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

Supporting Document 1

RISK AND TECHNICAL ASSESSMENT REPORT

APPLICATION A1056
DIMETHYL ETHER AS A PROCESSING AID FOR DAIRY INGREDIENTS & PRODUCTS

Executive Summary

Dimethyl ether is proposed for use as an extraction solvent for the separation of lipids from a range of dairy foods. At ambient pressure (1 atmosphere), dimethyl ether exists as a gas at temperatures above −24° C. It is compressed, under high pressure, for use as a liquid extraction solvent in the course of food processing. The evidence assessed provided adequate assurance that the proposed use of dimethyl ether is technologically justified and has been demonstrated to be effective in achieving its stated purpose.

Animal and human data on inhalational exposure to dimethyl ether indicate a very low degree of toxicity. Adverse effects have been reported only at atmospheric concentrations greater than 20,000 parts per million (ppm) for acute exposure and 2,000 ppm for chronic exposure. Because of its low boiling point, dietary exposure to dimethyl ether will be negligible due to rapid evaporation of any residual dimethyl ether present in food following processing. A maximum permitted level (MPL) for dimethyl ether of 2 mg/kg is proposed which is equivalent to the MPL for the two ether extraction solvents that are currently permitted for use in food manufacture: diethyl ether and dibutyl ether. This MPL is considered to be appropriate. Dimethyl ether is considered to pose no public health and safety issues associated with its proposed use.

The overall conclusion of this risk and technical assessment is that the use of dimethyl ether as a processing aid is technologically justified and raises no public health and safety issues.

Table of Contents

1. Introduction

1.1 Background

On 24 November 2010, Food Standards Australia New Zealand (FSANZ) received an Application from Fonterra Co-operative Group Limited, New Zealand, seeking an amendment to the Table to clause 13 of Standard 1.3.3 of the *Australia New Zealand Food Standards Code* (the Code) to permit the use of dimethyl ether as an extraction solvent processing aid.

Dimethyl ether is proposed for the extraction of lipids from a range of dairy foods. The Code currently includes two ether compounds permitted as extraction solvents: diethyl ether and dibutyl ether. Both of these extraction solvents are permitted for use in the manufacture of all foods. Residual levels of extraction solvents may remain in treated foods and the maximum permitted level (MPL) for each of these extraction solvents is 2 mg/kg. For dimethyl ether, the Applicant's proposed MPL is also 2 mg/kg.

1.2 Risk Assessment Questions & Scope

The following questions are addressed in this Risk and Technical Assessment Report:

- Is the use of dimethyl ether as an extraction solvent technologically justified?
- Are foods produced through the use of dimethyl ether safe for consumption?

This Risk and Technical Assessment Report addresses the above questions in order and comprises the following components:

(1) Food Technology Assessment, which describes the chemical properties of the compound and considers whether the use of dimethyl ether as an extraction solvent is technologically justified.

(2) Hazard Assessment, which evaluates the intrinsic toxicity of dimethyl ether and the potential for residual dimethyl ether to remain in food produced through its use.

2. Food Technology Assessment

2.1 Dimethyl Ether Characteristics

The following information regarding the identity and chemical and physical properties of the extraction solvent dimethyl ether has been taken from the Application and various references.

2.1.1 Identity

Common name: dimethyl ether

Chemical name (IUPAC): methoxymethane

Other names: methyl ether, oxybismethane, dimethyl oxide, wood ether

C.A.S. registry number: 115-10-6

Molecular formula: C_2H_6O

Structural formula: CH_3-O-CH_3

Molecular weight: 46.069 g/mol

Marketing names: Dymel A®, Demeon D®, Propel

2.1.2 Chemical and physical properties

Dimethyl ether is a colourless gas at room temperature and pressure with a characteristic sweet ethereal odour. It is readily liquefied when compressed to produce a colourless liquid. It is highly flammable but is safe when handled appropriately.

Relevant chemical and physical properties for dimethyl ether are provided in Table 1.

Table 1: *Chemical and physical properties of dimethyl ether*

Characteristic	Property
Boiling point	-24.8°C at 1 atmosphere
Freezing point (melting point)	-141.5°C at 1 atmosphere
Flash point	-41°C
Density of liquid	0.665 g/cm^3 at 25°C, when liquefied
Density of gas	1.92 g/L at 1 atmosphere and 25°C
Octanol/water partition coefficient	Log KOW 0.10
Vapour pressure	4450 mmHg (593 kPa) at 25°C
Solubility in water	7% by weight at 18°C and 1 atmosphere

As can be seen from Table 1, dimethyl ether is partially soluble in water. It is also soluble in organic solvents that are relatively polar, such as methanol, ethanol, isopropanol, diethyl

ether, chloroform, acetone, chlorinated hydrocarbons and toluene.

