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The New Zealand Mycotoxin Surveillance Program 06-14 Report Series

FW0617 Risk Profile Mycotoxin in the New Zealand Food Supply

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Scientific Interpretive Summary

This SIS is prepared by MPI risk assessors to provide context to the following report for MPI risk managers and external readers

The New Zealand Mycotoxin Surveillance Program 06-14 Report Series

FW0617 Risk Profile Mycotoxin in the New Zealand Food Supply

These reports are the outputs of MPIs ongoing mycotoxin surveillance programme. The nine reports form a series detailing the research undertaken over the last eight years to characterise and quantify the risk to the New Zealand public through the presence of mycotoxins in the food supply.

The nine reports are:

- Risk Profile: Mycotoxin in Foods 2006
- Aflatoxins in Maize Products 2008
- Aflatoxins and Ochratoxin A in Dried Fruits and Spices 2009
- Aflatoxins in Nuts and Nut Products 2010
- Dietary Exposure to Aflatoxins 2011
- Ochratoxin A in Cereal Products, Wine, Beer and Coffee 2011
- Trichothecene Mycotoxins in Cereal Products 2014
- Dietary Exposure to Ochratoxin A and Trichothecene Mycotoxins 2014
- Risk Profile: Mycotoxin in Foods 2014

Risk Profile Mycotoxin in the New Zealand Food Supply 2006

This report compiles the likely risks of the various categories of mycotoxins and previous occurrence data for New Zealand foods. This provides a single resource from which risk ranking future work on mycotoxins can be undertaken.

The report highlighted that Aflatoxins, Ochratoxin A and Trichothecenes had significant health concerns and data gaps on occurrence data prevented accurate risk assessments from being completed.

Other categories of mycotoxins, such as fumonisins and ergot alkaloids were prioritised as less of a dietary risk.

RISK PROFILE:
MYCOTOXINS IN THE NEW ZEALAND FOOD SUPPLY

Prepared as part of a New Zealand Food Safety Authority
contract for scientific services

by

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April 2006

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RISK PROFILE: MYCOTOXINS IN THE NEW ZEALAND FOOD SUPPLY

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SUMMARY

The purpose of a Risk Profile is to provide contextual and background information relevant to a food/hazard combination so that risk managers can make decisions and, if necessary, take further action. Risk Profiles include elements of a qualitative risk assessment, as well as providing information relevant to risk management. Risk profiling may result in a range of activities, e.g. immediate risk management action, a decision to conduct a quantitative risk assessment, or a programme to gather more data. Risk Profiles also provide information for ranking of food safety issues.

The current document contains individual risk profiles for the fungal toxins (mycotoxins) likely to be of greatest concern in New Zealand: aflatoxins, ochratoxin A, trichothecenes, fumonisins, zearalenone, ergot alkaloids and patulin. The information in the risk profiles was also used to provide a qualitative ranking of the risks to the New Zealander consumer due to mycotoxin exposure.

The following conclusions were reached:

- There is consistent evidence to support a causal link between chronic aflatoxin exposure and serious human disease (primary liver cancer). Exposure levels in New Zealand are likely to represent a very low level of risk, although better information on the contribution of maize to dietary aflatoxin exposure would decrease the uncertainty around this conclusion.
- There is some evidence to support a link between human kidney disease and exposure to ochratoxin A, however, further work is required to establish a causal relationship. Dietary exposure to ochratoxin A in New Zealand may approach tolerable daily intake levels and further investigation, particularly of the occurrence of ochratoxin A in bread and other wheat products, would help to clarify the situation.
- There is little evidence that the trichothecenes T2/HT2 toxin occur in New Zealand or Australian cereal crops. Confirmation of this observation would allow attention to be focused on other issues.
- There is very good evidence that trichothecenes are able to cause outbreaks of gastrointestinal disease in humans. Current New Zealand exposure estimates appear unreasonably low compared to estimates made in Europe, where crop contamination levels appear to be similar. Some European exposure estimates approach the tolerable daily intakes and it would seem prudent to continue some New Zealand focus on this issue, particularly the potential for trichothecene contamination of wheat and wheat-based products.
- While there is an increasing body of information linking fumonisin exposure to serious human diseases, there is virtually no information on the exposure of New Zealanders to these mycotoxins. While the fungal species that produce fumonisins have only rarely been reported in New Zealand, our considerable level of cereals imports mean that potential for dietary exposure still exists.
- Evidence linking zearalenone exposure to human disease states is fragmentary and inconsistent. However, the exposure of New Zealanders to zearalenone may be significant when compared to tolerable daily intakes. Further investigation of the role of wheat-based foods in zearalenone dietary exposure in New Zealand would help to clarify this issue.

- Ergotism represents a serious and real human health risk, however, in the context of current agricultural and food manufacturing practices, the dietary risk appears to be extremely low.
- While toxicological experiments have raised concerns about patulin exposure, there is no evidence linking patulin exposure to human disease. However, high levels of patulin contamination are indicative of poor manufacturing practice and a level of ongoing monitoring is probably justified.

Ranking of risk across different mycotoxins will involve a degree of subjectivity, as there is not absolute measure for the relative seriousness of different health effects. However, the proximity of estimates of OTA exposure to critical exposure limits suggests that improved estimates of New Zealand exposure should be ranked highly.

The seriousness of the health outcomes resulting from aflatoxin exposure and the relatively high weight of evidence supporting a casual role suggest that further work on sources of dietary exposure (e.g. maize) should also be ranked highly.

GLOSSARY OF TERMS, ABBREVIATIONS AND ACRONYMS

AFB_1, AFB_2, AFG_1, AFG_2, AFM_1
: Aflatoxin B_1, aflatoxin B_2, etc.

AMBS
: Australian Market Basket Survey. The previous name for the Australian Total Diet Survey

Codex
: the Codex Alimentarius Commission was created in 1963 by FAO and WHO to develop food standards, guidelines and related texts such as codes of practice under the Joint FAO/WHO Food Standards Programme

DON
: Deoxynivalenol

DAS
: Diacetoxyscirpenol

ESR
: Institute of Environmental Science and Research Limited

FAO
: the Food and Agriculture Organization of the United Nations

FB_1, FB_2, FB_3
: Fumonisin B_1, fumonisin B_2, fumonisin B_3

Food Standards Code
: the Australia New Zealand Food Standards Code. The Code is the official legal document that is given legal force via State, Territory, Commonwealth and New Zealand food legislation.

GAP
: Good Agricultural Practice is the nationally authorised safe uses of pesticides under actual conditions necessary for effective and reliable pest control. GAP encompasses a range of pesticide applications up to the highest authorised use, applied in a manner which leaves a residue which is the smallest practicable.

HACCP
: Hazard Analysis Critical Control Point. The systematic identification and management of risks associated with the manufacture, distribution and use of food ingredients

HT2
: HT-2 toxin

IUPAC
: The International Union of Pure and Applied Chemistry (IUPAC) is an international non-governmental organisation devoted to the advancement of chemistry.

JECFA
: the Joint FAO/WHO Expert Committee on Food Additives

NIV
: Nivalenol

NZFSA
: New Zealand Food Safety Authority

NZTDS	New Zealand Total Diet Survey
OTA	Ochratoxin A
PTWI	Provisional Tolerable Weekly Intake is the end-point used by JECFA for food contaminants such as heavy metals with cumulative properties. A PTWI is an estimate of the amount of a substance (contaminant) in food or drinking water that can be ingested weekly over a lifetime without appreciable health risk
T2	T-2 toxin
TDI	Tolerable Daily Intake is the end-point used by JECFA and other bodies for food contaminants with non-cumulative properties. A TDI is an estimate of the amount of a substance (contaminant) in food or drinking water that can be ingested daily over a lifetime without appreciable health risk.
Water activity	Water activity reflects the active part of moisture content or the part which, under normal circumstances, can be exchanged between the product and its environment
WHO	World Health Organization.

1 INTRODUCTION

The purpose of a Risk Profile is to provide contextual and background information relevant to a food/hazard combination so that risk managers can make decisions and, if necessary, take further action. The place of a risk profile in the risk management process is described in "Food Administration in New Zealand: A Risk Management Framework for Food Safety" (Ministry of Health/Ministry of Agriculture and Forestry, 2000). Figure 1 outlines the risk management process.

Figure 1: Risk Management Framework

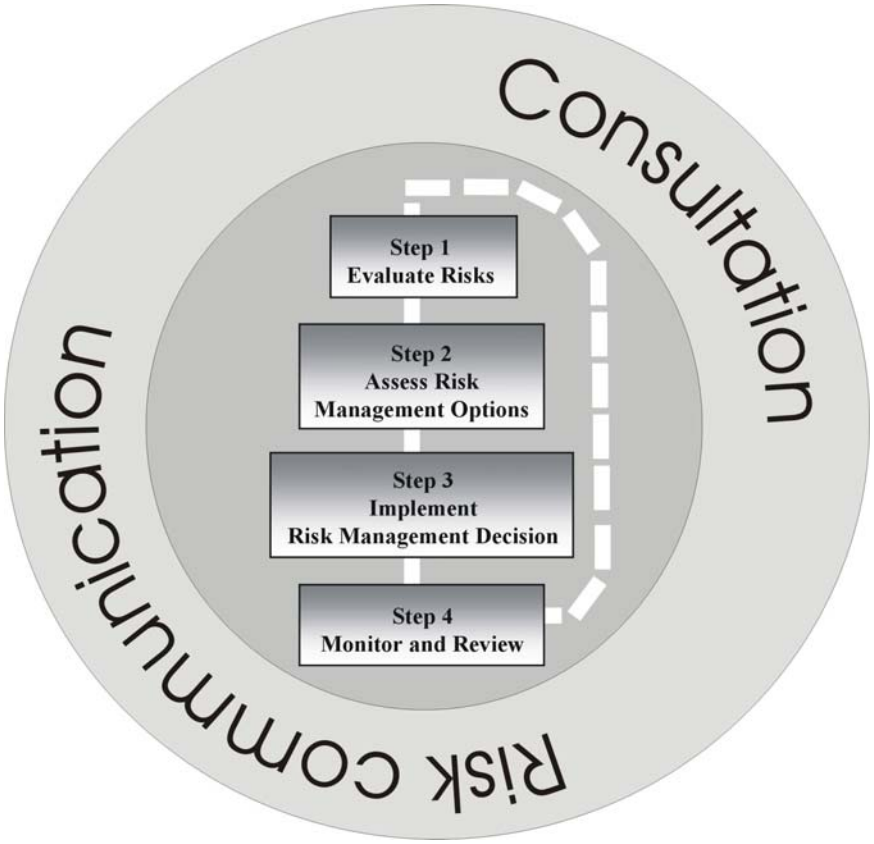


Figure reproduced from "Food Administration in New Zealand. A risk management framework for food safety" (Ministry of Health/Ministry of Agriculture and Forestry, 2000).

In more detail, the four step process is:

1. Risk evaluation

- identification of the food safety issue
- **establishment of a risk profile**
- ranking of the food safety issue for risk management
- establishment of risk assessment policy
- commissioning of a risk assessment
- consideration of the results of risk assessment

2. Risk management option assessment

- identification of available risk management options
- selection of preferred risk management option
- final risk management decision

3. Implementation of the risk management decision

4. Monitoring and review.

The Risk Profile informs the overall process, and provides an input into ranking the food safety issue for risk management. Risk Profiles include elements of a qualitative risk assessment. However, in many cases a full exposure estimate will not be possible, due to data gaps, particularly regarding the level of hazard in individual foods.

The Risk Profiles also provide information relevant to risk management. Based on a Risk Profile, decisions are made regarding whether to conduct a quantitative risk assessment, or take action, in the form of gathering more data, or immediate risk management activity.

This Risk Profile concerns seven mycotoxins or groups of mycotoxins (aflatoxins, ochratoxin A, trichothecenes, fumonisins, zearalenone, ergot alkaloids and patulin). An initial screening exercise was carried out which concluded that there was evidence that these mycotoxins were:

- A potential or actual human health risk in New Zealand or other countries; and
- Present in the New Zealand food supply.

Information on fungal species responsible for the production of each mycotoxin is reviewed in the relevant section, but has also been summarised in Appendix 1, for easy reference.

The sections in this Risk Profile are organised as much as possible as they would be for a conventional qualitative risk assessment, as defined by Codex (1999).

Hazard identification, including:

- A description of the chemical(s).
- A description of the food group.

Hazard characterisation, including:

- A description of the adverse health effects caused by the chemical.
- Dose-response information for the chemical in humans, where available.

Exposure assessment, including:

- Data on the occurrence of the hazard in the New Zealand food supply.
- Data on the consumption of the food group by New Zealanders.
- Qualitative estimate of exposure to the chemical (if possible).
- Overseas data relevant to dietary exposure to the chemical.

Risk characterisation:

- Information on the number of cases of adverse health effects resulting from exposure to the chemical with particular reference to the identified food (based on surveillance data) or the risk associated with exposure (based on comparison of the estimated exposure with exposure standards).
- Qualitative estimate of risk, including categorisation of the level of risk associated with the chemical in the food.

Risk management information

- A description of the food industry sector, and relevant food safety controls.
- Information about risk management options.

Conclusions and recommendations for further action

1.1 Main Information Sources

Information on the toxicology of and exposure to mycotoxins has been reviewed or otherwise considered by a number of groups. These assessments were major resources for the current project. Sources included:

- JECFA (the Joint FAO/WHO Expert Committee on Food Additives). Assessment reports were accessed at: http://www.inchem.org/
- SCF (the EU Scientific Committee on Food). Opinions were accessed at: http://europa.eu.int/comm/food/fs/sc/scf/index_en.html
- IARC (the International Agency for Cancer Research). Monographs were accessed from ESR's standing collection. Summaries can be accessed at: http://www.inchem.org/

The European Union under their scientific co-operation programme (SCOOP) have carried out assessments of food contamination and dietary exposure to various mycotoxins within Europe and Scandinavia. Reports of co-operation on aflatoxins, ochratoxin A, *Fusarium* toxins (trichothecenes, fumonisins, zearalenone), and patulin were obtained from a number of web and retail sources.

Reports on surveys carried out by the UK Food Standards Agency (FSA) and, before them, the Ministry of Agriculture, Fisheries and Food were also used extensively and can be accessed at: http://www.foodstandards.gov.uk/

More recent and additional information than that included in these resources was located by general searching of the World Wide Web (internet) and use of specific citation databases, including:

- PubMed. Accessed at: http://www.ncbi.nlm.nih.gov/entrez/query.fcgi?DB=pubmed
- Scopus. Accessed at: http://www.scopus.com/scopus/home.url

2 AFLATOXINS

2.1 Hazard Identification

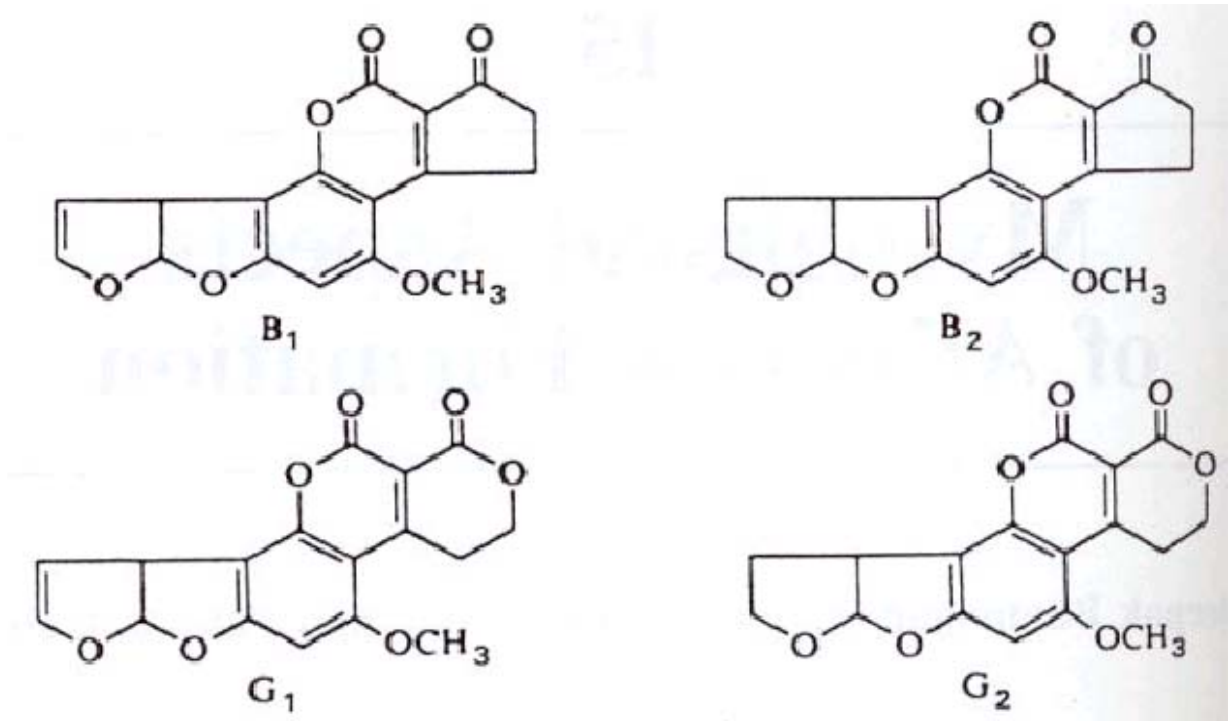
Aflatoxins are secondary metabolites produced by three species of *Aspergillus* mould: *A. flavus, A.. parasiticus* and *A. nomius* (JECFA, 1998). *A. flavus* occurs in all tropical and subtropical regions and is particularly associated with peanuts and other nuts, maize and other oilseeds. *A. parasiticus* is less widely distributed and is usually only associated with peanuts (Pitt and Tomaska, 2001).

