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22 March 2006

DRAFT ASSESSMENT REPORT

PROPOSAL P277

REVIEW OF PROCESSING AIDS (OTHER THAN ENZYMES)

DEADLINE FOR PUBLIC SUBMISSIONS: 6pm (Canberra time) 17 May 2006
SUBMISSIONS RECEIVED AFTER THIS DEADLINE WILL NOT BE CONSIDERED
(See 'Invitation for Public Submissions' for details)

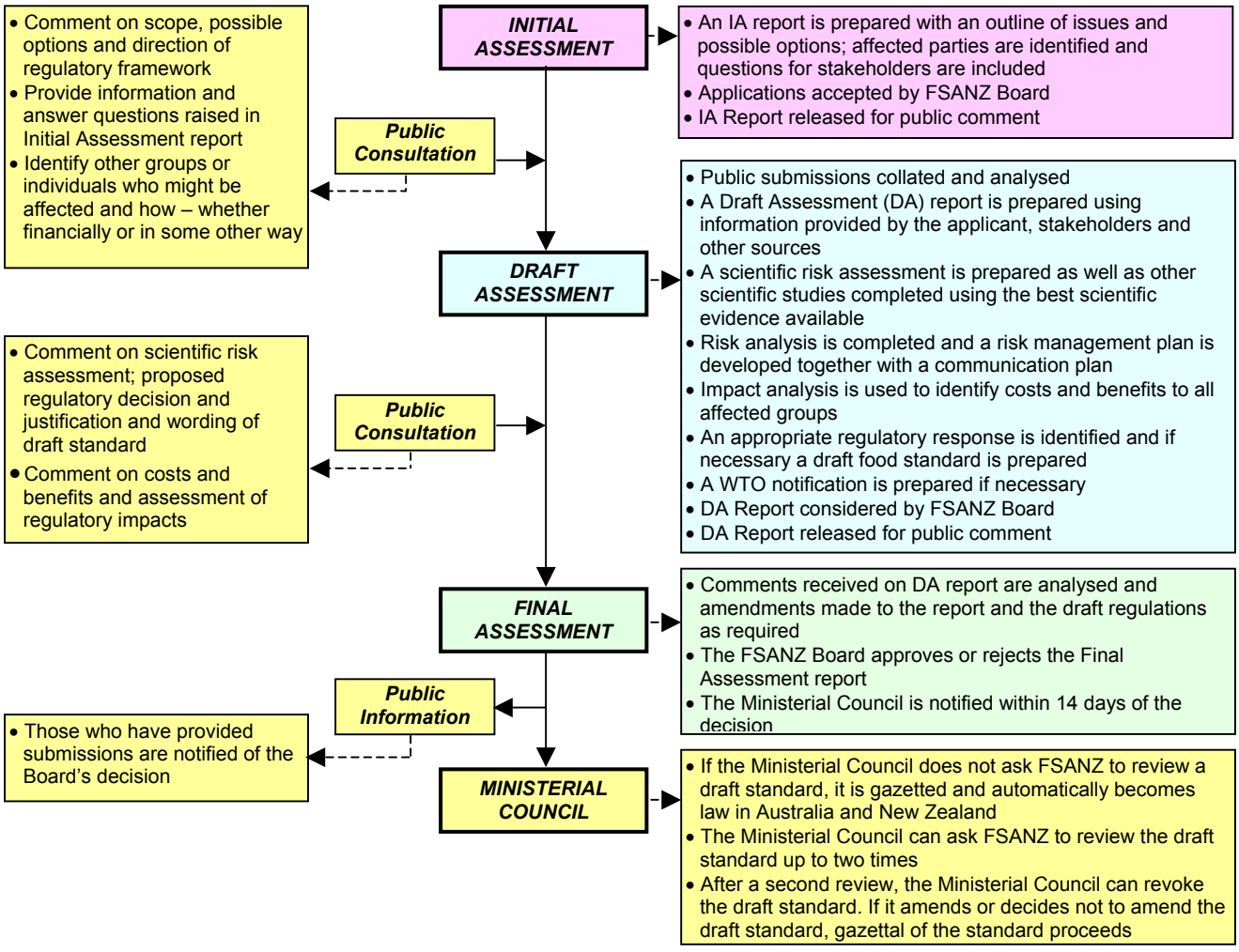
FOOD STANDARDS AUSTRALIA NEW ZEALAND (FSANZ)

FSANZ's role is to protect the health and safety of people in Australia and New Zealand through the maintenance of a safe food supply. FSANZ is a partnership between ten Governments: the Commonwealth; Australian States and Territories; and New Zealand. It is a statutory authority under Commonwealth law and is an independent, expert body.

FSANZ is responsible for developing, varying and reviewing standards and for developing codes of conduct with industry for food available in Australia and New Zealand covering labelling, composition and contaminants. In Australia, FSANZ also develops food standards for food safety, maximum residue limits, primary production and processing and a range of other functions including the coordination of national food surveillance and recall systems, conducting research and assessing policies about imported food.

The FSANZ Board approves new standards or variations to food standards in accordance with policy guidelines set by the Australia and New Zealand Food Regulation Ministerial Council (Ministerial Council) made up of Commonwealth, State and Territory and New Zealand Health Ministers as lead Ministers, with representation from other portfolios. Approved standards are then notified to the Ministerial Council. The Ministerial Council may then request that FSANZ review a proposed or existing standard. If the Ministerial Council does not request that FSANZ review the draft standard, or amends a draft standard, the standard is adopted by reference under the food laws of the Commonwealth, States, Territories and New Zealand. The Ministerial Council can, independently of a notification from FSANZ, request that FSANZ review a standard.

The process for amending the *Australia New Zealand Food Standards Code* is prescribed in the *Food Standards Australia New Zealand Act 1991* (FSANZ Act). The diagram below represents the different stages in the process including when periods of public consultation occur. This process varies for matters that are urgent or minor in significance or complexity.



INVITATION FOR PUBLIC SUBMISSIONS

FSANZ has prepared a Draft Assessment Report for Proposal P277; and prepared draft variations to the *Australia New Zealand Food Standards Code* (the Code).

FSANZ invites public comment on this Draft Assessment Report based on regulation impact principles and the draft variations to the Code for the purpose of preparing an amendment to the Code for approval by the FSANZ Board.

Written submissions are invited from interested individuals and organisations to assist FSANZ in preparing the Final Assessment for this Proposal. Submissions should, where possible, address the objectives of FSANZ as set out in section 10 of the FSANZ Act. Information providing details of potential costs and benefits of the proposed change to the Code from stakeholders is highly desirable. Claims made in submissions should be supported wherever possible by referencing or including relevant studies, research findings, trials, surveys etc. Technical information should be in sufficient detail to allow independent scientific assessment.

The processes of FSANZ are open to public scrutiny, and any submissions received will ordinarily be placed on the public register of FSANZ and made available for inspection. If you wish any information contained in a submission to remain confidential to FSANZ, you should clearly identify the sensitive information and provide justification for treating it as commercial-in-confidence. Section 39 of the FSANZ Act requires FSANZ to treat in-confidence, trade secrets relating to food and any other information relating to food, the commercial value of which would be, or could reasonably be expected to be, destroyed or diminished by disclosure.

Submissions must be made in writing and should clearly be marked with the word 'Submission' and quote the correct project number and name. Submissions may be sent to one of the following addresses:

Food Standards Australia New Zealand
PO Box 7186
Canberra BC ACT 2610
AUSTRALIA
Tel (02) 6271 2222
www.foodstandards.gov.au

Food Standards Australia New Zealand
PO Box 10559
The Terrace WELLINGTON 6036
NEW ZEALAND
Tel (04) 473 9942
www.foodstandards.govt.nz

Submissions need to be received by FSANZ by 6pm (Canberra time) 17 May 2006.

Submissions received after this date will not be considered, unless agreement for an extension has been given prior to this closing date. Agreement to an extension of time will only be given if extraordinary circumstances warrant an extension to the submission period. Any agreed extension will be notified on the FSANZ Website and will apply to all submitters.

While FSANZ accepts submissions in hard copy to our offices, it is more convenient and quicker to receive submissions electronically through the FSANZ website using the Standards Development tab and then through Documents for Public Comment. Questions relating to making submissions or the application process can be directed to the Standards Management Officer at the above address or by emailing slo@foodstandards.gov.au.

Assessment reports are available for viewing and downloading from the FSANZ website. Alternatively, requests for paper copies of reports or other general inquiries can be directed to FSANZ's Information Officer at either of the above addresses or by emailing info@foodstandards.gov.au.

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Executive Summary and Statement of Reasons

Introduction and background

FSANZ has prepared Proposal P277 to review Standard 1.3.3 – Processing Aids, excluding enzymes (clauses 15, 16 and 17 of Standard 1.3.3). Proposal P276 – Review of Enzyme Processing Aids, is currently reviewing the regulation of enzymes.

Standard A16, in the former Australian *Food Standards Code*, was formed as a result of Proposal P86 – Development of a Standard to regulate the Use of Processing Aids, which reviewed the toxicity of processing aids. This Standard was gazetted in the former Australian *Food Standards Code* in April 1996.

Standard 1.3.3 was established as a result of Proposal P188 – Review of Standard A16 - Processing Aids and was gazetted as part of the *Australia New Zealand Food Standards Code* (the Code) on 20 December 2000. Standard 1.3.3 was largely based on Standard A16 of the former Australian *Food Standards Code* with relevant New Zealand processing aids permissions from the New Zealand *Food Regulations 1984*. New Zealand permissions for processing aids were added without full evaluation or detailed consultation with food industries in New Zealand. The review of the processing aids standard was a high priority of the New Zealand Government at the time of the review of the two countries' food standards.

It is not the purpose of this Proposal to restructure Standard 1.3.3 in any major way or give new permissions, since the Standard was developed during the course of two earlier Proposals. However, this Proposal does allow interested parties to:

- provide new scientific evidence regarding the safety of currently permitted processing aids;
- make suggestions to correct any errors and review nomenclature;
- remove duplications and anomalies;
- improve consistency between this Standard and the rest of the Code; and
- improve the general operation and function of the Standard.

Safety of currently permitted processing aids

A total of forty chemical processing aids have been evaluated for their safety. The substances that were selected for evaluation had either:

- a maximum permitted level prescribed in the final food and not had their safety reviewed by FSANZ since 1993;
- had been relatively recently evaluated by the Joint FAO/WHO Expert Committee on Food Additives (JECFA), or other (inter) national governmental organisations; or
- had been identified by FSANZ, or other parties, as raising potential toxicological concerns.

The Safety Assessment Report proposed making a number of amendments to ensure consistency with the Australian and New Zealand drinking water guidelines, mainly related to maximum permitted limits. In addition, there are some amendments proposed due to safety concerns. These are:

- to exclude permission for chromium (VI) in the permission for chromium as a catalyst;
- to limit the permissions for potassium and sodium bromate as germination control agents in malting to the limit of determination for bromate rather than the current maximum permitted level of 0.1 mg/kg, to ensure there are no residues in food;
- to delete the permissions for trichloroethylene as an extraction solvent;
- to delete permissions for methylphenylpolysiloxane as a permitted antifoam agent; and
- to restrict the use of urea as a permitted microbial nutrient and microbial nutrient adjunct so as to exclude its use for alcoholic beverages.

Removing obsolete processing aids

The entry for permission for ethylene oxide in the Table to clause 14 as a sterilising agent ceased to have effect on 30 September 2003 so this permission will be deleted.

Correct errors, remove anomalies and improve consistencies within the Code

FSANZ stated in the Initial Assessment Report that the structure of Standard 1.3.3 will not be changed substantially by this Proposal.

However, FSANZ checked the consistency of nomenclature of similar chemicals used in the Standards that cover food additives and processing aids (Standard 1.3.1 and 1.3.3 respectively). A number of amendments have been proposed from this investigation to ensure nomenclature consistency.

Issues raised in submissions

The Initial Assessment Report for P277 was circulated for a round of public comment from 17 March 2004 till 26 May 2004. Three submissions were received which all supported the review.

One submission suggested that all safety reviews of processing aids should be done in accordance with the most recent Joint FAO/WHO Expert Committee on Food Additives (JECFA) safety assessments. FSANZ will take into account JECFA's reports but reserves the right to make an independent assessment of the data relevant to safety, including other more recent safety assessments, if appropriate.

The New Zealand Food Safety Authority (NZFSA) requested that the permission for urea as a microbial nutrient or microbial nutrient adjunct for wine manufacture should be removed, since urea can form ethyl carbamate (a suspected human carcinogen) by reaction with ethanol. The Safety Assessment supported this request and FSANZ proposes to remove the permission for urea as a microbial nutrient or microbial nutrient adjunct in alcoholic beverages. The permission for use of urea as a microbial nutrient or microbial nutrient adjunct in all other foods has been retained.

Public consultation

FSANZ seeks further comments from interested stakeholders on the following, but not exclusively limited, to:

- new scientific evidence regarding the safety of particular processing aids which may justify amending maximum permitted levels within Standard 1.3.3;
- recent international regulatory changes which may impact on specific processing aids;
- processing aids which are no longer used or likely to be used in the future;
- nomenclature of approved processing aids to better reflect current usage and international standards;
- errors and anomalies within the Standard; and
- the specific amendments proposed in this report.

External Advisory Group

An External Advisory Group (EAG) was established under section 43 of the FSANZ Act to assist FSANZ with this review Proposal. Members were drawn from experts from industry groups, regulatory agencies, academic and consumer groups with knowledge and expertise in food processing aids and their regulation. FSANZ staff involved with P277 – Review of Processing Aids (other than enzymes) met with the EAG in June 2004. Expert advice was received on the proposed amendments with further information received post this meeting.

FSANZ Decision

FSANZ has reviewed Standard 1.3.3 – Processing Aids, relating to processing aids (excluding enzymes) and has proposed a number of draft variations including some consequential draft variations to Standard 1.3.1 – Food Additives. These are proposed to ensure public health and safety, correct errors, remove duplications and anomalies, ensure consistency and improve the function of the Standard.

Statement of Reasons

The draft variations to Standard 1.3.1 – Food Additives and Standard 1.3.3 – Processing Aids of the Code are recommended for the following reasons:

- The proposed amendments are consistent with the protection of public health and safety.
- The proposed amendments ensure consistency within the Code and improved consistency, as far as is possible, with other international food standards.
- The proposed amendments have included information and consideration of submissions on issues received, as well as advice from an Expert Advisory Group, external to FSANZ.
- There will not be any expected added costs to food manufacturers, consumers or regulatory agencies arising from these proposed amendments.
- There are no other alternatives that are more cost effective than the proposed amendments to the Code.

FSANZ therefore seeks comments on this Draft Assessment Report, which will assist it in preparing the Final Assessment.

1. Introduction

Standard 1.3.3 – Processing Aids of the Code was largely developed as an inventory of usage of processing aids in Australia and is based on Standard A16 from the former Australian *Food Standards Code*.

Standard 1.3.3 is being comprehensively reviewed because the full list of processing aids permissions has not been formally evaluated. Standard 1.3.3 is a joint Australia and New Zealand Standard for processing aids. The Standard was developed during the review of the former Australian *Food Standards Code* and the New Zealand *Food Regulations 1984*. New Zealand permissions for processing aids from the New Zealand *Food Regulations 1984* were added without full evaluation or detailed consultation with food industries from New Zealand. The review of the processing aids standard was a high priority of the New Zealand government at the time of the review of the two countries' food standards.

This Proposal, P277, is to review permissions and evaluate processing aids other than enzymes in Standard 1.3.3. A separate Proposal P276 – Review of Enzyme Processing Aids, is currently reviewing the regulation of enzymes. The Initial Assessment Report for Proposal P276 was released in December 2003 for public comment, while the Initial Assessment Report for this Proposal was released for public comment from 17 March 2004 until 26 May 2004.

2. Regulatory Problem

2.1 Current Standard

The regulation of processing aids for all food in the Code is covered by Standard 1.3.3 – Processing Aids. This Standard regulates the use of processing aids in food manufacture, prohibiting their use in food, unless there is a specific permission within this Standard. Processing aids are defined in clause 1 as:

processing aid means a substance listed in clauses 3 to 18, where –

(a) the substance is used in the processing of raw materials, foods or ingredients, to fulfil a technological purpose relating to treatment or processing, but does not perform a technological function in the final food; and

(b) the substance is used in the course of manufacture of a food at the lowest level necessary to achieve a function in the processing of that food, irrespective of any maximum permitted level specified.

The various types of processing aids have been grouped into classes and regulated via Tables to clauses 3-18. This Proposal is to review all of Standard 1.3.3 excluding clauses 15, 16 and 17 which are permitted enzymes of animal, plant and microbial origin respectively (and which are the topic of a separate concurrent Proposal, P276).

3. Objective

The objective of this Proposal is to ensure that Standard 1.3.3 provides appropriate permissions for processing aids used in Australia and New Zealand and that any residues in food resulting from the use of processing aids are safe.

In developing or varying a food standard, FSANZ is required by its legislation to meet three primary objectives which are set out in section 10 of the FSANZ Act. These are:

- the protection of public health and safety;
- the provision of adequate information relating to food to enable consumers to make informed choices; and
- the prevention of misleading or deceptive conduct.

In developing and varying standards, FSANZ must also have regard to:

- the need for standards to be based on risk analysis using the best available scientific evidence;
- the promotion of consistency between domestic and international food standards;
- the desirability of an efficient and internationally competitive food industry;
- the promotion of fair trading in food; and
- any written policy guidelines formulated by the Ministerial Council.

The main section 10 objectives that this Proposal will meet are to ensure:

- the protection of public health and safety and that any amendments to the Standard are based on the best available scientific evidence;
- consistency, as far as possible, between domestic and international regulations of processing aids; and
- to ensure an efficient and internationally competitive food industry.

4. Background

4.1 Historical Background

The then National Food Authority (NFA) proposed (Proposal P86 – Development of a Standard to Regulate the Use of Processing Aids) the development of a standard for processing aids for Australia in 1995 (Standard A16). Proposal P86 was considered by the NFA in 1995 and Standard A16 was gazetted in the former Australian *Food Standards Code* in April 1996, after adoption by the Ministerial Council.

The reasons given by the NFA in April 1996 for the adoption of Standard A16 to provide permission for the use of processing aids during food processing and production in Australia were:

- processing aids were a special category of food additives which facilitate processing and production but did not perform any function in the final food product;

- traditionally processing aids had not been listed in the former Australian *Food Standards Code* (except in a number of standards such as the standards for alcoholic beverages) and their regulatory status was uncertain;

- prior to the inception of the NFA, the National Health and Medical Research Council (NHMRC) food committees had commenced work in this area and this Proposal was consistent, as far as possible, with the policy adopted in developing the NHMRC Guidelines for Processing Aids;

- a Standard for processing aids had been developed in order to ensure that all substances used in the preparation of food were standardised in the Australian *Food Standards Code*;

- the Standard was intended to maintain public health and safety and all entries in the schedule had undergone an evaluation to ensure that there were no toxicological concerns with permitting their use; and

- the Standard was intended to reflect current use and prohibit inappropriate use of processing aids.

Proposal P86 included a full toxicology evaluation of the processing aids incorporated into Standard A16. The Toxicology Report noted that the majority of processing aids are either not present in the final food or present at such low levels as not to constitute a concern for public health and safety. However, there were a number of processing aids that did leave residues in food or which have a demonstrated toxicity and these were fully evaluated. This was first to ensure they were suitable as food processing aids, and secondly, that the level present in food was safe. This Toxicology Report provided the scientific justifications for maximum permitted levels set for processing aids, if they were warranted on toxicity grounds.

A subsequent Proposal by the then Australia New Zealand Food Authority (ANZFA), P188 – Review of Standard A16 – Processing Aids, was raised as part of its review of the Australian *Food Standards Code.* This led to the development of Standard 1.3.3 of the Code. The Preliminary Assessment Report for Proposal P188 was released for public comment in October 1998, while the Full Assessment Report was released for public comment in August 1999. The Inquiry Report was released in December 1999 and the subsequent Standard, Standard 1.3.3, was gazetted on 20 December 2000 (as part of the *Australia New Zealand Food Standards Code*).

The objective of Proposal P188 was to update Standard A16 to recognise current practices in Australia and to take account of New Zealand requirements from the New Zealand *Food Regulations 1984*, in order to implement an *Australia New Zealand Food Standards Code*. There was no comparable standard for processing aids in the New Zealand *Food Regulations 1984*. Processing aids were either regulated as food additives or not specifically regulated. As Standard A16 had only recently been included in the Australian *Food Standards Code* it was considered that a detailed review for Australia would not be required.

4.2 Background on the regulation of processing aids internationally

The current system of regulation of processing aids in the Code for Australia and New Zealand differs from the regulation in many other countries.

Attachment 5 (The Regulation of Processing Aids Internationally) provides a brief summary of how processing aids are regulated in different countries and the similarities and differences with approaches.

Processing aids are regulated in the Code for Australia and New Zealand by being incorporated into a specific horizontal standard (meaning that the Standard applies across the whole of the food supply), which is different to systems used in many other countries, as well as for standards promulgated by the Codex Alimentarius Commission (Codex).

Codex has an Inventory of Processing Aids (IPA), but this list is not a standard, it does not have official status and is not currently up-to-date or complete.

Processing aids are regulated in Canada and the USA via different mechanisms. Canada does not have a separate standard for processing aids but processing aids are considered as a subset within the category of 'food additives', which are regulated.

The USA also does not appear to regulate processing aids in a separate standard. The Code of Federal Regulations regulates food chemicals, which include food additives (both direct and indirect food additives) and processing aids.

Some substances regulated as processing aids in Australia and New Zealand are considered (and therefore regulated) as food additives in Europe (European Union). Processing aids are regulated under Council Directive 88/344/EEC, however this directive only covers extraction solvents allowed in the production of foodstuffs and food ingredients. Processing aids fall outside the scope of the European Union Council Directives for food additives.

5. Relevant Issues

5.1 Safety of currently permitted processing aids

The Safety Assessment Report (**Attachment 2**) contains an assessment conducted on the processing aids listed in Standard 1.3.3. A total of forty chemical processing aids have been evaluated for their safety. The substances that were selected for evaluation had either:

- a maximum permitted level prescribed in the final food and not had their safety reviewed by FSANZ since 1993;
- had been relatively recently evaluated by the Joint FAO/WHO Expert Committee on Food Additives (JECFA), or other (inter) national governmental organisations; or
- had been identified by FSANZ, or other parties, as raising potential toxicological concerns.

Each of the selected substances was reviewed, using evaluation reports from other international organisations or agencies, where these were available. In general, substances that were determined to only leave relatively low residue levels in the final food, and/or that were found to have low oral toxicity were considered to raise no toxicological concerns.

Substances were considered to raise toxicological concerns if they were found to produce severe adverse effects, including carcinogenicity, in experimental animals where such effects could also reasonably be expected in humans, or where evidence already existed for such effects in humans.

For those substances used as processing aids in packaged water and water used as an ingredient in other foods, the maximum permitted levels were compared to the drinking water levels specified in the Australian Drinking Water Guidelines and the Drinking-water Standards for New Zealand. As packaged water has the potential to be used as a substitute for drinking water, it is important that the maximum permitted levels reflect the levels that have been established on health grounds for drinking water.

A summary of the conclusion reached for each substance evaluated is provided in Table 1.

Table 1: Summary of safety assessment conclusions

Substance	Safety assessment conclusions	Explanation
Acetone	No toxicological concerns	Readily metabolised at low levels, only minimal residues expected from use, substance has low oral toxicity at low levels of exposure.
Benzoic acid Benzyl alcohol	No toxicological concerns	Rapidly metabolised, long-term effects only seen following exposure to high levels, only minimal residues expected from use.
Benzoyl peroxide	No toxicological concerns	As per benzoic acid.
Butane Isobutane Propane	No toxicological concerns	Only low residues in food, substances of low oral toxicity
1-Butanol	No toxicological concerns	Low residue levels, metabolised to innocuous products, low oral toxicity.
Chlorine Calcium hypochlorite Sodium hypochlorite	No toxicological concerns but maximum permitted levels for use in packaged water should be brought into conformity with drinking water guidelines levels for Australia and New Zealand	Very few toxic effects associated with drinking water containing high chlorine levels. Main issue is the formation of disinfection by-products and their potential to cause adverse effects, such as cancer, in humans. None of the chlorination by-products studied to date found to be a potent carcinogen at concentrations normally found in drinking water.
Chlorine dioxide Sodium chlorite	No toxicological concerns but maximum permitted level for chlorine dioxide in packaged water should be brought into conformity with drinking water guideline levels for Australia and New Zealand.	No adverse effects observed in adults and neonates consuming water disinfected with chlorine dioxide. No evidence for carcinogenicity of chlorine dioxide and chlorite.

Substance	Safety assessment conclusions	Explanation
Chromium	There are toxicological concerns because the current permission does not specifically exclude the use of hexavalent chromium. No toxicological concerns with the use of other chromium compounds as catalysts.	Most toxic effects have been associated with hexavalent chromium compounds. Trivalent chromium appears to have low oral toxicity. Hexavalent chromium is a human carcinogen by the inhalation route. Potential carcinogenicity via oral exposure is unclear because of limited epidemiological and toxicological data.
β-Cyclodextrin	No toxicological concerns	Only very limited use, likely to result in only low residues. Substance has low oral toxicity.
Ethyl acetate	No toxicological concerns	Only limited toxicological information available. Ethyl acetate completely metabolised to innocuous products (ethanol and acetate), which are normal components of intermediary metabolism.
Hexanes	No toxicological concerns	Only low residue levels expected, adverse effects typically only at high levels of exposure.
Hydrogen peroxide	No toxicological concerns	Unlikely to leave significant residues, low levels of hydrogen peroxide not toxicologically significant.
Isopropyl alcohol	No toxicological concerns	Efficiently metabolised to innocuous substances normally found endogenously, does not accumulate in the body, metabolites do not raise toxicological concerns, low oral toxicity in animal studies.
Methylene chloride	No toxicological concerns providing use is limited to ensure residues in food are as low as practicable.	Relatively low oral toxicity in animals but some suggestive, although inconclusive, evidence of carcinogenicity.
Methylphenylpolysiloxane	Insufficient data to undertake safety assessment.	
Mineral oils Mineral oil based greases Paraffin	Difficult to determine if there are toxicological concerns because of uncertainties in the animal data. Current permissions should be maintained but reviewed once JECFA has finalised its evaluation. The nomenclature used in the Code for mineral oils should also be reviewed in light of discrepancies with that used by JECFA.	Wide range of systemic effects seen in studies with rats. Strain of rat used may not be appropriate model for humans. JECFA evaluation still ongoing, more studies required.
Nickel	No toxicological concerns	Substance has low systemic toxicity by the oral route, no evidence for carcinogenicity in either humans or experimental animals, only low residues in food expected.

Substance	Safety assessment conclusions	Explanation
Polyelectrolytes (acrylamide monomers)	No toxicological concerns however level of acrylamide should be kept as low as possible. The maximum permitted level for acrylamide monomers in packaged water should be brought into conformity with drinking water guideline levels for Australia and New Zealand.	Acrylamide is neurotoxic and carcinogenic by the oral route. The contribution to the total acrylamide intake from the use of polyelectrolytes as a processing aid would be relatively minor compared to the levels of acrylamide that can form in certain foods during frying and baking.
Potassium bromate Sodium bromate	There are toxicological concerns with the use of potassium and sodium bromate. Continued use of potassium and sodium bromate in malting would be acceptable only if the bromate levels remain below the limit of determination in the final food (beer).	Convincing evidence of renal toxicity and carcinogenicity in rats. Bromate also appears to be a potent genotoxic substance *in vivo*.
Potassium ethoxide Sodium ethoxide Sodium methoxide	No toxicological concerns.	No safety data available however the available information on their chemistry when used as catalysts indicates these compounds are converted to innocuous by-products (hydroxides and methanol or ethanol) following completion of the reaction, which are water soluble and removed during subsequent purification steps. Only very low residues would be expected to remain in the final product, if at all.
Silver ions	No toxicological concerns	Only poorly absorbed by gastrointestinal tract. No extensive systemic effects documented in either experimental animals or humans.
Sodium glucoheptonate	There may be toxicological concerns with maintaining a current maximum permitted level for sodium glucoheptonate measured as cyanide at 1 mg/kg. This level is significantly higher than the drinking water guideline level for cyanide of 0.08 mg/L established for Australia and New Zealand on the basis of health considerations. The maximum permitted level for cyanide should be brought into conformity with the drinking water guideline levels for Australia and New Zealand.	Cyanide has high acute toxicity, and may also have effects at lower levels following chronic exposure.
Sodium metabisulphite Sodium sulphite Sulphur dioxide	No toxicological concerns. *Sulphite sensitivity is unrelated to the general toxicity of sulphites. The risk to sulphite sensitive people from sulphites in food is managed through food labelling.*	Sulphites have a low systemic toxicity. Most common effects in animals are gastric lesions. Effect probably dependent on sulphite concentration in the stomach rather than daily dose. Contribution to the total intake of sulphites from use as processing aids likely to be minor compared to use as food additives.

Substance	Safety assessment conclusions	Explanation
Sodium nitrate	No toxicological concerns. The maximum permitted level should be brought into conformity with the drinking water guideline level for Australia and New Zealand. The drinking water guideline level has been established to protect bottle fed infants less than 3 months of age.	Nitrate is converted to nitrite once absorbed. Excess nitrite in humans may lead to impaired ability for haemoglobin to transport oxygen to tissues. Young infants particularly susceptible. Nitrate may react with other substances in the body to form *N*-nitroso compounds, some of which are known to be carcinogenic in animals.
Toluene	No toxicological concerns	Use as extraction solvent expected to result in minimal residues in food, and the contribution from food to the total toluene intake is considered to be minor. Low levels of toluene readily metabolised by humans. Adverse effects observed in rodent studies tend to occur at relatively high levels of exposure.
Trichloroethylene	There are toxicological concerns with its use as an extraction solvent. Use as an extraction solvent should be limited to ensure residues in food are as low as practicable.	Rapidly absorbed by the gastrointestinal tract, and rapidly metabolised. Many of its metabolites are themselves toxic. The primary targets for toxicity are the liver and kidneys. Effects on central nervous system and heart also observed after acute exposure to high levels. A multisite carcinogen in experimental animals. Suggestive, although inconclusive, evidence for increased risk of cancer from some epidemiological studies in humans.
Urea	There are toxicological concerns with the use of urea as a microbial nutrient and microbial nutrient adjunct for the manufacture of alcoholic beverages. The use of urea should be limited to exclude alcoholic beverages. There are no toxicological concerns with its use to manufacture concentrated gelatine solutions.	Urea reacts with ethanol in certain situations to produce ethyl carbamate (urethane). Ethyl carbamate is genotoxic and has been found to be a multisite carcinogen in all species tested, including non-human primates. Urea not the only precursor for ethyl carbamate formation but is the major precursor in alcoholic beverages. JECFA found that the ethyl carbamate intake from alcoholic beverages is of concern and recommended that measures to reduce the ethyl carbamate content in some alcoholic beverages should continue.

5.2 Removing any obsolete processing aids

FSANZ is using the opportunity of the current review of processing aids to ask if there are any obsolete processing aids which are no longer used, or likely to ever be used again in the food industry, in either Australia or New Zealand. Possible use in the rest of the world must also be considered since trading partners export food products to both Australia and New Zealand and these products must also meet the requirements of the Code.

FSANZ requested information from submitters on this point in the Initial Assessment Report. One submitter made comment that they do not support the removal of processing aids that may be considered obsolete, since it is impossible to determine when a processing aid may be required for use in the future, and to predict for what purposes.

Also removing 'obsolete' processing aids for Australia and New Zealand industries from the Code may cause trade issues if other countries still use these processing aids in food exported to either country. A submission for the concurrent Review of Enzyme Processing Aids (Proposal P276) cautioned that enzymes (or processing aids) should only be obsolete if they are not currently used in any country (not just Australia or New Zealand) to not inhibit international trade.

An obsolete processing aid permission which will be removed as part of this Proposal is that for ethylene oxide as a sterilisation agent in the Table to clause 14. The entry states that this permission ceased on 30 September 2003 so it is only a notice about an obsolete permission which should now be deleted.

