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

**Preliminary risk assessment of
3-monochloropropanediol (3-MCPD) glycidyl esters
from infant formula**

6 March 2020

Executive summary

3-MCPD esters and glycidyl esters are substances that can form during the processing of oils, when they are being decolourised and deodorised before their sale or use as an ingredient in other foods such as cooking oils, margarines and infant formulas.

Food safety and regulatory bodies around the world have known about 3-MCPD esters and glycidyl esters in food for several years but an internationally-agreed analytical method has not previously been available. There is some concern internationally about the levels of these substances in the food supply because there is evidence that they cause cancer in laboratory animals.

To understand how levels in Australian and New Zealand oils and infant formula compare to those found internationally, New Zealand Food Safety (NZFS), with input from Food Standards Australia New Zealand (FSANZ), coordinated a snap-shot analytical survey, which included 3-monochloropropanediol (3-MCPD) and glycidyl esters in cooking oils and infant formula. The survey also helped to identify a suitable analytical method to support future testing for 3-MCPD and glycidyl esters.

In total, 44 samples of oils and 56 samples of infant formula were analysed. Overall, the survey found that levels of both 3-MCPD esters and glycidyl esters in oils and infant formula were broadly consistent with those found internationally and generally very low. Results of the analytical survey can be found at https://www.mpi.govt.nz/food-safety/food-safety-and-suitability-research/food-science-research/chemical-hazard-and-mycotoxin-research/.

Based on the findings of the survey, FSANZ undertook a preliminary risk assessment of dietary exposure to 3 month old infants to identify any potential health and safety risks.

3-MCPD esters and glycidyl esters were evaluated by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) at their 83rd meeting in 2016. JECFA established a group provisional maximum tolerable daily intake (PMTDI)[1] of 4 µg/kg bw for 3-MCPD esters. For glycidyl esters, JECFA identified a $BMDL_{10}$[2] of 2.4 mg/kg bw/day as the point of departure for calculating a margin of exposure (MOE).[3]

Estimated dietary exposures to 3-MCPD esters for 3 month old infants ranged between 0.93 and 3.39 µg/kg bw/day, below the PMTDI, indicating that there are no public health concerns at current exposure levels. For glycidyl esters, the estimated dietary exposures for 3 month old infants ranged between 0.21 and 2.75 µg/kg bw/day. Based on these exposure estimates, the MOEs are within the range considered to be of possible concern by JECFA.

However, the preliminary nature of the survey with non-representative sampling of infant formula and limited data points, limit the potential to draw any firm conclusions. The benefits of continuing to provide formula to infants far outweighs any potential health concerns associated with low levels of glycidyl esters that may be present in some formula products. Infant formula is the only safe alternative to breast milk for infants.

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[1] The PMTDI represents the amount of a chemical in food or drinking water that can be ingested daily over a lifetime without appreciable health risk.

[2] $BMDL_{10}$: The benchmark dose lower confidence limit for a 10% increase in the incidence of an adverse effect.

[3] The ratio between the $BMDL_{10}$ and the estimated dietary exposure.

Australia and New Zealand have contributed to the development of an international code of practice by the Codex Alimentarius to reduce levels that occur in food. The Code of Practice was adopted in 2019 and will help manufacturers prevent and reduce levels of 3-MCPD esters and glycidyl esters in refined oils and food products containing refined oils.

An industry Toolbox was also developed several years ago, and industry has been encouraged to continue reducing levels to as low as reasonably achievable (ALARA) by adopting the measures outlined in this Industry Toolbox (BLL and FoodDrink Europe).

Now the Codex Code of Practice has been adopted, NZFS and FSANZ will look for opportunities to monitor its uptake and use, and to facilitating continued reductions to levels in vegetable oils and infant formula over time.

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Background

3-MCPD esters and glycidyl esters are substances that can form during the processing of oils, when they are being decolourised and deodorised before they are sold or used as an ingredient to manufacture other foods. Research has shown that the esters are broken down into 3-MCPD and glycidol after ingestion. These breakdown products are a potential public health concern as they can cause cancer in laboratory animals.