2.1.1 Structure and nomenclature

While the aflatoxins comprise a group of about 20 related compounds, the four major naturally-occurring compounds are aflatoxins B_1, B_2, G_1 and G_2. The 'B' and 'G' refer to the blue and green fluorescent colours produced by these compounds under UV light, while the subscripts '1' and '2' refer to major and minor components respectively (Pitt and Tomaska, 2001). The '2' compounds are dihydro derivatives of the major ('1') metabolites. Chemical structures are shown in Figure 2. Aflatoxins M_1 and M_2 are hydroxylated metabolites of the respective 'B' aflatoxins produced when ruminant animals consume aflatoxin-contaminated feed. The 'M' aflatoxins may be excreted in milk (Pitt and Tomaska, 2001). Aflatoxins are fat soluble (lipophilic).

Reference of 'aflatoxins' or 'total aflatoxins' can be taken to refer to the sum of B and G aflatoxins.

Figure 2: Structure of aflatoxins



Reproduced from Eaton and Groopman, (1994)

2.1.2 Occurrence

A. flavus produces only 'B' aflatoxins (AFB_1 and AFB_2), with only about 40% of isolates producing toxins. *A. parasiticus* produces both 'B' (AFB_1 and AFB_2) and 'G' (AFG_1 and AFG_2) aflatoxins, with virtually all isolates producing toxins (Klich and Pitt, 1988). The situation for *A. nomius* appears to be similar to that for *A. parasiticus.*

Aflatoxin B_1 is the most commonly occurring aflatoxin in foods and is also the compound which has been most thoroughly studied in toxicological studies.

A. flavus occurs widely in the environment, but *A. parasiticus* is considerably less common. However, some regional specificities exist and *A. parasiticus* is commonly isolated from peanuts in the United States, South Africa and Australia.

Fungal infection and consequent aflatoxin contamination can occur in field crops prior to harvest or during post-harvest storage if the moisture content of the crop exceeds critical values for fungal growth (JECFA, 1998). Fungal growth and subsequent toxin production are favoured by factors which place the host plant under stress such as high temperature, drought, and high insect activity.

Aflatoxin contamination is most commonly associated with peanuts and peanut products, dried fruit, tree nuts, spices, figs, crude vegetable oils, cocoa beans, maize, rice, cottonseed and copra (JECFA, 1998). Consumption of aflatoxin-contaminated feed by animals can lead to occurrence of aflatoxins (mainly the hydroxylated metabolite AFM_1) in meat, eggs and milk.

Most of these crops are not grown in New Zealand. Surveillance of fungal infections of New Zealand grown grain found no *Aspergillus* species (Sayer and Lauren, 1991). This is consistent with expert opinion, that aflatoxigenic species of *Aspergillus* are unlikely to occur in New Zealand (Pitt JI, personal communication).

2.1.3 Sampling for aflatoxin analysis

The distribution of aflatoxins throughout any contaminated product can be very uneven. Even contamination of the occasional nut or grain, less than 1 in 10,000 in a lot sample, can lead to a significant average level of contamination in the product. FAO in their paper on aflatoxins in peanuts and corn (FAO, 1993) note that only a small percentage of kernels are contaminated, and these may amount to no more than 0.03% of kernels when the lot concentration in peanuts is 5 μg/kg aflatoxin. Shotwell *et al*. (1974) reported finding over 400,000 μg/kg aflatoxin in individual contaminated corn kernels.

The process of testing a lot for aflatoxins involves three main steps; sampling the bulk lot of product, sub-sampling to provide a sample for analysis, and analytical determination (including sample extraction and clean-up). The uneven distribution makes sampling difficult, especially sub-sampling within the laboratory, if the final result is to give an estimation of the true level of contamination in the original product. Once a food has been ground and mixed, such as during processing into flour, the distribution of aflatoxins becomes more uniform and sample sizes can be smaller (Love, 1999). If the effect of non-

homogeneity is to be minimised, lot samples must be large and broken down in such a manner that the final test sample will contain a representative portion of every item.

Variability in test results can be reduced by (Whitaker and Park, 1994):

- Taking large lot samples (30 kg is recommended by the EU for lots of greater than 50 tonnes.
- Comminute whole sample before subsampling.
- Increase size of subsample.
- Increase number of analytical replicates.
- Use more precise quantification method (HPLC, rather than TLC).

2.2 Hazard Characterisation: Adverse Health Effects

The aflatoxins vary in their toxicity with AFB_1 generally agreed to be the most toxic compound. AFG_1 appears to be toxicologically similar to AFB_1, although it has been tested much less extensively. Aflatoxin M_1, the hydroxylated metabolite of AFB_1 appears to be approximately an order of magnitude less toxic than AFB_1 (Cullen *et al.*, 1987). The following discussion of adverse effects and toxicology generally relate to AFB_1 unless stated otherwise.

2.2.1 Conditions

AFB_1 has been demonstrated to exhibit both acute and chronic toxicity in a wide range of animal species (Eaton and Groopman, 1994). The liver is the principal target organ for acute (and chronic) toxicity. Effects on the lung, myocardium and kidneys have also been reported in some studies. Acute toxicity in humans has occasionally been reported in Africa and Asia following consumption of contaminated rice, maize or peanuts. Symptoms include vomiting, diarrhoea, abdominal pain and fever.

Chronic effects of aflatoxins in humans mainly relate to effects on the liver including primary liver cancer (PLC), chronic hepatitis, jaundice, hepatomegaly and cirrhosis. Most investigative studies have concentrated on the association between AFB_1 ingestion and primary liver cancer (JECFA, 1998).

2.2.2 Toxicity

2.2.2.1 Acute toxicity

Acute toxicity of AFB_1 has been determined in a wide range of animal species (summarised in Cullen and Newberne, 1994). LD_{50}, the lethal dose for 50% of test subjects, values ranged from 0.3 mg/kg body weight (rabbit, intraperitoneal) to 18 mg/kg body weight (rat or chicken, oral). In all species symptoms included acute liver haemorrhagic necrosis, while bile duct hyperplasia was also a common symptom.

While no estimates of acute human toxicity are available, estimates of sub-chronic human toxicity can be derived from limited cases of aflatoxicosis outbreaks.

- In 1974 contaminated corn caused illness in 397 people in a cluster of villages in Northwest India (Krishnamachari *et al.*, 1975). Of those affected 108 died, mainly from gastrointestinal haemorrhage. Levels of aflatoxin in the corn were found to be in the

range 0.25 to 15 mg/kg. The daily exposure to aflatoxin was estimated to be at least 55 μg/kg body weight for an unknown number of days. A 10-year follow-up found that survivors recovered fully with no long-term ill effects (FDA, 1992).

- In 1982 an outbreak of aflatoxicosis occurred in Kenya (Ngindu *et al*., 1982). There were 20 hospital admissions with a 60% case fatality rate. Aflatoxin exposure was estimated to be at least 38 μg/kg body weight for an unknown number of days.
- In a deliberate suicide attempt, a laboratory worker self-administered 12 μg/kg body weight of aflatoxin B_1 for two days followed by 11 μg/kg body weight of AFB_1 for fourteen days after an interval of six months. Except for transient rash, nausea and headaches there were no ill effects and a 14-year follow-up, including tests for liver function, demonstrated no long-term effects (FDA, 1992).
- A further outbreak of aflatoxicosis occurred in Kenya in 2004, due to aflatoxin contamination of stored maize. A total of 317 cases were reported, with 125 fatalities (Azziz-Baumgartner *et al*., 2005). Samples of maize were analysed and found to contain AFB_1 at levels up to 8 mg/kg. No estimate of dietary exposure was made.

2.2.2.2 Chronic toxicity

Aflatoxins are capable of causing liver cancer in most species studied and have been classified as human carcinogens (IARC, 1993).

Non-cancer chronic effects reported in humans include kwashiorkor (protein-energy malnutrition), Reye's syndrome and cirrhosis (Hall and Wild, 1994). However, these effects have not been reported as consistently as carcinogenic effects.

Oral administration of mixtures of aflatoxins or AFB_1 in a range of animal species has caused hepatocellular and/or cholangiocellular liver tumours in all species tested except mice (IARC, 1993; JECFA, 1998).

There is some evidence to suggest that humans are at lower risk of adverse outcomes through exposure to aflatoxins than other species and there is some disagreement in epidemiological studies as to whether aflatoxin exposure represents a cancer risk in isolation from other risk factors, such as hepatitis B (JECFA, 1998).

2.2.3 Toxicological assessment

JECFA reviewed the toxicity of aflatoxins most recently in 1998. They concluded that aflatoxins were human liver carcinogens and that AFB_1 was the most potent of the carcinogens, with aflatoxin M_1 (AFM_1) being approximately one order of magnitude less toxic. The potency of aflatoxins in hepatitis B positive individuals is substantially higher than in those not carrying the disease.

ANZFA (1999; now known as FSANZ) reviewed aflatoxin toxicity and concurred with the conclusions of JECFA.

IARC (International Agency for Research on Cancer) concluded that there was sufficient evidence in humans for the carcinogenicity of naturally occurring mixtures of aflatoxins and for AFB_1 (IARC, 1993). IARC uses the classification of "sufficient evidence of carcinogenicity" (Group 1) when it considers a causal relationship has been established

between exposure to the agent and human cancer, and that there can be reasonable confidence that this association is not the result of chance, bias or confounding (IARC, 1993). Additional information has been reviewed more recently without any amendment to the earlier opinion (IARC, 2002).

2.2.4 Proposed mechanisms of carcinogenicity

While a definitive mechanism for aflatoxin carcinogenesis in humans has not been determined, considerable research has been carried out with suggestive results.

Aflatoxins are categorised as 'bulky mutagens': a classification which includes polycyclic aromatic hydrocarbons and aromatic amines. Literature suggests that such mutagens cause a cell to become tumourigenic by reacting directly with DNA to form DNA adducts. These adducts or their breakdown products are responsible for generating mutations efficiently through mechanisms such as adduct-induced base ionization, adduct-induced base wobble, and adduct-induced base rotation (Loechler, 1994).

AFB_1 is metabolised in the liver by cytochrome P450 enzymes to the 8,9-epoxide, amongst other species. While shortlived, the epoxide is extremely reactive and is believed to be the principal mediator of cellular injury (McLean and Dutton, 1995). The epoxide can form adducts with a range of cellular macromolecules, including DNA, RNA and proteins.

The *p53* tumour suppressor gene has been found to be mutated in a majority of human cancers, with a wide variation in the number and type of mutations between cancers of different tissues (Greenblatt *et al.*, 1994). A particular example of this has been found in liver cancer subjects from regions of high aflatoxin exposure, involving a G→T transversion at the third base of codon 249 of the gene. Two independent studies in Africa (Bressac *et al.*, 1991) and China (Hsu *et al.*, 1991) reported this gene mutation to be present in approximately 50% of hepatocellular carcinomas (HCC) examined. No such codon 249 mutations were found in HCCs in Britain, an area of low aflatoxin exposure (Challen *et al.*, 1992). Subsequent studies have generally confirmed these trends (see review in Jackson and Groopman, 1999).

These ecological observations have been supported by *in vitro* mutagenesis studies in bacteria (Foster *et al.*, 1983) and human cancer cell lines (Aguilar *et al.*, 1993), which have shown that exposure to aflatoxins causes almost exclusive G→T transversion at the third base of codon 249.

Several studies which examined both codon 249 mutations and biomarkers of aflatoxin exposure in HCC cases failed to find a significant association between the occurrence of aflatoxin-DNA or aflatoxin-albumin adducts and codon 249 mutations (Hsieh and Atkinson, 1995; Soini *et al.*, 1996; Lunn *et al.*, 1997). However, it should be noted that the presence of aflatoxin adducts is an indication of recent aflatoxin exposure and the significance of these results is uncertain.

2.2.5 Carcinogenic potency of AFB_1

The carcinogenic potency of a chemical describes the mathematical relationship between exposure and response. While in simple cases this may relate to the slope of the dose-response curve, when derived from epidemiological studies the potency may include

contributions from a range of other factors such as disease status (e.g. hepatitis B) and other lifestyle factors (e.g. alcohol consumption). Potencies may be expressed in terms of additive risk due to a condition such as exposure to a carcinogen, or multiplicative or relative risk. The general form of these two models can be expressed as:

$r_M (t, E) = r_0(t) \times f_M(E)$ multiplicative model

$r_A(t, E) = r_0(t) + f_A(E)$ additive model

Where $r_M(t, E)$ and $r_A(t, E)$ are functions that describe cancer incidence as a function of age and exposure. For the aflatoxin models discussed in this document these figures will represent the total annual incidence of hepatocellular carcinoma per 100,000 of population. Similarly, $r_0(t)$ is the incidence rate for unexposed individuals, and $f_M(E)$ and $f_A(E)$ are functions describing the effect of exposure on the background incidence rate. In simple cases the 'f' term will be the product of an exposure estimate and a potency factor and will represent the absolute (f_A) or fractional (f_M) excess cancer incidence due to exposure to aflatoxins or some other carcinogen (JECFA, 1998).

JECFA (1998) reviewed estimates of additive potency from a range of studies and found estimates to be in a fairly consistent range of 0.10-0.38 incidence/year/100,000 of population for exposure of 1 ng/kg body weight/day, with the incidence referring to primary liver cancer. These figures made no correction for the contribution of hepatitis B positivity to primary liver cancer incidence.

Several investigators have modelled the risk of liver cancer for HBsAg (hepatitis B surface antigen) positive and HBsAg negative subjects separately and derived differential estimates of potency. These are summarised in Table 1.

Table 1: Potency estimates for risk of primary liver cancer in humans from aflatoxin exposure based on epidemiological data, with reference to hepatitis B status

Model type	Potency (incidence per 100,000 for exposure to 1 ng/kg body weight/day of aflatoxin) (upper 95th % CL)		Source Population	Reference
	HBsAg +ve	HBsAg -ve		
Additive	0.50 (0.77)	0.036 (0.079)	China (Guangxi Province)	Croy and Crouch, 1991 (in JECFA, 1998)
Additive	0.43 (0.64)	0.031 (0.06)	China (Guangxi Province)	Wu-Williams *et al.*, 1992
Additive	0.33	0.013	China (Guangxi Province)	Bowers *et al.*, 1993
Multiplicative (background rate = 2.8)	0.094 (0.19)	0.0037 (0.006)	China (Guangxi Province)	Wu-Williams *et al.*, 1992
Multiplicative (background rate = 3.4)	0.046 (0.08)	0.0018 (0.0032)	China (Guangxi Province)	Hosenyi, 1992
Multiplicative (background rate = 3.4)	0.11	0.011	China (Shanghai)	Qian *et al.*, 1994
Multiplicative (background rate = 3.4)	0.37	0.0082	Taiwan	Wang *et al.*, 1996

CL = Confidence Limit

Estimates of carcinogenic potency from the studies summarised in Table 1 are consistent in suggesting approximately 10-30 times greater potency of aflatoxins in subjects who are HBsAg positive, independent of model type.

JECFA considered available potency information and chose potency values of 0.3 cancers/year per 100,000 population per ng aflatoxin/kg body weight/day for HBsAg+ individuals with an uncertainty range of 0.05 to 0.5, and a potency of 0.01 cancers/year per 100,000 population per ng aflatoxin/kg body weight/day for HbsAg- individuals with an uncertainty range of 0.002 to 0.03 (JECFA, 1998).

These cancer potencies are based on epidemiological studies conducted in Asia and Africa. Gorelick *et al.* (1994) and others have questioned the applicability of these figures to populations in developed countries. They compared liver cancer rates between high and low aflatoxin-contamination areas of the United States and derived a lower potency estimate of 0.003 cancers/year per 100,000 population per ng aflatoxin/kg body weight/day (Gorelick *et al.,* 1994). This estimate of potency does not consider the impact of hepatitis B status, but notes that incidence of hepatitis B is much lower in the United States than in Asia and Africa.

Carcinogenic potency has also been determined by a number of investigators using animal models. The estimates (extrapolated to humans using a body weight to the 0.75 power scaling factor) range from 0.05 per 100,000 per year per 1 ng AFB_1/kg body weight/day (Syrian golden hamster; Moore *et al.*, 1982) to 37 per 100,000 per year per 1 ng AFB_1/kg body

weight/day (Fischer 344 rat; Cullen *et al.*, 1987). All of the estimates of potency derived from animal studies are greater than the potencies derived for HBsAg negative humans from epidemiological studies. The most likely explanation is that these differences are due to genuine lower sensitivity in humans, compared to animal species, explained in part by more efficient DNA repair mechanisms (JECFA, 1998).