5.3 Correct errors, remove anomalies and improve consistencies within the Code

It is not anticipated that the structure of Standard 1.3.3 will be changed substantially by this Proposal. The structure of the Standard was resolved during two earlier proposals; Proposal P86, that developed A16 in the former Australian *Food Standards Code*, and Proposal P188 which developed the current Standard 1.3.3 in the Code. Both these Proposals involved extensive consultation with various interested parties from food industries and regulatory agencies. There were full rounds of public consultations and submissions received to both Proposals.

The Initial Assessment for this Proposal asked interested parties to make suggestions to correct any errors, clarify nomenclature, remove duplications and anomalies, improve consistency between this Standard and the rest of the Code and improve the general operation and function of the Standard. No submissions were received addressing the overall structure of the Standard.

The consistency between the Standards that cover food additives and processing aids (Standard 1.3.1 – Food Additives and Standard 1.3.3 – Processing Aids) is particularly important since they contain many similar and some of the same chemicals. They were both developed independently of each other and at different times during the development of the Code. Therefore the nomenclature of chemicals in Schedule 2 of Standard 1.3.1 was compared with those in Standard 1.3.3, as well as those in the Codex lists[1]. Proposed amendments that resulted from these investigations, as well as discussions and communications, both internally and, with an External Advisory Group (see section 8.2) are listed in **Attachment 4**.

This Proposal is not a vehicle to give approvals for new, currently non-approved processing aids. Applicants would still need to make applications to request permissions to use new processing aids in the Code. Information on how to make an application to FSANZ is contained on FSANZ's website at www.foodstandards.gov.au, specifically at http://www.foodstandards.gov.au/standardsdevelopment/informationforapplic559.cfm.

[1] Codex Alimentarius document, 'Class Names and the International Numbering System for Food Additives', (2001) formerly found at, but not currently available at: ftp://ftp.fao.org/codex/standard/en/CXG_036e.pdf

5.4 Discussion of specific proposed amendments

5.4.1 Remove duplication

The food additives listed in Schedule 2, Miscellaneous additives permitted in accordance with GMP in processed foods specified in Schedule 1, of Standard 1.3.1 – Food Additives are also generally permitted processing aids under the approval contained in clause 3(b) of Standard 1.3.3 – Processing Aids. Therefore, this list of chemicals was compared to the list of permitted processing aids in the Tables to clauses 3-14 and 18 of Standard 1.3.3. It was found that there was duplication, sometimes when the same chemical was listed under different names in each list. To remove this duplication any processing aid listed in Standard 1.3.3 that is also listed in Schedule 2 of Standard 1.3.1 will be deleted.

Subclause 3(a) of Standard 1.3.3 allows that foods, including water, are considered generally permitted processing aids. So any processing aids listed within Standard 1.3.3 that are foods can be deleted to prevent duplicate permissions. These are noted in the Table below.

Those processing aids to be removed are listed in Table 2, with their corresponding name in Schedule 2 (or other reason) listed.

Table 2: Processing aids to be removed due to duplication

Processing aid to be deleted from Standard 1.3.3	**Corresponding name of the same chemical listed in Schedule 2 of Standard 1.3.1 (or other reason)**
Aluminium stearate	Aluminium, calcium, sodium, magnesium, potassium and ammonium salts of fatty acids (INS 470)
Calcium stearate	
Magnesium stearate	
Potassium stearate	
Potassium oleate	
Kaolin	Aluminium silicate (INS 559) (kaolin is an aluminium silicate)
Potassium hydrogen tartrate	Potassium tartrate (INS 336) Consequential amendment to the plural, potassium tartrates.
Dimethylpolysiloxane	Polydimethylsiloxane (INS 900a)
Polysorbate 60	Polyoxyethylene (20) sorbitan monostearate (INS 435)
Polysorbate 65	Polyoxyethylene (20) sorbitan tristearate (INS 436)
Polysorbate 80	Polyoxyethylene (20) sorbitan monooleate (INS 433)
Sodium stearoyl lactylate	Sodium lactylates (INS 481) (sodium lactylates includes sodium stearoyl lactylate)
Sodium stearoyl lactate	Sodium lactylates (INS 481) (sodium stearoyl lactate is an alternative name for sodium stearoyl lactylate)
Talc	Magnesium silicates (INS 553) (talc is a magnesium silicate)
Anhydrous sodium sulphate	Sodium sulphate (INS 514) Consequential amendment to the plural, sodium sulphates
Ethyl alcohol – from Table to clause 10	listed as a generally permitted processing aid in Table to clause 3 of Standard 1.3.3
Dextrin	Dextrins, white & yellow, roasted starch, (INS 1400)
Trehalose	a novel food, hence a food, and listed in the Table to clause 2 of Standard 1.5.1 – Novel Foods.

5.4.2 Amend nomenclature to ensure consistency

One aim of the review Proposal was to ensure nomenclature consistency of chemicals listed as food additives and processing aids within the Code. This is especially relevant to ensure the nomenclature of the same chemical in Standard 1.3.1 is identical to that in Standard 1.3.3. As indicated in Table 2 in the previous section there are a number of instances where there is duplication between these Standards but the substances have different names. That situation is resolved by deleting the reference, where warranted, to the processing aid permission.

FSANZ decided, where possible, to use the nomenclature used by the Joint WHO/FAO Expert Committee of Food Additives (JECFA), for processing aids. Therefore it is proposed to amend the nomenclature of a number of processing aids, as detailed in Table 3 below. One amendment is also for a typographical mistake.

Table 3: Amended nomenclature of processing aids

Current processing aid nomenclature in Standard 1.3.3	**Proposed amended nomenclature, to be consistent with JECFA (or other reason)**
Polyelectrolytes (acrylamide monomers)	Polyacrylamide (polyelectrolytes), to give more information about what the processing aid is. The acrylamide monomer is the contaminant of concern.
Polypropylene glycol alginate	Propylene glycol alginate (INS 405)
Polyoxyethylene 40 monostearate	Polyoxyethylene 40 stearate (INS 431)
Sodium fumate	Sodium humate This is a typographical mistake. It was listed as sodium humate in the former *Australian Food Standards Code*, Standard A16 – Processing Aids.

5.4.3 Amend limits to ensure consistency

FSANZ proposes to amend the processing aids used in packaged water and in water used as an ingredient in other foods permissions to be consistent with the Australian and New Zealand drinking water guidelines (Australian Drinking Water Guidelines[2] and Drinking-water Standards for New Zealand 2005[3]).

The proposed amendments to the Table to clause 11 of Standard 1.3.3 to ensure consistency with the Australian and New Zealand drinking water guidelines are listed in Table 4.

[2]Australian Drinking Water Guidelines (2004) National Water Quality Management Strategy, National Health and Medical Research Council http://www.nhmrc.gov.au/publications/_files/awgfull.pdf

[3] Drinking-water Standards for New Zealand (2005), Ministry of Health, New Zealand http://www.moh.govt.nz/moh.nsf/0/12F2D7FFADC900A4CC256FAF0007E8A0/$File/drinkingwaterstandardsnz-2005.pdf

Table 4: Amendments to the Table to clause 11 to ensure consistency with Australian and New Zealand drinking water guidelines

Substance	Current maximum permitted limits (mg/kg)	Proposed maximum permitted limits (mg/kg)
Calcium hypochlorite	10 (available chlorine)	5 (available chlorine)
Chlorine	10 (available chlorine)	5 (available chlorine)
Chlorine dioxide	10 (available chlorine)	1
Polyelectrolytes (acrylamide monomers) Change name to: Polyacrylamide (polyelectrolytes)	GMP	0.0002 (acrylamide monomer)
Sodium hypochlorite	10 (available chlorine)	5 (available chlorine)
Sodium nitrate	GMP	50 (as nitrate)
Styrene-divinylbenzene cross-linked copolymer	GMP	0.03 (styrene)

5.4.3.1 Polyacrylamide (polyelectrolytes)

Currently there is a permission to use polyelectrolytes in the Table to clause 11 (permitted processing aids used in packaged water and in water used as an ingredient in other foods).

Polyelectrolytes are polymers that are used as flocculating agents to clarify water. Polyelectrolytes that are applied as flocculants are mainly water-soluble polyacrylamides, polyphosphates and modified natural polymers[4]. Therefore, polyelectrolytes are not exclusively polyacrylamides. Polyelectrolytes are used to aggregate fine suspended or colloidal particles together to form larger particles which are then removed by filtration or sedimentation.

Both the Australian Drinking Water Guidelines[2] and the Drinking-water Standards for New Zealand (2005)[3] contain limits for the acrylamide monomer which is the substance of safety concern. The Safety Assessment Report concludes that the levels of acrylamide should be kept as low as possible. A maximum permitted level for acrylamide monomer of 0.0002 mg/L should be established to make it consistent with the Australian Drinking Water Guidelines. (The New Zealand limit for acrylamide monomer is 0.0005 mg/L).

The acrylamide monomer is the substance of concern for toxicity, but it is not the processing aid that is used. The term polyelectrolytes is proposed to be retained in the entry because a number of people will be familiar with its use to treat water.

Polyacrylamide is also the term referred to rather than polyelectrolytes in specifications, so it is proposed to change the term to polyacrylamide (polyelectrolytes) in the Code.

5.4.4 Amend limitations due to safety issues

A safety assessment was performed on individual processing aids that may have a safety concern if used in food, or may require more restricted permissions (Safety Assessment Report is found at **Attachment 2,** and the summary contained in section 5.1).

The proposed amendments due to safety concerns are listed in Table 5 along with the explanation.

[4] Encyclopedia of Food Sciences and Nutrition, Second Edition, Academic Press, (2003), p 2532

Table 5: Amendments due to safety concerns

Substance	Current permission	Proposed permission	Explanation
Chromium	as a catalyst (Table to clause 5)	Chromium (excluding chromium VI)	Safety concerns related to chromium VI.
Methylphenylpolysiloxane	as a antifoam agent (in Table to clause 4)	Delete permission	Insufficient data to undertake a risk assessment. Seek submissions on whether it is used and required as an antifoam agent.
Potassium bromate and sodium bromate	For germination control in malting (in the Table to clause 14) to a limit of 0.1 mg/kg	Change the maximum permitted level to the limit of determination of bromate	Safety concerns related to the use of bromate. It is proposed to allow no detectable residues of bromate in the final treated foods.
Sodium ethoxide and Sodium methoxide	as generally permitted processing aids in the Table to clause 3.	Remove them from the Table to clause 3, as generally permitted processing aids. Add them into the Table to clause 5, as catalysts, with a maximum permitted limit of 1.0 mg/kg, not GMP, to be comparable to potassium ethoxide	They are catalysts, like potassium ethoxide, and should not be listed as generally permitted processing aids. The safety assessment indicated no safety concerns for use as catalysts.
Sodium glucoheptonate	permitted in the Table to clause 11, at a maximum permitted level of 1 mg/kg (measured as cyanide).	Maximum permitted level to be reduced to 0.08 mg/kg (measured as cyanide)	Safety concerns related to cyanide. The limit to be consistent with the Australian and New Zealand drinking water guidelines.
Trichloroethylene	as a permitted extraction solvent (Table to clause 13), for all foods.	Delete permission for its use as an extraction solvent for all foods.	Safety concerns related to trichloroethylene. Seek submissions on whether it is used as an extraction solvent, and if there are viable alternatives. Is there a need for this approval and if so which foods are currently extracted or for which is permission sought? Justification for such requests are required.
Urea	A permitted microbial nutrient or microbial nutrient adjunct used in the manufacture of any food (in the Table to clause 18).	It is proposed to exclude permission for alcoholic beverages. Delete current permission in the Table to clause 18 and add a new entry into the Table to clause 14, excluding permission for alcoholic beverages.	Safety concerns related to the formation of ethyl carbamate in alcoholic beverages.

5.4.5 Miscellaneous amendments

There are a number of other issues which are proposed amendments which do not fit into the individual sections above. These are discussed in this section as individual cases.

5.4.5.1 Sodium fluoride and sodium fluorosilicate (sodium silicofluoride)

There are currently permissions for sodium fluoride and sodium fluorosilicate (sodium silicofluoride) as processing aids for packaged water and in water used as an ingredient in other foods (in the Table to clause 11 of Standard 1.3.3). It has been raised that both chemicals are not acting as processing aids, as it would seem that the permission was given to allow municipal water providers to treat water with fluoride for tooth decay prevention (for a community health outcome). This is not a technological function of a processing aid, but more like fortification for a public health outcome.

The issue that FSANZ must consider is whether removing the permission would cause any unintended consequences. FSANZ proposes the removal of the permissions for both chemicals and to consult on this issue to see if their removal would cause concerns.

Would the removal of permissions for sodium fluoride and sodium fluorosilicate (sodium silicofluoride) as processing aids to treat water used in packaged water and used as an ingredient in other foods cause unintended consequences for food manufacturers, food enforcement officers, or any other group? If so, what are the consequences, and can they be resolved by some other means?

5.4.5.2 White mineral oils, mineral oil based greases, paraffin

White mineral oil is listed as a generally permitted processing aid in the Table to clause 3. Mineral oil based greases are permitted as lubricants, release and anti-stick agents in the Table to clause 9, while paraffin is approved as a miscellaneous processing aid to coat cheese and cheese products in the Table to clause 14. Petrolatum (petroleum jelly), INS 905b, is also listed in Schedule 2 of Standard 1.3.1, so it is a generally permitted processing aid.

JECFA is currently evaluating mineral oils so it is proposed for white mineral oils, mineral oil based greases and paraffin that the current permissions and nomenclature in the Code be maintained, but be reviewed in three years, after the gazettal of the amendments resulting from this Proposal, since it seems premature to make changes until the issues are fully resolved. The draft variation to Standard 1.3.3 proposes the addition of an editorial note, indicating that white mineral oils will be reviewed three years from the gazettal of the editorial note, to ensure consistency with JECFA's assessment conclusion.

It is recommended in the Safety Assessment Report (**Attachment 2**) that the nomenclature for mineral oils in the Code should also be reviewed once JECFA has completed its evaluation to ensure consistency.

The current situation relating to mineral oils in JECFA and Codex is summarised below. Further work is being undertaken by JECFA for the safety assessment of white mineral oils.

JECFA has made nomenclature and specification changes with two new categories added into the JECFA specifications[5]. The two entries are high viscosity mineral oil, and medium and low viscosity mineral oil (further separated out into three classes, class I, II and III).

Mineral oil (high viscosity)

Added to the JECFA specifications, addendum 3 (1995).
INS 905a (in the JECFA specifications)
Listed as INS 905d in the General Standard for Food Additives (GSFA), Rev 6, 2005[6].
Synonyms: liquid paraffin, liquid petrolatum, food grade mineral oil, white mineral oil
Function: Release agent, lubricant, protective coating

Mineral oil (medium and low viscosity)

Added to the JECFA specifications, addendum 10 (2002).
Also called INS 905a (in the JECFA specifications).
Listed as INS 905e, only for class I, in the GSFA, Rev 6, 2005[6].
Synonyms: liquid paraffin, liquid petrolatum, food grade mineral oil, white mineral oil
Function: Release agent, lubricant, protective coating

Therefore there is some confusion over which INS numbers apply to these new terms.

There are three classes of mineral oil (medium and low viscosity) that are separated by viscosity (as well as carbon number at 5% distillation point and average molecular weight).

Class I, 8.5-11 mm^2/s (mm^2/s units also referred to as cSt, centistokes)
Class II, 7.0-8.5 mm^2/s
Class III, 3.0-7.0 mm^2/s

High viscosity mineral oils are also differentiated from the above classes on viscosity and carbon number.

The specifications for high viscosity, and medium and low viscosity oils (for the different classes) are very detailed and complicated, and are summarised in Table 6 below from the JECFA specifications.

[5] Joint FAO/WHO Expert Committee on Food Additives (JECFA) (1992), Food and Nutrition Paper 52, Compendium of Food Additives Specifications, Volumes 1 and 2, addenda 1-12, the Food and Agriculture Organisation of the United Nations, Rome

[6] Codex Alimentarius, General Standard for Food Additives, Food and Agriculture Organisation of the United Nations, World Health Organisation, Rome CODEX STAN 192-1995, Rev. 6 (2005). http://www.codexalimentarius.net/download/standards/4/CXS_192e.pdf

Table 6: JECFA specifications for mineral oils

Mineral oil		Viscosity at 100ºC, (cSt, centistokes) ASTM D455[1]	Carbon number at 5% distillation point	Average molecular weight	Boiling point at the 5% distillation point (ºC)
High Viscosity		≥11	≥28	≥500	>422
Medium and Low Viscosity	Class I	8.5-11	≥25	480-500	>391
	Class II	7.0-8.5	≥22	400-480	>356
	Class III	3.0-7.0	≥17	300-400	>287

Note: 1. ASTM is the American Society for Testing and Materials

Currently white mineral oil is considered a generally permitted processing aid since it is listed in the Table to clause 3. However, its function is as a lubricant, release and anti-stick agent so it should be removed from the Table to clause 3 and added to the Table to clause 9 (Permitted lubricants, release and anti-stick agents) to properly reflect its function. It is proposed to maintain the maximum permitted level of use as determined by GMP.

5.4.5.3 Editorial note for lactoperoxidase

Lactoperoxidase from bovine milk EC [31.11.1.7] is permitted for the purpose of reducing and/or inhibiting bacterial populations on meat surfaces in the Table to clause 14. There is an editorial note preceding this Table that relates to the lactoperoxidase permission. This note alerts that the mandatory labelling requirements of clause 4 of Standard 1.2.3 apply if meat has been treated with lactoperoxidase. The labelling requirements of clause 4 of Standard 1.2.3 relate to milk and milk products with no specific reference to lactoperoxidase. To aid in clarity of this editorial note it is proposed to add the phrase 'from bovine milk' after lactoperoxidase to indicate that the labelling requirements refer to the presence of milk products.

The new Editorial note in the clause to Table 14 is proposed to be:

> 'Where meat has been treated using lactoperoxidase from bovine milk, the mandatory labelling requirements in clause 4 of Standard 1.2.3 apply.'

5.4.5.4 Potassium ethoxide, sodium ethoxide and sodium methoxide

Sodium methoxide is used as a catalyst for the transesterification of fats and oils. Sodium ethoxide and potassium ethoxide can also perform this function but sodium methoxide is currently the favoured catalyst for this reaction.

Transesterification of vegetable oils is explained in a review article[7] which has formed the basis of the following information.

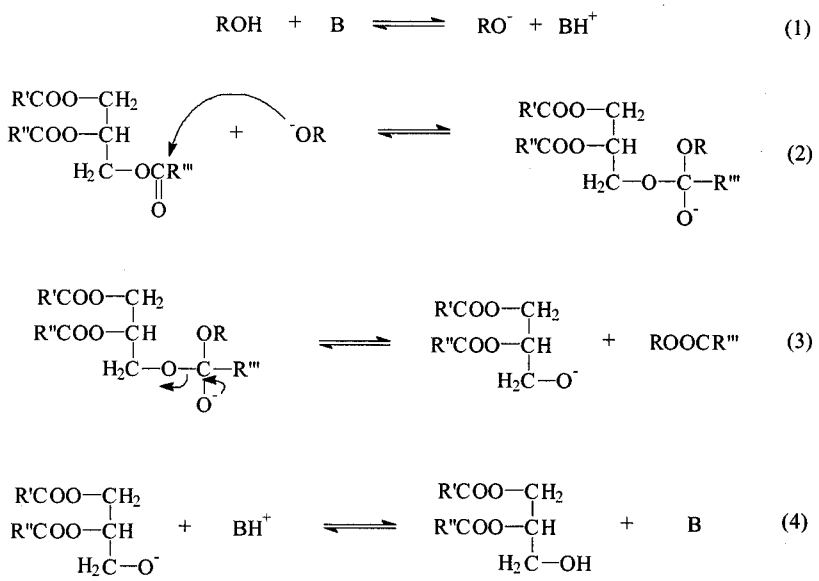
[7] Schuchardt, U., Sercheli, R. and Vargas, R.M., *J. Braz. Chem. Soc.*, Vol 9(1) 199-210, 1998, Transesterification of vegetable oils: a review.
http://www.biodieselgear.com/documentation/Transesterification_of_Vegetable_Oils.pdf

For the transesterification of vegetable oils, a triglyceride reacts with an alcohol in the presence of a strong acid or base, to produce a mixture of fatty acid alkyl esters and glycerol.

The general equation for a transesterification reaction is:

$$RCOOR' + R''OH \overset{\text{catalyst}}{\leftrightarrow} RCOOR'' + R'OH$$

Alkaline metal alkoxides, such as sodium methoxide, are used for base-catalysed transesterification, as listed in the scheme below. In this scheme, triglycerides (as well as diglycerides and monoglycerides) are converted by this mechanism to a mixture of alkyl esters and glycerol. Sodium methoxide can be used as a catalyst for the processing of fats and oils from animal and vegetable sources.



Mechanism schematic for base-catalysed transesterification of oils

Alkaline metal alkoxides are the most active catalysts, since they produce very high yields (>98%) in short reaction times (30 min), even at low molar concentrations (0.5 mol %). It requires the absence of water for the reaction. Alkaline hydroxides (potassium and sodium hydroxide) are cheaper than metal alkoxides, but they are less active.

The deactivation of sodium methoxide with water, after the catalytic reaction is completed produces methanol and sodium hydroxide. Likewise for sodium ethoxide and potassium ethoxide the reaction by-products are ethanol and sodium hydroxide, and ethanol and potassium hydroxide respectively.

$$NaOMe + H_2O \leftrightarrow MeOH + NaOH$$

The by-products of this hydrolysis reaction are well known substances which are water soluble and poorly soluble in the fats and oil phase. They are then removed during the further processing that the oils undergo after the catalysis reaction including washing with water, and deodorisation with elevated temperature and vacuum to remove volatile components and impurities.

Sodium ethoxide and sodium methoxide are proposed to be removed from the generally permitted processing aids table (Table to clause 3) and added to the current entry for potassium ethoxide in the Table to clause 5 (Permitted catalysts) to accurately reflect their function. As well their maximum permitted level should also be consistent with that for potassium ethoxide, listed as 1.0 mg/kg, rather than at levels determined by GMP.

5.4.6 Discussion of other issues that evaluation resulted in no change

A number of issues raised in submissions or part of the review of the Standard were assessed and found to not require any amendment to the Standard. These are listed in Table 7 below with the reason for the decision as indicated.

Table 7: Discussion of issues that resulted in no change

Issue considered	Discussion and reason for decision
Remove copper sulphate in the Table to clause 6, 11 and 18, since cupric sulphate is listed in schedule 2 of Standard 1.3.1 so is a generally permitted processing aid.	The reason for the suggestion is that cupric sulphate is another name of copper sulphate, so the specific permissions are duplications. However cupric sulphate is specifically copper II sulphate, but not copper I (being called cuprous) sulphate. Copper sulphate would include both valences, copper I and II, so it is proposed to not remove copper sulphate from the specific Tables.
Remove permission for short chain triglycerides in the Table to clause 7.	The reason is that short chain triglycerides can be considered foods, and are generally permitted processing aids (subclause 3(a) of Standard 1.3.3). However it is thought that not everyone may agree with this judgement so the specific permission in the Standard is proposed to be retained for clarity.
Amend and update the Tables to clauses 6 and 8, referring to ion exchange resins.	Specialist knowledge and assistance is required to ensure any changes are correct and do not either incorrectly broaden the permissions without appropriate assessment or remove current permissions. If required, a separate review of these resins could be made at a later time if appropriate assistance can be obtained.
Remove the permission for isopropyl alcohol in the Table to clause 10 since it is listed in the Table to clause 3 as a generally permitted processing aid.	It has a maximum permitted level of 1000 mg/kg in its permission in the Table to clause 10 so this restriction is proposed to be maintained.
The permission for sodium nitrate in the Table to clause 11 has been queried.	Sodium nitrate is a permitted boiler water treatment agent so there should be permission for it as a processing aid. There are a number of boiler water and water treatment chemicals permitted in this Table. There are nitrate limits in the Australian and New Zealand drinking water guidelines so keeping it ensures consistency.
Remove permissions for the extraction solvents from the Table to clause 13: • butane • isobutane • propane since they are listed in schedule 2 of Standard 1.3.1.	These gases are listed in schedule 2 of Standard 1.3.1, but their approval is for pressurised food containers only. They do not have general permissions as processing aids, so the specific approvals as extraction solvents, and their corresponding maximum permitted levels for specific foods should be maintained.

Issue considered	Discussion and reason for decision
Remove permissions for the use of potassium and sodium bromate for germination control in malting (given in the Table to clause 14).	The removal of permissions were sought since bromate is considered a category 2B (possibly carcinogenic to humans) carcinogen by the International Agency for Research on Cancer (IARC), discussed in more detail in the Safety Assessment Report (**Attachment 2**). A submission was received from the Australian Association of Brewers which requested these permissions be maintained since bromate is required for malting purposes for a small number of specialty malts produced at some malting companies. There are no alternatives. Data provided indicated that negligible levels of bromate (below the limit of detection) are found in beer produced from such malts. Therefore permission is maintained but it is proposed to limit the maximum permitted level to the limit of determination (as indicted above in section 5.4.4).

5.4.7 Issues requiring advice

There are a number of issues raised during the review of the Standard which have not been fully resolved and for which advice is sought. Some of these issues require advice on whether the chemical which has permission acts as a processing aid for the given purpose. Assistance from industry is sought to confirm reasons why permissions were given and whether they are still correct.

Table 8 below provides these issues and the information that is sought to justify the processing aid approval.

Table 8: Other issues for which advice is sought

Issue	Required advice or information to justify the current permission
Should glycine have permission as a processing aid in the Table to clause 10?	Glycine is listed in Codex as a food additive being a flavour modifier, with INS 640. It also has specific approval as a food additive for tabletop sweeteners in item 11.4 (tabletop sweeteners) in Schedule 1 of Standard 1.3.1. What role does it have as a processing aid? Does it act as a carrier or diluent?
Should L-leucine have permission as a processing aid in the Table to clause 10?	L-leucine is listed in Codex as a food additive being a flavour modifier, with INS 641. It also has specific approval as a food additive for tabletop sweeteners in item 11.4 (tabletop sweeteners) in Schedule 1 of Standard 1.3.1. What role does it have as a processing aid? Does it act as a carrier or diluent?

5.5 Issues from submissions

Public comment on the Initial Assessment Report for this Proposal was sought from 17 March 2004 till 26 May 2004. Three submissions were received which all supported the review. Along with the support they raised a number of issues which have been summarised in **Attachment 3**, and are discussed below and in other relevant sections.

5.5.1 Safety issues

One submitter suggested that all reviews of the safety of processing aids should be done in accordance with the most recent JECFA safety assessments. In general FSANZ will use JECFA's assessments as a principal authority, but FSANZ may also use other safety assessments, where relevant. This is discussed in more detail in section 5.1.

A submitter raised that they would like the permission for urea as a processing aid for wine manufacture to be removed, since urea can form ethyl carbamate (listed by the International Agency for research on Cancer (IARC) as a Group 2B, 'possibly carcinogenic to humans')[8] by reaction with ethanol. Urea is currently a permitted microbial nutrient or microbial nutrient adjunct (in the Table to clause 18) as well as having specific permission in the manufacture of concentrated gelatine solutions (in the Table to clause 14). To prevent the possible formation of ethyl carbamate in wine (or other products containing ethanol) a restriction to the approval for use of urea in wine in the Table to clause 18 was requested.

The Safety Assessment Report (**Attachment 2**) evaluated this issue and concluded that the permission for urea as a microbial nutrient and microbial nutrient adjunct should be excluded for alcoholic beverages to reduce the formation of ethyl carbamate in such products. This is fully discussed in the relevant section (urea) of the Safety Assessment Report, and the outcome discussed in section 5.4.4 where limitations have been proposed to permissions due to safety concerns.

5.5.2 Obsolete processing aids

One submitter did not support the removal of 'obsolete' processing aids, which has been discussed in section 5.2.

5.5.3 Other issues

One submitter made comment that processing aids may be contained in imported flavours and extracts, which Australian and New Zealand food manufacturers may not know or have full control over. Food manufacturers need to ensure that their products comply with the Code, regardless of where they source their ingredients, food additives or processing aids.

The inadequacy of some current specifications for approved processing aids was also raised in a submission. Soap and Perlite were used as examples. Both these processing aids have specifications in relevant sources within Standard 1.3.4 – Identity and Purity. Perlite has a specification in Food Chemicals Codex, while soap (which is a broad term) includes various specifications in several of these references.

5.6 Risk management

The risk assessment of the various processing aids has been summarised in section 5.1, while the full Safety Assessment Report is at **Attachment 2**.

[8] International Agency for Research on Cancer, Urethane - Summary of Data Reported and Evaluation, last updated 19 March 1998, http://www-cie.iarc.fr/htdocs/monographs/vol07/urethane.html

The various risk management discussions and decisions that occurred after the safety assessment and reviews of Standard 1.3.3 were undertaken are detailed in the various subsections in section 5.4. **Attachment 4** is a summary document of the suggested amendments and discussions that have arisen out of the review proposal to date. An earlier draft of this document was circulated to the External Advisory Group for a round of comment before it was finalised, as well as internal discussion within FSANZ. The document was then used to produce the legal drafting changes to Standard 1.3.3, with some consequential changes to Standard 1.3.1 – Food Additives, which are listed in **Attachment 1**.

6. Regulatory Options

FSANZ is required to consider the impact of various regulatory (and non-regulatory) options on all sectors of the community, which includes consumers, food industries and Governments in Australia and New Zealand. The benefits and costs associated with the proposed amendments to the Code will be analysed using regulatory impact principles.

The following two regulatory options are available for this Proposal.

Option 1. Maintain the *status quo* and not amend Standard 1.3.1 and Standard 1.3.3.

Option 2. Amend Standard 1.3.1 and Standard 1.3.3.

7. Impact Analysis

7.1 Affected Parties

The affected parties to this Proposal are:

- food manufacturers of every category who use processing aids in manufacturing and packaging their food products in Australia and New Zealand;
- consumers of food;
- manufacturers and suppliers of food processing aids; and
- Australian, State, Territory and New Zealand government enforcement agencies.

7.2 Impact Analysis

Because this Proposal is seeking to make amendments to Standards 1.3.1 and 1.3.3 to update permissions and maximum permitted levels from the most recent scientific safety evaluation, as well as amend error, anomalies and ensure consistencies between this Standard and the rest of the Code it is not expected that there should be any major costs or impacts to food manufacturers, consumers or regulatory agencies. It is anticipated that there will be benefits to consumers since the safety of processing aids has been reviewed considering the most recent scientific evaluations.

7.2.1 Option 1 – Status quo

7.2.1.1 Industry

Because this option requires no changes to the Code there should be no immediate impacts on industry. One disadvantage is that there will still be inconsistencies within the Code, specifically different nomenclature for the same chemicals which have approvals as both food additives and processing aids, which causes unnecessary confusion and leads to future enquiries to regulators. An added disadvantage for New Zealand industries is that the processing aids included from the former *New Zealand Food Regulations 1984* to the Standard have not been fully assessed.

7.2.1.2 Consumers

The disadvantage for consumers is that the safety of currently approved processing aids has not been assessed considering the most recent technical information. Other than that, there is no immediate effect on consumers due to this option.

7.2.1.3 Government

The impact of this option should be minimal for regulatory agencies. One disadvantage is that there will still be inconsistencies within the Code, specifically different nomenclature for the same chemicals which have approvals as both food additives and processing aids, which causes unnecessary confusion and leads to enquiries. Also, the New Zealand regulatory agencies had requested that a formal review of the Standard be conducted after the Code was first agreed to and a commitment was given that this would be performed. If option 1 was implemented this commitment would be broken.

This Proposal will not be approving any new processing aids so there should be little impact on regulatory agencies.

7.2.2 Option 2 – Amend Standard 1.3.1 and Standard 1.3.3

7.2.2.1 Industry

It is not expected that there should be any costs or detrimental effects on industry because of the outcomes of amending Standard 1.3.3 to update permissions and maximum permitted levels for currently approved processing aids considering the most recent scientific safety evaluations. The Proposal is also to amend errors, anomalies and ensure consistencies between this Standard and the rest of the Code.

This Draft Assessment Report containing the proposed amendments will be circulated for a round of public comment so if any proposed amendments will cause unnecessary or unintended imposts on industry, FSANZ can assess these costs verses the proposed benefits resulting from the change. Any such submissions will be assessed as part of the Final Assessment where final draft variations will be made.