New Zealand Food Safety (NZFS), with input from FSANZ, coordinated a snap-shot analytical survey of 3-monochloropropanediol 3-(MCPD), glycidol and their esters in selected edible vegetable oils and infant formula available at retail. The samples were analysed by ESR (the Institute of Environmental Science and Research) Food Chemistry Laboratory, Christchurch, New Zealand. ESR also tested for 2-monochloropropanediol (2-MCPD). Infant formula was tested because vegetable oils are a key ingredient and, in terms of dietary exposure, infants are a vulnerable population group and infant formula can be their sole source of nutrition.

The survey aimed to establish confidence in the selected analytical method and benchmark levels of these compounds found in products available in Australia and New Zealand against those found in similar products available overseas.

Methods and analytical survey

The methods and analytical results are described in detail in the NZFS report (https://www.mpi.govt.nz/food-safety/food-safety-and-suitability-research/food-science-research/chemical-hazard-and-mycotoxin-research/). In brief, 100 samples of vegetable oils and infant formula (including those noted as suitable from birth up to 12 months of age) were collected in Australia (n=50) and New Zealand (n=50) during August to October 2017. In total, 44 oils and 56 infant formula samples were tested. Infant formula products were purchased in both countries, however it should be noted that the country of purchase does not reflect the country the products were produced in.

The samples were analysed by ESR using Gas Chromatography Mass Spectrometry (AOCS Official method Cd 29a-13, 2013). Duplicate samples were dispatched to the United States Food and Drug Administration (US FDA) for analysis using an alternative direct, LC-MS based method for each ester individually as a means of validating the method selected by ESR.

The survey was successful in validating an analytical method for use in Australia and New Zealand, and provided some useful baseline data on products available in both countries. For vegetables oils, ESR noted that levels of both 3-MCPD esters and glycidyl esters are broadly consistent with those found in previous international surveys. For infant formula, ESR observed that levels of 3-MCPD are similar to average results found in international surveys; levels of glycidyl esters are, on average, at the low end of those found in studies conducted on samples sourced overseas.

There were insufficient samples of oils to undertake a risk assessment, therefore the oils were not considered further by FSANZ. There were sufficient samples of infant formula to undertake a preliminary risk assessment for this product category as a whole, the results from which may inform the need for a more detailed investigation.

FSANZ also undertook a comparison of the results with international regulatory limits, and a comparison with international concentration data in the GEMS/Food contaminants database (available on the World Health Organization (WHO) website). The results from this comparison can be found in Appendix 2.

Hazard identification and characterisation

3-MCPD esters and glycidyl esters were evaluated by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) at their 83rd meeting in 2016.

3-MCPD esters are substantially hydrolysed to 3-MCPD in the gastrointestinal tract and elicit toxicity as free 3-MCPD. JECFA established a group provisional maximum tolerable daily intake (PMTDI) of 4 µg/kg bw for 3-MCPD and 3-MCPD esters, expressed as 3-MCPD equivalents (WHO 2017). The PMTDI is based on a $BMDL_{10}$[4] of 0.87 mg/kg bw/day for renal tubule hyperplasia in male rats with the application of an uncertainty factor of 200. The uncertainty factor includes a factor of 2 to account for inadequacies in the available studies on reproductive toxicity.

Glycidyl esters (GEs) are substantially hydrolysed to glycidol in the gastrointestinal tract, and elicit toxicity as free glycidol. Glycidol is genotoxic and carcinogenic in experimental animals, inducing tumours in multiple tissues in rats and mice. JECFA identified a $BMDL_{10}$ of 2.4 mg/kg bw/day for mesotheliomas in the tunica vaginalis/peritoneum in male rats as the most sensitive endpoint on which to base a point of departure for calculating a margin of exposure (MOE)[5] (WHO 2017).

Dietary exposure assessment

Dietary exposures for infants to 3-MCPD (from 3-MCPD and 3-MCPD esters, expressed as 3-MCPD) and glycidyl esters (expressed as glycidol) were estimated by FSANZ based on the results from the analytical survey conducted by NZFS. Chronic dietary exposures were based on mean concentrations determined in the infant formula. Mean concentrations were derived for the samples analysed by ESR and separately for the results from samples analysed by US FDA. There were some not-detected (ND) concentrations in the ESR dataset, therefore three scenarios were assessed. The first where not detected concentrations were assigned a zero before deriving the mean (ND=0, or lower bound), the second where non-detects were assigned a value equal to half the limit of detection (LOD) (ND=1/2 LOD, or middle bound) and the third where non-detects were assigned a value equal to the LOD (ND=LOD, or upper bound). There were no non-detects in the US FDA dataset therefore one mean value was derived for each chemical.

