ANZFA
Australia New Zealand Food Authority

TE MANA WHAKARITE KAI
MO AHITEREIRIA ME AOTEAROA

5 May 1999
12/99

Development of Joint Australia New Zealand Food Standards

As part of the process of the Review of the *Food Standards Code*

REVIEW OF THE MAXIMUM PERMITTED CONCENTRATIONS OF NON-METALS IN FOOD

Full Assessment Report

Proposal P158

May 1999

The Authority should receive written submissions no later than **16 June 1999**

Submissions should be sent to:

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Australia New Zealand Food Authority

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Submissions will be placed on the Authority's public register (unless a claim of commercial confidentiality is made and accepted by the Authority) and may therefore be open to public scrutiny.

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*Not currently team members - provided comment on initial review papers.

The Authority appreciates the knowledge and expertise contributed by the above individuals, and acknowledges that the views contained in this paper do not necessarily represent the views of the individuals or their organisations.

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EXECUTIVE SUMMARY

Introduction

This paper forms part of the review of contaminants in food and specifically considers the maximum permitted concentrations (MPCs) for non-metal contaminants currently in the Australian *Food Standards Code* and in the *New Zealand Food Regulations 1984*. A formal proposal to review non-metal contaminants was agreed by the ANZFA Board in October 1997 and public submissions related to this proposal were requested in November 1997.

Revised standards have been proposed on the basis of an extensive review of the toxicological data and analysis of the dietary intake data for each of the contaminants based on available survey data and the results of the 1995 National Nutrition Survey. A risk assessment has been completed for each of the substances considered and risk management options considered.

Policy framework for the review

The policy framework for the review was detailed in the paper 'The Regulation of Contaminants and Other Restricted Substances in Food' which was prepared in October 1997 and revised, following consideration of public comments, in August 1998. This paper discusses the issues to be considered in reviewing contaminants in food as well as identifying the general principles to be used when establishing standards for contaminants.

The principles applied in the risk analysis of non-metal contaminants were detailed in the ANZFA policy paper 'Framework for the Assessment and Management of Food-Related Health Risks' This paper sets out the basic elements of risk assessment and management in relation to chemicals in food.

The possible use of guideline levels for contaminants to complement the use of MPCs in some cases is discussed in detail in the discussion paper 'The Use of Guideline Levels for Contaminants in Food'. The term 'guidelines' has been replaced by 'generally expected levels' or 'GELS'. GELS are proposed to be used where there is considered to be only a low public health and safety risk but where there is still a desire to maintain contaminant levels as low as reasonably achievable. No GELS have been proposed in this paper for non-metal contaminants but these could be considered in the future.

Non-metals considered in the review

The non-metal contaminants considered for review were as follows:

Acrylonitrile monomer;
Aflatoxin;
Ergot;
Erucic acid;
Fluorine;
Fusarium toxins;
Lupin alkaloids;
Methanol;
Ochratoxins;
Phomopsin;
Polychlorinated biphenyls;
Pyrrolizidine alkaloids;
Shellfish biotoxins;
- Paralytic shellfish poisons (PSP):
- Diarrhetic shellfish poisons (DSP):
- Amnesic shellfish poisons (ASP): and
- Neurotoxic shellfish poisons (NSP).

Vinyl chloride monomer; and
Vinylidene chloride monomer.

Conclusions of the review

- The review of the maximum permitted concentrations of non-metals in food has been conducted according to the principles and procedures previously agreed by the ANZFA Board and endorsed by ANZFSC.

- For each of the substances reviewed, the scientific evaluation has resulted in a characterisation of the risk associated with exposure to these substances through the consumption of food. Risk management options have been proposed for each substance which are consistent with the section 10 objectives of the *Australia New Zealand Food Authority Act 1991* to which the Authority must have regard when establishing or varying standards.

- New standards have been proposed for aflatoxin in tree nuts, diarrhetic shellfish poisons in bivalve molluscs, ergot in cereal grains, erucic acid in edible oils, lupin alkaloids in lupins seeds, methanol in alcoholic beverages and neurotoxic shellfish poisons in bivalve molluscs. Standards are unchanged for acrylonitrile monomer in all foods, aflatoxins in peanuts and peanut products, amnesic shellfish poisons and paralytic shellfish poisons in bivalve molluscs, phomopsins in lupin seeds, polychlorinated biphenyls in various foods and vinyl chloride and vinylidene in all foods. Standards have not been proposed at this time for fluoride, fusarium toxins, ochratoxins and pyrrolizidine alkaloids.

- The regulatory impact assessment has established that a combination of MPCs and GELs is the preferred regulatory option since it provides an adequate level of protection of public health and safety while not requiring an unnecessary level of surveillance to be performed by industry or enforcement agencies.

- Because of the current paucity of surveillance data available on most of the non-metal contaminants in food, no GELS have been proposed at this time.

BACKGROUND TO THE FOOD STANDARDS REVIEW

Australia New Zealand Food Authority

The Australia New Zealand Food Authority (the Authority) is a joint statutory body responsible for making recommendations on food standards which, when approved by the Australia New Zealand Food Standards Council (ANZFSC), are adopted by reference and without amendment into the food laws of the Australian States and Territories. In New Zealand for the time being, such standards apply as part of a system of dual standards, where the Australian Food Standards Code (AFSC) is recognised as an alternative to the New Zealand Food Regulations (NZFR). At a future date, standards in the NZFR will be repealed and the standards developed under the joint system will apply in both countries.

The Authority's other functions include:

- developing codes of practice for industry on any matter that may be included in a food standard;

- co-ordinating the surveillance of food in Australia;

- liaising with the Ministry of Health in New Zealand on arrangements for imported foods;

- conducting research and surveys in relation to food standards matters;

- developing food safety education initiatives in co-operation with the States and Territories; and

- assisting in the co-ordination of food recalls in Australia.

The Ministry of Health manages recalls in New Zealand. In Australia, the Authority develops assessment policies in relation to imported food.

Review of Food Standards

In July 1996 an Agreement between Australia and New Zealand came into force which established the Authority - a system for developing joint food standards and an *Australian New Zealand Food Standards Code.*

The aim of the Agreement is to extend the Australian food standard system to include New Zealand so that food standards developed by the Australia New Zealand Food

Authority and approved by Ministerial Council can be adopted throughout Australia and in New Zealand. The current review of the AFSC is an important element in developing joint standards. The provisions of the Agreement provide common policy objectives for developing food standards and a common approach to a transparent, timely, consultative and accountable standards setting process—both key features of the review process.
The Authority is seeking to ensure full New Zealand participation in the standards setting process and the review of food standards.

In developing or reviewing food standards, the Authority must have regard to the objectives outlined in section 10 of the *Australia New Zealand Food Authority Act 1991*.

Consistent with these statutory objectives and the policies of the Authority, the review will, where possible:

- reduce the level of prescriptiveness of standards to facilitate innovation by allowing wider permission on the use of ingredients and additives, but with consideration of the possible increased need for consumer information;
- develop standards which are easier to understand and make amendment more straightforward;
- replace standards which regulate individual foods with standards that apply across all foods or a range of foods;
- consider the possibility of industry codes of practice as an alternative to regulation; and
- facilitate harmonisation of food standards between Australia and New Zealand.

The review will also be carried out in accordance with the competition policy principles which have been adopted by the Council of Australian Governments (COAG). These principles require the review of all business regulation to remove unnecessary obstacles to competition, and an assessment of the social, environmental, and economic impacts as well as the impacts on health of proposed regulation on all affected sectors of the community.

Food Standards Setting in Australia and New Zealand

The Governments of Australia and New Zealand entered an Agreement in December 1995 establishing a system for the development of joint food standards. ANZFA is now developing a joint Food Standards Code (FSC) which will provide compositional and labelling standards for food in both Australia and New Zealand.

Until the joint *Australia New Zealand Food Standards Code* is finalised the following arrangements for the two countries apply:

- **Food imported into New Zealand other than from Australia** must comply with either the Australian *Food Standards Code*, as gazetted in New Zealand, or the New Zealand *Food Regulations 1984*, but not a combination of both. However, in all

cases maximum residue limits for agricultural and veterinary chemicals must comply solely with those limits specified in the New Zealand *Food Regulations 1984.*

- **Food imported into Australia other than from New Zealand** must comply solely with the Australian *Food Standards Code.*
- **Food imported into New Zealand from Australia** must comply with either the Australian *Food Standards Code*, as gazetted in New Zealand, or the New Zealand *Food Regulations 1984,* but not a combination of both.
- **Food imported into Australia from New Zealand** must comply with the Australian *Food Standards Code*. However, under the provisions of the Trans-Tasman Mutual Recognition Arrangement, food may **also** be imported into Australia from New Zealand provided it complies with the New Zealand *Food Regulations 1984.*
- **Food manufactured in Australia and sold in Australia** must for most products comply solely with the Australian *Food Standards Code.*

In addition to the above, all food sold in New Zealand must comply with the New Zealand *Fair Trading Act 1986* and all food sold in Australia must comply with the Australian *Trade Practices Act 1974,* and the respective Australian State and Territory *Fair Trading Acts.*

Any person or organisation may apply to ANZFA to have the *Food Standards Code* amended. In addition, ANZFA may develop proposals to amend the Australian *Food Standards Code* or to develop joint Australia New Zealand food standards. ANZFA can provide advice on the requirements for applications to amend the *Food Standards Code*.

REGULATORY IMPACT ANALYSIS

The Authority is required, in the course of development of regulations suitable for adoption in Australia and New Zealand, to consider the impact of various options (including non-regulatory options) on all sectors of the community, including consumers, the food industry and governments in both countries. The regulatory impact assessment will identify and evaluate, though not be limited to, the costs and benefits of the regulation, and its health, economic and social impacts.

To assist in this process, comment on potential impacts or issues pertaining to these regulatory options is sought from all interested parties in order to complete the development of the regulatory impact statement. Public submissions should clearly identify relevant impact(s) or issues and provide support documentation where possible.

WORLD TRADE ORGANIZATION (WTO)

Both Australia and New Zealand are members of the World Trade Organization and signatories to the agreements on the Application of Sanitary and Phytosanitary Measures (SPS agreement) and on Technical Barriers to Trade (TBT agreement).

Within Australia, a memorandum of understanding binding all States and Territories to the agreements has been put in place by the Council of Australian Governments (COAG).

In addition, the agreement between the Government of Australia and the Government of New Zealand on joint food standards explicitly requires the Authority to ensure that food standards are consistent with the WTO obligations of both countries.

The WTO agreements are predicated on a set of underlying principles that standards and other regulatory measures should be:

- based on sound scientific principles;
- developed using consistent risk assessment practices;
- transparent;
- no more trade-restrictive than necessary to achieve a legitimate objective;
- recognise the equivalence of similar measures in other countries; and
- not used as arbitrary barriers to trade.

As members of the WTO both Australia and New Zealand have an obligation to notify the WTO of changes to food standards to enable other member countries of the WTO to make comment. Notification is required in the case of any new or changed standards which may have a significant trade effect and which depart from the relevant international standard (or where no international standard exists). Matters raised in this proposal may be notified to the WTO as either SPS notifications or TBT notifications, or both.

SPS Notifications

These are primarily health related, and refer to any measure applied:

- to protect animal or plant life from risks arising from the entry, establishment or spread of pests, diseases or disease carrying organisms;
- to protect human or animal life or health from risks arising from additives, contaminants, toxins or disease-carrying organisms in foods, beverages or foodstuffs;
- to protect human life or health from risks arising from diseases carried by animals, plants or products thereof, or from the entry, establishment or spread of pests; and
- to prevent or limit other damage from the entry, establishment or spread of pests.

TBT Notifications

These are primarily not related to health, but are related to matters such as trade, food composition and labelling.

Notification for this Proposal

This matter does not warrant a TBT or SPS notification because the proposed regulations for non-metal contaminants in food are not more restrictive than relevant international standards.

INVITATION FOR PUBLIC SUBMISSIONS

The Authority has completed a full assessment of the proposal, prepared draft provisions for Standard 1.4.1 of the joint Australia New Zealand Food Standards Code and will now conduct an inquiry to consider the draft variations and their regulatory impact.

Written submissions containing technical or other relevant information which will assist the Authority in its consideration of the full assessment to review the standard maximum permitted concentrations of non-metal contaminants and its regulatory impact are invited from interested individuals and organisations. Technical information should be presented in sufficient detail to allow independent scientific assessment.

Submissions containing more general comment and opinion are also invited. The Authority's policy on the management of submissions is available from the Standards Liaison Officer upon request.

The processes of the Authority are open to public scrutiny, and any submissions received will ordinarily be placed on the public register of the Authority and made available for public inspection. If you wish any confidential information contained in a submission to remain confidential to the Authority, you should clearly identify the sensitive information and provide justification for treating it in confidence. The *Australia New Zealand Food Authority Act 1991* requires the Authority 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.

All correspondence and submissions on this matter should quote the full title, be addressed to the Project Manager - Proposal P158 and be sent to either of the addresses on the front page of this document. Submissions should be received by the Authority by **16 June 1999**. Submissions received after this date may not be able to be considered by the Authority in its consideration of this matter.
General queries on this matter and other Authority business can be directed to the Standards Liaison Officer at the above address or by Email on <slo@anzfa.gov.au>. Submissions should not be sent by Email as the Authority cannot guarantee receipt.

Requests for more general information on the Authority can be directed to the Information Officer at the above address or by Email <info@anzfa.gov.au>.

INTRODUCTION

A Proposal to review the maximum permitted concentrations (MPCs) of non-metal contaminants in food was agreed by the Authority in October 1997 as part of the review of food standards. This proposal considers those non-metal substances currently regulated in Standard A12 - Metals and Contaminants in Food together with other non-metal contaminants regulated elsewhere in the Food Standards Code. A number of other contaminants for which there is worldwide concern have also been included in this review.

This proposal was accompanied by a policy paper entitled 'The Regulation of Contaminants and Other Restricted Substances in Food'. The purpose of this policy paper was to:

- identify issues which needed to be considered when controlling food contaminants;
- identify general principles to be applied in establishing standards for contaminants and other restricted substances in food;
- raise some of the issues which need to be considered in the review of Standard A12; and
- indicate the general direction for the review of Standard A12.

Public comments on the Proposal and on the policy paper were sought at the time.

Contaminants to be considered for inclusion in the revised standard were selected on the basis of the following criteria:

- contaminants for which there is an existing standard in Australian or New Zealand regulations;
- contaminants for which there is an existing or proposed Codex standard; and
- contaminants for which there is a concern in Australia and/or New Zealand.

On this basis, the following contaminants were considered for review:

Acrylonitrile monomer	Aflatoxin	Ergot
Erucic acid	Fluorine	Fusarium toxins
Lupin alkaloids	Methanol	Ochratoxins
Phomopsin	Polychlorinated biphenyls	
Pyrrolizidine alkaloids	Vinyl chloride monomer	
Vinylidene chloride monomer		

Shellfish biotoxins
- Paralytic shellfish poisons (PSP)
- Diarrhetic shellfish poisons (DSP)

- Amnesic shellfish poisons (ASP)
- Neurotoxic shellfish poisons (NSP)

From November 1997 and throughout 1998, survey data on each of the non-metal contaminants was sought from a wide range of sources, including government enforcement agencies, industry and research institutes. This data, together with a review of the toxicology data, has been used to assess the risk associated with exposure to each of the non-metal contaminants and to provide risk management options.

RELEVANT PROVISIONS

Current Australian regulations in the *Food Standards Code*

STD	SUBSTANCE	CURRENT REGULATION
Std A12	Aflatoxin	15 ug/kg in peanut butter or peanut paste, nuts and the nut portion of products containing nuts. 5 ug/kg in all other foods.
	Acrylonitrile monomer	0.02 mg/kg in any food
	Ergot	Not detectable in a 2.25 litre sample of cereal grain (Proposed A303: 0.5 g/kg (w/w))
	Phomopsin	5 ug/kg in any food
	Polychlorinated biphenyls	0.2 mg/kg in fat of meat, fat of meat of poultry, milk, milk products, and eggs. 0.5 mg/kg in fish
	Vinyl chloride monomer	0.05 mg/kg in any food
	Vinylidene chloride	0.01 mg/kg in any food
Std G.1	Erucic acid	50 g/kg in total fatty acids present in rapeseed oil
Std B.1. B3	Lupin alkaloids	200 mg/kg in lupin flour, lupin kernel, lupin kernel meal, and lupin hulls

Std P.3, P4	Methanol	3 g/L in grape spirit, brandy 0.4g/L in whisky, rum, gin, vodka 8g/L in all other spirits 2g/L in white wine, white sparkling wine 3 g/L in other wine, sparkling wine and fortified wine.
Std D 1, D2	Paralytic shellfish poisons (PSP) Domoic acid (amnesic shellfish poisons or ASP)	0.8 mg/kg in the edible portion of bivalve molluscs or canned bivalve molluscs 20 mg/kg in the edible portion of bivalve molluscs or canned bivalve molluscs

Current New Zealand Standards in the *Food Regulations 1984*

STD	SUBSTANCE	CURRENT REGULATION
Reg. 257	Aflatoxin	0.015 mg/kg in peanut butter or shelled nuts, and the nut portion of products containing nuts. 0.005 mg/kg in all other foods.
Reg. 265	Acrylonitrile monomer Vinyl chloride monomer Vinylidene chloride	No person shall use, or permit to be used, in the preparation, packing, storage or delivery of a food for sale, any package, appliance, or container that yields or could yield to its contents any poisonous, injurious or tainting substance.
Reg. 257	Fluoride	3 mg/kg in all beverages and other liquid foods 15 mg/kg in shellfish 10 mg/kg in any other food except tea
Reg. 233	Methanol	0.4g/L of ethanol in whisky, rum, gin, vodka 3 g/L of ethanol in brandy, Tequila. 8g/L of ethanol in other spirits

Substances for which there are currently no regulations in Australia or New Zealand

Substance	Food Commodity
Ochratoxins	grains, dried fruit
Fusarium toxins	grains
Pyrrolizidine alkaloids	grains
Neurotoxic shellfish poisons (NSP)	bivalve molluscs
Diarrhetic shellfish poisons (DSP)	bivalve molluscs

Codex Standards

Substance	Codex Standard	Regulation
Aflatoxin	Std for cereals, pulses and legumes	Proposed: 15 µg/kg in peanuts 0.05 µg/kg in milk
Erucic acid	Std for edible low erucic acid rapeseed oil	5% in rapeseed oil
	Draft std for named vegetable oils	Proposed: 2% in rapeseed oil

ASSESSMENT OF ISSUES

Risk analysis framework

The principles that have been applied for the risk analysis of non-metal contaminants are detailed in the ANZFA policy paper 'Framework for the assessment and management of food-related health risks'. This paper sets out the basic element of risk assessment and management in relation to chemicals in food. In brief, the toxicology data on each of the non-metals has been reviewed in order to establish the tolerable daily (or weekly) intake, if possible. Survey data on the levels of contaminants in food has analysed and, if appropriate, used to estimate the dietary intake of the contaminant using the results of the recently released 1995 National Nutrition Survey. Risk management options have been considered on the basis of this risk assessment process. In most cases, maximum permitted concentrations (MPCs) have been recommended due to the relatively high public health and safety risks associated with exposure to these substances.

Guideline levels for contaminants

A proposal to consider establishing guideline levels for contaminants in food in place of standards in some cases was raised in the review of the cadmium MPCs (Proposal P144) and the ANZFSC meeting in July 1997 requested the Authority to develop within 12 months 'enforceable guidelines governing cadmium levels in foods other than those listed in Standard A12'. The issue of guidelines was also discussed briefly in the Contaminants Policy Paper circulated in October 1997 where the possibility was raised of extending the use of guidelines to all contaminants.

A more detailed Discussion Paper entitled 'The Use of Guideline Levels for Contaminants in Food' was prepared in June 1998 which was circulated to State, Territory and New Zealand Health departments. In this paper, it was proposed that, in some cases, guideline levels could replace or complement MPCs. This paper was considered at the ANZFAAC meeting in July 1998 and, following some minor changes, was considered by ANZFSC in July 1998. ANZFSC agreed in principle with the concept of guideline levels and that ANZFA should establish such guidelines for contaminants when appropriate.

At a 2-day Stakeholders Workshop on metal contaminants held in August 1998, it was decided that a more accurate term to describe the concept of guidelines was 'generally expected levels' or 'GELS' which would be expressed using the median (50th percentile) and 90th percentile.

