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

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Supporting document 1

Risk and technical assessment report – Application A1137

Polysorbate 20 as a Food Additive

Executive summary

The purpose of the application is to seek approval for the use of polyoxyethylene (20) sorbitan monolaurate, more commonly known as polysorbate 20, as a food additive. Polysorbate 20 is intended to be used as an emulsifier at levels of less than 0.05% (500 mg/kg(L)) in the final food product.

An assessment of the stated purpose of using polysorbate 20 as an emulsifier to surface treat meat and fish products indicates it is able to perform this role in the amounts and form proposed to be used. Its use is therefore technologically justified for its proposed stated purpose and it has proven advantages over currently permitted emulsifiers. There are internationally accepted specifications for polysorbate 20.

The submitted data, and information from other sources, are considered adequate to define the hazard of polysorbate 20. The available evidence shows that polysorbate 20 is not genotoxic. At the very high dose of 25% w/w in the diet, polysorbate 20 causes diarrhoea and associated weight loss and ill-health in laboratory rodents. However, these adverse effects would not be observed in humans since these levels are extremely high and not relevant to human consumption levels. There is no evidence that the polysorbates are reproductive or developmental toxicants. Although clinical data on human tolerance are limited, polysorbates are widely used as emulsifiers in foods and pharmaceuticals internationally, and have not been associated with adverse effects in consumers. Polysorbates 60, 65 and 80 are already permitted in the Australia New Zealand Food Standards Code (the Code) at levels consistent with Good Manufacturing Practice (GMP).

Polysorbates 20, 40, 60, 65 and 80 are chemically very similar, are metabolised by the same pathways and have similar adverse effects in laboratory animals. The group ADI set by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) in 1973 was based on chronic dietary studies of polysorbates 60, 65 and 80 in rats. A no observed adverse effect level (NOAEL) of 5% in the diet (equivalent to 2500 mg/kg bw/day) was based on the occurrence of diarrhoea and associated weight loss and ill-health at the next highest dose of 10 % (5000 mg/kg bw per day). From this NOAEL, JECFA established a group ADI for polysorbates of 0-25 mg/kg bw/day. Results of a chronic dietary study of polysorbate 80 in rats, conducted by the National Toxicology Program (NTP) in 1992, support the JECFA ADI, and FSANZ has found no evidence to suggest that the NOAEL for polysorbate 20 would be expected to be lower than those of the other polysorbates.

Given that the group ADI is intended to cover dietary exposure to all polysorbates, FSANZ undertook a dietary exposure assessment for polysorbate 20 plus all other permitted polysorbates. FSANZ completed a refined estimate of dietary exposure to polysorbates based on the most recent Australian and New Zealand consumption data and information on reported use levels by industry and/or Codex GSFA or EU maximum permitted levels. The estimated refined baseline mean and 90th percentile exposure to polysorbates expressed on a kilogram body weight basis ranged from 4.8–10.4 mg/kg bw/day and 10.7–23.7 mg/kg bw/day, respectively. When meat and fish products containing polysorbate 20 at the amount requested by the applicant were included, the estimated total mean and 90th percentile dietary exposures to polysorbates ranged from 5.0–10.8 mg/kg bw/day and 11.2–24.7 mg/kg bw/day, respectively. The requested permissions for polysorbate 20 result in only a small increase in dietary exposure. The refined estimated baseline exposures remain conservative and not considered to be reflective of actual dietary exposures. It would be unlikely that all foods within each permitted food category would contain polysorbates at maximum concentrations and it would be unlikely that every consumer would select all of the foods that they consume to be those containing polysorbates every day for a lifetime.

Based on a review of the toxicological data, including consideration of reviews by other regulatory agencies, FSANZ concludes that it is appropriate to include polysorbate 20 in a group ADI for polysorbates, and that the group ADI established by JECFA in 1973 for polysorbates, 0-25 mg/kg bw/day, remains appropriate. The mean and 90th percentile refined baseline exposure estimates of polysorbates already permitted in the Code were below the ADI of 25 mg/kg bw/day for all Australian and New Zealand population groups assessed. When the additional requested permission of polysorbate 20 was applied, mean and 90th percentile exposures for all population groups assessed did not exceed the ADI.

Based on dietary exposure assessment, it is expected that this group ADI will not be exceeded by the addition of polysorbate 20 to the proposed food categories requested in addition to the already permitted polysorbates in the Code.

On the basis of these considerations, the risk assessment concludes that there are no public health and safety concerns related to permitting polysorbate 20 as an emulsifier food additive for processed meat and meat products, and processed fish and fish products.

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1 Introduction

1.1 Objectives of the assessment

The purpose of the application is to seek approval for the use of polyoxyethylene (20) sorbitan monolaurate, more commonly known as polysorbate 20, as a food additive. Polysorbate 20 is intended to be used as an emulsifier at levels of less than 0.05% (500 mg/kg(L)) in the final food product.

There are no permissions for polysorbate 20 as a food additive in the Australia New Zealand Food Standards Code (the Code). An application to amend the Code to permit polysorbate 20 requires a pre-market assessment.

The objectives of this risk and technical assessment are to:

- determine whether the proposed technological purpose is clearly stated
- ensure polysorbate 20 performs the technological purpose in the quantity and form proposed
- evaluate any potential public health and safety concerns that may arise.

2 Food technology assessment

2.1 Introduction and description of substance

Polysorbates are a group of structurally-related substances that have a technological purpose as surface active agents (emulsifiers) when used as food additives. They are obtained by the reaction of sorbitol, fatty acids and ethylene oxide.

The individual polysorbates that make up the polysorbate group of food additive emulsifiers are listed in Table 1, with their common name, their Codex International Numbering System (INS) food additive number and their more detailed name listed by the Codex Standard CAC/GL 36/1989.

Table 1: Names and INS numbers of the different substances that make up the polysorbate group of food additives

Common name	INS No.	Detailed name
Polysorbate 20	**432**	**polyoxyethylene (20) sorbitan monolaurate**
Polysorbate 80	433	polyoxyethylene (20) sorbitan monooleate
Polysorbate 40	434	polyoxyethylene (20) sorbitan monopalmitate
Polysorbate 60	435	polyoxyethylene (20) sorbitan monostearate
Polysorbate 65	436	polyoxyethylene (20) sorbitan tristearate

Three other polysorbates are currently permitted in the Code as food additives. Polysorbates with the INS numbers 433, 435 and 436 are permitted in the table to section S16—2 as food additives, at levels consistent with Good Manufacturing Practice (GMP).

2.1.1 Identity

Details of the identity and structure of polysorbate are provided in Table 2.

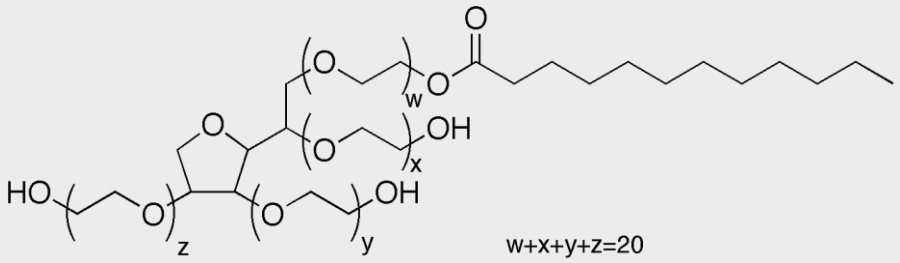
Polysorbates' nomenclature helps identify the structure of the individual substances and how they differ. The number 20 following polyoxyethylene in the name refers to the number of

oxyethylene (-CH_2CH_2O-) moieties in the chemical structure (i.e. w+x+y+z=20 in the structural formula in Table 2). The number following the simpler name, polysorbate, refers to the type of fatty acid associated with the polyoxyethylene sorbitan portion of the molecule. The number 20 indicates monolaurate, indicating it has been reacted with lauric acid.

Polysorbate 20 is defined in the Joint FAO/WHO Expert Committee on Food Additives (JECFA) and the European Commission Regulation (EU) No 231/2012 specifications. It is a mixture of partial esters of sorbitol and its mono and dihydrides, with edible lauric acid and condensed with approximately 20 moles of ethylene oxide per mole of sorbitol and its anhydrides. Therefore the molecular structure and molecular weight are nominal since the commercial product will be a blend of individual substances.

Both the JECFA and European Commission specifications for polysorbate 20 contain assay requirements for the preparation to meet (see later section on specification).

Table 2: Chemical names, identification and structure of polysorbate 20 (EFSA, 2015)

Chemical name	Polyoxyethylene (20) sorbitan monolaurate
International Union of Pure and Applied Chemistry (IUPAC) name	2-[2-[3,4-bis(2-hydroxyethoxy)oxolan-2-yl]-2-(2-hydroxyethoxy)ethoxy]ethyl dodecanoate
Common name	polysorbate 20
Other names	Tween^R 20, PEG (20) sorbitan monolaurate
INS No.	432
CAS Registry Number	9005-64-5
Chemical formula	$C_{58}H_{114}O_{26}$ (approximation of chemical formula)
Molecular weight	1,227.54 g/mol (nominal)
Structural formula:	

2.1.2 Technological purpose

Polysorbate 20 is a surface active agent, which when used as a food additive, has the technological purpose of an emulsifier. As defined in the table to section S14—2 an

emulsifier “facilitates the formation or maintenance of an emulsion between two or more immiscible phases”.

The application is proposing to use polysorbate 20 at levels of up to 500 mg/L, in solution as an emulsifier to act as a dispersion agent for natural antimicrobial agents (extracts of plants that are compliant with the Code). The antimicrobial solution is used as a surface spray or dipping solution to treat cooked processed meats, small goods and processed fish and fish products to prevent the growth of bacteria, yeasts and mould.

2.1.3 Technological justification

Polysorbate 20 has advantages for some applications as an emulsifier over the currently permitted polysorbates.

The emulsifier ensures the surface of the treated food is completely in contact with the antimicrobials of the spraying or dipping solution. The antimicrobials used are plant extracts from fruits, herbs and spices, along with weak organic acids to stabilise the preparation. The applicant explains that to disperse the active substances which have the antimicrobial function, requires an emulsifier that is safe and suitable for use in food, is pH tolerant due to the use of weak organic acids and has good surface wetting properties.

Trials conducted by the applicant have indicated that polysorbate 20 is the only emulsifier that satisfies these specific criteria:

- liquid at room and refrigerated temperatures
- stable at low pH
- water soluble and “film-forming” in aqueous solutions
- has sufficiently high “hydrophilic lipophilic balance (HLB)” to be able to form “oil in water” emulsions
- able to form stable dispersions of herb and spice extracts (essential oils, which are the active antimicrobials) in aqueous solutions.

Other permitted emulsifiers have been identified as unsuitable for the proposed purpose. Specifically, distilled monoglycerides (assumed to include mono- and di-glycerides of fatty acids (471)) and various fatty acids of glycerol (472a, 472b, 472c, 472e, 472f etc.) are not water soluble. Polysorbate 40 and 80 are not ‘film forming’, while polysorbate 60 is insoluble at refrigerated temperatures. Sorbitans (including 491 and 492) are not sufficiently water soluble, also being oil soluble.

The advantage of permitting polysorbate 20 as an emulsifier for adding to water-based antimicrobials is summarised by the applicant as “allowing water based plant extract antimicrobials to be applied to surfaces of raw and cooked meat and fish to limit food spoilage due to microbial growth, so extending the shelf life of these foods”.

2.1.4 Assessment of claimed benefits

The applicant performed and reported some antimicrobial efficacy studies comparing untreated meat products, current commercial sodium lactate/acetate treatment and the use of polysorbate 20 and the plant extracts as antimicrobials. Use of polysorbate 20 with the plant extract antimicrobials performed in an equivalent manner compared to the current sodium lactate/acetate treatment. These were for sliced ham stored at 4°C for 2, 7 and 42 days. As well, the zone of inhibition for various foodborne microbes (*Listeria monocytogenes*, *Staphylococcus aureus*, *E. coli* and *Campylobacter jejuni*) on agar plates was greater for polysorbate 20 and plant extract antimicrobials compared to the lactate/acetate treatment.

These results confirm the claimed benefit to the applicant that polysorbate 20 used as an emulsifier in conjunction with various plant based extracts containing active antimicrobials provides antimicrobial activity and concomitant shelf-life improvement. These results are for surface treatment of various meat and fish products.

2.2 Chemical properties

Polysorbate 20 has the technological function of an emulsifier since it forms an emulsion between oil and aqueous phases. It is classified as a non-ionic surfactant, is soluble in most solvents, but is insoluble in mineral oil and petroleum ether. Its solubility is based on its ability to act as both hydrogen bond donor and hydrogen bond acceptor (Pollard et al., 2006). The fatty acid tail (from lauric acid) provides the oil (non-polar) solubility function of the substance, while the sorbitan basic structure provides the polar solubility ability so enabling polysorbate 20 to function as an emulsifier.

2.3 Analytical method for detection

There are a range of different analytical methods for the analysis of polysorbates in food (EFSA 2015), including gas chromatography (GC), high performance liquid chromatography (HPLC) and supercritical fluid chromatography (SFC).

A number of analytical methods are provided in both the application and the European Food Safety Authority (EFSA) 2015 scientific opinion.

2.4 Manufacturing process

Polysorbates are most commonly prepared by reacting sorbitol with fatty acids using an acidic catalyst (e.g. phosphoric acid) and a caustic soda-type catalyst. The acidic catalyst drives the dehydration of the sorbitol to produce a mixture containing sorbitol and sorbitans (sorbitol monoanhydrides) among other by-products, the caustic soda-type catalyst driving the esterification. The sorbitan esters are then reacted with ethylene oxide (20 mole) in the presence of a catalyst, in this case potassium hydroxide, to produce the polysorbates.

There is an alternative method of production where the catalytic dehydration of sorbitol occurs, condensation with ethylene oxide, followed by esterification with fatty acids.

2.4.1 Product specification

Polysorbate 20 has a specification in the Combined Compendium of Food Additive Specifications prepared by JECFA. There are also specifications in the Food Chemicals Codex and the EU No 231/2012.

The commercial preparation of polysorbate 20 used in food preparation needs to meet the requirements of these international food additive specifications.

2.4.2 Product stability

Storage of polysorbates at room temperature results in hydrolysis of the fatty acid ester. To assist in preventing such degradation, product can be stored away from light, under an atmosphere of nitrogen and at low temperatures (EFSA 2015).

2.5 Food technology conclusion

FSANZ concludes polysorbate 20, when used as an emulsifier to surface treat meat and fish products, is able to perform this function in the amounts and form proposed to be used. Its

use is therefore technologically justified for its proposed stated purpose and it has proven advantages over other forms of emulsifiers. There are internationally accepted specifications and analytical methods available to check and quantify for the levels of polysorbate 20 in treated food.