7.2.2.2 Consumers

The advantage for consumers is that the safety of currently approved processing aids has been assessed considering the most recent technical information. Other than that there is no immediate effect on consumers due to this option.

7.2.2.3 Government

The impacts of this option should be minimal for regulatory agencies. One advantage is that inconsistencies within the Code, specifically different nomenclature for the same chemicals which have approvals as both food additives and processing aids will have been removed, so eliminating some unnecessary confusion and enquiries. This option would meet a commitment given to the New Zealand regulatory agencies that a formal review of the Standard be conducted after the Code was first agreed to.

This Proposal will not be approving any new processing aids so there should be little impacts on regulatory agencies.

8. Consultation

8.1 Public consultation

The Initial Assessment Report for P277 was circulated for a round of public comment from 17 March 2004 till 26 May 2004. Three submissions were received that all supported the review. A summary of submissions is contained in **Attachment 3**. Issues raised in these submissions are discussed in section 5.4 above.

FSANZ seeks further advice as part of this review. The questions and issues upon which advice is sought are listed below.

- Would deleting the permission for methylphenylpolysiloxane as an antifoam agent in the Table to clause 4 cause problems for the food industry? Deleting the permission is proposed since there is no data to perform a safety assessment to confirm its use to be safe. There is permission for the use of dimethylpolysiloxane as an antifoam agent.
- What role does glycine have as a processing aid in the Table to clause 10 – permitted carriers, solvents and diluents? What is the technological justification for the permission?
- What role does L-leucine have as a processing aid in the Table to clause 10 – permitted carriers, solvents and diluents? What is the technological justification for the permission?
- Does deleting permission for trichloroethylene as an extraction solvent cause issues in the food industry? Is there a need for trichloroethylene as an extraction solvent, or are there already permitted suitable alternatives? If there is a requirement for its use, and if so for which specific food types are required rather than 'all foods'? Justification for such permissions should be supplied.
- Would the removal of permissions for sodium fluoride and sodium fluorosilicate (sodium silicofluoride) as processing aids to treat water used in packaged water and in water used as an ingredient in foods cause unintended consequences for food manufacturers, food enforcement officers, or any other group? If so, what are the

consequences, and can they be resolved by some other means?

- Is there a problem with amending the permission for chromium to chromium (excluding chromium VI) as a permitted catalyst?
- Does changing the maximum permitted levels for potassium and sodium bromate as germination control agents for malting from 0.1 mg/kg to the limit of determination raise any issues?
- It is proposed to leave the current permissions and nomenclature for white mineral oil, mineral oil based greases and paraffin as currently listed for three years once this Proposal is gazetted where they can be re-evaluated after JECFA have completed their assessment. Is this reasonable and if not what alternative suggestion is there? White mineral oil is proposed not to be listed as a generally permitted processing aid, but as a permitted lubricant, release and anti-stick agent.
- Would putting a restriction on preventing urea from being listed as a microbial nutrient or microbial nutrient adjunct for alcoholic beverage (including wine and beer) production cause problems for such industries?
- Would changing the terminology of 'polyelectrolytes (acrylamide monomers)' to 'polyacrylamide (polyelectrolytes)' to better reflect its nature as an approved processing aid in the Table to clause 11 raise any issues? Is there a better alternative name?

8.2 External Advisory Group

The FSANZ Board agreed in May 2004 to the establishment of a committee under section 43 of the FSANZ Act and to the appointment of appropriate qualified and skilled people to an External Advisory Group (EAG) to provide advice to FSANZ to assist with completing the review of processing aids. This EAG has been drawn from experts from industry groups, regulatory agencies, academic and consumer groups with knowledge and expertise in food processing aids and their regulation.

The EAG met (with some people linked in via teleconference) in Sydney in June 2004. This meeting confirmed the terms of reference for the group and assisted in addressing issues received from submissions as well as providing expert advice on proposed amendments to the Standard. The issues raised during the review and how they are addressed were passed to the EAG for their expert input as part of the assessment process. In practice this meant an early working draft of **Attachment 4** was sent to the EAG for its considered comment.

The terms of reference of the EAG, plus the list of members is contained in **Attachment 6**.

8.3 World Trade Organization (WTO)

As members of the World Trade Organization (WTO), Australia and New Zealand are obligated to notify WTO member nations where proposed mandatory regulatory measures are inconsistent with any existing or imminent international standards and the proposed measure may have a significant effect on trade.

There are not any relevant international standards for processing aids and amending the Code to update and improve Standard 1.3.3 – Processing Aids is unlikely to have a significant effect on international trade. This issue has been fully considered at Draft Assessment and confirms this earlier conclusion.

Notification will not be recommended to the agencies responsible in accordance with Australia's and New Zealand's obligations under the WTO Technical Barrier to Trade (TBT) or Sanitary and Phytosanitary Measure (SPS) Agreements.

9. The Decision

The draft variations to Standard 1.3.1 – Food Additives and Standard 1.3.3 – Processing Aids of the Code are recommended for the following reasons:

- The proposed amendments are consistent with the protection of public health and safety.

- The proposed amendments ensure consistency within the Code and improved consistency, as far as is possible, with other international food standards.

- The proposed amendments have included information and consideration of submissions on issues received, as well as advice from an Expert Advisory Group, external to FSANZ.

- There will not be any expected added costs to food manufacturers, consumers or regulatory agencies arising from these proposed amendments.

- There are no other alternatives that are more cost effective than the proposed amendments to the Code.

ATTACHMENTS

1. Draft variations to the *Australia New Zealand Food Standards Code*
2. Safety assessment report
3. Summary of submissions
4. Suggested amendments and discussion
5. Regulation of processing aids internationally
6. Terms of reference and list of members of the External Advisory Group

Attachment 1

Draft variations to the *Australia New Zealand Food Standards Code*

To commence: on gazettal

[1] ***Standard 1.3.1*** *of the Australia New Zealand Food Standards Code is varied by –*

[1.1] *omitting from* Schedule 2*, the entries for –*

336	Potassium tartrate
514	Sodium sulphate

substituting

336	Potassium tartrates
514	Sodium sulphates

[2] ***Standard 1.3.3*** *of the Australia New Zealand Food Standards Code is varied by –*

[2.1] *omitting from the* Table to clause 3 –

Aluminium stearate
Calcium stearate
Kaolin
Magnesium stearate
Potassium hydrogen tartrate
Potassium oleate
Potassium stearate
Sodium ethoxide
Sodium methoxide
White mineral oil

[2.2] *omitting from the* Table to clause 3, Polyoxyethylene 40 monostearate, *substituting* –

Polyoxyethylene 40 stearate

[2.3] *omitting from the* Table to clause 3, Polypropylene glycol alginate, *substituting* –

Propylene glycol alginate

[2.4] *omitting from the* Table to clause 4*,* –

Dimethylpolysiloxane	10
Polysorbate 60	GMP
Polysorbate 65	GMP
Polysorbate 80	GMP

[2.5] *omitting from the* Table to clause 5, *the Substance*, Chromium, *substituting* –

Chromium (excluding chromium VI)

[2.6] *inserting in the* Table to clause 5 –

Sodium ethoxide	1.0
Sodium methoxide	1.0

[2.7] *omitting from the* Table to clause 7 –

Sodium stearoyl lactylate	GMP

[2.8] *omitting from the* Table to clause 9 –

Polysorbate 60	GMP
Sodium stearoyl lactate	GMP
Talc	GMP

[2.9] *inserting in the* Table to clause 9 –

White mineral oil	GMP

[2.10] *inserting after the* Table to clause 9 –

Editorial note:

The Joint FAO/WHO Expert Committee on Food Additives (JECFA) is currently reviewing mineral oils, including white mineral oil. To ensure consistency with the outcomes of this review, FSANZ will review the permission and nomenclature for white mineral oil three years from the gazettal of this Editorial note.

[2.11] *omitting from the* Table to clause 10 –

Anhydrous sodium sulphate	GMP
Ethyl alcohol	GMP
Talc	GMP

[2.12] *omitting from the* Table to clause 11 –

Sodium fluoride	GMP
Sodium fluorosilicate (Sodium silicofluoride)	GMP

[2.13] *omitting from the* Table to clause 11*, for the following substances, the maximum permitted levels, substituting* –

Calcium hypochlorite	5 (available chlorine)
Chlorine	5 (available chlorine)
Chlorine dioxide	1
Copper sulphate	2
Sodium glucoheptonate	0.08 (measured as cyanide)
Sodium hypochlorite	5 (available chlorine)
Sodium nitrate	50 (as nitrate)
Styrene-divinylbenzene cross-linked copolymer	0.03 (as styrene)

[2.14] *omitting from the* Table to clause 11 –

Polyelectrolytes (acrylamide monomers)	GMP

substituting

Polyacrylamide (polyelectrolytes)	0.0002 (as acrylamide monomer)

[2.15] *omitting from the* Table to clause 11, *the Substance*, Sodium fumate, *substituting* –

Sodium humate

[2.16] *omitting from the* Table to clause 13 –

Trichloroethylene	All foods	2

[2.17] *omitting the* Editorial note *before the* Table to clause 14, *substituting* –

Editorial note:

Where meat has been treated using lactoperoxidase from bovine milk, the mandatory labelling requirements in clause 4 of Standard 1.2.3 apply.

[2.18] *omitting from the* Table to clause 14 –

Ethylene Oxide This permission ceases to have effect on 30 September 2003. This permission is an Australia Only Standard. Subclauses 1(2), 1(3) and 1(4) of Standard 1.1.1 do not apply to this permission	Sterilisation of herbs, spices, and dried vegetables used as seasonings – herbs, spices, and dried vegetables used as seasonings sterilised by the application of ethylene oxide may only be sold or imported into Australia 21 days after such sterilisation	20
Polysorbate 80	Manufacture of edible collagen casings	GMP

[2.19] *omitting from the* Table to clause 14*, for the following substances, the maximum permitted levels, substituting* –

Potassium bromate	Germination control in malting	Limit of determination of bromate
Sodium bromate	Germination control in malting	Limit of determination of bromate

[2.20] *omitting from the* Table to clause 14 –

Urea	Manufacture of concentrated gelatine solutions	1.5 times the mass of the gelatine present

substituting

Urea	Manufacture of concentrated gelatine solutions	1.5 times the mass of the gelatine present
	Microbial nutrient and microbial nutrient adjunct for the manufacture of all foods, except alcoholic beverages	GMP

[2.21] *omitting from the* Table to clause 18 –

Dextrin
Polysorbate 80
Trehalose
Urea

Attachment 2

Safety Assessment Report

SAFETY ASSESSMENT OF CERTAIN PROCESSING AIDS

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SUMMARY AND CONCLUSIONS

A total of forty chemical processing aids have been evaluated for their safety. The substances that were selected for evaluation had either a maximum permitted level prescribed in the final food and not had their safety reviewed by FSANZ since 1993, had been relatively recently evaluated by the Joint FAO/WHO Expert Committee on Food Additives (JECFA), or other (inter) national governmental organisations, or had been identified by FSANZ, or other parties, as raising potential toxicological concerns.

Each of the selected substances was reviewed, using evaluation reports from other (inter)-national organisations or agencies, where these were available. In general, substances that were determined to only leave relatively low residue levels in the final food, and/or that were found to have low oral toxicity were considered to raise no toxicological concerns. Substances were considered to raise toxicological concerns if they were found to produce severe adverse effects, including carcinogenicity, in experimental animals where such effects could also reasonably be expected in humans, or where evidence already existed for such effects in humans.

For those substances used as processing aids in packaged water and water used as an ingredient in other foods, the maximum permitted levels were compared to the drinking water levels specified in the Australian Drinking Water Guidelines and the Drinking-water Standards for New Zealand. As packaged water has the potential to be used as a substitute for drinking water, it is important that the maximum permitted levels reflect the levels that have been established on health grounds for drinking water.

A summary of the conclusion reached for each substance evaluated is provided in Table 1.

Table 1: Summary of safety assessment conclusions

Substance	Safety assessment conclusions	Explanation
Acetone	No toxicological concerns	Readily metabolised at low levels, only minimal residues expected from use, substance has low oral toxicity at low levels of exposure.
Benzoic acid Benzyl alcohol	No toxicological concerns	Rapidly metabolised, long-term effects only seen following exposure to high levels, only minimal residues expected from use.
Benzoyl peroxide	No toxicological concerns	As per benzoic acid.
Butane Isobutane Propane	No toxicological concerns	Only low residues in food, substances of low oral toxicity
1-Butanol	No toxicological concerns	Low residue levels, metabolised to innocuous products, low oral toxicity.

Substance	Safety assessment conclusions	Explanation
Chlorine Calcium hypochlorite Sodium hypochlorite	No toxicological concerns but maximum permitted levels for use in packaged water should be brought into conformity with drinking water guidelines levels for Australia and New Zealand	Very few toxic effects associated with drinking water containing high chlorine levels. Main issue is the formation of disinfection by-products and their potential to cause adverse effects, such as cancer, in humans. None of the chlorination by-products studied to date found to be a potent carcinogen at concentrations normally found in drinking water.
Chlorine dioxide Sodium chlorite	No toxicological concerns but maximum permitted level for chlorine dioxide in packaged water should be brought into conformity with drinking water guideline levels for Australia and New Zealand.	No adverse effects observed in adults and neonates consuming water disinfected with chlorine dioxide. No evidence for carcinogenicity of chlorine dioxide and chlorite.
Chromium	There are toxicological concerns because the current permission does not specifically exclude the use of hexavalent chromium. No toxicological concerns with the use of other chromium compounds as catalysts.	Most toxic effects have been associated with hexavalent chromium compounds. Trivalent chromium appears to have low oral toxicity. Hexavalent chromium is a human carcinogen by the inhalation route. Potential carcinogenicity via oral exposure is unclear because of limited epidemiological and toxicological data.
β-Cyclodextrin	No toxicological concerns	Only very limited use, likely to result in only low residues. Substance has low oral toxicity.
Ethyl acetate	No toxicological concerns	Only limited toxicological information available. Ethyl acetate completely metabolised to innocuous products (ethanol and acetate), which are normal components of intermediary metabolism.
Hexanes	No toxicological concerns	Only low residue levels expected, adverse effects typically only at high levels of exposure.
Hydrogen peroxide	No toxicological concerns	Unlikely to leave significant residues, low levels of hydrogen peroxide not toxicologically significant.
Isopropyl alcohol	No toxicological concerns	Efficiently metabolised to innocuous substances normally found endogenously, does not accumulate in the body, metabolites do not raise toxicological concerns, low oral toxicity in animal studies.
Methylene chloride	No toxicological concerns providing use is limited to ensure residues in food are as low as practicable.	Relatively low oral toxicity in animals but some suggestive, although inconclusive, evidence of carcinogenicity.
Methylphenylpolysiloxane	Insufficient data to undertake safety assessment.	

Substance	Safety assessment conclusions	Explanation
Mineral oils Mineral oil based greases Paraffin	Difficult to determine if there are toxicological concerns because of uncertainties in the animal data. Current permissions should be maintained but reviewed once JECFA has finalised its evaluation. The nomenclature used in the Code for mineral oils should also be reviewed in light of discrepancies with that used by JECFA.	Wide range of systemic effects seen in studies with rats. Strain of rat used may not be appropriate model for humans. JECFA evaluation still ongoing, more studies required.
Nickel	No toxicological concerns	Substance has low systemic toxicity by the oral route, no evidence for carcinogenicity in either humans or experimental animals, only low residues in food expected.
Polyelectrolytes (acrylamide monomers)	No toxicological concerns however level of acrylamide should be kept as low as possible. The maximum permitted level for acrylamide monomers in packaged water should be brought into conformity with drinking water guideline levels for Australia and New Zealand.	Acrylamide is neurotoxic and carcinogenic by the oral route. The contribution to the total acrylamide intake from the use of polyelectrolytes as a processing aid would be relatively minor compared to the levels of acrylamide that can form in certain foods during frying and baking.
Potassium bromate Sodium bromate	There are toxicological concerns with the use of potassium and sodium bromate. Continued use of potassium and sodium bromate in malting would be acceptable only if the bromate levels remain below the limit of determination in the final food (beer).	Convincing evidence of renal toxicity and carcinogenicity in rats. Bromate also appears to be a potent genotoxic substance *in vivo*.
Potassium ethoxide Sodium ethoxide Sodium methoxide	No toxicological concerns.	No safety data available however the available information on their chemistry when used as catalysts indicates these compounds are converted to innocuous by-products (hydroxides and methanol or ethanol) following completion of the reaction, which are water soluble and removed during subsequent purification steps. Only very low residues would be expected to remain in the final product, if at all.
Silver ions	No toxicological concerns	Only poorly absorbed by gastrointestinal tract. No extensive systemic effects documented in either experimental animals or humans.

Substance	Safety assessment conclusions	Explanation
Sodium glucoheptonate	There may be toxicological concerns with maintaining a current maximum permitted level for sodium glucoheptonate measured as cyanide at 1 mg/kg. This level is significantly higher than the drinking water guideline level for cyanide of 0.08 mg/L established for Australia and New Zealand on the basis of health considerations. The maximum permitted level for cyanide should be brought into conformity with the drinking water guideline levels for Australia and New Zealand.	Cyanide has high acute toxicity, and may also have effects at lower levels following chronic exposure.
Sodium metabisulphite Sodium sulphite Sulphur dioxide	No toxicological concerns. *Sulphite sensitivity is unrelated to the general toxicity of sulphites. The risk to sulphite sensitive people from sulphites in food is managed through food labelling*.	Sulphites have a low systemic toxicity. Most common effects in animals are gastric lesions. Effect probably dependent on sulphite concentration in the stomach rather than daily dose. Contribution to the total intake of sulphites from use as processing aids likely to be minor compared to use as food additives.
Sodium nitrate	No toxicological concerns. The maximum permitted level should be brought into conformity with the drinking water guideline level for Australia and New Zealand. The drinking water guideline level has been established to protect bottle fed infants less than 3 months of age.	Nitrate is converted to nitrite once absorbed. Excess nitrite in humans may lead to impaired ability for haemoglobin to transport oxygen to tissues. Young infants particularly susceptible. Nitrate may react with other substances in the body to form *N*-nitroso compounds, some of which are known to be carcinogenic in animals.
Toluene	No toxicological concerns	Use as extraction solvent expected to result in minimal residues in food, and the contribution from food to the total toluene intake is considered to be minor. Low levels of toluene readily metabolised by humans. Adverse effects observed in rodent studies tend to occur at relatively high levels of exposure.
Trichloroethylene	There are toxicological concerns with its use as an extraction solvent. Use as an extraction solvent should be limited to ensure residues in food are as low as practicable.	Rapidly absorbed by the gastrointestinal tract, and rapidly metabolised. Many of its metabolites are themselves toxic. The primary targets for toxicity are the liver and kidneys. Effects on central nervous system and heart also observed after acute exposure to high levels. A multisite carcinogen in experimental animals. Suggestive, although inconclusive, evidence for increased risk of cancer from some epidemiological studies in humans.

Substance	Safety assessment conclusions	Explanation
Urea	There are toxicological concerns with the use of urea as a microbial nutrient and microbial nutrient adjunct for the manufacture of alcoholic beverages. The use of urea should be limited to exclude alcoholic beverages. There are no toxicological concerns with its use to manufacture concentrated gelatine solutions.	Urea reacts with ethanol in certain situations to produce ethyl carbamate (urethane). Ethyl carbamate is genotoxic and has been found to be a multisite carcinogen in all species tested, including non-human primates. Urea not the only precursor for ethyl carbamate formation but is the major precursor in alcoholic beverages. JECFA found that the ethyl carbamate intake from alcoholic beverages is of concern and recommended that measures to reduce the ethyl carbamate content in some alcoholic beverages should continue.

1. INTRODUCTION

Historical background

A proposal for the development of a standard to regulate the use of processing aids (Proposal P86) was raised in 1995 and resulted in the development of Standard A16, which was gazetted in the former Australian *Food Standards Code* in April 1996. The standard was developed for Australia only.

Proposal P86 included a toxicology evaluation of the processing aids subsequently incorporated into Standard A16. The toxicology report noted that the majority of processing aids are either not present in the final food or present at such low levels that they do not constitute a concern for public health and safety. However, a number of processing aids were found to leave residues in food or to have a demonstrated toxicity and these were assessed using evaluation reports from other sources; either other government agencies, or international organisations. This was to ensure that the levels present in food were safe. The toxicology report provided the scientific justifications for maximum residue levels set for processing aids, if they were warranted for the protection of public health and safety.

Standard A16 was subsequently reviewed under Proposal P188, as part of the review of the Australian *Food Standards Code*, resulting in the development of Standard 1.3.3 of the *Australia New Zealand Food Standards Code*. The objective of P188 was to update Standard A16 to recognise current practices in Australia and to take account of New Zealand requirements from the *New Zealand Food Regulations 1984*, in order to implement a joint Code with New Zealand. As Standard A16 had only recently been included in the Australian *Food Standards Code,* a detailed review (including a toxicology report) was not considered necessary.

Criteria used to determine inclusion in assessment

The following criteria have been used to determine which processing aids need to be evaluated for this Proposal.

(i) a maximum permitted residue is prescribed in the final food, and the substance has not been evaluated by FSANZ since 1993;

(ii) the substance has been (re)-evaluated by the Joint FAO/WHO Expert Committee on Food Additives (JECFA), or other (inter) national governmental organisations[9] since 1995; or

(iii) the substance has been identified by FSANZ, or other parties, as of potential toxicological concern.

For this assessment, evaluations from other (inter)-national agencies were used where available.

2. SAFETY ASSESSMENT

Acetone

Current permissions in the Code

Acetone is currently permitted as an extraction solvent for use in the manufacture of flavourings at a maximum permitted level of 2 mg/kg in the final food and the manufacture of other foods at 0.1 mg/kg (table to clause 13).

Available safety information

The safety of acetone was first evaluated by JECFA at their fourteenth meeting (WHO 1970), where its use as an extraction solvent was considered. The Committee commented that the small amounts likely to be found as residues in food are probably oxidised and metabolised by well-known pathways. They recommended the use of acetone be restricted to that determined by good manufacturing practice (GMP), which is expected to result in minimal residues. Within these limits, the Committee considered the residues would be unlikely to have any significant toxicological effect. The evaluation was considered tentative however as very little relevant data, including animal data were available.

A more substantive review of the safety of acetone was undertaken by the International Programme on Chemical Safety and was subsequently published as an Environment Health Criteria monograph (WHO 1998a). JECFA also recently considered the safety of acetone as a flavouring agent and concluded there were no safety concerns at current levels of intake when used as a flavouring agent (WHO 1999). More recently, the US EPA has also undertaken a comprehensive toxicological review of acetone (EPA 2003).

Acetone is one of three ketone bodies that occur naturally throughout the body. It can be formed endogenously in the mammalian body from fatty acid oxidation. Endogenous acetone is derived from the spontaneous and enzymatic breakdown of acetoacetate, and is subsequently eliminated from the body either by excretion in urine and exhaled air or by enzymatic metabolism. Under normal circumstances, metabolism is the predominant route of elimination, handling 70-80% of the total body burden.

[9] e.g. National Industrial Chemicals Notification and Assessment Scheme (NICNAS), National Health and Medical Research Council (NHMRC), European Scientific Committee on Food (SCF), European Food Safety Authority (EFSA), the United Stated Environmental Protection Agency (US EPA), Agency for Toxic Substances and Disease Registry (ATSDR), International Agency for Research on Cancer (IARC), and the Environmental Health Criteria (EHC)

The available data indicate that humans readily absorb acetone following oral administration. The water solubility of acetone allows for its broad distribution throughout the body, particularly into organs with high water content. Exogenously supplied acetone enters into many metabolic reactions in tissues throughout the body, but the liver appears to be the site of most extensive metabolism. Carbon from orally administered acetone has been detected in cholesterol, amino acids, fatty acids and glycogen in rat tissues, urea in urine and unchanged acetone and CO_2 in exhaled breath. Exhalation is the major route of elimination of exogenous acetone and its terminal metabolite (CO_2). The fraction of administered acetone that is exhaled as unchanged acetone is dose-related. Urinary excretion of acetone and its metabolites occurs, but this route of elimination is minor compared with exhalation of acetone and respiratory CO_2.

No human data or chronic animal studies are available for oral exposure to acetone. The majority of available studies consist of sub-chronic (13-week) drinking water or gavage studies in rats and mice. A number of genotoxicity studies are also available.

In a 13-week drinking-water study using rats, increases in kidney weights were observed in females receiving 20,000-ppm acetone (1600 mg/kg BW/day) and both males and females receiving 50,000-ppm acetone (3400 and 3100 mg/kg BW/day, respectively). Increases in liver weights were seen in both males and females receiving 20,000 (1700 mg/kg BW/day for males) and 50,000-ppm acetone. Increased testis weights and altered sperm mobility and morphology were also observed in males receiving 50,000-ppm acetone. Males given 20,000 and 50,000-ppm acetone showed increased in the incidence and severity of nephropathy. Nephropathy was not observed in the females. Other endpoints observed included changes to haematology parameters (increased leukocyte counts, decreased erythrocyte and reticulocyte counts and decreased haemoglobin levels) in males at 20,000 and 50,000-ppm acetone. These changes were considered to be consistent with mild macrocytic normochromic anaemia with a depressed regenerative response. In summary, the testis, kidney and haematologic system were identified as target organs for male rats, with a LOAEL of 1700 mg/kg BW/day, and a NOAEL of 900 mg/kg BW/day. A LOAEL for female rats was not identified.

A 13-week drinking water study was also conducted in mice. Acetone was administered in concentrations of 0, 1250 (males only), 2500, 5000, 10,000, 20,000 or 50,000 ppm (females only). Haematology and sperm morphology were not affected in any group. Organ weights for the males were similar to the controls for all treatment groups. Liver weights were increased in the high-dose females (11,000 mg/kg BW/day). Mild hepatic changes had been observed in males exposed to 20,000-ppm acetone (4900 mg/kg BW/day) in a 14-day study but these did not persist after 13 weeks of exposure. In summary, the liver was identified as the target organ in male and female mice, although it was noted that the liver effects may reflect enzyme induction only and may not be a true adverse effect. Effects that had been observed in the rat study were not evident in mice. The LOAEL for this study was 4900 mg/kg BW/day for males and 11,000 mg/kg BW/day for females, and the NOAELs were 2300 mg/kg BW/day and 5900 mg/kg BW/day, respectively. The LOAEL for male mice was selected on the basis of transient findings in a 14-day study.

In a 90-day gavage study, using rats dosed with 0, 100, 500 and 2500 mg acetone/kg BW/day, increases in liver and kidney weights were observed in the high-dose males and females.

Nephropathy incidence rates were similar between the treated and control groups, although an increase in the severity of tubular degeneration of the kidneys in mid and high-dose males and females was observed. The neuropathy exhibited a dose-response with respect to the number of animals affected. Based on organ weight changes and kidney lesions in males and females, the LOAEL for this study was 500 mg/kg BW/day and the NOAEL was 100 mg/kg BW/day.

Acetone has tested negatively for genetic toxicity in numerous non-mammalian systems, as well as in *in vitro* and in vivo mammalian systems. Positive results are restricted to a single test for aneuploidy in a yeast species exposed to high concentrations of acetone (6.82%) in its growth medium. Acetone is not considered to be genotoxic or mutagenic.

Evaluation and conclusion

Acetone is a normal cellular constituent that the body is capable of metabolising at low concentrations. Acetone does not accumulate in the body, and nor do its metabolites raise toxicological concerns. Studies on rodent exposure to orally administered acetone have identified several treatment related effects, most notably in the rat. Sub-chronic oral exposure resulted in kidney, testis and haematologic system effects in the rat; however the effects were typically mild. The nephrotoxic effects noted in rats tend to occur in males and only at high levels of exposure. The use of acetone as an extraction solvent is expected to result in minimal residues. Overall, there are **no toxicological concerns** with the use of acetone as a processing aid. The current maximum permitted levels and food groups are acceptable from a human safety perspective.

Benzoic acid and benzyl alcohol

Current permission in the Code

Benzoic acid is currently permitted as a microbial nutrient and microbial nutrient adjunct for use in the manufacture of any food (table to clause 18).

Benzyl alcohol is currently permitted as a carrier, solvent and diluent for use in the manufacture of any food up to a maximum permitted level of 500 mg/kg in the final food (table to clause 10), and as an extraction solvent in all foods at GMP levels (table to clause 13).

Benzoic acid and benzoyl alcohol are also permitted as food additives. Benzoic acid is permitted as a preservative in various foods at levels between 400 and 3000 mg/kg (Schedule 1) and benzoyl alcohol may be added to preparations of food additives (flavourings) up to 500 mg/kg in the final food (Schedule 1).

Available safety information

From a toxicological perspective, the benzyl derivatives – **benzoic acid**, the benzoate salts (calcium, potassium and sodium), benzaldehyde, benzyl acetate, **benzyl alcohol** and benzyl benzoate – can be considered together because they are metabolised along a common biochemical pathway. Also, because they are all metabolised to benzoic acid, the results of studies on one member of the group can be applied to other members of the group.

JECFA evaluated five benzyl derivatives as a group at its forty-sixth meeting, and assigned a group acceptable daily intake (ADI)[10] of 0-5 mg/kg BW as benzoic acid equivalents (WHO 1997). The group ADI was maintained at the fifty-seventh meeting of JECFA (WHO 2001). The Committee noted the occurrence of idiosyncratic human intolerance to benzoate but did not consider such data to be relevant to the establishment of an ADI for this group of compounds.

The Scientific Committee on Food (SCF) has also evaluated benzoic acid and its salts, including benzyl alcohol and related benzyl derivatives used as flavourings, and have established a full group ADI of 0-5 mg/kg BW (SCF 1994). The SCF has also performed a safety assessment on the use of benzyl alcohol as a carrier solvent for flavouring substances added to food and beverages at levels up to 300 mg/kg in the final food as consumed (SCF 2002). The SCF confirmed the inclusion of benzyl alcohol in the group ADI of 0-5 mg/kg BW for benzoic acid and benzoates.

Benzoate administered orally to humans is rapidly absorbed and excreted in the urine within 14 hours. The main metabolite is its glycine conjugate, hippuric acid, with the glucuronyl conjugate and free benzoic acid as minor pathways of excretion. The rate-limiting step in the excretion of hippuric acid is the availability of glycine. When glycine is depleted, free benzoic acid may sequester acetyl coenzyme A or be excreted unchanged or as the glucuronyl conjugate. In humans, the bolus dose of sodium benzoate causing 80% saturation of the maximal rate of hippuric acid secretion is 28 mg/kg.

Supplementation of the diet with glycine has been shown to alleviate the toxic effects in experimental animals induced by high doses of benzyl acetate and benzoic acid, including body-weight decrements and neurotoxic effects. Even with saturation of hippuric acid formation, however, clearance of compounds in the benzyl group is relatively rapid in both experimental animals and humans.

The benzyl derivatives have a low acute toxicity. In humans, acute toxicity symptoms from high doses are gastrointestinal irritation, central nervous system effects and convulsions. The effects, which have been attributed to a disturbance of the acid-base balance, are rapidly reversible.

Long-term studies in which benzyl acetate, benzyl alcohol, benzaldehyde, benzoic acid and sodium benzoate were administered in the feed or by gavage to mice and rats have been reviewed by JECFA (WHO 1997, WHO 2001). No definitive conclusions could be drawn from carcinogenicity studies of sodium benzoate in mice and rats, as the information provided was insufficient for this purpose, and survival rates in the study in rats were too low to allow it to be considered as conclusive. The Committee reviewed the studies considered in previous evaluations and an additional study in which benzaldehyde was administered in corn oil by gavage to rats at 200 or 400 mg/kg bw per day for 103 weeks and to mice at 200 or 400 mg/kg bw per day (males), or 300 or 600 mg/kg bw per day (females) for 103 weeks. On the basis of these studies, the Committee concluded that neither benzyl acetate nor benzyl alcohol is carcinogenic.

[10] The ADI is the amount of a food additive (or in this case, processing aid), expressed on a body-weight basis, that can be ingested daily over a lifetime without appreciable health risk.