The analytical results were not separated by country for the purpose of the dietary exposure assessment. This was due to a number of reasons including the limited number of samples overall, that a broader range of products would be available and consumed by infants which are likely to contain concentrations in the range of all products sampled, and many of the brands sampled are available in both countries.

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[4] $BMDL_{10}$: The benchmark dose lower confidence limit for a 10% increase in the incidence of an adverse effect.

[5] The MOE is defined as the ratio between the BMDL for the critical effect and the estimated dietary exposure.

The analytical results were given for concentrations of 3-MCPD or glycidol in the fat/oil component of the powder. Therefore, for the dietary exposure assessment the analytical results were converted to concentrations in the prepared formula ready for consumption (see Appendix 1 for further details).

Mean concentrations in the prepared infant formula used in the dietary exposure assessment for 3-MCPD for the ESR dataset were lower bound 7.6 µg/kg, middle bound 10.7 µg/kg and upper bound 13.8 µg/kg, and for the US FDA dataset the mean was 11.7 µg/kg. For glycidol, the mean concentrations in prepared formula for the ESR dataset were lower bound 1.7 µg/kg, middle bound 6.5 µg/kg and upper bound 11.2 µg/kg, and for the US FDA dataset the mean was 3.2 µg/kg. The concentration data are also shown in Table A1.1.

Exposure estimates were conducted for 3 month old infants, as infant formula can be the sole source of nutrition for this group. A model diet for the amount of infant formula consumed was used in the calculation of dietary exposure. The model diet was based on infant energy requirements, a representative mean body weight and an average energy content for the sampled infant formulas. High consumers were assessed by assuming a mean consumption of formula using a standard conversion of the mean multiplied by two to approximate a 90th percentile (P90) amount.

Further details about the methodology used for the dietary exposure assessment can be found in Appendix 1.

Estimated dietary exposures to 3-MCPD

Estimated mean dietary exposures to 3-MCPD from infant formula for 3 month old infants ranged between 0.93 (lower bound) – 1.69 (upper bound) µg/kg bw/day using the ESR analytical dataset and 1.44 µg/kg bw/day using the United States Food and Drug Administration (US FDA) analytical dataset (see Table 1).

Estimated P90 dietary exposures to 3-MCPD from infant formula for 3 month old infants ranged between 1.85 (lower bound) – 3.39 (upper bound) µg/kg bw/day using the ESR analytical dataset and 2.87 µg/kg bw/day using the US FDA analytical dataset (see Table 1).

The dietary exposure estimates using US FDA dataset lie between the ESR dataset estimates for ND=½ LOD and ND=LOD.

All dietary exposures are within the range of estimates published by JECFA for infants aged 0-12 months based on mean concentrations (<1 – 10 µg/kg bw/day based on mean consumption; <1 – 12 µg/kg bw/day based on high (P90 and P95) consumption) (JECFA 2017). The mean and high percentile dietary exposures estimated in this assessment using the US FDA analytical dataset are towards the lower end of the JECFA dietary exposure estimate ranges, noting that different age groups are used in these assessments.

Estimated dietary exposures to glycidyl esters (expressed as glycidol)

Estimated mean dietary exposures to glycidol from infant formula ranged between 0.21 (lower bound) – 1.37 (upper bound) µg/kg bw/day using the ESR analytical dataset and 0.40 µg/kg bw/day using the US FDA analytical dataset (see Table 1).

Estimated P90 dietary exposures to glycidol from infant formula ranged between 0.42 (lower bound) – 2.75 (upper bound) µg/kg bw/day using the ESR analytical dataset and 0.79 µg/kg bw/day using the US FDA analytical dataset (see Table 1).

All dietary exposures are within the range of estimates published by JECFA (mean exposures 0.1 – 3.6 µg/kg bw/day; high percentile (P90 and P95) exposures 0.3 – 4.9 µg/kg bw/day) (JECFA 2017). The mean and high percentile dietary exposures estimated in this assessment using the US FDA analytical dataset are towards the lower end of the international dietary exposure estimate ranges, noting that different age groups are used in these assessments.