3 Hazard assessment

3.1 Background

Polysorbate 20 has not previously been assessed by FSANZ. Three other polysorbates are currently permitted for use as food additives under Schedule 16 in the Code; polysorbates 80 (polyoxyethylene sorbitan monooleate), 60 (polyoxyethylene sorbitan monostearate) and 65 (polyoxyethylene sorbitan tristearate).

JECFA established a group ADI 0-25 mg/kg bw/day for polysorbates 20, 40, 60, 65 and 80 at their 17th meeting in 1973. The ADI was based on a No Observed Adverse Effect Level (NOAEL) of 2500 mg/kg bw/day in a chronic dietary study of polyoxyethylene sorbitan monostearate in rats with the application of a 100-fold safety factor.

3.1.1 Scope

The aims of the current hazard assessment are to:

- Review the available data on the toxicology of polysorbate 20 to determine its safety as a food additive
- Determine whether the group NOAEL for polysorbates is appropriate for polysorbate 20 or, if not, establish a health-based guidance value for polysorbate 20.

3.1.2 Evaluation of submitted data

The submitted data, together with information from other sources, were considered adequate to define the hazard of polysorbate 20.

3.2. Safety of polysorbate 20

3.2.1 Absorption, metabolism and excretion

Studies with radiolabelled polysorbates, administered orally to rats showed that the ester bond in polysorbates is hydrolysed in the intestine. The fatty acid moiety is absorbed and metabolised in the same way as dietary fatty acids. There is negligible cleavage of the bond between the polyoxyethylene moiety and the sorbitan moiety, and approximately 90% of the polyoxyethylene sorbitan is primarily excreted in the faeces. Excretion is practically complete at 24 hours after oral administration (as reviewed by the Food Safety Commission (2007) in Japan, and EFSA (2015)). FSANZ has found not identified new information on the absorption, distribution, metabolism and excretion of polysorbates postdating the reviews by those agencies. JECFA (WHO 1964) concluded in the report of its 7th meeting that there is no indication for any differentiation between the polysorbates in toxicological evaluation.

3.2.2 Acute studies in animals

Eagle and Poling (1956) reported acute oral toxicity values for polysorbate 20 of 18 mL/kg bw in the hamster and 36.7 mL/kg bw in the rat. Forty-seven hamsters, and 57 rats, were used in the study. Animals were observed for one week after dose administration by oral gavage.

Bartsch et al (1976) investigated the acute toxicity of a number of solvents, including polysorbate 20, in NMRI mice and Sprague-Dawley rats. Mice ranged in bodyweight from 15 to 25 g, and rats weighed 170-230 g. Each dose group comprised 10 animals; 5/sex. Food quality polysorbate 20 was administered undiluted for determination of oral toxicity. Animals were maintained, group-housed under standard husbandry conditions, for 7 days after dose administration. The acute oral toxicity of polysorbate 20 in both species was greater than 30 mL/kg, which was the highest dose tested.

The polysorbates as a group have low acute oral toxicity, estimated to be in the range 10 to 60 g/kg bw. In a number of the studies of acute oral toxicity of polysorbates, no toxicity was observed at the highest dose tested (reviewed by EFSA 2015).

3.2.3 Subchronic studies in animals

Four studies with polysorbate 20 considered by JECFA in or prior to 1973 are briefly reviewed here. These are the studies of Harris et al (1951a, b), Eagle and Poling (1956) and Poling et al (1956).

Harris et al (1951a) fed emulsifiers, including polysorbate 20, to Sprague Dawley rats. Polysorbate 20 was added to the diet at 25% w/w. Clinical findings associated with consumption of polysorbate 20 for up to 70 days included severe diarrhoea, perianal inflammation, weight loss, hunched posture, resistance to being handled, and death prior to scheduled termination. Feed efficiency was reduced and at necropsy, most of the rats fed polysorbate 20 had distended caeca. Histopathological findings included gastrointestinal irritation, renal tubular degeneration, reticuloendothelial hyperplasia, and incomplete maturation in the testes. Harris et al (1951b) also fed emulsifiers to hamsters, at 5% and at 15% w/w of the diet. These dietary levels of polysorbate 20 caused severe diarrhoea, weight loss, decreased feed efficiency, and death. Microscopic findings included gastrointestinal inflammation, renal tubular degeneration, and incomplete maturation of gonads in both sexes. The extremely high doses of polysorbate 20 used in these studies mean that the studies are not of value for the assessment of safety of polysorbate 20 at the much lower doses at which humans may be exposed through its use as a food additive.

Poling et al (1956) tested a number of polyoxyethylene derivatives in rats and hamsters. Polysorbate 20 was added to the diet of rats at 25% w/w for 21 weeks, and to the diet of hamsters at 5, 10, and 15% w/w for 28-39 weeks. Rats were weanling males of unspecified strain. There were 10 rats in the negative control group, and 10 in the polysorbate 20 group. Hamsters were also weanling males, 10/group. All animals were individually housed under controlled environmental conditions, with *ad libitum* access to food and water, and with determination of food consumption and bodyweight twice weekly. Rats fed polysorbate 20 had lower weight gain over 21 weeks than control rats despite greater food consumption. Treated rats developed severe diarrhoea and perianal inflammation. Polysorbate 20 at ≥5% in the diet of hamsters also resulted in decreased weight gain despite increased food consumption, and resulted in a dose-related increase in unscheduled mortality. Clinical signs observed at all doses of polysorbate 20, and which showed a dose-related increase in severity, included diarrhoea, poor hair coat and poor body condition. At ≥10% polysorbate 20, hamsters had tense bloated abdomens, and at 15%, they had perianal inflammation. Haematuria was observed in all groups but was more frequent in treated hamsters than in controls. Post-mortem findings from the studies were reported separately by Eagle and Poling (1956). Rats fed 25% polysorbate 20 showed increased incidences of renal hypertrophy, calculi in the kidneys and urinary bladder, and increased size of the caecum. Lesions in hamsters that showed a dose relationship with polysorbate 20 were small testes, misshapen kidneys, and enlarged caeca. Microscopic findings in rats included testicular atrophy, renal calcifications, obstructed renal tubules, lymphoid atrophy in spleen and mesenteric lymph nodes, hepatocyte atrophy, inflammation in the stomach and jejunum,

caecal haemosiderosis and calcification in the myocardium, aorta or coronary arteries. Microscopic lesions that showed a dose response relationship to polysorbate 20 in hamsters were hepatic haemosiderosis, hepatic cirrhosis, splenic haemosiderosis, splenic lymphoid atrophy, caecal haemosiderosis, and testicular atrophy. Similar to the studies of Harris et al (1951a,b) the dose levels at which adverse effect occurred greatly exceed those to which humans would be exposed through the diet.

The small number of subchronic studies that postdate the JECFA evaluation are not useful for establishment of a health-based guidance value and are described in subsection 3.2.8.

3.2.4 Chronic and carcinogenicity studies in animals

No recent chronic (≥12 months) studies of polysorbate 20 were submitted or identified in a literature review.

The group ADI for polysorbates established by JECFA in 1973 was originally identified as a conditional ADI in at the seventh meeting in 1963. This conditional ADI was based on two chronic dietary studies of polysorbates in rats, that by Fitzhugh *et al* (1959) and that of Oser and Oser (1956,1957). Briefly, the study by Fitzhugh et al (1959) was a two-year study in which rats (12/sex/group) were fed diets containing 0, 2%, 5%, 10% or 25% polysorbate 60. The NOAEL was 5%. At ≥ 10%, dietary polysorbate 60 caused diarrhoea and caecal enlargement, and there was some indication of fatty change in the liver at 25% polysorbate 60. The study by Oser and Oser (1956a,b; 1957) was a three-generation study of a number of emulsifiers, including polysorbates 60, 65 and 80, in Wistar rats (12 males and 20 females/group). Dose levels in the diet were 0, 5, 10 and 20% for all the polysorbates tested. The NOAEL was 5%. At ≥10%, many rats developed diarrhoea, and at 20% there were adverse effects on postnatal survival, lactation, duration of breeding activity, growth rate and feed efficiency. From these studies, JECFA concluded that the NOAEL for polysorbates in rats was 5% in the diet, equivalent to 2500 mg/kg bw/day. Using unspecified uncertainty factors, JECFA established a group ADI for dietary polysorbates in human beings of 0-25 mg/kg bw.

Chronic dietary toxicity/carcinogenicity study of polysorbate 80 in in F344/N rats and B6C3F1 mice (National Toxicology Program (NTP) 1992a) Regulatory status: GLP

The closely related compound polysorbate 80 (polyoxyethylene sorbitan monooleate; E433) was the test material in these studies. Dose levels in these studies were 0, 2.5 and 5% of the diet, for both species. No evidence of carcinogenicity was found in mice. At the highest dose, 5% polysorbate 80 in the diet, adverse findings in mice were an 11% decrease in bodyweight of females, and lesions of squamous hyperplasia and chronic inflammation in the forestomach was found in both sexes, although forestomach ulcers were found only in females. A NOAEL was not identified by the authors of the study, but FSANZ concludes that the NOAEL in mice was 2.5% polysorbate in the diet, equivalent to 3750 mg/kg bw/day. In rats, benign phaeochromocytoma in males was considered by the authors to be equivocal evidence of carcinogenicity. This is a common lesion in aged rats of this strain, and although the incidence in 5% males (29/50) was moderately higher than that in control males (21/50), the incidence in rats in the 2.5% group (19/50) was lower than that in the control group. Furthermore the incidence of hyperplasia of the adrenal medulla was increased in 2.5% males but not 5% males, when compared to control males. The authors of the study did not identify a NOAEL for polysorbate 80 in rats, but FSANZ concludes from the data that the NOAEL in this study is 5% dietary polysorbate 80, equivalent to 2500 mg/kg bw/day.

24-month dietary study of polysorbate 20 and polysorbate 60 in mice (Ewing and Tauber 1965)

This study was not considered by JECFA, but was cited by the Japanese Food Safety Commission.

The study was conducted in male C57BL/6 Jax mice that were 2 months of age at study start. Mice were group-housed (5/cage) and provided with food and water *ad libitum*. Mice were randomly assigned to five groups. The control group was fed the basal ration, while the treatment groups were fed diets supplemented with 5% polysorbate 20, 10% polysorbate 20, 5% polysorbate 60 or 10% polysorbate 60. Blood samples were collected from tail veins when mice were 4, 6, 9, 12, 16, 20 and 24 months of age. Blood samples were analysed for haemoglobin content, haematocrit, and erythrocyte count, and mean corpuscular volume, mean corpuscular haemoglobin and mean corpuscular haemoglobin concentration were calculated. Although all haematological parameters showed an expected age-related decline, group mean values for haemoglobin, haematocrit, erythrocyte count, MCV, and MCH showed significantly greater declines in mice fed 10% polysorbate 20 than in mice fed ≤5% polysorbate 20. However the mice did not become anaemic. The effects of polysorbate 60 were more pronounced, with statistically significant differences in haematological parameters evident in mice fed ≥5% polysorbate 60.

Treatment with polysorbate did not affect life-span, but mice fed the 10% polysorbate diets produced soft stools during the first months of the study and this effect persisted throughout the study in mice fed 10% polysorbate 60.

Drawbacks of this study are the limited number of parameters measured, and the small numbers of mice bled in the later stages of the study, which is presumably a reflection of age-related mortality. In addition, the reductions in group mean haematological parameters, although statistically significant, were minor in the clinical sense.

3.2.5 Genotoxicity

There have been a number of genotoxicity assays of polysorbates, although only two were of polysorbate 20. A negative result for polysorbate 20 in a gene mutation assay was obtained using mouse lymphoma cells, with and without metabolic activation, but the report was only an abstract with insufficient details (Coppinger et al 1981). A number of reverse bacterial mutation assays (Ames tests) of polysorbate 60 and of polysorbate 80 all produced negative results, both in the absence and the presence of metabolic activation, both polysorbate 60 and polysorbate 80 were negative in chromosome aberration assays using Chinese hamster fibroblasts, and polysorbate 60 was also negative, with and without a metabolic activation system, in an assay of cell transformation in primary golden hamster embryo cells (EFSA 2015).

Cytotoxicity and genotoxicity study of polysorbate 20 in A549 cells and human umbilical vein endothelial cells (Eskandani et al. 2013)

The study was conducted *in vitro* using A549 cells, which are a line of human lung carcinoma cells, and human umbilical vein endothelial cells (HUVEC). To assess the effects of polysorbate 20 on cellular viability, a 3-(4,5-dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide (MTT) assay was performed in triplicate. Cells were cultured to approximately 40-50% confluency prior to being exposed to concentrations of polysorbate 20 ranging from 0 to 10 µL/mL for 24 h. Cells were then incubated in the presence of MTT (2 mg/mL in PBS) and then to DMSO in Sorenson buffer. Absorbance was measured by spectrophotometry. Chromatin fragmentation of both types of cells was measured by 4′,6-diamidino-2-phenylindole (DAPI) staining assay. Cells were incubated with polysorbate 20 or with DMSO as a positive control. Cells were then fixed permabilized with Triton X-100, washed and stained with DAPI. DNA fragmentation in polysorbate 20-treated cells of both cell lines was assessed by extracting DNA and electrophoresing it in 1.2% agarose gel. Single cell-thin

layer gel electrophoresis (alkaline comet assay) was used on polysorbate 20-treated A549 cells. Slides were stained with ethidium bromide and DNA strand cleavage was expressed as the percentage of total DNA fluorescence that migrated in the tail of each nucleus. Finally, early and late apoptosis of polysorbate 20-treated cells of both types was assayed by fluorescein isothiocyanate (FITC)-labelled annexin V flow cytometry.

Both HUVECs and A549 cells showed a dose-and time-dependent reduction in cell growth when incubated in polysorbate 20, with an IC50 of approximately 0.3 and 0.4 µL/mL polysorbate 20, respectively. Treatment with 2 µL/mL polysorbate 20 resulted in greater than 90% cell death. Both types of cell also showed fragmentation of chromatin and DNA in the DAPI staining assay after exposure to polysorbate 20, similar to that observed with the positive control DMSO. DNA from treated cells showed obvious fragmentation and formation of ladders on agarose gel electrophoresis, consistent with induction of apoptosis. The alkaline comet assay of A549 cells showed considerable DNA cleavage in polysorbate 20-treated cells, in contrast to untreated cells. FITC-labelled annexin V flow cytometry showed that almost all polysorbate 20-treated cells were in early or late apoptosis after 24 h exposure.