A limited number of reproductive and developmental toxicity studies with benzyl alcohol, benzyl acetate, benzyl aldehyde and sodium benzoate are available which have been reviewed by both JECFA and the SCF (WHO 1997, WHO 2001, SCF 2002). Delayed development and reduced foetal and postnatal pup body weights have been observed in rats, mice, hamsters and rabbits, but only at doses that were maternally toxic. In a teratogenicity study with sodium benzoate, doses that induced severe maternal toxicity were associated with embryotoxic and fetotoxic effects and foetal malformations. A 4-generation study in rats, which were given the equivalent of 250 or 500 mg benzoic acid/kg BW/day, showed no effect on growth, fertility, lactation or survival. Overall, the available data do not indicate a potential for adverse reproductive or development effects.

JECFA has reviewed the results of genotoxicity tests for a number of benzyl derivatives, including benzoic acid and benzyl alcohol, and in view of the mainly negative results in the *in vitro* assays and the uniformly negative results in well-recognised *in vivo* assays, concluded that the benzyl derivatives are not genotoxic *in vivo*.

Evaluation and conclusion

In contrast to their use as food additives, the use of benzoic acid and benzyl alcohol as processing aids is unlikely to result in significant residues in food. Benzoic acid and benzyl alcohol are rapidly metabolised and long-term effects are generally only seen following exposure to relatively high levels. There are **no toxicological concerns** with the use of benzoic acid and benzyl alcohol as processing aids. The current maximum permitted levels and food groups are acceptable from a human safety perspective.

Benzoyl peroxide

Current permission in the Code

Benzoyl peroxide is currently permitted as a bleaching agent in all foods at a maximum permitted level of 40 mg/kg in the final food (measured as benzoic acid) (table to clause 12).

Available safety information

JECFA has evaluated the safety of benzoyl peroxide used as a bleaching agent in whey at a maximum concentration of 100 mg/kg (WHO 2005).

Benzoyl peroxide is manufactured by the reaction of benzoyl chloride, sodium hydroxide and hydrogen peroxide. Almost all the benzoyl peroxide used in food processing is converted to benzoic acid during heat treatment or storage. While traces of benzoyl peroxide may be present in the processed food, most, if not all, of the benzoyl peroxide ingested will be degraded to benzoic acid in the intestine.

In relation to its use as a bleaching agent in whey, the Committee considered this to represent only a minor contribution to the total dietary intake of benzoic acid for which a group ADI of 0-5 mg/kg BW exists. The Committee concluded that treatment of whey with benzoyl peroxide at a maximum concentration of 100 mg/kg does not pose a safety concern.

The International Agency for Research on Cancer (IARC) has considered both human and animal carcinogenicity data in relation to benzoyl peroxide (IARC 1999a), however all of the data relates to exposure via skin, which has little relevance to the oral route of exposure.

Little is known about the genotoxic properties of benzoyl peroxide. DNA damage has been observed in treated mammalian cells, but it is not mutagenic in bacteria and does not cause chromosomal damage in cultured mammalian cells or dominant lethal effects in mice.

The IARC concluded there is *inadequate evidence* in humans and only *limited evidence* in experimental animals for the carcinogenicity of benzoyl peroxide. The overall evaluation of the IARC was that benzoyl peroxide is *not classifiable as to its carcinogenicity to humans (Group 3)*.

Evaluation and conclusion

Only trace amounts of benzoyl peroxide are expected to be present in processed food, as most of the benzoyl peroxide is converted to benzoic acid during heat treatment and storage, or is degraded to benzoic acid in the intestine following ingestion. Therefore the same considerations as apply to benzoic acid and benzyl alcohol, also apply to benzoyl peroxide. Given the low levels present in food, its rapid metabolism (as benzoic acid) and the absence of toxicity at low levels, there are **no toxicological concerns** with the use of benzoyl peroxide as a processing aid. The current maximum permitted levels and food groups are acceptable from a human safety perspective.

Butane, isobutane and propane

Current permission in the Code

Butane, isobutane and propane are currently permitted as extraction solvents for use in flavourings at a maximum permitted level of 1 mg/kg and other foods at 0.1 mg/kg (table to clause 13).

Butane, isobutane and propane are also permitted as miscellaneous additives for use in accordance with GMP in processed foods specified in Schedule 1 of Standard 1.3.1 (pressurised food containers only).

Available safety information

All three substances are colourless gases. Isobutane has the same formula as *n*-butane (C_4H_{10}) but is structurally a different compound, which has different physical and chemical properties, compared to *n*-butane. Isobutane has a branched-chain structure, whereas *n*-butane has a straight-chain structure.

The toxicity of butane, isobutane and propane relates to their action as simple asphyxiants, which means they cause toxicity by displacing oxygen (IPCS 1997). There are no direct systemic effects, and no adverse effects following oral exposure have been reported.

All three substances have been evaluated by the SCF, both as extraction solvents (SCF 1981, SCF 1991) and as propellants (SCF 1999).

The Committee noted that from a toxicological point of view the content of non-volatile impurities in extraction solvents may be of greater significance with respect to presence in food as consumed, than small residues of the solvents themselves (SCF 1991). The Committee found it unnecessary to establish an ADI for butane, isobutane and propane and considered their use as extraction solvents acceptable providing their use is subject to a residue level per substance of 1 mg/kg in food consumed. The Committee added that if analytical data confirm that residues are normally below 1 mg/kg then the imposition of explicit conditions of use would be unnecessary.

JECFA evaluated propane in 1979 (WHO 1980) and concluded that propane has limited use and the residue in food is also limited. As such they decided it was not necessary to establish an ADI.

Evaluation and conclusion

The use of butane, isobutane, and propane is expected to result in only low residues in food. The available data do not indicate any adverse effects associated with oral exposure to these substances. Overall, there are **no toxicological concerns** with the use of butane, isobutane and propane as processing acids. The current maximum permitted levels and food groups are acceptable from a human safety perspective.

1-Butanol (Butyl Alcohol)

Current permission in the Code

Butanol is currently permitted as an antifoam agent in any food at levels up to 10 mg/kg in the final food (table to clause 4), an extraction solvent in all foods at levels up to 10 mg/kg in the final food (table to clause 13) and as a suspension agent for sugar crystals at levels up to 10 mg/kg in the final food (table to clause 14).

Available safety information

JECFA evaluated the safety of 1-butanol in 1997 and determined there are no safety concerns with the current level of intake when used as a flavouring agent (WHO 1998b). The Committee classified 1-butanol as a substance with a simple chemical structure and efficient mode of metabolism, suggesting a low order of toxicity by the oral route. The Committee concluded that 1-butanol can be predicted to undergo complete metabolism to endogenous products via the fatty acid and tricarboxylic acid pathways. In the opinion of the Committee, the endogenous levels of these metabolites would not give rise to perturbations outside the physiological range. Therefore, based on 1-butanol's simple chemical structure and known metabolism, the Committee had no safety concerns with its use as a flavouring agent.

A number of toxicity studies with 1-butanol have been reviewed by JECFA. No ADI has been allocated for 1-butanol.

In general, linear aliphatic alcohols exhibit low acute toxicity. Three acute oral toxicity studies are available for 1-butanol, indicating a LD_{50} between 790-4360 mg/kg BW.

In rats fed control diets or diets with 0.69, 1.38, 2.75 or 5.5% 1-butanol (equivalent to 690-5500 mg/kg BW) for 14 days, a statistically significant increase in the ratio of liver-to-body weight was reported in males at all but the lowest dose tested and in females only at the highest dose.

In a 28-day study using male rats fed diets containing 0, 1000, 3500 or 10 000 mg 1-butanol/ kg feed (about 90-940 mg/kg BW/day) in 2% corn oil, no deaths, gross lesions at necropsy or differences in liver and kidney weights were reported; there was a statistically significant increase in the ratio of adrenals-to-body weight at all doses compared to controls.

No adverse effects were observed when 6.9% 1-butanol (~ 5.6 mg/kg BW/day) and 25% sucrose were added to the drinking water of male rats for 13 weeks.

Both *in vitro* and *in vivo* genotoxicity studies have been conducted on 1-butanol. Negative results were obtained for both the Ames test in *S. typhimurium* TA102 and the sister chromatid exchange test in Chinese hamster ovary cells. A positive result was however found for 1-butanol in a forward mutation assay using Chinese hamster ovary cells at concentrations of 0.2-1.6 μg/ml. The Committee concluded this result was probably due to perturbations in the pH of the test medium.

Evaluation and conclusion

The use of 1-butanol as a processing aid is expected to result in only low residues in food. 1-Butanol is readily metabolised to innocuous substances and has been shown to have low oral toxicity. Overall, there are **no toxicological concerns** with the use of 1-butanol as a processing aid. The current maximum permitted levels and food groups are acceptable from a human safety perspective.

Chlorine, calcium hypochlorite and sodium hypochlorite

Current permission in the Code

Chlorine, calcium hypochlorite and sodium hypochlorite are permitted as processing aids for use in packaged water and in water used as an ingredient in other foods, up to a maximum permitted level of 10 mg/kg (available chlorine) in the final food (table to clause 11).

Chlorine, calcium hypochlorite and sodium hypochlorite are also permitted as bleaching, washing and peeling agents in all foods up to a maximum permitted level of 1.0 mg/kg (available chlorine) in the final food (table to clause 12).

Drinking water levels in Australia and New Zealand

The guideline health level for chlorine in the Australian Drinking Water Guidelines is 5 mg/L (as chlorine) (NHMRC 2004).

The maximum acceptable value for chlorine in the Drinking Water Standards for New Zealand is 5 mg/L (as chlorine), with the note that disinfection must never be compromised (Ministry of Health 2000).

Available safety information

Chlorine has been evaluated by JECFA as a flour treatment agent (WHO 1987a). In that evaluation, the Committee commented that no carcinogenic, teratogenic, or other toxic effects attributable to chlorination were observed in long-term and reproduction studies in which rats and mice were fed diets containing 75-79% dried cakes made from flour chlorinated at levels up to 2500 ppm. The Committee concluded that 0-2500 ppm Cl_2 was an acceptable level of treatment of flours for cake manufacturing.

JECFA has not evaluated the safety of active chlorine components when used in water as a disinfection agent, or for direct contact with food. Evaluations on the safety of chlorinated drinking water have however been undertaken by a number of other bodies including the IARC (IARC 1991), the IPCS (WHO 2000), and the National Health & Medical Research Council (NHMRC 2004).

In pure water, chlorine forms elemental chlorine (Cl_2), chloride ion (Cl^-) and hypochlorous acid (HOCl). As the pH increases, hypochlorous acid dissociates to hypochlorite ion (OCl^-). The term *free chlorine* (free available chlorine, free residual chlorine) refers to the concentrations of elemental chlorine, hypochlorous acid and hypochlorite ion that collectively occur in water. Several factors, including chlorine concentration, pH, temperature, exposure to light and the presence of catalysts or organic material, affect the stability of free chlorine in aqueous solution.

Chlorine is a strong respiratory irritant. Sodium hypochlorite (NaOCl) is also used as bleach and is frequently involved in human poisoning. These exposures, however, are not relevant to exposures from drinking water or from food sanitised with these chemicals. In animal studies using a naturally occurring non-radioactive chlorine isotope, chlorine was rapidly absorbed by the gastrointestinal tract, with the highest concentrations of the isotope being found in blood plasma. It is assumed that the toxicity of aqueous solutions containing chlorine, hypochlorous acid, or hypochlorite is similar since they are in dynamic equilibrium.

Very few toxic effects have been associated with drinking water containing high chlorine concentrations (NHMRC 2004). In one report, 150 people drank water with 50 mg/L during a period of mains disinfection, with no adverse effects. Several instances have been reported where military personnel drank water with chlorine concentrations up to 32 mg/L for several months with no ill effects. Mouth irritation and momentary constriction of the throat has been observed when the chlorine concentration exceeds 90 mg/L. Most people would refuse to drink water with a chlorine concentration over 25 mg/L. Long-term animal studies have shown no specific effects from the ingestion of chlorine.

Assessment of the mutagenicity of chlorine is complicated by its reactivity. Hypochlorite has been found to be mutagenic in tests with one strain of bacteria but not with another. Chromosome aberrations have been reported in tests with mammalian cells. Chlorine, hypochlorous acid and hypochlorite do not act as carcinogens or tumour initiators. Overall, it has been concluded, from the results of both animal and human studies, that chlorine and hypochlorite solutions probably do not themselves contribute to the development of cancer or any toxic effects (WHO 2000).

A WHO Working Group for the Guidelines for drinking-water quality (WHO 1993a) considered chlorine and established a tolerable daily intake (TDI) of 150 µg/kg BW for free chlorine. This TDI is derived from a NOAEL of approximately 15 mg/kg BW/day from a 2-year study in rats and mice undertaken by the National Toxicology Program, incorporating an uncertainty factor of 100.

Most attention has focused on the wide variety of disinfection by-products that result from reactions of chlorine and other disinfectants with both organic and inorganic precursors, which are found in virtually all water sources.

Natural organic matter (NOM) (which includes such substances as humic and fulvic acid), commonly measured by total organic carbon (TOC), serves as the organic precursors, whereas bromide ion (Br^-) serves as the inorganic precursor. Disinfection by-product formation is influenced by water quality (e.g., TOC, bromide, pH, temperature, ammonia, carbonate alkalinity) and treatment conditions (e.g., disinfectant dose, contact time, removal of NOM before the point of disinfectant application, prior addition of disinfectant).

Chlorine in the form of hypochlorous acid/hypochlorite ion ($HOCl/OCl^-$) reacts with bromide ion, oxidizing it to hypobromous acid/hypobromite ion ($HOBr/OBr^-$). Hypochlorous acid (a more powerful oxidant) and hypobromous acid (a more effective halogenating agent) react collectively with NOM to form chlorine disinfection by-products, including trihalomethanes (THMs), haloacetic acids (HAAs), haloacetonitriles (HANs), haloketones, chloral hydrate and chloropicrin. The dominance of chlorine disinfection by-product groups generally decreases in the order of THMs, HAAs and HANs. The relative amounts of TOC, bromide and chlorine will affect the species distribution of THMs (four species: chloroform, bromoform, bromodichloromethane [BDCM] and dibromochloromethane [DBCM]), HAAs (up to nine chlorinated/brominated species) and HANs (several chlorinated/brominated species). Generally, chlorinated THM, HAA and HAN species dominate over brominated species, although the opposite may be true in high-bromide waters. Other reaction products include chlorate (ClO_3^-) and 3-chloro-4-(dichloromethyl)-5-hydroxy-2[5*H*]- furanone (MX). MX and associated substances tend to be present at very low concentrations only (<0.1 µg/L). Although many specific chlorine disinfection by-products have been identified, a significant percentage of the total organic halogens still remain unaccounted for (WHO 2000).

A number of studies have suggested an association between chlorine disinfection by-products and various cancers. This association has been most consistent in relation to cancers of the bladder and rectum, but there are insufficient data to determine concentrations at which chlorination by-products might cause increased risk to human health (NHMRC 2004).

The IPCS noted in their evaluation that the epidemiological associations between chlorinated drinking water and human cancer have been subjected to several recent reviews, and the conclusions remain controversial (WHO 2000). None of the chlorination by-products studied to date has been found to be a potent carcinogen at concentrations normally found in drinking water. There is also insufficient epidemiological evidence to support a causal relationship between bladder cancer and exposures to chlorinated drinking water, THMs, chloroform or other THM species. The results of currently published studies also do not provide convincing evidence that chlorinated water or THMs cause adverse pregnancy outcomes.

The IARC also concluded there is *inadequate evidence* for the carcinogenicity of chlorinated drinking water in both humans and experimental animals, and so their overall evaluation was that chlorinated drinking water is *not classifiable as to its carcinogenicity to humans* (Group 3) (IARC 1991).

The WHO maximum guideline value for chlorine residue in drinking water is 5 mg/L (WHO 2004) and the WHO has also established guideline values in drinking water for the following by products: dibromochloromethane (100 μg/L), chloroform (200 μg/L), bromodichloromethane (60 μg/L), bromoform (100 μg/L), dichloroacetate (50 μg/L), trichloroacetate (100 μg/L), trichloroacetaldehyde (10 μg/L), dichloroacetonitrile (90 μg/L), dibromoacetonitrile (100 μg/L), trichloroacetonitrile (1 μg/L), 2,4,6-trichlorophenol (200 μg/L), cyanogen chloride (70 μg/L), chlorite (200 μg/L).

Evaluation and conclusion

In humans, very few toxic effects have been associated with drinking water containing high chlorine concentrations and long-term animal studies have shown no specific effects from the ingestion of chlorine. The available data, from both animal and human studies, indicates that chlorine and hypochlorite solutions probably do not themselves contribute to any toxic effects or the development of cancer. The main issue therefore is the formation of disinfection by-products and their potential to cause adverse effects, such as cancer, in humans. While some studies have suggested an association between chlorine disinfection by-products and various cancers, none of the chlorination by-products studied to date has been found to be a potent carcinogen at concentrations normally found in drinking water.

Overall, there are **no toxicological concerns** with the use of chlorine, calcium hypochlorite and sodium hypochlorite as processing aids in packaged water or as bleaching, washing and peeling agents.

The current maximum permitted levels and food groups for the use of chlorine, calcium hypochlorite and sodium hypochlorite as bleaching, washing and peeling agents are acceptable from a human safety perspective.

As packaged water can be used for as substitute for drinking water, the maximum permitted level for chlorine, calcium hypochlorite and sodium hypochlorite (measured as available chlorine) should be brought into conformity with the drinking water levels for Australia and New Zealand.

Chlorine dioxide and sodium chlorite

Current permission in the Code

Chlorine dioxide is currently permitted as a processing aid for use in packaged water and in water used as an ingredient in other foods at a maximum permitted level of 10 mg/kg (available chlorine) in the final food (table to clause 11).

Sodium chlorite is permitted as a bleaching agent, washing and peeling agent in all foods at a maximum permitted level of 1 mg/kg (available chlorine) in the final food (table to clause 12).

Levels in drinking water in Australia and New Zealand

The guideline health level for chlorine dioxide in the Australian Drinking Water Guidelines is 1 mg/L and for chlorite is 0.3 mg/L (NHMRC, 2004).

The maximum acceptable value for chlorine dioxide in the Drinking Water Standards for New Zealand is 0.3 mg/L for chlorite (as ClO_2) (Ministry of Health 2000).

Available safety information

The safety of chlorine dioxide and sodium chlorite has been evaluated by a number of bodies, including the WHO (2000), NHMRC (2004), ATSDR (2004) and US EPA (2000).

Chlorine dioxide is relatively unstable and rapidly dissociates, predominantly into chlorite and chloride, and to a lesser extent, chlorate. There is ready interconversion of these chemical species in water and in the gastrointestinal tract (EPA 2000). Chlorite and chlorate are in fact the major disinfection by-products formed by chlorine dioxide; there is no direct formation of organohalogen disinfection by-products (WHO 2000). Human exposure to chlorine dioxide and its by-products such as chlorite occurs primarily through ingestion of drinking water (ATSDR 2004). The taste and odour threshold for chlorine dioxide in water is 0.4 mg/L.

Chlorine dioxide, chlorite, and chlorate are all rapidly absorbed from the gastrointestinal tract into blood plasma and distributed to the major organs. All compounds appear to be rapidly metabolised. Chloride ion is the ultimate metabolite of chlorine dioxide, making up approximately 80-87% of radiolabelled chlorine excreted in the urine. The remainder is made up of chlorite (11-12%) and chlorate (2%). The metabolism of chlorite is similar to that of chlorine dioxide.

Available human and animal data indicate that oral exposure to relatively large amounts of chlorine dioxide or chlorite may result in irritation of the digestive tract, the severity of which appears to be dose-dependent. High-level oral exposure also results in increased levels of methaemoglobin in the blood, which reduces the ability of oxygen to bind to haemoglobin. These exposures, however, are not relevant to exposures from drinking water or from food sanitised with these chemicals.

In general, human ingestion studies have found no adverse effects in adults and neonates living in areas with chlorine dioxide-disinfected water. In a study with human volunteers, no adverse effects were observed after drinking water with either chlorine dioxide or chlorite concentrations up to 5 mg/L for a period of 12 weeks.

In studies with experimental animals, a number of effects have been observed. Both chlorine dioxide and chlorite appear to induce delays in neurodevelopment, as evidenced by delayed brain growth, decreased locomotor and exploratory behaviour, and altered auditory startle response in animals exposed during critical periods of neurodevelopment. These effects have been observed in rat pups whose mothers were exposed before mating and during gestation and lactation, and also in pups exposed directly via oral gavage during postnatal development. A NOAEL of 2.9 mg/kg BW/day for chlorite has been identified on the basis of decreased auditory startle response amplitude at 5.7 mg/kg BW/day.

Concurrent with the neurodevelopmental effects described above, changes have also been observed, although not consistently, in thyroid hormone levels in animals that were either directly exposed to chlorine dioxide or exposed to chlorine dioxide or chlorite via their mothers during pre and postpartum development. These effects were typically observed at dose levels ranging from 9-13 mg/kg BW/day. The toxicological significance of these changes is unclear.

The available data on the carcinogenicity of chlorine dioxide and chlorite do not indicate any concern, however only limited animal studies have been undertaken. Genotoxicity testing of both chlorine dioxide and sodium chlorite has produced both positive and negative results. Chlorine dioxide was not mutagenic (either with or without metabolic activation) in one Ames assay of *Salmonella typhimurium*, but was weakly positive in one strain of *S. typhimurium* in another assay, whereas sodium chlorite induced reverse mutations in *S. typhimurium* (with activation). Chlorine dioxide did not induce chromosomal aberrations in Chinese hamster fibroblast cells, whereas sodium chlorite did. Both chlorine dioxide and sodium chlorite were negative in *in vivo* assays for micronuclei and bone marrow chromosomal aberrations as well as sperm head abnormalities in mice.

Evaluation and conclusion

Delays in neurodevelopment have been observed in animal studies following *in utero* and postnatal exposure to ingested chlorine dioxide or chlorite. In humans, exposure to high levels can result in irritation of the digestive tract as well as a condition called methaemoglobinaemia, which results in an impaired ability for haemoglobin to transport oxygen to tissue. No adverse effects however have been observed in adults and neonates consuming water that has been disinfected with chlorine dioxide. In the limited studies conducted to date there is no evidence for carcinogenicity of chlorine dioxide and chlorite.

On the basis of the available data, there are **no toxicological concerns** with the use of chlorine dioxide as a processing aid for use in packaged water and in water used as an ingredient in other foods, or with sodium chlorite as a bleaching, washing and peeling agent.

The current maximum permitted level for sodium chlorite is acceptable from a human safety perspective. As packaged water can be used for as substitute for drinking water, the maximum permitted level for chlorine dioxide should be brought into conformity with the drinking water levels for Australia and New Zealand.

Chromium

Current permission in the Code

Chromium is currently permitted as a catalyst in the course of manufacture of any food up to maximum permitted level of 0.1 mg/kg in the final food (table to clause 5).

Available safety information

The safety of chromium has been evaluated by a number of different bodies including the IPCS (WHO 1988), IARC (IARC 1990a), ATSDR (ATSDR 2000a) and the US EPA (EPA 1998a). JECFA has not undertaken an evaluation of chromium.

In discussing the safety of chromium it is important to distinguish between the different oxidation states, as important differences exist in their properties and biological effects. Chromium has oxidation states ranging from –2 to +6, with the most commonly occurring being chromium metal (O), trivalent Cr(III), and hexavalent Cr(VI). Cr(VI) is reduced to the trivalent state in the presence of oxidisable organic matter. The oxidation of Cr(III) to Cr(VI) never occurs in biological systems (WHO 1988). Cr(III) is an essential nutrient where it plays a role in glucose, fat and protein metabolism by potentiating the action of insulin (ATSDR 2000a).

The bioavailability of chromium is probably the single most important factor in determining the toxicity of a specific chromium source (EPA 1998a). Gastrointestinal absorption of Cr(VI) occurs with greater efficiency than Cr(III). However, ingested hexavalent chromium is efficiently reduced to the trivalent state in the gastrointestinal tract, which means the rate of absorption of Cr(VI) compounds is still relatively poor. About 0.5-2.0 % of ingested Cr(III) is absorbed via the gastrointestinal tract of humans, compared to 2-10 % for Cr(VI) as potassium chromate. Once absorbed, chromium compounds are distributed to all organs of the body. Chromium is poorly taken up by cells in any valence state, but Cr(III) is taken up much less efficiently than Cr(VI). Hexavalent chromium is able to cross cell membranes through the phosphate and sulphate anion exchange carrier pathway, where it undergoes intracellular reduction to Cr(III). Cr(III) compounds may cross cell membranes but only with very low efficiency. Absorbed chromium is primarily eliminated in the urine. For unabsorbed chromium, the primary pathway of elimination after oral exposure is via the faeces.

In general, Cr(VI) compounds are more toxic than Cr(III) compounds (ATSDR 2000a). Toxic effects from trivalent chromium have been reported only following parenteral administration. Trivalent chromium, when administered to animals in food or water, does not appear to induce any harmful effects, even when given in large doses (WHO 1988). Most of the toxic effects, both acute and chronic (including carcinogenicity), have been associated with hexavalent chromium compounds.

The greater toxicity of Cr(VI) compounds is believed to be due in part to its intracellular reduction to Cr(III). The products of the metabolic reduction of Cr(VI) (free radicals, singlet oxygen, reactive Cr(IV) and (V) intermediates, and the newly generated Cr(III)) can produce a variety of DNA lesions, as well as cellular effects. It is these effects that are thought to be primarily responsible for the carcinogenic effects seen in humans and experimental animals following exposure to Cr(VI) compounds (ATSDR 2000a).

Hexavalent chromium has been shown to be genotoxic only in the presence of appropriate reducing agents *in vitro* or in viable cell systems *in vitro* and *in vivo*. Hexavalent chromium has been shown to be mutagenic in bacterial systems in the absence of a mammalian activating system, and not mutagenic when a mammalian activating system is present. Hexavalent chromium is also mutagenic in eukaryotic test systems, and clastogenic in cultured mammalian cells. Trivalent chromium is also genetically active but only in *in vitro* tests, where it can have a direct interaction with DNA.

Hexavalent chromium has been designated as a known human carcinogen by the inhalation route of exposure (EPA 1998a, NTP 2005). Results of occupational epidemiologic studies of chromium-exposed workers consistently demonstrate that chromium is carcinogenic by the inhalation route of exposure, with dose response relationships being established for chromium exposure and lung cancer.

In these studies exposure was to both hexavalent and trivalent compounds however, because only Cr(VI) has been found to be carcinogenic in animal studies, it was concluded that only Cr(VI) should be classified as a human carcinogen.

At present, the potential carcinogenicity of Cr(VI) by the oral route of exposure cannot be determined because of a lack of sufficient epidemiological and toxicological data. One study of miners exposed to chromium in drinking water has suggested an association with stomach cancer, but other human and animal studies have not reported similar effects (EPA 1998a).

The IARC has also examined the potential carcinogenicity of various chromium compounds and concluded there is sufficient evidence in humans for the carcinogenicity of Cr(VI) compounds as encountered during chromate production (inhalation exposure) (IARC 1990a). They also concluded there is inadequate evidence in humans and experimental animals for the carcinogenicity of metallic chromium and Cr(III) compounds.

Little data exist concerning other effects resulting from the ingestion of hexavalent chromium compounds. High oral doses of hexavalent chromium compounds have been reported to cause both reproductive and developmental toxicity in a number of species. Various testicular effects and alterations in sexual behaviour have been observed in male mice, rats and rabbits following oral exposure to doses ranging from 15-42 mg Cr(VI)/kg BW/day. Decreased mating and fertility, histological changes to the ovary and vagina, and decreased litter sizes have been observed in female rats and mice given following oral exposure to doses ranging from 37-66 mg Cr(VI)/kg BW/day. A number of developmental effects, including decreased foetal weight, increase resorptions and increased foetal abnormalities, have also been observed in the same dose range.

Evaluation and conclusion

The toxicity of chromium depends largely on its oxidation state. Different oxidation states have different bioavailability and different biological effects. Most of the toxic effects, both acute and chronic (including carcinogenicity), have been associated with hexavalent chromium compounds, whereas trivalent chromium, which is an essential nutrient, appears to have low oral toxicity. There is convincing evidence that hexavalent chromium is a human carcinogen by the inhalation route. The situation with regard to oral exposure is less clear because of limited epidemiological and toxicological data. Oral doses of hexavalent chromium have also been associated with reproductive and development toxicity in experimental animals.

Given the uncertain potential for carcinogenicity of hexavalent chromium by the oral route, and its other toxic effects in experimental animals, there **are toxicological concerns** with the current permission for chromium as a processing aid, because as written it does not preclude the use of hexavalent compounds. There would be no toxicological concerns with the use of other chromium compounds at the current maximum permitted level and food groups.

β-Cyclodextrin

Current permission in the Code

β-Cyclodextrin is currently permitted to extract cholesterol from eggs at GMP levels (table to clause 14).

Available safety information

β-Cyclodextrin has been evaluated by JECFA at is forty-first and forty-fourth meetings (WHO 1993c, 1996) and also by the SCF (SCF 1997), where similar conclusions were reached. An ADI of 0-5 mg/kg BW was allocated for β-cyclodextrin, based on the NOAEL of 1.25% in the diet (equal to 470 mg/kg BW/day) in a one-year study in dogs and applying a safety factor of 100.

β-Cyclodextrin is a cyclic heptamer composed of seven glucose units joined 'head-to-tail' by α-1,4 links. It is produced by the action of the enzyme cyclodextrin glycosyl transferase (CGT) on hydrolyzed starch syrups. CGT is obtained from *Bacillus macerans (now known as Paenibacillus macerans)*, *B. circulans* or related strains of *Bacillus*.

As a result of its cyclic structure, ß-cyclodextrin has the ability to form inclusion compounds with a range of molecules, generally of molecular mass of less than 250. The primary use of β-cyclodextrin is as a food additive, where it may serve as a carrier and stabiliser of food flavours, food colours and some vitamins. Intake of β-cyclodextrin from use as a food additive has been estimated at 1-1.4 g/day. The use of β-cyclodextrin to reduce the cholesterol content of eggs is predicted to make a much lower contribution to intakes than its use in food additive applications.

The toxicokinetic data available for β-cyclodextrin are limited but indicate that at low dietary concentrations, in both experimental animals and humans, β-cyclodextrin is probably not absorbed from the upper gastrointestinal tract but is hydrolysed in the colon by gut microflora and possibly endogenous enzyme activity. In studies with dogs, a small proportion (5%) of administered β-cyclodextrin is absorbed and excreted unchanged in the urine.

The available toxicity studies for β-cyclodextrin indicate it is a substance of low systemic toxicity in laboratory animals. In a one-year study in dogs, in which β-cyclodextrin was administered at dietary concentrations of 0, 0.62, 1.25 and 5.0%, the NOAEL was 1.25%, equal to 470 mg/kg BW/day, based on urinary effects in males (elevated urinary protein, elevated urinary calcium) and a slightly reduced body-weight gain at the high dose level. There were no adverse histopathological findings.

In a three-generation reproductive toxicity study in rats, where β-cyclodextrin was administered in the diet at dose levels of 0, 1.25, 2.5 or 5.0 %, the only adverse effect seen at higher doses was impaired pup growth during lactation which was probably secondary to reduced food consumption and body-weight gain in the dams at this dose level. The NOAEL was 1.25%, equal to between 560 and 2900 mg/kg BW/day, depending on the stage of the study.

Long-term toxicity/carcinogenicity studies have been undertaken in both the rat and the mouse using doses of 0, 25 (rat only), 75, 225, and 675 mg/kg BW/day. In the mouse study, β-cyclodextrin caused inflammatory changes in the lower gastrointestinal tract, which were considered to be the cause of death of some animals. The lowest dose level at which this occurred was 75 mg/kg BW/day (1/52 male affected) and the NOEL was 25 mg/kg BW/day. The lesions were considered to probably represent a species-specific reaction to β-cyclodextrin in some mice. No such effects were seen either in the carcinogenicity study in rats. No treatment-related neoplastic lesions were observed in the carcinogenicity studies.

β-Cyclodextrin was negative in *in vitro* tests for point mutations in bacterial and mammalian cells, and was also negative in an *in vitro* test for chromosome aberrations in human lymphocytes, as well as an *in vivo* micronucleus test.

