mean fatty acid composition between conventional soybean oil and SDA soybean oil.

variability that is found in conventional SBO. *Trans*-SDA is not detected in conventional SBO.

Table 1: Mean fatty acid concentration of SDA and *trans* fatty acids in conventional SBO compared with SDA SBO

Fatty acid	(% of total fatty acid)	
	Conventional SBO	**SDA SBO**
Intended changes		
Stearidonic acid (C18:4 n-3)	nd	**22.62**
Consequential changes		
Trans-SDA	nd	**0.26**
Trans-ALA	0.14	**0.51**

nd – not detected.

1.3 Existing dietary sources of SDA

The Western diet contains very little SDA with the major dietary source being seafood; although the amounts in seafood are very small. According to NUTTAB 2006[3], the amount of SDA in fish and other seafood is less than 0.2% of the total product or about 1% of all fatty acids in fish, such as Atlantic salmon. Thus, it follows that current intakes of SDA in Australian and New Zealand diets from food sources alone would be very low.

Seed oils from the borage family (such as echium and borage) are existing plant sources of SDA. Echium oil, derived from the plant *Echium plantagineum* (commonly known as Paterson's curse in Australia) is the richest commercially available source (3.5-9.0% SDA), followed by blackcurrant seed oil (BCSO) (2-6% SDA) (Whelan *et al*. 2009). These oils are not currently permitted novel foods[4] in Australia and New Zealand nor are they currently permitted in supplements[5] in Australia. However, fish oil supplements are readily available in both countries, although the SDA content of these is unknown and may vary depending on the source of the oil.

[3] NUTTAB 2006 is the most recent reference database of FSANZ. It contains the nutrient composition of approximately 2600 foods and up to 169 nutrients per food.
[4] Echium oil is an approved novel food in the European Union. The SDA content must be 10% or more of the total fatty acid content. It is permitted for use in a range of general purpose foods including: milk, yoghurt, cheese, spreadable fats and breakfast cereals.
[5] Therapeutic Goods Administration website located at www.tga.gov.au.

2. Nutritional implications of the increase in the SDA content of SDA soybean oil

2.1 Role of SDA in lipid metabolism

SDA is a short chain omega-3 PUFA that is involved in the synthesis of long chain omega-3 PUFAs. **Figure 1** illustrates that SDA is formed directly from ALA. ALA is the simplest omega-3 PUFA from which all other omega-3 PUFAs can be metabolically derived. In mammals this occurs via a series of enzymes (desaturases and elongases) that generate long chain omega-3 PUFAs (EPA, docosapentaenoic acid (DPA) and DHA) from the metabolism of short chain omega-3 PUFAs such as ALA. SDA is an intermediate fatty acid produced during this process. Although ALA is much more abundant in the food supply, its bioconversion to EPA is very inefficient with as little as 0.2% of plasma ALA undergoing conversion to EPA (Pawlosky *et al.* 2001).