It was concluded from this study that polysorbate 20 inhibits the growth of cells by inducing apoptosis by fragmentation of chromatin and DNA. The relevance of this study is uncertain because the assays used in this study are not part of the recommended suite of assays for assessment of genotoxic potential. While this study demonstrates cytotoxicity of polysorbate 20, it is not clear that it demonstrates genotoxicity, and therefore neoplastic potential, in viable cells.

3.2.6 Reproductive and developmental toxicity studies in animals

Dietary study of reproductive and developmental effects of polysorbate 20 and 60 in C57BL/6 mice (Paschall 1963).

Although this dissertation was completed in 1963, it was not included in the JECFA (WHO 1974) evaluation.

Mice were housed under controlled environmental conditions, although the description of those conditions does not meet modern standards of reporting. Females were individually housed. Males were group-housed except when used for breeding or when it was necessary to separate them to prevent fighting. The test materials were mixed into standard mouse chow to a concentration of 10%. There was one control group in which both males and females were fed diet containing no polysorbate compound. Groups in which polysorbate 20 was tested were a group in which both sexes were fed 10% polysorbate 20, a group in which only the males were fed polysorbate 20, and a group in which only the females were fed polysorbate 20. A further three groups had the same dietary exposures to polysorbate 60. There were approximately 15 breeding pairs in each group. Pups from the first litter of the control group, the group in which both parents were fed polysorbate 20, and the group in which both parents were fed polysorbate 60 were maintained from weaning on the same feed regimen as their parents, and used for breeding. A third generation was obtained from the same groups by the same approach. A total of four litters were obtained from the first (P) generation and the second (F1) generation, and three litters were bred from the third (F2) generation.

Measured parameters in litters included number of pups born, live/dead ratio, number surviving to postnatal day (PND) 4, total number of pups weaned/litter and sex ratio. At the end of the experiment, a selection of the P animals were weighed and killed, their gonad weights recorded, and sperm motility was measured in males.

The number of pups/litter was significantly depressed in all generations of mice fed polysorbate 20, compared to control mice, although the difference was not large. Average litter sizes for P, F1 and F2 generation mice were 6.4, 6.6 and 6.9 pups, compared to corresponding control values of 7.6, 6.3 and 7.1 pups. Dietary exposure to polysorbate 20 did not have a significant effect on the live/dead ratio of pups at birth, did not have a clear effect on survival of pups to PND 4, and did not affect pup survival to weaning or sex ratio at weaning. However, pups of dams fed polysorbate 20 were consistently lighter than those of controls at weaning (mean of 82% of control weight). This difference was largely attributable to poor weight gain in the third week of postnatal life, and disappeared by the time adult mice were weighed, which was at approximately 10 months of age. No treatment-related effects were found in weights of ovaries or testes of adult P generation mice, or on sperm motility.

There are deficiencies in the design of this study that confound interpretation of the results. The smaller litters and poorer pup weight gain of the treated dams may be due to a lower intake of calories and/or other dietary components, because no adjustment in the diet was made to correct for the addition of 10% polysorbate, with the concomitant reduction in the energy and nutrient content of the diet. There is a lack of information on the bodyweights of the dams during pregnancy and lactation. Another deficiency is that clinical signs in the mice were not recorded. In other studies, feeding of 10% polysorbate 20 in the diet has been reported to cause severe diarrhoea in mice. Smaller litters and poorer milk production would not be unexpected in female mice with chronic diarrhoea. Therefore, the adverse effects of polysorbate 20 on reproductive performance may be due to maternal toxicity, but maternal clinical signs were not recorded.

Developmental study of polysorbate 20 in rats (NTP 1992b)

This report is limited to an abstract, and the preface on the NTP website states that findings were not evaluated in accordance with the levels of evidence criteria established by NTP in March 2009. The preface also states that the findings and conclusions for this study should not be construed to represent the views of NTP or the US Government.

Timed-mated Sprague-Dawley-derived (CD) rats (24-25 per group) were gavaged with 0, 500 or 5000 mg/kg/day polysorbate 20, from gestational day (GD) 6 through to GD 15. Aqueous solutions were administered at a constant dose volume of 5 ml/kg bw. Rats were terminated on GD 20, the uterus was removed and examined to determine the number of resorptions, and of dead or live fetuses. Fetuses were weighed, and live fetuses were examined for external, visceral and skeletal defects.

All treated females survived to scheduled necropsy and 22-24 rats per group were pregnant. Regional alopecia was observed in some treated females in both dose groups. Maternal weight gain during treatment was decreased by 14% at 5000 mg/kg/day relative to the vehicle control group, but no effect was noted at 500 mg/kg/day. There were no treatment-related effects upon gravid uterine weight or on absolute or relative weights of maternal liver, kidneys or heart. Maternal relative food intake was comparable among treatment groups throughout gestation, but maternal water intake was elevated by 14% during treatment at 5000 mg/kg/day relative to the vehicle control group.

No differences between groups were noted for the number of corpora lutea per dam, the number of implantation sites per dam or the percent preimplantation loss per litter. No adverse effects were noted on the growth, viability or morphological development of the conceptuses.

In conclusion, the maternal LOAEL was 5000 mg/kg/day (based upon a 14% decrease in weight gain during treatment) and the maternal NOAEL was 500 mg/kg/day. The developmental NOAEL was greater than 5000 mg/kg/day.

3.2.7 Human tolerance studies

A small number of human studies were reviewed by the Food Safety Commission of Japan (2007). No adverse effects were observed in 13 premature babies and 2 term infants administered 0.12 to 1.0 g polysorbate 20, four times daily, as a pharmacologic additive. For the premature babies, this volume represented 250 to 2000 mg/kg bw/day.

Bolus administration of 4.4 g polysorbate 20 was well tolerated by two children. A study in five adults found no adverse effects from the dietary administration of 2 g polysorbate 20, three times daily, for one week (Food Safety Commission 2007). Although the value of these studies is limited by the small number of participants, they support the conclusion that polysorbate 20 is well tolerated in human beings.

3.2.8 Other studies

Jejunal perfusion study in the rat (Kimura and Yoshida 1982)

The toxic mechanisms of a variety of detergents were investigated in this study, which was conducted in young male Wistar rats, weighing approximately 120 g. Fasted rats were anesthetised and a proximal jejunal segment was perfused with Ringer's bicarbonate solution at a rate of 0.5 mL/min. To establish the normal rate of physiological desquamation of enterocytes, after 30 min equilibration, perfusate was collected for 120 min, in 30 min aliquots, and analysed for protein and for activities of sucrase, maltase and alkaline phosphatase. The liberation of the enzymes is a marker for enterocyte desquamation. To investigate the effects of detergents and dietary fibre on the levels of enzymes in perfusate, jejunal sections were perfused with test articles in Ringer's bicarbonate solution. Polysorbate 20 was used at 2% v/v, with or without the concurrent presence of 0.04% dietary fibre. The dietary fibre was 'Gobo', a common Japanese foodstuff from the root of the edible burdock, *Arctium lappa*. Perfusion with 2% polysorbate 20 resulted in an approximately threefold increase in release of sucrase, maltase and alkaline phosphatase, consistent with accelerated exfoliation in the small intestine. The increase in enzyme activity was prevented by the concurrent presence of dietary fibre.

This study is an exploration of toxic mechanism and includes only one dose level of polysorbate 20, and is therefore not useful for the establishment of a health-based guidance value.

Seven-day dietary study of polysorbate 20 in rats (Nakata and Kimura 1994)

Young male Wistar rats, weighing approximately 100 g, were the subjects of this experiment. Rats were individually housed under standard laboratory environmental conditions, and acclimated to a basal diet that contains 70% sucrose for seven days prior to the start of the experiment. Test diets were formulated by partially replacing the sucrose fraction of the basal diet, so that protein, lipid, vitamins and minerals were the same in all diets. Test materials were polysorbate 20 and gobo (*Arctium lappa*) dietary fibre (GDF).

Rats were assigned to four groups of five rats/group, and fed for seven days with either the basal diet, a diet containing 10% polysorbate 20, a diet containing 10% GDF, or a diet containing both 10% polysorbate 20 and 10% GDF. Faeces were collected on the last four days of the in-life phase. On Day 8, rats were decapitated, a section of jejunum was excised, washed and homogenized for determination of sucrase activity.

The group consuming the 10% polysorbate diet exhibited a significantly lower group mean bodyweight gain than that of other groups, 63% that of the control group. The group mean bodyweight gain of the other two treatment groups was comparable to that of the control

group. The group mean food intake of the 10% polysorbate group was 85% that of the control group, but the food intakes of the other two treatment groups were higher than that of the control group. Dry weight of collected faeces was increased fivefold, relative to that of the control group, in the group fed 10% GDF, and increased tenfold, relative to that of the control group, in the group fed 10% polysorbate 20 and 10% GDF. The group fed 10% polysorbate 20, however, developed severe diarrhoea, so dry weight of faeces was not determined. Pooled faeces of rats fed polysorbate 20, with or without GDF, contained four- to fivefold the amount of concanavalin A-binding glycoprotein (CBGP) as faeces of control rats. On SDS-polyacrylamide gel electrophoresis (SDS-PAGE), CBGP from rats fed GDF, with or without polysorbate 20, showed a similar profile to that of control rats whereas the SDS-PAGE profile of CBGP from rats fed polysorbate 20 without GDF showed only the higher molecular weight bands of CBGP. There was no significant difference in group mean intestinal sucrase between rats in the control group, rats in the 10% GDF group and rats in the 10% polysorbate 20 + 10% GDF group, but group mean intestinal sucrase of the 10% polysorbate 20 group was 69% that of the control group, a significant difference. The authors attributed differences in quantity of CBGP and its SDS-PAGE profile to increased renewal of the small intestinal epithelium by dietary fibre, but solubilisation of the small intestinal epithelium by polysorbate 20. The concluded that GDF ameliorated the effects of polysorbate 20 by prompting more rapid renewal of the epithelium which overcame the destructive effects of polysorbate 20.

This study is a mechanistic study in which only one dose of polysorbate 20 was used, and is therefore not useful for the identification of a health-based guidance value.

28-day oral gavage study of polysorbates in hyperlipidaemic mice (Li et al 2011)

This study involved the use of a number of polysorbates and only the aspects of the study related to polysorbate 20 are summarized here. The subjects were C57BL/6J mice. Mice were housed under standard laboratory husbandry conditions and hyperlipidaemia was induced by feeding of a high-fat diet for 28 days. Hyperlipidaemia was considered to be present if serum lipids were increased approximately threefold over those of mice in the negative control group that were fed a standard diet. For the purpose of investigating the effects of polysorbate 20, the groups comprised 6 mice/sex/group. Groups were a negative control group, a hyperlipidaemic group gavaged daily with normal saline at 0.2 mL/10 g bw, a hyperlipidaemic group gavaged daily with lovastatin at 30 mg/kg bw, a hyperlipidaemic group gavaged daily with cholestyramine at 2000 mg/kg bw, and a group gavaged daily with polysorbate 20 at 1600 mg/kg bw. The vehicle was normal saline at 0.2 mL/10 g bw. Treatment was continued for 28 days. Bodyweight was measured weekly through the in-phase phase. At the end of the in-life phase, mice were fasted for 16 hours, blood was collected under anaesthesia and mice were killed. Heart, liver and stomach were collected, fixed, and processed for light microscopy.

Treatment with polysorbate 20 was associated with a group mean decline in total cholesterol of 18.76%, relative to group mean cholesterol of hyperlipidaemic mice gavaged with only saline. However, since only one dose of polysorbate 20 was used in this study, the study is not useful for the identification of a health-based guidance value.

3.2.9 Regulatory status in other countries

EFSA

EFSA issued a Scientific Opinion on polysorbates 20, 80, 40, 60 and 65 in 2015. It considered all these polysorbates together because of their close similarities in structure and metabolic fate. EFSA identified the pivotal study to be a chronic dietary study of the toxicity and carcinogenicity of polysorbate 80 conducted in F344 rats by the NTP (NTP 1992a). From

this study a NOAEL of 5% in the diet, equivalent to 2500 mg/kg bw/day, was identified. EFSA applied an uncertainty factor of 100 to derive a group ADI of 25 mg/kg bw/day for polysorbates 20, 80, 40, 60 and 65 (EFSA 2015).

United States of America

The USA permits the use of polysorbate 20 in foods under the Code of Federal Regulations Title 21 §172.515 Synthetic flavoring substances and adjuvants, and §178.3400 Emulsifiers and/or surface-active agents.

Japan

Polysorbate 20 is approved as a designated food additive by the Ministry of Health, Labour and Welfare. The most recent evaluation of the safety of polysorbates by the Food Safety Commission was published in June 2007. This evaluation established a group ADI for polysorbates of 10 mg/kg bw/day, based on diarrhoea observed at 1000 mg/kg bw/day in a 13-week study of polysorbate 60 in rats and the application of an uncertainty factor of 100.

Singapore

Use of polysorbate 20 at GMP levels is approved under the Sixth Schedule, Permitted Emulsifiers and Permitted Stabilisers, in Regulation 21(2) of the Food Regulations.

3.3 Discussion

The ester bond in polysorbate 20 is hydrolysed by pancreatic lipase in the intestine. There is negligible cleavage of the bond between the polyoxyethylene moiety and the sorbitan moiety, and polyoxyethylene sorbitan is primarily excreted in the faeces.

The available evidence shows that polysorbate 20 is not genotoxic, although it may be cytotoxic in vitro. Results of repeat-dose subchronic studies showed that at the very high dose of 25% w/w in the diet, polysorbate 20 causes diarrhoea and associated weight loss and ill-health in laboratory rodents.

Because polysorbates 20, 40, 60, 65 and 80 are chemically very similar, are metabolised by the same pathways and have similar adverse effects in laboratory animals, a group ADI is appropriate for this group of emulsifiers. The group ADI set by JECFA in 1973 was based on chronic dietary studies of polysorbates 60, 65 and 80 in rats, in which the NOAEL of 5% in the diet, equivalent to 2500 mg/kg bw/day. From this NOAEL, JECFA derived a group ADI for dietary polysorbates in human beings of 0-25 mg/kg bw/day. FSANZ has found no evidence to suggest that the NOAEL for polysorbate 20 would be expected to be lower than those of the other polysorbates. The group ADI established by JECFA remains appropriate although in the opinion of FSANZ, the pivotal study is currently the chronic dietary toxicity/carcinogenicity study of polysorbate 80 conducted in F344 rats by the NTP (1992a).

Data on developmental and reproductive toxicity of the polysorbates are limited, but there is no evidence that the polysorbates are reproductive toxicants, or cause adverse effects on development at doses below those that cause maternal toxicity.

Data on human tolerance of polysorbates are also limited. FSANZ notes that polysorbates 60, 65 and 80 are already permitted in the Code at GMP. Polysorbates are widely used as emulsifiers in foods and pharmaceuticals internationally, and have not been associated with adverse effects in consumers.