Table 1: Estimated mean and P90 dietary exposures to 3-MCPD and glycidol from infant formula for 3 month old infants, in µg/kg bw/day

Chemical	Analytical dataset	Scenario	Dietary exposure (µg/kg bw/day) Mean	P90
3-MCPD	ESR	ND=0	0.93	1.85
		ND=½ LOD	1.31	2.62
		ND=LOD	1.69	3.39
	US FDA		1.44	2.87
Glycidol	ESR	ND=0	0.21	0.42
		ND=½ LOD	0.79	1.58
		ND=LOD	1.37	2.75
	US FDA		0.40	0.79

Risk characterisation

3-MCPD

The PMTDI set by JECFA for 3-MCPD is 4 µg/kg bw/day (JECFA 2017).

Using the ESR analytical dataset, the estimated dietary exposures to 3-MCPD from infant formula for 3 month old infants are 25 – 40% PMTDI at the mean and 45 – 85% PMTDI at the P90. The lower end of the range is for the ND=0 scenario; the upper end of the range is for the ND=LOD scenario.

Using the US FDA analytical dataset, the estimated dietary exposures to 3-MCPD from infant formula for 3 month old infants are below the PMTDI: 35% PMTDI at the mean and 70% PMTDI at P90. The estimates using US FDA data are similar to the ESR ND=½ LOD scenario estimates.

See Table 2 for further details.

Estimated mean and P90 dietary exposures for 3 month old infants were below the PMTDI for all scenarios and analytical datasets assessed. Therefore exposures to 3-MCPD are not of health concern.

Table 2: Estimated mean and P90 dietary exposures to 3-MCPD from infant formula for 3 month old infants, as a %PMTDI

Analytical dataset	Scenario	Dietary exposure %PMTDI	
		Mean	P90
ESR	ND=0	25	45
	ND=½ LOD	35	65
	ND=LOD	40	85
US FDA		35	70

Glycidol

There is no health based guidance value for glycidol set by JECFA, therefore estimated dietary exposures have been compared to the $BMDL_{10}$ of 2.4 mg/kg bw/day for a Margin of Exposure (MOE) estimate[6] (JECFA 2017).

Using the ESR analytical dataset, the estimated mean and P90 dietary exposures to glycidol from infant formula for 3 month old infants give MOEs of 1,700 – 12,000 at the mean and 900 – 5,800 at the P90. The lower end of the range is for the ND=LOD scenario; the upper end of the range is for the ND=0 scenario.

Using the US FDA analytical dataset, the estimated mean and P90 dietary exposures to glycidol from infant formula for 3 month old infants give MOEs of 6,100 and 3,000, respectively. See Table 3 for further details.

With the exception of the mean exposure for the ESR ND=0 scenario, the MOEs for glycidol, at the mean and P90 estimated dietary exposures were generally low for a compound that is genotoxic and carcinogenic, and within the range considered to be of possible concern to human health by JECFA.

While the MOEs are low, FSANZ notes that they are comparable to those observed internationally and that the benefits of continuing to provide formula to infants far outweighs any potential health concerns associated with low levels of these contaminants in some formula products. Infant formula is the only safe alternative to breast milk for infants under six months of age.

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[6] Margin of Exposure (MOE) = $BMDL_{10}$ ÷ dietary exposure to glycidol on a body weight basis.

Table 3: Estimated mean and P90 dietary exposures to glycidol from infant formula for 3 month old infants, expressed as a Margin of Exposure (MOE)

Analytical Dataset	Scenario	Margin of Exposure	
		Mean	P90
ESR	ND=0	12,000	5,800
	ND=½ LOD	3,000	1,500
	ND=LOD	1,700	900
US FDA		6,100	3,000

Risk management and next steps

Since these contaminants were identified, industry and food safety bodies around the world have been working to reduce their occurrence in foods. There are a number of risk management measures in place, including a Toolbox developed to help industry reduce levels.

FSANZ and NZFS were involved in developing the Codex Code of Practice for the reduction of 3-MCPD esters and glycidyl esters in refined oils and food products made with refined oils. This Code of Practice was adopted in 2019. The Code of Practice sets out explicit guidance for producers and users to reduce the presence of 3-MCPD and glycidyl esters in refined oils, such as rapeseed, soya bean, sunflower, safflower, walnut and especially palm oils. This will ensure the production of a safe product to protect consumer health and ensure trade flow of refined oils by producing countries.