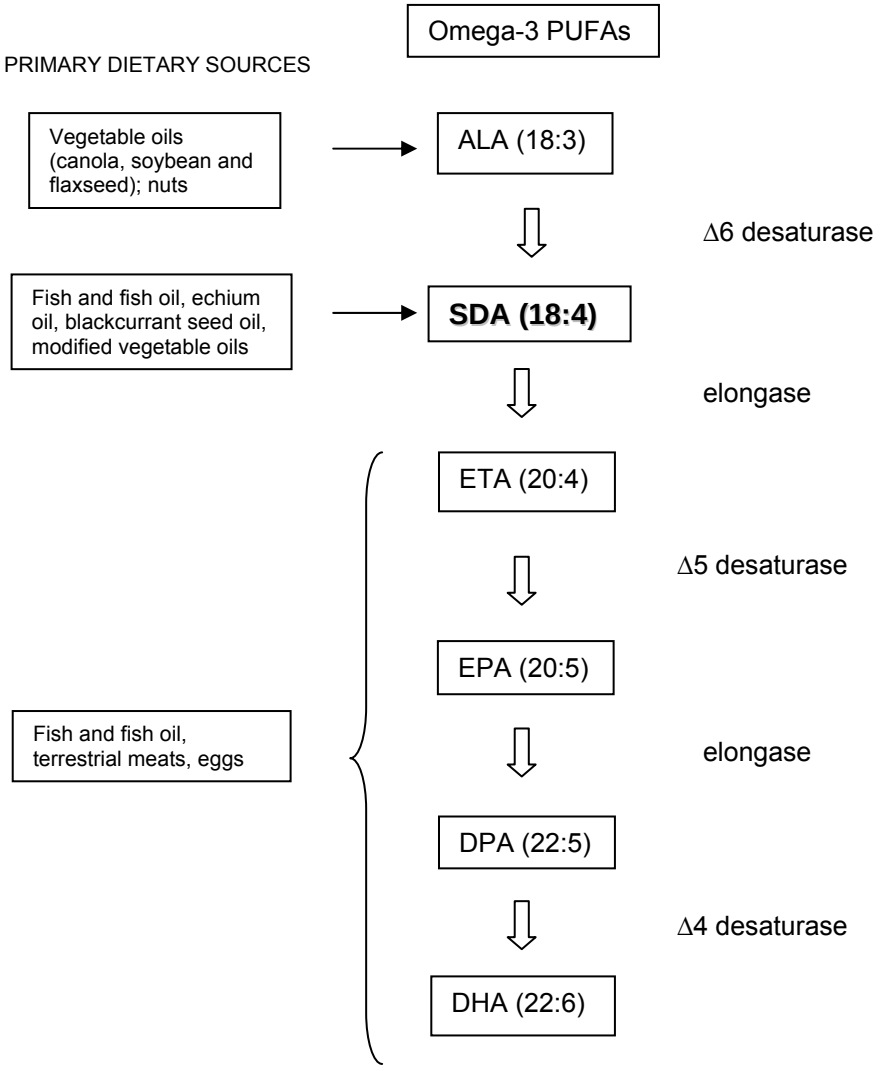

Figure 1: Metabolism of omega-3 acids (Jones and Kubow, 2006).

2.2 Is SDA converted into EPA in human tissues?

To assess the extent of conversion of SDA to EPA in human tissues, FSANZ reviewed the relevant clinical trial data provided by the Applicant. Studies included were those that involved healthy human participants and those that reported tissue levels of EPA as an outcome measure in response to consumption of SDA, either alone or blended with other oils/fatty acids in a supplement. Where other oils were included in the treatment used in the study, they were excluded if they contained more than 1% of their fatty acids as EPA. One additional study cited in the papers provided by the Applicant was also included. An additional search of the literature by FSANZ, based on the inclusion criteria described above, did not identify any further studies.

The available database was five published papers involving randomised, double-blind, placebo-controlled trials (RCTs) and one published open label trial (see **Table A1** at the end of this report for study details). Two of the studies included SDA-enriched soybean oil from genetically modified soybeans (Harris *et al*., 2008; Lemke *et al*., 2010) and one of these explicitly stated that it was derived from MON87769 soybeans (Lemke *et al*., 2010).

2.2.1 The effect of consumption of SDA on blood levels of EPA

EPA, when consumed from food sources such as fatty fish or in supplement form, is readily incorporated into circulating lipids (Miles *et al*. 2004). Hence, this analysis assesses and compares the extent of conversion of SDA-rich oils and EPA-rich oils to EPA in blood plasma and in erythrocytes. The EPA levels in these blood fractions are assumed to reflect the conversion levels of omega-3s in other human tissues.

Table 2 shows the results from the five RCTs ordered according to SDA dose; four of these include an EPA comparison group. The results show a statistically significant response in erythrocyte EPA from SDA compared with placebo, but only at higher levels of intake (about 3.7 g/day SDA or greater) (Harris *et al*., 2008; Lemke *et al*., 2010). Although Lemke *et al*. (2010) was a 12 week study, the authors reported that similar results were observed after only eight weeks of supplementation. James *et al*. (2003) did not provide a comparison of the treatment and placebo groups; however, their results suggest a significant difference between the SDA-treated group and the placebo group, particularly for plasma EPA. At intake levels of about 1.0 g/day SDA or less (Wu *et al*., 1999; Miles *et al*., 2004) there is no apparent trend towards increased levels of erythrocyte or plasma EPA compared with placebo.