In conclusion, the group ADI for polysorbates, including polysorbate 20, is 0-25 mg/kg bw/day.

4 Dietary exposure assessment

4.1 Background

The applicant seeks permission to use polysorbate 20 (INS 432) for use as an emulsifier in surface spray or dipping solutions used to treat cooked processed meats/small goods and processed fish and fish products. There are existing permissions in the Code for three other polysorbates (polysorbate 80 (INS 433), polysorbate 60 (INS 435) and polysorbate 65 (INS 436)), all of which have GMP permissions in a range of food categories.

Polysorbates have a group ADI. This means that the estimated dietary exposure to all permitted polysorbates needs to be considered for A1137 in order to be able to make a determination regarding any risks to public health and safety. Therefore, before a dietary exposure assessment could be undertaken for the proposed additional use of polysorbate 20, a baseline level of polysorbates exposure using current existing permissions was required. The scenarios therefore conducted for the assessment were a baseline based on current permissions and an extension of use including baseline permissions and those proposed for polysorbates 20.

Dietary exposure assessments require data on the concentrations of the chemical of interest in the foods requested, and consumption data for the foods that have been collected through a national nutrition survey. The dietary exposure assessment was undertaken using FSANZ's dietary modelling computer program, Harvest[1]. As food additive permissions in the Code apply to both Australia and New Zealand, dietary exposure assessments were undertaken for both countries.

A summary of the general FSANZ approach to conducting the dietary intake assessment for this Application is at Appendix 1. A detailed discussion of the FSANZ methodology and approach to conducting dietary intake assessments is set out in *Principles and Practices of Dietary Exposure Assessment for Food Regulatory Purposes* (FSANZ 2009).

4.2 Food consumption data used

As dietary exposure assessments needed to be undertaken for both Australia and New Zealand, dietary survey data for both countries were required.

The food consumption data used for the dietary exposure assessments were:

- **2002 New Zealand National Children's Nutrition Survey** (2002 NZ NCNS): one day of consumption data for 3,275 New Zealand children aged 5–14 years (Ministry of Health 2003; Ministry of Health 2005).
- **2008–09 New Zealand Adult Nutrition Survey** (2008 NZ ANS)**:** one day of consumption data for 4,721 New Zealanders aged 15 years and above (Ministry of Health 2011a; Ministry of Health 2011b).
- **2011–12 Australian National Nutrition and Physical Activity Survey** (2011-12 NNPAS): two days of consumption data for 7,735 Australians aged 2 years and above (ABS 2014).

[1] Harvest is FSANZ's custom-built dietary modelling program that replaced the previous program, DIAMOND, which does the same calculations just using a different software program.

The design of these nutrition surveys vary and the key attributes of each, including survey limitations, are set out in Appendix 1.

One day of food consumption data from both of the NZ surveys were used for the dietary exposure assessment whereas the average of two days of data from the 2011-12 NNPAS was used for Australia. The two day average exposures better reflect longer term estimates of dietary exposure and therefore are a better estimate of chronic dietary exposure.

The hazard identification and characterisation did not identify any population sub-groups for which there were specific safety considerations in relation to exposure to polysorbates. In addition, the food categories requested in the application for addition of polysorbate 20 are consumed by all sectors of the Australian and New Zealand populations. Therefore, the dietary exposure assessments were conducted for the general Australian and New Zealand populations based on the dietary survey data available. A dietary exposure assessment was conducted for children because children generally have higher exposures due to their smaller body weight, and they consume more food per kilogram of body weight compared to adults. The population groups listed in Table 3 were used for the dietary exposure assessment.

Table 3: Population groups used in the dietary exposure assessment

Country	Survey	Age group	No. respondents (Day 1 only)	No. respondents (Day 1 & 2)
Australia	2011-12 NNPAS	5 – 14 years	n/a	1014
		15 years and above	n/a	6421
		2 years and above	n/a	7735
New Zealand	2002 NZ NCNS	5 – 14 years	3,275	n/a
	2008 NZ ANS	15 years and above	4,721	n/a

4.3 Initial estimate of baseline dietary exposure to polysorbates

FSANZ usually undertakes dietary exposure assessments for food additives using a tiered approach. The first assessment using worst case assumptions and the least required resources, with refinements made following this assessment if needed. Therefore an initial dietary exposure assessment for polysorbates was conducted which was based on MPLs from the Code.

Due to the Code permissions for currently permitted polysorbates being at GMP, an actual concentration needed to be determined for use in the dietary exposure assessment. Numerical concentrations readily available to conduct the first estimate of baseline dietary exposure estimates were from Codex General Standard for Food Additives (GSFA) and European Union (EU) maximum permitted levels (MPLs). Therefore, these concentrations were used for the relevant food categories where permissions exist in Australia and New Zealand along with the most recent Australian and New Zealand consumption data to determine baseline polysorbates dietary exposure. The concentrations used for this initial assessment are shown in Table 4.

Estimated dietary exposures were compared to the group ADI of 0-25 mg/kg bw/day. Based on Codex GSFA and EU MPLs for polysorbates, estimated mean dietary exposures to polysorbates across all Australian and New Zealand population groups assessed ranged between 65-150% ADI and 90th percentile exposures ranged between 120-290% ADI. The highest 90th percentile exposure of 290% ADI was for New Zealand children 5-14 years,

based on day 1 of food consumption data (the Australian 2 day average for same age group was 250% ADI). The exposure estimates derived from this scenario are conservative since it assumes that all foods in every category contain polysorbates at the MPL and the consumer will be continuously (over a lifetime) exposed to polysorbates at these levels.

4.4 Refined estimate of baseline dietary exposure to polysorbates

In order to determine a more realistic estimate of dietary exposure, more specific concentration data were required. Therefore, a request was made to the food industry in Australia and New Zealand for use levels of polysorbates, collection of which data was facilitated by the Australian Food & Grocery Council and New Zealand Food & Grocery Council.

The refined baseline polysorbates exposure was estimated using: (1) the most recent nutrition survey data which includes consumption amounts for foods with permissions for polysorbate use; (2) current reported use levels by industry in the GMP permitted food categories in Schedule 15 of the Code and/or Codex GFSA MPL concentrations where no industry data was provided; and (3) industry brand market share data.

The dietary exposure assessment for the extension of use was estimated from the refined baseline exposure based on existing permissions and that from meat and fish products containing polysorbate 20 at the amount requested by the applicant.

4.4.1 Food categories and concentrations of polysorbates used for the refined baseline and extension of use scenarios

The applicant requested permission for the use of polysorbate 20 as an emulsifier at levels of less than 0.05% (500 mg/kg) in the final food product for cooked processed meats/small goods and processed fish and fish products. This value was used for the extension of use scenario.

For the refined baseline scenario, the food industry in Australia and New Zealand were requested to provide current use levels of polysorbates in the GMP permitted food categories listed in Schedule 15 of the Code along with product market share data. A decision tree (Figure A1.1 in Appendix 1) was used to determine the final polysorbates concentration to use in the refined baseline dietary exposure assessment as it was anticipated that industry data for 100% of foods in 100% of categories would not be possible to obtain. A conservative approach was taken for food categories where there was limited industry data which follows FSANZ's normal tiered approach to conducting dietary exposure assessments.

In general, weighted concentrations for each food group were calculated based on the industry use level and industry market share, with the MPL (from Codex or EU) used for the remaining market share. Where market share data weren't/were not able to be provided by industry, Euromonitor (Euromonitor International 2018) was used to obtain market share data where available.

The food category codes used by the applicant to provide their use data were based on the Australia New Zealand Food Classification System (ANZFCS) in Schedule 15 of the Code. However, the food classification codes in Harvest can vary slightly and may also be split into sub-groups (Figure A2.1 in Appendix 2) in order to allow specific permissions to be applied directly to very specific categories of foods. To assess the populations' dietary exposure of polysorbates, the food categories proposed by the applicant and the food categories which have existing GMP permissions were assigned to the relevant Harvest food classification codes.

The food categories and concentrations used in the refined baseline and extension of use dietary exposure assessments are detailed in Table 4.

Table 4: Polysorbate concentrations used for the dietary exposure assessments

Harvest Food Category Code	Harvest Food Category Name	Initial baseline∞	Weighted concentration used in dietary exposure assessment (mg/kg)		% of industry (I) data vs Codex/EU MPL used
			Refined baseline*	Refined baseline + Polysorbate 20	
0	Preparations of food additives	n/a	0	0	
1.1.1	Liquid milk (including buttermilk) - UHT goat milk only	n/a	0	0	No Industry data or MPL
1.1.2	Liquid milk products & flavoured liquid milk	3000	1170	1170	I: 61% , MPL: 39%
1.2.2	Fermented milk products and rennetted milk products	1000	653	653	I: 35% , MPL: 65%
1.3	Condensed milk & evaporated milk	n/a	0	0	I: 100%
1.4.1.1.3	Cream, unflavoured, red fat (canned)	1000 (UHT cream only)	218	218	I: 78% , MPL: 22%
1.4.2	Cream products (flavoured, whipped, thickened, sour cream etc)	1000	210	210	I: 81% , MPL: 19%
1.4.2.2.2.1	Cream products, whipped/thickened, whole fat, aerosol	1000 (UHT cream only)	218	218	I: 78% , MPL: 22%
1.4.2.2.2.2	Cream, regular thickened, 35% fat, UHT treated	1000 (UHT cream only)	218	218	I: 78% , MPL: 22%
1.5	Dried milk, milk powder, cream powder	4000	1632	1632	I: 59% , MPL: 41%
1.6	Cheese & cheese products	0	0	0	
1.6.1	Unripened cheeses	80	16.5	16.5	I: 81% , MPL: 19%
2.1	Edible oils essentially free of water	0	0	0	Only permitted in oils and spreads used for baked goods, so zero allocated as polysorbate use is picked up in baked goods
2.2.1.2	Butter products	0	0	0	
2.2.1.3	Margarine and similar products	0	0	0	
2.2.2	Oil emulsions (<80% oil)	0	0	0	
3	Ice cream and edible ices	1000	558	558	I: 58% , MPL: 42%
4.1.3	Fruits and vegetables that are peeled, cut, or both peeled and cut	n/a	0	0	I: 100%

Table 4: Polysorbate concentrations used for the dietary exposure assessments

Harvest Food Category Code	Harvest Food Category Name	Weighted concentration used in dietary exposure assessment (mg/kg)			% of industry (I) data vs Codex/EU MPL used
		Initial baseline∞	Refined baseline*	Refined baseline + Polysorbate 20	
4.3	Processed fruits and vegetables	n/a	0	0	I: 100%
4.3.1.4	Dried herbs & spices	2000	1280	1280	I: 36% , MPL: 64%
4.3.5	Candied fruits & vegetables	3000	3000	3000	MPL: 100%
4.3.6	Fruit & vegetable preparations including pulp	3000	3000	3000	MPL: 100%
5.1	Chocolate & cocoa products	5000	3895	3895	I: 22% , MPL: 78%
5.1.6	Cocoa based spreads, including fillings	1000	1000	1000	MPL: 100%
5.2	Sugar confectionery (excluding bubble gum & chewing gum)	1000	653	653	I: 35% , MPL: 65%
5.2.1	Bubble gum & chewing gum	5000	755	755	I: 85% , MPL: 15%
5.4	Icings and frostings	3000	3000	3000	MPL: 100%
6.3	Processed cereal and meal products	n/a	0	0	I: 100%
6.4	Flour products (including noodles & pasta)	5000	0	0	Concentrations applied at sub-group level
6.4.1.1	Flour products, noodle, instant	5000	0	0	There was no reported use of polysorbates in pasta or noodles by industry. This was also supported by an extensive ingredient label search.
6.4.1.2	Flour products, noodle, {not instant}	5000	0	0	
6.4.2	Flour products, pasta only	5000	0	0	
7	Breads & bakery products	0	0	0	Concentrations applied at sub-group level
7.1	Bread and related products	3000	0	0	Technical advice received from two separate bread manufacturers indicated polysorbates are not typically used in plain breads and the main use of polysorbates for baking would be as a stabiliser in oil in water emulsions in manufactured fats and whipping gels for batters. This was also supported by an extensive ingredient label search.
7.2	Biscuits, crackers, cakes, pastries & scones	3000	3000	3000	MPL: 100%

Table 4: Polysorbate concentrations used for the dietary exposure assessments

Harvest Food Category Code	Harvest Food Category Name	Weighted concentration used in dietary exposure assessment (mg/kg)			% of industry (I) data vs Codex/EU MPL used
		Initial baseline∞	Refined baseline*	Refined baseline + Polysorbate 20	
7.2.1.1	Biscuits & crackers, sweet	3000	1614	1614	I: 46% , MPL: 54%
7.2.1.2	Biscuits & crackers, savoury	3000	1840	1840	I: 63% , MPL: 37%
7.2.2.1	Cakes	3000	2846	2846	I: 15% , MPL: 85%
8.2	Processed meat/ poultry/ game products in whole/ cut pieces (e.g. ham, bacon, smoked chicken)	5000	3635	4135	I: 27% , MPL: 73%
8.3	Processed comminuted meat, poultry & game products	5000	3670	4170	I: 26.5% , MPL: 73.5%
8.3.2	Sausage & sausage meat	5000	5000	5500	MPL: 100%
8.4	Edible casings	1500	1500	1500	MPL: 100%
8.5	Animal protein products	n/a	0	0	No Industry data or MPL
9.2	Processed fish & fish products	n/a	0	0	No Industry data or MPL
9.3	Semi-preserved fish & fish products	n/a	0	0	No Industry data or MPL
9.4	Fully preserved fish including canned fish products	n/a	0	0	I: 100%
10.2	Liquid egg products	n/a	0	0	No Industry data or MPL
10.3	Frozen egg products	n/a	0	0	No Industry data or MPL
10.4	Dried or heat coagulated egg products	n/a	0	0	No Industry data or MPL
11.1.1	Rainbow sugar	n/a	0	0	No Industry data or MPL
11.3.1	Dried honey	n/a	0	0	No Industry data or MPL
11.4	Tabletop sweeteners	n/a	0	0	No Industry data or MPL
12.1.2	Reduced sodium salt mixture	n/a	0	0	No Industry data or MPL
12.1.3	Salt substitute	n/a	0	0	No Industry data or MPL
12.5	Yeast & yeast products	n/a	0	0	I: 100%
12.6	Vegetable protein products	n/a	0	0	No Industry data or MPL