No GELS have been proposed in this paper for non-metal contaminants but these could be considered in the future. A discussion paper on GELS is available from ANZFA. GELS have been proposed for some metal contaminants where there is considered to be only a low public health and safety risk but where there is still a desire to maintain contaminant levels as low as reasonably achievable, in accordance with policy principles for regulating contaminants.

Principles used for controlling contaminants

The principles to be used in controlling the level of contamination in foods and for setting MPCs were established by ANZFA in June 1997 and endorsed by ANZFSC in July 1997. These principles were presented in the policy paper "The Regulation of Contaminants and Other Restricted Substances in Food". The following general principle was established:

"Contaminant levels in food should be as low as reasonably achievable"

The principle is based on the premise that contaminants have no intended function in food and their associated health risks may not yet be fully understood.

ANZFA also applies the following additional principles when evaluating the establishment of MPCs for contaminants. These are secondary to the broader section 10 objectives of *the Australia New Zealand Food Authority Act 1991:*

1. An MPC will be established only where it serves an effective risk management function; and MPCs will be set for:

   a) all primary commodities (described using Codex food commodity groupings) which provide, or may potentially provide, a significant contribution to the total dietary contaminant intake, as indicated by dietary exposure assessments; and

   b) nominated processed foods where the setting of an MPC for the primary commodity is judged to be ineffective.

2. An MPC will be set at a level which is consistent with public health and safety as determined by an appropriate risk assessment procedure based on dietary modelling[1] and which is reasonably achievable from sound primary production and natural resource management practices. Australian and New Zealand data will normally be used for this purpose.

3. In setting an MPC, consideration will be given to Australia and New Zealand's international trade obligations under the World Trade Organization's Sanitary and Phytosanitary (SPS) agreement and Technical Barrier to Trade (TBT) agreement.

4. There are a number of measures, other than MPCs, that might be used to reduce contaminant levels in the food supply and consequent dietary intakes. Other measures include improving primary commodity production practices

[1] Dietary modelling is a technique which combines dietary intake data or model diets with concentration data for food chemicals to estimate dietary exposure to that food chemical.

and developing appropriate education programs for population groups with potential for high exposure to particular contaminants.

The principle criteria used for determining whether and MPC or a GEL is appropriate for a particular contaminant is the potential public health and safety risk. If the risk is high, or there is potential for the risk to be high without strict controls, for the average or high consumer, than an MPC will be used. In some cases, an MPC may be considered necessary to encourage good agricultural practice and good manufacturing practice in order to avoid a situation of high public health and safety risk developing. If there is no evidence that there is a significant public health risk, even for the high consumer, a GEL may be appropriate. When considering the public health and safety risk associated with exposure to contaminants, all sources of exposure need to be considered.

Risk analysis outcomes

A brief outline of the results of the risk analysis is provided below. Summaries of the risk analyses are provided in Appendix 2 and detailed reports on individual contaminants are available from ANZFA upon request.

Food contact materials: acrylonitrile, vinyl chloride and vinylidene chloride

These are substance which may contaminate food as a result of leaching from food packaging or as a result of contact with food. The risk assessments conducted on each of these substances have concluded that each is a potential carcinogen, and although there is no evidence of adverse health effects resulting from low level exposure to these substances via food, it is proposed to retain the maximum levels in foods to the levels of detection, as shown below.

Substance	**Food**	**Maximum permitted concentration**
Acrylonitrile	All food	0.02 mg/kg
Vinyl chloride	All food	0.01 mg/kg
Vinylidene chloride	All food	0.01 mg/kg

Mycotoxins: aflatoxins, ochratoxins, phomopsin, fusarium toxins and ergot

Aflatoxin, ochratoxin, fusarium toxins and phomopsin are mycotoxins which contaminate foods as a result of fungal growth on the food. Ergot is the sclerotium (dormant winter form) of the fungus *Claveceps* that contaminates many cereal grains.

Aflatoxins

The major source of aflatoxins in the diet is from the consumption of peanuts and peanut products. Pistachios and other tree nuts may also have high levels of aflatoxins. Aflatoxins are considered potent mutagens and carcinogens and, as such, human exposure should be maintained at levels which are as low as reasonably

achievable. Considerable effort is made both in growing and storing peanuts to reduce the aflatoxin level and the maximum level proposed is considered the lowest achievable. The high levels of aflatoxin found in some tree nuts is considered sufficient justification for the same level to be applied to these foods (see below). The current MPC for 'other foods' is not considered necessary and is inconsistent with one of the principles used for establishing MPCs for contaminants, namely, that MPCs will be established for primary commodities which provide, or may potentially provide, a significant contribution to the total dietary contaminant intake.

Ochratoxins

Concern regarding contamination of food with ochratoxins has largely been confined to northern Europe, particularly in relation to barley and other grains. There has also been recent concerns regarding occurrence of ochratoxins in dried fruit. There is currently on-going work in Australia to establish the extent of ochratoxin contamination of foods. Ochratoxin is regarded as a possible human carcinogen. No standards are proposed at this stage as there is considered to be insufficient data available to establish whether there is a risk to public health. This issue will be considered further by ANZFA as survey data become available.

Phomopsins

The fungus which infects plants and produces phomopsins is mainly found on lupins. On other plants, the spoilage tends to make the plant inedible. Contaminated lupin seeds can be isolated effectively from uncontaminated seeds by sorting based on the discolouration caused by the infection, however, residual levels of phomopsins remain in the sorted seeds. Phomopsins bind to tubulin in cells, preventing cell division. Of particular concern is the evidence that phomopsins can cause liver tumors in rats at extremely low levels of exposure. The toxicity data on phomopsins is, however, very limited and an adequate risk assessment is not currently possible. Maintaining the levels of phomopsins in food as low as reasonably achievable is considered the appropriate risk management strategy. It is proposed that the current level of 5 μg/kg be maintained but that further analysis of phomopsin levels in lupins used for direct consumption be investigated as well as in flour prepared from lupins. Further work on the mechanism of phomopsin toxicity would also be beneficial.

Fusarium toxins

Concern in relation to fusarium toxins has largely been related to levels in maize and maize products in North America. There is currently only limited information in relation to contamination in Australia and New Zealand. Fusarium species produce a variety of toxins including T-2 toxin, tricothecenes, zearalenone and fumonisins which can produce toxicity involving the gastrointestinal tract, reproductive and cardiovascular systems, and potential immunotoxicity and cancer.

Further survey work on the levels of fusarium toxins in foods is now being conducted. A risk assessment on these toxins therefore will be finalised when this data become available. No standards for fusarium toxins are proposed at this stage.

Ergot

Ergot contamination of grains, particularly rye, is largely an issue for countries which have cool, damp weather. It has become an issue for Australia and New Zealand as a result of the importation of rye from Canada. Ergot contains biologically active alkaloids which can cause a variety of significant toxic symptoms in humans. The risk associated with ergot and the need for a standard has been considered in a recent application to ANZFA (A303) from the Bread Research Institute of Australia. The recommendation from consideration of this application was that a maximum level of 0.05% (w/w) ergot in grain be established. ANZFSC is still considering this recommendation. In this review, it have been proposed that the 0.05% level is appropriate, but that a definition of 'ergot' be included in the Standard, as shown below.

Substance	**Food**	**Maximum permitted concentration**
Aflatoxin	Peanuts and peanut products Tree nuts and tree nut products	0.015 mg/kg 0.015 mg/kg
Phomopsins	Lupin seeds	0.005 mg/kg
Ergot[1]	Cereal grain	500 mg/kg

1. Ergot refers to the sclerotium of dormant winter form of the fungus, *Claviceps purpuria*.

Shellfish biotoxins : PSP, ASP, NSP and DSP

There are four major groups of shellfish toxins, namely, paralytic shellfish poisons, diarrhetic shellfish poisons, amnesic shellfish poisons and neurotoxic shellfish poisons, which can be found in bivalve molluscs and cause serious and, in some cases, long-term toxicity in humans. There is, however, a poor understanding of the dose-response relationship associated with this toxicity and the current regulatory levels are pragmatically derived on the basis of the limited information available on the dose levels which do not appear to cause toxic symptom in humans. The levels of shellfish toxins are generally low but rise dramatically when there is an algal bloom. There are currently food standards for PSP and ASP in Australia, but not in New Zealand. In New Zealand, shellfish toxins are controlled under fisheries regulations.

Data on the incidence of shellfish toxin poisonings both in Australia and New Zealand and worldwide indicates that the incidence of poisonings is increasing. In New Zealand, there is a coordinated shellfish biotoxin monitoring programme in place. In Australia, there is limited monitoring undertaken and limited national coordination.

The available data suggests there is a potential for significant health risk from shellfish contaminated with PSP, ASP, NSP or DSP and that the level of contamination should be kept as low as reasonably achievable. It is proposed that standards should be established for all four shellfish toxins, as shown below.

Substance	**Food**	**Maximum permitted concentration**
Amnesic shellfish poisons (domoic acid equivalents)	Bivalve molluscs	20 mg/kg
Diarrhetic shellfish poisons (okadaic acid equivalents)	Bivalve molluscs	0.2 mg/kg
Neurotoxic shellfish poisons	Bivalve molluscs	200 MU[1]/kg
Paralytic shellfish poisons (saxitonxin equivalent)	Bivalve molluscs	0.8 mg/kg

1. As defined in 'Recommended procedures for examination of seawater and shellfish' Irwin N. (ed.) 4th Ed. 1970. American Public Health Association Inc.

Inherent substances in foods: erucic acid, lupin alkaloids, methanol, pyrrolizidine alkaloids, fluoride

Erucic acid

Erucic acid is a 22-carbon mono-unsaturated fatty acid with a single double bond at the omega 9 position which constitutes about 30-60% of the total fatty acids of rapeseed oils and mustard seed oils. High exposure to erucic acid is associated with myocardial lipidosis and heart lesions in experimental animals. The new Canola varieties of rapeseed contain less than 2% of the total fatty acids as erucic acid. The dietary modelling indicates that high consumers of rapeseed oils may approach the PTWI for erucic acid if the level were to exceed 2% of total fatty acids. It proposed, therefore, to reduce the maximum permitted level of erucic acid in edible oils from the current level of 5% to 2% which is consistent with the draft Codex standard.

Lupin alkaloids

Lupins contain quinolizidine alkaloids which can cause neurotoxicity in animals. The level of alkaloids in lupins can be reduced by a debittering process, but more recently

plant breeding has produced a low alkaloid lupin ('sweet lupin') which can be consumed as the seed or used to produce lupin flour. Little is known about the metabolism or toxicity of lupin alkaloids but the limited data suggests that humans may be more sensitive to the toxic effects than animals and there are reports of lethality at relatively low levels of acute intake. There is little information on the level of dietary exposure to these alkaloids but using conservative assumptions regarding the use of lupin flour, the estimated dietary exposure is below the tentative safe exposure level.
It has not been possible, however, to estimate the level of intake of alkaloids from direct use of the seeds. A potential 'at-risk' group in relation to lupin alkaloid toxicity may be those who suffer from coeliac disease since lupin seeds do not contain gluten and may be an attractive replacement for wheat flour.

Given the uncertainty regarding the potential risk associated with exposure to lupin alkaloids, it is proposed that the current MPC of 200 mg/kg in seeds be retained and that further research on the toxicity and fate of these alkaloids be encouraged.

Methanol

Methanol is available from the consumption of fruit and vegetables or from fermented beverages. Methanol is a breakdown product from the enzymic degradation of naturally-occurring fruit pectins. In wines, the levels range from trace amounts to approx. 0.6 g/L. The toxicity associated with methanol consumption is as a result of metabolism to formaldehyde and formic acid. Humans are particularly sensitive to methanol toxicity which is expressed as metabolic acidosis, ocular toxicity and blindness, nervous system depression, coma and death. While there is no evidence to suggest the current levels of methanol in foods is a concern, there is justification to maintain the levels of methanol as low as reasonably achievable using current manufacturing techniques.

Consideration was given to simplifying the current standards and expressing the MPC in mass per volume of beverage, however, given the concentration of methanol varies in proportion to the concentration of ethanol, this could not be achieved without a considerable relaxation of the standard for some beverages. The MPCs shown below have been proposed.

Pyrrolizidine alkaloids

Pyrrolizidine alkaloids (PAs) are found in various species of plants which may contaminate various grain crops. They are also found in comfrey and herbal medicines which are deliberately ingested. There is extensive evidence of toxicity in humans from poisoning outbreaks involving PAs in various parts of the world. The major toxicological effect of chronic exposure to PAs in humans is hepatocellular injury, cirrhosis and veno-occlusive disease. There is no evidence of carcinogenicity in humans although this has been observed at high dose levels in rats. The major source of exposure to PAs is contaminated grains although there is little data on the levels of PAs in foods as consumed. Complete characterisation of the potential health risk from

exposure to PAs is not possible until further dietary exposure is available. No MPC for PAs is proposed at this time.

Fluoride

There are currently MPCs for fluoride (the ionic form of fluorine) in the New Zealand regulation but not in the Australian FSC. Chronic exposure to excess fluoride produces dental (enamel) fluorosis and skeletal fluorosis. Dental fluorosis is generally considered as a cosmetic effect rather than a functional disability.

The level of fluoride in food is generally controlled by the levels found or added to drinking water. This level is controlled by the current drinking water guidelines and is generally in the range of 0.7 to 1 mg/kg in drinking water. There is no evidence of public health and safety concerns at this level of intake and it is proposed that no MPCs for fluoride in food be established.

Substance	**Food**	**Maximum permitted concentration**
Erucic acid	Edible oils	20 g/kg
Lupin alkaloids	Lupin seeds	200 mg/kg
Methanol	Red wine, white wine and fortified wine Whisky, rum, gin and vodka Other spirits, fruit wine, vegetable wine and mead	3 g per litre of ethanol content 0.4 g per litre of ethanol content 8 g per litre of ethanol content

Environmental contaminants: polychlorinated biphenyls

Polychlorinated biphenyls (PCBs) contaminate the environment as a result of industrial processes involving chlorination. PCBs are very stable and enter the food chain because of their environmental persistence. In the body, they accumulate in the liver and adipose tissue. PCBs can produce a variety of toxic effects in mammalian species, including neurological effects and reproductive effects. Risk assessment of PCBs is complicated by poorly controlled toxicity studies available and by the paucity of dietary exposure data but there is enough concern to propose maintaining the current MPCs.

Substance	**Food**	**Maximum permitted concentration**

Polychlorinated biphenyls	Mammalian fat Poultry fat Milk and milk products Eggs Fish	0.2 mg/kg 0.2 mg/kg 0.2 mg/kg 0.2 mg/kg 0.5 mg/kg

ASSESSMENT AGAINST SECTION 10 OBJECTIVES

The protection of public health and safety

There is adequate information on the toxicity of each of the non-metals to indicate that the proposed maximum permitted concentrations (MPCs) would be adequate to protect public health and safety for both average and high level consumers. Detailed risk assessments have been performed in all cases and MPCs established where appropriate.

The provision of adequate information relating to food to enable consumers to make informed choices to prevent fraud and deception

There are no issues regarding this objective.

The promotion of fair trading in food

The standards will apply to all foods produced in or imported into New Zealand and Australia.

The promotion of trade and commerce in the food industry

The revised standards will promote trade and commerce in the food industry by having standards which are achievable and which provide consistency between New Zealand and Australia.

Promotion of consistency between domestic and international food standards where these are at variance

The proposed joint Australia New Zealand food standards will provide identical food standards in New Zealand and Australia. The proposed standard will also be consistent with Codex standards and, therefore, will promote trade internationally.

REGULATORY IMPACT ASSESSMENT

The Authority is required to prepare a Regulatory Impact Statement (RIS) when considering a variation to the *Food Standards Code* or when undertaking any legislative review such as the review of the *Food Standards Code*. The RIS must be agreed to by the Australia New Zealand Food Standards Council (ANZFSC). The aim of an RIS is to identify and assess any social, economic and/or environmental impacts arising from the regulatory options proposed. In New Zealand, compliance cost statements are required to be undertaken. These statements are similar in their objectives to the Australian RIS.

REGULATORY IMPACT STATEMENT

Identification of affected parties:

1. Governments in Australia and New Zealand

2. Primary industry and processed food manufacturers

3. Consumers in Australia and New Zealand

Options (including alternatives to regulation)

Option 1 - use MPCs in all cases
Retain MPCs for all non-metal contaminants where control of contamination is considered necessary.

Option 2 - use GELs in all cases
Delete all MPCs and rely on GELs to encourage good agricultural practice and good manufacturing practice and control contamination.

Option 3 - use a combination of MPCs and GELs
Retain MPCs in situations where there is an appreciable risk to public health and safety and establish GELs to encourage good agricultural practice and good manufacturing practice where there is low risk to public health and safety.

Analysis

Option 1 - use MPCs in all cases

	Advantages/Benefits	**Disadvantages/Costs**
Industry	• maximum legal limits clearly identified	• extensive monitoring in all cases would be necessary, and compliance costs high. • there may be unnecessary discarding of food in some cases. • imported food may be unable to met the std in some cases.
Consumers	• public health and safety is ensured.	• there may be unnecessary concerns regarding some contaminants. • may result in reduced availability of some foods at certain times.

Government	• maximum legal limits clearly identified.	• enforcement costs will be higher. • in some cases, the MPCs cannot be supported on public health and safety grounds. • may evoke a WTO challenge.

Option 2 - use GELs in all cases

	Advantages/Benefits	**Disadvantages/Costs**
Industry	• occasional contamination over the GELs may be tolerated. • level of monitoring may be less and thus costs.	• food over the GEL may cause public health and safety risk in some cases.
Consumers	• None	• No distinction between substances with low and high public health and safety risks. • food over the GEL may cause public health and safety risk in some cases.
Government	• GELS are suitable when the public health and safety risk is low. • will not evoke a WTO challenge.	• No distinction between substances with low and high public health and safety risks. • No legal limits in cases where public health and safety is at risk. • GELs may be treated as pseudo standards.

Option 3 - use a combination of MPCs and GELs

	Advantages/Benefits	**Disadvantages/Costs**
Industry	• clear distinction between substances with low and high public health and safety risks. • level of monitoring can reflect the level of risk.	None

Consumers	• public health and safety will be appropriately protected for substances with low and high risk.	None
Government	• maximum limits for substances with high risk will be identified and for low risk substances will be kept as low as reasonable achievable. • meets international obligations.	• GELS may be used as pseudo standards in some cases.

Assessment of impact of proposed regulation

Option 1 proposes to retain MPCs for all non-metal contaminants in food in all cases. This would be inconsistent with the principles agreed by ANZFSC for establishing MPCs since some of the MPCs would not serve an effective risk management function and would be established on primary commodities which did not provide a significant contribution to the total dietary contaminant intake. It would also be a greater economic burden for industry and enforcement agencies, by requiring extensive surveillance of all contaminants.

Option 2 proposes removal of all MPC and reliance on GELs for all contaminants. This would not provide an effective control for those substances which could be a high risk to public health and safety. This option would therefore be inconsistent with protection of public health and safety.

Option 3 is the preferred option since it provides an adequate level of protection of public health and safety while not requiring an unnecessary level of surveillance to be performed by industry or enforcement agencies.

OTHER RELEVANT MATTERS

Review of Standard A12

The current review of Standard A12 is divided into three parts, namely:

(i) metals (Proposal P157).

(ii) non-metals (Proposal P158) .

(iii) prohibited and restricted botanicals arising from the use of flavourings (Proposal P(unspecified at this time)).

It is anticipated that the botanicals will become a separate standard, namely, Standard 1.4.4 - Prohibited and Restricted Botanicals, while the metal and non-metals will form a new standard, namely, Standard 1.4.1 - Contaminants.

Review of methods of analysis

Currently, there are methods of analysis for paralytic shellfish poisons (PSP) and domoic acid in Standard D1 - Fish. It is proposed that these methods of analysis will be reviewed as part of a separate proposal specifically dealing with methods of analysis. These methods, therefore, are not discussed further in this report. For NSP, the unit of measure is the MU which is defined in APHA publication 'Recommended procedures for examination of seawater and shellfish'. While this method may ultimately be included in a separate standard in the joint FSC, it is included in the standard at this stage for consistency and for public comment.