Over recent years many methods have been developed to reduce 3-MCPD esters and glycidyl esters in the production of vegetable fats and oils. Industry are encouraged to continue reducing levels to as low as reasonably achievable (ALARA) by adopting an Industry Toolbox (BLL and FoodDrink Europe). The Toolbox provides a number of strategies that can be used across all stages of the supply and manufacture to mitigate the occurrence of 3-MCPD esters and glycidyl esters. FSANZ has liaised with industry to ensure industry are aware of the measures in the Toolbox and are working to encourage an ongoing reduction in the potential levels in products.

FSANZ is also collaborating with international agencies, sharing data and information, with a view to identifying further mitigation measures.

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Appendix 1 – Approach to estimating dietary exposures to 3-MCPD and glycidol

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 (see Equation 1).

Equation 1: Dietary exposure calculation

Dietary exposure = food chemical concentration x food consumption

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. Further detailed information on conducting dietary exposure assessments at FSANZ is provided in *Principles and Practices of Dietary Exposure Assessment for Food Regulatory Purposes (Food Standards Australia New Zealand 2009)*, available at: http://www.foodstandards.gov.au/science/exposure/documents/Principles%20_%20practices%20exposure%20assessment%202009.pdf.

Population group(s)

The analysed food in this study is infant formula, with sampled products including those that are suitable from 0-12 months of age. Consequently, the population group that was included in the dietary exposure assessment was infants. The specific population group assessed was infants who are exclusively formula-fed: infants aged 3 months. This allows an assessment of 3-MCPD and glycidol dietary exposures from infant formula without the contribution of consumption of solid foods. In addition, consumption amounts of infant formula for older infants up to 12 months of age tend to be lower as the proportion of solid food in the diet increases, as does body weight.

Food consumption data used

As there are no data available from the 2011-12 Australian National Nutrition and Physical Activity Survey (2011-12 NNPAS) or the New Zealand National Children's Nutrition Survey (2002 NZNNS) for children aged less than 2 years, a model diet was constructed to estimate dietary exposures to 3-MCPD and glycidol in infants aged 3 months.

As the 3 month old infant model diet is based on mean food consumption amounts only, a distribution of food consumption was not available and hence, a distribution of 3-MCPD and glycidol dietary exposures was not able to be produced. Therefore, the 90th percentile dietary exposures were estimated using the calculation shown in Equation 2.

Equation 2: 90th percentile dietary exposure calculation for the 3 month old infant model diet

$$90\text{th percentile exposure} = \text{mean exposure} \times 2^{*}$$

* (World Health Organization et al. 1985)

How the 3 month old infant diet was constructed

The recommended energy intake for a three-month-old boy (343 kJ/kg bw/day) (United Nations University et al. 2004) and the 50th percentile weight (6.4 kg) (World Health Organization 2006) for the same age and sex were used as the basis for the model diet for 3 month old infants. Boys' weights were used because boys tend to be heavier than girls at the same age and therefore have higher overall energy and food requirements. The entire energy requirement in the 3 month old infant diet is derived from infant formula. The body weight of 6.4 kg was used to estimate dietary exposures for 3 month old infants on a body weight basis.

The energy content of infant formula is required for the calculation of the amount of infant formula in the model diet for infants aged 3 months. The latest nutrient data set published for Australian foods (AUSNUT), does not contain energy concentrations for infant formula, only for *Infant formula, 6-12 months, prepared with water* (Food Standards Australia New Zealand 2016). Therefore, an average of the labelled energy concentrations from the sampled infant formula products was examined and assumed to be 280 kJ/100 ml. This derived energy concentration was used in the calculation of the amount of infant formula consumed by 3 month old infants: 785 grams infant formula per day.

Concentrations of 3-MCPD and glycidol

The same infant formula samples were analysed for 3-MCPD and glycidol by two laboratories; ESR and the US FDA. The analyses by the two laboratories are considered to be two separate datasets for the purposes of dietary exposure assessment. This enables a comparison to be made between the dietary exposures estimates made using each of the two datasets.

All analytical results provided by the US FDA were quantified (i.e. above the limit of detection (LOD)) for both 3-MCPD (56/56 samples) and glycidol (56/56 samples). In contrast, thirty-eight of the 56 samples analysed by ESR for 3-MCPD and 54 of the 56 samples analysed for glycidol were below the LOD.