Table 4: Polysorbate concentrations used for the dietary exposure assessments

Harvest Food Category Code	Harvest Food Category Name	Weighted concentration used in dietary exposure assessment (mg/kg)			% of industry (I) data vs Codex/EU MPL used
		Initial baseline∞	Refined baseline*	Refined baseline + Polysorbate 20	
13.3	Formulated meal replacements and formulated supplementary foods	n/a	0	0	I: 100%
13.3.2.9	Very low energy drinks and liquid meal replacements	1000	971	971	I: 3% , MPL: 97%
13.4	Formulated supplementary sports foods	n/a	0	0	No Industry data or MPL
13.5	Food for special medical purposes	1000	1000	1000	MPL: 100%
13.5.2.2	Toddler formula products	n/a	0	0	I: 100%
14.1.1.2	Carbonated, mineralised and soda waters	n/a	0	0	I: 100%
14.1.2.1	Fruit and vegetable juices	n/a	0.25	0.25	I: 100%
14.1.2.2	Fruit and vegetable juice products	n/a	20	20	I: 100%
14.1.3	Water-based flavoured drinks	500	57	57	I: 52%, MPL: 48%
14.1.4	Formulated beverages	500	159	159	I: 68%, MPL: 32%
14.1.5	Coffee (or substitute), tea, herbal infusion & similar (excluding caffeinated instant tea)	n/a	0	0	I: 100%
14.2.5	Wine based drinks and reduced alcohol wines	120	120	120	MPL: 100%
14.2.4.1	Fruit wine products and vegetable wine products	120	120	120	MPL: 100%
14.2.5	Spirits and liqueurs	120	120	120	MPL: 100%
14.3	Alcoholic beverages not included in item 14.2	120	120	120	MPL: 100%
20	Foods not included in items 0 to 14		0	0	Concentrations applied at sub-group level
20.1.1.4	Beverages, non-alcoholic, chocolate, dry mix	n/a	0	0	I: 100%
20.1.1.6	Beverages, non-alcoholic, no chocolate/coffee, dry mix	n/a	0	0	I: 100%
20.2.1.1.1.2	Desserts, dairy, custard, chocolate flavoured	3000	2704	2704	I: 10%, MPL: 90%
20.2.1.1.3.2	Desserts, dairy, custard, non-chocolate	3000	2704	2704	I: 10%, MPL: 90%

Table 4: Polysorbate concentrations used for the dietary exposure assessments

Harvest Food Category Code	Harvest Food Category Name	Weighted concentration used in dietary exposure assessment (mg/kg)			% of industry (I) data vs Codex/EU MPL used
		Initial baseline∞	Refined baseline*	Refined baseline + Polysorbate 20	
	flavoured				
20.2.1.2.3.2.1	Dessert, no-dairy, no choc/coffee; pavlova/meringue	3000	377	377	I: 100% (Concentration provided by industry but no market share data available)
20.2.2.1	Grains & cereals with fruit & nut	n/a	0	0	I: 100%
20.2.2.3	Cereal products, bars	n/a	0	0	I: 100%
20.2.3.1.2.1	Bakery products, sweet, no choc; bread, yeast - hot X bun	3000	524	524	I: 100% (Concentration provided by industry but no market share data available)
20.2.4.2.2	Snack foods, not dairy or fat based, not confectionary	n/a	8	8	I: 100%
20.2.5.2	Prepared dishes, vegetable based	n/a	280	280	I: 100%
20.2.5.3.6.1	Prepared dishes, pies & pastries, Asian style	3000	2768	2768	I: 8%, MPL: 92%
20.2.5.3.6.2	Prepared dishes, pies & pastries, non-Asian style	3000	2214	2214	I: 26%, MPL: 74%
20.2.6.2	Gravy, sauces and condiments	5000	2820	2820	I: 44%, MPL: 56%
20.2.6.2.5	Sauce, horseradish, commercial	5000	3138	3138	I: 49%, MPL: 51%
20.2.7.1	Mayonnaise	3000	2866	2866	I: 44%, MPL: 56%
20.2.7.2	Salad dressings	3000	3032	3032	I: 55%, MPL: 45%
20.2.8.1	Soups, liquid	1000	655	655	I: 34%, MPL: 66%
20.2.8.2	Soups, dry mix	1000	247	247	I: 56%, MPL: 24%

∞Concentrations based on using 100% Codex GFSA and/or EU maximum permitted levels.
* Based on use levels provided by the food industry.
n/a – no Codex GFSA and/or EU maximum permitted levels available for Harvest food category.

4.4.2 Assumptions and limitations of the refined dietary exposure assessment

The aim of the dietary exposure assessment was to make the most realistic estimation of polysorbates exposure possible. However, where significant uncertainties or gaps in the data existed, conservative assumptions were generally used to ensure that the estimated dietary exposure was not an underestimate of exposure.

Assumptions made in this refined dietary exposure assessment included:

- Maximum concentration levels of polysorbates used by industry in each permitted food category were applied to the dietary exposures assessment for the refined baseline, in keeping with FSANZs normal tiered approach to dietary exposure assessments.

- Polysorbates indirectly added as a result of carryover from flavourings, colourings etc. and where quantities of levels within ingredients were not known, were not included in the dietary exposures assessment.

- If there were no available industry data from Australia or New Zealand for polysorbates use in a permitted food category, an MPL (Codex, EU or other) was used if available, otherwise a zero was assumed.

- If industry data from Australia and/or New Zealand was available for polysorbate use (or non-use) in a permitted food category and market share data was available (either from industry or other sources such as Euromonitor), a weighted concentration was derived. If less than 100% of the market was represented by the industry provided data, the remaining proportion was assigned the Codex or EU MPL if available and a weighted concentration derived. The MPLs were used for the portion of the category for which no industry data was available as it could not be assumed that concentration data from one company is representative of all foods in the category.

- If there was no available market share for the food category, then the highest of all concentration values provided was used.

- If there were data for both Australia and New Zealand, generally the higher of the two was used for the dietary exposure assessments for both countries on the assumption that food manufactured in either country could be imported, sold and consumed in the other. If data for only one country was available, then this value was assigned for both countries. The final concentrations that were assigned to each of the permitted food categories were then used in the dietary exposure assessment.

- Zero concentrations were applied to Category 7.1 Breads & related products and 6.4 Flour products (including pasta & noodles) in the dietary exposures assessment[2].

In addition to the specific assumptions made in relation to this dietary intake assessment, there were a number of limitations:

- Due to uncertainties or gaps arising from the limited amount of industry data on polysorbate use or non-use and product market share, the remaining proportion of

[2] Technical advice from two separate bread manufacturers indicated polysorbates are not typically used in plain breads and the main use of polysorbates for baking would be as a stabiliser in oil in water emulsions in manufactured fats and whipping gels for batters. This was also supported by ingredient label searches which found no polysorbate use. Pasta and noodles were also found to have no polysorbate use from extensive ingredient label searches.

market share was assigned the Codex or EU MPL, thus the concentrations used were conservative and may have led to an overestimation of the real exposures to polysorbates.

- For some food categories there were no industry use data or an MPL available, therefore a zero concentration was assigned. These categories included foods such as animal protein products, liquid egg products, rainbow sugar, dried honey, tabletop sweeteners and salt substitutes. For many of these there were no consumers in the national nutrition surveys therefore this is unlikely to lead to an underestimate of dietary exposure.

- When less than 100% of the market was represented by industry provided data and the remaining proportion was assigned the Codex or EU MPL to derive a weighted concentration, it has likely skewed the real percentage of food contributors to polysorbates dietary exposures.

4.5 Dietary exposure assessment results

The estimated dietary exposures to polysorbates were calculated for 'consumers' of polysorbates only and were reported in three ways:

- estimated mean and 90th percentile dietary exposures in milligrams of polysorbates per day, derived from each individual's ranked daily exposures
- estimated dietary exposures derived on a per kilogram body weight basis using each individual's body weight
- estimated exposures to polysorbates as a percentage of the ADI.

The major food contributors to the estimated dietary exposures to polysorbates were also calculated for each population group assessed. Major food contributors were calculated from consumers' total exposures from foods consumed that contained the additive in the dietary exposure assessment.

4.5.1 Estimated polysorbate exposure from foods with added polysorbates

4.5.1.1 Estimated refined baseline dietary exposures to polysorbates

The estimated refined baseline mean and 90th percentile exposure to polysorbates for consumers ranged from 341–400 mg/day and 695–931 mg/day respectively across the population groups assessed. When expressed on a kilogram body weight basis, the estimated mean and 90th percentile exposures ranged from 4.8–10.4 mg/kg body weight/day and 10.7–23.7 mg/kg body weight/day, respectively (Refer to Table A3.1 Appendix 3 for detailed results).

The estimated refined baseline mean and 90th percentile daily exposures to polysorbates on a per kilogram body weight basis are summarised in Figure 4.1.

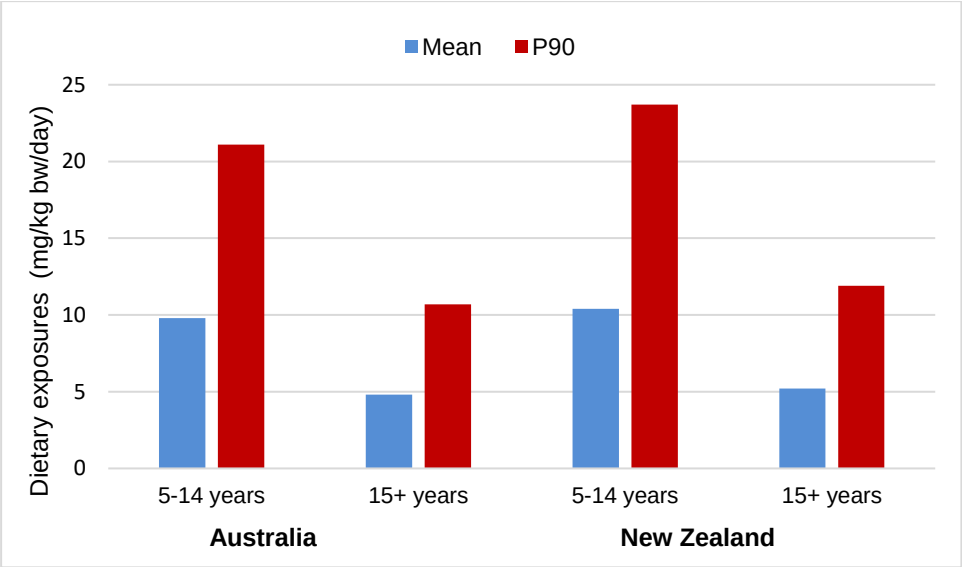


Figure 4.1: Estimated refined baseline mean and 90th percentile (P90) daily dietary exposures (mg/kg bw/day) to polysorbates for all population groups assessed

4.5.1.2 Estimated dietary exposures to polysorbates for the extension of use scenario (Refined baseline + Polysorbate 20)

The estimated total mean and 90th percentile dietary exposures to polysorbates for consumers based on polysorbates exposure derived from existing permissions and that from meat and fish products containing polysorbate 20 at the amount requested by the applicant, ranged from 354–416 mg/day and 730–973 mg/day respectively across the population groups assessed. When expressed on a kilogram body weight basis, the estimated mean and 90th percentile exposures ranged from 5.0–10.8 mg/kg body weight/day and 11.2–24.7 mg/kg body weight/day, respectively. (For detailed results refer to Table A3.1 Appendix 3).

The estimated total mean and 90th percentile daily exposures to polysorbates on a per kilogram body weight basis are summarised in Figure 4.2.

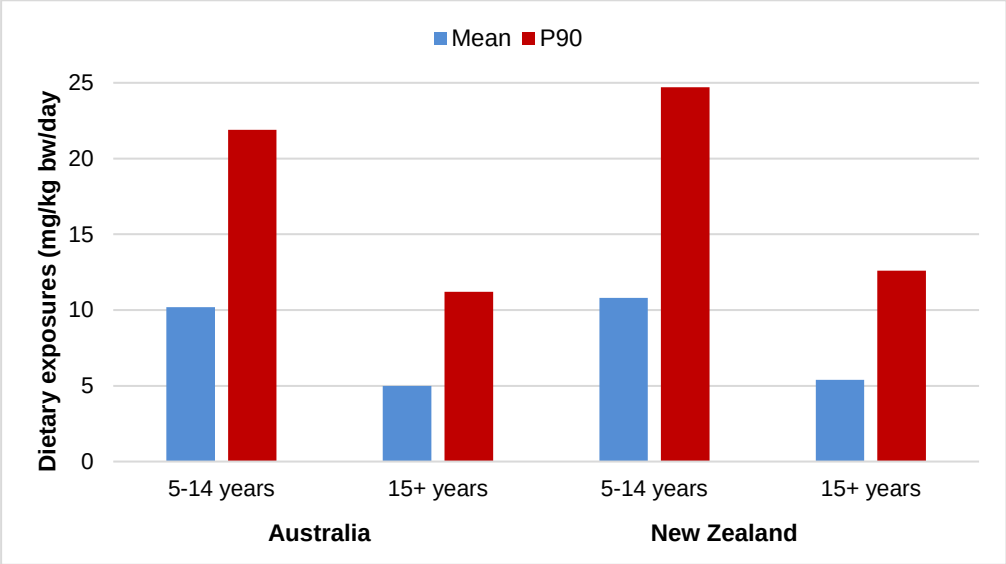


Figure 4.2: Estimated total mean and 90th percentile (P90) daily dietary exposures (mg/kg bw/day) to polysorbates for all population groups assessed

4.5.2 Foods with added polysorbates that contributed to exposure

The foods that were major contributors to estimated total polysorbates dietary exposure (providing ≥5%) were calculated from consumers' mean intake from all foods consumed that were proposed to contain the additive. These results should be interpreted with caution given the weighted nature of the concentration data used for the assessment that included a varying proportion of industry use levels and MPLs across the foods included. This may skew the foods contributing to the dietary exposure and may not truly reflect the contributors in reality.

For all populations and age groups assessed, category 'Gravy, sauces & condiments' was the largest contributor to polysorbates with exposure ranging from 17–25%. The other major contributors to polysorbates exposures in all population groups assessed were 'Prepared dishes, pies & pastries, savoury' (6–17%), 'Sausage & sausage meat containing raw, unprocessed meat' (13–16%) and 'Processed meat/poultry/game products' (9–14%). Of these additional major contributors, 100% of the Codex MPL was used for the sausage category, resulting in a greater contribution to polysorbate dietary exposure than is likely in reality. Several food categories were major contributors to exposure to polysorbates in only some of the population groups assessed.

These major contributors are shown in Table 5 for all population groups assessed. The detailed results are set out in Table A3.2 Appendix 3.