2.3 Exposure Assessment

2.3.1 Aflatoxins in the New Zealand food supply

Table 2 summarises available information on levels of aflatoxin in food available in New Zealand. The method of analysis was thin layer chromatography (TLC).

Table 2: Aflatoxins in New Zealand foods

Year	Food	Samples tested	Results Number positive (percent, range µg/kg aflatoxins measured)	Reference
Surveys				
1977	Peanut kernels	16	2 (13%, 5-6 AFB_1)	Stanton, 1977
	Barley	8	ND	
	Rice	5	ND	
	Other*	9	ND	
1991	Peanuts#	10	4 (40%, 30-200 Total)	Lake *et al.*, 1991
	Peanut butter	3	ND	
	Tree nuts	4	ND	
	Popcorn	1	ND	
	Figs	3	ND	
1999	Peanut confectionery	87	9 (10%, 3-200 Total)	Stanton, 1999
	Peanut sauces	49	12 (24%, 1-13 Total)	
	Peanut butter	17	6 (35%, 1-9 Total)	
	Raw peanuts	2	1 (50%, 26 Total)	
2000	Corn (maize) snacks	24	ND	Stanton, 2000a
	Maize products	7	ND	
	Breakfast cereals	25	ND	
	Other cereals, flour and rice	24	ND	
	Pasta, noodles, biscuits	10	ND	
	Peanuts	34	ND	
	Tree nuts and oilseeds	27	ND	
	Pulses	14	ND	
	Dried fruit	35	ND	
Import Monitoring§				
1996	Peanuts	46	6 (13%, 3-87 Total)	
1997	Peanuts	169	12 (7%, 7-118 Total)	
	Pistachios	2	ND	
1998	Peanuts	67	1 (1.5%, 15 Total)	
	Pistachios	8	ND	

Year	Food	Samples tested	Results Number positive (percent, range µg/kg aflatoxins measured)	Reference
1999	Peanuts Peanut butter Pistachios	100 7 13	6 (6%, 10-355 Total) 2 (29%, 4-20 Total) 1 (8%, 40-245 Total)	
2000	Peanuts Peanut butter	103 19	10 (10%, 2-250 Total) ND	
2001	Peanuts Peanut butter Pistachios	96 27 16	2 (2%, 7-40 Total) ND 3 (19%, 7-305 Total)	
2002	Peanuts Peanut butter Pistachios	144 46 18	7 (5%, 1-445 Total) ND 1 (6%, 8 Total)	
2003	Peanuts Peanut butter Pistachios	103 25 28	7 (7%, 6-384 Total) ND ND	
2004	Peanuts Peanut butter Pistachios	121 36 34	22 (18%, 1-645 Total) 3 (8%, 2-8 Total) 6 (18%, 1-157 Total)	

AFB_1 = aflatoxin B_1 Total = aflatoxins $B_1 + B_2 + G_1 + G_2$

ND = Not detected. Limit of detection = 1 µg/kg for most studies, except Stanton (1977) which had limits of detection in the range 2-4 µg/kg

* One sample of each of peanut butter, soya beans, soya bean oil, sunflower seed oil, wheat flour, soya flour, wholemeal flour, pearl barley and whole millet

Includes two samples rejected at border inspection

§ Import monitoring data is expressed in terms of lots or consignments. Testing of a lot for aflatoxin may involve testing of up to 22 individual samples. Data reported here only applies to testing carried out by ESR. Concentrations reported are from individual subsamples.

Aflatoxins have not been detected in foods available on the New Zealand market, other than peanuts and peanut products. However, this observation should be treated with some caution since relatively small numbers of non-peanut foods have been examined. In particular, import testing of pistachios has regularly detected aflatoxin-positive shipments, but no retail surveillance has been carried out for this commodity.

Raw milk samples are analysed for AFM_1 as part of the NZFSA's Dairy residue Monitoring Programme (http://www.nzfsa.govt.nz/consumers/food-safety-topics/chemicals-in-food/residues-in-food/dairy-residue-monitoring-programme.htm). Results available from 2002/2003 and 2003/2004 show positive detection of AFM_1 in one sample out of 250, at a level above the limit of detection, but below the default maximum residue limit of 0.1 mg/kg.

2.3.2 Aflatoxins in the Australian food supply

A significant proportion of food imported into New Zealand originate in Australia. FSANZ (then ANZFA) reviewed risks associated with aflatoxins in foods (ANZFA, 1999). Information relevant to the current risk profile is summarised in Table 3.

Table 3: Aflatoxins in Australian foods (1983-1997)

Food	Samples tested	Results Number positive (percent, maximum µg Total aflatoxins /kg)	Data source
Almonds	70	1 (1%, 12)	AGAL
Almonds	135	ND	AMDC
Cashews	109	ND	AGAL
Cashews	223	1(0.5%, 30)	AMDC
Cereals	147	ND	AGAL
Cereals	248	41 (17%, 12)	AMDC
Coffee, tea	624	ND	AGAL
Coffee, tea	17	ND	AMDC
Confectionery	29	1 (3%, 143)	AGAL
Dairy products	16	ND	AGAL
Dairy products	227	10 (4%, 2)	AMDC
Fruit (fresh and dried)	93	ND	AGAL
Fruit (fresh and dried)	20	2 (10%, 4)	AMDC
Hazelnuts	55	ND	AGAL
Hazelnuts	100	1 (1%, 20)	AMDC
Maize	89	53 (65%, 295)	AMDC
Maize meal	4	4 (100%, 120)	AMDC
Maize – corn flakes	265	1 (0.4%, 3)	AMDC
Miscellaneous foods	90	14 (16%, 169)	AGAL
Miscellaneous foods	1035	246 (24%, 40)	AMDC
Miscellaneous nuts	121	9 (7%, 104)	AGAL
Miscellaneous nuts	496	98 (20%, 1085)	AMDC
Peanuts	1135	98 (9%, 819)	AGAL
Peanuts	11956	4100 (34%, 4000)	AMDC
Pistachios	494	26 (5%, 710)	AGAL
Pistachios	54	3 (6%, 40)	AMDC
Satay products	65	34 (52%, 128)	AGAL
Satay products	20	10 (50%, 29)	AMDC
Walnuts	52	ND	AGAL
Walnuts	162	12 (7%, 5)	AMDC

ND = Not detected, AGAL = Australian Government Analytical Laboratories, AMDC = Australian Mycotoxin Data Centre

Maize, peanuts and peanut products were the most commonly contaminated foods, of those analysed. While it is not known what the intended use of the maize samples was (human or animal nutrition), the frequency of aflatoxin contamination of maize appears to be high, although there is little evidence of aflatoxin in processed maize products (corn flakes). These

results are consistent with reports that the dry milling process, which produces corn flakes, results in a 90-94% decrease in the levels of aflatoxin in corn (JECFA, 1998). The low incidence of aflatoxin in corn flakes may be due to the processing steps reducing toxin levels to an undetectable amount, rather than absence of the toxins in the intact kernels. The incidence of aflatoxins in peanut products (satay products) is higher than in peanuts. This may be due to lower grade nuts being used for further processing.

The 20th Australian Total Diet Survey (FSANZ, 2002) analysed breads, biscuits, rice, oats, processed wheat bran, breakfast cereals (including infant cereal), instant coffee, peanut butter, almonds and milk chocolate for aflatoxins, with aflatoxins not being detected in any food above the limit of reporting of 1 μg/kg.

Klieber (2001) examined the aflatoxin content of chilli and paprika products available in Australia. Of 90 samples of chilli powder, paprika powder, crushed chilli, whole chilli, minced chilli and chilli sauce, 91% contained total aflatoxin at levels greater than 5 μg/kg. Maximum levels of 89 μg/kg were detected in paprika powder.

2.3.3 Overseas Context

An enormous body of information is available on the incidence and levels of aflatoxins in a variety of commodities and processed foods in a variety of countries. Results of representative surveys are given in Table 4.

Table 4: Worldwide data on occurrence of aflatoxins in food

Country	Year	Food	Aflatoxin measured	Samples positive/total (%)	Concentration (range, mean or maximum; µg/kg)	Reference
Canada	1998-2002	Beer	AFB_1	12/304 (4)	Range = 0.0007 – 0.23	Mably *et al.* (2005)
Cyprus	1992-96	Corn/maize	AFB_1	2/170 (1)	Max = 1	Ioannou-Kakouri *et al.*, 1999
Cyprus	1992-96	Barley	AFB_1	0/127 (0)		Ioannou-Kakouri *et al.*, 1999
Cyprus	1992-96	Wheat	AFB_1	0/55 (0)		Ioannou-Kakouri *et al.*, 1999
Cyprus	1992-96	Rice	AFB_1	0/56 (0)		Ioannou-Kakouri *et al.*, 1999
Cyprus	1992-96	Breakfast cereals and others	AFB_1	0/78 (0)		Ioannou-Kakouri *et al.*, 1999
Cyprus	1992-96	Coffee beans	AFB_1	0/171 (0)		Ioannou-Kakouri *et al.*, 1999
Cyprus	1992-96	Cocoa products	AFB_1	0/10 (0)		Ioannou-Kakouri *et al.*, 1999
Cyprus	1992-96	Raisins	AFB_1	0/22 (0)		Ioannou-Kakouri *et al.*, 1999
Cyprus	1992-96	Figs and figpie	AFB_1	4/24 (17)	Range = 1.4 – 6	Ioannou-Kakouri *et al.*, 1999
Cyprus	1992-96	Dates	AFB_1	0/5 (0)		Ioannou-Kakouri *et al.*, 1999
Cyprus	1992-96	Beans, broad beans, chick peas, lentils	AFB_1	0/390 (0)		Ioannou-Kakouri *et al.*, 1999
Cyprus	1992-96	Sunflower and pine seeds	AFB_1	0/8 (0)		Ioannou-Kakouri *et al.*, 1999
Cyprus	1992-96	Pumpkin seeds	AFB_1	0/190 (0)		Ioannou-Kakouri *et al.*, 1999
Cyprus	1992-96	Sesame seeds	AFB_1	4/211 (2)	Max = 2	Ioannou-Kakouri *et al.*, 1999
Cyprus	1992-96	Sesame products	AFB_1	5/130 (4)	Max = 1	Ioannou-Kakouri *et al.*,

Country	Year	Food	Aflatoxin measured	Samples positive/total (%)	Concentration (range, mean or maximum; µg/kg)	Reference
						1999
Cyprus	1992-96	Pepper, turmeric and others	AFB_1	1/6	Max = <0.4	Ioannou-Kakouri *et al*., 1999
Cyprus	1992-96	Desiccated coconut	AFB_1	0/71 (0)		Ioannou-Kakouri *et al*., 1999
Cyprus	1992-96	Almond, cashew, hazelnut	AFB_1	0/1107 (0)		Ioannou-Kakouri *et al*., 1999
Cyprus	1992-96	Walnut	AFB_1	6/560 (1)	Range = <0.4 – 0.2	Ioannou-Kakouri *et al*., 1999
Cyprus	1992-96	Chestnut	AFB_1	10/118 (8)	Max = <0.4	Ioannou-Kakouri *et al*., 1999
Cyprus	1992-96	Brazil nut	AFB_1	10/51 (20)	Range = 8.3 - 20	Ioannou-Kakouri *et al*., 1999
Cyprus	1992-96	Pistachio	AFB_1	53/856 (6)	Range = 1.4 - 206	Ioannou-Kakouri *et al*., 1999
Cyprus	1992-96	Peanut	AFB_1	179/1860 (10)	Range = <0.4 – 700	Ioannou-Kakouri *et al*., 1999
Cyprus	1992-96	Peanut butter	AFB_1	21/74 (28)	Range = 1.2 - 73	Ioannou-Kakouri *et al*., 1999
Cyprus	1992-96	Nut products	AFB_1	0/12		Ioannou-Kakouri *et al*., 1999
Cyprus	1992-96	Raw milk	AFM_1	3/71 (4)	Range = 0.03 – 0.04	Ioannou-Kakouri *et al*., 1999
Cyprus	1992-96	Pasteurised milk	AFM_1	9/31 (29)	Range = 0.01 – 0.04	Ioannou-Kakouri *et al*., 1999
Cyprus	1992-96	Baby milk, evaporated milk (imported)	AFM_1	0/10 (0)		Ioannou-Kakouri *et al*., 1999
Japan	1988-92	Peanut butter	Total	3/4 (75)	Range = 0.7 – 2	Taguchi *et al*., 1995
Japan	1988-92	Peanuts	Total	1/34 (3)	Max = 0.1	Taguchi *et al*., 1995
Japan	1988-92	Tree nuts (almond, cashew, macadamia, pistachio, walnut)	Total	0/68 (0)		Taguchi *et al*., 1995
Japan	1988-92	Nutmeg	Total	2/3 (67)	Range = 0.4 – 1.0	Taguchi *et al*., 1995

Country	Year	Food	Aflatoxin measured	Samples positive/total (%)	Concentration (range, mean or maximum; µg/kg)	Reference
Japan	1988-92	Pepper (black, white)	Total	1/17 (6)	Max = 0.6	Taguchi *et al.*, 1995
Japan	1988-92	Pepper (red)	Total	1/2 (50)	Max = 0.8	Taguchi *et al.*, 1995
Japan	1988-92	Other spices (garlic, ginger, mustard)	Total	0/9 (0)		Taguchi *et al.*, 1995
Japan	1988-92	Cereals (corn products, rice, wheat, buckwheat, Job's tears)	Total	0/9 (0)		Taguchi *et al.*, 1995
Japan	1988-92	Bean products	Total	0/5 (0)		Taguchi *et al.*, 1995
Japan	1988-92	Cheese	Total	0/41 (0)		Taguchi *et al.*, 1995
Japan	1988-92	Beef	Total	0/3 (0)		Taguchi *et al.*, 1995
UK	1994	Herbs and spices (Pepper, cinnamon, coriander, turmeric, cumin, cardamom, mixed, oregano, pimento, fennel, tarragon)	Total	0/67 (0)		MAFF, 1994a
UK	1994	Herbs and spices	Total	Chilli 13/33 (39) Curry powder 10/29 (34) Cayenne 4/8 (50) Paprika 1/9 (11) Ginger 3/8 (38) Fenugreek 1/2 (50)	Max = 47.5 Max = 5.2 Max = 14.8 Max = 1.8 Max = 8.4 Max = 2.5	MAFF, 1994a
UK	1994-95	Peanuts	Total	5/47 (11)	Max = 105	MAFF, 1996a
UK	1994-95	Peanut butter	Total	13/42 (31)	Max = 21	MAFF, 1996a
UK	1994-95	Other nut butters	Total	0/12 (0)		MAFF, 1996a
UK	1994-95	Pistachios	Total	8/43 (19)	Max = 175	MAFF, 1996a
UK	1994-95	Brazil and other nuts	Total	0/13 (0)		MAFF, 1996a
UK	1994-95	Figs and fig products	Total	Figs 1/29 (3) Dried figs 16/20 (80) Fig paste 9/10 (90)	Max = 16 Max = 89 Max = 76	MAFF, 1996a
UK	1995	Milk	AFM_1	Full fat (Summer) 21/48 (44) Skim/semi-skim (Summer) 18/38 (47)	Max = 0.22 Max = 0.03 Max = 0.02 Max = 0.03	MAFF, 1995a

Country	Year	Food	Aflatoxin measured	Samples positive/total (%)	Concentration (range, mean or maximum; µg/kg)	Reference
				Full fat (Winter) 31/40 (78) Skim/semi-skim (Winter) 19/36 (53)		
UK	1995	Milk products	AFM_1	Dried milk 0/31 (0) Infant formula 4/62 (6) Plain yoghurt 4/13 (31) Fruit yoghurt 2/17 (12)	 Max = 0.05 Max = 0.04 Max = 0.03	MAFF, 1995a
UK	1995	Cheese	AFM_1	Cheddar 4/12 (33) Leicester 7/13 (54) Cheshire 10/13 (77) Lancashire 10/11 (91) Wensleydale 9/11 (82) Double Gloucester 9/13 (69)	Max = 0.09 Max = 0.09 Max = 0.17 Max = 0.21 Max = 0.22 Max = 0.13	MAFF, 1995a
UK	1996	Farm milk	AFM_1	Winter 11/40 (28) Summer 2/39 (5)	Max = 0.09 Max = 0.03	MAFF, 1996b
UK	1996	Retails foods (dried apricots, beer, desiccated coconut, fresh coconut, currants, dates, olives, raisins, sultanas)	Total	0/161 (0)		MAFF, 1997
UK	1996	Cereals (barley, oats, rye, wheat)	Total	0/74 (0)		MAFF, 1997
UK	1998-99	Maize, raw	Total	Country of origin: France 15/97 (15) Argentina 12/37 (32) Other European 3/5 (60)	 Max = 6.0 Max = 29.1 Max = 4.9	MAFF, 1999a
UK	2000	Rice	Total	17/100 (17)	Range = 0.2 - 1.8	FSA, 2002a
UK	2000-01	Tree nuts (almonds, Brazil nuts, cashews, chestnuts, hazelnuts, pecans, pinenuts, walnuts)	Total	0/33 (0)		FSA, 2002b
UK	2000-01	Pistachios	Total	8/52 (15)	Max = 106.9	FSA, 2002b
UK	2000-01	Peanuts	Total	3/19 (16)	Max = 70.9	FSA, 2002b
UK	2000-01	Peanut butter	Total	22/55 (40)	Max = 11.2	FSA, 2002b