CONCLUSIONS

The review of the maximum permitted concentrations of non-metals in food has been conducted according to the principles and procedures previously agreed by the ANZFA Board and endorsed by ANZFSC.

For each of the substances reviewed, the scientific evaluation has resulted in a characterisation of the risk associated with exposure to these substances through the consumption of food. Risk management options have been proposed for each substance which are consistent with the section 10 objectives of the *Australia New Zealand Food* Authority Act 1991 to which the Authority must have regard when establishing or varying standards.

New standards have been proposed for aflatoxin in tree nuts, diarrhetic shellfish poisons in bivalve molluscs, ergot in cereal grains, erucic acid in edible oils, lupin alkaloids in lupins seeds, methanol in alcoholic beverages and neurotoxic shellfish poisons in bivalve molluscs. Standards are unchanged for acrylonitrile monomer in all foods, amnesic shellfish poisons and paralytic shellfish poisons in bivalve molluscs, phomopsins in lupin seeds, polychlorinated biphenyls in various foods and vinyl chloride and vinylidene in all foods. Standards have not been proposed at this time for fluoride, fusarium toxins, ochratoxins and pyrrolizidine alkaloids.

The regulatory impact assessment has established that a combination of MPCs and GELs is the preferred regulatory option since it provides an adequate level of protection of public health and safety while not requiring an unnecessary level of surveillance to be performed by industry or enforcement agencies.

Because of the current paucity of surveillance data available on most of the non-metal contaminants in food, no GELS have been proposed at this time.

ATTACHMENTS

1. Draft variation to the Australian *Food Standards Code* and proposed new Joint Australia New Zealand Food Standard

2. Summaries of the toxicological evaluations and risk assessments on non-metal contaminants. The full reports are available on request to ANZFA.

    Acrylonitrile monomer
    Aflatoxin
    Ergot
    Erucic acid
    Fluoride
    Fusarium toxins (summary only)
    Lupin alkaloids
    Methanol
    Ochratoxins (summary only)
    Phomopsins
    Polychlorinated biphenyls
    Pyrrolizidine alkaloids
    Shellfish biotoxins
        - Paralytic shellfish poisons (PSP)
        - Diarrhetic shellfish poisons (DSP)
        - Amnesic shellfish poisons (ASP)
        - Neurotoxic shellfish poisons (NSP)
    Vinyl chloride monomer
    Vinylidene chloride monomer

3. Public Comment Received

DRAFT VARIATION TO THE AUSTRALIAN FOOD STANDARDS CODE

Standard 1.4.1

Contaminants

Purpose

This Standard sets out the maximum permitted concentrations (MPCs) of specified contaminants in nominated food groups.

Contents

1 Interpretation
2 Maximum permitted concentrations of metals
3 Maximum permitted concentrations of non-metals
4 Maximum permitted concentrations of non-metals arising from the use of flavourings
5 Sampling plan for mercury in fish and fish products

Clauses

1 Interpretation

In this Standard, unless the contrary intention appears:-

(1) **metal** means a contaminant listed in bold type in column 1 of Table 1 of this Standard, and includes compounds of a metal;

non-metal means a contaminant listed in bold type in column 1 of the Table to clause 3, or Table 3 in this Standard;

maximum permitted concentration means the maximum level of a metal or a non metal which is permitted to be present in a food, expressed in milligrams of the metal or a compound of the metal or non metal per kilogram of the food (mg/kg);

(2) Where food contains a metal and any other chemical species of that metal, all chemical species of that metal shall be expressed as the metal;

(3) The maximum permitted concentration shall be determined for the edible content of the food that is ordinarily consumed;

(4) The concentration for a food which is dried, dehydrated or concentrated is to be calculated on the basis of the mass of the food, or the mass of the ingredients of the food, prior to drying, dehydration or concentration determined from one or more of the following:

(a) the manufacturer's analysis of the food;
(b) calculation from actual or average quantity in water in the ingredients used;
(c) generally accepted data.

2 Maximum permitted concentration of metals

P157 to finalise

3 Maximum permitted concentrations of non metals

(1) In this clause:

food means the food or class of foods listed in unbolded type in column 1 of the Table to clause 3 in this Standard;

MU means the unit of measure described in 'Recommended procedures for examination of seawater and shellfish" Irwin N. (ed.) 4th Ed. 1970, American Public Health Association Inc.

ergot means the sclerotium or dormant winter form of the fungus, *Claviceps purpuria.*

(2) The maximum permitted concentration (MPC) for a non metal in food is listed in column 2 of the Table to this clause, expressed in mg/kg, unless otherwise specified.

Table to clause 3

Column 1	Column 2
Acrylonitrile	
All food	0.02
Aflatoxin	
Peanuts and peanut products	0.015
Tree nuts (as specified in Schedule 3 to Standard A14) and tree nut products	0.015
Amnesic shellfish poisons (Domoic acid equivalent)	
Bivalve molluscs	20
Diarrhetic shellfish poisons (Okadaic acid equivalent)	
Bivalve molluscs	0.2
Ergot	
Cereal grains	500
Lupin alkaloids	
Lupin seeds	200
Methanol	
Red wine, white wine and fortified wine	3 g per litre of ethanol content
Whisky, Rum, Gin and Vodka	0.4 g per litre of ethanol content
Other spirits, fruit wine, vegetable wine and mead	8 g per litre of ethanol content
Neurotoxic shellfish poisons	
Bivalve molluscs	200 MU/kg
Paralytic shellfish poisons (Saxitoxin equivalent)	
Bivalve molluscs	0.8
Phomopsins	
Lupin seeds	0.005
Polychlorinated biphenyls	
Mammalian fat	0.2
Poultry fat	0.2
Milk and milk products	0.2
Eggs	0.2
Fish	0.5
Vinyl chloride	
All food	0.01

Vinylidene chloride All food	0.01

4 Maximum permitted concentration of non-metals arising from the use of flavourings

P195 to finalise

5 Sampling plan for mercury in fish and fish products

P157 to finalise

CONSEQUENTIAL AMENDMENTS TO THE AUSTRALIA NEW ZEALAND FOOD STANDARDS CODE

The Australia New Zealand Food Standards Code is varied by deleting from Standard 2.4.1-

Prescribed name

2. Edible oils is not a prescribed name.

Composition

3. (1) Edible oils may contain incidental amounts of free fatty acids, unsaponifiable constituents and other lipids.

Editorial Note: 'Other lipids' include natural gums, natural waxes and phosphatides.

(2) Edible oils must not contain more than 50 g/kg of erucic acid.

Process declaration

4. Where the specific name of an oil is used in a food label, the food label must include a statement that describes the nature of any process which has been used to alter the fatty acid composition of the edible oil.

Editorial Note: For example, hydrogenation is a process used to alter the fatty acid composition of fatty acids in an edible oil.

substituting-

2 Composition

(1) Edible oils may contain incidental amounts of free fatty acids, unsaponifiable constituents and other lipids.

Editorial Note: 'Other lipids' include natural gums, natural waxes and phosphatides.

(2) Edible oils must not contain more than 20 g/kg of erucic acid.

3 Process declaration

Where the specific name of an oil is used in a food label, the food label must include a statement that describes the nature of any process which has been used to alter the fatty acid composition of the edible oil.

Editorial Note: For example, hydrogenation is a process used to alter the fatty acid composition of fatty acids in an edible oil.

SUMMARY OF INDIVIDUAL TOXICOLOGICAL AND RISK ASSESSMENT REPORTS

The following summary reports are provided:

Substance	Page
Acrylonitrile monomer	**2**
Aflatoxins	**6**
Ergot	**10**
Erucic acid	**14**
Fluoride	**18**
Fusarium toxins	**21**
Lupin alkaloids	**22**
Methanol	**26**
Ochratoxins	**31**
Phomopsin	**32**
Polychlorinated biphenyls	**37**
Pyrrolizidine alkaloids	**42**
Shellfish toxins	**45**
Vinyl chloride monomer	**50**
Vinylidene chloride monomer	**53**

ACRYLONITRILE MONOMER

SUMMARY OF THE TOXICOLOGICAL REVIEW AND RISK ASSESSMENT

Introduction

Acrylonitrile is a colourless, liquid, man-made chemical used to make plastics, acrylic fibres, and synthetic rubber. The most important routes of exposure are inhalation and dermal, for both production and processing to polymers and other products. While acrylonitrile is a liquid, the use of high temperatures during various stages of synthesis/reaction and the high volatility of acrylonitrile indicates that the major exposure route of concern to occupationally exposed workers is inhalation. Acrylonitrile is released during industrial production and processing to air and waste water.

The major potential source for indirect or consumer exposure is via the use of materials, textiles, furnishings etc. which may contain a very small percentage of unreacted acrylonitrile monomer, or via food which is packaged in containers made from acrylonitrile plastics eg, margarine containers, vegetable oil bottles, fruit juice containers etc.

The occupational exposure limit for acrylonitrile in a number of EU countries and also in Australia and the US is 4.5 mg/m^3 or 2 ppm. A specific acrylonitrile limit of 0.02 mg/kg has been laid down in the Commission Directive 90/128/EEC, relating to plastics materials and articles intended to come into contact with foodstuffs. It should be noted that this was based on the limit of detection and applies to food content not to the residual monomer in plastic.

The Australian Food Standards Code currently states that: 'the proportion of acrylonitrile in any food shall not be greater than 0.02 mg/kg'. This level was established in 1980 and was set on the limit of detection for acrylonitrile in food.

The New Zealand Regulations (1984) control contamination from packaging materials under Regulation 265-Use of harmful containers prohibited. The regulation states: 'No person shall use, or permit to be used, in the preparation, packing, storage or delivery of a food for sale, any package, appliance, or container that yields or could yield to its contents any poisonous, injurious, or tainting substance'.

No specific Codex standards have been established for food in contact with packaging substances.

In the US, plastics are considered under Part 109-Unavoidable contaminants in food for human consumption and food-packaging material. The legislation states: 'The manufacturer of food must at all times utilise quality control procedures which will reduce contamination to the lowest level currently feasible'.

Toxicological data

In animals, orally administered acrylonitrile is rapidly absorbed and distributed fairly uniformly throughout the body with highest concentrations occurring in blood, liver, kidney, lung, adrenal cortex and stomach. Metabolism results in at least 10 different metabolites of acrylonitrile with mercapturic acids being major metabolites of acrylonitrile *in vivo*. Excretion of the metabolic products is mainly via the urine either as thiocyanate or as products of conjugation. There is no evidence of accumulation of acrylonitrile or its metabolites in tissues over the long term.

Acute exposures at high concentrations produce clinical signs in animals of excitation, watery eyes, agitation, salivation, lachrymation, urination and defecation which is characteristic of cyanide-type toxicity. This is followed by a convulsive phase in which the animal undergoes clonic seizures. The acute LD50 has been estimated to be 93 mg/kg bw in rats and 27 mg/kg bw in mice.

Repeat dose oral studies in animals results in an irritational effect on the gastrointestinal tract (inflammation of the oesophagus and stomach).

Long-term administration (2 years) of acrylonitrile to rats by the oral route (in the drinking water from 8.5 to 25 mg/kg bw/day) has resulted in statistically significant increases of tumour incidences at multiple sites, including: astrocytomas of the brain, squamous cell carcinomas of the Zymbal gland and carcinomas and papillomas of the non-glandular stomach.

In humans, specific case reports indicate that chronic exposure to acrylonitrile is associated with neuropathological effects following inhalational exposure. Effects reported include nausea, vomiting, diarrhoea, gastritis, general weakness, chest pain, headaches, irritability and irritation of the mucosa of the respiratory tract. These clinical symptoms mimic those described in experimental animals and are reported to be due to metabolism of the parent compound to cyanide.

Although acrylonitrile has produced positive results in a number of *in vitro* mutagenicity tests, it has not been found to be genotoxic *in vivo*. Acrylonitrile produced no significant increase in chromosomal aberrations in bone marrow cells from rats up to 21 mg/kg bw/day, and no significant effect in a dominant lethal assay in rats at doses up to 60 mg/kg bw/day. Studies on unscheduled DNA synthesis in liver and brain of rats exposed to doses of 50 mg/kg showed increased DNA synthesis in the liver but not in the brain, suggesting limited potential for acrylonitrile to be genotoxic. However, this has recently been questioned in a current review of the genotoxicity potential.

Acrylonitrile has teratogenic effects when administered in the drinking water by gavage to rats but only at maternal toxicity levels (65 mg/kg bw). Overall, it can be concluded that existing animal data do not show any clear indication of fertility,

reproductive or teratogenic effects of acrylonitrile at doses below those producing maternal toxicity.

The available evidence human epidemiological studies, and, in particular, recent completed studies suggest that there is little evidence to support a causal relationship between acrylonitrile exposure and cancer in humans. Additionally, the IARC has recently revised there categorisation of acrylonitrile as a carcinogen from category 2A to category 2B on the basis of the recent epidemiological data.

Whilst there appears to be an extensive data base on the effects of acute or chronic exposure to acrylonitrile via the inhalational route (in animals and humans), limited studies are available via the oral route. Particularly relevant to this is that previous epidemiological studies have suggested a link between acrylonitrile exposure and lung cancer and additionally prostate cancer. However, many of these studies have limitations including insufficient quantification of exposure, short follow-up, small study population, and inadequate evaluation of confounding associations (USDHHS, 1990). Furthermore, there is no data to compare the pharmacokinetics between animals and humans and although epidemiology studies have indicated that the lung may the target organ in humans, no lung tumours have been demonstrated in animal studies (Page, 1990).

In conclusion, animal studies have not established NOELs and as such an ADI could not be set. Although there is negligible risk to the consumer of acrylonitrile ingestion via migration from plastics to foods, the fact that acrylonitrile is a carcinogen via oral and inhalational routes in animals suggests there is still a need to limit overall exposure to a level which is a low as reasonably achievable.

Dietary exposure assessment

Foods may become contaminated with acrylonitrile as a result of the migration of the monomer from chemical containers of acrylonitrile polymers. Acrylonitrile has also been found to desorb from polyacrylonitrile resins and partition into cooking oil. Other foods which may be contaminated by acrylonitrile from their containers include luncheon meat, peanut butter, margarine, fruit juice and vegetable oil.

From the available limited US data, levels in foods have ranged from not detectable (<2.5 ppb) to 35 ppb. Whilst data suggests there is a potential for migration to foods, the current manufacturing practices employed ensure that limited (if any) migration of the monomer occurs from current packaging materials. There is no available Australian or New Zealand data on the levels of acrylonitrile in food.

Risk characterisation

Acrylonitrile is classified as carcinogenic on the basis of a number of chronic/carcinogenicity studies in animals following oral administration or via inhalation (these later studies not reviewed). The common target organs identified were the central nervous system (brain and spinal cord), gastro-intestinal tract (tongue,

non-glandular stomach and small intestine), Zymbal gland and mammary gland. A dose-relationship was noted between the incidences of astrocytomas and dose level of acrylonitrile. A NOEL could not be established.

Genotoxicity studies suggest that the DNA active compound is the metabolite epoxide cyanoethylene oxide (CEO). CEO is mutagenic *in vitro*, but acrylonitrile is negative in *in vivo* genotoxicity tests. It is postulated that the lack of *in vivo* mutagenicity may be due to inactivation of CEO via glutathione conjugation resulting in failure of acrylonitrile to reach the target tissues.

Epidemiological studies in occupationally exposed individuals has not demonstrated conclusively a correlation between exposure to acrylonitrile and cancer in humans.

Acrylonitrile is a common industrial chemical. Exposure of humans can occur around factories where it is made or used, near chemical waste sites (via improper storage or disposal) or as a consequence of use of products manufactured from acrylonitrile such as plastics used in food. The two most likely exposure pathways are via the air or contaminated drinking water. Minor exposure can occur from materials, textiles, furnishings etc. which may contain a very small percentage of unreacted acrylonitrile monomer, or via food which is packaged in containers made from acrylonitrile plastics eg, margarine containers, vegetable oil bottles, or fruit juice containers.

The overall conclusion is that while there is no evidence of adverse health effects resulting from the low level exposure to acrylonitrile via food, the potential carcinogenic effects indicate that exposure to this substance should be kept as low as possible.

Risk management

It is proposed to retain the current level of 0.02 mg/kg (ie, at the limit of detection) for acrylonitrile in food (see below). This would be consistent with the JECFA (1984) recommendations that human exposure to acrylonitrile in food as a result of its migration from food-contact materials should be reduced to the lowest levels technologically attainable. It is also consistent with the current EC limit of 0.02 mg/kg.

Substance	**Food**	**Proposed MPC (mg/kg)**
Acrylonitrile	All food	0.02

AFLATOXINS

SUMMARY OF THE TOXICOLOGICAL REVIEW AND RISK ASSESSMENT

Introduction

Aflatoxins are a family of mycotoxins produced mainly by two closely related fungus species, *Aspergillus flavus* and *Aspergillus parasiticus*. The suite of toxins produced is specific for each species. *A. flavus* can produce aflatoxins B1, B2 and cyclopiazonic acid (CPA), but only about 40% of isolates are toxigenic. *A. parasiticus* produces aflatoxins B1, B2, G1 and G2 but not cyclopiazonic acid, and almost all known isolates are toxigenic. The importance of *A. flavus* and *A. parasiticus* lies not only in their toxigenicity, but also in the fact that they are extremely common in stored commodities including grains, oilseeds, nuts and spices. They appear to have a close affinity with particular crop plants, especially cottonseed, maize and peanuts, which permits early entry to developing seeds or nuts. This affinity partially explains the high incidence of aflatoxins in these commodities. In addition, aflatoxin production by these species appears to be favoured by the presence of oil, so that other nuts, including pistachios, walnuts and Brazil nuts, and all types of oilseeds, sometimes contain high aflatoxin concentrations.

Aflatoxins are difuranocoumarin derivatives. Aflatoxins B1, B2, G1 and G2 are produced in nature by the moulds described above. The letters B and G refer to the fluorescent colours (blue and green, respectively) observed under long wave ultraviolet light, and the subscripts 1 and 2 to their separation patterns on thin layer chromatography plates. Aflatoxins M1 and M2 are produced from their respective B aflatoxins by hydroxylation in lactating animals, and are excreted in milk at a rate of approximately 1.5% of ingested B aflatoxins.

The Australian *Food Standards Code* states that "The proportion of aflatoxins in food shall not be greater than -

(a) in peanut butter or peanut paste, nuts and the nut portion of products containing nuts, 15 ug/kg;
(b) in all other foods, 5 ug/kg.

The New Zealand *Food Regulations 1984* states that "The proportion of aflatoxins in food shall not exceed the following:

(a) In peanut butter, shelled nuts, and the nut portion of products containing nuts, 0.015 mg/kg;
(b) In all other food, 0.005 mg/kg.

The draft Codex Standard (at Step 8) is 15 µg/kg for peanuts and 0.05 µg/kg for milk.

Toxicological data

Aflatoxins are potent mutagenic and carcinogenic substances and this aspect of their toxicity is the focus of this report. Extensive experimental evidence has shown that aflatoxins are capable of inducing liver cancer in most species studied. However,

assessment of the risk of liver cancer in humans has proved to be difficult because of the confounding factors influencing tumour formation.

A 1997 report by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) has considered in detail the data on the carcinogenicity of aflatoxins in animals and humans, together with an analysis of the confounding factors which influence tumour incidence and potency estimates in humans. Some of the points made in this report are provided below.

The liver is the primary target organ in most species, but tumours of other organs have also been observed in animals treated with aflatoxin. The effective dose of aflatoxin B1 for induction of liver tumours varied over a wide range in different animals species when the carcinogen was administered by continuous feeding, generally for the lifetime of the animal. Effective doses were 10-30 μg/kg in the diet in fish and birds. Rats responded according to strain at levels of 15-1,000 μg/kg , while some strains of mice showed no response at doses up to 150,000 μg/kg. Tree shrews responded to 2,000 μg/kg. In subhuman primate species, aflatoxin B1 potency in induction of liver tumours differed widely, squirrel monkeys developing liver tumours when fed aflatoxin B1 at 2,000 μg/kg for 13 months, and three other monkey species developing a low (7-20%) incidence of liver tumours when fed average doses of 99-1,225 mg/animal over 28-179 months.

Some epidemiological evidence indicates the possibility that humans are at substantially lower risk from aflatoxins than other species. While some studies suggest that intake of aflatoxin poses a detectable risk in the absence of other factors, other studies suggest that it poses risks only in the presence of confounding factors such as hepatitis B infection.