Table 5: Major food contributors (≥5%) to estimated total polysorbates exposures

Category code	Food Category name	Percentage contribution (%)#♦			
		Australia		New Zealand	
		5-14 years$^{\Psi}$	15+ years*	5-14 years$^{\Psi}$	15+ years*
20.2.6.2	Gravy, sauces & condiments	18	25	17	18
20.2.5.3.6.2	Prepared dishes, pies & pastries, savoury	6	6	17	12
8.3.2	Sausage & sausage meat containing raw, unprocessed meat	16	14	13	16
8.2	Processed meat/poultry/game products whole/cut pieces	13	14	9	13
8.3	Processed comminuted meat, poultry & game products	5	<5	9	6
7.2.1.2	Biscuits & crackers, savoury	5	<5	<5	<5
	All other food categories	37	36	32	33
Total		**100**	**100**	**100**	**100**

♦ Zero concentration applied to Category 7.1 Breads & related products & 6.4 Flour products (including pasta & noodles) in DEA
$^{\infty}$ Derived using the Australian 2011-12 NNPAS (2 day average exposure)
$^{\Psi}$ Derived using the NZ NCNS 2002 (Day 1)
* Derived using the NZ ANS 2008 (Day 1)
# A major contributors is one which contributes ≥5% to dietary exposures
All % contributions are expressed as a percentage of the grand total contribution

4.6 Dietary Exposure assessment conclusion

FSANZ determined a refined estimate of baseline polysorbates dietary exposure based on the most recent Australian and New Zealand consumption data and information on reported use levels by industry and/or Codex or EU MPLs. As industry data was not available for all products manufactured nor complete information regarding if polysorbates are used or not, several assumptions needed to be made to determine a concentration of polysorbates to be used in the assessment. The data gaps and assumptions made are likely to mean that the refined estimate is still an overestimation of the actual exposure to polysorbates in reality.

The estimated refined baseline mean and 90th percentile exposure to polysorbates expressed on a kilogram body weight basis ranged from 4.8–10.4 mg/kg body weight/day and 10.7–23.7 mg/kg body weight/day, respectively. When meat and fish products containing polysorbate 20 at the amount requested by the applicant were included, the estimated total mean and 90th percentile dietary exposures to polysorbates ranged from 5.0–10.8 mg/kg body weight/day and 11.2–24.7 mg/kg body weight/day, respectively. The requested permissions for polysorbate 20 result in only a small increase in dietary exposure.

The highest contributing food category to the total exposure estimates for all population groups was 'Gravy, sauces & condiments'. 'Prepared dishes, pies & pastries, savoury', 'Sausage & sausage meat containing raw, unprocessed meat' and 'Processed meat/poultry/game products' were also major contributors for all population groups. Interpreting the results of major food contributors needs to be done with caution. This is because using weighted concentrations in the exposure assessment where less than 100% of the market was represented by industry provided data and the remaining proportion assigned the Codex or EU is likely to skew the proportions derived and they may be different in reality.

The revised estimated baseline exposures remain conservative and not considered as the most refined estimate of actual dietary exposures as it would be unlikely that all foods within each permitted food category would contain polysorbates at maximum concentrations and unlikely that every consumer would select all of the foods that they consume to be the ones containing polysorbates on every day of their life. Hence, it is unlikely to reflect usual dietary exposures from polysorbate-containing foods, nor the total maximum exposure of polysorbates were permission for extended use to be approved.

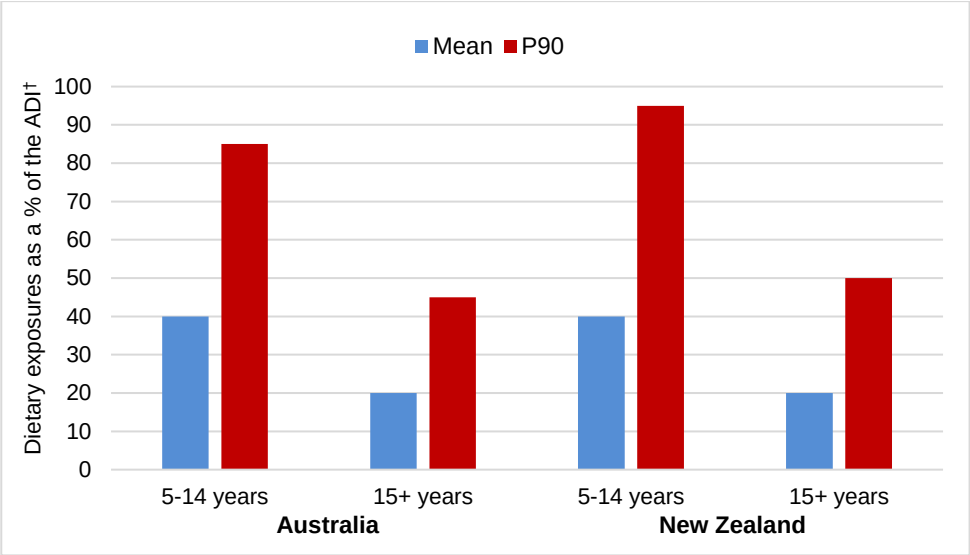
5 Risk characterisation/conclusion

Based on review of the toxicological data, including consideration of reviews by other regulatory agencies, FSANZ concludes that it is appropriate to include polysorbate 20 in a group ADI for polysorbates, and that the group ADI established by JECFA in 1973 for polysorbates, 0-25 mg/kg bw/day, remains appropriate. This ADI was used to compare against the estimated dietary exposures.

5.1 Estimated refined baseline dietary exposures as a proportion of the ADI

The estimated mean and 90th percentile refined baseline dietary exposures for all the population groups assessed were below the ADI at between 20%–40% and between 45%–95% respectively (Figure 5.1).

The highest exposure was for New Zealand children aged 5–14 years at 95% of the ADI at the 90th percentile based on a single day of food consumption data. The Australian 2 day average for same age group was also assessed in order to determine a better estimate of longer term chronic dietary exposure for this group, for which the 90th percentile exposure was 85% ADI. The distribution of food consumption amounts for one 24 hour period is much broader than that averaged across 2 days given that all foods are not consumed on a daily basis. Therefore the number of days of food consumption data affects the distribution of dietary exposures when averaged across two days, resulting in the tails of the exposure distribution coming in and a lower 90th percentile exposure compared to one day of data only.



†If exposure is between between10 and 100% it has been rounded to the nearest 5%.

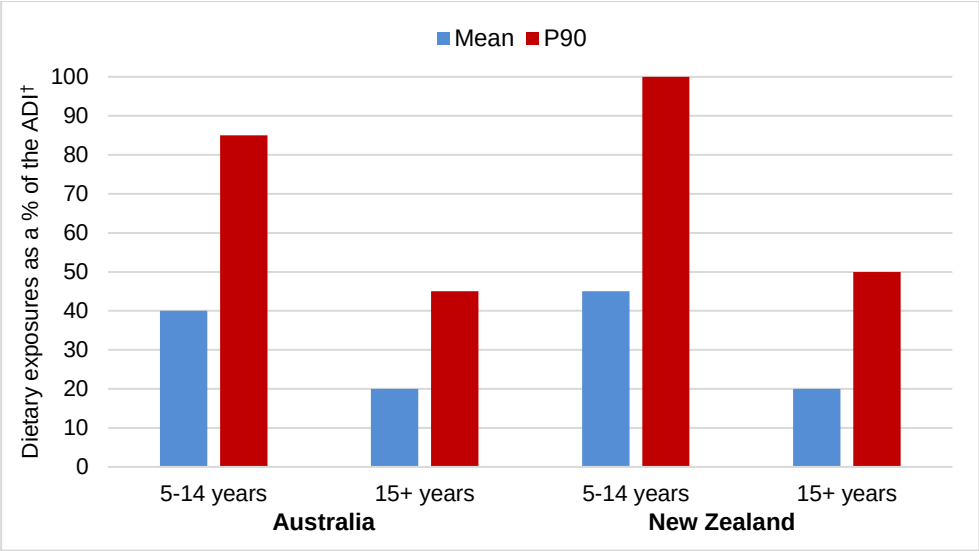
Figure 5.1: Estimated refined baseline mean and 90th percentile (P90) daily dietary exposures to polysorbates as a % of the ADI for all population groups assessed

5.2 Estimated total dietary exposures (refined baseline exposures + Polysorbate 20)

The estimated mean and 90th percentile total dietary exposures expressed as a percentage of the ADI for all the population groups assessed ranged between 20%–45% and between 50%–100% respectively (Figure 5.2).

When the additional requested permission of polysorbate 20 was applied, there was an increase in exposure in only some population groups by 5% of the ADI. Mean and 90th percentile total dietary exposures for all population groups assessed did not exceed the ADI under this extension of use scenario. New Zealand children have estimated 90th percentile dietary exposures at 100% of the ADI, however as discussed above given the concentration data used and only one day of consumption data, this exposure would be lower in reality.

Based on dietary exposure assessment, it is anticipated that this group ADI will not be exceeded by the addition of polysorbate 20 to the proposed food categories requested in addition to the permitted polysorbates in the Code.



†If exposure is between between10 and 100% it has been rounded to the nearest 5%.

Figure 5.2: ***Estimated total mean and 90th percentile (P90) daily dietary exposures to polysorbates as a % of the ADI for all population groups assessed***

References

ABS (2014) National Nutrition and Physical Activity Survey, 2011-12, Basic CURF, CD-ROM. Findings based on ABS CURF data. Australian Bureau of Statistics, Canberra.

Bartsch W, Sponer G, Dietmann K and Fuchs G (1976). Acute toxicity of various solvents in the mouse and rat. Arzneimittelforschung 26: 1581-1583

Coppinger WJ, Brennan SA and Thompson ED (1981). Testing of surfactants for mutagenic potential in the L5178Y TK+/- mouse lymphoma assay. Environmental Mutagenesis 3:320

Eagle E and Poling CE (1956). The oral toxicity and pathology of polyoxyethylene derivatives in rats and hamsters. Journal of Food Science 21: 348-361

EFSA (2015). Scientific Opinion on the re-evaluation of polyoxyethylene sorbitan monolaurate (E 432), polyoxyethylene sorbitan monooleate (E 433), polyoxyethylene sorbitan monopalmitate (E 434), polyoxyethylene sorbitan monostearate (E 435)and polyoxyethylene sorbitan tristearate (E 436) as food additives. EFSA Journal 13(7): 4152, 74 pp. doi:10.2903/j.efsa.2015.4152

Eskandani M, Hamishehkar H and Dolatabadi JEN (2013). Cyto/genotoxicity study of polyethylene (20) sorbitan monolaurate (Tween 20). DNA and Cell Biology 32(9): 498-503

Ewing KL and Tauber OE (1965). Hematologic picture of mice during chronic ingestion of high levels of polyoxyethylene sorbitan derivatives. Toxicology and Applied Pharmacology 7: 320-328

Euromonitor International (2018) Passport [online] Available at: https://www.portal.euromonitor.com/portal/magazine/homemain

Fitzhugh OG, Bourke AR, Nelson AA and Frawley JP (1959) Chronic oral toxicities of four stearic acid emulsifiers. Toxicology and Applied Pharmacology 1(3): 315-331

Food Safety Commission (2007) Evaluation Report of Food Additives “Polysorbate 20, Polysorbate 60, Polysorbate 65 and Polysorbate 80”.

FSANZ (2009) Principles and practices of dietary exposure asessment for food regulatory purposes. Report prepared by Food Standards Australia New Zealand, Canberra.

Kimura T and Yoshida A (1982). Toxicity of detergent feeding and effect of the concurrent feeding of dietary fiber in rats. Nutrition Reports International 26: 271–279.

Li X, Wang L, Li Y, Ho Y, Yang D, Chen Y, Hu X and Xue M (2011). Polysorbates as novel lipid-modulating candidates for reducing serum total cholesterol and low-density lipoprotein levels in hyperlipidemic C57BL/6J mice and rats. European Journal of Pharmacology 660: 468-475

Ministry of Health (2003) NZ Food NZ Children: Key results of the 2002 National Children's Nutrition Survey. Ministry of Health, Wellington.

Ministry of Health (2005) 2002 National Children's Nutrition Survey: National Confidentialised Unit Record File (CURF) User Document. Ministry of Health, Wellington.

Ministry of Health (2011a) Methodology report for the 2008/09 New Zealand Adult Nutrition

Survey. Ministry of Health, Wellington.

Ministry of Health (2011b) A focus on nutrition: Key findings of the 2008/09 New Zealand Adult Nutrition Survey. Ministry of Health, Wellington.

Nakata S and Kimura T (1994). Mechanism involved in the ameliorating effect of dietary fiber on the toxicity of a non-ionic surface-active agent and amaranth to the diet of rats. Bioscience, Biotechnology, and Biochemistry 58: 998–1001

NTP (1992a). NTP Toxicology and Carcinogenesis Studies of Polysorbate 80 (CAS No. 9005-65-6) in F344/N Rats and B6C3F1 Mice (Feed Studies). National Toxicology Program Technical Report Series 415:1-225. https://ntp.niehs.nih.gov/ntp/htdocs/lt_rpts/tr415.pdf

NTP (1992b). TER91010 Developmental toxicology of polyoxyethylene sorbitan monolaurate in Sprague-Dawley CD rats.
https://ntp.niehs.nih.gov/testing/types/dev/abstracts/ter91010/ter91010.html

Oser BL and Oser, M (1956) Nutritional Studies on Rats on Diets Containing High Levels of Partial Ester Emulsifiers: I. General Plan and Procedures; Growth and Food Utilization. Journal of Nutrition 60(3): 367-390

Oser BL and Oser, M (1956) Nutritional Studies on Rats on Diets Containing High Levels of Partial Ester Emulsifiers: II. Reproduction and Lactation. Journal of Nutrition 60(4): 489-505

Oser BL and Oser, M (1957) Nutritional Studies on Rats on Diets Containing High Levels of Partial Ester Emulsifiers: IV. Mortality and Post-Mortem Pathology; General Conclusions. Journal of Nutrition 61(2): 235-252

Paschall HD(1963). Effects of feeding emulsifiers on reproduction of C57BL/6 mice. Retrospective Theses and Dissertations, Iowa State University Digital Repository Paper 2489

WHO (1964) World Health Organization Technical Report Series No. 281 Specifications for the identity and purity of food additives and their toxicological evaluation: Emulsifiers, stabilizers, bleaching and maturing agents. Seventh report of the Joint FAO/WHO Expert Committee on Food Additives.
http://apps.who.int/iris/bitstream/handle/10665/40595/WHO_TRS_281_(p1-p100).pdf;jsessionid=6FF92601F51632C5A79A7DE865838249?sequence=1

WHO (1974) World Health Organization Technical Report Series No. 539 FAO Nutrition Meetins Report Series No. 53. Toxicological evaluation of certain food additives with a review of general principles and of specifications. Seventeenth Report of the Joint FAO/WHO Expert Committee on Food Additives.
http://fsanzapps/applications/A1137/Shared%20Documents/Application/Appendices/Appendix%206%20JECFA%2017th%20report%201973.pdf

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 food chemicals is estimated by combining food consumption data with food chemical concentration data. The process of doing this is called 'dietary modelling'.