Due to there being analytical results below the LOD for both 3-MCPD and glycidol in the ESR dataset, three separate scenarios (bounds) were examined where not detected concentrations were assigned a numerical concentration in order for a mean concentration to be derived. The three scenarios were as follows:

Assumption	Bound	Scenario name
Not detected equals zero	Lower bound	ND=0
Not detected equals half the LOD	Middle bound	ND= ½ LOD
Not detected equals the LOD	Upper bound	ND = LOD

The dietary exposure estimates represent a range between the lower bound (ND=0) and the upper bound (ND=LOD). The upper bound is highly protective of consumers as it assumes that the component is always present at a concentration equivalent to the LOD if there is no detection.

As there were no non-detections in the US FDA dataset, no 'bound' needed to be derived and a single mean concentration was calculated for both 3-MCPD and glycidol.

Analytical results for 3-MCPD and glycidol were reported as mg/kg of fat. Label data for each individual sample was used to convert the analytical values from a 'fat basis' to an 'as consumed' infant formula basis. This included using the label reported value for the percent of fat in the formula and the amount of water specified on each label to make up that specific formula. Following this calculation, mean analytical results were derived for use in the dietary exposure assessments (see Table 1).

Table A1.1 Mean concentrations of 3-MCPD and glycidol in infant formula (as consumed) as used in the dietary exposure assessment

		Concentration (µg / kg formula)	
Analytical dataset	Scenario	3-MCPD	Glycidol
ESR	ND=0	7.6	1.7
	ND=½ LOD	10.7	6.5
	ND=LOD	13.8	11.2
US FDA		11.7	3.2

Note:

1. 1 litre of infant formula is equal to 1,050 grams.

Assumptions, limitations and uncertainties in the dietary exposure assessment

The aim of the dietary exposure assessment was to make the most realistic estimation of dietary exposures to 3-MCPD and glycidol as possible. However, where significant uncertainties in the data existed, assumptions that are protective of consumers were used to ensure that the estimated dietary exposure was not an underestimate of exposure and vulnerable populations are adequately protected.

Assumptions made in the dietary exposure assessment included:

- Unless otherwise specified, 'as consumed' infant formula, on average, contains 3-MCPD and glycidol at the concentrations specified in Table A 1.1
- In the calculation of 3-MCPD and glycidol concentrations in infant formula, 1 litre of infant formula equals 1,050 grams
- infants aged 3 months are exclusively infant formula fed and there is no contribution to 3-MCPD or glycidol dietary exposures through foods and beverages other than infant formula
- the mean x 2 is a reasonable representation of a 90th percentile
- there is no contribution to 3-MCPD and glycidol dietary exposures through the use of complementary or other medicines (e.g. fish oil supplements)
- the GEMS/Food contaminants database concentrations for *3-MCPD fatty acid esters* and *glycidyl fatty acid esters* are in the form of 3-MCPD and glycidol
- the GEMS/Food contaminants database terms 'as consumed' and 'as is' for infant formula powder refer to the dry powder
- dietary exposures for 3 month old infants can be compared with the dietary exposures from JECFA for 0-12 month old infants, noting that different age groups are used in these assessments
- Analyses for 3-MCPD fatty acid esters and glycidyl fatty acid esters conducted between 2010 and 2015 are able to be compared with the analyses from the NZFS study (for both ESR and US FDA analytical datasets).

In relation to limitations, it is noted that this is a snap-shot survey with a non-representative sample of infant formula. Therefore, there are not enough data points to be able to determine distributions of the concentrations of the contaminants examined within brands or specific types of products. As such, the data can only be used as a whole with all samples combined to determine summary contaminant concentrations.

Appendix 2 – Comparison of analytical concentrations with international concentration data and regulations

ESR undertook a comparison of the analytical results for infant formula from the current survey with concentrations of 3-MCPD and glycidol from studies reported in the literature. ESR observed levels of 3-MCPD are similar to average results found in international surveys; levels of glycidyl esters are, on average, at the low end of those found in studies conducted on samples sourced overseas.

FSANZ also undertook a comparison of the results with international regulatory limits, and a comparison with international concentration data in the GEMS/Food contaminants database (available on the World Health Organization (WHO) website).