Evaluation and conclusion

The use of β-cyclodextrin as a processing aid is limited to a very specific use, namely to reduce the cholesterol content of eggs. The limited use of β-cyclodextrin is likely to result in only very low residues in food. The available data indicate that β-cyclodextrin is a substance of low systemic toxicity. Overall, there are **no toxicological concerns** with the use of β-cyclodextrin as a processing aid to reduce the cholesterol content of eggs at GMP levels.

Ethyl acetate

Current permission in the Code

Ethyl acetate is currently permitted as a carrier, solvent or diluent in any food at GMP levels (table to clause 10), as an extraction solvent in all foods up to a maximum permitted level of 10 mg/kg in the final food (table to clause 13), and for the cell disruption of yeast at GMP levels (table to clause 14).

Available safety information

Both JECFA and the US EPA have evaluated the safety of ethyl acetate.

JECFA assigned an ADI of 0-25 mg/kg BW in 1967 on the basis of the known metabolic fate of ethyl acetate, as no toxicological data were available (WHO 1968). The ADI was maintained by JECFA at its forty-sixth meeting (WHO 1997), where ethyl acetate was evaluated along with fourteen other ethyl esters used as flavouring agents in foods.

Ethyl acetate is completely hydrolysed in the human body to ethanol and its component carboxylic acid (acetic acid), both of which are endogenous intermediates in human metabolism and considered to be innocuous products. JECFA concluded there were no safety concerns at the estimated level of current intake of ethyl acetate (as a flavouring).

JECFA estimated that, in the unlikely event that all foods containing all of the 15 ethyl esters as flavouring substances were consumed simultaneously on a daily bases, the daily intake for individuals in Europe and the USA would be 1000 and 870 μg/kg BW, respectively. The equivalent estimated daily per capita intakes of ethanol are 460 and 410 μg/kg BW, respectively. The endogenous synthesis of ethanol has been estimated to be approximately 40-80 mg/kg BW per day, which is of the order of 100-200 times the estimated daily intake per kg body weight derived from the ethyl esters. The Committee concluded that the use of ethyl acetate as a flavouring agent would therefore not present safety concerns at the estimated levels of current intake.

One toxicological study was available of unknown quality, where no adverse effects were reported when rats were given a drinking-water-fusel oil mixture containing ethyl acetate at a dose corresponding to 4 mg/kg BW per day for 56 weeks.

The US EPA evaluated ethyl acetate in 1988 (EPA 1988). Ethyl acetate is considered to be fairly non-toxic (oral LD_{50} in rats: 11.3 g/kg). Only one sub-chronic study in rats was available. Groups of rats were gavaged daily with 0, 300, 900 and 3600 mg/kg BW/day of ethyl acetate. Male rats exposed to the highest dose (3600 mg/kg BW/day) showed significant toxic effects, which resulted in depressed body and organ weights, and depressed food consumption. Female rats exposed to the high dose showed slight but non-significant depression of the above parameters compared with controls. The next lower dose (900 mg/kg BW/day) did not produce any adverse effects in either male or female rats and was therefore considered a NOAEL. An uncertainty factor of 1000 was applied to the NOAEL to derive an oral reference dose (RfD) of 0.9 mg/kg BW/day (or 63 mg/day for a 70-kg person). Because of the lack of other toxicological data, there was only low to medium confidence in the RfD.

Evaluation and conclusion

Although there is limited toxicological information available for ethyl acetate, the data indicates it is completely metabolised by the body to innocuous products (ethanol and acetate), which are normal components of intermediary metabolism. Overall, there are **no toxicological concerns** with the use of ethyl acetate as a processing aid. The current maximum permitted levels and food groups are acceptable from a human safety perspective.

Hexanes

Current permission in the Code

Hexanes are currently permitted for use as extraction solvents in all foods up to a maximum permitted level of 20 mg/kg in the final food (table to clause 13).

Available safety information

'Hexane' or 'hexanes' is a commercial product consisting of a mixture of hydrocarbons with six carbon atoms and includes *n*-hexane and its isomers 2-methylpentane and 3-methylpentane as well as small amounts of other hydrocarbons. Where intended for specialised oil extractions for food use, the purity of *n*-hexane products are typically in the range 95-99 % *n*-hexane (ATSDR 1999).

Because of the high volatility of *n*-hexane, exposure to *n*-hexane occurs predominantly by the inhalation route. Prolonged occupational exposure by this route has resulted in significant neurotoxicity, the principal toxic effect being peripheral neuropathy (ATSDR 1999).

n-Hexane has a very low solubility in water (9.5 mg/L at 25ºC), and significant oral exposure through food or drinking water has not been reported (ATSDR 1999). As a consequence, little toxicokinetic and toxicological information exists for oral (or dermal) exposure to *n*-hexane in humans or laboratory animals. No studies are available that specifically address the absorption of *n*-hexane following ingestion by the oral route, although absorption can be inferred because significant levels of one of the *n*-hexane metabolites has been measured in the serum of rats receiving *n*-hexane by gavage (ATSDR 1999). *n*-Hexane is metabolised by mixed-function oxidases in the liver to a number of metabolites, including 2,5-hexanedione, which is believed to be the toxic agent in *n*-hexane induced neurotoxicity.

Little information is available on the levels of *n*-hexane in food. Recent studies have found that residual *n*-hexane residues for refined food products would be less than 2 ppm. Such small amounts are regarded as toxicologically insignificant (ATSDR 1999).

JECFA has not set an ADI for n-hexane but stressed that the solvent should be used only in accordance with GMP to ensure minimal residues in food (WHO 1971).

In a recent evaluation, the ATSDR found the database for oral exposure to be insufficient to derive a safe level of exposure (ATSDR 1999). Only three animal studies (two in rats, one in chickens) were located regarding neurological effects after oral exposure to *n*-hexane. No human studies are available.

Decreases in motor nerve conduction velocities were noted in rats following exposure to 1250 mg/kg/day *n*-hexane for four and eight weeks.

No changes in behaviour or clinical signs of peripheral neuropathy were noted. In another study, groups of male rats were exposed by gavage to *n*-hexane and its metabolites (2-hexanol, 2-hexanone, 2,5-hexanedione, 2,5-hexanediol, 5-hydroxy-2-hexanone) for 90-120 days. The doses were 570, 1140, and 4000 mg/kg/day *n*-hexane. Practical grade hexane (40% *n*-hexane) was also tested at 4000 mg/kg/day. Clinical signs of neurotoxicity (severe hind limb weakness or paralysis) were not observed over the 90-day dosing period at 570 and 1140 mg/kg/day, but were observed at the high dose after 101 days in three out of four rats. Clinical signs of neurotoxicity were also observed with all other chemicals tested except practical grade hexane. The most rapid onset of clinical symptoms (17 days) was observed in rats dosed with 2,5-hexanedione. Histological evidence of tibial nerve alteration was found in rats receiving the highest dose, including in one rat receiving practical grade hexane. Body weight reduction was noted at all dose levels tested and testicular atrophy was also noted in rats receiving the highest dose of *n*-hexane, with this effect being reproduced in rats receiving 2,5-hexanedione.

The database on the genotoxic potential of *n*-hexane is limited but *n*-hexane does not appear to be mutagenic in *in vitro* or *in vivo* test systems.

Evaluation and conclusion

The use of hexane as extraction solvents is reported to leave only very low residue levels in food. The database on the oral toxicity of hexanes is limited, however adverse effects are typically only observed at relatively high levels. The low residues of hexane expected to result from its use as a processing aid are considered to be of little toxicological significance. There are **no toxicological concerns** with the use of hexane as a processing aid (extraction solvent). The current maximum permitted levels and food groups are acceptable from a human safety perspective.

Hydrogen peroxide

Current permission in the Code

Hydrogen peroxide is currently permitted for the following uses:

- in packaged water and in water used as an ingredient used in other foods at a maximum permitted level of 5 mg/kg in the final food (table to clause 11);
- as a bleaching, washing and peeling agent in all foods at a maximum permitted level of 5 mg/kg in the final food (table to clause 12);
- as an inhibiting agent for dried vine fruits, fruit and vegetable juices, sugar, vinegar and yeast autolysate at a maximum level of 5 mg/kg in the final food (table to clause 14);
- to remove glucose from egg products at a maximum level of 5 mg/kg in the final food (table to clause 14); and
- for the removal of sulphur dioxide at a maximum level of 5 mg/kg in the final food (table to clause 14).

Available safety information

Hydrogen peroxide was evaluated by JECFA in 1965 and again in 1973 for the purpose of establishing an ADI (WHO 1966, WHO 1974). Only limited toxicological and other information were available to the Committee. The Committee noted that when hydrogen peroxide is used as an antimicrobial in dairy products or other foodstuffs, the excess is destroyed. Toxicological considerations therefore apply only to the possible formation of toxic substances, but not to residual hydrogen peroxide. Small amounts of hydrogen peroxide given orally have been found to produce no toxicological effects, because of the rapid decomposition by the catalase of intestinal cells. The Committee commented that biochemical studies and short-term animal studies with hydrogen peroxide treated milk and cheese support the view that milk treated with hydrogen peroxide may be safe, although long-term studies are lacking. No ADI was allocated because of the instability of the compound in contact with food.

Hydrogen peroxide has been evaluated for potential carcinogenicity (IARC 1999b). No human data were available. Hydrogen peroxide has been tested in mice by oral administration, where both adenomas and carcinomas of the duodenum were observed. Hydrogen peroxide is formed intracellularly as a result of certain enzymatic reactions. Hydrogen peroxide, either from this source or externally applied, generates hydroxyl radicals that initiate lipid peroxidation chain reactions within exposed cells and can lead to DNA damage and cell death. DNA damage has been demonstrated in bacteria and in cultured mammalian cells. In addition, hydrogen peroxide induced mutations in bacteria, yeast and other fungi and there is some evidence that it can do so in Chinese hamster V79 and mouse lymphoma L5178Y cells at the *hprt* locus. Chromosomal aberrations and sister chromatid exchanges are induced in both human and other mammalian cells *in vitro*, but it did not induce chromosomal aberrations in the bone-marrow cells of exposed rats.

IARC concluded there is inadequate evidence for carcinogenicity in humans and only limited evidence in experimental animals. Hydrogen peroxide is therefore not classifiable as to its carcinogenicity to humans (Group 3).

Evaluation and conclusion

The use of hydrogen peroxide at low levels in food is unlikely to leave significant residue levels. The compound's instability also means it will rapidly decompose. Overall, there are **no toxicological concerns** with the use of hydrogen peroxide as a processing aid. The current maximum permitted levels and food groups are acceptable from a human safety perspective.

Isopropyl alcohol

Current permission in the Code

Isopropyl alcohol is currently permitted as a generally permitted processing aid at GMP levels (table to clause 3) and as a carrier, solvent and diluent up to a maximum permitted level of 1000 mg/kg in the final food (table to clause 10).

Available safety information

The safety of isopropyl alcohol (isopropanol) has been evaluated by JECFA (WHO 1999) and the European Food Safety Authority (EFSA 2005). Isopropanol was evaluated most recently by JECFA at its fifty-first meeting. The use of isopropanol as an extraction solvent, carrier solvent and flavouring agent is considered acceptable and no ADI has been established. In relation to its use as a flavouring agent, the Committee concluded there are no safety concerns at current levels of intake. Isopropanol is expected to be metabolised via well-known biochemical pathways to innocuous metabolic and/ or endogenous substances. In the opinion of the JECFA, the endogenous levels of metabolites would not give rise to perturbations outside the physiological range.

In studies with mice and rats, 56% and 26% of an oral dose of isopropanol was exhaled as acetone and CO2, respectively. Unmetabolised isopropanol was not detected. Approximately 5% was excreted in urine as a metabolite tentatively identified as propyl-2-glucuronic acid ester, together with small amounts of acetone and traces of isopropanol.

Only very limited human data and no chronic/carcinogenicity animal studies are available for oral exposure to isopropanol. The available studies consist of a short term drinking water studies in rats, a reproductive study in rats, plus several developmental and genotoxicity studies.

Isopropanol was ingested by groups of eight adult human male volunteers at doses of 0, 2.6, or 6.4 mg/kg BW/day for six weeks. No significant changes were observed in the chemical or cellular composition of blood or urine, in the ability of the liver to excrete sulfobromophthalein, in the optical properties of the eye, or in the general well being of the subjects.

The potential toxicity of isopropanol has been investigated in a 12-week study with male rats given 0, 870, 1300, 1700, and 2500 mg/kg BW/day in their drinking water. Body weights were statistically significantly decreased in rats at 1700 or 2500 mg/kg BW/day. Statistically significant, dose-related changes in relative liver weights were observed at the three highest doses; significant increases in testis weights were observed at 2500 mg/kg bw per day; significant increases in relative kidney weights were seen at the three highest doses; and statistically significant increases in relative adrenal weights were observed at the two highest doses. Increased formation of hyaline casts and increased hyaline droplet content were observed in the proximal tubules of the kidneys in a dose-dependent fashion. The NOAEL for the study was 870 mg/kg BW/day.

A two-generation reproduction study with isopropanol was undertaken in rats using doses of 0, 100, 500 or 1000 mg/kg BW/day by gavage for at least 10 weeks prior to mating. Findings in the parental animals consisted of increased body weight gain during lactation in the mid and high-dose females, increased liver and kidney weights in the mid and high-dose groups of both sexes, and centrilobular hepatocyte hypertrophy in some high-dose P_2 males.

Kidney lesions were observed in the P_1 males in the mid and high-dose groups and all treated P_2 males, however, this effect was considered unique to the male rat and of no toxicological significance to humans. Increased mortality was seen in the high-dose F_1 offspring during the early postnatal period with not other clinical signs being seen in offspring from either generation. A statistically significant reduction in the male mating index was observed in the high-dose P_2 males with no other reproductive effects being seen. The NOAEL for reproductive toxicity was 500 mg/kg BW/day.

Developmental studies have been undertaken in rats and rabbits. In rats, the only treatment related effects in the dam were a reduction in maternal body weight and gravid uterine weight in the group receiving 1200 mg/kg BW/day on gestational days 6-15. Foetal litter body weights were significantly reduced at the 800 and 1200 mg/kg BW/day dose levels but no teratogenic effects were observed. The NOAEL for developmental toxicity was 400 mg/kg BW/day. In rabbits, the dams were more sensitive to toxic effects from isopropanol, exhibiting profound clinical signs (laboured respiration, cyanosis, lethargy, peripheral vasodilation) at 480 mg/kg BW/day. No developmental effects, including teratogenicity, were observed at any of the dose levels tested. In a developmental neurotoxicity study using rats, no treatment related effects were observed on motor activity and parameters of other behavioural tests, brain weights and morphology of the central and peripheral nervous system, at doses up to 1200 mg/kg BW/day on gestational days 6-21.

In genotoxicity studies, negative results have been obtained for the Ames assay (with or without metabolic activation), the Chinese hamster ovary HGPRT-forward mutation assay and the mouse micronucleus assay, and the sister chromatid exchange test in Chinese hamster lung fibroblasts

Evaluation and conclusion

Isopropanol is efficiently metabolised by well-known biochemical pathways to innocuous substances, which are normally found endogenously. Isopropanol does not accumulate in the body and nor do its metabolites raise toxicological concerns. The available animal studies indicate that isopropanol is a substance of relatively low oral toxicity. Overall, there are **no toxicological concerns** with the use of isopropanol as a processing aid. The current maximum permitted levels and food groups are acceptable from a human safety perspective.

Methylene Chloride (Dichloromethane)

Current permission in the Code

Methylene chloride is currently permitted for use as an extraction solvent for decaffeinated tea and coffee and as an extraction solvent for flavourings up to a maximum permitted level of 2 mg/kg in the final food (table to clause 13).

Available safety information

Evaluations of the safety of methylene chloride have been undertaken by JECFA (WHO 1980, 1983, 1993b), ATSDR (2000b), the IARC (1999c), the US EPA (1985a, 1985b), as well as by FSANZ in 1995 (as the National Food Authority; NFA 1995) and 1999 (as the Australia New Zealand Food Authority; ANZFA 1999).

Methylene chloride had been examined by JECFA for the establishment of an ADI. The Committee established a temporary ADI of 0-0.5 mg/kg BW, and recommended that the solvent should be used according to GMP, which would result in minimum residues and prevent any significant toxicological effects (WHO 1980). In a subsequent evaluation, the Committee withdrew the previously allocated ADI and recommended that the use of methylene chlorine as an extraction solvent should be limited in order to ensure that its residues in foods are as low as practicable (WHO 1983). The Committee considered the available lifetime studies in rats and mice, due to a number of shortcomings, were inadequate for a complete evaluation of the possible carcinogenicity of methylene chloride. In the more recent evaluation, the Committee concluded that the use of methylene chloride as an extraction solvent in food processing should be limited to current uses (as an extraction solvent for spice oleoresins and the decaffeination of tea and coffee, and for food additives in which previous specifications drawn up by the Committee included residues of methylene chloride) (WHO 1993b).

In the assessment undertaken by the NFA in 1995, which was based on the JECFA evaluation in 1993, it was concluded that the use of methylene chloride as a extraction solvent in food processing should be limited to the use for spice oleoresins and the decaffeination of tea and coffee (NFA 1996). A maximum permitted residue of 5 mg/kg was adopted for decaffeinated coffee, and 2 mg/kg for flavours. In 1998, ANZFA received an Application for the use of methylene chloride as a processing aid for the decaffeination of tea. The toxicological assessment concluded that methylene chloride has low acute oral toxicity in laboratory animals and long-term administration does not appear to be associated with an increased incidence of tumours or adverse reproductive or developmental effects (ANZFA 1999). A tolerable intake in humans of 50 µg/kg BW/day was established on the basis of dose-related haematological changes in rats. The maximum dietary exposure to methylene chloride from decaffeinated tea was estimated to be below the tolerable daily intake and not expected to lead to any adverse effects in humans.

Methylene chloride is readily absorbed from the gastrointestinal tract and distributed to the blood, liver, lung, kidneys, body fat, and nervous tissues of animals and humans. Methylene chloride is readily eliminated mainly by exhalation of the parent compound and the metabolites carbon dioxide and carbon monoxide. Systemic accumulation of methylene chloride does not occur. Methylene chloride has been shown to cross the placenta in pregnant rats.

Methylene chloride is metabolised to CO and CO_2 by two pathways; one dependent on oxidation by mixed-function oxidases; and the other on glutathione S-transferases. The mixed-function oxidase pathway appears to be the preferred metabolic route at low concentrations of methylene chloride, while at higher concentrations this pathway becomes saturated, making a larger percentage of methylene chloride available for metabolism by the glutathione-dependent pathway. The metabolic production of CO from methylene chloride leads to the formation of carboxyhaemoglobin, the cause of the hypoxic state commonly seen in accidental poisoning by methylene chloride.

Studies on the effects of oral exposure to methylene chloride are limited. Only a small number of animal studies have been undertaken, and very little human data is available. The majority of available information on the toxicity of methylene chloride in both experimental animals and humans relates to inhalation exposure and therefore is not relevant to this assessment.

Some haematological effects (increased erythrocyte count, mean haematocrit and haemoglobin levels) have been observed in studies with rats receiving doses up to 250 mg/kg BW/day in drinking water for 2 years. The NOAEL for this study was 6 mg/kg BW/day. Similar effects have not been observed in mice.

Some limited liver effects have also been observed in both short and long terms studies with rats and mice given methylene chloride in drinking water. Histological changes to the liver consisting of increased foci of cellular alteration and fatty changes have been observed in rats receiving 55 mg/kg BW/day for 2 years (NOAEL 6 mg/kg BW/day) and histological evidence of increased liver fat have been observed in mice receiving 236 mg/kg BW/day (NOAEL 175 mg/kg BW/day). Single and repeat doses of high levels of methylene chloride have also produced elevations in serum enzyme levels indicative of liver toxicity.

A variety of neurobehavioural effects, such as increased motor activity and decreased learning ability have been observed in experimental animals after inhalation exposure to high concentrations of methylene chloride. The neurotoxicity depends on both a direct, non-specific narcotic action on the central nervous system, and an equally non-specific carbon monoxide-induced hypoxic effect. No data is currently available on neurotoxic effects via oral exposure.

No studies are available regarding carcinogenic effects in humans following oral exposure to methylene chloride. Studies in animals are said to provide suggestive evidence that ingestion of methylene chloride may increase the incidence of liver cancer.

In a 2-year study in rats receiving 5, 50, 125, or 250 mg/kg BW/day of methylene chloride in the drinking water the incidence of combined hepatocellular carcinoma and neoplastic nodules was statistically significantly increased in female rats in the 50 and 250 mg/kg BW dose groups. The incidence of hepatocellular carcinoma alone was not significantly increased. The combined incidence of hepatocellular carcinoma and neoplastic nodules in controls and the four dose groups however was similar to that for historical controls. Male rats showed no increase in liver tumours. In a similar study in mice, receiving 0, 60, 125, 185, or 250 mg/kg BW/day there was an increased incidence of combined neoplastic nodules and hepatocellular carcinoma in males. The increase was not dose-related, but the pair wise comparisons for the two mid- dose groups were reported to be statistically significant. The hepatocellular carcinoma incidence alone for male mice (which was about 55 to 65% of the total) was not significantly elevated. Female mice did not have increased liver tumour incidence. This study is regarded as suggestive but not conclusive evidence for carcinogenicity of methylene chloride. The US EPA has classified methylene chloride as a probable human carcinogen.

The IARC has classified methylene chloride as *possibly carcinogenic to humans (Group 2B)*. This classification is based on *sufficient evidence* in experimental animals and *inadequate evidence* in humans for the carcinogenicity of methylene chloride (IARC 1999c). The majority of information and data considered by the IARC relates to inhalation exposure. The oral studies in experimental animals were found to give inconclusive results.

In terms of genotoxic effects, *in vitro* results have been mixed in bacterial assays and in tests using mammalian cells. Methylene chloride has cause chromosomal aberrations in some studies, but not in others.

Given the evidence of *in vitro* clastogenicity and its negative results in unscheduled DNA synthesis and DNA binding studies, methylene chloride may be a weak mutagen in mammalian systems. Methylene chloride has been evaluated in several *in vivo* assay systems producing many negative but also some positive results. It appears there may be tissue-specific variation in the metabolism of methylene chloride, which may explain the variability in the genotoxicity results (ATSDR 2000b).

Evaluation and conclusion

Methylene chloride is readily absorbed from the gastrointestinal tract and distributed to body tissues where it is then either exhaled unchanged as methylene chloride, or metabolised to carbon monoxide and carbon dioxide. In rodents, oral administration of methylene chloride has produced some haematological and liver effects. Carcinogenicity studies with orally administered methylene chloride have given inconclusive results although there is some suggestive evidence that ingestion of methylene chloride may increase the incidence of liver cancer in rodents. The available data do not indicate that methylene chloride is a substance of high systemic toxicity, and there is only equivocal evidence of carcinogenicity, therefore there are **no toxicological concerns** with the use of methylene chloride as an extraction solvent providing its use is limited in order to ensure that its residues in food are as low as practicable. The current maximum permitted levels and restricted uses are acceptable from a human safety perspective.

Methylphenylpolysiloxane

Current permission in the Code

Methylphenylpolysiloxane is currently permitted as an antifoam agent up to a maximum permitted level of 10 mg/kg in the final food (table to clause 4).

Available safety information

Methylphenylpolysiloxane is a type of silicone oil. JECFA has not evaluated methylphenylpolysiloxane but has evaluated another type of silicone oil called dimethylpolysiloxane (WHO 1980). An ADI of 0-1.5 mg/kg BW was established by the Committee with the comment that the ADI applies only to compounds with 200-300 subunits. No toxicological monograph was prepared.

No information on the chemistry, toxicokinetics or safety of methylphenylpolysiloxane is currently available.

Of the limited animal studies that have been undertaken with dimethylpolysiloxane, none have indicated any significant toxicity. The metabolic studies, including those in humans, indicate that the orally administered dimethylsiloxanes are mainly excreted unchanged in the faeces. It is unclear if these results are relevant to an assessment of the safety of methylphenylpolysiloxane.

Evaluation and conclusion

Insufficient data are available to enable an assessment to be made of the safety of methylphenylpolysiloxane as a processing aid.

Mineral oils/ mineral oil based greases/ paraffin

Current permissions in the Code

White mineral oil is permitted for use as a generally permitted processing aid at GMP levels (table to clause 3), mineral oil based greases are permitted for use as lubricants, release and anti-stick agents at GMP levels (table to clause 9) and paraffin is permitted as a coating for cheese and cheese products at GMP levels (table to clause 14).

Available safety information

JECFA has evaluated mineral oils (highly refined paraffinic and naphthenic liquid hydrocarbons) on a number of previous occasions, the most recent evaluation being at their fifty-ninth meeting in 2002 (WHO 2003). The synonyms for mineral oil include liquid paraffin, liquid petrolatum, food grade mineral oil and white mineral oil.

For the purposes of evaluation, and to define the materials more clearly, the Committee, at its forty-forth meeting, had prepared individual specifications for micro-crystalline wax and for two groups of mineral oils: mineral oils (high-viscosity) and mineral oils (medium- and low-viscosity) (WHO 1996). Medium and low viscosity mineral oils have a boiling point above 200ºC**,** and high viscosity mineral oils have a boiling point above 350ºC**.** The medium and low viscosity mineral oils were further divided into three classes – class I, class II and class III.

For the purpose of characterisation of the different types of oils and waxes, the criteria viscosity, average relative molecular mass and carbon number at 5% distillation-point were used in the specifications (see Table 2).

Table 2: Classification of mineral hydrocarbons

Name	Viscosity at 100˚C (mm^2/s)	Average relative molecular mass	Carbon number at 5% distillation-point
Microcrystalline wax	≥ 11	≥ 500	≥ 25
High melting point wax			
Low melting point wax	3.3	380	22
Mineral oil (high viscosity)	≥ 11	≥ 500	≥ 28
P100 (H)	11	520	29
Mineral oil (medium and low viscosity) Class I	8.5-11	480-500	≥ 25
P70	9.0	480	27
Medium viscosity liquid petroleum	8.7	480	25
P70 (H)	8.6	480	27
Mineral oil (medium and low viscosity) Class II	7.0-8.5	400-480	≥ 22
N70 (H)	7.7	420	23
Mineral oil (medium and low viscosity) Class III	3.0-7.0	300-400	≥ 17
P15 (H)	3.5	350	17
N15 (H)	3.5	330	17

The Committee last evaluated mineral oils at its forty-fourth meeting, when four 90-day studies in rats using a range of mineral oils and waxes representative of materials in commercial use were reviewed. The materials tested included low-, medium- and high-viscosity mineral oils (N10 (A), N15 (H), P15 (H), N70 (A), N70 (H), P70 (H) and P100 (H)); paraffin waxes (low-melting-point wax and intermediate-melting-point wax); and microcrystalline waxes (high-melting-point wax and high-sulphur wax). All the substances, with the exception of the microcrystalline waxes, appeared to accumulate in the tissues of the animals to varying degrees, depending on the material and dose. Except for P70 (H) and P100 (H) oils, there was evidence of accumulation of the mineral hydrocarbons and effects indicative of a reaction to a foreign body at one or more doses. The types of effects seen were similar and included focal histocytosis, increased weights of liver, lymph nodes, spleen and kidneys, granulomas or micro-granulomas of the liver, haematological changes typical of a mild, chronic inflammatory reaction and biochemical changes indicative of mild hepatic damage.

The ADI of 0–20 mg/kg BW for mineral oils with the specifications of high-viscosity oils and of high melting point and high sulphur waxes was based on NOAELs at the highest dose tested (2% in the diet) in 90-day studies rats. The NOAELs for all the other materials except P70 (H) oil (i.e. class II and III medium- and low-viscosity oils and low-melting-point wax) were based on an increased incidence of histocytosis in the lymph nodes at the next highest dose. For P70 (H) oil, the NOAEL was based on an increased incidence of pigmented macrophages in male rats at a dietary concentration of 2%, a minor effect considered of doubtful biological significance. Accordingly, because effects were observed at all doses, the ADIs for low-melting-point and intermediate-melting-point waxes were withdrawn. A group temporary ADI of 0–0.01 mg/kg BW was allocated for class II and III medium- and low-viscosity mineral oils, the temporary nature of the ADI being due to uncertainty about the long-term significance of the inflammatory response to accumulated dietary mineral hydrocarbons. A temporary ADI of 0–1 mg/kg BW was allocated for P70 (H) oil.

At its forty-fourth meeting, the Committee considered that, although the types of effects seen were essentially reactions to a foreign body, it was possible that a prolonged inflammatory response of the type observed could result in functional changes in the immune system and that this aspect required further investigation. It also noted that the oils and waxes for which high NOAELs were observed contained a greater proportion of hydrocarbon components of high relative molecular mass (high carbon number) and had higher viscosities than those materials with a low NOAEL, which contained a greater proportion of hydrocarbon components of lower relative molecular mass (low carbon number).

At its fifty-ninth meeting, the Committee reviewed a number of new studies, including the results of a combined 2-year study of toxicity and carcinogenicity and a 1-year study of toxicity with a 1-year recovery period with P70 (H) and P100 (H) oils (with the specifications of class-I medium- and low-viscosity mineral oils and of high-viscosity mineral oil, respectively) conducted in parallel. In addition, the Committee received and reviewed a number of studies conducted with low- and medium-viscosity mineral oils, including: a 2-year study of the carcinogenicity of a medium-viscosity liquid petroleum (class I medium- and low-viscosity mineral oil); studies of pharmacokinetics and studies of humoral immune function after administration to P15 (H) mineral oil (class III medium- and low-viscosity mineral oil) in Fischer 344 and Sprague-Dawley rats; and a 90-day study of histopathological responses and compositional analysis of absorbed hydrocarbons with N15 (H), N70 (H) and P70 (H) oils (classes III, II and I medium- and low-viscosity mineral oils, respectively).

The Committee also reviewed several studies of low-melting-point paraffin wax, as they were considered to provide information relevant for the evaluation of low- and medium-viscosity mineral oils relating to the difference in response to mineral hydrocarbons in Fischer 344 and Sprague-Dawley rats.

As the materials tested in the long-term studies, P70 (H) and P100(H) oils, were not associated with induction of liver granulomas in Fischer 344 rats, the studies did not help the Committee to determine the long-term consequences or reversibility of the liver granulomas that had been seen in previous studies in response to consumption of low- and medium-viscosity mineral oils and low-melting-point waxes by Fischer 344 rats. In addition, the Committee was unable to interpret the effects in the study of humoral immune function in response to dietary administration of P15 (H) oil.

The results of the studies on the effects of P15 (H) oil and low-melting-point wax in Fischer 344 and Sprague-Dawley strains indicated that the more extensive response of Fischer 344 rats, in particular that of females, is associated with greatly enhanced retention of mineral hydrocarbons in the tissues, which is probably due to a reduced ability to metabolise absorbed hydrocarbons. The Committee concluded that additional studies are needed in order to determine whether the Fischer 344 rat is an appropriate model of human response to dietary intake of food-grade mineral hydrocarbons. In particular, elucidation of the metabolic differences between Fischer 344 rats and other strains and species, including humans, would be useful.

Neither P70 (H) nor P100 (H) oil was carcinogenic in the combined study of toxicity and carcinogenicity reviewed by the Committee. The effects observed even at the lowest dose, i.e. enhanced reticuloendothelial-cell hyperplasia, increased weights of mesenteric lymph nodes and increased incidence and grade of vacuolation of hepatocytes, were shown not to progress to more severe effects, and there was no indication that accumulated test material contributed to suppression or activation of an inflammatory response. Consequently, these effects were considered to be indicators of exposure to mineral hydrocarbon rather than adverse effects.

The NOAEL for P70 (H) oil was identified as the highest dose tested in the combined study of toxicity and carcinogenicity in rats, 1200 mg/kg BW/day, to which a safety factor of 100 was applied. An ADI of 0-10 mg/kg BW was allocated for class I medium- and low-viscosity mineral oils, which include P70 (H) oil. An ADI of 0–20 mg/kg BW already existed for P100 (H) oil.