Results from the open label study (Surette *et al*., 2004) (data not shown in Table 2), show that the EPA composition of plasma increased significantly from baseline to week 4 ($p<0.05$) in response to consumption of echium oil (equivalent to about 1.9 g/d SDA).

Table 2: Summary of results from the RCTs of the effect of SDA on erythrocyte and plasma EPA

Study (Duration: SDA dose)	Treatment	Outcome	Mean % of total fatty acids ± SD		p value	
			Baseline	End of study	Treatment compared with placebo	SDA compared with EPA
Wu *et al*. (1999) (8 weeks: 0.13 g/d)	Placebo	Erythrocyte EPA	1.10±0.05 (SEM)	1.05±0.06 (SEM)		
	BCSO		**0.92±0.08 (SEM)**	**0.97±0.06 (SEM)**	**NR**	
James *et al*. (2003) (6 weeks: 0.75 g/d for 3 weeks followed by 1.5 g/d for the next 3 weeks	ALA (placebo)	Erythrocyte EPA	0.88±0.17	1.01±0.18		
	EPA		0.81±0.14	2.56±0.65	NR	
	SDA		**0.96±0.19**	**1.44±0.24**	**NR**	**NR**
	ALA (placebo)	Plasma EPA	1.16±0.31	1.43±0.40		
	EPA		1.04±0.2	4.48±1.35	NR	
	SDA		**1.27±0.30**	**2.38±0.51**	**NR**	**NR**
Miles *et al*. (2004) (12 weeks: ~1 g/d))	Placebo	**EPA** in plasma triacylglycerols	0.28±0.03	0.45±0.19		
	EPA-oil		0.38±0.06	0.86±0.25	NS	
	SDA-oil		**0.37±0.09**	**0.47±0.11**	**NS**	**NS**
	Placebo	**EPA** in plasma cholesterol esters	0.28±0.03	0.45±0.19		
	EPA-oil		0.38±0.06	0.86±0.25	NS	
	SDA-oil		**0.37±0.09**	**0.47±0.11**	**NS**	**NS**
	Placebo	**EPA** in plasma phospholipids	0.28±0.03	0.45±0.19		
	EPA-oil		0.38±0.06	0.86±0.25	NS	
	SDA-oil		**0.37±0.09**	**0.47±0.11**	**NS**	**NS**
Harris *et al*. (2008) (16 weeks: ~3.7 g/d)	ALA (placebo)	Erythrocyte EPA	0.52±0.22	0.52±0.18		
	EPA		0.47±0.21	1.73±0.44	<0.0001	
	SDA		**0.42±0.13**	**1.21±0.59**	**0.0005**	**0.07**
Lemke *et al*. (2010)[§] (12 weeks: 4.2 g/d)	Placebo	Erythrocyte EPA	0.48±0.23	0.40±0.07		
	EPA		0.44±0.26	1.16±0.06	<0.001	
	SDA		**0.45±0.22**	**0.94±0.06**	**<0.001**	**0.008**

NS - not significant (i.e. p≥0.05); NR - not reported.

[§] Baseline results are initial mean intention to treat (ITT) and end of study results are adjusted final ITT.

2.2.2 Relative effectiveness of conversion of SDA to EPA

James *et al*. (2003) estimated the numerical relative effectiveness of EPA:SDA:ALA based on the results from their study. From the erythrocyte and plasma phospholipid EPA levels they concluded that the ratio was approximately 1.0:0.3:0.07. Thus, 1 g of dietary SDA is approximately equivalent to 300 mg dietary EPA in terms of increasing plasma and erythrocyte concentrations of EPA. However, the trial results indicate that about 3.7 g/day of SDA is required before a statistically significant response in erythrocyte EPA is observed (see **Table 2**).