Dietary exposure = food chemical concentration x food consumption

FSANZ's approach to dietary modelling is based on internationally accepted procedures for estimating dietary exposure to food chemicals (FSANZ 2009). 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 the ranked individual person's exposures from the nutrition survey.

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/science/riskanalysis/Pages/default.aspx.

FSANZ has developed a custom-built computer program 'Harvest' to calculate dietary exposures. Harvest is a newly built program and replaces the program 'DIAMOND' that had been used by FSANZ for many years. Harvest has been designed to replicate the calculations that occurred within DIAMOND using a different software package. Harvest was used for this assessment to extract the exposure data based on levels of added polysorbates in foods for Australian and New Zealand consumers.

Further detailed information on 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/science/exposure/documents/Principles%20_%20practices%20exposure%20assessment%202009.pdf.

A1.1 Food consumption data used

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

- The 2011-12 Australian National Nutrition and Physical Activity Survey (2011-12 NNPAS)
- The 2002 New Zealand National Children's Nutrition Survey (2002 NZ NCNS)
- The 2008-09 New Zealand Adult Nutrition Survey (2008 NZ ANS).

The design of each of these surveys varies somewhat and key attributes of each are set out below. Further information on the national nutrition surveys used to conduct dietary exposure assessments is available on the FSANZ website at http://www.foodstandards.gov.au/science/exposure/Pages/dietaryexposureandin4438.aspx.

A1.1.1 2011-12 Australian National Nutrition and Physical Activity Survey (2011-12 NNPAS)

The 2011–12 Australian National Nutrition and Physical Activity Survey (NNPAS) undertaken by the Australian Bureau of Statistics is the most recent food consumption data for Australia. This survey includes dietary patterns of a sample of 12,153 Australians aged from 2 years and above. The survey used a 24-hour recall method for all respondents, with 64% of respondents also completing a second 24-hour recall on a second, non-consecutive day. The data were collected from May 2011 to June 2012 (with no enumeration between August and September 2011 due to the Census). Day 1 and Day 2 24-hour recall data for respondents were used for this assessment. These data were weighted for use in the calculation. Consumption and respondent data from the survey were incorporated into the Harvest program from the Confidentialised Unit Record Files (CURF) data set (ABS 2014).

A1.1.2 2002 New Zealand National Children's Nutrition Survey (2002 NZ NCNS)

The 2002 NZ NCNS was a cross-sectional and nationally representative survey of 3,275 New Zealand children aged 5–14 years. The data were collected during the school year from February to December 2002. The survey used a 24-hour food recall and provided information on food and nutrient intakes, eating patterns, frequently eaten foods, physical activity patterns, dental health, anthropometric measures and nutrition-related clinical measures. It was also the first children's nutrition survey in New Zealand to include a second day diet recall data for about 15% of the respondents, and dietary intake from both foods (including beverages) and dietary supplements. Only the Day 1 24-hour recall data for all respondents (excluding supplements) were used for this assessment. These data were weighted for use in Harvest.

A1.1.3 2008-09 New Zealand Adult Nutrition Survey (2008 NZ ANS)

The 2008 NZ ANS provides comprehensive information on the dietary patterns of a sample of 4,721 respondents aged 15 years and above. The survey was conducted on a stratified sample over a 12 month period from October 2008 to October 2009. The survey used a 24-hour recall methodology with 25% of respondents also completing a second 24-hour recall. The information collected in the 2008 NZ ANS included food and nutrient intakes, dietary supplement use, socio-demographics, nutrition related health, and anthropometric measures. Only the Day 1 24-hour recall data for all respondents (excluding supplements) were used for this assessment. These data were weighted for use in Harvest.

A1.2 Limitations of dietary exposure assessments

Dietary exposure assessments based on 2011-12 NNPAS, 2002 NZ NCNS and 2008 NZ ANS food consumption data provide the best estimation of actual consumption of a food and the resulting estimated dietary exposure assessment for the Australian population aged 2 years and above, as well as the New Zealand populations aged 5–14 years and 15 years and above, respectively. However, it should be noted that NNS data do have limitations.

- Diets derived from one or two 24-hour food recall surveys are used as the basis for drawing conclusions on lifetime eating patterns. This normally leads to conservative dietary exposure assessments, particularly where exposure arises from the consumption of non-habitually eaten foods.
- Participants in 24-hour food recalls may over- or under- report food consumption, particularly for certain types of foods.

Further details of the limitations relating to dietary intake assessments undertaken by FSANZ are set out in the FSANZ document, *Principles and Practices of Dietary Exposure Assessment for Food Regulatory Purposes* (FSANZ 2009)

Is industry data available from AUS and/or NZ for polysorbate use in food categories in Schedule 15 with GMP permissions?

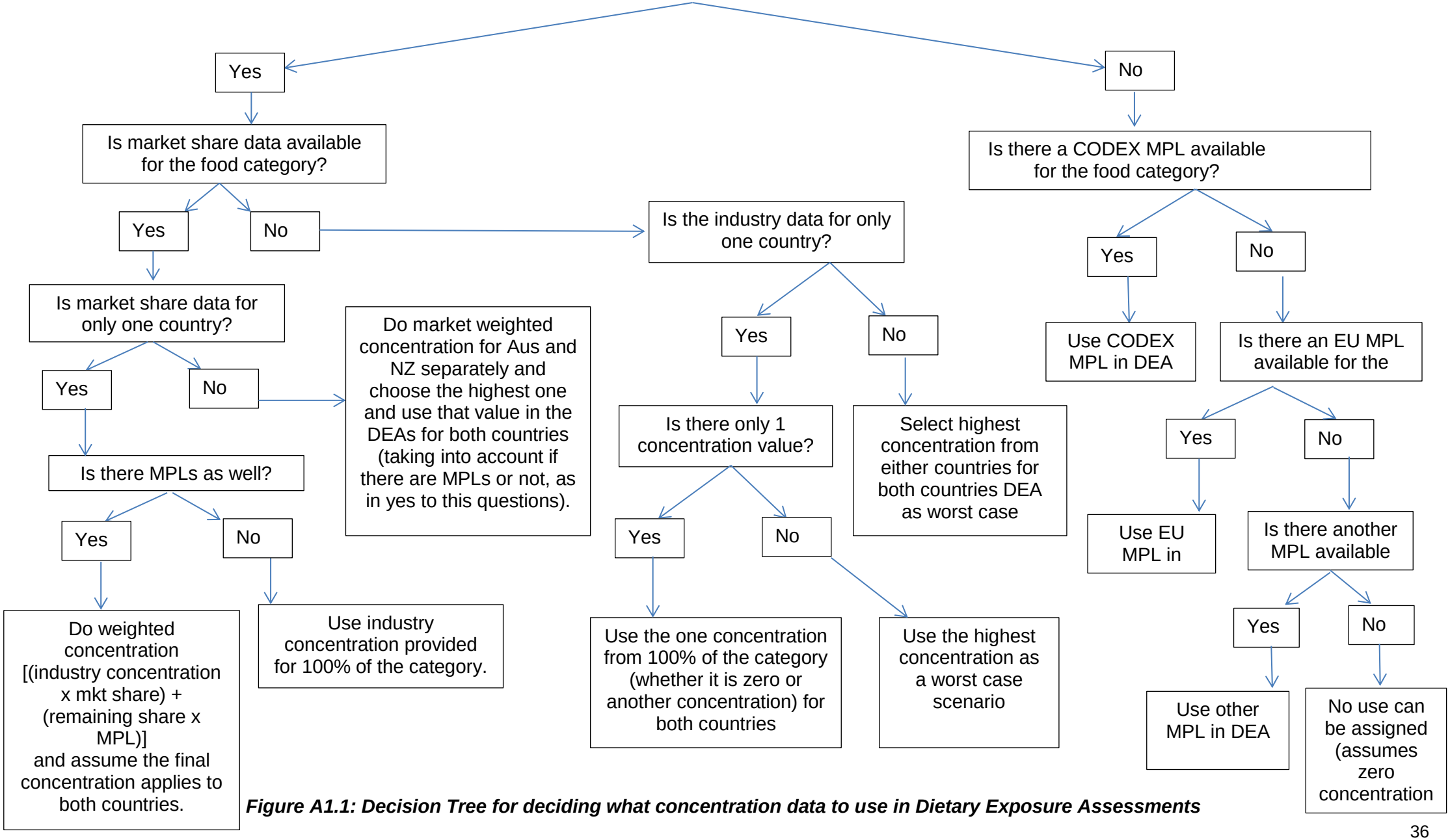


Figure A1.1: Decision Tree for deciding what concentration data to use in Dietary Exposure Assessments

Appendix 2: Food classifications used in Harvest modelling

Foods that are permitted to contain added polysorbates at GMP are specified in the Code and/or related Schedules. However, these foods are coded in Harvest according to classification names and codes that can vary slightly from the Code and may also be split into sub-groups. To estimate polysorbate exposure from foods with added polysorbates, concentrations for specific foods were assigned to the relevant Harvest food classification codes, as listed in Table A2.2 below:

Table A2.2: Classification names and codes from the Food Standards Code and the corresponding Harvest code used for the dietary exposure assessment

Food Standards Code (Standard 1.3.1 – Schedule 15)		**Harvest**	
Category Code	**Category Description**	**Classification Code**	**Classification Name**
0	Preparations of food additives	0	General provisions
1.1.1	Liquid milk (including buttermilk) – only UHT goats milk	1.1.1.5	Liquid milk, unflav, UHT goat milk only
1.1.2	Liquid milk products and flavoured liquid milks	1.1.2 *(excludes* *1.1.2.1.1* *1.1.2.2.1* *1.1.2.3.1* *1.1.2.4.1* *1.1.2.5.1* *1.1.2.5.1.1)*	Liquid milk prod and flav liquid milks *(excludes unflavoured liquid milk products)*
1.2.2	Fermented milk products and rennetted milk products	1.2.2	Fermented & rennetted milk & milk products, flavoured
1.3	Condensed milk and evaporate milk	1.3	Condensed milk and evaporated milk
1.4.1	Cream, reduced cream and light cream *(Only UHT creams and creams ≥ heat treatments)*	1.4.1.1.3 1.4.2.2.2.1 1.4.2.2.2.2	Cream, unflavoured, red fat (canned) Cream products, whipped/thickened, whole fat, aerosol Cream, regular thickened, 35% fat, UHT treated
1.4.2	Cream products (flavoured, whipped, thickened, sour cream etc)	1.4.2	Cream products (flavoured, whipped, thickened, sour cream etc)
1.5	Dried milk, milk powder, cream powder	1.5	Dried milk, milk powder, cream powder
1.6	Cheese and cheese products	1.6 1.6.1	Cheese and cheese products Unripened cheese
2.1	Edible oils essentially free of water	2.1	Edible oils essentially free of water
2.2.1.2	Butter products	2.2.1.2	Butter products
2.2.1.3	Margarines and similar products	2.2.1.3	Margarines and similar products
2.2.2	Oil emulsions (>80% oil)	2.2.2	Oil emulsions (>80% oil)
3	Ice cream and edible ices	3	Ice cream and edible ices
4.1.3	Fruits and vegetables that are peeled, cut, or both peeled and cut	4.1.3	Peeled &/or cut fruits & vegetables
4.3	Processed fruits and vegetables	4.3 4.3.1.4 4.3.5 4.3.6	Processed fruits and vegetables Dried herbs and spices Candied fruits & vegetables Fruit & vegetable preparations including pulp
5.1	Chocolate and cocoa products	5.1 5.1.6	Chocolate and cocoa products Cocoa based spreads
5.2	Sugar confectionary	5.2 5.2.1	Sugar confectionary Bubble gum and chewing gum
5.4	Icings and frostings	5.4	Icings and frostings
6.3	Processed cereal and meal products	6.3	Processed cereal and meal products

Food Standards Code (Standard 1.3.1 – Schedule 15)		Harvest	
Category Code	**Category Description**	**Classification Code**	**Classification Name**
6.4	Flour products (including noodles and pasta)	6.4 6.4.1.1 6.4.1.2 6.4.2	Flour products (including noodles & pasta) Flour products, noodle, instant Flour products, noodle {not instant} Flour products, pasta only
7	Breads and bakery products	7 7.1 7.2 7.2.1.1 7.2.1.2 7.2.2.1	Breads and bakery products Bread and related products Biscuits, crackers, cakes, pastries & scones Biscuits and crackers, sweet Biscuits and crackers, savoury Cakes
8.2	Processed meat, poultry and game products in whole or cut pieces	8.2	Processed meat, poultry and game products in whole or cut pieces
8.3	Processed comminuted meat, poultry and game products, other than listed in item 8.3.2	8.3	Processed comminuted meat, poultry and game products
8.3.2	Sausage and sausage meat containing raw, unprocessed meat	8.3.2	Sausage and sausage meat containing raw, unprocessed meat
8.4	Edible casings	8.4	Edible casings
8.5	Animal protein products	8.5	Animal protein products
9.2	Processed fish and fish products	9.2	Processed fish and fish products
9.3	Semi preserved fish and fish products	9.3	Semi preserved fish and fish products
9.4	Fully preserved fish including canned fish products	9.4	Fully preserved fish including canned fish products
10.2	Liquid egg products	10.2	Liquid egg products
10.3	Frozen egg products	10.3	Frozen egg products
10.4	Dried or heat coagulated egg products	10.4	Dried or heat coagulated egg products
11.1.1	Rainbow sugar	11.1.1	Rainbow sugar
11.3.1	Dried honey	11.3.1	Dried honey
11.4	Table-top sweeteners	11.4	Table-top sweeteners
12.1.2	Reduced sodium salt mixture	12.1.2	Reduced sodium salt mixture
12.1.3	Salt substitute	12.1.3	Salt substitute
12.5	Yeast and yeast products	12.5	Yeast and yeast products
12.6	Vegetable protein products	12.6	Vegetable protein products
13.3	Formulated meal replacements and formulated supplementary foods	13.3 13.3.2.9	Formulated meal replacements and formulated supplementary foods Very low energy drinks & meal replacement liquids
13.4	Formulated supplementary sports foods	13.4	Formulated supplementary sports foods
13.5	Foods for special medical purposes	13.5 13.5.2.2	Foods for special medical purposes Toddler formula products, not soy based, dry base
14.1.1.2	Carbonated mineralised and soda waters	14.1.1.2	Carbonated mineralised and soda waters
14.1.2.1	Fruit and vegetable juices	14.1.2.1	Fruit and vegetable juices
14.1.2.2	Fruit and vegetable juice products	14.1.2.2	Fruit and vegetable juice products
14.1.3	Water based flavoured drinks	14.1.3	Water based flavoured drinks
14.1.4	Formulated beverages	14.1.4	Formulated beverages
14.1.5	Coffee, coffee substitutes, tea, herbal infusions and similar products	14.1.5 14.1.5.1 14.1.5.3.1	Coffee, coffee substitutes, tea, herbal infusions and similar products Coffee beverage Tea, caffeinated
14.2.3	Wine based drinks and reduced alcohol wines	14.2.3	Wine based drinks and reduced alcohol wines
14.2.4.1	Fruit wine products and vegetable wine products	14.2.4.1	Fruit wine products and vegetable wine products
14.2.5	Spirits and liqueurs	14.2.5	Spirits and liqueurs