No data were available that would permit allocation of a full ADI for medium- and low-viscosity mineral oils in classes II and III. The Committee noted that the new information indicated that the observed effects of these mineral oils, on which the temporary ADI is based, may be both strain- and sex-specific. The Committee therefore extended the temporary group ADI of 0–0.01 mg/kg BW for class II and III medium- and low-viscosity mineral oils until 2006, pending information on the relevance to humans of the response of Fischer 344 and Sprague-Dawley rats to these materials. In order for the data to be applicable to as wide a range of mineral oils as possible, the Committee suggested that commercial mineral oils of the lowest viscosity be used in such studies. Further studies might be required, depending on the outcome of the new studies. The ADIs for the various mineral oils are summarised in Table 3.

Table 3: ADIs established by JECFA for various mineral oils

Viscosity	Class	Oils included	ADI (mg/kg BW)
High		High-viscosity oil P100 (H)	0-20
Medium and low	I	Medium-viscosity oil P70 (H)	0-10
Medium and low	II	Medium-viscosity oils N70 (H) and N70 (A)	0-0.01 (temporary)
Medium and low	III	Low-viscosity oils P15 (H), N15 (H) and N10 (A)	0-0.01 (temporary)

In its most recent evaluation JECFA also assessed the intake of mineral oils (WHO 2003). Dietary intake was assessed from data on the levels of use in foods and on migration from coatings and packaging materials into foods, combined with national data on food consumption in the 1990s. In both the United Kingdom and the United States, the average total intake of mineral hydrocarbons (excluding petroleum jelly) from food use was estimated to be 0.47 mg/kg BW/day; the intake at the 90th percentile of consumption by the population of the United Kingdom was 0.80 mg/kg BW/day. Class III medium- and low-viscosity mineral oils (including P15 (H) oil) accounted for 0.21 mg/kg bw per day in the UK and 0.25 mg/kg BW/day in the US; these values are 21 and 25 times the temporary ADI of 0–0.01 mg/kg BW, respectively, whereas class I and II medium- and low-viscosity mineral oils and high-viscosity mineral oil (including P70 (H) and N70 (H) oils, respectively) accounted for 0.18 and 0.19 mg/kg BW/day, respectively. As these different categories of mineral oil have different ADIs, but data on intake are not available for separate categories, the intake of each category cannot be compared with the corresponding ADI. Use of solid hydrocarbons (e.g. microcrystalline wax (high-melting-point wax) and paraffin wax (low-melting-point wax)) accounted for the remainder of the total intake.

The intake of high-viscosity and class I, II and III medium- and low-viscosity mineral oils that have migrated into food from coating and packaging materials was estimated to be 0.001 mg/kg BW in both the UK and the US, while the combined intake of paraffin wax and microcrystalline wax from this source was estimated to be 0.005 and 0.006 mg/kg BW/day, respectively.

Naturally occurring hydrocarbons are widely distributed in many edible plants and animals, and they contribute significantly to the overall dietary intake of hydrocarbons. For example, the dietary intake of naturally occurring hydrocarbons was estimated to be 0.47, 0.25 and 0.19 mg/kg BW/day in the populations of the European Union, the UK and the US, respectively. It is clear, therefore, that account should be taken of intakes from naturally occurring hydrocarbons when evaluating the safety of mineral oils.

While a number of adverse effects have been observed in Fischer 344 rats following oral exposure to various mineral oils, a number of other reports indicate such effects may not be consistently observed in other strains of rats, or other species.

In a review of the oral toxicity of mineral oils, Nash et al (1996) noted that sub-chronic oral ingestion of refined white mineral oil has been found to produce micro-granuloma in the liver and histocytosis in the mesenteric lymph nodes of F334 rats. However, no evidence of any adverse event such as tumour formation related to the ingestion of white oils has been reported.

Also, in contrast to findings in F344 rats, several sub-chronic and chronic oral administration studies using Sprague-Dawley or Long-Evans strains of rat and other species (i.e. beagle dogs) have resulted in the absence of gross or histological effects. In dogs, an +increased frequency of soft faeces in most treatment groups suggested a slight laxative effect from mineral oils in the diet (Smith et al 1995).

A Panel of medical and veterinary pathologists has reviewed published and unpublished reports dealing with studies of various white mineral oils and waxes in F344 and Sprague-Dawley rats (Carlton et al 2001). The Panel also reviewed mineral oil-induced alterations in tissues of human patients (liver, hepatic lymph node and spleen). The Panel concluded that the mitral valve alterations had little if any toxicological significance as the focal infiltrate was minimal in severity, occurred in controls, occurred in association with murine cardiomyopathy, and were unlike the responses in the liver and mesenteric lymph nodes. The Panel agreed that the lesions observed in the liver and mesenteric lymph nodes of F344 rats exposed to mineral oils were different morphologically from changes observed in lymph node, liver, and spleen of humans that were mineral oil-users. According to the Panel, the mineral oil-induced lesions can be considered incidental and inconsequential in humans.

Evaluation and conclusion

The term *mineral oil* refers to a relatively broad class of substances with varying viscosities and other physical properties. When these substances are administered to Fischer 344 rats, similar types of effects are seen with the different types mineral oils. These effects consist of increased liver, spleen, lymph node and kidney weight, haematological changes typical of a mild, chronic inflammatory reaction and biochemical and histological changes indicative of liver damage. The no-effect-levels effects from the high viscosity oils were higher than for the medium and low viscosity oils, hence different ADIs have been derived for the different categories of mineral oils. No evidence for carcinogenicity has been found in any of the studies conducted to date. Some uncertainty exists as to whether the Fischer 344 strain of rat is an appropriate model of human response; given studies with other strains of rat, as well as other species, have failed to produce the same effects. JECFA noted that the observed effects of these mineral oils may be both strain- and sex-specific.

JECFA has assessed the dietary intake of mineral oils using both UK and US data. These intake estimates indicate that the intake for low viscosity mineral oils may exceed the current temporary ADI established for this class of mineral oils by a large margin. Ordinarily this may raise toxicological concerns, however, given the uncertainty with the toxicological studies, it's not yet clear whether the temporary ADI of 0-0.01 mg/kg BW for this class of mineral oils is appropriate and/or likely to be retained. JECFA has concluded that additional studies are necessary to determine if the Fischer 344 rat is an appropriate model of human response.

Given the available data and the uncertainty regarding the appropriateness of the F344 rat as a model for humans **it is difficult to determine if there that are toxicological concerns** associated with the use of mineral oils as processing aids. An added difficulty is the incongruence between the categories of mineral oils specified by JECFA for the purposes of risk assessment, and the current nomenclature used in the Code.

Given the JECFA evaluation of mineral oils is still ongoing, the current permissions for mineral oils should be maintained with the proviso that they be reviewed once JECFA has finalised its evaluation. It is also recommended that the nomenclature for mineral oils currently used in the Code be reviewed in light of the discrepancies with that used by JECFA.

Nickel

Current permission in the Code

Nickel is currently permitted as a catalyst up to a maximum permitted level of 1.0 mg/kg in the final food (table to clause 5).

Available safety information

A number of bodies have evaluated the safety of nickel, including the ATSDR (2003), IPCS (WHO 1991), IARC (1990b) and the US EPA (1998b). JECFA has not evaluated nickel. The WHO has established a drinking water guideline for nickel of 0.02 mg/L (WHO 2004).

Nickel is introduced into the environment from both natural and anthropomorphic sources. Nickel from soil and water is absorbed and metabolised by plants and microorganisms and these small quantities of nickel are widely present in all foods and water. Some foods, such as pulses and cocoa products, may contain relatively high amounts of nickel, but these quantities have not been correlated with adverse health effects (WHO 1991). Food is the dominant source of nickel exposure for the general population, with water generally being a minor contributor to total daily intake.

Nickel can be absorbed via inhalation, ingestion or via the skin. Respiratory absorption with secondary gastrointestinal absorption of nickel (insoluble and soluble) is the major route of entry during occupational exposure. Dermal absorption is negligible, quantitatively, but is important in the pathogenesis of contact hypersensitivity. Gastrointestinal absorption of nickel is variable and depends on the composition of the diet. Gastrointestinal absorption of nickel is greatest when it is given in water, compared to in food. Once absorbed, nickel is distributed to the kidneys, liver, heart, lung, adipose tissue, peripheral nerve tissues and the brain. Placental transfer of nickel has been observed in rodents. Non-absorbed nickel is eliminated in the faeces.

The targets of nickel toxicity appear to be similar across exposure routes, with the exception of portal of entry effects. The primary targets are the respiratory tract following inhalation exposure, the reproductive system and the developing organism following inhalation or oral exposure, and the immune system following inhalation, oral or dermal exposure.

Most of the information on the toxicity of nickel to humans comes from occupational exposure therefore much of this data is of limited relevance for exposure from food. Of interest is the occurrence of nickel sensitivity, which has been observed both in workers as well as the general population following both dermal contact and oral exposure.

The available data from animal studies point to a number of different effects. In a 2-year study in rats receiving 0, 5, 50 and 125 mg Ni/kg BW in the diet, there were alterations in several organ to body weight ratios in both sexes at the 50 and 125 mg/kg BW/day doses.

No other effects were reported and no significant effects were observed in animals receiving 5 mg/kg BW/day, considered to be the NOAEL for the study. This particular study was used by the WHO to derive a TDI for nickel in water of 5 μg/kg BW, incorporating an uncertainty factor of 1000 (WHO 2004).

In addition to the systemic effects in animal studies, two other sensitive endpoints exist: neonatal mortality, which is frequently observed in animal studies, and dermatotoxicity, which is commonly seen in humans. While no reproductive effects have been associated with nickel exposure to humans, effects have been observed in several studies in laboratory animals.

Exposure of rats and mice to relatively low oral doses (1.9 mg/kg BW/day) of nickel chloride or nickel sulphate by either gavage or in drinking water resulted in histological alterations in the epididymis and seminal vesicles as well as sperm alterations. Other studies in rats and dogs, where the nickel was administered via the diet, have not found similar histological alterations following oral exposure to nickel for up to 2 years. Significant alterations in fertility have been observed in some but not all studies. A multigenerational study involving exposure to nickel chloride did not find any significant alteration in the fertility of rats. Some minor reproductive effects have also been observed following inhalation exposure.

The available animal data from developmental toxicity studies suggest that the foetus and the neonate are sensitive targets for nickel toxicity. The most commonly reported endpoint is foetal loss and decreased survival in both rat and mouse offspring in studies involving male-only exposure, female-only exposure and combined male and female exposure prior to mating and during gestation and lactation in single generation, multilitter, and multigenerational studies. Differences in study design and the method of administration of the nickel (in the form of nickel chloride) complicates the identification of a threshold for developmental effects. The lowest LOAEL values range from 3 to 90 mg Ni/kg BW/day and the highest NOAEL values range from 4 to 45 mg Ni/kg BW/day. Maternal toxicity, particularly decreased body weight gain, was evident at these dose levels, which complicates the interpretation of these data.

The immunotoxicity of nickel has been established in humans and animals following inhalation, oral and dermal exposure. In humans, the immune response to nickel is elicited as allergic contact dermatitis, a rash that develops shortly after exposure to metallic nickel or nickel compounds. Nickel sensitisation typically involves initial exposure to a large nickel dose; thereafter much lower doses will elicit a response. The prevalence of nickel sensitisation in the general population is said to be approximately 11%, with the highest prevalence among young women. Small oral doses of approximately 0.02 mg Ni/kg BW are often enough to cause a flare up of dermatitis among sensitised individuals. In experimental animals, alterations in parameters of non-specific immunity and humoral and cell-mediated immunity have been observed following both oral and inhalation exposure.

The carcinogenic effect of nickel is well documented in occupationally exposed individuals. A number of studies of nickel-exposed workers have found significant increases in the incidence of both lung and nasal tumours. The IARC has concluded that inhaled nickel compounds are *carcinogenic to humans* (Group 1) and that metallic nickel is *possibly carcinogenic to humans* (Group 2B) on the basis of sufficient evidence in both humans and experimental animals (IARC 1990b). There is however a lack of evidence for carcinogenicity following oral exposure in both humans and experimental animals.

The data on genotoxicity for nickel collectively show that nickel compounds are generally inactive in bacterial mutation assays, but active in mammalian cells. In all the gene mutation studies using mammalian cells, any response following exposure to nickel compounds was associated with considerable cytotoxicity. Tests for chromosome aberration in cultured mammalian cells generally show a positive result. Studies of chromosome aberration *in vivo* however indicate that nickel compounds are generally not clastogenic.

Evaluation and conclusion

The available data indicate that oral exposure to nickel is of lesser importance than inhalation in terms of human health risk. Nickel absorption from the gastrointestinal tract is generally poor, although nickel in drinking water is absorbed to a greater extent, particularly on an empty stomach. This may pose a risk for those individuals who are sensitised to nickel. Nickel, by the oral route, appears to have a relatively low systemic toxicity and there is a lack of evidence for carcinogenicity, in both humans and experimental animals, from oral exposure to nickel. The use of nickel as a catalyst is not expected to result in significant residues of nickel in food and is likely to contribute only in a very minor way to the total nickel content of food. Overall, there are **no toxicological concerns** with the use of nickel as a processing aid. The current maximum permitted level is acceptable from a human safety perspective.

Polyelectrolytes (acrylamide monomers)

Current permission in the Code

Polyelectrolytes are currently permitted as processing aids for use in packaged water and in water used as an ingredient in other foods at GMP levels.

Drinking water levels for Australia and New Zealand

The Australian Drinking Water Guidelines state that based on health considerations the concentration of acrylamide in drinking water should not exceed 0.0002 mg/L (NHMRC 2004).

In the Drinking Water Standards for New Zealand, the maximum acceptable value for acrylamide in drinking water is 0.0005 mg/L (Ministry of Health 2000).

The guideline value of 0.0002 mg/L set for drinking water in Australia was set at the limit of determination because it is within the values derived from health considerations, and is considered to provide an adequate degree of protection. The higher value of 0.0005 mg/L in the Drinking Water Standards for New Zealand, which is the same as the guideline level established by the WHO for acrylamide in drinking water (WHO 2004), is based on an estimated lifetime risk of one additional cancer per hundred thousand people.

Available safety data

Acrylamide occurs as a minor impurity in polyacrylamide, which is used as a flocculant aid in water treatment. When non-ionic and anionic polyacrylamides are used in water treatment at a typical dose level of 1 mg/L, the maximum theoretical concentration of acrylamide has been estimated at 0.0005 mg/L, with practical concentrations 2-3 times lower (NHMRC 2004). Residual levels from the use of cationic polyacrylamides may be higher.

JECFA undertook an evaluation of acrylamide at its sixty-fourth meeting, at the request of the Codex Committee on Food Additives and Contaminants (JECFA 2005). The Committee had not previously evaluated acrylamide. Concerns about dietary exposure to acrylamide had arisen as a result of studies conducted in Sweden in 2002, which showed high levels of acrylamide were formed during the frying or baking of a variety of foods. The Committee concluded that adverse effects based on non-neoplastic endpoints are unlikely at the estimated average intakes for the general population based on national estimates, but that morphological changes in nerves cannot be excluded for some individuals with very high intakes. In terms of neoplastic endpoints, the Committee considered that as acrylamide is a compound that is genotoxic and carcinogenic, the estimated intakes may indicate a human health concern. The Committee notes that ongoing studies of neurotoxicity and neurodevelopmental effects in rats will more clearly define whether effects may arise from long term, low doses of acrylamide. The committee recommended that acrylamide be re-evaluated when results of ongoing carcinogenicity and long term neurotoxicity studies become available and that appropriate efforts to reduce acrylamide concentrations in food should continue.

In experimental animals, acrylamide is readily absorbed from the gastrointestinal tract following oral administration and then widely distributed to tissues. Acrylamide can also cross the placenta. Once absorbed, acrylamide is metabolised to glycidamide, a chemically reactive epoxide. An alternative pathway for metabolism is conjugation with glutathione. Acrylamide and its metabolites are rapidly eliminated in the urine, primarily as mercapturic acid conjugates of acrylamide and glycidamide.

Numerous studies in a number of animal species have shown that the nervous system is the principal site for the toxic effects of acrylamide. Epidemiological studies of human industrial and accidental exposure indicate this is also the case for humans.

In experimental animals, sufficient, repeated exposure to acrylamide causes a degenerative peripheral nerve change that results from an accumulation of damage at the sites of toxicity. Continued dosing with acrylamide has been shown to induce nerve terminal degeneration in brain areas critical for learning, memory and other cognitive functions and these lesions may precede the morphological changes in nerves. In rats exposed to acrylamide in drinking water for 90 days, the NOAEL for morphological changes in nerves detected using electron microscopy was 0.2 mg/kg BW/day and no exposure-related non-neoplastic lesions were found at other tissues at dose levels below 5 mg/kg BW/day.

In reproduction studies, male rodents showed reduced fertility, dominant lethal effects, and adverse effects on sperm count and morphology at oral doses of >7 mg/kg BW/day. In female rats, no adverse effects on fertility or reproduction have been observed apart from slight reductions in rat offspring body weight at oral doses of 2.5 mg/kg BW/day and above. In developmental toxicity studies, acrylamide was fetotoxic in mice only at a maternally toxic dose of 45 mg/kg BW/day, and was not teratogenic in mice or rats. In a developmental neurotoxicity study, in which acrylamide was dosed orally from gestational day 6 to lactation day 10, the NOAEL for developmental neurotoxicity was 10 mg/kg BW/day. The overall NOAEL for developmental effects was 2 mg/kg BW/day.

Glycidamide has shown mutagenicity in the Ames test, but acrylamide has not. Acrylamide is both clastogenic and mutagenic in mammalian cells *in vitro* and *in vivo*.

In addition, dominant lethality studies have shown acrylamide to be a germ cell mutagen in male rodents. The mutational spectra produced by acrylamide and glycidamide in transgenic mouse cells are consistent with formation of promutagenic purine DNA adducts *in vivo*. Metabolism of acrylamide to glycidamide appears to be a prerequisite for the genotoxicity of acrylamide *in vitro* and in experimental animals.

Acrylamide in drinking water has been tested for carcinogenicity in two experiments with rats (dose ranging from 0-3 mg/kg BW/day). There were increases in tumour incidences at a variety of sites. Information about total tumour bearing animals was not available from either study. JECFA undertook a dose response analysis of the animal carcinogenicity data in order to derive a benchmark dose (BMD) and BMDL (benchmark dose level) associated with a 10% extra risk of tumours (JECFA 2005). This procedure resulted in a range of BMD and BMDL values for each endpoint considered. The lowest range of BMDLs was found for total mammary tumours (0.3 – 0.46 mg/kg BW/day). The Committee used 0.3 mg/kg BW/day (the lowest end of the range) as the point of departure for the induction of mammary tumours in rats. The Committee considered that the pivotal effects of acrylamide for risk assessment were its genotoxicity and carcinogenicity.

Acrylamide has been evaluated by the IARC and has been classified as *probably carcinogenic to humans* (Group 2A) on the basis of a positive cancer bioassay result; supported by evidence that acrylamide is efficiently transformed to a chemically reactive genotoxic intermediate, glycidamide, in both rodents and humans (IARC 1994).

Evaluation and conclusion

Acrylamide is both neurotoxic and carcinogenic by the oral route of exposure. Given that high levels of acrylamide can form in certain foods during frying and baking, the contribution to the total acrylamide intake from the use of polyelectrolytes as a processing aid is expected to be relatively minor. Overall, there are **no toxicological concerns** with the use of polyelectrolytes as processing aids for use in packaged water and water used as an ingredient in other foods, however, in line with the recent recommendation of JECFA that efforts to reduce acrylamide concentrations in food should continue, it is important that the levels of acrylamide should be kept as low as possible. A maximum permitted level for acrylamide monomer of 0.0002 mg/L should be established to bring it into conformity with the Australian Drinking Water Guidelines.

Potassium bromate and sodium bromate

Current permission in the Code

Potassium bromate and sodium bromate are currently permitted as processing aids for germination control in malting at levels of 0.1 mg/kg.

Available safety information

Potassium bromate was evaluated as a flour treatment agent at the seventh, twenty-seventh, and thirty-third meetings of JECFA (WHO 1964, 1983, 1989). In the course of those evaluations the general principle was reiterated that bromate should not be present in foods as consumed, and that the use of potassium bromate could only be approved in such circumstances.

Evidence was considered that, at levels of flour treatment up to 62 mg/kg, no bromate residues were detected in the bread, with the principle breakdown product being bromide. The Committee determined the acceptable level of treatment for flour for bread-making to be 0-60 mg potassium bromate/kg flour. The Committee had no toxicological data on other food products treated with bromate and were aware that some applications could give rise to significant residues. Accordingly, no acceptable level of treatment could be established for foods other than flour intended for baking.

In a subsequent evaluation, the Committee noted that recent oral long-term toxicity/ carcinogenicity studies of potassium bromate have revealed renal-cell tumours, peritoneal mesotheliomas, and thyroid follicular-cell tumours in rats and slightly increased incidence of renal-cell tumours in hamsters (WHO 1993b). In view of these findings and the results obtained from in vivo as well as in vitro mutagenicity studies, it was concluded that potassium bromate is a genotoxic carcinogen. Experiments using new sensitive methods have also demonstrated that, when it is used for flour-treatment at what were regarded as acceptable levels, bromate is nevertheless present in bread. On the basis of the new safety data and the new data on residual bromate in bread, the Committee concluded that the use of potassium bromate as a flour-treatment agent was not appropriate. The previous acceptable level of treatment of flours for bread making was therefore withdrawn. The Committee was unable to address the use of potassium bromate in beer making owing to the lack of data on its levels in beer.

Both the IARC (1999d) and US EPA (2001) have undertaken more recent evaluations of bromate.

The gastrointestinal tract rapidly absorbs bromate. It is distributed throughout the body, appearing in plasma and urine unchanged and in other tissues as bromide. Bromate is reduced to bromide in several body tissues, probably by glutathione (GSH) or other sulphydryl-containing compounds. Most bromate is excreted in the urine, either as bromide or bromate, but some may be eliminated in the faeces.

No long-term studies on the human health effects of bromate are available. Subchronic and chronic studies in rats indicate that the kidney is the target organ of bromate toxicity, although very few of these studies actually provide dose-response data. Specific kidney effects observed include necrosis and degenerative changes in renal tubules and urothelial hyperplasia. On the basis of these kidney effects, a NOAEL of 1.5 mg potassium bromate/kg BW/day and a LOAEL of 7.9 mg/kg BW/day have been identified. Similar kidney effects have been seen in humans and rats following acute exposure. Bromate may also be a male reproductive toxicant, causing a decrease in epididymal sperm density, however such effects occur at higher doses than the kidney effects. A major uncertainty with the kidney effects observed in rats is its relevance to humans, as no such effects have been observed in mice.

Bromate is mutagenic in bacteria and causes chromosomal aberrations in cultured mammalian cells. In *in vivo* studies, administration of potassium bromate to rats and mice either orally of via intraperitoneal injection resulted in increases in micronuclei in femoral bone marrow cells, dose-dependent increases in the number of aberrant metaphase cells in bone marrow, as well as dose-dependent increases in frequency of micronucleated polychromatic erythrocytes.

Potassium bromate has been tested for carcinogenicity in several studies in rats and in one study each in mice and hamsters. In rats, it produced renal tubular tumours (adenomas and carcinomas) and thyroid follicular tumours in animals of each sex and peritoneal mesotheliomas in males. A dose-response relationship was observed for all three tumour types in rats, both in terms of incidence as well as severity/progression. In mice, it produced a low incidence of renal tubular tumours in males. In hamsters, the incidence of renal tubular tumours was marginally increased. Potassium bromate did not increase tumour incidence in bioassays in newborn rats and mice, but it enhanced the induction of kidney tumours by *N*-nitrosoethylhydroxyethylamine in several experiments. On the basis of these findings in experimental animals, the IARC has classified potassium bromate as *possibly carcinogenic to humans* (Group 2B) (IARC 1999d).

Research undertaken by Brewing Research International in 1990, the results of which have been submitted to FSANZ, indicates that no detectable bromate residues remain in the wort (limit of detection = 0.005 mg/L) or in beer (limit of detection = 0.0025 mg/L) when the malt has been treated with potassium bromate, including at levels greatly in excess of those used commercially.

Evaluation and conclusion

Bromate is rapidly absorbed following oral exposure and widely distributed in the body. Very limited information is currently available on effects in humans but there is convincing evidence of renal toxicity and carcinogenicity in rats. Bromate also appears to be a potent genotoxic substance *in vivo*. While some uncertainty exists regarding the relevance to humans of the adverse effects seen in rats, cases of acute exposure in humans have also produced severe kidney effects. In addition, the development of tumours at multiple sites in rats supports the human cancer potential of bromate, as the more tumour sites observed, the more likely that some of the mechanisms involved will be relevant to humans.

On the basis of the available evidence **there may be toxicological concerns** with the use of potassium and sodium bromate as processing aids, if their use were to result in detectable residues in food. Current information indicates the use of potassium and sodium bromate for germination control in malting does not result in detectable bromate residues in beer. The continued use of potassium and sodium bromate in malting is therefore acceptable providing the bromate levels remain below the limit of determination in beer.

Potassium ethoxide, sodium ethoxide and sodium methoxide

Current permission in the Code

Potassium ethoxide is currently permitted as a catalyst with a maximum permitted level of 1.0 mg/kg in the final food (table to clause 5). Sodium ethoxide and sodium methoxide are permitted for use as generally permitted processing aids at GMP levels (table to clause 3).

Available safety information

JECFA has not evaluated any of these substances and no information could be found on the toxicokinetics or safety of these substances as processing aids.

Potassium and sodium ethoxide and sodium methoxide are all alkaline metal alkoxides that are used as catalysts for the interesterification of fats and oils. Alkaline metal alkoxides are the most active catalysts, since they produce very high yields (>98%) in short reaction times (30 min), even at low molar concentrations (0.5 mol %). It requires the absence of water for the reaction.

Following completion of the reaction, the catalyst is deactivated with water, producing methanol and sodium hydroxide, in the case of sodium methoxide, or ethanol and either sodium or potassium hydroxide in the case of sodium or potassium ethoxide. The by-products of this deactivation reaction are well known substances, which are water soluble and poorly soluble in the fats and oil phase. They are then removed during the further processing that the oils undergo after the catalysis reaction including washing with water, and deodorisation with elevated temperature and vacuum to remove volatile components and impurities (deodorisation).

Evaluation and conclusion

Only limited information is available on the toxicity of sodium or potassium ethoxide and sodium methoxide. However, the available information on their chemistry when used as catalysts indicates they are converted to innocuous by-products following completion of the reaction, which are then subsequently removed. Only very low residues would be expected to remain in the final product, if at all. Overall, there are **no toxicological concerns** with the use of sodium ethoxide, potassium ethoxide and sodium methoxide as catalysts.

Silver ions

Current permission in the Code

Silver ions are permitted as processing aids for use in packaged water and in water used as an ingredient in other foods up to a maximum permitted concentration of 0.01 mg/kg in the final food (table to clause 11).

Drinking water levels for Australia and New Zealand

The Australian Drinking Water Guidelines state that based on health considerations the concentration of silver in drinking water should not exceed 0.1 mg/L (NHMRC 2004).

In the Drinking Water Standards for New Zealand, the maximum acceptable value for silver in drinking water is 0.02 mg/L (Ministry of Health 2000).

Available safety information

JECFA evaluated the use of silver as a colour at their 21st meeting but postponed a decision regarding an ADI (WHO 1977). JECFA has not further evaluated silver. The ATSDR (1990) and the US EPA (1996) have also evaluated silver. More recent evaluations were unable to be located.

Humans are exposed to small amounts of silver from dietary sources. The oral intake of silver from a typical diet has been estimated to range from 27-88 ug/day. Although silver can be found in biological substances it is not considered an essential trace element for mammals.

Over a lifetime, individuals that have not had excessive exposure to silver can accumulate a small but measurable amount of silver. It has been estimated that a person aged 50 years would have an average retention of 0.23-0.48 g silver.

The gastrointestinal tract absorbs approximately 10% of ingested silver. The distribution of silver to various body tissues depends upon the route and quantity of silver administered and the chemical form. An oral dose of silver, following absorption, undergoes a first pass through the liver resulting in excretion in the bile, thereby reducing systemic distribution to body tissues. In rats, following oral administration, high concentrations of silver were observed in tissues of the reticuloendothelial system in the liver, spleen, bone marrow, lymph nodes, skin and kidney. Silver was also observed in the tongue, teeth, salivary gland, thyroid, parathyroid, heart, pancreas, gastrointestinal tract, adrenal glands and brain. The deposition of silver in tissues is the result of the precipitation of insoluble salts, such as silver chloride and silver phosphate. Ingested silver is eliminated primarily in the faeces, with only minor amounts excreted in the urine.

In humans, the critical effect following the ingestion of silver is argyria, a medically benign but permanent bluish-grey discolouration of the skin. Argyria results from the deposition of silver in the dermis and also from silver-induced production of melanin. Although the deposition of silver is permanent, it is not associated with any adverse health effects. No pathologic changes or inflammatory reactions have been shown to result from silver deposition. Argyria has really only been observed in connexion with occupational or medical exposure or after cosmetic application of silver. Silver compounds have been used for medical uses for centuries. In the nineteenth and early twentieth centuries, silver arsphenamine was used in the treatment of syphilis; more recently it has been used as an astringent in topical preparations. While argyria occurred more commonly before the development of antibiotics, it is now a rare occurrence. Ingestion of silver also causes deposition of silver granules in the skin of animals.

In experimental animals, toxic effects from silver have been reported primarily for the cardiovascular and hepatic systems. Exposure of rats to 0.1% silver nitrate in drinking water to rats for 218 days (approximately 89 mg/kg BW/day) resulted in a statistically significant increase in the incidence of ventricular hypertrophy. Pigmentation was observed in body organs, but the ventricular hypertrophy was not attributed to silver deposition. Hepatic necrosis and ultra structural changes to the liver have been induced by silver administration to vitamin E and/or selenium deficient rats. It has been hypothesised that this toxicity is related to a silver-induced selenium deficiency that inhibits the synthesis of the seleno-enzyme glutathione peroxidase. In animals supplemented with selenium and/or vitamin E, exposures of silver as high as 140 mg/kg BW/day (100 mg Ag/L drinking water) were well tolerated. Deposits of silver in the central nervous system, accompanied by hypoactive behaviour, has also been reported in mice receiving 18 mg Ag/kg BW/day in drinking water for 4 months.

No data are available on the carcinogenicity of silver. Silver salts are not mutagenic in tests with bacteria, but can induce damage in mammalian DNA.

Evaluation and conclusion

Humans are exposed to small amounts of silver through the diet. Silver can be absorbed by the gastrointestinal tract, although the rates of absorption tend to be relatively poor.

The evidence from human exposure and studies in experimental animals does not point to silver having extensive systemic effects. The most well documented effect in humans is a condition called argyria, an irreversible pigmentation of the skin. This effect is not considered adverse, and nor is it relevant to consideration of the use of silver as a processing aid, which is only expected to result in minimal residues. Overall, there are **no toxicological concerns** with the use of silver as a processing aid. The current maximum permitted level is acceptable from a human safety perspective, and is below the levels for silver specified in the Australian Drinking Water Guidelines and the Drinking Water Standards for New Zealand.

Sodium glucoheptonate

Current permission in the Code

Sodium glucoheptonate is currently permitted as a processing aid for use in packaged water and in water used as an ingredient in other foods up to a maximum permitted concentration of 1 mg/kg (measured as cyanide) in the final food.

Available safety information

Glucoheptonic acid is obtained by treating glucose with HCN yielding a cyanohydrin, which is saponified to glucoheptonic acid. The sodium salt is prepared from corn syrup. Sodium glucoheptonate is freely soluble in water. Sodium glucoheptonate can therefore contain a measurable amount of cyanide.

No other relevant information could be located on the chemistry, toxicokinetics or safety of sodium glucoheptonate.

The WHO has evaluated cyanide in the context of considering cyanogenic glycosides (WHO 1993b). A Poisons Information Monograph is also available for cyanides (IPCS 1988).