Country	Year	Food	Aflatoxin measured	Samples positive/total (%)		Concentration (range, mean or maximum; µg/kg)	Reference
UK	2000-01	Other nut butters	Total	2/7 (29)		Max = 4.8	FSA, 2002b
UK	2001	Milk	AFM_1	Retail conventional Retail organic Farm-gate conventional Farm-gate organic	0/40 (0) 0/10 (0) 3/40 (8) 0/10 (0)	Range = 0.01 – 0.021	FSA, 2001
UK	2003	Baby foods, various	Total	1/169 (0.5)		Max = 0.05	FSA, 2004
UK	2003	Maize-based retail foods (sweetcorn, corn on the cob, baby food, corn oil, cornflour, polenta, maize meal, maize pasta, maize-based snacks, tortillas)	Total	1/292 (0.3)		Max = 0.38	FSA, 2005
UK	2004	Spices	Total	Paprika Chilli powder Cayenne pepper	26/26 (100) 29/31 (94) 4/4 (100)	Range = 0.4 – 5.7 Range = 0.6 – 14.6 Range = 0.2 – 7.0	FSA, 2005a
USA	1986	Shelled corn/maize	Total	Southeast Corn belt Virginia-Maryland Arkansas-Texas Rest of USA	19/59 (32) 0/31 (0) 2/8 (25) 3/23 (13) 0/27 (0)	Mean = 70, Max = 364 Mean = 12, Max = 20 Mean = 11, Max = 12	Wood, 1989
USA	1986	Milled corn/maize products	Total	Southeast Corn belt Virginia-Maryland Arkansas-Texas Rest of USA	17/61 (28) 2/22 (9) 0/4 (0) 0/8 (0) 0/44 (0)	Mean = 21, Max = 53 Mean = 8, Max = 8	Wood, 1989
USA	1986	Manufactured corn-based products	Total	0/23 (0)			Wood, 1989
USA	1986	Almond	Total	Domestic Imported	1/26 (4) 1/5 (20)	Max = 6 Max = 10	Wood, 1989
USA	1986	Almond butter and spread	Total	0/5 (0)			Wood, 1989
USA	1986	Brazil nut (imported)	Total	6/12 (50)		Mean = 20, Max = 42	
USA	1986	Cashew	Total	0/3			Wood, 1989
USA	1986	Cashew, coconut, hazelnut,	Total	0/24			Wood, 1989

Country	Year	Food	Aflatoxin measured	Samples positive/total (%)	Concentration (range, mean or maximum; µg/kg)	Reference
		pinenut, walnut candy (imported)				
USA	1986	Hazelnut	Total	0/1 (0)		Wood, 1989
USA	1986	Macadamia	Total	0/1 (0)		Wood, 1989
USA	1986	Pecan	Total	Domestic 0/35 (0) Imported 3/17 (18)	Mean = 135, Max = 334	Wood, 1989
USA	1986	Pistachio	Total	Domestic 7/22 (32) Imported 10/21 (48)	Mean = 58, Max = 252 Mean = 41, Max = 133	Wood, 1989
USA	1986	Pistachio candy (imported)	Total	1/1 (100)	Max = 78	Wood, 1989
USA	1986	Walnut	Total	Domestic 2/27 (7) Imported 2/4 (50)	Mean = 35, Max = 41 Mean = 4, Max = 8	Wood, 1989
USA	1986	Peanuts, in shell	Total	0/9 (0)		Wood, 1989
USA	1986	Peanuts, shelled	Total	6/55 (11)	Mean = 68, Max = 329	Wood, 1989
USA	1986	Peanut butter	Total	Domestic 17/104 (16) Imported 1/3 (33)	Mean = 14, Max = 27 Max = 43	Wood, 1989
USA	1986	Peanut paste (imported)	Total	3/4 (75)	Mean = 9, Max = 11	Wood, 1989
USA	1986	Peanut candy (imported)	Total	10/18 (55)	Mean = 10, Max = 20	Wood, 1989
USA	1986	Peanut oil (crude)	Total	5/8 (62)	Mean = 246, Max = 310	Wood, 1989
USA	1986	Peanut products	Total	1/6 (17)	Max = 2	Wood, 1989
USA	1986	Fluid milk and milk products	Total	0/182 (0)		Wood, 1989
USA	1986	Barley	Total	0/3		Wood, 1989
USA	1986	Canned corn, mixed vegetables	Total	0/10		Wood, 1989
USA	1986	Melon seed (imported)	Total	2/4 (50)	Mean = 26, Max = 29	Wood, 1989
USA	1986	Pumpkin seed (imported)	Total	0/6 (0)		Wood, 1989
USA	1986	Sesame seed (imported)	Total	0/20 (0)		Wood, 1989
USA	1986	Various herbs and spices (imported)	Total	0/59 (0)		Wood, 1989
USA	1986	Chilli powder (imported)	Total	9/12 (75)	Mean = 10, Max = 30	Wood, 1989
USA	1986	Ginger (imported)	Total	1/3 (33)	Max = 2	Wood, 1989

Country	Year	Food	Aflatoxin measured	Samples positive/total (%)	Concentration (range, mean or maximum; µg/kg)	Reference
USA	1986	Nutmeg (imported)	Total	5/5 (100)	Mean = 13, Max = 2	Wood, 1989

There is evidence that aflatoxins present in animal feed can be transmitted to human foods, such as eggs and meat. Oliveira *et al*. (2000) fed laying hens AFB_1 contaminated feed (300 or 500 μg AFB_1/kg feed) for eight weeks. AFB_1 was detected at levels in the range 0.05 – 0.16 μg/kg in eggs from the high dose group only. Wolzak *et al*. (1985) fed hens a diet containing 3310 μg AFB_1/kg and 1680 μg AFB_2/kg of feed for 28 days. Aflatoxin content of eggs reached a maximum after 4-5 days with a mean combined residue content of less than 0.5 μg/kg. No aflatoxin residues were detected in eggs 5-7 days after withdrawal of contaminated feed. In contrast, Zaghini *et al.* (2005) fed hens a diet containing 2.5 mg/kg (2500 μg/kg) of AFB_1 and detected no residues of AFB_1 or AFM_1 in eggs after 2 and 3 weeks.

Oliveira *et al.* (2003) fed quail relatively low doses of AFB_1 (25, 50 or 100 μg/kg of feed for 90 days. Aflatoxin residues in eggs were in the range 0.01 – 0.08 μg AFB_1/kg, 0.03 – 0.37 μg AFM_1/kg, 0.01 – 1.03 μg AFB_{2a}/kg and 0.01 –0.03 μg aflatoxicol/kg.

Laying hens and male broiler were fed diets containing 50 μg AFB_1/kg (Micco *et al*., 1988). AFB_1 was detected in the liver, kidney, thigh muscle and skin of some birds, while AFM_1 was detected in liver, kidney and thigh. Some differences in residues patterns were observed between broilers and layers. Bintvihok *et al*. (2002) fed quail, ducks, hens and broilers a diet containing 3 mg/kg (3000 μg/kg) of AFB_1 for 7 days. Free and conjugated AFB_1 and 'other' aflatoxins (AFM_1, AFB_{2a}, AFP_1, AFQ_1, AFR_0) were detected in liver sample from all species, with free AFB_1 levels in the range 0.13 – 7.83 μg/kg. Free AFB_1 was only detected in the muscle tissue from quail, while other aflatoxins were detected in muscle of all species at levels of free aflatoxins in the range 0.11 – 0.82 μg/kg.

Aflatoxins can occur in meat and meat products either due to consumption of aflatoxin-contaminated feed or due to direct growth of the fungi on meat. Aziz and Youssef (1991) reported the presence of *A. flavus* and *A. parasiticus* on Egyptian meat products (beefburger, hotdog, kubeba, sausage, luncheon meat) and the occurrence of AFB_1 and AFB_2 in some samples of meat products at levels in the range 2 – 150 μg/kg. Stubblefield *et al*. (1991) detected AFB_1 and AFM_1 in livers of pigs fed aflatoxin-contaminated corn (12 of 160 samples) at levels of 0.02 – 0.24 μg/kg and 0.03 – 0.44 μg/kg respectively. No aflatoxin residues were detected in associated muscle tissue samples.

While there is evidence that aflatoxin residues can be transmitted to foods of animal origin, the resultant residue concentrations are generally low. Animal feeding practices in New Zealand will mean that the potential for aflatoxins residues in stock animals is extremely low. The diverse nature of ingredients used in the poultry feed industry mean that there is some potential for aflatoxin residues in poultry feed and, consequently, in eggs and poultry meat, although concentrations will be very low.

Overseas data suggests that there is potential for New Zealanders to be occasionally exposed to aflatoxins through consumption of a range of foods, other than peanuts.

2.3.4 New Zealand estimates of dietary exposure

Thomson (1996) estimated the chronic exposure of New Zealanders to total aflatoxins, through consumption of peanuts and peanut butter, at 0.0001 μg/kg body weight/ day.

Peanuts are consumed at a relatively low level by New Zealanders (2.7 g/person/day; ANZFA, 2001b). New Zealand imported approximately 5,400 tonnes of peanuts in the year to September 2005, principally from Australia (59%) and China (36%).

2.3.5 Overseas estimates of dietary exposure

Table 5 summarises results of overseas studies, which have derived estimates of dietary exposure to aflatoxins.

There is a significant divide between estimates of aflatoxin exposure in developing countries, where estimates may be as high as several hundred ng/kg body weight/day, and developed countries, where estimates are generally less than 5 ng/kg body weight/day (0.005 µg/kg body weight/day) and often less than 1 ng/kg body weight/day (0.001 µg/kg body weight/day). An estimate of New Zealand exposure is similar to estimates for European countries, Australia and temperate regions of the United States (0.0001 µg/kg body weight/day or 0.1 ng/kg body weight/day; Thomson, 1996).

The estimates of aflatoxin exposure for different regions of the United States (Stoloff, 1983) clearly demonstrates the impact of the ecology of aflatoxigenic fungi. In the USA, maize may be grown either in sub-tropical regions (Southeast) or temperate (North and West). Maize grown in the Southeast is susceptible to aflatoxin contamination and the population in this area are potentially exposed to high levels of aflatoxins. Maize from the temperate regions of the North and West is rarely, if ever, contaminated with aflatoxin and the contribution of maize to total aflatoxin exposure in these regions is minimal (Stoloff, 1983).

Table 5: Overseas estimates of dietary exposure to aflatoxins

Country	Year	Population group	Exposure (ng/kg bw/day, total aflatoxin unless otherwise stated)	Main foods contributing	Reference
Australia	1994	**Mean energy intake** Adult male (75 kg bw) Adult female (59 kg bw) Boy, 12 years (40 kg bw) Girl, 12 years (42 kg bw) Toddler, 2 years (12 kg bw) **95th percentile energy intake** Adult male (75 kg bw) Adult female (59 kg bw) Boy, 12 years (40 kg bw) Girl, 12 years (42 kg bw) Toddler, 2 years (12 kg bw)	 0.2 0.2 0.3 0.1 0.2 0.2 0.3 0.5 0.2 0.3	Aflatoxins only detected in peanut butter	Marro, 1996
Australia	1996	**Mean energy intake** Adult male (75 kg bw) Adult female (59 kg bw) Boy, 12 years (40 kg bw) Girl, 12 years (42 kg bw) Toddler, 2 years (12 kg bw) **95th percentile energy intake** Adult male (75 kg bw) Adult female (59 kg bw) Boy, 12 years (40 kg bw) Girl, 12 years (42 kg bw) Toddler, 2 years (12 kg bw)	 1.1 1.2 2.4 1.0 1.6 1.8 1.9 3.8 1.5 1.9	Aflatoxins only detected in peanut butter	Hardy, 1998
Australia	2001	Mean population (60 kg body weight) 95th percentile consumer	0.2 3.4	Only peanuts considered	Pitt and Tomaska, 2001

Country	Year	Population group	Exposure (ng/kg bw/day, total aflatoxin unless otherwise stated)	Main foods contributing	Reference
Australia	2000-2001	Same as for Hardy (1998), with addition of infant diet	No aflatoxins detected in any food tested	No aflatoxins detected in any food tested	FSANZ, 2002
Belgium	1997	Average inhabitant (60 kg bw)	0.2 (AFB_1) 0.055 (AFM_1)	Nuts (peanuts, pistachios) Milk and milk products, cheese	SCOOP, 1997a
China	1980-1997		0-91 (AFB_1)	Not specified	Chen, 1997 (in JECFA, 1998)
China	1990	Standard man, 18-45 years, 60 kg body weight	0-10 (AFB_1) AFM_1 was not detected in any food tested	Cereals composite	Chen and Gao, 1993
China (Southern Guangxi)	1978-84	Not stated	11.7-2027 (AFB_1)	Maize	Yeh *et al.*, 1989
China (Fusui County)	Not stated	Adult males Adult females	200 (AFB_1) 8 (AFB_1)	Maize	Wang *et al*., 2001
Denmark	1997	Average adult (70 kg bw)	<0.1 (AFM_1)	Milk and milk products	SCOOP, 1997a
France	1997	Adult (60 kg bw)	1.3 (AFB_1)	Cereals and cereal products	SCOOP, 1997a
France	2000-2001	Adult, 15+ years, mean 95th percentile Child, 3-14 years, mean 95th percentile Adult, 15+ years, mean 95th percentile Child, 3-14 years, mean 95th percentile	0.12 (Total) 0.35 (Total) 0.32 (Total) 0.89 (Total) 0.09 (AFM_1) 0.21 (AFM_1) 0.22 (AFM_1) 0.55 (AFM_1)	Eggs and egg products Cereals and cereal products Ultra-fresh dairy products Ultra-fresh dairy products	Lelbanc *et al*., 2005
Gambia	1988	Not stated	4-115 (AFB_1)	Not specified	Wild *et al.*, 1992 (in IARC, 1993)
Germany	1997	Adult (75.9 kg bw) Child (13.5 kg bw) Adult (75.9 kg bw) Child (13.5 kg bw)	0.03 (AFB_1) 0.3 (AFB_1) 0.04 (AFM_1) 0.2 (AFM_1)	Nuts and nut products Milk, cheese	SCOOP, 1997a

Country	Year	Population group	Exposure (ng/kg bw/day, total aflatoxin unless otherwise stated)	Main foods contributing	Reference
India (Southern)	NS	Rural 1-5 years 5-12 years 12-18 years >18 years	6-101 (Total) 5-80 (Total) 18-63 (Total) 4-57 (Total)	Maize	Vasanthi *et al*., 1997
Kenya	1969-1970	Not stated	3.5-14.8 (AFB_1 + AFB_2)	Not specified	Peers and Linsell, 1973
Korea	2002	Adult (55 kg)	1.2-5.8 (AFB_1)	Rice	Park *et al*., 2004
Mozambique	1969-1974	Not stated	38.6-184 (AFB_1)	Maize, peanuts	Van Rensburg *et al.*, 1985
Netherlands	1997	Adult (50 kg bw) Infant (15 kg bw)	0.37 (AFB_1) 0.046 (AFM_1) 0.19 (AFM_1)	Peanuts and figs and their products Pasteurised and unpasteurised milk	SCOOP, 1997a
Swaziland	1972-73	Not stated	5.1-43.1 (AFB_1)	Not specified	Peers *et al.*, 1976 (in IARC, 1993)
Swaziland	1982-83	Not stated	11.4-159 (AFB_1) 20-297 (Total)	Maize	Peers *et al.*, 1987
Sweden	1996-1998	Adult average (18-74 years) High (95^{th} percentile) consumer	0.8 2.1	Pistachios, Brazil nuts	Thuvander *et al.*, 2001
Thailand	1969-70	Three households in each of three areas in each of three seasons	0-151 (AFB_1) <1-213 (Total)	Not specified	Shank *et al.*, 1972
Transkei*	1976-77	Not stated	16.5 (AFB_1)	Maize, peanuts	Van Rensburg *et al.*, 1985
UK	1997	Adult (70.1 kg)	0.03 (AFB_1) 0.06 (AFM_1)	Peanuts and figs and their products Not specified	SCOOP, 1997a
USA	1910-1934 1935-1959	Southeast total population North and West total population Southeast total population North and West total population	221 (AFB_1) 0.22 (AFB_1) 121 (AFB_1) 0.34 (AFB_1)	Maize	Stoloff, 1983
USA	1960-79	Not stated	2.7 (AFB_1)	Not specified	Bruce, 1990

* Transkei was incorporated into South Africa in 1994

2.4 Risk Characterisation

2.4.1 Adverse health effects in New Zealand

No cases of acute aflatoxicosis have been reported in New Zealand. While it is not possible to definitively identify cases of chronic adverse affects from exposure to aflatoxins, it is pertinent to consider New Zealand's rates of primary liver cancer and the prevalence of hepatitis B and C infection, as these factors have all shown inter-relations in the major epidemiological studies carried out in relation to aflatoxin exposure overseas (Table 6).