James *et al*. (2003) also noted that the ∆6 desaturase catalysed conversion of ALA to SDA is the rate limiting step in the production of long chain omega-3 fatty acids in the body. Therefore, higher tissue levels of long chain omega-3 fatty acids would be expected to occur in response to SDA compared with a similar amount of ALA.

Harris *et al*. (2008) noted that their results for relative effectiveness[6] of conversion of SDA to EPA, when calculated based on changes in erythrocyte levels, were lower than those reported in James *et al*. (2003) (16.6% vs 30%[7]). Lemke *et al*. (2010) reported a similar conversion of dietary SDA to EPA in erythrocyte membranes (17.1%) to that of Harris *et al*. (2008).

Harris and colleagues (2008) considered that several factors might be contributing to the differences observed between their study and the James *et al*. (2003) study: different chemical forms of SDA, the difference in study duration, or the types of subjects included. Another possible explanation is that each of the classes of fatty acids can interfere with the metabolism of the other. For example, an excess of omega-6 PUFAs in the diet can reduce the metabolism of omega-3 PUFAs (Jones and Kubow, 2006). As James *et al*. (2003) attempted to minimise linoleic acid intake, an omega-6 PUFA, this may explain the higher conversion rates experienced in this study compared with Harris *et al*. (2008) who did not control for fatty acid intake, except to recommend avoidance of fatty fish and Lemke *et al*. (2010) who recommended a reduction in usual fat intake.

Table 3 summarises the study design differences between the three studies. The comparison suggests that gender and BMI, in addition to the form of SDA and control of omega-6 intake, may influence the relative effectiveness of conversion of SDA to EPA. The other two RCTs (Wu *et al*., 1999; Miles *et al*., 2004) did not report results for relative effectiveness of conversion of SDA to EPA

Table 3: Differences in study design among RCTs that reported results for relative effectiveness of conversion of SDA to EPA

Study	Form of SDA (capsules or oils)	Control of fatty acid intake	Subject differences	% of women in the study	Duration	Relative effectiveness of conversion of SDA to EPA in erythrocytes
James *et al*. (2003)	Ethyl esters (capsules)	Attempted to minimise omega-6 intake	Mean BMI: 26.4	36%	6 weeks	30%*
Harris *et al*. (2008)	Triglycerides (capsules)	Recommended avoidance of fatty fish	Mean BMI in the 3 treatment groups: 30-31	58%	16 weeks	17%
Lemke *et al*. (2010)	Triglycerides (capsules and oils)	No change in diet but did recommend an adjustment in fat intake to account for the treatment oils.	Mean BMI in the 3 treatment groups: 28.5-30	~55%	12 weeks	17%

* Relative effectiveness of conversion of SDA to EPA in the James *et al*. (2003) paper was based on erythrocyte and plasma EPA levels.

[6] Harris *et al*. (2008) refer to "efficiency of conversion", but FSANZ considers 'relative effectiveness of conversion' to be a more correct term, and it is used in this report.

[7] Harris *et al*. (2008) cite a 27% difference in the effectiveness of conversion of SDA to EPA from the James *et al*. (2003) study. However, FSANZ has used 30% as indicated in the James *et al*. (2003) study; the results of which are described above.

2.2.3 Residual levels of SDA after conversion to EPA

Four of the studies (Wu *et al*., 1999; James *et al*., 2003; Harris *et al*., 2008; Lemke *et al*., 2010) reported that the percentage of SDA in erythrocytes at the end of the study compared with baseline in the SDA treatment groups was small to negligible indicating that the conversion of SDA to the longer chain omega-3s is nearly 100%. Miles *et al*. (2004) reported that SDA did not appear in detectable amounts in any of the plasma fractions investigated or in peripheral blood mononuclear cells (PBMCs) in the SDA treated group. James *et al*. (2003) also noted that when SDA was provided as an ethyl ester that it was not detectable in plasma triacylglycerols, cholesterol esters or phospholipids, or in phospholipids, platelets or PBMCs, indicating that SDA is readily metabolised to EPA without any significant accumulation of eicosatetraenoic acid (ETA).