Cyanide is rapidly absorbed by the gastrointestinal tract and after absorption is rapidly distributed in the body through the blood. The concentration of cyanide is higher in erythrocytes than in plasma. It is known to combine with iron in both methaemoglobin and haemoglobin present in erythrocytes. Cyanide is detoxified by the enzyme rhodanase, forming thiocyanate, which is excreted in the urine. Acute toxicity results when the rate of absorption of hydrogen cyanide is such that the metabolic detoxification capacity of the body is exceeded. Cyanide has a special affinity for ferric ions, which are found in cytochrome oxidase, the terminal oxidative respiratory enzyme within the mitochondria. This enzyme is an essential catalyst for tissue utilization of oxygen. When cytochrome oxidase is inhibited by cyanide, cellular respiration is inhibited and histotoxic anoxia occurs as aerobic metabolism becomes inhibited.

Chronic low-dose neurotoxic effects (demyelinating nervous conditions) and thyroid effects have been suggested by epidemiological studies of populations ingesting naturally occurring plant glycosides. These glycosides are present in a wide variety of plant species, most notably cassava. There is no evidence of any carcinogenic effects and cyanide is not mutagenic.

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The FAO/WHO has set an ADI for cyanide of 0.05 mg/kg BW (FAO 1965). The WHO has established a guideline value for cyanide in drinking water of 0.07 mg/L (WHO 2004). The guideline value is considered to be protective for acute and long-term exposure. In New Zealand and Australia, the level of cyanide specified for drinking water is 0.08 mg/L (NHMRC 2004, Ministry of Health 2000). The drinking water levels are based on a TDI of 12 μg/kg BW/day, based on a LOAEL of 1.2 mg/kg BW/day for effects on behavioural patterns and serum biochemistry in a 6-month study in pigs (WHO 2004).

Evaluation and conclusion

Insufficient data are available to enable an assessment to be made of the safety of sodium glucoheptonate as a processing aid. The use of sodium glucoheptonate may result in cyanide residues in the final food. Most toxicological concern with cyanide relates to its high acute toxicity, although there are suggestions cyanide may also have effects at much lower doses following chronic exposure. There **may be toxicological concerns** with maintaining a current maximum permitted level for sodium glucoheptonate measured as cyanide at 1 mg/kg. This level is significantly higher than the drinking water level for cyanide of 0.08 mg/L established for Australia and New Zealand on the basis of health considerations. Because packaged water may be used as a substitute for drinking water, it would be appropriate to bring the maximum permitted level for cyanide into conformity with the drinking water levels for Australia and New Zealand.

More data from industry on the use of sodium glucoheptonate and typical cyanide levels following processing would be useful for risk assessment purposes.

Sodium metabisulphite, sodium sulphite and sulphur dioxide

Current permission in the Code

Sodium metabisulphite is permitted for the following uses:

- a bleaching, washing and peeling agent for root and tuber vegetables up to a maximum permitted level of 25 mg/kg in the final food (table to clause 12);
- a dough conditioner up to a maximum permitted level of 60 mg/kg in the final food (table to clause 14);
- for removal of excess chlorine up to a maximum permitted level of 60 mg/kg in the final food (table to clause 14);
- softening of corn kernels for starch manufacture up to a maximum permitted level of 60 mg/kg (in the starch) (table to clause 14);
- treatment of hides for use in gelatine and collagen manufacture at GMP levels (table to clause 14).

Sodium sulphite is permitted as a dough conditioner up to a maximum permitted level of 60 mg/kg (table to clause 14).

Sulphur dioxide is permitted for use for the control of nitrosodimethylamine in malting and for the treatment of hides for use in gelatine and collagen manufacture up to a maximum permitted level of 750 mg/kg in the final food (table clause 14).

Related substances include sulphuric acid, which is permitted as a generally permitted processing at GMP levels (table to clause 3), and sodium sulphide, which is permitted for the treatment of hides for use in gelatine and collagen manufacture at GMP levels (table to clause 14).

Sulphur dioxide and various sulphites are also permitted for use in various foods and food products as a food additive at levels ranging from 10-3000 mg/kg in Schedule 1 of Standard 1.3.1 – Food Additives.

Available safety information

JECFA has evaluated sulphites on numerous previous occasions. A group ADI for sulphur dioxide and its equivalents was established at its thirtieth meeting (WHO 1987b). This ADI encompassed the sulphur dioxide equivalents arising from sodium metabisulphite, potassium metabisulphite, sodium sulphite, and sodium hydrogen sulphite. Calcium hydrogen sulphite, sodium thiosulphate, and potassium hydrogen sulphite were subsequently included in the group ADI.

Sulphite is readily absorbed by the gastrointestinal tract and once absorbed is oxidised *in vivo* to sulphate, catalysed by the enzyme sulphite oxidase located in the mitochondrial intramembranous space. Sulphite oxidase is widely distributed in mammalian tissues, with most activity being found in liver, heart, and kidney. As a result of rapid metabolism by sulphite oxidase, sulphite does not accumulate in the tissues on chronic administration, but is eliminated in the urine mainly as sulphate. In general, there is a large reserve capacity of sulphite oxidase and so systemic toxicity of sulphites is low. This conclusion is supported by clinical experience with total parenteral nutrition solutions preserved with sulphiting agents.

In their evaluation, JECFA noted there are two main issues in relation to sulphites and sulphur dioxide – general toxicity and idiosyncratic intolerance. The latter does not appear to be related to sulphite oxidase deficiency in humans. As general toxicity and idiosyncratic intolerance appeared to be unrelated, they can be considered separately.

The group ADI of 0.7 mg/kg BW/day is based on studies conducted in rats and pigs, where exposure to sulphites was found to cause gastric lesions in both long and short-term studies. The NOAEL was 70 mg/kg BW/day. There was little evidence of toxicity in other organs, even at higher dose levels. The occurrence of gastric lesions is therefore regarded as the most sensitive adverse effect. In establishing the ADI, a safety factor of 100 was applied to the NOAEL to take account of species differences and individual human variation. The Committee noted that gastric effects arise from local irritation therefore the effects would be more dependent on concentration in the stomach than daily dose. Adverse effects are therefore more likely to occur following regular ongoing consumption of foods having high concentrations of sulphites. There is currently no evidence that the gastric effects observed in animals have occurred in humans.

While sulphiting agents can interact with DNA and may induce mutations in bacteria, *in vivo* mutagenicity studies in mammals were negative, as were long-term carcinogenicity studies on potassium and sodium metabisulphite in mice and rats, respectively.

The most commonly reported adverse reaction to sulphur dioxide or sulphite in humans is bronchoconstriction and bronchospasm, particularly among a sensitive sub-group of asthmatics.

Less commonly, symptoms similar to anaphylaxis, flushing, hypotension, and tingling sensations have been reported. JECFA noted in their evaluation that appropriate labelling was the only feasible means of offering protection to susceptible individuals (WHO 1987b).

Evaluation and conclusion

Sulphite is readily absorbed by the gastrointestinal tract and once absorbed is rapidly oxidised to sulphate and excreted in the urine. In general, sulphites have a low systemic toxicity. The most common effects observed in rats and pigs are gastric lesions. Such effects are more dependent on concentration of sulphites in the stomach than daily dose, therefore adverse effects are more likely to occur following regular ongoing consumption of foods having high concentrations of sulphites. There is no evidence that such effects occur in humans. The contribution to the total intake of sulphites from the use of sulphur dioxide and sulphites as processing aids is likely to be relatively minor compared to their use as food additives. Overall, there are **no toxicological concerns** with the use of sulphur dioxide and sulphites as processing aids. The maximum permitted levels and food groups are acceptable from a human safety perspective.

A small section of the population, mainly people who suffer from asthma, are sensitive to sulphites and may react with allergy-like symptoms. Sensitivity to sulphite is unrelated to the general toxicity of sulphites and therefore must be considered separately. The risk to sulphite-sensitive people from sulphites in food is generally managed through food labelling.

Sodium nitrate

Current permission in the Code

Sodium nitrate is currently permitted as a processing aid for use in packaged water and water used as an ingredient in other foods at GMP levels.

Nitrate salts are also listed as food additive in Schedule 1, Standard 1.3.1 and in Standard 2.6.2 – Non-alcoholic Beverages and Brewed Soft Drinks the maximum limit is 45 mg/L (as NO_3^-).

Permissions in drinking water in Australia and New Zealand

The Australian Drinking Water Guidelines state that based on health considerations, the guideline value of 50 mg NO_3/L (as nitrate) has been set to protect bottle fed infants less than 3 months of age (NHMRC 2004). Adults and children over 3 months of age can safely consume up to 100 mg NO_3/L.

In the Drinking Water Standards for New Zealand, the maximum acceptable value for nitrate in drinking water is 50 mg/L (expressed as NO_3), with the remark that the sum of the ratio of the concentrations of nitrate and nitrite to each of these respective maximum acceptable values should not exceed 1 (Ministry of Health 2000).

Available safety information

JECFA has reviewed nitrate on numerous previous occasions, and most recently at its forty-fourth and fifty-ninth meetings (WHO 1995, 2003).

The Committee had previously allocated an ADI of 0–5 mg/kg BW, expressed as sodium nitrate. This ADI was based on a NOAEL of 500 mg/kg BW/day for body-weight gain at a higher dose in a long-term study in rats and a short-term study of toxicity in dogs, with a safety factor of 100.

Following the consideration of additional toxicological and epidemiological data at its forty-fourth meeting, the Committee noted that nitrate per se can generally be considered to be of relatively low toxicity. As the toxicity of nitrate results from its conversion to nitrite and the possible endogenous formation of *N*-nitroso compounds, and the toxicokinetics and biotransformation of nitrate in the rat are different from those in humans, rats are less suitable than rabbits, dogs and pigs for use in assessing the toxicity of nitrate in humans. However, the toxicological data are too limited to allow a safety evaluation on the basis of the results of studies on these species. For these reasons, the Committee considered both the toxicity studies on nitrate in laboratory animals and those on nitrite in combination with data on the conversion of nitrate to nitrite.

The Committee concluded that nitrate itself was not genotoxic, and the results of studies of carcinogenicity with nitrate were negative except when extremely high doses of both nitrate and nitrosatable precursors were administered. The available epidemiological data were considered to provide no evidence for an association between exposure of humans to nitrite and the risk for cancer. On the basis of this information, the NOAEL of 370 mg/kg BW/day, expressed as nitrate ion, in a long-term study in rats was considered to be the most appropriate for the safety evaluation.

When the proportion of nitrate converted to nitrite in humans was taken as 5% for the average individual and 20% for those with a high level of conversion, and when the NOAEL for nitrite (6 mg/kg BW/day, expressed as nitrite ion) was used to calculate the 'transposed' NOAEL for nitrate, expressed as nitrate ion, these values were estimated to be 160 and 40 mg/kg BW/day for average and high responders, respectively. As these figures were derived in part from data on human pharmacokinetics, use of a safety factor of less than 100 was considered to be justified.

On the basis of the NOAEL of 370 mg/kg BW/day, expressed as nitrate ion, and a safety factor of 100, an ADI of 0–5 mg/kg BW expressed as sodium nitrate or 0–3.7 mg/kg BW expressed as nitrate ion was allocated. On the basis of the 'transposed' NOAEL for nitrate of 160 mg/kg BW/day for normally responding persons (5% rate of conversion) and a safety factor of 50, an ADI of 0–3.2 mg/kg BW, expressed as nitrate ion, could be allocated. These two methods of deriving the ADI for nitrate thus resulted in similar figures, therefore the previously established ADI of 0–3.7 mg/kg BW, expressed as nitrate ion, was retained. Because nitrate may be converted to nitrite in significant amounts and infants below the age of 3 months are more vulnerable to the toxicity of nitrite than adults, the ADI does not apply to such infants.

At its fifty-ninth meeting, JECFA concluded that the pivotal observed toxic effects of nitrate are consequent on its conversion to nitrite *in vivo*. The Committee established an ADI of 0-0.07 mg/kg BW for nitrite on the basis of the NOAEL of 6.7 mg/kg BW/day for effects on the heart and lung in the 2-year study in rats and a safety factor of 100. As the new data on nitrite would not provide a basis for a significant change in the previous ADI for nitrate, the Committee retained the ADI of 0-5 mg/kg BW expressed as sodium nitrate, or 0-3.7 mg/kg BW, expressed as nitrate ion, established at its forty-fourth meeting.

Ingested nitrate is primarily absorbed from the upper part of the human digestive tract. Once absorbed, nitrate is rapidly distributed to the salivary glands and probably to other exocrine glands. On average, 25% of oral nitrate intake is secreted in the saliva. After absorption and equilibrium in body fluids, nitrate is rapidly excreted in urine. In humans, about 65–70% of any orally administered dose of nitrate was excreted in urine. Excretion was maximal about 5 hours after dosage and essentially complete within 18 hours. The most important metabolite of nitrate is nitrite. However, nitrite is converted rapidly and may not be readily detected. Once nitrate has been metabolised to nitrite, further metabolism can occur to hydroxylamine, ammonium and ultimately to urea. Nitrate can be reduced to nitrite by both enteric bacteria and mammalian nitrate reductase activity. Many species of microorganisms resident in the gastrointestinal tract have nitrate reductase activity. In humans, nitrate is converted to nitrite by microorganisms in the saliva. The major site for this reduction appears to be at the base of the tongue where a stable, nitrate-reducing microflora are established.

The toxicity of nitrate to humans is thought to be solely due to its reduction to nitrite. The major biological effect of nitrite in humans is its involvement in the oxidation of normal haemoglobin to methaemoglobin which is unable to transport oxygen to the tissues. This condition is called methaemoglobinaemia. Young infants are more susceptible to methaemoglobin formation than older children and adults. Other susceptible groups include pregnant women and people with a deficiency of glucose-6-phosphate dehydrogenase or methaemoglobin reductase.

In animals, laboratory experiments suggest that neither nitrite nor nitrate acts directly as a carcinogen. There is concern that nitrite may react with foods rich with secondary amines to form *N*-nitroso compounds in the stomach: many of these compounds are known to be carcinogenic in animals. Some epidemiological evidence suggests a relationship between nitrate and gastric cancer in humans, but this has not been confirmed in more definitive analytical studies. Overall, the epidemiological studies conducted to date have showed no consistently increased risk for cancer with increasing consumption of nitrate and do not provide evidence that nitrate is carcinogenic to humans.

Nitrate is not mutagenic in tests with bacteria and mammalian cells *in vitro*. Chromosome aberrations have been observed in the bone marrow of rats but may be due to the formation of *N*-nitroso compounds. Nitrite is mutagenic in both *in vivo* and *in vitro* experiments using mammalian cells.

Evaluation and conclusion

Nitrate *per se* is generally considered to have low toxicity. The toxicity of nitrate to humans is thought to be solely due to its conversion to nitrite once it has been absorbed following ingestion. Excess nitrite in humans may lead to a condition called methaemoglobinaemia, which results in an impaired ability for haemoglobin to transport oxygen to tissues. Young infants, in particular, are susceptible to the occurrence of methaemoglobinaemia. There is no evidence that either nitrate or nitrite act directly to cause cancer in either laboratory animals or humans, although concern has been expressed that nitrite may react with other substances in the body to form *N*-nitroso compounds, some of which are known to be carcinogenic in animals.

Overall, there **are no toxicological concerns** with the use of sodium nitrate as a processing aid for use in packaged water and water used as an ingredient in other foods.

However, given that these products could be used as a substitute for drinking water, it would be appropriate for the maximum permitted level for sodium nitrate to be brought into conformity with the drinking water level of 50 mg/L currently specified for Australia and New Zealand. This level has been established to protect bottle fed infants less than 3 months of age.

Toluene

Current permissions in the Code

Toluene is currently permitted as an extraction solvent in all foods at 1 mg/kg (Table to clause 13).

Available safety information

Toluene is the common name for methylbenzene. JECFA evaluated the safety of toluene as an extraction solvent in 1981 (WHO 1981) and the International Programme on Chemical Safety (IPCS) also undertook a review of toluene, which was subsequently published as an EHC Monograph (WHO 1986). More recently, both the US EPA and the ATSDR have evaluated the safety of toluene (EPA 1994, ATSDR 2000c). The IARC has also recently considered the carcinogenicity of toluene (IARC 1999e).

JECFA allocated an 'ADI not specified', concluding that residues of toluene occurring in food when the substance is used in accordance with GMP, would not pose any toxicological hazard. This was based on the low toxicity of toluene in experimental animals, its rapid hepatic metabolism and excretion from the body, and its lack of carcinogenicity in a lifetime inhalation study in rats. The Committee noted that since toluene absorbed from oral ingestion must pass through the liver, it is likely that at low levels of exposure, metabolism will occur before it can pass to other tissues. In the IPCS review it was noted that the presence of small amounts of toluene in drinking water and food adds only minor quantities to a person's total daily intake.

Toluene appears to be completely absorbed following oral exposure, although the rate of absorption appears to be slower than pulmonary absorption (ATSDR 2000c). The metabolism and excretion of orally administered toluene is similar to inhaled toluene. The primary site for toluene metabolism is the liver, with the majority of absorbed toluene being metabolised to benzoic acid, which is subsequently conjugated to glycine to form hippuric acid (WHO 1986). It is excreted in this form via the urine. Small amounts of toluene also undergo ring hydroxylation to form o-, m-, and p-cresol, which are excreted in the urine as sulphate or glucuronide conjugates. A proportion of the absorbed toluene (20 - 40%) is eliminated unchanged in expired air. After a single exposure, the elimination of toluene and its metabolites is almost complete in 24 hours. The ingestion of ethanol has been found to have a dramatic effect on the metabolism and subsequent excretion of toluene, with studies showing that ethanol inhibits the major metabolic pathway for toluene (ATSDR 2000c). The available data suggest that children past early neonatal development are able to metabolise toluene as efficiently as adults, at low exposure levels (ATSDR 2000c).

Studies on the effects of oral exposure to toluene are limited. Only a minimal number of animal studies have been undertaken, and very little human data is available.

In animals, oral studies with toluene are limited but effects observed include cardiovascular, neurological, hepatic and renal effects in mice and rats exposed to doses up to 2500 mg/kg BW/day for 13 weeks. A higher dose of 5000 mg/kg BW/day was lethal within one week of administration. Histopathologic lesions in the liver consisted of hepatocellular hypertrophy and were also noted in the brain and urinary bladder. In the brain, mineralised foci and necrosis of neuronal cells were observed in both male and female rats. Neurological effects, including ataxia and tremor were observed in mice and rats exposed to 2500 and 5000 mg/kg BW/day. No neurological effects were seen at doses of 625 mg/kg BW/day. The NOAEL for the study in rats was 312 mg/kg BW/day based on liver and kidney weight changes in male rats at 625 mg/kg BW and in mice was 1250 mg/kg BW/day.

Orally administered toluene has been reported to be teratogenic in mice. Exposure to 870 mg/kg BW on days 6 - 15 significantly increased the incidence of cleft palate. A level of 430 mg/kg BW was without effect. These results contrast to those from inhalation studies where toluene does not appear to be teratogenic in mice, rats, or rabbits, although embryotoxic/fetotoxic effects have been observed in rats and rabbits at doses that were non-toxic for the dams.

One oral study on carcinogenic effects in animals is available where toluene was administered at doses of 500 and 800 mg/kg BW/day to male and female rats for 104 weeks. This study showed an increase in the total number of malignant tumours in both males and females. However, the increased incidences were not dose-related and the confidence in this study is reported to be low (ATSDR 2000c). Toluene has been tested for carcinogenicity by inhalation exposure in one study in mice and in one study in rats. No significant increase in the incidence of tumours was observed. Repeated application of toluene to the skin of mice did not result in an increased incidence of skin tumours.

Data on effects in humans have primarily involved individuals exposed to toluene via inhalation either in experimental or occupational settings or during episodes of intentional abuse of solvent mixtures containing toluene. In these cases the primary effect of toluene is on the central nervous system (CNS).

A number of epidemiological studies have been undertaken that have assessed occupational toluene exposure (by the inhalation route) as a possible risk factor for cancer. Cancers of most tissue sites were not significantly associated with toluene exposure in any study and there was a weak consistency in the findings of those studies that did find an association (ATSDR 2000c). The majority of these studies primarily involved subjects exposed to mixtures of solvents including toluene, therefore the information from these studies is inadequate to assess the carcinogenic potential for toluene

The IARC found there is inadequate evidence in humans for the carcinogenicity of toluene, whereas in experimental animals there is evidence suggesting a lack of carcinogenicity of toluene. On this basis, toluene was considered *not classifiable as to its carcinogenicity to humans* (Group 3).

In terms of genotoxicity, toluene has been tested in a number of microbial, isolated mammalian cell, and whole organism test systems. The results have usually been negative (WHO 1986, EPA 1994, ATSDR 2000c). In the few studies in which a positive result has been found, the purity of the toluene was not stated.

Evaluation and conclusion

The use of toluene as an extraction solvent is expected to result in minimal residues in food, and the contribution from food to the total toluene intake is also considered to be minor. Low levels of toluene are readily metabolised by humans. Studies on rodent exposure to orally administered toluene have identified several treatment related systemic effects, most notably in the central nervous system, liver and kidney. These effects tend to occur at relatively high levels of exposure, with rats being more sensitive than mice. Overall, there are **no toxicological concerns** with the use of toluene as a processing aid. The current maximum permitted levels and food groups are acceptable from a human safety perspective.

Trichloroethylene

Current permissions in the Code

Trichloroethylene is currently permitted as an extraction solvent in all foods at a maximum permitted level of 2 mg/kg (Table to clause 13).

Available safety information

JECFA evaluated the safety of trichloroethylene as an extraction solvent at its twenty-seventh meeting (WHO 1983). An ADI for trichloroethylene has not been allocated. The Committee recommended that the use of trichloroethylene as an extraction solvent should be limited in order to ensure that its residues in food are as low as practicable. The Committee withdrew the specification for trichloroethylene in 2000 because requested information on the nature, level(s), and methods of analysis for stabilizers in food-grade trichloroethylene, assay requirements, method of assay, and requirements and methodology for volatile impurities were not provided.

The International Programme on Chemical Safety (IPCS) also undertook a review of trichloroethylene, which was subsequently published as an EHC Monograph (WHO 1985). Evaluations of trichloroethylene have also been undertaken more recently by the ATSDR (ATSDR 1997), IARC (IARC 1995) and the National Toxicology Programme (NTP 2005).

Trichloroethylene is rapidly absorbed by the gastrointestinal tract and distributed throughout the body. It primarily concentrates in the fatty tissues such as the liver, brain and body fat. Trichloroethylene can also readily pass through the placenta into the foetus. Trichloroethylene is rapidly metabolised through oxidation by cytochrome P-450 and conjugation with glutathione (GSH), with the metabolites being primarily excreted in the urine. Trichloroethylene metabolism in mice, rats and humans is qualitatively similar, producing the same primary metabolites, which include trichloroethanol, trichloroethanol-glucuronide, and trichloroacetic acid (TCA). Minor metabolites include oxalic acid, dichloroacetic acid (DCA), and N-(hydroxyacetal)-aminoethanol as well as the glutathione (GSH) conjugates of trichloroethylene and its metabolites. Metabolism is said to play an important role in the toxicity of trichloroethylene because many of its metabolites are themselves toxic (ATSDR 1997).

Based on effects reported in humans and/or animals, the primary targets for trichloroethylene toxicity appear to be the liver and kidneys. Effects on the central nervous system and the heart have also been observed, particularly following acute exposure to high levels.

The toxicity of trichloroethylene does not seem to be heavily dependent on the route of exposure (ATSDR 1997), with similar effects being observed following inhalation and oral exposure. The specific organ toxicity of trichloroethylene can vary depending on the species and this is most likely attributed to interspecies differences in metabolism.

Several studies have shown hepatotoxicity in mice that received trichloroethylene for intermediate periods, although the effects may be sex specific. Male mice exposed for 6 weeks showed a dose-related progression of hepatic alterations, beginning with liver enlargement at 100 mg/kg BW/day, enlarged liver cells at 400 mg/kg BW/day, and focal necrosis at 1600 mg/kg BW/day. While liver enlargement appears to be the primary liver effect, this is not consistently observed in all studies, and in some long-term studies with mice, no liver effects have been reported at doses up to 1738 mg/kg BW/day. Liver effects were not observed in rats treated by gavage with 2000 mg/kg BW/day for 13 weeks.

No clear evidence of renal effects has been observed in studies with humans chronically exposed to trichloroethylene in drinking water. Renal effects have however been observed in both rats and mice, with rats being more sensitive than mice. Long-term administration of trichloroethylene to rats (500-1100 mg/kg BW/day) and mice (1200-2300 mg/kg BW/day) resulted in treatment-related chronic nephropathy, characterised by degenerative changes in the tubular epithelium. In a carcinogenicity study in rats, non-neoplastic renal effects included toxic nephrosis at doses of 500 and 1000 mg/kg BW/day, as well as cytomegaly of the renal tubular cells coupled with toxic nephropathy.

There is no information available on the potential genotoxic effects in humans following oral exposure. Results from both *in vivo* animal studies and *in vitro* studies are inconclusive with regard to the potential genotoxicity of trichloroethylene. In mammalian cell culture studies, trichloroethylene did not induce chromosomal aberrations in Chinese hamster ovary (CHO) cells, unscheduled DNA synthesis in rat hepatocytes, or gene mutation in human lymphoblastoid cells, but it did induce sister chromatid exchange in CHO cells, gene mutation in mouse lymphoma cells, and morphological transformation of rat embryo cells. In rodent *in vivo* studies trichloroethylene did not induce unscheduled DNA synthesis, sister chromatid exchange, dominant lethal mutations or chromosomal aberrations. Trichloroethylene gave mixed results for DNA single strand breaks in mouse liver and positive results for micronucleus formation in mice.

While trichloroethylene may itself not be genotoxic, some of its metabolites are reactive and potentially genotoxic compounds (ATSDR 1997). For example, the metabolite 1,2-dichlorovinyl-cysteine (DCV), which is a product of DCA conjugation to GSH in the kidney, is mutagenic in *Salmonella typhimurium* and may induce primary DNA damage in mammalian cells *in vitro* and *in vivo*. The production of DVC in humans is believed to occur by a minor pathway that is unlikely to become saturated and lead to kidney damage (ATSDR 1997).

A number of epidemiological studies have been conducted to try and determine if there is a link between the incidence of leukaemia and other cancers and oral exposure to trichloroethylene. While some of these studies have shown an association between oral exposure to trichloroethylene and an increased incidence of certain types of cancers, other studies have not shown such an association at much higher levels of exposure. The associations drawn from these studies are therefore said to be suggestive yet inconclusive (ATSDR 1997).

Animal studies have shown increases in various types of cancers following inhalation or oral exposure to trichloroethylene, including cancer of the liver in mice, and cancer of the kidney and testes in rats. Oral exposure to trichloroethylene or its metabolites preferentially induces peroxisome proliferation in mouse liver, which may be related to the carcinogenic response in this species. It has been hypothesised that some of the potential for tumour induction may be related to the formation of trichloroethylene metabolites such as DCA and TCA.

Trichloroethylene is listed in the NTP's Report on Carcinogens (NTP 2005) as *reasonably anticipated to be a human carcinogen* (NTP 2005). This conclusion is based on limited evidence from studies in humans, as well as the results of studies with experimental animals, which indicates there is an increased incidence of malignant and/or combination of malignant and benign tumours at multiple tissue sites in multiple species, and information suggesting that trichloroethylene acts through mechanisms that indicate it would likely cause cancer in humans. The IARC has also evaluated trichloroethylene and have classified it as *probably carcinogenic to humans* (Group 2A), on the basis of limited evidence in humans and sufficient evidence in experimental animals (IARC 1995).

Evaluation and conclusion

Trichloroethylene is rapidly absorbed by the gastrointestinal tract and distributed throughout the body, where it is rapidly metabolised. Many of its metabolites are themselves toxic. The primary targets for trichloroethylene toxicity appear to be the liver and kidneys. Effects on the central nervous system and the heart have also been observed, particularly following acute exposure to high levels. Trichloroethylene is a potent carcinogen in experimental animals, producing tumours at multiple sites and in multiple species. There is also suggestive evidence from some epidemiological studies in humans for an association between oral exposure to trichloroethylene and an increased incidence of certain types of cancers. On the basis of the available data, **there are toxicological concerns** with the use of trichloroethylene as an extraction solvent for foods. The use of trichloroethylene as an extraction solvent should be limited in order to ensure that its residues in food are as low as practicable.

Urea

Current permissions in the Code

Urea is currently permitted as a processing aid for the manufacture of concentrated gelatine solutions at a maximum permitted level of 1.5 times the mass of the gelatine present. Urea is also permitted as a microbial nutrient and microbial nutrient adjunct for use in the course of manufacture of any food.

Available safety information

The safety of urea when used as a food additive in sugar free chewing gum was evaluated by JECFA at their forty-first meeting (WHO 1993c). JECFA reviewed biochemical studies, short-term toxicity studies in dogs and ruminants, carcinogenicity studies in rats and mice, mutagenicity studies, and studies on effects in human volunteers. The Committee noted that most of the available data were either inadequate or of little relevance for the evaluation of urea as a food additive.

It was concluded that since urea is a natural end product of amino acid metabolism in humans, and that approximately 20 g/day is excreted in the urine of adults (proportionately less in children), the use of urea at levels of up to 3% in chewing gum was of no toxicological concern.

The main safety concern relating to the use of urea is its potential to react with ethanol to produce ethyl carbamate (urethane), the ethyl ester of carbamic acid. In a recent evaluation by JECFA, it was concluded that ethyl carbamate is genotoxic and is a multisite carcinogen in all species tested (JECFA 2005). Ethyl carbamate has also been classified as a group 2B carcinogen by the IARC, which means the agent is *possibly carcinogenic to humans* (IARC 1987).

Ethyl carbamate has been tested in a large number of studies of genotoxicity *in vitro* and *in vivo*. The results of assays for point mutations were uniformly negative for mouse lymphoma cells, while assays in bacterial, yeast and other types of mammalian cells produced variable results. Results of assays in somatic cells *in vivo* (including tests for induction of chromosomal aberrations, micronucleus formation and sister chromatid exchange) were almost uniformly positive. The assay of micronucleus formation in mice showed the strongest positive response.

The acute oral toxicity of ethyl carbamate is low, the oral LD_{50} in rodents being approximately 2000 mg/kg BW. In rodents, singles doses of 1000 mg/kg BW cause anaesthesia. Repeated administration of ethyl carbamate in drinking water for 13 weeks resulted in an increase in mortality in mice and rats receiving doses of about 500-600 mg/kg BW/day. In the same study, mice given ethyl carbamate at doses of ≥150 mg/kg BW/day showed reduced body weight gain and effects on lungs, kidney, heart, spleen, lymph nodes, thymus, bone marrow and ovaries. No such effects were seen at 50 mg/kg BW/day. Similar effects, except in the lungs, were also seen in rats at the same doses. Co-administration of 5% ethanol with the ethyl carbamate attenuated many of the adverse effects.

Ethyl carbamate is a multisite carcinogen with a short latency period. Single doses or short-term oral dosing at 100-200 mg/kg BW have been shown to induce tumours in mice, rats and hamsters. In non-human primates given ethyl carbamate at a dose of 250 mg/kg BW/day by the oral route for five years, a variety of tumour types analogous to those observed in rodents (including adenocarcinoma of the lung, hepatocellular adenoma and carcinoma and hepatic haemangiosarcoma) were induced over an observation period of up to 22 years. Treatment of female mice with single or multiple doses of ethyl carbamate during gestation or lactation was found to increase the incidence or multiplicity of tumours in the adult offspring compared with untreated controls.

In a newly available lifetime study of carcinogenicity, male and female mice were given drinking water containing ethyl carbamate at different concentrations, equalling intakes of approximately 0, 1, 3 or 9 mg/kg BW/day. Treatment with ethyl carbamate resulted in dose-dependent increased incidences of alveolar and bronchiolar, hepatocellular and Harderian gland adenoma or carcinoma, hepatic haemangiosarcoma, and mammary gland adenocanthoma or adenocarcinoma (females only). Small, but still statistically significant, increases were also observed in the incidence of a number of other tumours. Dose-related increases in non-neoplastic lesions affecting the blood vessels of the liver, heart and uterus as well as eosinophilic foci of the liver were also observed.

The most sensitive sites for tumour induction were the lung and Harderian gland. There was also a treatment-related increase in the combined incidence of any tumour type at any site. The co-administration of ethyl carbamate and ethanol resulted in marginal changes in the incidence of some of the neoplasms attributed to ethyl carbamate alone, but overall, co-administration of ethanol had no consistent effect on the carcinogenicity of ethyl carbamate.