Table 6: Incidence of liver cancer, hepatitis B and hepatitis C in New Zealand

Year	Liver cancer *		Hepatitis B#		Hepatitis C#	
	New cases	Rate (per 100,000)	New cases	Rate (per 100,000)	New cases	Rate (per 100,000)
1995	114	Non-Maori 1.8 Maori 11.0	125	3.3 (European 1.8, Maori 8.6, Pacific Islanders 1.5)	88	2.4 (European 2.5, Maori 2.5, Pacific Islanders 0.5)
1996	131	Non-Maori 2.5 Maori 7.1	104	2.8 (European 1.5, Maori 6.3, Pacific Islanders 4.5)	59	1.6 (European 1.4, Maori 0.8)
1997	153	Non-Maori 2.6 Maori 8.9	138	3.7 (European 1.5, Maori 8.0, Pacific Islanders 9.0)	92	2.5 (European 1.9, Maori 2.5)
1998	143	Non-Maori 2.3 Maori 8.0	88	2.4 (European 1.5, Maori 4.6, Pacific Islanders 4.5)	102	2.7 (European 2.5, Maori 2.1)
1999	NA	NA	94	2.5 (European 1.4, Maori 4.2, Pacific Islanders 4.0)	96	2.6 (European 2.4, Maori 2.3, Pacific Islanders 0.5)
2000	NA	NA	79	2.1 (European 1.1, Maori 3.0, Pacific Islanders 4.5)	80	2.1 (European 1.3, Maori 1.5, Pacific Islanders 0.5)
2001	NA	NA	56	1.5 (European 0.7, Maori 2.7, Pacific Islanders 4.0)	59	1.6 (European 1.2, Maori 1.3)

NA Not available

* New Zealand Health Information Service, 1999; 2000; 2001; 2002

From Episurv database (Liz Sneyd, ESR Keneperu Science Centre, personal communication)

Hepatitis B notifications have declined from about 600 per year in the mid-1980s to the most recently reported incidence of 30 in 2005 (http://www.nzpho.org.nz/view_data.asp#NotifiableDisease). This decline has been influenced by the introduction of immunisation for infants of HBsAg (a surface antigen of the Hepatitis B virus)-positive mothers (1985), followed by immunisation of all neonates (1988) (MoH, 2002).

Blakely *et al.* (1999) examined the HBsAg status of 193 confirmed cases of hepatocellular carcinoma (HCC) in New Zealand between 1987 and 1994. It was found that 77% of Maori, 80% of Pacific Island, and 89% of Asian HCC cases were HBsAg positive, while only 6% of European HCC cases were HBsAg positive. This explained between 78 (Maori) and 92% (Asian) of the excess risk of HCC compared to the rate in Europeans.

2.4.2 Adverse health effects overseas

2.4.2.1 Incidence of primary liver cancer

Liver cancer is the fifth most frequently occurring cancer worldwide (Bosch *et al.*, 1999). Rates of liver cancer in developing countries are generally two to three times higher than in developed countries. Regions with the highest age-adjusted incidence rates are; East Asia (27.6-36.6 per 100,000 of population), sub-Saharan Africa (20.8-38.1 per 100,000 of population) and some countries in West Africa (30-48 per 100,00 of population). The areas of lowest liver cancer risk are reported to be Northern Europe, Australia, New Zealand and the Caucasian populations of North and South America with rates for males below 5.0 per 100,00 of population (Bosch *et al.*, 1999).

2.4.2.2 Epidemiological studies

A number of epidemiological studies have been conducted, mainly in Asia, to examine links between primary liver cancer (PLC) or hepatocellular carcinoma (HCC), hepatitis B and aflatoxin exposure. While PLC may involve cell types other than the hepatocytes, it can generally be assumed that PLC and HCC are synonymous. HBsAg refers to a surface antigen of the hepatitis B virus. These studies are summarised below.

China (Guangxi Province)

Yeh *et al.* (1989) followed a cohort of 7917 men aged 25-64 in southern Guangxi province, China. Hepatitis B status of members of the cohort was determined by testing for the HBsAg surface antigen. Average aflatoxin exposures were determined on a commune by commune basis from staple food monitoring. A positive linear relationship was observed between regional aflatoxin exposure and mortality due to PLC. Prevalence of HBsAg was high and homogeneous across the study areas (21-25%).

China

Campbell *et al.* (1990) conducted a cross-sectional study of risk factors for PLC over 48 survey sites in the People's Republic of China. The survey sites represented an approximately 600-fold range in aflatoxin exposure, 39-fold range in PLC mortality rates, and a 28-fold range in HBsAg carrier prevalence. Aflatoxin exposure was estimated from urinary aflatoxin metabolite levels. The study showed no association between aflatoxin exposure and PLC mortality.

China (Shanghai)

An ongoing prospective cohort study in Shanghai, China of 18,244 middle-aged men examined urinary levels of AFB_1 and its metabolites, and DNA-aflatoxin adducts (Ross *et al.*, 1992; Qian *et al.*, 1994, Yuan *et al.*, 1995). Two assessment points in the study have so far been reported, with liver cancer cases being matched with liver cancer-negative controls from the study group and compared for hepatitis B status and urinary aflatoxin level. At the first assessment point (after 35,299 person years) it was concluded that up to 50% of liver cancer cases may be due to aflatoxin exposure.

At the second assessment point (Qian *et al.*, 1994) a highly significant association was found between the presence of at least one urinary aflatoxin metabolite, HBsAg positivity and PLC risk. Risk was particularly elevated in subjects with both biomarkers, but the number of subjects was quite small. Considerable debate has followed publication of this study (see JECFA, 1998 for a summary) and it should be noted that there was no dose-dependent association between dietary aflatoxin exposure estimates and either PLC risk or urinary metabolite status.

Gambia

Wild *et al.* (1993) collected blood samples from 117 Gambian children aged 3-4 over a one month period. Bloods were analysed for aflatoxin-albumin adducts as a marker of aflatoxin exposure, markers of hepatitis B infection , and liver enzymes as markers of liver damage. A significant positive correlation between aflatoxin adduct levels and liver damage biomarker levels was found, even after exclusion of subjects positive for hepatitis B.

Thailand

Srivatanakul *et al* (1991) conducted a case-control study to assess risk factors for PLC in Thailand, using aflatoxin-albumin adduct as a biomarker of aflatoxin exposure. Hepatitis B was the predominant risk factor, with neither aflatoxin adduct nor hepatitis C being significantly associated with cancer risk. This study has been criticised for lacking sufficient statistical power to detect aflatoxin or hepatitis C as independent risk factors (JECFA, 1998).

Taiwan

Hatch *et al.* (1993) conducted a survey over eight regions of Taiwan, which provided a significant range of estimates of aflatoxin exposure and rates of PLC. It was concluded that aflatoxins had an independent role in PLC in Taiwan.

Wang *et al* (1996) conducted a case-control study on the effect of aflatoxin on PLC in Taiwan. Fifty-six cases of PLC were matched with 220 healthy controls and blood and urine samples analysed for aflatoxin and hepatitis biomarkers. HBsAg carriers had significantly increased cancer risk and, after adjustment for HBsAg status, there was a significantly elevated cancer risk for subjects with high levels of urinary aflatoxin metabolites.

Sudan

Omer *et al.* (1998) conducted a small case-control study (24 cases and 34 controls) to determine risk factors for hepatocellular carcinoma (HCC). Peanut butter and peanuts were collected from two regions of Sudan (West Sudan, high levels of contamination, and Central Sudan, lower levels of contamination). HCC was weakly, but significantly, associated with AFB_1 index (an indicator of exposure), with an odds ratio (OR) of 1.5. The study showed no association between HCC and hepatitis virus infection.

United States

Hoque *et al.* (1999) examined sera and tissue samples from 23 patients with hepatocellular carcinoma for biomarkers of hepatitis virus and aflatoxin exposure. Aflatoxin-DNA and aflatoxin-lysine adducts were detected in some patients. However, the small size of the study and the lack of suitable controls means that few conclusions can be drawn.

Conclusions

In reviewing these studies and other information on molecular biomarkers the JECFA committee concluded that "exposure to aflatoxins appears to present an additional risk which is enhanced by simultaneous exposure to hepatitis B virus, and possibly hepatitis C virus. This relationship, which may affect not only carcinogenic potency but also metabolism, biochemistry and pharmacology of the aflatoxins, and other multiple etiological agents for primary liver cancer, makes it difficult to interpret the epidemiological studies in the context of the risk of primary liver cancer from aflatoxins" (JECFA, 1998). However, the strength of evidence as evaluated by IARC (1993; 2002) clearly demonstrates an independent causal association between aflatoxin exposure and human liver cancer incidence.

2.4.2.3 Risk assessments and other activity overseas

JECFA

The latest assessment of aflatoxins carried out by the Joint FAO/WHO Expert Committee on Food Additives (JECFA) summarised recent studies relevant to aflatoxins in foods (JECFA, 1998). The assessment made the following comments:

- The committee considered that the weight of scientific evidence supports a conclusion that aflatoxins should be treated as carcinogenic food contaminants, the intake of which should be reduced to levels as low as reasonably achievable.
- The potency of aflatoxins in HbsAg+ (hepatitis B surface antigen) individuals is substantially higher than the potency in HbsAg- individuals.
- Vaccination against hepatitis B will reduce the prevalence of carriers, which would reduce the potency of aflatoxins in vaccinated populations and reduce liver cancer risks.
- Analysis of the application of hypothetical standards (10 μg/kg or 20 μg/kg aflatoxin in food) to model populations with a low prevalence of HBsAg+ individuals and/or with a low mean intake of aflatoxin (less than 1 ng/kg body weight/day) is unlikely to exhibit a detectable difference in population risk.
- The committee has previously noted that reductions can be achieved through avoidance measures such as improved farming and proper storage practice and through enforcing standards for food or feed within countries and across borders.

FSANZ/ANZFA

FSANZ (then ANZFA) carried out an assessment of aflatoxins in food in 1999 (ANZFA, 1999). It was concluded that "while most problems associated with aflatoxins are associated with peanuts, several varieties of tree nuts may also be contaminated on occasions".

European Commission

The European Commission carried out a risk assessment of aflatoxins under their tasks for scientific co-operation (SCOOP) programme (SCOOP, 1997a). The study found that:

- Aflatoxins are found in a wider range of foods than traditionally thought.
- The estimation of dietary intake is limited by different approaches to obtaining consumption data and indicators of total dietary intake of aflatoxins depend completely on the number and types of individual foods considered within the summation.

2.5 Risk Management Information

2.5.1 Relevant food controls: New Zealand

2.5.1.1 Establishment of regulatory limits

The New Zealand Food Regulations 1984 specify a limit for total aflatoxin contamination of 'peanut butter, shelled nuts, and the nut portion of products containing nuts' of 0.015 ppm (15 ppb) and a limit of 0.005 ppm in 'all other foods'.

The Australia New Zealand Food Standards Code, which has replaced the New Zealand Food Regulations 1984, specifies a maximum limit for total aflatoxins in peanuts and tree nuts of 0.015 ppm, but includes no provisions for other foods.

The New Zealand (Mandatory) Food Standard 1997 prescribes imported peanut and pistachio nuts, peanut butter and nutmeg; requiring their testing at time of import for the presence of mycotoxins (fungal toxins).

Love (2000) reviewed New Zealand import testing procedures for peanuts and compared them to several other countries, concluding that advantages of the New Zealand system were "Its ability to reject almost all shipments with levels of aflatoxin above 15 µg/kg, and the increased ability to identify hot spots in a damaged shipment because of the number of sites checked".

2.5.2 Relevant food controls: overseas

2.5.2.1 Establishment of regulatory limits

In 2003 approximately 100 countries reported having mycotoxin regulations in place (van Egmond and Jonkers, 2003). Aflatoxins are by far the most commonly regulated mycotoxins. Regulatory limits may be expressed in terms of AFB_1, in terms of total aflatoxins or occasionally in terms of the sum of AFB_1 and AFG_1 (van Egmond and Jonkers, 2003).

For regulatory limits expressed in terms of AFB_1 limits range from 1 to 20 µg/kg, with the most common limit being 2 µg/kg. This limit applies to most foods for direct human consumption within EU and associated countries (29 countries). The next most common limit for AFB_1 is 5 µg/kg (21 countries).

The range of regulatory limits for total aflatoxins found was 0-35 µg/kg, with a median of 10 µg/kg (van Egmond and Jonkers, 2003). The EU limit of 2 µg/kg for AFB_1 is also expressed

as 4 µg/kg total aflatoxins and this was the most common regulatory limit for total aflatoxins (29 countries), followed by 20 µg/kg (17 countries).

Regulatory limits for AFM_1 were reported from 60 countries (van Egmond and Jonkers, 2003) with the most common limit being 0.05 µg/kg (34 countries, including EU and associated countries), followed by 0.5 µg/kg (22 countries).

JECFA examined the impact of several regulatory scenarios on the dietary exposure to aflatoxins from consumption of maize and peanuts. The scenarios were assessed in terms of contamination profiles of commodities from three sources: Europe, USA and China. Exposure estimates were derived for all five GEMS/Food Regional Diets (Europe, Africa, Middle East, Latin America, East Asia. Results for the European diet are summarised in Table 7.

Table 7: Estimated dietary exposure to aflatoxins from consumption of maize and peanuts under various scenarios for the GEMS/Food European diet

	Aflatoxin exposure if samples exceeding stated aflatoxin level are excluded (ng/person/day)			
	>10 µg/kg	**>15 µg/kg**	**>20 µg/kg**	**None**
Total aflatoxins				
European residue levels	6.5	6.5	7	67
USA residue levels	8.0	9.5	12	117
AFB_1				
European residue levels	18	18	18.5	49
Chinese residue levels	42	45	50	162

From JECFA (1998)

The JECFA analysis concluded that the most significant effect on aflatoxin intake was the limiting of contamination to less than 20 µg/kg. Minor further reductions can be achieved by decreasing the limit level to 15 or 10 µg/kg.

2.5.2.2 Codes of Practice

Codes of Practice for prevention and reduction of aflatoxin contamination have been formulated by the Codex Alimentarius Commission (Codex) and are available at the following sites:
Peanuts (http://www.codexalimentarius.net/download/standards/10084/CXC_055_2004e.pdf)
Tree nuts (http://www.codexalimentarius.net/download/standards/10221/CXP_059e.pdf)
Feed for milk producing animals (http://www.codexalimentarius.net/download/standards/331/CXP_045e.pdf)

In addition Codex have also prepared a general standard for prevention and reduction of mycotoxin contamination of cereals (http://www.codexalimentarius.net/download/standards/406/CXC_051e.pdf).

2.5.2.3 Management of aflatoxin formation in crops

The level of aflatoxins in a food crop and the resulting food products may be influenced at a number of steps in the process from paddock to plate (Park *et al.*, 1999), including:

- Pre-harvest. Development of cultivars with improved resistance to fungal infection and management of risk factors (water stress, insect infestation, fungal levels).
- Harvesting. Minimisation of physical damage and harvesting at correct moisture content.
- Post-harvest procedures. Physical separation of infected grains (usually on the basis of colour) can substantially decrease the level of contamination.
- Storage. Accumulation of moisture, heat, and physical damage can increase fungal infestation and consequent aflatoxin formation.
- Processing.

2.5.2.4 Post-harvest treatment to reduce aflatoxin levels

A number of techniques have been investigated to reduce aflatoxin contamination in food and feed. Techniques include:

Mechanical segregation. Most of the aflatoxin contamination associated with maize may be found in a relatively small number of kernels. Separation of infected from non-infected kernels on the basis of appearance does not appear to have received much attention for maize, but has been applied with some success to peanuts and Brazil nuts (Phillips *et al*., 1994).

Density segregation. Flotation and density segregation of maize has demonstrated a noticeable reduction in aflatoxin contamination (Huff and Hagler, 1985). While this technique is compatible with wet milling of maize, it is unlikely to be practical for maize destined for dry milling.

Thermal inactivation. Aflatoxins are heat stable and are not completely destroyed by boiling or autoclaving (Phillips *et al*., 1994). Roasting has been shown to decrease, but not eliminate, aflatoxin contamination in maize.

Irradiation. Gamma irradiation did not degrade aflatoxin in peanut meal, while exposure to sunlight for 14 hours resulted in destruction of approximately 50% of aflatoxin B_1 in naturally contaminated groundnut flakes (Shantha *et al.,* 1986). However, exposure to UV light appears to activate aflatoxins as mutagens (Phillips, 1984).