Comparison with European Union regulatory limits

The European Union (EU) regulatory limit for glycidyl esters (as glycidol) in infant formula, follow-on formula and foods for special medical purposes intended for infants and young children (liquid) is 6.0 µg/kg (as of 1July 2019) (European Commission 2018). While the mean concentration of glycidol from the US FDA analytical dataset (3.2 µg/kg) is below this limit, a small number of infant formula samples (3 / 56) had glycidol concentrations above the 6.0 µg/kg limit.

There is no EU regulatory limit for 3-MCPD in infant formula.

Comparison with international concentration data

For the NZFS infant formula analysis, analytical results for 3-MCPD and glycidol were reported by both labs as mg/kg of fat. An analysis of the fat content of the infant formula powder was also available. This fat concentration of each infant formula powder sample was used to convert the analytical values from a 'fat basis' to a 'infant formula powder' basis. Following this calculation, mean analytical results were derived (see

Table A2.1) for comparison with international infant formula powders. This was only conducted for the US FDA data set because it used a lower LOD and all samples had detectable concentrations. Where concentration data were available on an 'as consumed' formula basis, comparisons were also made with international data.

Table A2.1: 3-MCPD and glycidol concentrations in 'as prepared' infant formula and infant formula powder, using the US FDA analytical dataset

	US FDA analytical concentration (µg / kg)			
	3-MCPD		Glycidol	
	As consumed	Powder	As consumed	Powder
Mean	11.7	89.8	3.2	24.9
P50	7.7	60.3	1.6	12.1
Range	0.6 – 81.1	4.7 – 645	0 – 58.6	0 – 466

Note: all 56 analysed samples had quantified concentrations of 3-MCPD and glycidol (i.e. there were no ND results).

JECFA used the GEMS/Food contaminants database to derive summary 3-MCPD and glycidol concentrations for use in its assessment at its eighty-third meeting in 2016 (JECFA 2017). Summary concentration data were published in the monograph from the meeting (JECFA, 2018) and are included in the discussion further below.

FSANZ used the GEMS/Food contaminants database available on the WHO website (World Health Organization 2018) for this analysis. The final data to derive summary concentrations of 3-MCPD and glycidol in infant formula included in this analysis may differ to that used by JECFA in their assessment for a number of reasons. For example, the number of fields and some other detailed information provided in the publically available dataset may differ compared to the complete database and raw data available to JECFA. For data available in the GEMS/Foods contaminants database, 3-MCPD fatty acid esters analyses were conducted between 2010 and 2015, with the analyses for glycidyl fatty acid esters being conducted between 2012 and 2015, and the years of data analysed may have differed between FSANZ and JECFA. Data cleaning and editing, and data exclusions may have also been different depending on the purposes of the assessments.

Analytical methods have changed over time, and mitigation to decrease levels of 3-MCPD and glycidyl esters has also been occurring over time. Based on this and the assumptions and limitations noted above, a comparison of the survey results and international datasets can only provide a guide to the similarities in concentrations.

Concentrations of 3-MCPD were provided in the GEMS/Food contaminants database as *3-MCPD fatty acid esters* and glycidol as *glycidyl fatty acid esters*. It was not known to FSANZ from the level of detail available in the publically available dataset what the analytical method was or whether the free and esterified forms are expressed as 3-MCPD and glycidol or whether free forms have been converted to the esterified form. For the purposes of comparison with the US FDA analytical dataset, FSANZ assumed that the GEMS/Foods contaminants database concentrations are in the form of 3-MCPD and glycidol.

The results from the FSANZ analysis of the GEMS/Food contaminants database data are summarised in Table A2.2 for 3-MCPD and Table A2.3 for glycidol.

3-MCPD

The mean concentration of 3-MCPD in infant formula powder from the samples purchased in Australia and New Zealand (approx. 90 µg/kg) is lower than that for Hong Kong SAR (112 µg/kg) and Brazil (136 µg/kg). Since mean concentrations can be influenced by outliers in the data, median / P50 concentrations were also examined. The P50 concentration of 3-MCPD in samples purchased in Australia and New Zealand (approx. 60 µg/kg) is lower than that for Hong Kong SAR (87 µg/kg) and Brazil (115 µg/kg).