In relation to the potency of aflatoxins, aflatoxin B1 is the most potent and most of the toxicological data available relates to it. Aflatoxin M1, the hydroxylated metabolite of B1 has a potency approximately one tenth that of B1. The potency of aflatoxins in hepatitis B positive individuals is substantially higher than the potency in hepatitis B negative individuals. Vaccination against hepatitis B will reduce the prevalence of carriers which would likely reduce the potency of the aflatoxins in vaccinated populations and consequently reduce liver cancer risks.

Dietary intake assessment

Information on aflatoxins in the Australian diet comes from three major sources:

(i) a data bank from the Australian Government Analytical Laboratories (AGAL) containing 16000 entries from all AGAL laboratories during the period 1992 to 1997;

(ii) a data bank from AGAL in New South Wales for 1997 and part of 1998; and

(iii) data derived from information gathered for inclusion in the 'Australian Mycotoxin Data Centre Newsletter' (AMDC) since 1983 and published by Food Science Australia.

In New Zealand, a limited survey of foods was conducted in 1991.

Foods categories in which aflatoxin contamination was recorded rather frequently include peanuts and peanut products; and satay sauces; pistachios; and some other miscellaneous foods. However, the wide variability in the levels of aflatoxin do not permit a mean level of exposure for the population to be determined.

Foods where either no aflatoxins have been found, or where levels found are sufficiently low to constitute a negligible risk from aflatoxin contamination include almonds and other tree nuts including cashews, hazelnuts, walnuts, pecans and macadamias; cereals and cereal products including bread and baked goods; confectionery, where that does not include a peanut component; dairy goods, including fresh and dried milk and cheese; fresh and dried fruit including sultanas and dates; coffee and tea.

Risk characterisation

Aflatoxins are considered potent mutagens and carcinogens, although there is now some evidence to suggest that their carcinogenic potency in humans may be influenced considerably by concurrent infection with hepatitis B virus. Nevertheless, in weighing up the scientific evidence, which includes epidemiological data, laboratory animal studies and *in vivo* and *in vitro* metabolism studies, JECFA concluded that aflatoxins should be treated as carcinogenic food contaminants, the intake of which should be reduced to levels as low as reasonably achievable. However, JECFA did not believe that there was a firm foundation for setting absolute limits for aflatoxin intake by humans at this time.

Analysis of Australian and New Zealand commodities have indicated that problems associated with aflatoxin are almost entirely confined to peanuts. Other products where there has been some contamination include maize, milk and pistachios.

Risk management

Aflatoxin formation in peanuts is the result of a number of factors such as the presence of *Aspergillis* fungi in the soil, drought stress prior to harvest, inadequate drying rates after harvest, and inadequate storage. Farm management practices which can reduce aflatoxin formation include irrigation, crop rotation, rapid harvesting and mechanical drying, and precleaning to remove extraneous material. Following storage and shelling, the most critical process in aflatoxin reduction is colour sorting which removes discoloured peanuts which includes those infected with *Aspergillis* fungi. All of the above techniques for risk reduction are used in the production of Australian-grown peanuts, however, residual levels of aflatoxin are found in domestic peanuts.

Given the public health and safety concerns associated with exposure to aflatoxin, maintaining a level of human exposure which is as low as reasonably achievable is appropriate. The extensive data now available on aflatoxin levels in foods indicates that peanuts are the major source of aflatoxin in the diet.

It is proposed that the MPC of 15 µg/kg by maintained for peanuts and tree nuts and for products which are derived from peanuts and tree nuts in order to maintain low levels of aflatoxin in both domestic and imported products. It is also proposed that the MPC for 'other foods' be removed as it is unnecessary and inconsistent with the draft Codex Standard. The proposed drafting for the joint ANZ Food Standards Code is:

Substance	**Food**	**Proposed MPC (mg/kg)**
Aflatoxin	Peanuts and peanut products Tree nuts (as specified in Schedule 3 to Standard A14) and tree nut products	0.015 0.015

ERGOT

SUMMARY OF THE TOXICOLOGICAL REVIEW AND RISK ASSESSMENT

Introduction

Ergot is the sclerotium (the dormant winter form) of the fungus *Claviceps* that contaminates many cereals, predominantly rye, wheat and triticale. It is particularly predominant in the northern hemisphere countries such as Canada where the cool, damp weather is ideal for ergot germination. Ergot is recognised by the hard purple bodies that replace the grains of the affected head.

Contained in the sclerotia are biologically active alkaloids which have previously been proven to be extremely toxic to humans and livestock when ingested in sufficient amounts. Depending on the organism involved, *Claviceps purpurea or Claviceps fusiformis,* clinical manifestations are different.

Chemical properties

Chemically, the alkaloids are derivatives of lysergic and isolysergic acid and clavine compounds, and many individual alkaloids have been identified.

The Association of Official Agricultural Chemists does not list an analytical method for ergot alkaloid determination in grain, although a number of methods have been reported such as thin layer chromatography, high performance chromatography, colorimetric and immunoassay techniques.

The levels of ergot contamination in cereal grain has generally been expressed as a percentage of sclerotia on a weight-for-weight basis, with relatively few studies identifying individual alkaloids. When alkaloids are referred to, it is usually the total alkaloid content.

Processing of cereal grain contaminated with ergot has been found to reduce the ergot concentration considerably, although no precise data is available on the level of reduction achievable.

Current Regulations

The Australian *Food Standards Code* currently states that "Ergot shall not be detectable in a 2.25 litre sample of cereal grain". There is no reference to ergot in the NZ regulations.

In the USA, the Code of Federal Regulations does not contain any reference to ergot. The US Department of Agriculture states that wheat and rye containing more than 0.3% ergot and triticale containing 0.10% ergot be designated 'ergoty'.

In Canada, the Canadian Grain Commission has a tolerance level for rye of 0.05% for No. 1 grade, 0.20% for No. 2 grade and 0.33% for No. 3 grade.

The EU specifies ergot among miscellaneous impurities in wheat, durum wheat and rye, and sets an ergot content of 0.05% as a minimum quality standard for these cereal grains.

There is no Codex standard for ergot in rye grain or flour. The Codex Draft Standard for wheat and durum wheat specifically refers to a maximum level of ergot of 0.05%.

Application A303

The Australia New Zealand Food Authority received an application (A303) on 28 February 1996 from The Bread Research Institute of Australia to amend Standard A12 clause (5) of the Australian Food Standards Code to provide an appropriate and realistic tolerance level for ergot in cereal products. The applicant requested that ANZFA should give consideration to deletion of the requirement for an MPC for ergot, or alternatively, establish an appropriate limit based on protection of public health and safety. ANZFA made a recommendation to ANZFSC in March 1997 that a maximum permitted level be established at 0.05% (w/w) ergot in grain. ANZFSC is still considering this recommendation.

Toxicological data

In toxicity studies on domestic animals, cattle appear to be more sensitive than sheep, pigs, primates or poultry. Signs of acute toxicity in animals are restlessness, mydriasis, excess salivation, vomiting, piloerection, muscular weakness, tachypnoea, dyspnoea, tail gangrene and, at high doses, convulsions. Chronic toxicity studies revealed that ischaemia in the limbs is characteristic and cattle exhibit signs of lameness and gangrene as a result of the peripheral vasoconstrictive activity. No evidence of genotoxicity has been reported in the limited *in vitro* studies available.

Historically, ergot poisoning in humans has been associated with consumption of bread prepared from flour containing >1% (w/w) ergot, with fatal cases reported at 7% (w/w) ergot in bread. Clinical signs of toxicity in humans are gangrene, feeble peripheral pulse, swelling and weakness of the limbs, diarrhoea and vomiting. From the available literature on therapeutic uses of ergot alkaloids, there is evidence of considerable variability in the toxicity of individual alkaloids. There are also human case reports of effects on the heart (myocardial ischaemia), on the vascular effects (numbness, absent peripheral pulses), on the nervous system (muscle twitching, spasms, paralysis, convulsions), on the endocrine system (decreased prolactin levels), and on the reproductive system (effects on implantation, foetal development, and lactation).

According to the published literature, the lowest level of contamination of grain which resulted in health effects was seen in Ethiopia in 1978 where grain reported to contain 0.75% (w/w) ergot was consumed. In another incident in India in 1956/7, in samples taken from households where poisoning occurred, the grain (millet) contained between 1.5 - 17.4% (w/w) ergot. In this case, the total alkaloid levels in the whole grain which caused poisoning ranged between 15 and 199 mg/kg. The concentration

of alkaloids in whole grain which did not cause poisoning ranged from 0.2 to 26 mg/kg. The overlap in these dose ranges may be related to the different levels of washing in individual households. When the level of alkaloids in the grain was related to the dietary intake, the quantity of alkaloids which could be ingested without toxic effects was estimated to be about 28 μg/kg bw/day.

Dietary exposure assessment

Levels in food

Traditionally, ergot contamination has been expressed as a percentage of sclerotia on a weight-for-weight basis rather than as amounts of individual alkaloids. In the early 1980s, surveys in North America revealed that the average total alkaloid content in contaminated cereal was 0.24% (w/w). A study of total ergot alkaloids from rye and wheat in South-East Asia found the total alkaloid content in the sclerotia of rye was 700 mg/kg and in wheat was 920 mg/kg . A survey of cereals and cereal products in Switzerland using a HPLC procedure found average total alkaloid concentrations were as follows: wheat flour, 4.2 ug/kg; very course wheat flour, 103.4 ug/kg; and rye flour, 139.7 ug/kg. The estimated daily intake of total alkaloids in Switzerland was reported to be 5.1 ug/person (0.08 μg/kg bw/day).

Canadian data published in 1992 on levels of alkaloids in grain sold over a 3-6 year period found the following alkaloids: ergometrine, ergosine, ergotamine, ergocornine, alpha-ergocryptine, and ergocristine. The predominant alkaloids were ergocristine and ergotamine. The level of total alkaloids found in the various commodities was as follows: rye flour, 70-414 μg/kg; rye bread/crispbread, 4.8-100 μg/kg; bran/bran cereal, 12-69 μg/kg; triticale, 46-283 μg/kg; and wheat flour, 15-68 μg/kg.

The National Food Agency of Denmark in 1995 analysed for ergot alkaloids in wheat, rye, oatmeal, barley and mixed bran. Barley and oats contained low levels of alkaloids (up to 0.9 μg/kg maximum content), whereas the range in wheat and rye was from 14-33 μg/kg which gave an estimated intake of 5.7 μg/person/day.

Estimated dietary intake

From the data available from the 1995 National Nutrition Survey, the population group with the highest level of intake wheat flour is males aged 12-15 years, with a 95th percentile intake of 340 g per day. If it is assumed that the approximate conversion factor for wheat flour to whole wheat is 1.20, then a high level of consumption of whole wheat for this group is 408 g per day, which is equivalent to 7.2 g/kg bw/day (average weight 57 kg). At the proposed maximum level of 0.05% (w/w) ergot in grain, the maximum amount of sclerotia consumed would be 204 mg. While it is known that the level of total alkaloids in the sclerotia is highly variable, the level of alkaloids in the sclerotia of wheat has been reported to be approximately 0.1%, therefore, the maximum total intake of alkaloids consumed would be 0.20 mg/day (approximately 3 μg/kg bw/day).

From the surveys considered above, the actual mean levels of intake in countries where ergot-contaminated grain is more common is much lower than this theoretical maximum level.

Risk characterisation

The toxicity associated with high levels of ergot exposure is of a serious nature but appears to be well controlled by modern agricultural practices. There have been no ergot-related poisoning outbreaks in the last 20 years. From the data obtained from the Ethiopian and Indian outbreaks, the level of intake of ergot alkaloids considered to be without adverse effects is 28 μg/kg bw/day. The estimated maximum intake from grains contaminated at 0.05% is 3 μg/kg bw/day which is well within safe limits of exposure.

Furthermore, published data indicates that food processing generally reduces the levels of ergot alkaloids in foods. Treatment of sclerotia with 1% chlorine and 200^{O}C resulted in a 90% reduction in alkaloid levels. Autoclaving sclerotia resulted in a 25% reduction in alkaloid levels. Baking bread with ergot-infected grains resulted in a 60-100% reduction in alkaloid levels in whole wheat bread, a 50-86% reduction in all-rye bread, and a 25-74% reduction in triticale pancakes.

Risk management

Based on the available information considered in application A303, the Authority recommended that a maximum level of 0.5 g/kg (0.05%w/w) ergot in grain (post cleaning but prior to milling) would be a practical and achievable level for contamination in cereal grains. The Canadian Grain Commission and the US Department of Agriculture impose a 0.3% (w/w) maximum ergot limit on grain for export. However, this level is applicable to the lowest grade of grain (No.3). The level of 0.05% refers to the highest grade (Grade 1), ie, grain of the best quality. These limits serve to ensure the quality, and reliability of the grain and are primarily quality standards. Therefore, the Australian/New Zealand standard would be based on an acceptable internationally recognised standard for ergot contaminated cereal grain of the highest quality (Grade 1).

It is proposed that a maximum level of 0.05% (w/w) ergot in cereal grain be incorporated into the joint ANZ Food Standards Code as shown below. This is consistent with the outcome of Application A303 which is currently with ANZFSC. In order to further clarify this standard, it is proposed that a definition of 'ergot' be included, as shown.

Substance	Food	Proposed MPC (mg/kg)
Ergot[1]	Cereal grain	500

1. Ergot refers to the sclerotium or dormant winter form of the fungus, *Claviceps purpuria*.

ERUCIC ACID

SUMMARY OF THE TOXICOLOGICAL REVIEW AND RISK ASSESSMENT

Introduction

Erucic acid is a 22–carbon monounsaturated fatty acid with a single double bond at the omega 9 position. Erucic acid constitutes about 30–60% of the total fatty acids of rapeseed, mustard seed and wallflower seed and up to 80% of the total fatty acids of nasturtium seeds. Erucic acid has also been found in some marine animal oils.

In response to potential safety concerns associated with high dietary exposure to erucic acid (myocardial lipidosis and heart lesions in laboratory rats), efforts were made, using selective breeding, to transfer a low erucic acid trait into agronomically adapted cultivars of *Brassica napus* and *B. campestris*, which are used in the production of rapeseed oils. These varieties of rape were superseded by the canola varieties in the 1980s. Canola varieties have improved agronomic characteristics, such as increased yield and improved disease resistance. By definition, canola refers to *B. napus* and *B. campestris* lines containing less than 2% of the total fatty acids as erucic acid. These canola varieties comprise almost the entire rapeseed crop produced in the world today. In 1997, the erucic acid content of 50% of the Australian canola crop was 0.3% or less of the total fatty acids. The maximum reported erucic acid level was 1.6% of the total fatty acids.

Canola oil has virtually replaced all uses for rapeseed oil and can be used by itself as a salad or vegetable oil. However, it is usually blended with other vegetable oils in the production of margarine, shortening, salad oil and vegetable oil.

Currently, Standard G1 (Edible Fats and Oils) of the Australian *Food Standards Code* specifies that edible fats and oils should not contain more than 50 g/kg (5%) of erucic acid in the total fatty acids present therein. The New Zealand Food Regulations do not specify any levels for erucic acid. The Codex Standard for Edible Low Erucic Acid Rapeseed Oil specifies that the oil should not contain more than 5% erucic acid. Although, in the draft Codex Standard for Named Vegetable Oils, this specification has been reduced to 2%.

Toxicological data

Erucic acid, as a fatty acid, is digested, absorbed and metabolised, for the most part, like other fatty acids. This process involves hydrolysis of the ingested triacylglycerols by the intestinal lipases in the small intestine, absorption of the liberated fatty acids by the intestinal cells, then passage into the circulation via the lymph. The length of the fatty acid, its degree of saturation and the digestibility of the triacylglyceride molecule into which it is incorporated will all influence this process. In humans, the digestibility of erucic acid containing triacylglycerols is near maximal (99%), whereas in rats their digestibility is somewhat lower (77%).

Once absorbed, fatty acids are distributed to tissues bound to serum albumin. Fatty acids represent the major fuel source of the heart and skeletal muscles. All cells are capable of oxidising fatty acids and this primarily occurs in the mitochondria, yielding ATP. The process is known as mitochondrial β–oxidation. The peroxisomes are also capable of β–oxidation. Erucic acid, however, like other long chain fatty acids, is poorly oxidised by the mitochondrial β–oxidation system, probably because erucic acid is poorly utilised as a substrate by the β–oxidation enzymes. Heart muscle seems particularly poor at oxidising erucic acid. Furthermore, erucic acid also appears to inhibit the overall rate of fatty acid oxidation, by the mitochondria. In liver, the presence of erucic acid appears to induce the peroxisomal β–oxidation system, leading to a gradual decline in erucic acid accumulation and also reduced inhibition of fatty acid oxidation. This is thought to reduce the influx of erucic acid to the heart. Unmetabolised erucic acid can be found in the faeces.

The human health concern with erucic acid arises from two findings. Firstly, experimental studies have demonstrated an association between dietary erucic acid and myocardial lipidosis in a number of species. Myocardial lipidosis is reported to reduce the contractile force of heart muscle. The occurrence of myocardial lipidosis can be explained by the effect that erucic acid has on the mitochondrial β–oxidation system. Secondly, studies have also demonstrated an association between dietary erucic acid and heart lesions in rats. So far, however, there is no evidence that dietary erucic acid can be correlated to either of these effects in humans. Furthermore, there is no conclusive evidence which indicates that the development of myocardial lipidosis is causally linked to the development of myocardial necrosis. However, given what is know about erucic acid metabolism, it seems reasonable to expect that humans would also be susceptible to myocardial lipidosis following exposure to high levels of erucic acid.

All of the available animal studies rely on short term or sub–chronic oral exposure to oils containing various proportions of erucic acid. The most common effect associated with short–term, and to a lesser extent, sub–chronic exposure to these oils is myocardial lipidosis. This effect is observed soon after the commencement of oil feeding and appears to be increased in its severity, in a dose–dependent manner, if erucic acid is present. Clinical signs are typically absent; reduced weight gain only occasionally being correlated with erucic acid dose.

Increased myocardial lipidosis is associated with doses of erucic acid at 1500 mg/kg bw/day in rats, although in nursling pigs this occurs at 900 mg/kg bw/day. Nursling pigs appear to tolerate less erucic acid than adult pigs before myocardial lipidosis is evident, suggesting that the immature myocardium and/or liver may be less able to oxidise long–chain fatty acids. The severity of the observed myocardial lipidosis appears to decline with time. This is most likely due to the induction of the peroxisomal oxidation system in the liver, with subsequent downstream effects on the heart. It is not clear whether this adaptation to the oxidation of long–chain fatty acids by the liver, and possibly also the heart, has any long term adverse consequences.

In pigs and monkeys, there appears to be no other adverse findings that can be associated with erucic acid consumption, other than myocardial lipidosis. In rats,

however, the animals typically also develop myocardial necrosis followed by fibrosis, at erucic acid doses of 6600 mg/kg bw/day. It is not apparent from these studies if this necrosis has any long term effects, although it has been reported that the lifespan of rats exhibiting such lesions is not affected. The male rat is reported to be predisposed to the development of this type of heart lesion, particularly in response to the feeding of oils, with or without erucic acid.

No chronic, genotoxicity or carcinogenicity data are available. A single generation reproductive study was done in rats and guinea pigs where doses of erucic acid up to 7500 mg/kg bw/day were not associated with any adverse reproductive or developmental effects.

In establishing a NOEL for the effects of erucic acid, short term studies are considered the most appropriate as myocardial lipidosis appears rapidly after only short exposures, and is at its most severe early in the exposure period. The available sub–chronic studies are inadequate for deriving a no-effect level because of the absence of myocardial lipidosis in many of the studies as well as inappropriate dosing regimes. A NOEL of 750 mg/kg bw/day, based on the occurrence of increased myocardial lipidosis at 900 mg/kg bw/day in nursling pigs, is considered appropriate.

A number of human epidemiological studies are available which have attempted to establish if there is any association between dietary erucic acid and the occurrence of heart disease, myocardial lipidosis or erucic acid accumulation in the heart. The studies indicate that erucic acid may occur in human heart muscle in geographic areas where vegetable oils containing erucic acid are consumed. However, the available evidence does not indicate an association between myocardial lesions, of the type observed in rats, or significant myocardial lipidosis, and the consumption of rapeseed oil. None of these studies enable a tolerable level for human exposure to be established.