Food Standards Code (Standard 1.3.1 – Schedule 15)		Harvest	
Category Code	**Category Description**	**Classification Code**	**Classification Name**
14.3	Alcoholic beverage not included in item 14.2	14.3	Alcoholic beverage not included in item 14.2
20	Foods not included in items 0 to 14	20	Mixed foods commercial
		20.1.1.4	Beverages, non-alcoholic, choc, dry mix
		20.1.1.6	Beverages, non-alcoholic, choc, dry mix
		20.2.1.1.1.2	Desserts, dairy, choc; custard & blanc mange mix/powder
		20.2.1.1.3.2	Desserts, dairy, no choc/coffee; custard & blanc mange mix/powder
		20.2.1.2.3.2.1	Desserts, no dairy, no choc/coffee; pavlova/meringue
		20.2.2.1	Grains and cereals, with fruit/nut
		20.2.2.3	Cereal products, bars
		20.2.3.1.2.1	Bakery products, sweet, no choc, bread, yeast, hot cross bun
		20.2.4.2.2	Snack foods, not dairy or fat based, not confectionary
		20.2.5.2	Prepared dishes, fruit/vegetable/legume based
		20.2.5.3.6.1	Prepared dishes, pies & pastries, Asian style
		20.2.5.3.6.2	Prepared dishes, pies & pastries, savoury, {not Asian}
		20.2.6.2.	Gravy, sauces & condiments
		20.2.6.2.5	Sauce, horseradish
		20.2.7.1	Mayonnaise
		20.2.7.2	Salad dressings
		20.2.8.1	Soups, liquid
		20.2.8.2	Soups, dry mix

Appendix 3: Dietary Exposure Assessment Results

Table A3.1: Mean and 90th percentile (P90) estimated refined baseline and total (baseline + PS20) dietary exposure to Polysorbates for all age and population groups assessed

Survey	Age Group (no. of respondents)	No. of consumers	Cons. as a % of respond.	Refined baseline Mean exposure			Refined baseline P90 exposure			Refined baseline + Polysorbate 20 Mean exposure			Refined baseline + Polysorbate 20 P90 exposure		
				mg/day	*mg/kg BW/day$^{\beta}$*	*% ADI*	*mg/day*	*mg/kg BW/day$^{\beta}$*	*% ADI*	*mg/day*	*mg/kg BW/day**	*% ADI*	*mg/day*	*mg/kg BW/day**	*% ADI*
NNPAS 2011-12 (Day 1&2)	5-14 years$^{\infty}$ (1014)	1014	100.0	341	9.8	40	695	21.1	85	354	10.2	40	730	21.9	85
	15+ years$^{\infty}$ (6421)	6395	99.6	361	4.8	20	801	10.7	45	373	5.0	20	837	11.2	45
	All ages$^{\infty}$ (2+years) (7735)	7709	99.7	353	5.8	25	770	13.0	50	366	6.0	25	806	13.5	55
NZ ANS 2008 (Day 1)	5-14 years $^{\Psi}$ (3275)	3242	99.0	373	10.4	40	832	23.7	95	386	10.8	45	858	24.7	100
NZ NCNS 2002 (Day 1)	15+ years* (4721)	4479	94.9	400	5.2	20	931	11.9	50	416	5.4	20	973	12.6	50

β Individual respondents' exposures are divided by their own body weight before deriving mean and P90 dietary exposures.
Mean body weights for each group: Australians 5-14 years = 38 kg, 15+ years = 77 kg, all ages (2+ years) = 70 kg, New Zealand 5-14 years = 40 kg, All ages (15+ years) = 79 kg
∞ Derived using the Australian 2011-12 NNPAS (2 day average exposure)
ψ Derived using the NZ NCNS 2002 (Day 1)
* Derived using the NZ ANS 2008 (Day 1)

Table A3.2 Foods contributing to total dietary exposure to polysorbates

Classification code	Harvest Classification name	Percentage contribution (%)♦				
		Australia			New Zealand	
		5-14 years∞	15+ years∞	2+ years∞	5-14 yearsψ	15+ years*
0	**General provisions**	**0**	**0**	**0**	**0**	**0**
1	**Dairy products (excluding butter & butter fats)**	**8**	**9**	**9**	**7**	**6**
1.1.1	Liquid milk (incl buttermilk)	0	0	0	0	0
1.1.2	Liquid milk products & flavoured liquid milk	3	5	4	4	2
1.1.2.1.1	Liquid milk products & flavoured liquid milk, incr fat, unflavoured	0	0	0	0	0
1.1.2.2.1	Liquid milk products & flavoured liquid milk, whole, unflavoured	0	0	0	0	0
1.1.2.3.1	Liquid milk products & flavoured liquid milk, red fat, unflavoured	0	0	0	0	0
1.1.2.4.1	Liquid milk products & flavoured liquid milk, low/skim, unflavoured	0	0	0	0	0
1.1.2.5.1	Liquid milk, PSE, unflavoured	0	0	0	0	0
1.1.2.5.1.1	Liquid milk, PSE, unflavoured, low fat/skim	0	0	0	0	0
1.2.2	Fermented & rennetted milk & milk products, flavoured	4	3	3	3	3
1.3	Condensed milk & evaporated milk	0	0	0	0	0
1.4	Cream & cream products	0	0	0	0	0
1.4.1.1.3	Cream, unflavoured, red fat	0	0	0	<1	<1
1.4.2	Cream products (e.g. flavoured, whipped, thickened, sour)	<1	<1	<1	<1	<1
1.4.2.2.2.1	Cream products, whipped/thickened, whole fat, aerosol	<1	<1	<1	<1	<1
1.4.2.2.2.2	Cream, regular thickened, 35% fat, UHT treated	<1	<1	<1	<1	<1
1.5	Dried milk, milk powder, cream powder	<1	<1	<1	<1	1
1.6	Cheese and cheese products	0	0	0	0	0
1.6.1	Unripened cheese	0	<1	<1	0	<1
2	**All Edible oils & oil emulsions**	**0**	**0**	**0**	**0**	**0**
2.1	Edible oils essentially free of water	0	0	0	0	0
2.2.1.2	Butter products	0	0	0	0	0
2.2.1.3	Margarines and similar products	0	0	0	0	0
2.2.2	Oil emulsions (>80% oil)	0	0	0	0	0
3	**Ice cream and edible ices**	**4**	**2**	**2**	**2**	**<1**
4	**All Fruit & vegetables (including fungi/ nuts/ seeds/ herbs/ spices)**	**1**	**1**	**1**	**2**	**1**
4.1.3	Peeled &/or cut fruits & vegetables	0	0	0	0	0
4.3	Processed fruits and vegetables	0	0	0	0	0

Classification code	Harvest Classification name	Percentage contribution (%)♦				
		Australia			New Zealand	
		5-14 years∞	15+ years∞	2+ years∞	5-14 yearsψ	15+ years*
4.3.1.4	Dried herbs and spices	<1	<1	<1	<1	<1
4.3.5	Candied fruits & vegetables	0	<1	<1	0	0
4.3.6	Fruit & vegetable preparations including pulp	1	1	1	2	1
5	**Confectionary**	**4**	**3**	**3**	**4**	**3**
5.1	Chocolate and cocoa products	4	3	3	2	3
5.1.6	Cocoa based spreads	0	0	0	<1	<1
5.2	Sugar confectionary	<1	<1	<1	1	<1
5.2.1	Bubble gum and chewing gum	0	0	<1	<1	0
5.2.1.1	Bubble gum and chewing gum, I/S	0	0	<1	<1	0
5.4	Icings and frostings	0	<1	<1	<1	<1
6	**Cereals and cereal products**	**0**	**0**	**0**	**0**	**0**
6.3	Processed cereal and meal products	0	0	0	0	0
6.4	Flour products (including noodles & pasta)	0	0	0	0	0
6.4.1.1	Flour products, noodle, instant	0	0	0	0	0
6.4.1.2	Flour products, noodle {not instant}	0	0	0	0	0
6.4.2	Flour products, pasta only	0	0	0	0	0
7	**All Breads & bakery products**	**12**	**7**	**7**	**7**	**7**
7.1	Bread and related products	0	0	0	0	0
7.2	Biscuits, crackers, cakes, pastries & scones	2	2	2	2	3
7.2.1.1	Biscuits and crackers, sweet	2	1	1	1	1
7.2.1.2	Biscuits and crackers, savoury	5	2	2	2	2
7.2.2.1	Cakes	3	2	2	1	1
8	**All Meat & meat products (including poultry & game)**	**33**	**31**	**31**	**32**	**36**
8.2	Processed meat, poultry and game products in whole or cut pieces	13	14	14	9	13
8.3	Processed comminuted meat, poultry and game products	5	3	3	9	6
8.3.2	Sausage and sausage meat containing raw, unprocessed meat	16	14	14	13	16
8.4	Edible casings	0	0	0	0	0
8.5	Animal protein products	0	0	0	0	0
9	**All Fish & fish products**	**<1**	**<1**	**<1**	**<1**	**<1**
9.2	Processed fish and fish products	<1	<1	<1	<1	<1

Classification code	Harvest Classification name	Percentage contribution (%)♦				
		Australia			New Zealand	
		5-14 years∞	15+ years∞	2+ years∞	5-14 yearsψ	15+ years*
9.3	Semi preserved fish and fish products	0	0	0	0	0
9.4	Fully preserved fish including canned fish products	0	0	0	0	0
10	**All Egg & egg products**	**0**	**0**	**0**	**0**	**0**
10.2	Liquid egg products	0	0	0	0	0
10.3	Frozen egg products	0	0	0	0	0
10.4	Dried or heat coagulated egg products	0	0	0	0	0
11	**Sugars, honey & related products**	**0**	**0**	**0**	**0**	**0**
11.1.1	Rainbow sugar	0	0	0	0	0
11.3.1	Dried honey	0	0	0	0	0
11.4	Table-top sweeteners	0	0	0	0	0
12	**All Salts & condiments**	**0**	**0**	**0**	**0**	**0**
12.1.2	Reduced sodium salt mixture	0	0	0	0	0
12.1.3	Salt substitute	0	0	0	0	0
12.5	Yeast and yeast products	0	0	0	0	0
12.6	Vegetable protein products	0	0	0	0	0
13	**All Foods intended for particular dietary uses**	**0**	**<1**	**<1**	**0**	**0**
13.3	Formulated meal replacements and formulated supplementary foods	0	0	0	0	0
13.3.2.9	Very low energy drinks & meal replacement liquids	0	<1	<1	0	0
13.4	Formulated supplementary sports foods	0	0	0	0	0
13.5	Foods for special medical purposes	0	0	0	0	0
13.5.2.2	Toddler formula products, not soy based, dry base	0	0	0	0	0
14	**All Non-alcoholic & alcoholic beverages**	**3**	**3**	**3**	**4**	**3**
14.1.1.2	Carbonated mineralised and soda waters	0	0	0	0	0
14.1.2.1	Fruit and vegetable juices	<1	<1	<1	<1	<1
14.1.2.2	Fruit and vegetable juice products	<1	<1	<1	<1	<1
14.1.3	Water based flavoured drinks	2	3	3	3	2
14.1.4	Formulated beverages	<1	<1	<1	<1	<1
14.1.5	Coffee, coffee substitutes, tea, herbal infusions and similar products	0	0	0	0	0
14.2.3	Coffee beverage	0	0	0	0	0
14.2.4.1	Tea, caffeinated	0	0	0	0	0

Classification code	Harvest Classification name	Percentage contribution (%)♦				
		Australia			New Zealand	
		5-14 years∞	15+ years∞	2+ years∞	5-14 yearsψ	15+ years*
14.2.3	Wine based drinks and reduced alcohol wines	0	<1	<1	<1	<1
14.2.4.1	Fruit wine products and vegetable wine products	0	0	0	0	0
14.2.5	Spirits and liqueurs	<1	<1	<1	<1	<1
14.3	Alcoholic beverage not included in item 14.2	0	0	0	0	0
20	**Mixed foods commercial**	**35**	**44**	**42**	**42**	**44**
20.1.1.4	Beverages, non-alcoholic, choc, dry mix	0	0	0	0	0
20.1.1.6	Beverages, non-alcoholic, choc, dry mix	0	0	0	0	0
20.2.1.1.1.2	Desserts, dairy, choc; custard & blanc mange mix/powder	<1	<1	<1	<1	<1
20.2.1.1.3.2	Desserts, dairy, no choc/coffee; custard & blanc mange mix/powder	2	1	1	1	1
20.2.1.2.3.2.1	Desserts, no dairy, no choc/coffee; pavlova/meringue	<1	<1	<1	0	0
20.2.2.1	Grains and cereals, with fruit/nut	0	0	0	0	0
20.2.2.3	Cereal products, bars	0	0	0	0	0
20.2.3.1.2.1	Bakery products, sweet, no choc, bread, yeast, hot cross bun	<1	<1	<1	<1	<1
20.2.4.2.2	Snack foods, not dairy or fat based, not confectionary	<1	<1	<1	<1	<1
20.2.5.2	Prepared dishes, fruit/vegetable/legume based	2	4	4	3	3
20.2.5.3.6.1	Prepared dishes, pies & pastries, Asian style	2	3	3	<1	3
20.2.5.3.6.2	Prepared dishes, pies & pastries, savoury, {not Asian}	6	6	6	17	12
20.2.6.2	Gravy, sauces & condiments	18	25	24	17	18
20.2.6.2.5	Sauce, horseradish	0	0	0	0	0
20.2.7.1	Mayonnaise	<1	<1	<1	<1	<1
20.2.7.2	Salad dressings	<1	<1	<1	<1	1
20.2.8.1	Soups, liquid	1	2	2	<1	4
20.2.8.2	Soups, dry mix	<1	<1	<1	<1	<1
Grand Total		**100**	**100**	**100**	**100**	**100**

∞ Derived using the Australian 2011-12 NNPAS (2 day average exposure)
ψ Derived using the NZ NCNS 2002 (Day 1)
* Derived using the NZ ANS 2008 (Day 1)
All % contributions are expressed as a percentage of the grand total contribution