For concentrations of 3-MCPD in infant formula prepared ready for consumption, the mean concentration in Australian and New Zealand samples was 11.7 µg/kg. JECFA reported the mean 3-MCPD ester concentrations (expressed as 3-MCPD equivalents) in infant formulas or follow-on formulas that were used in the JECFA dietary exposure calculations in an 'as consumed' form. Mean concentrations ranged between not detected and 51 µg/kg. The concentrations for the non-European countries assessed (Brazil, Canada, Japan and the USA) had means in the range of 19-51 µg/kg. The mean concentrations reported by JECFA for specific European countries (France, Germany, Greece, Italy, the Netherlands, Spain) were all <1 µg/kg. The JECFA assessment only considered data from 2012 to 2016 from the GEMS/Food contaminants database.

From the FSANZ analysis of the GEMS/Food contaminants database for formulas as consumed, the mean concentrations in the Canadian infant formula samples was 40 µg/kg, and for samples for the World Health Organization (WHO) European Region (i.e. no specific country identified) was 649 µg/kg; both higher than Australian and New Zealand samples. The median concentration for Australia and New Zealand formulas ready to consume was 7.7 µg/kg, which was lower than those for the Canadian infant formula samples (28 µg/kg) and the WHO European Region samples (62 µg/kg).

Glycidol

The mean concentration of glycidol in infant formula powder samples purchased in Australia and New Zealand (24.9 µg/kg) is lower than that for samples from Brazil (195 µg/kg) in the GEMS/Food contaminants database. Since mean concentrations can be influenced by outliers in the data, median / P50 concentrations were also examined. The P50 concentration of glycidol in samples purchased in Australia and New Zealand (12.1 µg/kg) was lower than that for samples from Brazil (155 µg/kg).

The mean concentration in infant formula samples as consumed for Australia and New Zealand was 3.2 µg/kg. JECFA reported concentration data from their assessment from the GEMS/Food contaminants database (Brazil, Canada, Japan, USA) to be means between 5 and 35 µg/kg, with an additional two published studies from Europe with means of between 11 and 17 µg/kg. From the FSANZ analysis of the GEMS/Food contaminants database for formulas as consumed, the mean concentrations in the Canadian infant formula samples was 16.5 µg/kg and for WHO European Region was 41.4 µg/kg. The median concentration for Australia and New Zealand samples was 1.6 µg/kg and from the GEMS data were not detected for Canada and 13.5 µg/kg for the WHO European Region samples.

Conclusion

Based on the evaluation of ESR's comparison of concentration data from this survey with international concentrations from some available literature, and the FSANZ comparison of the concentration data with international data from the GEMS/Food Contaminants Database, FSANZ concludes that the results from this survey for both 3-MCPD and glycidol in infant formula are within the range of those found internationally.

Table A2.2: International 3-MCPD concentrations in infant formula, as derived by FSANZ using the GEMS/Food contaminants database

Country	Food	Form of food[♦]	No. samples	3-MCPD fatty acid esters concentration (µg / kg)[*⌃]		
				Mean	P50	Range
WHO European Region	Infant formulae powder	'As consumed'	49	649	62	ND – 3,030
Canada	Infant formulae powder	'As consumed'	21	40	28	0 – 89
Brazil	Infant formulae powder	'As is'	40	136	115	ND – 600
Hong Kong SAR	Infant formulae powder	'As is'	9	112	87	26 – 290

*   The GEMS/Food contaminants database uses the assumption that ND=0.

⌃   Assumed that free and esterified 3-MCPD are expressed as the free form.

♦   Assumed that 'as consumed' refers to made up ready to drink and 'as is' refers to the dry infant formula powder.

Table A2.3: International Glycidyl fatty acid esters[^] concentrations in infant formula, as derived by FSANZ using the GEMS/Food contaminants database

Country	Food	Form of food[♦]	No. samples	Glycidyl fatty acid esters concentration (µg / kg)[*^]		
				Mean	P50	Range
WHO European Region	Infant formulae powder	'As consumed'	17	41.4	13.5	ND – 134
Canada	Infant formulae powder	'As consumed'	20	16.5	ND	ND – 70
Brazil	Infant formulae powder	'As is'	40	195	155	ND – 750

*   The GEMS food database uses the assumption that ND=0.

^   Assumed that free and esterified glycidol are expressed as the free form.

♦   Assumed that 'as consumed' refers to made up ready to drink and 'as is' refers to the dry infant formula powder.