Thus, based on the evidence from the five RCTs, there are negligible amounts of residual SDA in the various blood fractions considered in these studies.

2.2.4 The effect of consumption of SDA on the omega 3 index

The omega-3 index is the combined proportion of EPA and DHA in erythrocyte membranes, expressed as a percent of total fatty acids, and is correlated with cardiac membrane EPA and DHA (Harris *et al*. 2004). As dietary intake recommendations relate to both these fatty acids, the omega-3 index provides a mechanism for observing the effect of SDA- and EPA-rich oils on EPA and DHA in human tissues.

Two studies (Harris *et al*., 2008; Lemke *et al*. 2010) reported results for the omega-3 index in response to intake of SDA (see **Table 4**). In both studies, the omega-3 index in the SDA treatment group was significantly greater than the placebo group, and similar results were observed in the EPA treatment group as would be expected. There were no differences between the omega-3 index in the SDA or EPA group in either of these studies.

Table 4: Summary of results of the effect of SDA intake on the omega 3 index

Study (Duration: dose)	Treatment	Omega-3 index Mean % of total fatty acids ± SD		p value	
		Baseline	End of study	Treatment compared with placebo	SDA compared with EPA
Harris *et al*. (2008) (16 weeks: ~3.7 g/d)	ALA (placebo)	4.36±0.95	4.21±0.81		
	EPA	4.07±0.86	5.10±0.82	0.026	
	SDA	**4.02±0.90**	**4.80±1.00**	**0.042**	**0.69**
Lemke *et al*. (2010) [§] **(**12 weeks: 4.2 g/d)	ALA (placebo)	4.45±1.10	4.18±0.11		
	EPA	4.19±1.10	4.79±0.10	<0.001	
	SDA	**4.29±1.16**	**4.62±0.10**	**0.006**	**0.196**

[§] Baseline results are initial mean intention to treat (ITT) and end of study results are adjusted final ITT.

3. Nutritional implications of the increase in the TFA content of SDA soybean oil

As mentioned in Section 1.2, there is a consequential increase in trans-SDA (from zero to 0.26% of total fatty acids) and trans-ALA (from 0.14% to 0.51% of total fatty acids) as a result of increasing the SDA and, to a lesser extent, the ALA content of SDA soybean oil. *Trans* fatty acids (TFAs) in the diet raise LDL-cholesterol and lower HDL-cholesterol, thus contribute to an increased risk of coronary heart disease. The WHO, in its report on diet, nutrition and chronic diseases (WHO 2003), recommended that TFAs comprise no more than 1% of total dietary energy[8]. The NHMRC and NZMoH (2006) recommend that saturated fatty acids and TFAs combined comprise no more than 8-10% of dietary energy.

FSANZ conducted a formal scientific review of TFAs in the Australian and New Zealand food supplies in 2007[9] and updated this review in 2009[10]. In 2009, FSANZ reported that mean total TFA intake from both ruminant and manufactured sources is estimated to be 0.5-0.6% of total dietary energy, with more than 90% of Australians and more than 85% of New Zealanders having intakes below 1% of total energy intake. This result is in keeping with WHO's revised recommendation on TFA intake (see footnote below). The following draws further on information discussed in these documents.

In 2004, the Danish food authorities adopted legislation which introduced a limit of no more than 2 g of TFA per 100 g of fats or oil in the food product as sold to the consumer, with some exceptions for ruminant TFAs occurring in animal fats. In 2008, Switzerland adopted similar legislation. Based on this upper limit, the NSW Food Authority (NSWFA) analysed 456 samples from six different food categories: takeaway foods, fats and oils, snack foods, meat products, and bakery products. These data were collected between September 2008 and April 2009 from a range of supermarkets and takeaway shops. The results were reported in FSANZ's 2009 review of TFAs. Overall, 82.3% of products had a level of TFAs below 2% (i.e. the recommended maximum level set by Denmark), and many of these foods had undetectable levels of TFAs.