Dimethyl ether is quite stable under an inert atmosphere. It also does not form any reaction products when it is used to treat food.

2.1.3 Production

Dimethyl ether is produced from the catalytic dehydration of methanol under conditions of high temperature and pressure.

2.1.4 Specifications

There are no specifications for dimethyl ether in the relevant monographs of clause 2 and 3 of Standard 1.3.4 – Identity and Purity. Therefore a specification monograph for dimethyl ether is required to be added to the Schedule of Standard 1.3.4.

FSANZ has amended the Applicant's proposed specification based on that used for aerosol grade dimethyl ether (used as a propellant for various uses for commercial care products such as hairspray). FSANZ has removed reference to appearance and odour and some parameters as these are not important for regulatory specifications. The proposed specification for dimethyl ether is provided in Table 2, to be added into the Schedule of Standard 1.3.4.

Table 2: *Proposed specification for dimethyl ether*

Characteristic	Specification
Purity	Minimum of 99.8%
Methanol	Not greater than 200 mg/kg

2.1.5 Methods of analysis

The Application contains details of an analytical method for dimethyl ether residues on treated food.

The method used is a gas chromatography method (GC) with detection via flame ionisation (FID) or mass spectroscopy. The Applicant notes that the limit of detection for their analytical method for determining dimethyl ether residues in treated food is 2 mg/kg, while the limit of quantification is estimated to be 5 mg/kg.

2.2 Technological function

Dimethyl ether is proposed by the Applicant as a new extraction solvent processing aid. Extraction solvent processing aids used during the manufacture and processing of foods are regulated by clause 13 – Permitted extraction solvents of Standard 1.3.3. There are already a number of permitted extraction solvents including two ethers, diethyl ether and dibutyl ether.

The Applicant, supported by scientific literature, claims dimethyl ether has a number of advantages over other extraction solvents that make it the solvent of choice for a number of specific uses.

The main purpose of using dimethyl ether as an extraction solvent is to extract lipids from both liquid and dry foods. The solvent has unique properties that make it an effective solvent for extracting both polar and non-polar lipids from food. One of these properties is that it can

extract lipids without denaturing the residual proteins in the food, which for some uses is a very important and useful attribute.

Dimethyl ether has unique extraction properties compared to other extraction solvents due to the following attributes:

- It is a gas at room temperature and pressure so residues can be easily removed from treated food.

- It is a powerful polar solvent when it is compressed to a liquid and used for extraction near its critical point (40-50° C).

- It is inert, so there are no by-products produced during extraction.

- Because it is used at relatively mild extraction conditions of temperature and pressure its use does not damage the food it is extracting, which retain most, if not all, of their natural properties such as appearance, flavour, solubility and bioactivity.

- Since it is partially soluble in water it is able to extract lipids from aqueous foods.

Dimethyl ether is considered a near-critical liquid when used as an extraction solvent. Near-critical liquids are found to be very powerful extraction solvents when used as pressurised extraction solvents because of the dual properties:

- They have the solute carrying capacity of a liquid (similar density).

- They have similar mass-transfer rates to gases (their viscosity is similar to gases and diffusivity is intermediate between a gas and a liquid).

The Application explains the general process used to extract solid food with dimethyl ether.

- The food is loaded into stainless steel extraction baskets.

- Dimethyl ether is liquefied by being compressed to 40 bar, heated to 40-50°C and then pumped through the vessels containing the food.

- The dimethyl ether phase containing the extracted and dissolved polar and non-polar lipids pass into one or more separation vessels.

- The separation vessel has its pressure lowered so that the lipids are no longer soluble in dimethyl ether and so precipitate out of solution. The lipid extract is recovered from the base of the vessel and the dimethyl ether gas is recovered, re-pressurised and recycled through the process.

- Once the extraction process has been completed the extraction vessels are depressurised, the dimethyl ether is recovered for reuse, the lipid extract is obtained and the lipid-depleted original food is also recovered from the extraction baskets.

There are two categories of food applications for which dimethyl ether could be used as an extraction solvent. The first is to remove polar lipids from the food so producing a lower fat version of the food. The second category is to extract a valuable lipid extract from one source of food and then use this as a value-added ingredient in other foods, often to produce food with added proposed health benefits.

The following examples of food that have been extracted by dimethyl ether in trials and pilot plant studies have been provided in the Application. As well there are various literature studies on the use of dimethyl ether as an extraction solvent for various foods.

2.2.1 Examples of use of dimethyl ether for dairy products

This Application has concentrated on the use of dimethyl ether as an extraction solvent for dairy based foods since the Applicant is a major dairy company.