In the absence of adequate human data, the NOEL of 750 mg/kg bw/day, established for pigs, can be extrapolated to humans in order to establish a tolerable level of human exposure. If an uncertainty factor of 100 (10 for extrapolation to humans, 10 for variation within humans) is applied to this NOEL the tolerable level for human exposure would be 7.5 mg erucic acid/kg bw/day, or about 500 mg erucic acid/day for the average adult. This is regarded as the provisional tolerable daily intake (PTDI) for erucic acid.

Dietary intake assessment

The majority of exposure to erucic acid comes from canola oil. This is because other oils, such as high erucic acid rapeseed oil and mustard seed oil, would not comply with the *Food Standards Code* because of their high erucic acid content and, therefore, should not appear on the market in Australia.

The estimated dietary intake of erucic acid for high consumers of canola oil, assuming the oil contains erucic acid at the highest reported survey level, is about 350 mg/day.

This represents about 86% of the PTDI. For the average consumer, the dietary intake is 124 mg/day or 28% of the PTDI.

Risk characterisation

An association between erucic acid and an increased incidence of myocardial lipidosis in animals has been demonstrated. It is not apparent from human data whether this effect also occurs in humans in response to the consumption of erucic acid. The occurrence of increased lipidosis in animals is generally short lived; the myocardium and liver eventually adapting to the oxidation of erucic acid. The long term effects, if any, of this adaptation are not known.

A tolerable level of human exposure was able to be established on the basis of the animal studies. There is a 120 fold safety margin between this level and the level which is associated with increased myocardial lipidosis in nursling pigs.

The dietary exposure assessment has concluded that the majority of exposure to erucic acid by the general population would come from the consumption of canola oil. The dietary intake of erucic acid by an individual consuming at the average level is well below the PTDI, therefore, there is no cause for concern in terms of public health and safety. However, the individual consuming at a high level has the potential to approach the PTDI. This would be particularly so if the level of erucic acid in canola oil was to exceed 2% of the total fatty acids.

Risk management

Given that there may be public health and safety concerns for high consumers of canola oils if the erucic acid content were to exceed 2%, it is proposed that a maximum allowable level for erucic acid in edible oils be maintained in a joint Australia New Zealand Food Standards Code. It is further proposed that this level apply to all edible oils, as other rapeseed oils and mustard seed oils can contain high levels of erucic acid.

As canola has largely replaced all uses of rapeseed oil and comprises almost the entire rapeseed crop produced in the world today and, by definition, contains 2% erucic acid or less, it is proposed that the maximum allowable level be lowered from 5% to 2%. This would be consistent with public health and safety, as determined by the risk assessment, and is also a level which is reasonably achievable in modern canola varieties. In addition, this level is likely to harmonise with proposed Codex levels for erucic acid.

It is proposed that Clause 3(2) of Standard 2.4.1–Edible Oils of the proposed Australia New Zealand Food Standards Code be amended by substituting 20 g/kg of erucic acid for 50 g/kg of erucic acid.

FLUORIDE

SUMMARY OF THE TOXICOLOGICAL REVIEW AND RISK ASSESSMENT

Introduction

Fluoride is the ionic form of fluorine, and is one of the most reactive elements. The ingestion of fluoride during the pre-eruptive development of the teeth has a cariostatic effect and due to its unique ability to stimulate new bone formation it has recently been used as an experimental drug for the treatment of osteoporosis.

The Australian *Food Standards Code* does not set a limit for fluoride in food other than in Standard S5-Packaged Water and Packaged ice which may not contain more than 1.7 mg/L of fluoride. This level was established in 1987.

In New Zealand, fluoride is regulated in the First Table to Regulation 257 and is permitted in the following foods:

All beverages and other liquid food	3 ppm
Shellfish	15 ppm
Any other food except tea	10 ppm

No specific Codex standards have been established for fluoride.

Toxicology data

Fluoride is rapidly absorbed through the gastrointestinal tract with an efficiency between 30-90% depending on individual variability in metabolic handling and on whether fluoride is ingested from the water or the diet. Most of the body's fluoride is found in calcified tissues to which it is not irreversibly bound. Mobilisation of fluoride occurs during the process of bone remodelling. The elimination of absorbed fluoride occurs via the kidneys.

Acute toxicological studies in animals have found that the oral LD50 for soluble fluorides is in the range 20-100 mg/kg bw, whereas, via intravenous, intraperitoneal or subcutaneous routes the LD50 is half of the oral dose. Clinical signs consist of increased salivation, lacrimation, vomiting, diarrhoea, muscular fibrillation, respiratory and cardiac depression. Acute toxicity in humans usually occurs as a result of accidental or suicidal ingestion of fluoride, and results in gastro-intestinal effects, severe hypocalcaemia, nephrotoxicity and shock. The LD50 in humans ranges from 6-100 mg/kg bw.

Chronic exposure to excess fluoride in animals and humans produces dental (enamel) fluorosis and skeletal fluorosis. Dental fluorosis can occur during the pre-eruptive development of teeth, is largely regarded as a cosmetic effect rather than a severe functional disability, and ranges from a slight aberration in the normal enamel (a few white specks to occasional white spots) to hypoplasia of the tooth (with discrete confluent pitting and widespread brown stains). The minimal daily intake fluoride in

infants that may cause mild fluorosis has been estimated to be at 0.1 mg/kg bw/day. This is in agreement with the reported levels of 0.1 to 0.3 mg/kg bw/day necessary to initiate fluorosis in animals.

The most significant toxic effect of chronic excess fluoride in humans is skeletal fluorosis. Symptoms consist of increases in bone density, bone morphometric changes and exostoses and can progress to crippling skeletal fluorosis with accompanying muscle wasting and neurological defects. The development of skeletal fluorosis and its severity is directly related to the level and duration of exposure. Most research has indicated that an intake of at least 10 mg/day for 10 or more years is needed to produce clinical signs of the milder forms of the condition. Advances stages of skeletal fluorosis are associated with intakes of fluoride ranging from 20-80 mg/day for 10 or more years.

Previous reviews of the literature have not found an association between fluoride ingestion and teratogenic or reproductive effects, although the studies are extremely limited.

Past studies using standard genotoxicity tests have failed to show that fluoride can induce mutagenic effects. Some of the *in vitro* studies suggested that fluoride was capable of mutagenic activities (mutations in mouse lymphoma cells, sister-chromatid exchanges and micronuclei in cultured Chinese hamster ovary cells), however, *in vivo testing* gave conflicting results.

Current reviews have suggested that:

- animal studies have not established an association between fluoride exposure (even extremely high and life long exposure) and cancer; and
- there is no detectable risk cancer in humans from optimally fluoridated water.

Fluoride in concentrations normally encountered in the food and water are considered to be of low risk to human health (although there is the possibility of mild dental fluorosis for some individuals). This is supported by the literature in which many studies have failed to demonstrate associations between fluorosis and ingestion of fluoride from food, beverages and water and additionally, the use of fluoride mouthrinses and professionally applied fluorides. Further research is needed to establish whether fluoride protects against or contributes to or has no effect on bone fractures or in treating osteoporosis.

Sources of dietary exposure

Sources of food and beverage products that may contribute to excess fluoride ingestion are fluoridated water, infant formula (reconstituted with optimally fluoridated water) , infant foods (cereals), seafoods, soft drinks, tea and reconstituted juice products processed with fluoridated water. However, there is wide variation in fluoride concentrations of some categories of products and dietary intakes.

Risk characterisation

Like other trace elements, fluoride can become toxic when the quantity ingested exceeds the homeostatic control mechanisms. An excess intake of fluoride in humans may manifest as: (a) acute poisoning (b) skeletal fluorosis and (c) mottled tooth enamel (dental fluorosis). In terms of frequency of occurrence only the last category is commonly encountered.

In the past, cases of skeletal fluorosis have been observed following chronic exposure to high fluoride-containing water. However, this required high doses (20-80 mg/day) of fluoride over a considerable period of time (>10 years) and has historically been restricted to tropical and subtropical areas, and is complicated by factors such as malnutrition.

Risk management

The 1996 Australian Drinking Water Guidelines established jointly by the NHMRC and the Agricultural and Resource Management Council of Australia and New Zealand contains drinking water guidelines for fluoride. Typical fluoride concentrations in unfluoridated water supplies range from <0.05 mg/L to 1.5 mg/L and in fluoridated supplies, the target concentration is between 0.7 and 1 mg/L.

The Guidelines suggest that the concentration of fluoride in the drinking water should not exceed 1.5 mg/L. This guideline level was set to protect children from the risk of dental fluorosis but it was recognised that there is a narrow margin between concentrations producing beneficial effects to teeth and those producing fluorosis. It was recommended that if the 1.5 mg/L value is exceeded (in circumstances where it is not practicable to defluoridate) then parents should be advised to use rainwater or bottled water for children up to about 6 years of age to limit or prevent dental fluorosis. The current New Zealand standard of 3 ppm for all beverages is twice the current maximum recommended level in drinking water and would not be considered acceptable in relation to preventing dental fluorosis.

The overall conclusion is that there is no evidence of public health and safety concerns from current dietary exposures to fluoride. The Authority considers that the issue of dietary intake of fluoride is adequately covered by the current water quality guidelines. The issue of dental fluorosis in infants from excess fluoride consumption is being addressed in Proposal P93 - Infant Formula.

It is proposed that no MPCs for fluoride be established in the Joint ANZ Code.

FUSARIUM TOXINS

SUMMARY OF THE TOXICOLOGICAL REVIEW AND RISK ASSESSMENT

Introduction

Fusaria are a widespread fungi occurring abundantly in or on the soil and thriving in decaying vegetation, plant debris and other organic substrates. Some occur as parasites or saprophytes on subterranean or aerial parts of wild and cultivated plants. The genera is found worldwide in a variety of climates in different geographic regions. While many species in this genus are field fungi, many are able to develop and multiply post-harvest and in storage. *Fusarium* fungi are pathogenic to plants and crops but their role in animal or human mycoses is minimal. Pathogenicity in animals and humans is almost entirely related to their ability to produce toxins.

Fusarium species produce a variety of toxins including T-2 toxin, nivalenol, deoxynivalenol, acetodeoxynivalenol (collectively known as tricothecenes) zealalenone and fumonisins. Many of these toxins are highly stable and continue to exist long after the *Fusarium* spp. that produced them have died. Natural occurrence of most *Fusarium* toxins in feed or foodstuffs is minimal, although some, like zearalenone and deoxynivalenol (DON) have been shown to occur naturally in corn and corn-based food. The toxicity associated with *Fusarium* toxins is broad, involving the gastrointestinal tract, reproductive and cardiovascular systems, as well as potential increases in immunosuppression and cancer.

Mycotoxin levels are dependent on essentially three factors, namely, the presence of a toxigenic *Fusarium* species, an appropriate substrate for fungal growth, and an environment conducive to the growth of the fungus. The most important environmental parameters are the moisture level or water activity of the substrate and the temperature.

A detailed evaluation report on the toxicity and risk assessment of *fusarium* toxins will be prepared in 1999 as further survey data on the level of these toxins in foods in Australia and New Zealand becomes available. Survey data on the levels of fusarium toxins in maize and maize products is currently being sought by the Grains Research and Development Corporation.

Conclusion

Because of the need for further monitoring of *fusarium* toxins in produce in Australia and New Zealand, and the on-going work on *fusarium* toxins elsewhere in the world, it is considered premature at this time to be considering establishing maximum permitted concentrations in foods. This issue will be considered further in 1999 as part of ANZFA work but no recommendations will be made as part of the review of Standard A12.

LUPIN ALKALOIDS

SUMMARY OF THE TOXICOLOGICAL REVIEW AND RISK ASSESSMENT

Introduction

Quinolizidine alkaloids are found in various plants including those belonging to the Lupinus genus, and are considered to be poisonous at high levels - generally recognised to be 1-2% alkaloid concentration in the plant. The levels and combinations of these alkaloids are highly variable between species, and they contribute to the majority of alkaloids found in lupins. Piperidine alkaloids are also found in lupins and are suspected to be toxic and teratogenic. The Australian Food Standards Code currently has a maximum permitted concentration of 200 mg/kg for alkaloids in lupins.

The native levels of alkaloids in seeds or meal can be reduced through "debittering" processes or by washing with water. Plant breeding programs have concentrated on the hybridisation and crop optimisation of species with low native levels of alkaloids (so-called 'sweet' lupins). Evidence suggests that the mean alkaloid content of marketable sweet lupin seed averages 130-150 mg/kg (Petterson et al, 1987).

Lupin alkaloids may be found in any derivative of the seed or plant, including flours and meal, pastas and pastries, dairy product substitutes, and coffee substitutes. Also, goats milk has been claimed to contain high levels of alkaloids as a result of browsing on affected pasture by goats. Historically, lupin was restricted to traditional use, or as a feedstuff but more recently lupin products are increasingly being introduced into food for human consumption.

Toxicological Data

The lupin alkaloids of interest in human and animal health are sparteine, lupanine (a ketonic derivative of sparteine) and anagyrine.

In acute studies sparteine intoxication occurs at significantly lower levels than for lupanine in single dose parenteral or oral administration. Mice appear to be more sensitive to alkaloids, with oral LD_{50} of 410 mg/kg compared to 1664 mg/kg in rats. There is a small difference in the LD_{50} values of sparteine and lupanine in the mouse, when given by the intraperitoneal (IP) route. The relative difference was confirmed in the guinea pig. In the rat it is apparent alkaloids administered IP have a lower LD_{50} value than for PO administration. LD_{50} for mixtures of alkaloids are much higher when compared to those of pure lupanine and sparteine, by peroral (PO) administration. The symptoms of acute toxicity indicate neurological effects, especially loss of motor co-ordination and muscular control.

In 3-month studies, no deaths among rats occurred, the only significant effects which could be linked to treatment consisted of decreased haemoglobin levels in males and increased white blood cell count in females at the dose of 500mg/kg bw/day. No

significant toxicological effects were observed when rats were fed a diet containing up to 90 mg/kg bw/day lupin alkaloids.

In a 9-month feeding study, the alkaloid related toxicity was limited to the liver of female rats. This was observed as relatively reduced weight at the intake of 12 mg/kg bw/day alkaloids. This study was limited for the purposes of establishing a LOEL as only a single dose level was used throughout the treatment period.

A reproductive study combined with the above feeding study in rats, revealed no adverse effects on fertility, lactation or any other reproductive parameters observed at the dietary level of 12 mg/kg bw/day lupin alkaloids - the only dose tested. A study in cows was inadequate to assess development toxicity of lupin alkaloids.

With the exception of one anecdotal report regarding humans, the quinolizidine alkaloid, anagyrine, is generally thought to be teratogenic only in cattle. However, the reported effects in animals, should be taken into account in the absence of human or more extensive quantitative animal data.

In a special study to investigate neurotoxicity of certain lupin alkaloids, sparteine and lupanine appeared to inhibit ganglionic transmission of the sympathetic nervous system. In the parasympathetic nervous system lupanine suppresses the effects of pre-ganglionic stimulation of the pneumo-gastric nerve. The lowest level where no effect was observed was 5 mg/kg (i.v. dose) in the dog and 0.5 mg/kg (i.v. dose) in the cat. It is difficult to extrapolate from intravenous dosage to dietary levels, however as neurological effects were apparent in acute toxicity studies, it may be useful to note that these effects are reflected in this study.

Human toxicity studies were restricted to anecdotal reports. There were no quantitative studies available, but the literature indicates that certain alkaloids are of concern to human health after acute exposure. In one case, an acute dose of 11 mg/kg was observed to be lethal when lupin alkaloids were ingested.

Hazard Characterisation

Establishing a NOEL in animals

The available toxicological reports investigated lupin alkaloid toxicity using acute and sub-chronic exposures. Reversibility of effects of intoxication in acute studies is indicated, ie, when lupin diets are discontinued, symptoms of toxicity disappear. Acute toxicity consists of neurological symptoms such as nausea, respiratory arrest, weakness and coma. Limited neurotoxicity studies confirm this, but are inadequate for the purposes of determining a NOEL/LOEL.

Short term (3 month) studies in rats indicated an absence of toxicity at doses of around 90-105 mg/kg bw/day. An overall NOEL from animal studies is 90 mg/kg bw/day.

Establishing a tolerable level of exposure for humans

Although the reports of the human studies are anecdotal or dated, they seem to indicate a marked difference in sensitivity between animals and humans with regard to acute toxicity. A summary of the available reports show that at 11 mg/kg, there is a report of lethality in humans. This suggests there are significant metabolic differences between humans and rats with regard to lupin alkaloids, and that rats may not be a suitable model for establishing levels of tolerable exposure in humans.

Since there is very little known about metabolism and pharmacology of lupin alkaloids in animals and no information is available in humans, it is not considered appropriate to extrapolate the animal NOEL derived from the rat studies to humans. Tolerable levels for animals cannot be applied with any confidence in estimating tolerable long-term human exposure.

In the absence of medium or long-term human data which is indicative of potentially toxic dose levels in humans, or which enables an estimate of a tolerable level of exposure, it is proposed to apply a 1000-fold uncertainty factor to the dose level reported to result in human lethality, namely, 11 mg/kg. Using this conservative assumption, the tolerable level of exposure for humans is 0.01 mg/kg/day.

Levels in Food and Dietary Exposure Assessment

There are no suitable dietary survey data available from which to determine food consumption levels of lupin alkaloids. There is, however, some evidence that suggests that the quantity of lupin flour in any flour-based product does not exceed 10% for technological reasons. Dietary exposure has, therefore, been estimated by assuming that of all flour products in the market place, only 5% are likely to contain lupin flour at a level of 10% of total flour volume. Levels of dietary alkaloids can then be calculated based on the alkaloid concentration typically present in lupins harvested for human consumption - most recently reported being 130mg alkaloids/kg seed. Using the mean, median and 95%ile consumption rates of wheat flour gained from the 1995 National Nutrition Survey (NNS), dietary exposure per day is calculated by assuming that average adult weight is 70 kg.

The exposure calculations indicate that high consumers of flour based products such as pasta, pastry and cakes and biscuits would be likely to have a daily exposure to lupin alkaloids of 0.002 mg/kg bw/day at the 95th percentile of consumption which is below the estimated PTDI of 0.01 mg/kg bw/day. Normal consumers at the mean and median level of consumption are well below this figure. It is not possible to calculate the exposure to alkaloids from products prepared in the home from lupin seeds, due to lack of data.

There is no information available on the heat or cooking stability of lupin alkaloids, though they are recognised to be soluble in water or organic solvents, as shown by debittering processes. Alkaloids are generally thought to be very chemically stable.

Risk Characterisation

The available data on lupin alkaloids is limited and does not allow a full characterisation of the risk of exposure to humans. There is particular concern that the apparent toxicity in humans is considerably higher than in the experimental animals which have been tested. A tolerable level of exposure for humans has tentatively been established at 0.01 mg/kg/day. The available information on potential exposure suggests that at current levels of use, human exposure, for the majority of the population, is below this tolerable level of exposure. However, the small margin-of-safety suggests that further data on the potential toxicity of lupin alkaloids should be obtained before there is an extension of the use of lupin flour in food for any sector of the population.

One potential 'at-risk' group are those with coeliac disease. The seeds of lupins do not contain gluten and, thus, are attractive as ingredients in the listed diets for sufferers of this disease, as a replacement for wheat flour. If use the lupin flour increases in the sub-population with coeliac disease, this group needs to be made aware of preparation techniques to lower the content of these alkaloids.

Very little is known or available in the literature about the effects of cooking on the toxicity of lupin alkaloids. In the absence of information to the contrary, and in setting a tolerable level of human exposure, it must be assumed that there is no reduction in the final food product of these alkaloids.

In order to further characterise the potential human risk associated with lupin alkaloids, additional research is required on: (i) the metabolism and pharmokinetics of alkaloids in humans; (ii) the basis for toxicity in humans and a more accurate estimate of the tolerable level of intake, particularly in the long-term; and (iii) dietary exposure and consumption patterns and the effects of cooking.