Thus, the level of TFAs in SDA soybean oil (<1% of total fatty acids) is likely to make only a minor contribution to the overall TFA content of foods in which SDA soybean oil is an ingredient. For comparison, the TFA content of five blended edible oils, included in NSWFA's analysis in 2009, reported a range of 0.3 to 3.10 g/100 g of oil. In August 2010, Australian CHOICE magazine published data on the nutritional information of commercially available cooking oils[11]. These data are based on analysis conducted by CHOICE. Soybean oil was not one of the categories analysed but the TFA content of numerous other cooking oils was published. **Table 5** shows a summary of the range of TFA content in the oils included in CHOICE's analysis. Based on these data, the TFA content of SDA soybean oil is within the TFA range of commercially available cooking oils.

[8] In 2009, WHO revised its recommendation on TFA intakes, from advising that populations should have TFA intakes below 1% of total energy on average, to advising that the great majority of the population should have TFA intakes below 1% of total energy.
[9] FSANZ's 2007 report on TFAs can be found at http://www.foodstandards.gov.au/scienceandeducation/publications/transfattyacidsrepor4561.cfm
[10] FSANZ's 2009 report on TFAs can be found at http://www.foodstandards.gov.au/scienceandeducation/publications/transfattyacidsrepor4560.cfm
[11] CHOICE's analysis included 14 different types of supermarket cooking oil.

Table 5: TFA content of edible cooking oils as reported by 'CHOICE'

Cooking oil	TFA (g/100 mL) (range, where applicable)
Mustardseed oil	0
Almond oil	NS
Canola oil	<0.5-<1
Grapeseed oil	0.9
Corn oil	0.8
Avocado oil	0
Olive oil	0-0.5
Sunflower oil	0.5-1.8
Macadamia oil	0-NS
Canola & red palm fruit oil	0
Peanut oil	NS-0.9
Vegetable oil/cooking oil (not further defined)	0.46-0.92
Rice bran oil	0
SDA soybean oil	**0.76% of total fatty acids (equivalent to 0.67 g TFA per 100 mL)**

NS - not significant.

Source: Data on cooking oils other than SDA soybean oil were obtained from the CHOICE website http://www.choice.com.au/Reviews-and-Tests/Food-and-Health/Food-and-drink/Groceries/Cooking-oils/page/Nutritional%20information%20table.aspx accessed on 8 November 2010.

4. Potential adverse effects

Five of the six studies included in this assessment considered potential adverse effects in response to consumption of oils rich in SDA. Miles *et al*. (2004) was the one study that did not report adverse effects. No reasons were given as to why four of the original 74 participants dropped out of the study. Results for the other five studies are presented below.

Wu et al. (1999) reported that haematology, blood and urine chemistry, and blood lipid profiles were normal and did not change significantly after two months of supplementation with black currant seed oil[12]. There were also no adverse effects on the immune response[13] between placebo and the treatment groups among the study participants. Although 11 of the original 40 subjects did not complete the study, their reasons for dropping out did not appear to be related to the treatment used in this study.

[12] The black currant seed oil used in the Wu *et al*. (1999) study contained 15% γ-linolenic acid (GLA), in addition to SDA (2-6%). The investigation of GLA on the immune response was the primary purpose of this study.

[13] The immune response was assessed in several ways: a 'delayed-type hypersensitivity response'; lymphocyte proliferation; interleukin and prostaglandin production; lymphocyte sub-populations and membrane fluidity.

James *et al*. (2004) measured tumour necrosis factor α and interleukin 1β in their study. Both of these inflammatory cytokines are known to decrease in response to the ingestion of fish oil; the mechanism however is not known. The study showed that both tumour necrosis factor α and interleukin 1β decreased in the subjects who received SDA, although this decrease also occurred in the placebo and EPA treated groups such that there were no statistically significant differences between the groups at the end of the study. There were also no consistent differences among the fatty acids regarding their effect on lipopolysaccharide-stimulated synthesis of prostaglandin E_2[14] or on thromboxane A_2[15] synthesis during blood clotting. And there were no significant differences between groups in concentrations of fasting triacylglycerol or of total, LDL or HDL cholesterol. One subject in the EPA group withdrew from the study; the reason was not provided.