Solvent extraction. A number of solvent systems, including binary and tertiary systems, are capable of extracting aflatoxins from contaminated meal with minimal effect on protein content or nutritional quality. However, these techniques appear to be impractical and cost prohibitive for large scale detoxification (Phillips *et al*., 1994).

Ammoniation. Treatment with ammonia (ammonium hydroxide or ammonia gas) has been shown to reduce aflatoxin levels in maize by more than 99% (Brekke *et al*., 1977). Ammoniation of maize is permitted in the United States in states were aflatoxin contamination of maize may be severe (Texas, North Carolina, Georgia and Alabama only), and in Mexico (Phillips *et al*., 1994). The products of ammoniation have been shown to be significantly less toxic than AFB_1.

Sodium bisulphite treatment. Sodium bisulphite has been shown to react with aflatoxins under various conditions of temperature, concentration and time to form water-soluble reaction products (Hagler *et al*., 1982). The reaction appears to proceed by formation of an adduct. Although there is currently no information on the biological activity of the adduct, it has been hypothesised that the mode of addition (addition of a sulfo group across the double bond of the bisfuran ring of the aflatoxin) will result in detoxification as the double bond involved is necessary for the reaction of aflatoxins with DNA (Tabata *et al*., 1999).

Treatment with other food additives. Tabata *et al*. (1994) demonstrated degradation of pure aflatoxins by hydrochloric acid, sulphuric acid, sodium bicarbonate, sodium carbonate, sodium hydroxide, sodium sulphite, sodium hypochlorite, potassium metabisulphite, sodium bisulphite, sodium hydrosulphite, hydrogen peroxide, sodium chlorite and ammonium peroxodisulphate. Potassium bromate, potassium nitrate and sodium nitrite had no effect on aflatoxins. When aflatoxins were added to corn, sodium bisulphite (0.5%, 48 hours, 60˚C) treatment resulted in an 80% reduction in aflatoxin B_1 levels, while sodium chlorite (0.25%, pH 4, 48 hours, 60˚C) and ammonium peroxodisulphate (0.25%, 48 hours, 60˚C) treatment resulted in complete degradation of aflatoxins.

Ozonation. Ozone is a powerful oxidant which has been shown to be effective in degrading aflatoxins in contaminated maize (McKenzie *et al*., 1998). Naturally contaminated maize (1200 µg AFB_1/kg) was treated with electrochemically produced ozone (92 hours, 200 mg/minute), resulting in greater than 95% reduction in levels of AFB_1. The efficacy of the treatment was confirmed by feeding trials with one-day-old turkey poults, with poults fed AFB_1 contaminated corn treated with ozone being indistinguishable from controls, while poults fed AFB_1 contaminated corn (no ozone treatment) exhibited reduced weight gain and liver weight, liver discolouration, and altered serum enzyme activities and blood chemistry (McKenzie *et al*., 1998).

Selective chemisorption. A variety of absorbent clay materials have been studied for their ability to selectively bind aflatoxins, resulting in diminished aflatoxin uptake and distribution to the blood and target organs. Addition of these materials to naturally contaminated animal feeds has shown a protective effect from toxic effects of aflatoxins (summarised in CAST, 2003).

2.5.3 Influence of food processing on aflatoxin levels

Roasting of peanuts can reduce the level of aflatoxin contamination by 50-80% (JECFA, 1998).

Dry milling of maize, to produce products such as flaking grit, coarse grits, regular grits, cornmeal, cones and cornflour, reduces aflatoxin levels to approximately 6-10% of the original concentrations (Park, 2002). Similar patterns are seen with dry milling of rice and wheat (Park, 2002).

Processing of maize reduces aflatoxin levels. Wet milling of maize to produce starch and other by-products reduces the concentration of aflatoxins in the resultant starch to less than 1% of the levels in the raw grain (JECFA, 1998). Starch is the main human food output of the wet milling process, with the other components generally used for animal feed (gluten, fibre)

or for further processing (germ for oil extraction).Table 8 summarises results of three studies looking at the partitioning of aflatoxins between mill fractions during the wet milling process.

Table 8: Distribution of aflatoxins between maize wet milling fractions

Fraction	Percentage of total aflatoxins		
	Yahl *et al.* (1971)	**Bennett and Anderson (1978)**	**Romer (1984)**
Steep water and solubles	42	40	50
Fibre	30	38	28
Gluten	17	13	11
Germ	10	6	11
Starch	1	1	0.2

Extrusion cooking of maize flour in the presence of sodium metabisulphite has been reported to decrease AFB_1 levels by 10-25% (Cazzaniga *et al*., 2001). Of three factors studied (extrusion cooking temperature, moisture content of flour and presence of additive) only the presence of the additive, sodium metabisulphite, had a significant effect on AFB_1 levels.

Production of tortillas, tortilla chips and corn chips involves an alkaline cooking process (nixtamalisation). This process has been shown to remove 30-85% of aflatoxin (Torres *et al*., 2001).

Domestic cooking of spices and herbs naturally contaminated with AFB_1 (microwaving or heating in a gas oven) did not result in reduction of AFB_1 levels (MAFF, 1994a).

Fermentation can result in decreases in aflatoxin contamination and Chu *et al*. (1975) demonstrated a 70-80% reduction in AFB_1 levels through the beer brewing process.

AFM_1 was found to be associated with the casein fraction of milk and is stable during the pasteurisation process (Wiseman *et al*., 1983). The production of butter results in very low levels of AFM_1 in the butter, with the majority appearing in the buttermilk or rinse water (Wiseman and Marth, 1983). Production of cheese from AFM_1-contaminated milk results in concentration of the AFM_1, with levels in the cheese approximately 3-6 times those in the milk (van Egmond, 1983).

2.6 Conclusions

2.6.1 Description of risks to New Zealand consumers

There is consistent epidemiological evidence linking aflatoxin exposure to human primary liver cancer. Plausible mechanisms for carcinogenesis have been proposed and there is some biochemical data to support these hypotheses. However, the cancer risk due to aflatoxin is substantially increased in the presence of other liver diseases (hepatitis B, hepatitis C) and there are some questions concerning aflatoxin exposure as an independent risk factor.

Studies indicate that aflatoxigenic *Aspergillus* species are not present in New Zealand crops (Sayer and Lauren, 1991) and it is generally believed that these toxins only form in tropical

or sub-tropical situations. The major potential sources of aflatoxin exposure for the general New Zealand population are probably imported maize and peanuts and their products.

The majority of maize imports into New Zealand are from Australia and are not subject to testing for aflatoxins. Australian data suggest that maize in Australia is frequently contaminated with aflatoxins. This is consistent with a large body of information from a variety of countries. Processing of maize, by dry or wet milling, results in a substantial decrease in aflatoxin levels. Other processes, such as extrusion cooking and alkaline steeping produce further decreases in aflatoxin levels.

Very limited analyses of maize and maize-based products available on the New Zealand market revealed no aflatoxins, at a limit of detection of 1 μg total aflatoxin/kg (Stanton, 2000a). This is consistent with Australian data, which only reported one detection of aflatoxins amongst 265 analyses of corn flakes (ANZFA, 1999).

Importations of peanuts and peanut products into New Zealand continue to show a proportion of contaminated shipments However, import testing procedures will reduce the proportion of contaminated shipments that reach the retail market. Love (2000) reviewed New Zealand testing procedures and compared them to several other countries, concluding that advantages of the New Zealand system were "Its ability to reject almost all shipments with levels of aflatoxin above 15 μg/kg, and the increased ability to identify hot spots in a damaged shipment because of the number of sites checked". While a proportion of aflatoxin-contaminated product will inevitably make its way onto the New Zealand retail market, this is likely to be a relatively rare occurrence. In a limited survey of peanuts from retail outlets (34 samples), none were found to contain detectable levels of aflatoxin.

Estimates of the aflatoxin exposure of New Zealanders suggest that it is at the lower end of the range of international estimates – probably in the range 0.1-2.5 ng/kg bw/day, and is similar to estimates for European countries and temperate areas of North America. Based on the consensus carcinogenic potency values from epidemiological studies adopted by JECFA (0.01 cancers/year per 100,000 population per ng aflatoxin/kg body weight/day for HbsAg negative individuals), this level of exposure would result in an excess liver cancer risk of 0.0005-0.01 cancers/100,000 population/year compared to current rates of liver cancer in New Zealand of 2-11/100,000/year, depending on ethnicity. The risk for hepatitis B positive individuals will be approximately 30 times higher.

It should be noted that the single estimate made of aflatoxin exposure in New Zealand may be an underestimate, due to the paucity of data on aflatoxin-contamination of maize imported into New Zealand and the possible contribution of foods of animal origin. A recent exposure assessment carried out for the French population suggested that eggs and egg products were a major source of aflatoxin exposure (Leblanc *et al*., 2005).

2.6.2 Commentary on risk management options

The current import monitoring regime is the only feasible risk management strategy available to New Zealand and assessments carried out suggest that the current approach offers a high level of protection with respect to importation of aflatoxin-contaminated peanuts and pistachios. No controls exist for aflatoxin contamination of other imported foods, such as maize.

2.6.3 Data gaps

A wider survey of maize and maize product imported into New Zealand would give more statistical certainty to the negative findings of Stanton (2000a). Information on aflatoxin contamination in animal feed would also provide important information for assessment of aflatoxin exposure in New Zealand.

3 OCHRATOXIN A (OTA)

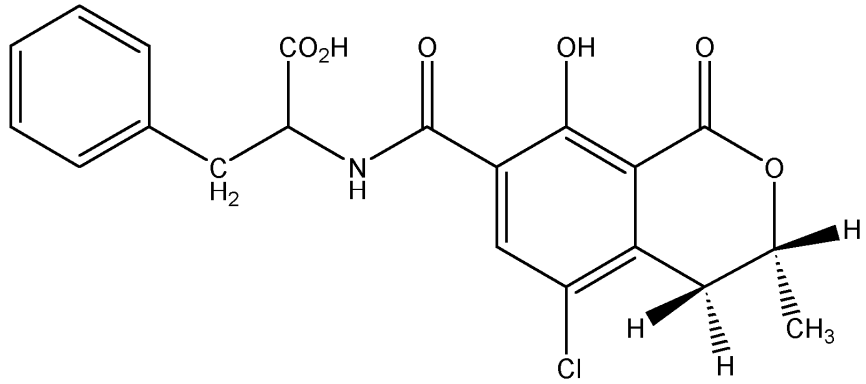
3.1 Hazard identification

Ochratoxin A (OTA) is produced by *Aspergillus ochraceus* and a related *Aspergillus* species, *A. carbonarius,* as well as some isolates of *A. niger*, and by *Penicillium verrucosum* (JECFA, 2001a). These organisms differ in their geographical distribution and ecological niche, in the commodities affected, and at the point at which they are likely to infect commodities.

3.1.1 Structure and nomenclature

OTA contains a chlorinated isocoumarin moiety linked via a carboxyl group to L-phenylalanine. Ochratoxin B (a dechlorinated analogue of OTA) and ochratoxin C (an ethyl ester of OTA) have also been detected, but OTA is by far the major contaminant found in crop plants (Walker, 1999)

Figure 3: Structure of OTA



3.1.2 Occurrence

P. verrucosum is a cool climate organism (0-31˚C, optimum 20˚C), occurring only in cool temperate regions, and is able to grow at water activities as low as 0.8 (Pitt and Hocking, 1997). It is the source of OTA formation in stored cereals and cereal products in European countries and Canada. Due to the high stability of OTA this can also result in the presence of OTA in animals fed contaminated cereals. *P. verrucosum* does not occur in the tropics (JECFA, 2001a).

A. ochraceus grows at moderate temperatures (8-37˚C, optimum 24-31˚C) and at water activities above 0.8 (optimum 0.95-0.99) (Pitt and Hocking, 1997). It occurs occasionally on a wide range of stored food products, but is seldom the cause of substantial concentrations of OTA (JECFA, 2001a).

A. carbonarius grows at high temperatures (max 40˚C, optimum 32-35˚C) and is associated with maturing fruit, particularly grapes. It is the major source of OTA in fresh grapes, dried vine fruits and wine (JECFA, 2001a).

OTA contamination is principally found in cereals, but can also occur in coffee, cocoa, nuts, dried vine fruits, grape juice and wine, beer, and pork and pork products made from animals fed OTA contaminated feed (Walker, 1999).

Sayer and Lauren (1991) did not report isolation of any of these OTA-forming fungal species from New Zealand grain sampled at harvest. However, no information was found on occurrence of these fungal species on stored grain in New Zealand. Similarly, no information was found on *Aspergillus* infection of grapes or other fruits in New Zealand. However, it has been reported that bunch rot of vines due to *A. niger* probably occurs in New Zealand, but hasn't been officially reported (http://www.hortnet.co.nz/publications/hortfacts/hf905020.htm).

3.2 Hazard Characterisation: Adverse Health Effects

3.2.1 Conditions

OTA is principally nephrotoxic. Consumption of OTA-contaminated barley in Europe has been associated with a major renal disease of pigs, known as porcine nephropathy (CAST, 2003).

While not conclusively established, OTA has been strongly implicated in a human kidney disease known as Balkan endemic nephropathy (BEN; CAST, 2003). OTA is common in foods from BEN affected areas (former Yugoslavia, Bulgaria and Romania). Further weight is added to this hypothesis by the fact that OTA is also carcinogenic in rats and mice and patients with BEN frequently exhibit kidney tumours (urothelial urinary tract tumours) (CAST, 2003; Pfohl-Leszkowicz *et al*., 2002). The disease has a slow progressive course leading to renal failure. While populations in BEN unaffected areas are also exposed to OTA, there is evidence to suggest that exposure frequency and blood OTA levels are higher in those suffering BEN (Pfohl-Leszkowicz *et al*., 2002). It has been proposed that BEN may have a multi-nephrotoxin aetiology, with OTA, citrinin and as-yet uncharacterized *Penicillium*-nephrotoxins being involved (Pfohl-Leszkowicz *et al*., 2002).

Scott (2005) has summarised epidemiological studies in Bulgaria, Croatia, Romania, Spain, the Czech Republic, Turkey, Italy, Egypt, Algeria and Tunisia that demonstrate higher levels of blood OTA in patients with kidney and urinary disorders than healthy controls. However, it was noted that these associations do not necessarily constitute a causal relationship.

3.2.2 Toxicity

3.2.2.1 Acute toxicity

No cases of acute human ochratoxicosis have been reported (JECFA, 2001a).

The LD_{50} following oral administration in laboratory animals ranges from 0.2 mg/kg body weight in dogs to 46-58 mg/kg body weight in mice (JECFA, 2001a). In rats, neonates are more sensitive than adults (JECFA, 2001a), while females are more sensitive than males (Pfohl-Leszkowicz *et al*., 2002).

3.2.2.2 Chronic toxicity

OTA is nephrotoxic in all mammalian species tested, with the main target being the renal proximal tubule, where OTA exerts both cytotoxic and carcinogenic effects (JECFA, 2001a). In rodents, the doses causing carcinogenicity were higher than those resulting in nephrotoxicity.

OTA is genotoxic both *in vitro* and *in vivo*, however the mechanism is uncertain and it is not known whether it exerts its genotoxicity through direct interaction with DNA or via a reactive metabolite (JECFA, 2001a).

OTA can cross the placenta and is embryotoxic and teratogenic in rodent species. It is also immunosuppressive in rodents, inhibiting proliferation of B and T lymphocytes. All of these effects occur only at doses much higher than those causing nephrotoxicity (JECFA, 2001a).

3.2.3 Toxicological assessment

JECFA have concluded that the adverse effect occurring at the lowest dose in animal species was nephrotoxicity and that this was also likely to be true in humans (JECFA, 2001a). JECFA established a Provisional Tolerable Weekly Intake (PTWI) for OTA of 112 ng/kg body weight/week (16 ng/kg body weight/day), based on renal function deterioration in pigs with a lowest observed effect level of 0.008 mg/kg body weight/day (JECFA, 1991). Due to the fact that a no observed effects level dose was frequently not observed a higher than usual safety factor of 500 was applied in deriving the PTWI. The PTWI was subsequently rounded down to 100 ng/kg body weight/week (14 ng/kg body weight/day; JECFA, 1995a).

Other toxicological evaluations have focused on carcinogenic endpoints, based on long-term rodent studies. A Canadian risk assessment derived Provisional Tolerable Daily Intakes (PTDIs) for OTA in the range 1.2-5.7 ng/kg body weight/day, equating to an excess lifetime cancer risk of 1:100,000 (see Kuiper-Goodman, 1996 for a summary). The Nordic Council of Ministers used a similar approach in establishing a Tolerable Daily Intake (TDI) for OTA of 5 ng/kg body weight/day (Kuiper-Goodman, 1996). The EU Scientific Committee on Food concluded that it would be prudent to reduce exposure to OTA as much as possible to ensure that exposures are towards the lower end of the range of tolerable daily intakes derived by various organizations (SCF, 1998).

IARC have concluded that there is sufficient evidence for the carcinogenicity of OTA in experimental animals and have classified it as a possible human carcinogen (Group 2B; IARC, 1993).