Risk Management

Proposed Regulation

Given the considerable uncertainty regarding the potential toxicity of lupin alkaloids, it is proposed that the current maximum permitted level in the Australia Food Standards Code of 200 mg/kg be retained in the joint ANZ Standards and applied to lupin seeds as shown below:

Substance	Food	Proposed MPC (mg/kg)
Lupin alkaloids	Lupin seeds	200

METHANOL

SUMMARY OF THE TOXICOLOGICAL REVIEW AND RISK ASSESSMENT

Introduction

Methanol (methyl alcohol) is a colourless, volatile and flammable liquid which is poisonous and has a slight alcoholic odour when pure. Poisoning may occur from ingestion, inhalation or absorption through the skin.

Methanol occurs as a natural consequence of metabolic processes in humans, other animals and plants. It is found in blood, urine, saliva and expired air and equates to a background body burden of 0.5 mg/kg of bodyweight. Additional exposure to methanol occurs through the diet. Methanol is available from the ingestion of fruits and vegetables, from the consumption of fruit juices and fermentation beverages, and from the use of the synthetic sweetener aspartame, which on hydrolysis yields 10% of its weight as free methanol, which is available for absorption.

In the manufacture of particular alcoholic beverages, methanol is produced as a breakdown product of the enzymic degradation of naturally occurring fruit pectins. This is a spontaneous process which increases during fruit ripening, and is artificially enhanced in the wine making process by the addition of commercial pectinases to achieve improved clarification of the wine. In general, there is more methanol in red wine than in white, and fruit wines have especially high levels. The amount of methanol in wines ranges from trace levels to approximately 0.6 g/L, with an average of about 0.1 g/L.

Brandy is produced as an alcoholic distillate of wine and therefore also may contain a small amount of methanol. Fruit brandies are higher in methanol than grape brandies. In general, it has been shown that the presence of methanol in distilled spirits is directly linked to the pectin content of the raw material, and thus concentrations vary with the type of distilled spirit concerned.

Regulatory history

In 1980, the NHMRC established a working party on wines, spirits and liqueurs to conduct a comprehensive review of standards for alcoholic beverages. The Working Party, together with the Food Science and Technology Subcommittee (FST) and Food Standards Committee (FSC) made recommendations on maximum permissible levels of methanol initially only for spirits, but later for other beverages including wines. The levels were based on very limited toxicological information and data from industry and AGAL on methanol concentrations detected in various types of alcoholic beverages.

The initial decision to recommend a blanket level for methanol for all alcoholic beverages was gradually modified, in response to consumer and industry advice, to provide individual commodity standards based on the levels of methanol naturally

occurring in the various types of beverages concerned. The process of review for each type of alcoholic beverage is detailed in Appendix 1 to the full report in Attachment 4.

Current Standards

	AUSTRALIA	NEW ZEALAND
Fruit Wine, Vegetable Wine and Mead	**STANDARD P2**	**REGULATION 226**
	3 g/L of ethanol	no methanol clause
Spirits and Liqueurs	**STANDARD P3**	**REGULATION 233**
Spirits	8 g/L of ethanol	8 g/L of ethanol
Grape spirit	3 g/L of ethanol	
Brandy	3 g/L of ethanol	3 g/L of ethanol
Fruit Brandy	8 g/L of ethanol	
Whisky	0.4 g/L of ethanol	0.4 g/L of ethanol
Rum	0.4 g/L of ethanol	0.4 g/L of ethanol
Gin	0.4 g/L of ethanol	0.4 g/L of ethanol
Vodka	0.4 g/L of ethanol	0.4 g/L of ethanol
Tequila	3 g/L of ethanol	3 g/L of ethanol
Grappa	8 g/L of ethanol	
Liqueurs	8 g/L of ethanol	
Wine, Sparkling Wine and Fortified Wine	**STANDARD P4**	**REGULATIONS 219,220**
White wine, White sparkling wine	2 g/L of ethanol	no methanol clause
Other wine, sparkling wine and fortified wine	3 g/L of ethanol	no methanol clause

In France, maximum limits are set by the International Office of Vine and Wine at 0.3 g / L for red wine and 0.15 g / L for white wine. Concentrations of methanol permitted in brandies in the USA, Canada and Italy range from 6-7 g/L of ethanol. There is no Codex standard for methanol in alcoholic beverages.

Toxicological data

Methanol is readily absorbed following ingestion and is rapidly distributed to tissues according to all tissues. Peak absorption from the gastrointestinal tract occurs in 30-60 minutes depending on the amount of food in the stomach. A small amount of methanol is excreted unchanged by the lungs and kidneys but the bulk of the methanol is metabolised primarily in the liver by sequential oxidation to formaldehyde, formic acid and carbon dioxide. The oxidative step from formaldehyde to formic acid is rapid, but the further breakdown of formate into carbon dioxide is primarily via a tetrahydrofolate-dependent pathway.

Tetrahydrofolate is derived from folic acid in the diet and is the major determinant of the rate of formate metabolism. The toxic effects of formate are due to an inactivation

of the iron containing enzymes which subsequently interferes with the oxidative phosphorylation pathway.

There are profound differences in the rate of formate oxidation in different species which determine the sensitivity to methanol. In humans and other primates, the metabolism of formate occurs only poorly due to the limited availability of folic acid, leading to an accumulation of formic acid in the body, following methanol consumption. In contrast, other species including rodents, rabbits and dogs are generally folate-sufficient and can readily detoxify formate. Elimination of methanol from the blood appears to be slow in all species, especially when compared with ethanol. In humans, clearance occurs with a half life of 1 day or more for high doses (greater than 1 g/kg) and about 3 hours for low doses (less than 0.1 g/kg). Maximum excretion of formic acid in urine may occur as late as the second or third day following ingestion.

Humans (and non-human primates) are uniquely sensitive to methanol poisoning and the toxic effects are characterised by formic acidaemia, metabolic acidosis, ocular toxicity, nervous system depression, blindness, coma and death. Damage to the retina is incurred by the localised metabolism of methanol by alcohol dehydrogenase (ADH) to formaldehyde and then to formic acid which is severely toxic to the high energy requirements of the eye. Visual disturbances following acute exposure generally develop between 12 and 48 hours after methanol ingestion and range from mild photophobia and blurred vision to markedly reduced visual acuity and complete blindness. Nearly all of the available information on methanol toxicity in humans relates to the consequences of acute rather than chronic exposures. However, a limited number of case reports and epidemiological studies indicate that chronic exposure to methanol may cause effects qualitatively similar to those observed from relatively high levels of acute exposure, including in some cases CNS and visual disorders. The principal concern is that the blood levels of methanol may accumulate over a period of consumption of alcoholic beverages since its clearance is inhibited by the presence of relatively high amounts of ethanol which competitively inhibits methanol oxidation by alcohol dehydrogenase. Thus, while ethanol ingestion stops the degradation of methanol into its more toxic metabolites, allowing it to be cleared from the body by other routes, chronic intake of alcohol beverages may mask the accumulation of methanol which can become hazardous when ethanol levels fall.

Two important determinants of human susceptibility to methanol toxicity appear to be (1) concurrent ingestion of ethanol, which slows the entrance of methanol into the metabolic pathway, and (2) hepatic folate status, which governs the rate of formate detoxification.

Methanol caused significant increases in mutation frequencies in L5178Y mouse lymphoma cells and there is also some evidence that oral administration increased the incidence of chromosomal damage in mice. There is no evidence from animal studies to suggest that methanol is a carcinogen, although the lack of an appropriate animal model is recognised. Methanol can cause embyotoxicity when administered during pregnancy.

A widely used occupational limit for methanol exposure by inhalation is 200 ppm, which is designed to protect workers from any of the effects of methanol-induced acidosis and ocular and nervous system toxicity.

This is equivalent to an acute ingestion of methanol up to 20 mg/kg bw by healthy or moderately folate deficient humans This level of intake is generally not considered to result in formate accumulation above endogenous levels.

Dietary intake assessment

Exposure to methanol occurs from the ingestion of fruits and vegetables, from the consumption of fruit juices and fermentation beverages, and from the use of the synthetic sweetener aspartame. Estimates of intakes from these sources vary considerably, however, methanol in alcoholic beverages represents the major dietary source.

Data obtained in the 1995 National Nutrition Survey have been used to estimate maximum potential methanol intake from the consumption of different types of alcoholic beverages. The 95th percentile level of intake for those identified as consumers in the survey was as follows: red wine, 745 g/day; white wine, 841 g/day; and fortified wine, 357 g/day. At an average ethanol concentration of 12%, standard red and white wines could contribute an upper level of intake of approximately 100 g ethanol per day. At the current maximum permitted level of methanol for wines (3 g/L of ethanol), this corresponds to an intake of 306 mg methanol per day for the high consumer of wine. In addition, the data indicates a potential intake of methanol of approximately 194 mg per day from the consumption of fortified wines if the methanol level were at the maximum allowable level (3 g/L of ethanol).

The highest potential consumption levels revealed by the survey data, were in the category of 'other alcoholic beverages' (1549 g/day), which includes ciders, wine coolers and low alcohol wines. At a maximum permissible methanol level of 8 g/L of ethanol, this amounts to a potential intake of methanol around 0.96 g per day.

Conclusion

Risk characterisation

Acute poisoning with methanol from the consumption of alcoholic beverages is unlikely given current manufacturing practices and regulatory provisions. Of greater concern, however, are the health and safety considerations of long term alcohol consumption and the possible incremental damage, particularly ocular effects, of repeated low level methanol exposure.
While there is no formal acceptable daily intake (ADI) for methanol, a pragmatic level of 20 mg/kg bw/day has been used as the level which does not result in formate accumulation above endogenous levels.

Although the assessment of the risks associated with chronic exposure to low doses of methanol is confounded by factors such as wide individual variability to methanol toxicity and variable folate status, there is sufficient concern regarding the potential adverse public health risks to justify limiting methanol exposure via alcoholic beverages. Given there is potential for adulteration of alcoholic beverages with methanol, a maximum permitted level is warranted to ensure that the methanol concentration will be as low as reasonably achievable using current manufacturing techniques.

Proposed Regulation

Consideration was given to reducing the number of categories of wines and spirits and also expressing the maximum permitted concentration of methanol in mass per volume of beverage. However, given that the concentration of methanol varies in proportion to the concentration of ethanol, this could not be achieved without a considerable relaxation of the standard for some beverages. For this reason, it is proposed to maintain the current method of expression of methanol limits.

To simplify the current standards, however, the following MPCs are proposed

Substance	**Food**	**MPC**
Methanol	Red wine, white wine and fortified wine	3 g/L of ethanol content
	Whisky, Rum, Gin and Vodka	0.4 g/L of ethanol content
	Other spirits, fruit wine, vegetable wine and mead	8 g/L of ethanol content

These concentrations are based on the fact that the source of the carbohydrate used to produce the product determines the ultimate amount of methanol in the beverage. Accordingly, products derived from malt and grains are naturally low in methanol and the proposed level is sufficient to prevent possible adulteration. The concentration proposed for all categories of wine is considered achievable, even for fortified wines which traditionally contain the highest amounts of methanol. The highest concentrations of methanol probably occur in fruit brandies and grappa, but analytical data suggest that most of these alcoholic beverages, if produced according to good manufacturing practice, will meet the proposed level.

OCHRATOXINS

SUMMARY OF THE TOXICOLOGICAL REVIEW AND RISK ASSESSMENT

Introduction

Ochratoxin A was originally described in 1968 as a toxic metabolite of *Aspergillus ochraceus*, but it was soon found that only a minority of isolates of *A. ochraeus* are producers. Moreover, extensive further work has shown that *A. ochraeus* rarely occurs as the dominant fungus in foods. For those reasons, the risk of ochratoxin A contamination of foods due to growth of *A. ochraeus* appears to be quite low.

In the 1970s, ochratoxin A was detected in Scandinavian pig meats as a result of contamination of feed grains by a *Penicillium* species. *P. verrucosum*. This species grows in barley and other grains in Northern Europe and to a lesser extent in Canada. Ochratoxin A is consumed by European populations in pig meat and in bread and other cereal products. Ochratoxin A is regarded as a possible human carcinogen.

Recent developments

Until recent, the above two organism were considered to be the only sources of ochratoxinA, however, the occurrence of ochratoxin A in coffee beans and some north African foods could not readily be explained as these fungi were rarely isolated in these cases. In 1994 and again in 1996, there were reports that *Aspergillus niger* and *A. carbonarius* can sometimes produce ochratoxin A.

In early 1998, ochratoxin A was found in the United Kingdom in dried vine fruits from Greece and Turkey, and in wine from Germany. *Aspergillus* species commonly occur on grapes before and after drying.

In Australia, a recent survey by the CSIRO has indicated that grapes and drying vine fruits are often contaminated by *Aspergillus* species and may also contain ochratoxin A. These surveys are still continuing.

Conclusion

Because of the uncertainties surrounding the source of ochratoxin A contamination in food and the on-going work in this area in Australia and elsewhere, it is considered premature at this time to be considering establishing a maximum permitted concentration in foods. This issue will be considered further in 1999 as part of ANZFA work and a detailed toxicology evaluation and risk assessment report will be prepared. No recommendations, therefore, will be made as part of the review of Standard A12.

PHOMOPSIN

SUMMARY OF THE TOXICOLOGICAL REVIEW AND RISK ASSESSMENT

Introduction

The phomopsins are a family of mycotoxins produced by the fungus *Phomopsis leptostromiformis*. The main host for the fungus is lupins, the fungus being capable of infecting most parts of the plant. The fungus is also capable of infecting other plants, such as chestnuts and mangoes, although the resulting spoilage may limit consumption of affected products. Under normal storage conditions, infected lupin seed can exhibit significant levels of phomopsin contamination. While the majority of lupin seed is used in animal feed, lupin products are also increasingly being introduced into food for human consumption. Therefore, whole lupin seed and flour may represent a source of human exposure to phomopsins. Furthermore, phomopsins have been shown to be resistant to destruction by extensive processing, including cooking.

Contamination of lupin seeds by phomopsins is associated with discolouration of the seed. Commercial grading equipment has been shown to be very effective in selecting seeds which have reduced phomopsin levels. Also, lupin breeding programs have produced varieties resistant to the fungus. These resistant lines may still be colonised by the fungus but there is a significant reduction of phomopsin contamination of the seed.

Currently, Standard A12 of the Australian *Food Standards Code* specifies that the proportion of phomopsins in any food shall not be greater than 5 µg/kg. The New Zealand Food Regulations do not specify any levels for phomopsins and there are no Codex standards for phomopsins.

Toxicological data

There is very limited data available on the metabolism and kinetics of phomopsins, due in part to the lack of suitably radio–labelled phomopsins. Limited evidence from toxicity studies suggest that phomopsins may be only partially absorbed from the gastrointestinal tract. Once absorbed, the phomopsins appear to be metabolised in the liver to a reactive form. The studies available using other routes of exposure also suggest that liver metabolism is essential to the toxicity of phomopsins. There is some evidence from animal toxicity studies to indicate that phomopsins, or their metabolites, may be excreted via the kidneys.

The toxicity of phomopsins appears to be related largely to their ability to bind to tubulin. This results in the inhibition of important cellular functions such as spindle formation during mitosis, and the intracellular transport of lipids. Other observed effects include distortions of cell nucleus shape plus apparent disruptions to membrane systems within the cell. These toxic effects appear largely confined to the liver.

The ingestion of phomopsins has, so far, only been associated with adverse effects in animals. In particular, the ingestion of phomopsin–contaminated lupin stubble has been linked to lupinosis, a disease of sheep. Given the apparent mechanism of toxicity, however, it is reasonable to conclude that humans would also be vulnerable to the toxic effects of phomopsins.

The majority of available animals studies rely on acute or sub–chronic exposure using subcutaneous or intraperitoneal routes, or in the case of sheep, intraruminal routes. Data on oral exposure is mainly limited to reports from observations of field–affected animals, and these reports tend to be qualitative in nature.

The most common sign of toxicity seen in animals following acute and sub–chronic exposure, regardless of the exposure route, is liver toxicity. Liver failure is the most common cause of death in these animals. The most sensitive clinical indicator for this toxicity is inappetence in the affected animals. Reduced appetite has been observed in animals where gross liver damage is not yet apparent and, in sheep, has been associated with an intraruminal dose of 12.5 μg/kg bw/day. This may approximate a LOEL for this exposure route. Animals receiving sub–lethal doses of phomopsins exhibit some capacity to recover once treatment discontinues.

The acute and sub–chronic toxicity studies have shown that a number of parameters may affect the toxicity of phomopsins. Firstly, susceptibility to the toxin appears to vary between species. For example, sheep appear to be far more susceptible than rats to the toxic effects of a given dose of phomopsins. Secondly, limited evidence, from both acute and sub–chronic toxicity studies, suggests that the toxicity of phomopsins may vary depending on the route of exposure, with a given dose of phomopsins being less toxic by the oral route. This suggests that the absorption of phomopsins by the gastrointestinal tract may be limited or that phomopsins undergoes some degradation after ingestion. Thirdly, the toxicity of a given total dose of phomopsins appears to be greater if it is administered in smaller fractions over an extended period of time. This may indicate a cumulative effect.

The only data available for chronic toxicity are qualitative observations in cases of chronic lupinosis in sheep. As with acute and sub–chronic exposure, the liver appears to be the principal target organ of toxicity. The qualitative nature of the chronic studies did not enable the determination of a LOEL or NOEL for these effects.

There is very little data on which to assess the potential genotoxicity of phomopsins. Negative results have been obtained in bacterial mutagenicity assays. However, some equivocal evidence exists, from cultured mammalian cells, that phomopsins may induce chromosomal aberrations. No information was available on the *in vivo* genotoxicity of phomopsins.

Studies on the reproductive toxicity of phomopsins was not available. In a single developmental toxicity study using rats, significant embryotoxicity was observed. However, significant maternal toxicity was also observed at all dose levels tested. Therefore, it was not possible to attribute the observed embryonic deaths to the direct

action of phomopsins. Additional developmental studies using more appropriate dose levels are warranted.

The carcinogenicity data reported, while not derived using an oral route of exposure, are a serious concern. Data from a sub–chronic study using the subcutaneous route indicates that there is an unequivocal association between phomopsin treatment and an increased incidence of liver cholangiocarcinomas and hepatocellular carcinomas in rats at a dose level of 30 µg/kg bw/day administered for 17 weeks. The potential for carcinogenicity of phomopsins following oral exposure remains unclear.

Overall, it can be concluded that phomopsins are potent cytotoxic agents which predominantly target the liver and which are clearly liver carcinogens in the rat. Some animal species appear more vulnerable than others to the toxic effects of phomopsins. Phomopsins may also be less toxic by the oral route, although still capable of causing severe disease, eg., lupinosis of sheep. The cytotoxic nature of phomopsins suggest that humans would also be vulnerable to its toxic effects, however, the available animal studies do not allow a determination of a safe level of dietary exposure to phomopsins. In the absence of a NOEL for phomopsins from animals studies and no data of potential toxicity in humans, it is not possible to determine a tolerable level for human exposure.

Dietary intake assessment

The survey data available for phomopsins is limited to Australian data and restricted to lupin seed only.

Surveys have found that up to 20% of harvested seed can be infected by *P. leptostromiformis* . A survey of commercial lupin seed from Western Australia, Victoria and New South Wales has found levels of phomopsins ranging from <6 µg to 360 µg/kg. Levels as high as 4522 µg/kg in seed have also been detected.

In a survey of unsorted lupin seed from the 1991/92 harvest in Western Australia, the mean level of contamination by phomopsins was found to be 6.1 µg/kg, with 32% of samples exceeding the 5 µg/kg maximum permitted concentration specified in the Australian *Food Standards Code*. If the seed was sorted on the basis of discolouration, analyses showed that the major portion of the phomopsins is present in the discoloured portions (mean phomopsin level 355.1 µg/kg), with the mean level of phomopsins in clean seed measuring 1.3 µg/kg. This indicates that seed sorting is an effective means of reducing phomopsin contamination of seed.

There is no data available on the levels of phomopsins carried over to lupin flour. Therefore, it is not clear to what extent the milling process may remove phomopsin contamination. In addition, no data is available for other potential sources of exposure such as other lupin products, offal, milk etc.
Therefore, there is insufficient survey information to enable a dietary exposure assessment to be done. However, sub–populations groups most likely to have high exposure to phomopsins would be those consuming large amounts of lupin products.