The Application contains a list of foods (either the whole food or an ingredient added to the food) that may contain dairy ingredients derived from processing with dimethyl ether. It includes the following:

- Liquid milk and liquid milk based drinks (toddler milks only)
- Fermented and rennetted milk products (e.g. yoghurt and yoghurt based products)
- Dried milk, milk powder, cream powder (toddler milk powders only)
- Cheese and cheese products
- Ice cream and edible ices
- Chocolate and cocoa products
- Infant formula products
- Foods for infants
- Formula meal replacements and formulated supplementary foods

The Applicant proposes to be able to use dimethyl ether as an extraction solvent for two types of purpose:

1. To extract lipids from various dairy based foods to produce low fat versions of these products, to then be sold and marketed as such. Low fat dairy products and ingredients are a market category for consumers seeking a lower fat healthier alternative to standard higher fat products. Other advantages from producing lower fat products and ingredients are that they are more stable than their full fat counterparts due to the tendency of milk fat to oxidise and become rancid.

2. To extract a range of valuable polar lipids, such as phospholipids and glycolipids, that can be added to other foods as ingredients with possible health benefits. An example of such an extracted value-added ingredient in the Application is the so-called ‘dairy lecithin’. These extracts from milk are claimed to contain various polar lipids that could be viewed as value-added ingredients important for human health. They contain polar lipids such as sphingomyelin, phosphatidylserine, cerebrosides and gangliosides. These lipids are either unique to milk or are contained in greater concentrations than extracted from soy or egg. Further, the dimethyl ether extracts of dairy lipids (lecithin) are claimed to be free of chemical residues compared to standard unrefined or further refined lecithin produced using a variety of other chemical solvents and chemical treatments. The dimethyl ether extracts of dairy lecithin can be further treated with supercritical carbon dioxide to remove the neutral lipids (e.g. triglycerides and cholesterol) so producing a more refined dairy lecithin free of chemical residues where

the ingredients are not altered due to the treatment conditions used.

The Application and other references provided many examples supporting the advantages of using dimethyl ether as an extraction solvent compared to other approved extraction solvents such as carbon dioxide and propane. Examples noted included extracting lipids from whey protein concentrate dairy powders. The Applicant provided examples of using dimethyl ether to defat protein powder and to extract lipids from buttermilk powder.

Since dimethyl ether can also extract lipids from liquids it could be used to extract low fat whey protein concentrates and dairy lecithin from aqueous dairy streams such as whey protein concentrates. The Application notes that dimethyl ether has the unique ability to extract both polar and non-polar lipids from liquid dairy streams. In this case dimethyl ether does denature the globular whey proteins.

2.3 Food Technology Conclusion

Dimethyl ether has been shown to function as an extraction solvent for treating various food matrices. The technological function as an extraction solvent processing aid is to extract polar lipids from both solid and aqueous foods when it is used as a near critical liquid produced by compressing the gas and slightly heating it. The analysis concludes that dimethyl ether performs the technological function as an extraction solvent processing aid, which is the stated purpose of the Application.

3. Hazard Assessment

3.1 Introduction

The pharmacokinetic and toxicological properties of dimethyl ether have been investigated in inhalation studies in animals and humans (summarised below). EFSA recently published a scientific opinion on the safety of dimethyl ether when used as an extraction solvent in food manufacturing (EFSA 2009). US EPA has evaluated unpublished inhalation toxicity studies on dimethyl ether and concluded that there is no need to establish a maximum permissible level for residues of dimethyl ether arising from its use in pesticide formulations (US EPA 2005).

3.2 History of Use

Dimethyl ether has a long history of use as an aerosol propellant in personal care products and in pesticide formulations. The use of dimethyl ether as a food extraction solvent is recent (see Overseas Approvals, below).

3.3 Overseas Approvals

Dimethyl ether was recently approved for use in the European Union as a food extraction solvent (EC 2010). It is approved for the removal of fat from animal protein raw materials. The approved ‘maximum residual limit’ of dimethyl ether is 9 µg/kg in the defatted protein product. This limit corresponds to the detection limit of the analytical method provided to EFSA (EFSA 2009).

The US EPA has granted an exemption from the requirement of a tolerance for residues of dimethyl ether arising from its use as an inert ingredient (propellant) in pesticide formulations applied to growing crops or raw agricultural commodities (US EPA 2005).