3.3 Exposure Assessment

3.3.1 OTA in the New Zealand food supply

Only a single study was identified which examined the OTA content of foods in New Zealand (Stanton, 2000b). Table 9 summarises the results of this study.

Table 9: OTA in New Zealand foods

Product type	Number analysed	No. samples with OTA (percentage)	Mean * (µg/kg)	Range of positives (µg/kg)
Breakfast cereals	22	6 (27)	0.10	0.1 - 0.77
Cereals	26	10 (38)	0.13	0.1 - 0.85
Wheat products	10	0 (0)	0.0	
Maize products	9	0 (0)	0.0	
Pulses	14	2 (14)	0.05	0.1, 0.60
Coffee, milo, cocoa	23	17 (74)	1.04	0.3 - 3.5
Dried fruit	35	16 (46)	1.54	0.2 - 22
Wine, grape juice, beer	18	2 (12)	0.04	0.03, 0.67
Pâté	3	0 (0)	0.0	

From Stanton, 2000b

* mean calculated assuming that 'not detected' results were equal to zero

While some of the cereals and cereal products (breakfast cereals) containing OTA were of New Zealand manufacture, this does not preclude the inclusion of imported grain. The foods containing the highest levels of OTA (coffee, dried fruit) were imported. However, the two wines in which OTA was detected were manufactured in New Zealand.

3.3.2 OTA in the Australian food supply

The 20th Australian Total Diet Survey analysed bread, biscuits, rice, oats, processed wheat bran, breakfast cereals, instant coffee, peanut butter, almonds and milk chocolate for OTA. OTA was not detected in any samples at a limit of reporting of 0.001 mg/kg (FSANZ, 2002). However, results from other survey work (see Tables 9 and 10) suggest that this limit of detection is too high to produce meaningful results.

Hocking *et al*. (2003) detected OTA is 90/601 (15%) of Australian wines. However, 85% of positive detections were at concentrations less than 0.2 µg/l, and only one result exceeded 0.5 µg/l.

OTA contamination of cereals in Australia is not believed to be a problem (Webley and Jackson, 1998). However, no survey data were located to support this opinion.

The lack of any other significant information on OTA in Australian foods has been confirmed by Pitt and Tomaska (2002).

3.3.3 Overseas Context

An enormous body of information is available on the incidence and levels of OTA in a variety of commodities and processed foods overseas. Much of this has been summarised by JECFA (2001a). The majority of these data (85%) are from European studies. Table 10 is a reproduction of the summary of these studies compiled by JECFA (2001a).

Table 10: Worldwide data on occurrence of OTA in food

Food	Years (Range)	Countries	Samples tested	Weighted mean OTA concentration (µg/kg)	Maximum level of OTA (µg/kg)
Beer	1993-1999	Canada, Denmark, United Kingdom, Spain, Europe, Italy, Japan, Germany	660	0.025	0.65
Cereals (all)			2700	0.94	
- Barley	1990-1999	Germany, Norway, USA, United Kingdom, Uruguay, Finland, Canada	350	0.53	33
- Maize	1991-1999	Germany, United Kingdom, Croatia, Brazil, Uruguay	95	7.5	614
- Oats	1986-1999	Sweden, Norway, Denmark, Finland, United Kingdom, Germany	280	0.44	56.6
- Rice	1993-1998	Uruguay, United Kingdom, Dubai, Germany	45	0.06	0.28
- Rye	1986-1999	Sweden, Norway, Denmark, United Kingdom, Germany	790	1.2	121
- Wheat	1986-1999	Germany, Netherlands, Norway, Sweden, Brazil, USA, Finland, Denmark, Dubai, United Kingdom, Uruguay	1200	0.38	430
Cereal products	1994-1999	United Kingdom, Tunisia, Dubai, Canada, Germany	1500	0.19	29.8
Cocoa and chocolate	1993-1998	Netherlands, Uruguay, United Kingdom, Germany	270	0.18	2.4
Coffee, green and roasted			1900	0.86	
- green	1995-1999	USA, United Kingdom, Sweden, Germany	130	1.0	27.3
- roasted	1993-1999	Netherlands, USA, Denmark, United Kingdom, Canada, Dubai, Spain, Switzerland, Brazil,	1700	0.76	12.1

Food	Years (Range)	Countries	Samples tested	Weighted mean OTA concentration (µg/kg)	Maximum level of OTA (µg/kg)
		Germany			
- instant	1995-1999	USA, United Kingdom, Canada, Sweden, Spain, Brazil, Germany	290	1.4	9.5
Dried vine fruit	1993-1999	Uruguay, USA, United Kingdom, Germany	860	2.3	53.6
Grape juice	1994-1998	United Kingdom, Germany, Japan	68	0.44	5.3
Pig kidney	1995-1999	Denmark, Germany, France	380	0.12	14.7
Products of animal origin	1993-1999	Uruguay, Denmark, United Kingdom, Germany, France	810	0.052	
Wine, all			1800	0.32	
- red wine	1992-1999	Netherlands, United Kingdom, Italy, France, Germany	1300	0.4	15.6
- white wine	1992-1999	Netherlands, United Kingdom, Italy, Germany	260	0.1	8.9

It should be noted that the studies summarised by JECFA differed considerably in limits of quantitation (LOQ) (0.001-50 μg/kg). It is not surprising that studies with high detection limits 5-50 μg/kg generally failed to detect OTA (JECFA, 2001a). Most studies (95%) used the same analytical methodology (liquid chromatography with fluorescence detection) with LOQs generally less than 0.5 μg/kg. The balance used thin layer chromatography (TLC) with LOQs greater than or equal to 5 μg/kg.

Average levels of OTA in coffee and dried fruits are very similar between the overseas summary (JECFA, 2001a) and analyses of New Zealand foods. This is not surprising, as the sources of these products are likely to be similar in both cases. OTA levels in cereals, wine and meat products appear to be lower in New Zealand (Stanton, 2000b) than in the international summary of JECFA (2001a). Results for these products will reflect contamination in the New Zealand environment and, initially, suggesting that contamination of foods with OTA may be less in New Zealand than in Europe. Although, the small number of samples analysed in New Zealand and the wide diversity of results reported for Europe suggest that any conclusions should be drawn with caution.

OTA has the potential to be retained by animals consuming OTA-contaminated feed and transmitted to foods of animal origin. Skaug (1999) detected OTA in 6/40 conventional cow's milk samples (range 0.011-0.058 μg/l) and 5/47 organic milk samples (range 0.015-0.028 μg/l). OTA was not detected in 20 infant formula samples.

Laciaková *et al*. (2001) detected OTA in hens eggs. However, this was due to penetration of the toxin through the egg shell, rather than transmission from the hen.

There is no evidence to suggest that OTA-contaminated feed can result in residues in the meat of ruminant animals (cattle, sheep, goats, horses).

Meat products from pigs consuming OTA-contaminated feed have been shown to contain OTA and a survey of 325 pigmeat products (mainly sausages) found OTA in 18% of samples at concentrations in the range 0.1-3.4 μg/mg (Gareis, 1996). Higher levels are found in pig kidneys and in pig blood (SCOOP, 1997b). Jørgensen (1998) detected OTA in pork (82% of samples, maximum 1.3 μg/kg), duck (58%, 0.09 μg/kg), duck liver (57%, 0.16 μg/kg), goose (42%, 0.10 μg/kg), goose liver (33%, 0.06 μg/kg) turkey (59%, 0.11 μg/kg), turkey liver (18%, 0.28 μg/kg), and chicken (55%, 0.18 μg/kg).

3.3.4 New Zealand estimates of dietary exposure

Thomson (1996) estimated New Zealand exposure to OTA to be 2.4 ng/kg body weight/day. This was based on Danish data for OTA concentrations in cereals and it should be viewed as speculative only. It is uncertain whether this exposure assessment will under- or over-estimate the true situation. Exclusion of foods such as dried fruit, wine and coffee will lead to under-estimation, while use of European contamination concentration data may potentially lead to over-estimation.

Import data for the year ending September 2005 showed that New Zealand imports significant quantities of dried fruit, particularly apples (402 tonnes; 67% from China, 21% from Chile), apricots (2021 tonnes; 77% from Turkey), grapes (8,630 tonnes; 61% from

Turkey, 14% from USA), dates (1117 tonnes; 88% from Iran), figs (208 tonnes; 83% from Turkey) and prunes (948 tonnes; 80% from USA).

Unroasted coffee (6774 tonnes) is imported from a range of countries, including Vietnam (36%), Colombia (13%), Papua New Guinea (12%) and Brazil (11%), while roasted coffee (1371 tonnes) is principally imported from Australia (73%).

New Zealand's wine imports (53,000 tonnes) are dominated by product from Australia (73%) and South Africa (10%).

3.3.5 Overseas estimates of dietary exposure

Table 11 summarises results of overseas studies which have derived estimates of dietary exposure to OTA.

Table 11: Overseas estimates of dietary exposure to OTA

Country	Year	Population group	Estimated dietary exposure (ng OTA/kg bw/day)	Main contributing food(s)	Reference
Canada		Not specified	1.1-4.5	Cereal, pig meat	Kuiper-Goodman *et al*, 1996
Denmark	1997	Adult, 70 kg body weight	2.0	Rye bread, wheat bread	SCOOP, 1997b
Europe	NR		3.5		CCFAC, 1998
France	1997	Adult, 60 kg body weight	1.5	Bread	SCOOP, 1997b
France	2000-2001	Adult, 15+ years, mean 95th percentile Child, 3-14 years, mean 95th percentile	2.2 3.6 4.1 7.8	Bread, pasta, biscuits, cakes	Leblanc *et al.*, 2005
Germany	1997	Adult, 75.9 kg body weight	0.9	Wheat bread, beer, roasted coffee	SCOOP, 1997b
Italy	1997	Adult, 60 kg body weight	4.6	Cereals	SCOOP, 1997b
Netherlands	1997	Adult, 70 kg body weight	2.0	Wheat	SCOOP, 1997b
Spain	1997	Adult, 70 kg body weight	0.7	Wheat	SCOOP, 1997b
Sweden	1997	Adult, 70 kg body weight	1.5	Wheat	SCOOP, 1997b
United Kingdom	NR	50 volunteers	0.26-3.54	Not specified	Gilbert *et al*, 2001
United Kingdom	1997	Adult, 70.1 kg body weight	1.4	Wheat	SCOOP, 1997b

OTA was not detected in any of the food samples analysed in the 20th Australian Total Diet Survey (FSANZ, 2002). However, as previously mentioned the limits of detection were insufficiently low for meaningful analysis of this contaminant. Pitt and Tomaska (2002) estimated Australian exposure to OTA, based on an assumption that cereals would not contribute to OTA exposure and using European exposure estimates for wine, dried fruit and coffee, at 0.24 ng/kg body weight/day (about 10% of the New Zealand estimate).

All estimates in Table 11 are from developed countries and show exposure to OTA being dominated by contamination of cereals and cereal products. These exposure estimates are similar to the speculative estimate made for New Zealand (Thomson, 1996). This is not surprising as the New Zealand estimate was based on European food concentration data.

Pitt and Tomaska (2002) concluded that, in the absence of exposure from OTA contaminated cereals, dried vine fruits are the major contributors to dietary OTA exposure.

3.4 Risk Characterisation

3.4.1 Adverse health effects in New Zealand

No cases of human ochratoxicosis have been reported in New Zealand and no reports were identified linking kidney disease in New Zealand to exposure to fungal toxins.

The incidence of renal disease in New Zealand is apparently increasing, with 447 new cases reported in 2004 compared to 248 in 1994 and 117 in 1984 (http://www.anzdata.org.au/anzdata/AnzdataReport/28thReport/files/AppendixIII.pdf). The incidence of new patients entering treatment for end stage renal failure in New Zealand (11/100,000 in 2004) is similar to Australia (9.5/100,000 in 2004). Ochratoxicosis is not listed amongst causes of kidney disease in New Zealand or Australia (http://www.anzdata.org.au/anzdata/AnzdataReport/28thReport/files/Ch02NewPatients.pdf). In New Zealand, diabetic nephropathy is the most common type of end stage renal disease (ESRD) (40%), followed by glomerulonephritis (24%) and hypertension (16%).

3.4.2 Adverse health effects overseas

Limited data are available for overseas populations. In 1999 the USA reported over 89,000 new recipients of care for end stage renal disease (ESRD) or approximately 30 cases/100,000 of population (http://kidney.niddk.nih.gov/statistics/statistics.htm), with the primary causes of disease being the same as for the New Zealand population (diabetes, hypertension, glomerulonephritis). No mention is made of fungal toxins in the US summary.

In areas of Croatia and Bulgaria where Balkan Endemic Nephropathy occurs the age adjusted incidence has been reported to be as high as 500/100,000 (Pfohl-Leszkowicz *et al*., 2002). The incidence of urothelial tumours in these regions was also high (40-70/100,000 compared to high incidence areas of Italy with rates of 2-6/100,000).

3.4.2.1 Risk assessments and other activity overseas

JECFA

JECFA most recently reviewed information on OTA in 2001 (56th meeting; JECFA, 2001a). The previously determined PTWI was confirmed at this meeting and concluded that the mechanisms by which OTA causes nephrotoxicity and carcinogenicity are unknown, but that carcinogenicity appeared to follow after nephrotoxicity. JECFA encouraged further studies into fungal ecology, OTA exposure and epidemiological investigations of the role of OTA in chronic kidney disease.

European Commission

The EU Scientific Committee on Food most recently considered OTA in 1998 (SCF, 1998). The opinion expressed summarised tolerable threshold limits derived by other organizations, noting that higher limits were derived using nephrotoxicity as an endpoint than those based on carcinogenicity. The Committee noted an increasing concern about the genotoxicity of OTA and concluded that it would be prudent to reduce exposure to OTA as much as possible.

Canada

Kuiper-Goodman *et al*. (1996) reported the outcomes of a risk assessment based on the carcinogenicity of OTA and derived exposure limits for an excess cancer risk of 1 in 100,000 in the range 1.2-5.7 ng OTA/kg body weight/day.

Codex

Codex, through the 31st meeting of the Codex Committee on Food Additives and Contaminants (CCFAC, 1998), reviewed a position paper on OTA (prepared by Sweden) and concluded that:

- Levels of OTA need to be as low as technically feasible;
- A Code of Practice for reduction of OTA in cereals should be established;
- A Codex maximum limit for OTA in cereals of 5 μg/kg be established; and
- Codex should establish sampling plans and methods of analysis for OTA in cereals.

3.5 Risk Management Information

3.5.1 Relevant food controls: New Zealand

3.5.1.1 Establishment of regulatory limits

New Zealand does not currently have regulatory limits for OTA.

3.5.2 Relevant food controls: overseas

3.5.2.1 Establishment of regulatory limits

Regulations for the 25 countries (counting the EU as a single country) which reported regulation of OTA in foods (but not feeds) are given in Table 12 (van Egmond and Jonker, 2003).

Table 12: Regulatory limits for OTA in various countries (food regulations only)

Country	Commodity description	Regulatory limit (µg/kg)
Bulgaria	Dried vine fruits	5
	Cereals and processed products thereof for direct human consumption	3
	Cereals to be subject to sorting, or other physical treatment, before human consumption	5
	Spices	10
	Green coffee beans	8
	Roasted coffee	4
	Beer	0.2
	Grape juice	3
Cuba	Coffee, cereals	5
Czech Republic	Child and baby nourishment	1
	Flours and cereal products	3
	Foodstuffs, type A (not specified)	5
	Foodstuffs, type B (not specified)	10
Denmark	Pig kidney	
	- viscera condemned	10
	- whole carcass condemned	25
Estonia	Pig liver	10
	Cereal, cereal flours, cereal groats and flakes, past products, ordinary baker's wares, fine baker's wares, isolates, concentrates and hydrolysates of cereals protein	5
EU	Raw cereal grains (including raw rice and buckwheat)	5
	All products derived from cereals (including processed cereal products and cereal grains intended for direct human consumption)	3
	Dried vine fruits (currants, raisins and sultanas)	10
Greece	Coffee, raw and processed	20
Hungary	Cereals (including rice and *Fagopyrum* sp.	5
	Every cereal product including milled products and those cereal products used for direct human consumption	3
	Raisin (currant, sultana), roasted coffee and coffee products, other plant originated foods	10
	Green/unroasted coffee	15
Indonesia	Coffee	Not detectable

Country	Commodity description	Regulatory limit (µg/kg)
Iran	Dates, dried grapes (raisins and sultanas), figs and all dried fruits	10
	Baby food based on cereals with milk	1
	Baby instant food (ready to use)	1
	Barley	50
	Maize	50
	Rice	5
	Wheat	5
	Legumes	20
Israel	Cereal, cereal products and other foods	50
Italy	Coffee	8
	Roasted coffee	4
	Cocoa and derived products	0.5
	Beer	0.2
	Pig meat and derived products	1
	Fruit juice	50
	Baby food	0.5
Latvia	Cereals	5
Lithuania	Following EU regulations	
Morocco	Cereals	30
Poland	Following EU regulations	
Romania	Alimentary products	20
	Alimentary products for babies	5
Serbia and Montenegro	All foodstuffs	10
Singapore	Cereal, raw coffee beans	2.5
	Roasted coffee beans	2.5
Slovakia	Milk, meat, poultry, flour and its products, rice, vegetables, potatoes	5
	Infant formulae	1
	Food for children	1
	Other foodstuffs	10
Slovenia	Following EU regulations	
Sudan	Wheat	15
Switzerland	Spices	20
	Dried fruit	20
	Infant formulae and follow-on formulae	0.5
	Processed cereal-based foods and baby foods for infants and young children	0.5
	All foodstuffs	5
Turkey	Raw grain	5
	Foodstuffs produced from grain	3
	Dried raisins	10
Uruguay	Rice, barley, beans, coffee, corn	50

From van Egmond and Jonker (2003)

3.5.2.2 Codes of Practice

Codex have developed a draft Code of Practice for the prevention of OTA contamination in cereals (http://www.who.int//fsf/Chemicalcontaminants/ochratoxin00_17.pdf). The Code identifies grain storage moisture content as the critical variable in control of OTA contamination and recommends a range of practices based on GAP at the preharvest, harvest, preservation (drying), storage and transport stages). These practices are generally targeted at minimising plant stress, minimising physical and insect damage, eliminating fungal vectors, achieving rapid and effective grain drying and maintaining the grain in a dry environment, free of mould and insects.