Risk characterisation

Phomopsins have been shown in animal studies to be a potent liver toxins and carcinogens in rats. Although no direct evidence of toxicity in humans is available, their mechanism of action is such that humans are likely to be susceptible to their toxic effects. Phomopsins appear to be less toxic by the oral route than by other routes but still capable of causing severe liver disease in sheep following oral ingestion. Phomopsins also appear to be stable during cooking. The paucity of toxicity data available does not make it possible at this time to identify a NOEL in animal studies or assign a tolerable level for human exposure.

The survey data on the levels of phomopsin in food is confined to lupin seed. Phomopsin levels in food are not surveyed as part of the Australian or New Zealand Total Diet Surveys, nor are its levels routinely surveyed in other food groups such as milk, offal, meat etc. Furthermore, the extent to which lupin flour and other lupin products are included in foods is not known, therefore, a dietary exposure assessment for phomopsins is not possible.

The difficultly of establishing a tolerable level of human exposure to phomopsins, combined with a paucity of exposure data, makes it difficult to clearly characterise the potential public health and safety risk from exposure to phomopsins in food. However, the available data suggests that phomopsins are highly toxic in all mammalian species tested and may be a health concern in humans exposed to lupins or products derived from lupins. Given these concerns, particularly with regard to the potential carcinogenicity of phomopsins, it would be prudent to ensure that human exposure be kept as low as is reasonably achievable.

In order to further characterise the potential public health risks associated with phomopsins, further research is required on: (i) the extent of phomopsin contamination of lupin seed used for direct human consumption, flour prepared from lupin seeds; and offal from animals grazing on lupin stubble; (ii) the potential toxicity of phomopsin following long term low level exposure.

Risk management

Given the public health and safety concerns associated with exposure to phomopsins, maintaining a level of human exposure which is as low as reasonably achievable is appropriate. While the current MPC of 5 μg/kg was based the level of detection at the time the MPC was established, the sensitivity of analytical techniques for detecting phomopsin have improved such that it is now possible to detect phomopsin in picogram amounts. It is doubtful whether such low levels would be reasonably achievable.

Ninety five percent of samples of clean lupin seed from individual sidings are able to meet the current MPC (with 50 % of samples having phomopsin levels of 0.4 µg/kg, or less). Therefore, seed sorting seems to be a reasonably reliable method for ensuring that the majority of seed has less than 5µg/kg phomopsin. The remaining 5 % of samples, however, have been shown to have level up to 10 µg/kg phomopsin after sorting.
Thus, although sorting is reasonably effective at reducing phomopsin levels, it is not totally reliable to maintain the levels below 5 µg/kg. The current MPC of 5 µg/kg, however, seems to be reasonably achievable for 95% of lupin seeds.

It is proposed, therefore, that the current MPC of 5 µg/kg be retained and that in the absence of information on the presence of phomopsin in other foods, that this MPC be restricted to lupin seeds, as shown below.

Substance	**Food**	**Proposed MPC (mg/kg)**
Phomopsins	Lupin seeds	0.005

POLYCHLORINATED BIPHENYLS

SUMMARY OF THE TOXICOLOGICAL REVIEW AND RISK ASSESSMENT

Introduction

Polychlorinated biphenyls (PCBs) are members of a large class of organic compounds known as halogenated aromatic hydrocarbons which do not occur naturally in the environment. Rather, they are manufactured by the addition of chlorine atoms to biphenyls in the presence of a suitable catalyst and are chemically similar to the chlorinated organic compounds used in pesticides. PCBs can exist as 209 individual congeners (forms), however, only about 130 congeners are likely to occur in commercial PCB mixtures.

PCBs were first produced commercially in the 1920s, although it was not until the 1950s that the industrial application of PCBs increased significantly. They were used as capacitor, hydraulic and transformer fluids, in carbonless copying paper and as plasticisers in paint. PCBs are dispersed into the environment through the atmosphere and following release into water. PCBs are also mobilised in soil or landfills. PCBs degrade very slowly and, as a result, they accumulate and persist for many years in the environment, resulting in contamination of the food chain. In response to public concern over the bioaccumulation of PCBs, many industrialised countries, including Australia, have taken steps to control and restrict the flow of PCBs into the environment.

Commercial PCBs are clear oils at room temperature and do not crystallise, even at low temperatures, but turn into solid resins. PCBs are non-flammable and form non-explosive vapours that are heavier than air and are chemically very stable under normal conditions. However, when heated, other, more toxic compounds such as polychlorinated dibenzofurans (PCDFs) can be produced.

Degradation of PCBs in the environment is dependent on the degree of chlorination of the biphenyl, and, in general, the greater the chlorination of a PCB, the longer it will persist in the environment. The half-life of PCBs varies according to the specific congener and ranges from 1 day to 70 years.

Current sources of PCB release include volatilisation from landfills containing transformer, capacitor and other PCB-wastes, sewage, sludge, spills, dredge spoils and improper disposal to open areas. Pollution may occur during the incineration of industrial waste. Explosions or overheating of transformers and capacitors may release significant amounts of PCBs into the environment.

The current regulations in the FSC were established in 1978, based on the level of detection at the time, as follows:

Fat of meat, fat of meat of poultry, milk, milk products and eggs at 0.2 mg/kg and in fish 0.5 mg/kg.

The New Zealand *Food Regulations 1984* do not prescribe levels for PCBs in foods, nor does Codex.

The FDA regulates PCBs under the Food, Drug and Cosmetic Act (FD&CA), establishing tolerances of PCBs in several foods and in feeds for food-producing animals. The tolerances are 1.5 mg/kg (fat basis) in milk and manufactured dairy products, 3 mg/kg (fat basis) in poultry, 0.3 mg/kg in eggs, 0.2 mg/kg in finished animal fed, 2 mg/kg in animal feed components of animal origin, 2 mg/kg in fish and shell fish (edible portion) and 0.2 mg/kg in infant and junior foods. FDA established action levels of 3 mg/kg in red meat.

Toxicological data

In general, PCBs appear to be rapidly absorbed by the gastrointestinal tract after oral exposure. Once absorbed, PCBs are most likely distributed via the lymphatic system. Overall, PCBs are rapidly cleared from the blood and accumulate in the liver and adipose tissue, or are metabolised in the liver.

Animal feeding studies, mostly using rodents, have shown that the range and severity of the toxic effects of PCBs is correlated with the PCB congener/mixture used. In acute studies using different Aroclors (commercial PCB mixtures), the oral LD_{50} range in rats ranged from 1000 to 10,000 mg/kg bw, indicating low acute toxicity in rats.

Sub-chronic and chronic exposure studies indicate that the liver is the organ most susceptible to the toxic effects of PCBs. In rats, sub-chronic oral exposure to the individual PCB congener 126 (3,3',4,4',5-pentachlorobiphenyl) at a dose of 0.1 µg/kg bw/day was associated with changes in liver enzyme activity and increased liver weights, whereas similar effects were associated with congener 128 (2,2',3,3',4,4'-hexachlorobiphenyl) at an oral dose of 0.42 mg/kg day/bw. Chronic oral toxicity studies in rats using different commercial PCB mixtures have indicated hepatocellular adenofibrosis for Aroclor 1254 at a dose of 5 mg/kg bw/day, whereas oval cell and bile-duct proliferation was seen in Kanechlor 300 treated animals at a dose of 50 mg/kg bw/day. These studies illustrate that oral exposure to different PCBs (individual congeners and mixtures) are associated with varying degrees of liver toxicity.

Sub-human primates appear to be more sensitive to PCBs than rodents. Adverse effects (nail bed deformations and prominent tarsal glands) in female Rhesus monkeys orally exposed to Aroclor 1254 were observed at a dose of 80 µg/kg bw/day. Male Rhesus monkeys exposed to Aroclor 1242 exhibited swollen and irritated eyelids at a dose of 0.12 mg/kg bw/day.

The evidence for genotoxicity of PCBs is equivocal. Studies have shown that some PCBs may be clastogenic *in vitro*. *In vivo* studies using rats indicated that PCBs may be linked to DNA breakage, but this effect was reversible.

PCBs appear to be associated with adverse reproductive effects in rodents. Mice chronically exposed to Aroclor 1254 in the diet at a dose of 0.25 mg/kg bw/day indicated pronounced reproductive toxicity in the form of depressed fertility and

decreased survival of exposed animals. Foetotoxity was observed as low birth weights in rats orally exposed to 25 mg/kg bw/day of Kanechlor 500.
In mice, cleft palates were associated with oral exposure to the individual PCB congener 3',4, 4', 5, 5'-hexachlorobiphenyl at 2 mg/kg bw/day and hydrophrenosis at 4 mg/kg bw/day.

PCB exposure appears to be linked with neurotoxicity in rodents and non-human primates. Behavioural testing of the offspring of pregnant rats fed Kanechlor 500 in the diet indicated delayed learning in male progeny exposed to 5 mg/kg bw/day on days 15-21 of gestation. Female Rhesus monkeys administered an oral dose of 0.084 mg/kg/bw day of Aroclor 1248 gave birth to offspring that exhibited hyperactive behaviour and retarded learning ability.

Decreased thymus weights and reduced killer cell activity were observed in rats exposed to Aroclor 1254 by gastric intubation at a dose of 10 mg/kg bw/day. Aroclor 1248 at a dose of 0.05 mg/kg/bw day appeared to decrease gamma-globulin levels in orally exposed Rhesus monkeys. It appears that PCBs affect immune responsiveness, however, functional immunity in animals does not appear to be affected by exposure to PCBs.

Oral exposure to PCBs has been shown to be associated with slight alterations in steroid hormone levels and metabolism in animals. However, developmental studies examined in this evaluation did not indicate any abnormal masculinisation or feminisation of foetuses during development, suggesting that exposure to PCBs did not functionally impair mammalian sexual development.

Data concerning the toxicological effects of PCBs in humans appear to be based on two accidental poisonings from contaminated rice oil in Japan and Taiwan. Clinical symptoms were seen in victims three to four months after exposure. Follow-up studies have shown that some victims developed neurological symptoms and malignancies. These toxic effects were originally attributed to PCBs present in the oil. However, further examination of the poisonings indicates that the symptoms were most probably caused by the presence of the more potently toxic polychlorinated dibenzofurans.

The choice of a particular NOEL for human health risk assessment should be identified for the most sensitive effect in the most sensitive species. The Joint (FAO/WHO) Expert Committee on Food Additives (JECFA) has identified non-human primates as the species most sensitive to the toxic effects of PCBs and has assigned a NOEL of 0.04 mg/kg bw/day, based on the general toxicity of Aroclor 1242 in monkeys. However, the limitations of the available data and the toxicological differences in PCB mixtures that were used in animal feeding studies has made it difficult to establish a value for tolerable intake for humans.

Dietary intake assessment

The major foods in which PCB contamination occurs are fish, milk, other dairy products and meat. Median levels in fish reported from various countries are about 100 µg/kg, compared with less than 20 µg/kg for other foods. An important exception

is human breast milk, in which PCB median levels ranging from 15 to 100 µg/kg on a whole milk basis.

The 1987 and 1992 Australian Market Basket Survey (AMBS) detected PCBs in fish and seafood, albeit within the current permitted level of 0.5 mg/kg. However, the last two Surveys carried out in 1994 and 1996 did not detect PCBs in any foods tested. The New Zealand Total Diet Survey 1990-1991 failed to detect PCBs in foods.

The dietary intake of PCBs by various populations has been estimated by JECFA to range from 0.005 to 0.2 µg/kg bw/day, depending on the type of food consumed and the method used to estimate the dietary PCB intake. This range is considered by JECFA to be within acceptable exposure limits based on comparison with the NOEL set for the Rhesus monkey of 0.04 mg/kg bw/day.

PCB intakes of breast fed infants can range from 2 to 12 µg/kg bw/day. As a consequence, infants may be at a higher risk than the general population because of their small size and immaturity, and the fact that breast milk contributes significantly to an infant's total dietary intake of PCBs. However, even the infant exposure is within the acceptable exposure limits set by JECFA of 0.04 mg/kg bw/day.

Risk characterisation

Toxicological evaluation of PCBs is complicated by many factors, the first of which is the paucity of data concerning human exposure to, and the effects of, PCBs. Much of the animal toxicity data are based on testing mixtures that contain many PCB congeners with varying degrees of chlorination and different stereochemical structures. Differences in toxicity between PCB congeners may also be associated with specific metabolites and/or their specific intermediates.

Oral exposure to PCBs is associated with adverse effects in animals, the most consistent and pronounced is the occurrence of liver tumours in rodents. However, the available human data (mainly from accidental exposures) is equivocal in respect of an association between PCBs and increased cancer mortality.

The Australian Market Basket Survey and the New Zealand Total Diet Survey have indicated that PCBs are undetectable in the Australian and New Zealand food supply. Therefore, it appears that the general population is not being exposed to unacceptable levels of PCBs from food. On the other hand, PCBs are detected in breast milk and infants may represent a higher risk group than the general population. However, PCB intake from breast milk is still within the acceptable exposure limits.

In order to further characterise the potential public health risks associated with PCBs, further research is required on the analysis of PCBs in food in Australia and New Zealand.

Risk management

Considering the uncertainty surrounding the potential toxicity of PCBs, their persistence within the environment and the necessity to achieve low PCB levels within the Australian and New Zealand food supply, it is proposed that the current MPCs be retained as show below.

Substance	Food	Proposed MPC (mg/kg)
Polychorinated biphenyls	Mammalian fat	0.2
	Poultry fat	0.2
	Milk and milk products	0.2
	Eggs	0.2
	Fish	0.5

PYRROLIZIDINE ALKALOIDS

SUMMARY OF THE TOXICOLOGICAL REVIEW AND RISK ASSESSMENT

Introduction

Pyrrolizidine alkaloids (PAs) which may find their way into human and animal food in Australia are derived mainly from the plants *Heliotropium europaeum, Echium plantagineum, Symphytum* spp. and *Crotalaria retusa.* The *Sympthytum* spp. (comfrey) are deliberately ingested while the remaining species are weeds in various grain crops. There is a long history of toxicity in livestock caused by grazing on PA-containing plants. There has also been a number of outbreaks of human poisoning as a result of ingestion of contaminated grain as well as case reports of poisoning caused by intentional ingestion of herbal medicines containing PAs.

Toxicological data

The PAs of relevance to human health are the hepatotoxic PAs which are esters of 1-hydroxymethyl dehydropyrrolizidine. Such compounds are metabolised in the liver to electrophilic derivatives referred to as pyrroles. These pyrroles cause damage in the hepatocytes in which they are generated, but depending on their persistence in aqueous media, can pass from the hepatocytes into the adjacent sinusoids and damage endothelial lining cells of the sinusoids and smallest hepatic veins. These effects give rise in man to hepatocellular injury, cirrhosis and veno-occlusive disease.

The pyrroles react with macromolecules in the cells in which they are either formed or gain access leading to the formation of S-bound protein adducts and DNA cross-linking. The pyrroles have been shown to have mutagenic activity, mainly in *Drosophila* and many have been shown to be carcinogenic, mainly in the rat. There is no evidence of pyrrolizidine alkaloid-induced cancer in humans.

In laboratory and domestic animals, marked anti-mitotic activity due to the pyrroles has been demonstrated but this is not a prominent feature of their toxicity in humans. The main pathological feature of this effect in animals is in the liver, and less so in other tissues. In humans, the major toxicological effect of chronic exposure to PAs is veno-occlusive disease. The available data on cases of veno-occlusive disease in humans indicates a tentative no-observed-effect level (NOEL) of 10 μg/kg bw/day can be established. If an uncertainty safety factor of 10 to account for human variability is applied to this NOEL, the provisional tolerable daily intake (PTDI) for pyrrolizidine alkaloids in humans is 1 μg/kg bw/day.

If a PTDI were to be established on the basis of potential carcinogenicity, the most relevant study is a long term study in rats, where a NOEL for hepatic haemagioendothelioma was reported to be 300 μg/kg. If an uncertainty factor of 100 (to account for extrapolation to humans and for individual variability) were applied to this NOEL, the PTDI would be 3 μg/kg bw/day. This is well above the highly conservative level in the current German regulations for an allowable intake of PAs from herbal medicine, namely, 0.0014 μg/kg bw/day for a 70 kg person.

Dietary intake assessment

Apart from the deliberate use of herbal remedies and nutritional supplements containing PAs, humans can become inadvertently exposed through consumption of contaminated food. The foods which have been found to contain PAs include grains, honey, milk, offal and eggs. It is still unknown whether there are residues of PAs in meat.

In Australian honey, levels of alkaloid up to 1 mg/kg have been recorded from hives where bees foraged exclusively on *Echium* spp., however, blending and bulking of honey from different sources would substantially reduce this level. In the liver and kidney of domestic animals, PA levels have ranged from <10 to 73 μg/kg while in eggs, the levels ranged from 5 to 168 μg/kg. In relation to milk from domestic animals, it is likely that no more than about 0.1% of the ingested alkaloid base will be excreted in milk. PAs and PA N-oxides are known to be excreted in cows milk, but due to milk bulking, it is unlikely that significant exposures would come from this source. In relation to human milk, PAs have been found in human milk during PA poisoning epidemics and cases of veno-occlusive disease have occurred in both neonates and other infants by this means.

Substantial contamination of grain commodities has been recorded in various countries due to both contamination by seeds of PA-containing weeds growing in the crop as well as plant dust fragments from the same plants. The levels of PAs found in various grain commodities in Australia have ranged from <50 to >6000 μg/kg, but there has been no systematic analysis of the levels in grains entering the food supply. There is currently no data to indicate whether PAs occur in oilseed crops.

On the basis of the very limited data available, the major source of dietary exposure to PAs is grains, with eggs, offal and honey minor dietary contributors. However, on the basis of the currently available data, it is not possible to estimate the potential dietary exposure to PA from these food sources.

Risk characterisation

The target organ for PA toxicity in both experimental animals and humans is the liver. In animals, this toxicity is manifested as anti-mitotic activity leading to extensive fibrosis, nodular regeneration, parenchyma and cancer, while in humans, the major effects are hepatocellular injury, cirrhosis and veno-occlusive disease. There is no evidence from the significant human epidemics which have occurred that PAs cause liver cancer in humans. Further research on the mechanisms of PA-induced hepatotoxicity may clarify the apparent differences in species specificity. At this time, the major toxicological endpoint for humans is considered to be veno-occlusive disease.

While there is survey data to suggest that significant levels of PAs can be found in some foods, and particularly in grains, there is virtually no data on the levels of PAs in foods as consumed. The effectiveness of measures taken to control *Heliotrope* seed contamination of grains is unknown. A realistic dietary exposure assessment for PAs, therefore, is not possible at this time.

In order to further characterise the public health risk associated with pyrrolizidine alkaloids, further research is required on: the levels of pyrrolizidine alkaloids in all foods, but particularly grains and foods derived from grains; (ii) the mechanisms of PA-induced hepatotoxicity in order to clarify the apparent differences in species specificity.

Establishing a tolerable level of exposure for humans (PTDI)

It is proposed for the purposes of conducting an assessment of the risk associated with PA exposure that the figure of 1 μg/kg bw/day be regarded as the provisional tolerable daily intake for pyrrolizidine alkaloids in humans.

Further characterisation of the potential human health risk from exposure to pyrrolizidine alkaloids in food is not possible because there is currently inadequate dietary exposure information.

Risk management

No maximum permitted concentration (MPC) is proposed for pyrrolizidine alkaloids in foods at this time.

SHELLFISH TOXINS

SUMMARY OF THE TOXICOLOGICAL REVIEW AND RISK ASSESSMENT

Introduction

Microscopic unicellular algae (mostly 20 to 200 mm size) form an important component of the plankton diet of shellfish such as mussels, oysters and scallops. Under favourable environmental conditions of light, temperature, salinity, water column stability and nutrients, algal populations of only a few cells can quickly multiply into dense blooms containing millions of cells per litre which can discolour the seawater. Of the estimated 2000 living dinoflagellate species, about 30 species produce toxins that can cause human illness from shellfish or fish poisoning. When humans eat seafood contaminated by these microalgae, they may suffer a variety of gastro-intestinal and neurological illnesses. The most common poisonings from shellfish are paralytic shellfish poisoning (PSP) which in extreme cases can lead to death through respiratory paralysis, diarrhetic shellfish poisoning (DSP) which causes severe gastro-intestinal problems and can promote stomach tumours, neurotoxic shellfish poisoning (NSP) which causes respiratory distress, and amnesic shellfish poisoning (ASP) which can lead to permanent brain damage (short-term memory loss).