Harris *et al*. (2008) reported no significant differences between groups for any of the physiological endpoints considered (heart rate, blood pressure, body weight), the lipid endpoints (total, LDL-, HDL-cholesterol, triglycerides) or on platelet function. No serious adverse events were reported. Non-serious adverse events related to gastrointestinal distress were evenly distributed across all three groups. Twelve of the 45 participants initially enrolled withdrew for reasons described as “non-serious adverse events”.

Lemke *et al*. (2010), the study with the highest dose of SDA, investigated the effect of SDA on fasting serum total cholesterol, LDL-cholesterol, HDL-cholesterol and triglycerides. No statistically significant results were reported between the SDA treatment group and the placebo group; nor between the SDA treatment group and the EPA treatment group. Self-reported adverse events, such as gastrointestinal disorders, did not differ between treatment groups; nor did body weight or BMI. Similar numbers of participants in each treatment group did not complete the study protocol. The two main reasons non-completion were attributed to “withdrawal of consent” and “loss to follow up”; none of these were attributed to adverse events associated with the treatments. There was one case of gastroenteritis with dehydration that occurred in the SDA group and one case of gastroenteritis in the control group. These were considered serious adverse events that resolved completely after treatment was discontinued. However, the authors did not comment on the attribution of the treatments to these events.

In the open label study, Surette *et al*. (2004) reported no significant differences between baseline and week 4 in serum total, LDL- or HDL-cholesterol. However, there was a significant fall in serum triglycerides of 21% ($p<0.05$) as a result of consuming echium oil. None of the reported adverse events were considered to be associated with echium oil. There were no dropouts in this study.

[14] Prostaglandin E_2 causes the constriction of blood vessels.
[15] Thromboxane A_2 is involved in the formation of blood clots.

5. Conclusion

Dietary SDA results in significant increases in EPA in blood plasma and erythrocytes compared with a placebo group, and the conversion of SDA to EPA in these tissues is relatively complete.

The clinical data indicate that the relative effectiveness of conversion of dietary SDA to EPA in plasma and erythrocytes ranges from 17-30%, compared with the relative effectiveness of conversion of ALA to EPA in these blood fractions of <1%. As with all sources of SDA, conversion to EPA is variable, depending on a number of individual and concurrent dietary factors.

While SDA is consumed in small quantities in the Australian and New Zealand diets at present, the available evidence indicates that there is unlikely to be any adverse effects from an increase in the consumption of SDA. In addition, although the TFA content in SDA soybean oil is higher than in conventional soybean oil, the level (0.67 g TFAs per 100 mL) is well within the range in commonly consumed edible oils (0-1.8 g TFAs per 100 mL); hence it is unlikely to increase overall TFA intakes in Australia and New Zealand above their current levels.

Thus, SDA soybean oil has the potential to be used as an alternate source of omega-3 PUFAs and, in so doing, indirectly contribute to the recommended increased intakes of long chain omega-3 PUFAs in the Australian and New Zealand populations

Table A1: Details of studies identified that consider changes in tissue concentrations of EPA in response to SDA intake