As part of its evaluation of ethyl carbamate, JECFA undertook a dose response analysis of the animal carcinogenicity data in order to derive a benchmark dose (BMD) and BMDL (benchmark dose level) associated with a 10% extra risk of tumours (JECFA 2005). For this analysis the Committee considered the pivotal study to be the long-term study of carcinogenicity in mice, and that the observed increased incidence of alveolar and bronchiolar adenoma or carcinoma as the critical endpoint. The values for the BMDLs ranged from 0.3 to 0.5 mg/kg BW.

The Committee prepared international estimates of dietary intake assessment of ethyl carbamate from both food and alcoholic beverages and compared these to the BMD and BMDL values for tumours associated with administration of ethyl carbamate (JECFA 2005). When the estimated intake of ethyl carbamate in foods (15 ng/kg BW/day) was compared with the BMDL value obtained for the incidence of alveolar and bronchiolar tumours in male and female mice, the margin of exposure (MOE) was 20,000. When alcoholic beverages were included in the estimated intake (80 ng/kg BW/day), the MOE was 3,800. On the basis of these calculations, the Committee concluded that intake of ethyl carbamate from foods excluding alcoholic beverages would be of low concern, but intakes from food and alcoholic beverages combined is of concern, therefore mitigation measures to reduce concentrations of ethyl carbamate in some alcoholic beverages should be continued.

Ethyl carbamate occurs naturally in a number of fermented foods and beverages, such as wine, spirits, beer, bread, soy sauce and yoghurt. JECFA concluded that cyanate is probably the ultimate precursor in most cases, reacting with ethanol to form the carbamate ester (JECFA 2005). Cyanate may originate from different sources such as carbamyl phosphate, the oxidation of hydrogen cyanide, *N*-carbamyl compounds such as urea and citrulline, or from hitherto unknown substances with labile carbamyl groups (Zimmerli & Schlatter 1991).

In the reaction between urea and ethanol to form ethyl carbamate, heat is required in order for considerable amounts of ethyl carbamate to be formed. Foods where this reaction might occur comprise wine, sake and probably bread. Most of the ethyl carbamate content of wines is formed after fermentation, by a reaction between ethanol and ethyl carbamate precursors. Hence, the concentrations of ethanol and ethyl carbamate precursors as well as temperature and the time of storage are important parameters for ethyl carbamate formation. Although it is very probable that urea is a major ethyl carbamate precursor in wine, it seems not to be the only one.

Over the past few years, major reductions in the concentration of ethyl carbamate have been achieved either by reducing the concentration of the main precursor substances in the food or by reducing the tendency for these substances to react to form cyanate (e.g. by exclusion of light from bottled spirits). In the United States, the use of urea as a fermentation supplement in wine is prohibited. The US Bureau of Alcohol, Tobacco, Firearms and Explosives has found that the use of urea is not considered acceptable in good commercial practice among wine producers and has rescinded the listing of urea as an authorized treatment. (Federal Register, Vol 55, No 118, 24974-24982, 06/19/1990).

Evaluation and conclusion

Urea does not itself raise any toxicological concerns, however it has the potential to react with ethanol in certain situations to produce a substance called ethyl carbamate (urethane). Ethyl carbamate is genotoxic and has been found to be a multisite carcinogen in all species tested, including non-human primates.

Ethyl carbamate can be formed from various substances present in foods and beverages. Although urea is not the only precursor for ethyl carbamate formation, it does seem to be the major precursor in alcoholic beverages. In the most recent evaluation by JECFA, it was concluded that while ethyl carbamate intake from foods would be of low concern, ethyl carbamate intake from food and alcoholic beverages combined is of concern, therefore, mitigation measures to reduce the concentration of ethyl carbamate in some alcoholic beverages should continue.

On the basis of the available information, **there are toxicological concerns** with the use of urea as a microbial nutrient and microbial nutrient adjunct for use in the manufacture of alcoholic beverages. The permission for the use of urea as a microbial nutrient and microbial nutrient adjunct should be limited to exclude alcoholic beverages.

There are **no toxicological concerns** with the use of urea as a processing aid for the manufacture of concentrated gelatine solutions. The maximum permitted level is acceptable from a human safety perspective.

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Attachment 3

Summary of submissions

Round One

Submitter Organisation	Name
Nestlé Australia Limited	Robyn Banks
Food Technology Association of Victoria Inc.	David Gill
New Zealand Food Safety Authority	Carole Inkster

Submitter	Position	Comments
Nestlé Australia Limited	In general supports the review	Supports the review of processing aids where there are safety issues with particular processing aids. However it does not support the removal of processing aids that may be considered obsolete. The reasons for this are: • It is impossible to determine what processing aids may be required for use in the future for various purposes. • The use of any such 'obsolete' processing aid (which has been removed from the Code) by other countries for imported products would deem such products not approved for sale in Australia and New Zealand. (Therefore processing aids could only be considered obsolete if they are no longer used or likely to be used by any food manufacturing country in the world).
Food Technology Association of Victoria Inc.	Agrees with the review	Supports option 2 – to conduct the review and make amendments to the Standard as appropriate and made the following comments. • Pointed out that several processing aids that are listed in section 5.1 of the Initial Assessment Report that FSANZ will evaluate their safety have recently been reviewed by JECFA. • Suggested that all reviews should be done in accordance with JECFA, whose reviews should be relied on for all decisions. • Noted that some of these processing aids which will have a safety assessment are known to be used in imported flavours and extracts which (Australian and New Zealand) users may not fully have control over. • Expressed concern about whether all listed processing aids have specifications listed in any of the references in Standard 1.3.4 (or clause 11 of Standard 1.3.1 for flavourings) and whether they meet them. Two examples it listed are soap and Perlite.

Submitter	Position	Comments
New Zealand Food Safety Authority	Fully supports the review	Fully supports option 2 to review the Standard and make amendments as required. It also looks forward to participating in the EAG. Made mention of an earlier New Zealand government agencies submission to the formation of the draft new *Australia New Zealand Food Standards Code* dated 17 May 2000, which raised concerns about the new processing aids standard. This submission noted that the new standard was based on the old 1996 Australian standard (A16). However there are a number of new processing aids which have not been evaluated by JECFA or had a full safety assessment performed when A16 was developed (P86). So therefore it fully supported and welcomed this Proposal to undertake this assessment as detailed in section 5.1 of the Initial Assessment Report. One specific issue they would like to be assessed as part of this review. • This is to reiterate their view (previously expressed as a submission to A474 – Winemaking, dated 14/11/03) that the permission to use urea as a processing aid for wine be removed from the Code (currently contained in the Table to clause 18 of the Standard).

Attachment 4

Suggested amendments and discussion

The Tables contain both suggested amendments, as well as discussions about issues where it was decided not to make changes, with discussion of the reasons.

Table to clause 3 – Generally permitted processing aids

Suggested action	Reason, comment
Remove - aluminium stearate - calcium stearate - magnesium stearate - potassium stearate - potassium oleate	Since they are included under the general item in schedule 2 of Std 1.3.1, as: aluminium, calcium, sodium, magnesium, potassium and ammonium salts of fatty acids (INS 470)
Remove kaolin	Since it is an aluminium silicate, which is listed in schedule 2, Std 1.3.1 as INS 559
Remove potassium hydrogen tartrate Change potassium tartrate to potassium tartrates in Schedule 2 of Standard 1.3.1.	Since potassium tartrate is listed in schedule 2 of Std 1.3.1, as INS 336. Codex has INS 336 as potassium tartrates, so would appear that potassium hydrogen tartrate would already be approved. Make a consequential amendment to Schedule 2, Standard 1.3.1 to the plural term, potassium tartrates.
Change the name of polypropylene glycol alginate to the more commonly used term propylene glycol alginate (PGA).	It is believed they may be two different compounds but propylene glycol alginate (PGA) is the processing aid used and so this term should be used in place of polypropylene glycol alginate. JECFA uses this proposed name, INS 405.
Change the name of polyoxyethylene 40 monostearate to polyoxyethylene 40 stearate	An alternative name, more commonly used. JECFA, as well as others, uses the proposed alternative name, polyoxyethylene 40 stearate, INS 431.
Remove Sodium ethoxide Sodium methoxide	They are catalysts for the interesterification of fats and oils, so should be listed in the Table to clause 5, not as generally permitted processing aids. They should have a maximum permitted level of 1.0 mg/kg, like potassium ethoxide.
Remove White mineral oil	It is considered a lubricant, release and anti-stick agent so it should be removed from the Table to clause 3 and added into the Table to clause 9. The maximum permitted level should be maintained at GMP.

Table to clause 4 – Antifoam agents

Suggested action	Reason, comment
Remove dimethylpolysiloxane	Since it is listed in schedule 2 of Std 1.3.1, as: polydimethylsiloxane, which is an alternative name for the same compound, INS 900a.
Remove - polysorbate 60 - polysorbate 65 - polysorbate 80	Since they are listed in schedule 2 of Std 1.3.1, under different names as indicated polyoxyethylene (20) sorbitan monostearate (INS 435) polyoxyethylene (20) sorbitan tristearate (INS 436) polyoxyethylene (20) sorbitan monooleate (INS 433).

Table to clause 5 – catalysts

Suggested action	Reason, comment
Change permission for chromium to chromium (excluding chromium VI)	The safety concern is only for chromium (VI). Chromium (VI) has toxicological concerns.
No change Potassium ethoxide	The safety assessment has indicated that there is no safety issue with the current permission.
Add Sodium ethoxide and sodium methoxide	Remove the entry from the Table to clause 3, since they, like potassium ethoxide, are catalysts used for the interesterification of fats and oils. Their maximum permitted levels should be the same as that currently for potassium ethoxide, that is 1.0 mg/kg.

Table to clause 6 – Decolourants, clarifying, filtration and adsorbent agents

Suggested action	Reason, comment
Remove copper sulphate **No**	Since cupric sulphate, which is another name for copper sulphate is listed in schedule 2 of Std 1.3.1, INS 519. Conclusion was not to remove it since cupric (II) sulphate does not include cuprous (I) sulphate, while copper sulphate includes both.

Table to clause 7 – Desiccating preparations

Suggested action	Reason, comment
Remove sodium stearoyl lactylate	Since sodium lactylates, which includes this compound is listed in schedule 2 of Std 1.3.1, INS 481. JECFA and Codex lists sodium stearoyl lactylate as INS 481i. Codex also lists 481, like schedule 2, as sodium lactylates.
Remove, short chain triglycerides **No**, leave as is to ensure clarity.	Since they may be considered to be foods, in which case they already have approval as a generally permitted processing aid, due to subclause 3(a) of Std 1.3.3.

Table to clause 8 – Ion exchange resins

Suggested action	Reason, comment
No change	Require specialist industry assistance in how to review this table (as well as the Table to clause 6).

Table to clause 9 – Lubricants, release and anti-stick agents

Suggested action	Reason, comment
Remove sodium stearoyl lactate	Since sodium stearoyl lactate is an alternative name for sodium stearoyl lactylate. As stated above under table to clause 7, sodium lactylates, which includes this compound is listed in schedule 2 of Std 1.3.1, INS 481. JECFA and Codex lists sodium stearoyl lactylate as INS 481i. Codex also lists 481, like schedule 2, as sodium lactylates.
Remove polysorbate 60	Since it is listed in schedule 2 of Std 1.3.1, as mentioned above in Table to clause 4, under a different name as INS 435.
Remove talc	Since talc is considered to come under magnesium silicates, which is listed in schedule 2 of Std 1.3.1, as INS 553. Talc is listed in Codex as 553iii and also in JECFA as talc/talcum INS 553iii.
Add White mineral oil	Remove the entry from the Table to clause 3 since it is a lubricant, release and anti-stick agent at GMP.
Add an editorial note relating to white mineral oil.	JECFA is currently reviewing mineral oils so it is considered premature to make changes to the permissions until this review has been completed. Therefore it is proposed to insert an editorial note to the effect that FSANZ will review white mineral oil three years after the gazettal of this note (to allow time for JECFA to complete their review).

Table to clause 10 – Carriers, solvents and diluents

Suggested action	Reason, comment
Remove anhydrous sodium sulphate Change sodium sulphate to the plural term, sodium sulphates, in Schedule 2 of Standard 1.3.1.	Since sodium sulphate (not specifically anhydrous) is listed in schedule 2 of Std 1.3.1, INS 514. Codex lists 514, as sodium sulphates, but schedule 2 does not. Make a consequential amendment to schedule 2 of Standard 1.3.1 to the plural.
Remove ethyl alcohol (ethanol)	Since it is already listed in the Table to clause 3 as a generally permitted processing aid.

Suggested action	Reason, comment
Check, remove glycine **No**, seek submissions on this issue	Codex lists glycine as INS 640, flavour modifier. It can act as a carrier, or diluent. Comment is that glycine is used in table top sweeteners and has approval in Schedule 1 of Standard 1.3.1. Keeping this permission allows its use as either a food additive or a processing aid.
Remove isopropyl alcohol **No**	Since it is already listed in the Table to clause 3 so a generally permitted processing aid. No keep the specific permission since it has a maximum permitted level of 1,000 mg/kg.
Remove talc	Same reason as listed in the entry for Table to clause 9. Talc can be considered to come under magnesium silicates, INS 553 which is listed in schedule 2 of Std 1.3.1.
Check, remove L-leucine **No**, seek submissions on this issue.	A similar comment to the above entry for glycine. It can act as a carrier, or diluent. Comment is that glycine is used in table top sweeteners and has approval in Schedule 1 of Standard 1.3.1. Keeping this permission allows its use as either a food additive or a processing aid.

Table to clause 11 – Processing aids used in packaged water used as an ingredient in other foods

Suggested action	Reason, comment
Remove copper sulphate **No** Amend the maximum permitted level for copper from GMP to 2	Cupric sulphate, which is another name for copper sulphate is listed in schedule 2 of Std 1.3.1, INS 519. Same comment as mentioned above for the Table to clause 6 entry so propose to not remove. To be consistent with the Australian Drinking Water Guidelines and the New Zealand guidelines.
Remove sodium fumate and replace with sodium humate	Since believe this is an incorrect spelling, believe the name should be humate, which is listed as an approved boiler water treatment chemical in the US CFR section 173.310 - Boiler water additives. Seems like it was a typographical error that was not been picked up. It was listed as sodium humate in the old Australian Food Standards Code, Standard A16 – Processing Aids.
Amend the maximum permitted level for chlorine from 10 (available chlorine) to 5 (available chlorine)	To be consistent with both the Australian Drinking Water Guidelines and the New Zealand guidelines.
Amend the maximum permitted level for chlorine dioxide from 10 (available chlorine) to 1	To be consistent with the Australian Drinking Water Guidelines.
Amend the maximum permitted level for calcium hypochlorite from 10 (available chlorine) to 5 (available chlorine)	To be consistent with the Australian Drinking Water Guidelines.

Suggested action	Reason, comment
Amend the maximum permitted level for polyelectrolytes (acrylamide monomers) from GMP to 0.0002 (acrylamide monomer). Change the name from polyelectrolytes (acrylamide monomers) to Polyacrylamide (polyelectrolytes), and the maximum permitted limit to refer to acrylamide monomer.	To be consistent with both the Australian Drinking Water Guidelines (0.0002 (acrylamide)) and the New Zealand guidelines (0.0005 (acrylamide)). Polyelectrolytes are polymers that act as flocculating agents to clarify water. There are safety limits on acrylamide in water so polyelectrolytes made from polyacrylamide should have the same acrylamide limits. The specifications in the Code refer to polyacrylamide, not polyelectrolytes so that term should be referenced for permissions, while keeping the term polyelectrolytes is useful for clarity, and for people familiar with the term for water treatment.
Remove permission for sodium fluoride Seek submissions on this issue	It is not considered a processing aid, and its removal should not cause any issues.
Remove permission for sodium fluorosilicate (sodium silicofluoride) Seek submission on this issue	It is not considered a processing aid, and its removal should not cause any issues.
Amend the maximum permitted level for sodium glucoheptonate from 1 mg/kg measured as cyanide to 0.08 mg/kg (measured as cyanide)	To be consistent with both the Australian Drinking Water Guidelines and the New Zealand guidelines. The limit of 1 mg/kg cyanide of the US Code of Federal Regulations section 173.310 relates to the processing aid (sodium glucoheptonate) not the treated water.
Amend the maximum permitted level for sodium nitrate from GMP to 50.	To be consistent with the Australian and New Zealand drinking water guidelines. Sodium nitrate is approved as a boiler water treatment in the US CFR section 173.310.
Amend the maximum permitted level for styrene-divinylbenzene cross-linked copolymer from GMP to 0.03 (styrene)	To be consistent with the Australian Drinking Water Guidelines and New Zealand guidelines.

Table to clause 13 – Extraction solvents

Suggested action	Reason, comment
Query the permissions for: - butane - isobutane - propane **Do not** change permissions	The gases are listed in schedule 2 of Standard 1.3.1, but for pressurised food containers only. That is they do not have general permission as food additives so require specific listing as extraction solvents.
Remove the permission for trichloroethylene, as an extraction solvent for all foods. Seek submissions on this issue.	There is a safety issue with trichloroethylene. Is it used anywhere as an extraction solvent?

Table to clause 14 – Processing aids with miscellaneous function

Suggested action	Reason, comment
Add the phrase 'from bovine milk' after lactoperoxidase in the editorial note, so that the sentence reads: Where meat has been treated using lactoperoxidase the mandatory labelling requirements in clause 4 of Standard 1.3.3 apply.	To ensure clarity, that the mandatory labelling requirements of clause 4 of Standard 1.2.3 relate to milk residues, not lactoperoxidase.
Remove the entry for ethylene oxide	The permission ceased to have effect on 30 September 2003, so the entry is superfluous.
Remove polysorbate 80	Since as noted above (entry in Table to clause 4), it is approved in schedule 2 of Std 1.3.1, under another name, as INS 433.
Remove permission for the use of potassium bromate and sodium bromate for germination control in malting. **No**, leave as is, since permission is still required, but make the maximum permitted level to be the limit of determination for bromate. The Safety Assessment made this recommendation to ensure there are no residues in the final food.	For safety reasons due to the assessment of bromate as a category 2B (possibly carcinogenic to humans) carcinogen (International Agency for Research on Cancer). Australian Associated Brewers (AAB) sent through a submission that they are still used in some special malts so asked that permissions be left in.
Add A permission for urea as a microbial nutrient and microbial nutrient adjunct, for all foods excluding alcoholic beverages, to a limit of GMP.	It is proposed to remove its general permission in the Table to clause 18, to then exclude permissions for alcoholic beverages. This is because there is a safety concern about it use due to the involvement of urea in the formation of ethyl carbamate (carcinogen) in wine production (and other fermentation processes).

Table to clause 18 – Microbial nutrients and microbial nutrient adjuncts

Suggested action	Reason, comment
Remove copper sulphate **No**	Since as noted above (entries in Tables to clause 6 and 11), it is approved in schedule 2 of Standard 1.3.1, under another name, cupric sulphate, as INS 519. Same comment as before.
Remove, dextrin	Since dextrins, white & yellow, roasted starch, INS 1400, is listed in schedule 2 of Std 1.3.1. Believe this entry should cover the simple term dextrin.
Remove polysorbate 80	Since as listed above (entries in Tables to clause 4 and 14), it is approved in schedule 2 of Std 1.3.1, under another name, as INS 433.
Remove trehalose	Considered as a novel food or novel food ingredient (listed in Table to clause 2 of Std 1.5.1 – Novel foods, from recent Application, A453). So already has permission as a generally permitted processing aid (subclause 3(a) of Std 1.3.3) since novel foods are foods.

Suggested action	Reason, comment
Remove Urea Provide a limitation that urea is not approved for alcoholic beverage production (includes wine production).	This comes from a submission to the Initial Assessment report from the New Zealand Food Safety Authority. A safety concern about it use due to the involvement of urea in the formation of ethyl carbamate (carcinogen) in wine production (and other fermentation processes). The safety assessment supports a restriction. Make a consequential amendment to include a permission for the use of urea as a microbial nutrient and microbial nutrient adjunct, for all foods excluding alcoholic beverage (including wine production). to be added to the Table to clause 14.

Attachment 5

Regulation of Processing Aids Internationally

The current system of regulation of processing aids in Australia and New Zealand is different to how they are regulated in many other countries. This is a summary of how processing aids are regulated elsewhere and the differences and similarities with approaches.

Australia and New Zealand

The regulations for food additives and processing aids for Australia and New Zealand are in general horizontal standards; Standard 1.3.1 – Food Additives and Standard 1.3.3 – Processing Aids respectively. Horizontal standards mean that the standards are general standards that regulate across all the individual commodity standards (viewed as individual vertical standards (unless these standards have their own specific regulations which apply only to them). The food additives listed in Schedule 2 of Standard 1.3.1 (miscellaneous additives permitted in accordance with GMP in processed foods specified in Schedule 1) are also treated as generally permitted processing aids. Foods (including water) are also treated as generally permitted processing aids.

Codex

The only international food regulatory system is provided by the Codex Alimentarius Commission (Codex). Codex uses the following definitions for food additive and processing aid.

> ***Food additive*** means any substance not normally consumed as a food by itself and not normally used as a typical ingredient of the food, whether or not it has nutritive value, the intentional addition of which to food for a technological (including organoleptic) purpose in the manufacture, processing, preparation, treatment, packing, packaging, transport or holding of such food results, or may be reasonably expected to result (directly or indirectly), in it or its by-products becoming a component of or otherwise affecting the characteristics of such foods. The term does not include contaminants or substances added to food for maintaining or improving nutritional qualities[11,12].
>
> ***Processing aid*** means any substance or material, not including apparatus or utensils, and not consumed as a food ingredient by itself, intentionally used in the processing of raw materials, foods or its ingredients, to fulfil a certain technological purpose during treatment or processing and which may result in the non-intentional but unavoidable presence of residues or derivatives in the final product[1].

From these two Codex definitions it would appear that processing aids are regarded as a sub-set of food additives. The distinguishing features separating processing aids from other food additives are that:

- they must be intentionally used during the processing of raw materials, foods or ingredients;
- they are used to fulfil a technological purpose during treatment or processing and not a function in the final food; and

[11] Codex Alimentarius, Second Edition (revised 1995) Volume 1A (General Requirements), Food and Agriculture Organisation of the United Nations, World Health Organisation, Rome p 11-13.
[12] Codex Alimentarius, General Standard for Food Additives, Food and Agriculture Organisation of the United Nations, World Health Organisation, Rome *CODEX STAN 192-1995, Rev. 5 (2005).*

- the presence of any residue or derivative of the substance must be non-intentional and unavoidable.

Codex does not have a standard for processing aids. Codex is developing a General Standard for Food Additives[2]. Codex also has an Inventory of Processing Aids (IPA)[13]. This Codex Inventory of Processing Aids was prepared by the Codex Committee on Food Additives and Contaminants (CCFAC) and adopted by the Codex Alimentarius Commission in 1989. The objectives for preparing the Inventory were:

(1) to develop information on substances used as processing aids; and
(2) to identify processing aids whose safety should be evaluated by the Joint FAO/WHO Expert Committee on Food Additives (JECFA).

The Codex IPA list is not intended to be complete or a 'positive list' of permitted processing aids. The list has been updated from the original list of 1989 up until 2004. The New Zealand Codex representatives offered to update the list and to develop a discussion paper for Codex Committee for Food Additives and Contaminants (CCFAC) on how to address processing aids (submitted to the thirty-six session of CCFAC in March 2004). CCFAC has decided that the IPA is a list with no regulatory status. CCFAC has not resolved how to develop a standard for processing aids. There is confusion about its status, as some stakeholders may incorrectly believe that substances in the list have been assessed by Codex as being safe for use in food.

Canada

Canada regulates processing aids as a subset within the broad definition of food additive[14] within the Food and Drug Regulations.

> 'food additive' means any substance the use of which results, or may reasonably be expected to result, in it or
> its by-products becoming a part of or affecting the characteristics of a food, but does not include
> (a) any nutritive material that is used, recognized, or commonly sold as an article or ingredient of food,
> (b) vitamins, mineral nutrients and amino acids, other than those listed in the tables to Division 16,
> (c) spices, seasonings, flavouring preparations, essential oils, oleoresins and natural extractives,
> (d) agricultural chemicals, other than those listed in the tables to Division 16,
> (e) food packaging materials and components thereof, and
> (f) drugs recommended for administration to animals that may be consumed as food; (*additif alimentaire*)

Division 16 – Food Additives within the Food and Drug Regulations contains 15 tables (Tables I to XV) that group various food additives under their type and function. A number of these are functionalities that would be considered processing aids in the Code, such as enzymes (Table V – Food additives that may be used as food enzymes).

[13] Codex Alimentarius, Inventory of Processing Aids, CAC/MISC 3, 1999
[14] Food and Drug Regulations, Part B Foods, Division 1, page 36, (2003) found on the website: http://www.hc-sc.gc.ca/food-aliment/friia-raaii/food_drugs-aliments_drogues/act-loi/pdf/e_b-text-1.pdf

The United States of America

The regulation of food additives and processing aids in the United States of America is regulated by the Code of Federal Regulations, Title 21 – Foods and Drugs. The definitions of both food additive and processing aid (see below) are found in section 170.3 – Definitions within Part 170 – Food Additives[15].

> Food additives includes all substances not exempted by section 201(s) of the act, the intended use of which results or may reasonably be expected to result, directly or indirectly, either in their becoming a component of food or otherwise affecting the characteristics of food. A material used in the production of containers and packages is subject to the definition if it may reasonably be expected to become a component, or to affect the characteristics, directly or indirectly, of food packed in the container. ``Affecting the characteristics of food'' does not include such physical effects, as protecting contents of packages, preserving shape, and preventing moisture loss. If there is no migration of a packaging component from the package to the food, it does not become a component of the food and thus is not a food additive. A substance that does not become a component of food, but that is used, for example, in preparing an ingredient of the food to give a different flavor, texture, or other characteristic in the food, may be a food additive.
>
> ``Processing aids'': Substances used as manufacturing aids to enhance the appeal or utility of a food or food component, including clarifying agents, clouding agents, catalysts, flocculents, filter aids, and crystallization inhibitors, etc.

A report from the National Academy of Sciences/National Research Council in 1972, titled 'A Comprehensive Survey of Industry on the Use of Food Chemicals Generally Recognized as Safe' provides these definitions. Both these definitions indicate some differences in the approach to regulating and defining food additives and processing aids in the USA compared to that within Australia and New Zealand. The definition of processing aids comes under a variety of different definitions of terms that describe the physical or technical functional effects for which direct human food ingredients (not termed food additives) may be added to foods. The Code of Federal Regulations (CFR) regulates food chemicals, which include food additives and processing aids. The CFR also has sections that regulate direct and indirect food additives.

Europe (European Union)

The risk assessment of food additives (and processing aids) for the European Union now comes under the authority of the European Food Safety Authority, while their regulation occurs under the European Commission (EC). The definitions of food additive and processing aid are contained in an European Communities Council Directive[16].

> 'Food additive' means any substance not normally consumed as a food in itself and not normally used as a characteristic ingredient of food whether or not it has nutritive value, the intentional addition of which to food for a technological purpose in the manufacture, processing, preparation, treatment, packaging, transport or storage of such food results, or may be reasonably expected to result, in it or its by-products becoming directly or indirectly a component of such foods.

[15] Code of Federal Regulations, Title 21 – Food and Drugs, part 170 – Food Additives, section 170.3 – Definitions (2003) found on the website : http://a257.g.akamaitech.net/7/257/2422/04nov20031500/edocket.access.gpo.gov/cfr_2001/aprqtr/pdf/21cfr170.3.pdf

[16] Consolidated Text, (1989) L0107-10/09/1994, Council Directive 89/107/EEC

> 'Processing aid' means any substance not consumed as a food ingredient by itself, intentionally used in the processing of raw materials, foods or their ingredients, to fulfil a certain technological purpose during treatment or processing and which may result in the unintentional but technically unavoidable presence of residues of the substance or its derivatives in the final product, provided that these residues do not present any health risk and do not have any technological effect on the finished product.

There are specific labelling regulations for foodstuffs[17] with requirements that ingredients (which include specific requirements for food additives) be labelled. It would appear that processing aids do not need to be labelled on food products[7]. The following has been extracted from this reference.

> 1. Ingredients shall be listed in accordance with this Article
> and Annexes I, II and III.
> 4. (c) The following shall not be regarded as ingredients:
> (ii) additives:
> — whose presence in a given foodstuff is solely due to the fact that they were contained in one or more ingredients of that foodstuff, provided that they serve no technological function in the finished product,
> — which are used as processing aids.

United Kingdom

In the United Kingdom the regulations of food additives are under The Miscellaneous Food Additive Regulations 1995[18] (and updated amendments) which implement the appropriate European Parliament and Council Directives. Miscellaneous additives are defined as 'food additives other than colours and sweeteners' (but does not include processing aids). Regulation 2(1) within this regulation contains the following definitions.

> 'food additive' means—
> (a) any substance not normally consumed as a food in itself and not normally used as a characteristic ingredient of food, whether or not it has nutritive value, the intentional addition of which to food for a technological purpose in the manufacture, processing, preparation, treatment, packaging, transport or storage of such food results, or may reasonably be expected to result, in it or its by-products becoming directly or indirectly a component of such foods; or
> (b) a carrier or carrier solvent;
> [but does not include— *(a number of exemptions which are not copied here)]*.
>
> 'processing aid' means any substance not consumed as a food by itself, intentionally used in the processing of raw materials, foods or their ingredients to fulfil a certain technological purpose during treatment or processing, and which may result in the unintentional but technically unavoidable presence of residues of the substance or its derivatives in the final product, provided that these residues do not present any health risk and do not have any technological effect on the finished product;

This regulation states that:

> 'Processing aids are not covered by Directive 95/2/EC or by these Regulations'.

It would therefore appear there is no separate regulation for food processing aids. There is no apparent legal requirement to label for processing aids on food packages.

[17] Directive 2000/13/EC of the European parliament and of the council (20 March 2000)
[18] The Miscellaneous Food Additives Regulations (1995), Statutory Instrument 1995 No 3187, on the website: http://www.legislation.hmso.gov.uk/si/si1995/Uksi_19953187_en_1.htm#end

Attachment 6

Terms of reference and list of members for the External Advisory Group

Terms of reference for the External Advisory Group

Within the scope of Proposal P277 – Review of Processing Aids (Other than Enzymes), the terms of reference for the External Advisory Group are to:

1. provide input and expert advice on amendments suggested to update the various Tables to clauses of Standard 1.3.3 of the approved processing aids and their maximum permitted levels in food.

2. provide technical advice specifically relating to:

    - generally permitted processing aids;
    - permitted antifoam agents;
    - permitted catalysts;
    - permitted decolourants, clarifying, filtration and adsorbent agents;
    - permitted desiccating preparations;
    - permitted ion exchange resins;
    - permitted lubricants, release and anti-stick agents;
    - permitted carriers, solvents and diluents;
    - permitted processing aids used in packaged water and in water used as an ingredient in other foods;
    - permitted bleaching agents, washing and peeling agents;
    - permitted extraction solvents;
    - permitted processing aids with miscellaneous functions; and
    - permitted microbial nutrients and microbial nutrient adjuncts.

3. provide advice in relation to:

    - new scientific evidence regarding the safety of particular processing aids which may justify amending maximum permitted levels within Standard 1.3.3;
    - recent international regulatory changes which may impact on specific processing aids;
    - processing aids which are no longer used or likely to be used in the future;
    - names of approved processing aids to better reflect current usage and international standards;
    - errors and anomalies within the Standard; and
    - improvements to make the Standard easier to read and use.

External Advisory group (EAG) list of members

Name	Position	Company
Mr Kim Leighton	Assistant Director Scientific & Technical	Australian Food & Grocery Council
Mr Bill Smith	Technical Manager Echuca	H.J. Heinz Co Australia Ltd
Ms Julie Newlands	Manager, Regulation	Unilever Australasia
Mr John van den Beuken	Programme Manager (Composition) Food Standards Group	New Zealand Food Safety Authority
Dr Mike Rockell		Massey University, NZ
Bill Porter	Team Leader – Regulatory Affairs	NSW Food Authority
Dr John Germov	Senior Lecturer in Sociology	School of Social Sciences, Faculty of Education & Arts, University of Newcastle