Poisonous seafood neither looks nor tastes different from uncontaminated seafood, and cooking and other treatments of shellfish do not destroy the toxins. Shellfish and finfish farming areas infested by toxic algal species therefore need to run costly monitoring programmes to check for toxic algae in the water and, whenever these are present, regular tests for toxins in associated seafood products need to be carried out.

Toxicity data and human poisoning cases

The shellfish toxins generally comprise more than one individual chemical species, but there is little data on the toxicity of the individual chemical components.

The symptoms of toxicity for the four toxins being considered are shown below.

Clinical symptoms of toxicity

Biotoxin	Symptoms		Treatment
	Mild Case	*Extreme Case*	
Paralytic Shellfish Poisoning (PSP)	Within 30 min: tingling sensation or numbness around lips, gradually spreading to face and neck; prickly sensation in fingertips and toes; headache, dizziness, nausea, vomiting, diarrhoea.	Muscular paralysis; pronounced respiratory difficulty; choking sensation; death through respiratory paralysis may occur within 2–24 hrs after ingestion.	Patient has stomach pumped and is given artificial respiration. No lasting effects.
Diarrhetic Shellfish Poisoning (DSP)	After 30 min to a few hrs (seldom more than 12 hrs): diarrhoea, nausea, vomiting, abdominal pain.	Chronic exposure may promote tumour formation in the digestive system.	Recovery after 3 days, irrespective of medical treatment.
Amnesic Shellfish Poisoning (ASP)	After 3–5 hrs: nausea, vomiting, diarrhoea, abdominal cramps.	Decreased reaction to deep pain; dizziness, hallucinations, confusion; short-term memory loss; seizures.	
Neurotoxic Shellfish Poisoning (NSP)	After 3-6 hrs: chills, headache, diarrhoea; muscle weakness, muscle and joint pain; nausea and vomiting.	Paraesthesia; altered perception of hot and cold; difficulty in breathing, double vision, trouble in talking and swallowing.	

PSP toxins block the sodium channels of excitable membranes of the nervous system and associated muscles, inhibiting action potentials and nerve transmission impulses. In vertebrates, the peripheral nervous system is particularly affected; typical symptoms of poisoning include tingling and numbness of the extremities, progressing to muscular incoordination, respiratory distress and muscular paralysis leading to death by asphyxiation in extreme cases. Globally, PSP is responsible for some 2000 cases of human poisoning per year (15% mortality), ranging from temperate waters of Europe, North America and Japan, to the Southern Hemisphere in South Africa, Australia, India, New Zealand, Thailand, Brunei, Sabah, the Philippines and Papua New Guinea.

Cases of DSP poisoning causing severe vomiting, nausea and diarrhoea symptoms in shellfish consumers were first recorded in the Netherlands in the 1960s and in Japan in the late 1970s. Since then similar problems have been recognised in Spain, France, Scandinavia, Thailand, Chile, Canada and New Zealand. The clinical symptoms of DSP often may have been mistaken for those of bacterial gastric infections and the problem

may be much more widespread than currently thought. Unlike PSP, no human fatalities have been reported and patients usually recover within 3 days. However, some of the toxins involved could act as stomach tumour promotors and thus produce chronic problems in shellfish consumers.

ASP was first documented in a serious outbreak of shellfish poisoning in eastern Canada in 1987. The memory loss associated with extreme cases of human intoxication led to the description of the syndrome as amnesic shellfish poisoning. A limited number of human mortalities have also been associated with ASP in Canada, with immunodepressed patients being most at risk. Humans affected had consumed mussels containing 300-1200 μg/g of domoic acid. To date the only positive detection of domoic acid in Australian shellfish refers to scallop viscera from Lakes Entrance, Victoria (August 1993) (one sample 26 μg/g; all others <20 μg /g) but the causative organism was not identified in that case. As a precautionary measure, the then Victorian Department of Health and Community Services forbid the sale or supply of scallops other than those which had the viscera removed. Maximum levels of domoic acid detected in New Zealand mussels have been up to 187 μg/g (Marlborough Sounds, Dec. 1994) with scallop digestive glands containing up to 600 μg/g. There have been no poisoning outbreaks in New Zealand.

The toxins associated with NSP are termed brevetoxins and exert their toxic effect by specific binding to site-5 of voltage-sensitive sodium channels. In humans, the symptoms of NSP intoxication include respiratory distress, as well as eye and nasal membrane irritation, caused principally by exposure to sea-spray aerosols and by direct contact with toxic algal blooms while swimming. No human fatalities from brevetoxin poisoning have ever been reported. The toxins implicated in neurological shellfish poisoning are considered to be primarily ichthyotoxins (fish killing toxins).

Risk characterisation

The serious and in some cases long-term nature of the toxicity associated with seafood toxins makes them a particularly important public health issue. However, there is still a very poor understanding of the target organs for toxicity and of the nature of any dose-response relationship associated with this toxicity. For these reasons, it is still difficult to identify a safe level of exposure to the respective toxins and, therefore, to provide an estimate of the margin of safety at various levels of exposure. Estimates of toxic dose levels have been made at times of algal blooms but it is difficult to get accurate estimates from this data. An acceptable daily intake (ADI) has not been established for any of the seafood toxins.

Dietary exposure estimates for shellfish toxins cannot be conducted in the same way as for other contaminants in food because of the sporatic nature of the contamination, with significant temporal and regional variation in the level of contamination. For the majority of samples tested, the levels of toxins are either zero or very low unless there is an algal bloom when the levels rise dramatically. The use of a overall mean or median contaminant level of toxin to determine normal consumption levels of toxin is therefore of little value.

For PSP, the available data suggests that moderate symptoms of toxicity can occur at intake levels of 120μg of saxitoxin. At the current regulatory level of 80 μg/100g of edible shellfish flesh, this level could be reached after consuming 150g of contaminated shellfish. The margin of safety in this case, therefore, is very small.

The data available suggest that there is a potential for significant health risk from consumption of shellfish contaminated with PSP, ASP, DSP or NSP and that the level of contamination should be kept as low as reasonably achievable.

Risk management

The current regulatory levels used in Australia and New Zealand (Health standards in Australia and Fisheries regulations in New Zealand) are pragmatically derived but are internationally recognised and have proved thus far to be effective in protecting public health. Until there is more information available on the individual toxins and the dose-response relationships with the major toxic endpoints, there is little basis for changing the current regulatory standards.

It is proposed the following regulations be established as food standards in the Joint Australia New Zealand Food Standards Code:

Paralytic shellfish poisoning (PSP)

It is proposed that the current regulatory standard which is used in both Australia and New Zealand, namely, 80 μg saxitoxin equivalent per 100 g edible shellfish flesh (0.8 mg/kg) be adopted as the joint Australia/New Zealand standard.

Amnesic shellfish poisoning (ASP)

It is proposed that the regulatory level currently used in Australia and New Zealand, namely, 20 mg domoic acid per kg of the edible shellfish flesh, be adopted as the joint Australia/New Zealand standard.

Diarrhetic shellfish poisoning (DSP)

It is proposed that the current New Zealand MAF standard of 20 μg okadaic acid per 100 g of the edible shellfish flesh (0.2 mg/kg) be adopted as the joint Australia/New Zealand standard.

Neurotoxic shellfish poisoning (NSP)

It is proposed that the current New Zealand MAF regulatory level of 20 MU/100g of edible shellfish flesh (200 MU/kg) be adopted as the joint Australia/New Zealand standard.

The proposed standards are as follows.

Substance	**Food**	**Proposed MPC**
Paralytic shellfish poisons (Saxitoxin equivalent)	Bivalve molluscs	0.80 mg/kg
Amnesic shellfish poisons (Domoic acid equivalent)	Bivalve molluscs	20 mg/kg
Diarrhetic shellfish poisons (Okadaic acid equivalent)	Bivalve molluscs	0.20 mg/kg
Neurotoxic shellfish poisons	Bivalve molluscs	200 MU[1]/kg

1. As defined in 'Recommended procedures for examination of seawater and shellfish' Irwin N. (ed.) 4th Ed. 1970, American Public Health Association Inc.

VINYL CHLORIDE MONOMER

SUMMARY OF THE TOXICOLOGICAL REVIEW AND RISK ASSESSMENT

Introduction

Vinyl chloride is a colourless vapour with a mild sweet odour which can exist in liquid form if it is kept under high pressure. Most of the vinyl chloride produced is used to make polyvinyl chloride (PVC). The most likely sources of exposure are inhalational (ie in air near plastics industries, hazardous waste sites and landfills), drinking water (from contaminated wells and PVC pipes) and from food in contact with PVC. PVC is used in the plastics industry to make a variety of products, some of which are used for covering foods.

The Australian *Food Standards Code* currently states that: "The proportion of vinyl chloride in any food shall not be greater than 0.05 mg/kg." This level was established in 1976 and was set on the limit of detection for vinyl chloride in food.

The New Zealand *Food Regulations 1984* control contamination from packaging materials under Regulation 265-Use of harmful containers prohibited. The regulation states: 'No person shall use, or permit to be used, in the preparation, packing, storage or delivery of a food for sale, any package, appliance, or container that yields or could yield to its contents any poisonous, injurious, or tainting substance'.

In Europe, the EC Directive 97/48/EC has established a maximum level for vinyl chloride of 0.01 mg/kg based on the level of detection.

In the US, plastics are considered under Part 109-Unavoidable contaminants in food for human consumption and food-packaging material. The legislation states: 'The manufacturer of food must at all times utilise quality control procedures which will reduce contamination to the lowest level currently feasible'.

No specific Codex standards have been established for food in contact with packaging substances.

Toxicological data

Orally administered vinyl chloride is rapidly absorbed. The metabolism is dose-dependent and a saturable process. Low oral doses are metabolised and excreted primarily in the urine. In contrast higher doses are mainly excreted, unchanged via the lung. The principal urinary metabolites are derived from the oxidative metabolism of vinyl chloride, involving the cytochrome P-450 system.

Virtually no previous studies have been undertaken in animals to ascertain the acute toxicological effects via the oral route. However, LC50s ranging from 294-595 g/m^3 have been determined for a range of animal species as inhalation is the main route of exposure in occupationally exposed humans.

Vinyl chloride is carcinogenic in rats at a dose of 1.3 mg/kg bw/day when administered via the oral route. The liver was one of the principal sites for occurrence of tumours. The Joint (FAO/WHO) Expert Committee on Food Additives (JECFA) review in 1984 suggested that a NOEL could not be established from the available sub-chronic and/or chronic animal studies.

No studies have reported cancer in humans following oral exposure to vinyl chloride. Epidemiological studies indicate a clear correlation between the incidence of liver angiosarcomas and occupational exposure to vinyl chloride or PVC. However, there is a paucity of data on the specific dose that is required via the inhalational route. Other cancers associated with occupational exposure to vinyl chloride include cancers of the brain, lung, pancreas, digestive tract, respiratory tract, lymphocytic system, and malignant skin melanoma.

Dietary exposure assessment

The most common route of exposure to vinyl chloride is via air (most likely near industrial sites, hazardous waste sites, and landfills); tobacco smoke, water and in food via migration from packaging materials.

Risk characterisation

Reports of adverse health effects in humans exposed to vinyl chloride have come almost exclusively from studies of workers exposed by inhalation in the workplace. Interpretation of these epidemiological studies is limited by the absence of data on the actual levels of exposure. However, studies in animals by both the inhalational and oral routes have provided an indication of the doses of vinyl chloride that may be associated with adverse effects.

Long-term effects attributable to inhalational exposure to vinyl chloride in humans include bone resorption, Raynaud's syndrome, scleroderma and fibrosis of the liver. Cancers associated with occupational exposure to vinyl chloride include cancers of the brain, lung, pancreas, digestive tract, respiratory tract, lymphocytic system, and malignant skin melanoma.

Chronic/carcinogenicity studies in animals via both the oral route has found that vinyl chloride is carcinogenic in rats, the liver one of the principal sites for occurrence of tumours. Other tumours reported include pulmonary angiosarcomas, extrahepatic abdominal angiosarcomas, and tumours of the Zymbal gland (unique to rats). A NOEL in experimental animals has not been established.

Genotoxicity studies suggest a correlation between the incidence of chromosomal aberrations and duration and level of exposure in occupationally exposed workers to inhaled vinyl chloride.
However, there is no evidence of genotoxicity effects in humans as a result of exposure to vinyl chloride which has migrated from packaging to food.

Foods may become contaminated with vinyl chloride as a result of migration of the monomer from plastics in contact with food. From the available data levels have ranged from not detectable (<0.01 ppm) to 18 ppm. The last Australian study conducted in 1975 which monitored vinyl chloride migration in a wide range of Australian food products found minimal levels in selected foods.

The overall conclusion is that while there is no evidence of adverse health effects resulting from the low level of exposure to vinyl chloride via food, the potential carcinogenic effects indicate that exposure to this substance should be kept as low as possible.

Risk management

It is proposed to reduce the maximum permitted concentration (MPC) for vinyl chloride in food to 0.01 mg/kg on the basis that exposure to this substance should be kept as low as possible.

The level of 0.01 mg/kg is the new level of detection for vinyl chloride. This level is consistent with the recently proposed EC level (97/48/EC). This would also be consistent with the 1984 JECFA recommendations that human exposure to vinyl chloride in food as a result of its migration from food-contact materials should be reduced to the lowest levels technologically attainable. The proposed level is shown below.

Substance	Food	Proposed MPC (mg/kg)
Vinyl chloride	All food	0.01

VINYLIDENE CHLORIDE

SUMMARY OF THE TOXICOLOGICAL REVIEW AND RISK ASSESSMENT

Introduction

Vinylidene chloride (VDC) is used extensively as a co-monomer in the manufacture of food packaging materials where low permeability to oxygen and water vapour is required together with resistance to oils, grease or alcohol and the ability to heat seal.

The Australian *Food Standards Code* currently states that: 'the proportion of vinylidene chloride in any food shall not be greater than 0.01 mg/kg'. This level was established in 1984 and was set on the limit of detection for vinylidene chloride in food.

The New Zealand *Food Regulations 1984* control contamination from packaging materials under Regulation 265-Use of harmful containers prohibited. The regulation states: 'No person shall use, or permit to be used, in the preparation, packing, storage or delivery of a food for sale, any package, appliance, or container that yields or could yield to its contents any poisonous, injurious, or tainting substance'.

No specific Codex standards have been established for food in contact with packaging substances.

In Europe, the EC (90/128/EEC) established a maximum level for vinylidene chloride of 0.05 mg/kg based on the level of detection.

In the US, plastics are considered under Part 109-Unavoidable contaminants in food for human consumption and food-packaging material. The legislation states: 'The manufacturer of food must at all times utilise quality control procedures which will reduce contamination to the lowest level currently feasible'.

Toxicological data

VDC is readily absorbed in animals following oral ingestion, is widely distributed in rats reaching maximal levels in the liver and kidneys but does not accumulate within the body. The major routes of metabolism involve oxidation and conjugation with glutathione and/or phosphatidyl ethanolamine prior to further conversions. It is eliminated as metabolites in the bile and urine, or at saturation via the breath.

VDC is toxic in animals after inhalation and ingestion. LD50 values following oral administration were approximately 1500 and 200 mg/kg in rats and mice, respectively. As with the inhalational route, the principal organs affected by oral administration of vinylidene chloride are the liver, kidneys, and lungs. No studies are available in humans on acute toxicity by the oral route.
Short-term (approximately 3 months) oral dosing studies in rats up to 1 mg/kg bw/day in rats and 2 mg/kg bw/day in dogs did not show any evidence of toxicity other than minimal reversible hepatic damage in rats.

Chronic/carcinogenic studies in rats for one year up to a dose of 30 mg/kg bw/day produced minimal hepatic changes, although a clear NOEL could not be established. There was some evidence from a separate study that renal inflammation could be induced in rats, following long-term oral administration of vinylidene chloride at 5 mg/kg bw/day. No evidence of increased tumour incidences could be established, however, some of these studies used insufficient numbers of animals and inadequate numbers of dose levels. On the basis of the currently available data NOELs could not be established for these studies.

Although VDC is genotoxic in a number of *in vitro* assays, including mammalian cells, there is only limited evidence for genotoxicity *in vivo*.

No effect on reproduction or foetal development has been found, other than those associated with maternal toxicity.

In humans severely overexposed to VDC (16000 mg/m3 by inhalation) via occupational exposure depression of the nervous system and kidney, liver and cardiovascular damage has been reported. Epidemiological studies have shown no evidence of carcinogenicity in humans, but were inadequate to evaluate VDCs carcinogenic risk.

Dietary intake assessment

The main sources of exposure to VDC are via the air, particularly in industrial areas, water and soil, and packaging materials. Occupational exposure to VDC results mainly from inhalation, but skin and eye contamination may also occur.

Generally, levels of vinylidene chloride reported to migrate into food have been quite low consistent with the high barrier properties of vinylidene chloride co-polymers.

Risk characterisation

The principle target organs for toxicity are the liver, kidneys, and lungs. On the basis of the currently available data a NOEL could not be established, however, a LOEL of 0.5 mg/kg bw/day produced minimal changes to liver histology. There is no evidence of carcinogenicity in rat studies. Although VDC is genotoxic in a number of *in vitro* assays, including mammalian cells, there is limited evidence of genotoxicity *in vivo*. Epidemiological studies have shown no evidence of carcinogenicity in humans, although the studies were considered inadequate. No effect on fertility has been observed and no foetal abnormalities occur, other than those associated with maternal toxicity.

Food may be contaminated by the migration of residual vinylidene chloride monomer from packaging materials containing VDC polymers. However, from the limited survey data available there is no evidence that VDC migration levels are high.

Overall, there does not appear to any public health and safety problems associated with oral exposure to vinylidene chloride at the levels found in foods due to migration from food packaging materials. There is, however, still a paucity of data in relation to potential carcinogenicity and, therefore, levels in food should be maintained as low as reasonably achievable.

Risk management

It is proposed that the current level of 0.01 mg/kg (ie, the limit of detection) should be retained, as shown below.

Substance	Food	Proposed MPC (mg/kg)
Vinylidene chloride	All food	0.01

PUBLIC COMMENTS

1. Comments in relation to the policy paper on the review of contaminants

Qld Dept of Primary Industries (Denis Hamilton)

- Generally in favour of proposing MPCs from non-toxicology data and then comparing the likely intakes with the toxicologically acceptable intakes at the risk assessment step.

- It is not in the interests of long-term sustainability to contaminate up to a permitted level, and MPCs need to be kept as low as possible for this reason.

- Prefer food standards to be reasonably comprehensive, rather than have guidelines develop for trading purposes.

Wrightson Nutrition

- A distinction needs to be made between contaminants and other restricted substances, particularly essential nutrients such as selenium, copper and zinc.

- Classification of essential nutrients as contaminants doesn't permit the management to optimal levels of nutrients in food.

South Australian Health Commission

- Need to consider other sources of exposure to contaminants besides food.
- A definition of a contaminant is a key requirement of the document.

- Further discussion of guidelines in a separate document.

- Suggest 'maximum permitted concentration' is more accurate than 'maximum level'

- No justification is given for removal of sampling plans and analytical protocols.

New Zealand Ministry of Health

- ANZFA should establish transparent scientific rationale for the development of any contaminant standard, including justification for development of any contaminant standard.

- Consideration should be given to New Zealand-specific dietary consumption patterns.

- Consideration should be given to WTO obligations.

- ANZFA should provide regulatory impact assessments for each standard.

- The mechanism for scientific peer-review of any new standard should be clearly identified.

New Zealand Ministry of Commerce

- Any future reference to COAG principles and regulatory impact statements should make reference to the New Zealand Quality of Regulation package including the draft Code of Good Regulatory Practice. If adopted by the NZ Govt agencies could be required to prepare Regulatory Impact Statements.

CSIRO Division of Animal Health

- ANZFA should also consider establishing standards for natural substances which inadvertently contaminate foods during agricultural production such as pyrrolizidine alkaloids and corynetoxins.

2. Comments in relation to P158 - Review of non-metals

BRI Australia Ltd

- Continue to support A303- Ergot in cereal grain- to provide an appropriate an realistic tolerance level of 0.5 mg/kg for ergot in cereal products.

- A standard of 0.5 mg/kg for ergot would be based on an internationally accepted standard.