First Author, Year Trial objective	Initial n (m/f)	Final n (m/f)	Health status	Age (years)	Duration (weeks)	Treatment groups			Comments
RCTs						SDA	EPA	Placebo	
Harris, 2008 **Objective**: To compare the effects of EPA and an SDA-enriched soy bean oil on red blood cell EPA and DHA levels.	45 (ITT analysis)	33 (14/19) (PP analysis)	Overweight, healthy	21-70	16	~3.7 g/d SDA + 2.42 g/d ALA	~1 g/d EPA + 1.7 g/d ALA	1.7 g/d ALA	Subjects were asked to maintain a consistent lifestyle (diet, exercise, alcohol intake, sleep habits etc.) and to avoid intake of fatty fish for the duration of the study. Treatments provided as capsules. Compliance was defined as >=80% consumption of oils/capsules. There were no differences between the ITT and PP analysis.
James, 2003 **Objective**: To determine whether dietary SDA can increase tissue EPA and DHA in healthy humans and compare its efficacy with EPA and ALA.	45 (29/16)	44	Healthy, BMI: 20-30	18-65	3 3 3	Run-in 0.75 g/d SDA 1.5 g/d SDA (SDA provided in pure form as an ethyl ester)	Run-in 0.75 g/d EPA 1.5 g/d EPA	Run-in 0.75 g/d ALA 1.5 g/d ALA	Subjects were asked to avoid dietary n-6 fatty acids and to substitute monounsaturated fatty acids where possible. They were provided with some foods to facilitate this action. Also provided with diet diaries and instructed in keeping weighed food records on certain days. No significant change in participant's body weight during the study. One dropout in the EPA group. Treatments provided as capsules. Compliance was 99.5±0.77%.
Miles, 2004b **Objective**: To identify whether SDA can be used to increase the EPA content of plasma lipids and cells and to understand more about the effects of ALA, SDA and EPA in humans.	74 males	70 males	Healthy	21-44	12	9 g/d 'SDA-oil' (11.7% SDA) Referred to as 'echium oil' in the study.	9 g/d 'EPA-oil' (27.5% EPA + 1.6% SDA) Referred to as 'EPA oil' in the study	9 g/d 80:20 mix of palm and sunflower oils Referred to as 'placebo' in the study	Eight treatment groups were included in this study, but only three groups are compared here. Treatments provided as capsules. The placebo oil closely resembled the fatty acid composition of the UK diet.

First Author, Year Trial objective	Initial n (m/f)	Final n (m/f)	Health status	Age (years)	Duration (weeks)	Treatment groups			Comments
Lemke, 2010 Objective: To investigate the effect of SDA oil on improving markers of hearty health, in particular the omega-3 index expressed as % of total fatty acids.	252 (ITT analysis)	181 (CP analysis)	Healthy (BMI 25-35)	21-70	12	1.0 g/day SBO capsule + 14.7 g/d SDA enriched soybean oil (equiv to 4.2 g/d SDA)	1.0 g/d EPA capsule + 14.7 g/d soybean oil	1.0 g/day Soybean oil capsule + 14.7 g/d soybean oil (equiv to 1.0 g/d ALA)	Subjects maintained their normal diet and exercise throughout the study, with the exception of reducing fat in their usual diet to accommodate the test oils. Subjects completed 3-day dietary records at the start and at the end of the study. No differences in fat, protein, carbohydrate or energy were observed. Treatments provided as capsules and edible oils. Baseline demographics did not differ between the ITT and CP populations. Compliance ranged from 85 to 105%*.
Wu, 1999 Objective: To investigate the effect of black currant seed oil (2.9% SDA) on the immune response of healthy elderly subjects.	40	29 (16/13)	healthy	>= 65	8	4.5 g/day black currant seed oil This is estimated to equate to 0.13 g/d SDA.	NA	4.5 g/day Soybean oil	Subjects were asked to continue with typical food intake, dietary habits and lifestyle. Subjects completed 3-day dietary records during the first month of the study. Treatments provided as capsules. Compliance was not reported.
Open label trials									
Surette, 2004 **Objective**: To investigate the effect of dietary echium oil (12.5% SDA) on tissue fatty acid content and serum triacylglycerol concentrations in hypertriglyceridaemic humans.	11 (6/5)	11 (6/5)	Hypertri-glyceridaemic adults; otherwise healthy.	>= 20 (mean =56)	4	15 g/day echium oil This is estimated to equate to 1.9 g/d SDA.	NA	NA	Subjects were given instructions to follow the American Heart Association's National Cholesterol Education Program Step 1 diet. Treatments provided as capsules. Compliance ranged from 85 to 105%*.

Abbreviations: g/d – grams per day; NA – not applicable.
Compliance levels above 100% indicate that participants consumed more of the treatment than was required.

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