3.4 Absorption, Distribution, Metabolism and Excretion

EFSA reviewed unpublished inhalation data in rats and stated that dimethyl ether is rapidly absorbed and distributed in various tissues and organs, reaching a steady state concentration 30 minutes after exposure. It is reported to be excreted unchanged, largely via exhaled air within a very short time, with levels returning to background levels within 90 minutes. Further, in rats exposed to 1000 ppm of dimethyl ether for 60 minutes, concentrations of dimethyl ether ranged from 14 to 22 mg/kg in muscle, fat, lungs, liver, spleen, kidney, heart, brain and blood. Concentrations in organs appeared to be directly proportional to atmospheric concentrations of dimethyl ether in the range 750 to 2000 ppm (EFSA 2009).

3.5 Toxicity

Unpublished inhalational toxicity studies have been evaluated by US EPA (2005) and EFSA (2009). Information from these evaluations is summarised below.

3.5.1 Acute toxicity

The most obvious acute effect of inhalational exposure to high concentrations of dimethyl ether is anaesthesia, as is the case with diethyl ether which was once used as a general anaesthetic. Narcotic effects have been reported in humans at an atmospheric concentration of 120000 ppm.

Rats exposed for four hours to an atmosphere containing dimethyl ether at a concentration of 20000 ppm did not show any effect, while the lethal concentration for 50% of the rats (LC_{50}) was 164000 ppm.

3.5.2 Sub-chronic toxicity

Four- and 13-week inhalation studies have been conducted in rats and hamsters. Animals were exposed for six hours per day. In both species there were no biologically significant effects on any of the parameters investigated (behaviour, body weight, clinical chemistry, haematology, urinalysis, gross pathology, organ weights and histopathology) at atmospheric concentrations as high as 20000 ppm, the highest concentration tested.

3.5.3 Chronic toxicity and carcinogenicity

A two-year inhalation study in rats exposed to atmospheres of dimethyl ether at concentrations up to 25000 ppm for six hours per day, five days per week, showed no evidence for carcinogenicity potential. Clinical chemistry, haematology and histopathology findings were unremarkable. A slight decrease in survival was observed in the 10000 ppm group compared to the control group. The next lowest concentration level of 2000 ppm was considered to be the no observed adverse effect concentration (NOAEC) in this study.

3.5.4 Genotoxicity

Unpublished *in vitro* and *in vivo* studies with dimethyl ether have shown no evidence for genotoxicity potential, with or without metabolic activation. Bacterial mutagenicity assays involved incubation of plates in atmospheres containing dimethyl ether at concentrations up to 120000 ppm. Concentrations tested *in vivo* were up to 20000 ppm.

3.5.5 Reproductive and developmental toxicity

Two unpublished studies in pregnant rats have been evaluated by US EPA and EFSA. Inhalation exposure to dimethyl ether was from days 6 to 15 of gestation. The maximum concentration tested was 20000 and 28000 ppm in the respective studies. The rat strain differed for each study (Wistar and Sprague-Dawley) and no teratogenic effects were observed in either strain. In Sprague-Dawley rats, an increased incidence of skeletal variations was reported at the two highest concentrations tested (5000 and 20000 ppm). The NOAEC was therefore proposed to be the next lowest concentration of 1250 ppm.

3.6 Residual Levels in Food

The Applicant proposes a maximum permitted level (MPL) for dimethyl ether of 2 mg/kg which is equivalent to the detection limit of the method described by the Applicant. It was stated that no residual dimethyl ether was detectable in the following: defatted protein powder and the lipid extract produced after extracting buttermilk powder with dimethyl ether, after further treatment such as standing at room temperature for 1 day, or fluidisation of the powder for at least 30 minutes using either compressed air or carbon dioxide. Incorporation of the ingredient in final food products will further dilute any residual dimethyl ether.

3.7 Dietary Exposure

FSANZ considers that a dietary exposure assessment for dimethyl ether is not necessary because of its low toxicity and the negligible levels that will be present in food.

3.8 Discussion

While the inhalational toxicity of dimethyl ether is not directly relevant to potential exposure to trace amounts of dimethyl ether present in food matrices, the data indicate that the compound is of very low toxicity with regards to all toxicological aspects investigated. Data on acute, sub-chronic, chronic and reproductive/developmental toxicity via the inhalation route indicate that adverse effects are only evident at exceedingly high atmospheric concentrations. Because of its low boiling point, dietary exposure to dimethyl ether will be negligible due to rapid off-gassing of any residual dimethyl ether present in food following processing.

The proposed MPL for dimethyl ether is 2 mg/kg, which is equivalent to the limit of detection of the method described by the Applicant. The presence of dimethyl ether in food at levels below the MPL raises no public health and safety concerns.

3.9 Hazard Assessment Conclusion

Data on inhalation exposure to dimethyl ether indicate a very low degree of toxicity and dietary exposure to the compound will be negligible.

The use of dimethyl ether as an extraction solvent processing aid raises no public health and safety issues.

4. References

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