3.5.2.3 Management of OTA formation in crops

Control of OTA production in foods depends on the crop type and its location, as these factors will influence which fungal species is likely to grow and produce toxins (JECFA, 2001a). *A. ochraceus* occurs primarily in stored foods, while *A. carbonarius* and *A. niger* appear to be saprophytes occurring on fruit, that can gain entry due to the fruit being damaged. Little information is available on *P. verrucosum*, but it is generally believed to be a storage fungus.

Management of *A. carbonarius* and *A. niger* in fruit crops is dependent upon minimizing physical damage, specifically:

- Control of pathogenic fungi;
- Control of mechanical damage, from pruning, leaf reduction and harvesting; and
- Control of splitting.

3.5.2.4 Management of OTA formation during crop storage

OTA formation in cereals is principally due to infection with *P. verrucosum.* Control of OTA formation in stored grain is principally achieved by reducing grain moisture content and preventing the grain from becoming wet again. A moisture content below 17-19% (equivalent to a water activity of 0.8 or less) will prevent OTA formation by *A. ochraceus* (JECFA, 2001a).

Fumigants, added to grain stores to control insect pests will, in some cases, also achieve control of fungal growth. However, many of the fumigants that are effective in this respect are being phased out due to environmental or human toxicity concerns (JECFA, 2001a).

3.5.3 Influence of processing on OTA levels

3.5.3.1 Wheat

OTA tends to be concentrated in the outer bran layers of cereals (Scudamore, 2005). Wheat cleaning, including abrasive scouring, was shown to remove 44% of OTA (Scudamore *et al*., 2003). Straight run white flour contained about 75% less OTA than the parent wheat. However, breadbaking had little additional impact on OTA levels.

Scudamore *et al*. (2004) examined the impact of extrusion on OTA contaminated whole wheat flour. Even under the harshest extrusion conditions examined OTA reduction was no greater than 40%.

3.5.3.2 Barley

OTA levels increase during the malting of barley, with increases as high as 20 times being reported. However only 20% of the OTA in the malt remains in the finished beer (Scudamore, 2005). These results are similar to those reported by Baxter *et al*. (2001) of 13 to 32% of the OTA in the malt surviving in the beer.

3.5.3.3 Coffee

Coffee is processed by two main methods to the point where the bean can be roasted. Natural processing usually involves drying of the fruit (usually in the sun, but occasionally mechanically) to produce 'cherry coffee'. The coffee can be stored in the cherry form or shelled and stored as green coffee. Wet processing involves mechanical removal of the skin and most of the mesocarp, followed by fermentation to remove remaining mesocarp (Frank, 1999).

OTA production occurs only during drying of green coffee beans, due to growth of *A. carbonarius, A. ochraceus* or *A. niger* (Bucheli and Taniwaki, 2002). Rapid and effective drying will prevent or minimize OTA production (Taniwaki *et al*., 1999). OTA production in coffee can be controlled by application of Good Manufacturing Practice (GMP). Storage of properly dried green coffee does not appear to result in any further development of OTA.

Despite the demonstrated thermal stability of OTA, roasting of coffee has been shown to result in up to 100% reduction in OTA levels from those in the green coffee (Bucheli and Taniwaki, 2002), although results are extremely variable with some researchers reporting little decrease in OTA levels during roasting (Viani, 1996). Blanc *et al*. (1998) carried out experiments on three tonnes of naturally OTA-contaminated green coffee and demonstrated that roasting reduced OTA levels to about 16% of the levels in the green coffee, while soluble coffee manufacture further reduced the level of contamination down to about 13%.

3.6 Conclusions

3.6.1 Description of risks to New Zealand consumers

Evidence for a role for OTA in the causation of human kidney disease is suggestive, but not conclusive. The progression of the condition known as Balkan Endemic Nephropathy (BEN) is similar to effects observed in laboratory animals exposed to OTA. Diets in BEN-affected areas are known to be heavily contaminated with OTA.

New Zealand does not exhibit regions of endemic kidney disease and the general incidence of kidney disease in New Zealand, although rising, is not high. Major causes of kidney disease in New Zealand are well characterised, and do not include food contaminants.

The study of Stanton (2000b) demonstrated the presence of OTA in the New Zealand food supply. While many of the contaminated foods available in New Zealand are likely to be

imported (e.g. coffee/cocoa/milo, dried fruits) the study of Stanton indicates that New Zealand-produced cereals and fruits may also contain OTA. The limited results available suggest that contamination of the New Zealand food supply is at a level similar to or lower than that reported for European countries (SCOOP, 1997b) and similar non-European countries (USA, Canada; JECFA, 2001a).

Exposure estimates for OTA carried out overseas have generally identified cereals in general and wheat in particular as the major contributors to OTA exposure. Although no OTA analyses have been carried out on New Zealand breads, Stanton (2000b) detected OTA in 6/14 (43%) of wheaten or rye flour samples analysed, suggesting that wheat products may be a significant contributor to OTA exposure in New Zealand. However, OTA concentrations found in New Zealand foods are not high by international standards and the exposure of New Zealanders to OTA is likely to be similar to or lower than for many European countries and, hence, within currently agreed tolerable limits.

While the study of Stanton (2000b) examined the OTA content of New Zealand retail flours, the OTA content of bread was not examined. As bread is the major wheat-based food consumed in New Zealand, information on the OTA content of retail breads would be of interest. New Zealand's temperate climate means that in some seasons wheat may be harvested at higher than optimum moisture contents and these conditions would increase the risk of OTA formation.

3.6.2 Commentary on risk management options

New Zealand does not currently exercise direct risk management measures to control the entry of OTA into the human food chain. Control of OTA in New Zealand produced food is likely to occur as a consequence of GAP and GMP practices, designed to achieve other quality and safety objectives.

3.6.3 Data gaps

The major data gap at present is the establishment of a definitive link between OTA exposure and adverse human health effects, although expert bodies such as JECFA and SCF feel that there is sufficient evidence to recommend that exposure be kept as low as possible.

In New Zealand information on OTA contamination in bread is not currently available.

4 TRICHOTHECENES

4.1 Hazard identification

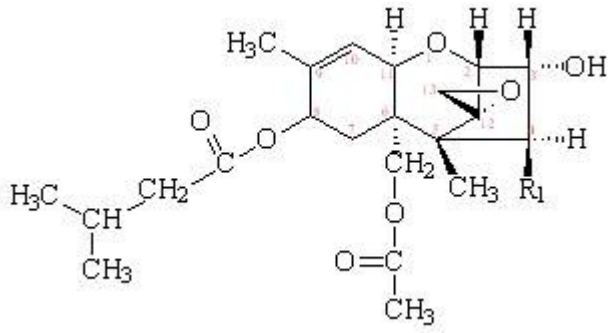
The trichothecenes are a family of approximately 150 structurally related compounds produced by fungi of the genera *Fusarium, Cephalosporium, Myrothecium, Stachybotrys, Trichoderma* and others. Trichothecenes of significance in food are produced by *Fusarium* species, including *F. poae, F. sporotrichioides, F. acuminatum, F. graminearum, F. culmorum, F. crookwellense, F. avenaceum* and *F. equiseti* (CAST, 2003). The toxins in this group that have received the most attention are deoxynivalenol (DON), nivalenol (NIV), T-2 toxin (T2) and HT-2 toxin (HT2), with lesser attention paid to diacetoxyscirpenol (DAS) and other trichothecene toxins. Focus on these toxins has been due to the fact that they are the major toxins formed in foods and/or there is evidence for their involvement in human disease. The current analysis will focus on DON, NIV, T2 and HT2. Trichothecenes have been reported in cereal grain crops worldwide (Schothorst and van Egmond, 2004).

4.1.1 Structure and nomenclature

The trichothecenes are sesquiterpenoids possessing a tetracyclic 12,13-epoxytrichothecene skeleton. They can be conveniently divided into four categories according to similarity of functional groups (Ueno, 1977). The first class is characterised by a functional group other than a ketone at C-8 (type A) and include T2 and HT2. The second category of trichothecenes has a carbonyl function at C-8 (type B) typified by DON and NIV. The third category is characterised by a second epoxide group at C-7,8 or C-9,10 (type C), and the fourth contains a macrocyclic ring system between C-4 and C-15 with two ester linkages (type D). Type C and type D trichothecenes are not normally associated with food.

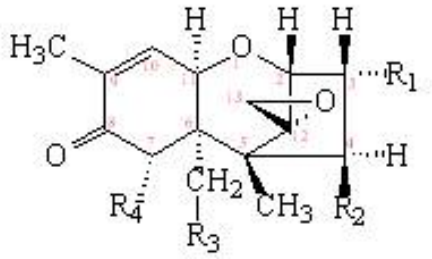
Structural summaries are reproduced in Figure 4 from a WHO summary (WHO, 1990).

Figure 4: Structure of type A and B trichothecenes



Type A

T2 (R_1 = OAc), HT2 (R_1 = OH)



Type B

DON (R_1 = OH, R_2 = H, R_3 = OH, R_4 = OH), NIV (R_1 = OH, R_2 = OH, R_3 = OH, R_4 = OH),

4.1.2 Occurrence

Type A trichothecenes (T2, HT2) are frequently associated with *F. tricintum, F. poae, F. sporotrichioides, F. acuminatum, F. equiseti* and *F. semitectum* (WHO, 1990). Trichothecene formation by these fungal species has been reported in Europe and North America and occasionally in Asia, but not in Africa or Australia (CAST, 2003). Type B trichothecenes (DON, NIV) are frequently associated with *F. graminearum* and *F. culmorum* (WHO, 1990). Trichothecene formation by these species, particularly *F. graminearum* appears to be almost universal (CAST, 2003). Type C and type D trichothecenes are not normally associated with food.

Table 13 summarises information on *Fusarium* species occurring and production of trichothecenes in New Zealand crops.

Table 13: Trichothecene production by *Fusarium* species in New Zealand crops

Crop	Fungal species ('>' indicates order of detection frequency)	Trichothecenes detected	Study reference
Maize (Manawatu)	*F. graminearum* *F. culmorum* *F. subglutinans* *F. acuminatum*	T2, DON, DAS detected, but no details of which species produced which mycotoxins	Hussein *et al.*, 1987

Crop	Fungal species ('>' indicates order of detection frequency)	Trichothecenes detected	Study reference
Maize (Waikato)	*F. graminearum* >*F. semitectum* > *F. crookwellense**	No analyses carried out for mycotoxins	Sayer, 1991
Wheat (Waikato)	*F. graminearum* >*F. avenaceum, F. crookwellense, F. poae*	No analyses carried out for mycotoxins	Sayer and Lauren, 1991
Wheat (East Coast)	*F. culmorum* > *F. poae*		
Wheat (Manawatu)	*F. graminearum, F. culmorum* > *F. avenaceum, F. crookwellense, F. poae*		
Wheat (South Island)	*F. avenaceum* > *F. poae, F. culmorum*		
Barley (Waikato)	*F. graminearum* >*F. avenaceum, F. crookwellense, F. poae*		
Barley (East Coast)	*F. avenaceum, F. culmorum, F, equiseti,*> *F. poae*		
Barley (Manawatu)	*F. poae* > *F. avenaceum, F. crookwellense, F. culmorum, F. graminearum*		
Barley (South Island)	*F. avenaceum, F. poae* > *F. culmorum, F. graminearum*		
	F. poae > *F. avenaceum*		
Oats (East Coast)	*F. avenaceum* > *F. culmorum* > *F. poae*		
Oats (South Island)	*F. graminearum* > *F. crookwellense* > *F. semitectum*		
Maize (North Island)			
Maize, wheat, barley, oats (all New Zealand)	*F. graminearum*	NIV, DON	Lauren *et al*., 1992
	F. culmorum	NIV, (DAS)#	
	F. avenaceum		
	F. crookwellense	NIV, (DAS)#	
	F. poae	DAS	
	F. semitectum		
	F. equiseti		
	F. tricinctum		
Wheat, barley (North Island)	*F. graminearum* > *F. avenaceum* > *F. poae* > *F. crookwellense* > *F. culmorum*	No analyses carried out for mycotoxins	Cromey *et al*., 2001
Wheat, barley (South Island	*F. avenaceum* > *F. culmorum* > *F. graminearum* > *F crookwellense*	No analyses carried out for mycotoxins	Cromey *et al*., 2001
Maize (Manawatu)	*F. graminearum* > *F. culmorum* > *F. acuminatum, F. subglutinans*	No analyses carried out for mycotoxins	Hussein *et al*., 2002

* Order given here is for field maize. In stored maize the proportion of *F. semitectum* was greater than *F. graminearum.*

Detections of DAS were infrequent in comparison to detections of NIV

While there are differences between different studies, *F. graminearum* appears to be the *Fusarium* species that most commonly infects grain crops in the North Island. *F. graminearum* is associated with production of Type B trichothecenes (NIV, DON). Monds *et al.* (2005) examined the mycotoxin-producing potential of a number of *F. graminearum* isolates from New Zealand grains and found that the isolates either produced NIV or DON or neither, but rarely both NIV and DON in significant amounts.

South Island crops are more likely to be infected with *F. avenaceum*. Bosch *et al*. (1989) demonstrated significant rodent toxicity in extracts from *F. avenaceum* and found high levels of moniliformin in these extracts and a haemorrhagic factor (wortmannin) in one extract.

There have been no reports of significant trichothecene production by *F. avenaceum* isolates in New Zealand. *F. avenaceum* is the most common *Fusarium* species infecting crops in Northern Europe and has been reported to produce the mycotoxins moniliformin, beauvericin and enniatins (Morrison *et al.,* 2002).

Other species common in New Zealand grain are known trichothecene producers, including *F. culmorum* (DON, NIV), *F. poae* (HT2, T2, DAS, NIV), and *F. crookwellense* (NIV, DAS).

The study of Hussein *et al*. (1987) is unique in reporting detection of T2. Although T2 has been looked for, it has not been detected in subsequent studies and there must be some questions regarding these early findings.

4.2 Hazard Characterisation: Adverse Health Effects

A number of incidents of human toxicosis have been associated with trichothecene contaminated foods. However, it should be noted that in most cases the implicated food may contain more than one known mycotoxin and may potentially contain other, as yet uncharacterized, toxins.

In 1987, an outbreak of acute disease affecting approximately 50,000 people in the Kashmir Valley of India was attributed to consumption of bread made from rain-damaged wheat (Bhat *et al*., 1989). The wheat contained DON (0.34-8.4 mg/kg in 11 of 24 samples), acetylDON (0.6-2.4 mg/kg in 4 of 24 samples), NIV (0.03-0.1 mg/kg in 2 of 24 samples) and T2 (0.55-4.0 mg/kg in 3 of 24 samples). Cases exhibited mainly minor gastrointestinal symptoms (abdominal pain, diarrhoea, bloody stool and vomiting) for approximately two days. Onset of disease occurred approximately 15 minutes to one hour after consumption of bread. It was noted that samples were not collected until four months after the outbreak.

4.2.1 Conditions

4.2.1.1 Deoxynivalenol (DON)

No human deaths attributed to DON have been reported (JECFA, 2001b).

The acute effects are similar to microbial food poisoning (nausea, vomiting, diarrhea, abdominal pain, headaches, dizziness and fever). The condition is sometimes known as red mould toxicosis (JECFA, 2001b).

A number of epidemiological studies in China have associated consumption of DON-contaminated maize or wheat to chronic conditions such as oesophageal cancer, gastric cancer and endemic osteoarthritis (JECFA, 2001b). There was consistent evidence of higher levels of DON in grains in affected areas compared to control areas.

IARC classified DON in 1993 as not classifiable as to its carcinogenicity to humans (Group 3; IARC, 1993). Subsequent chronic rodent studies support its non-carcinogenicity (Iverson *et al*., 1995).

4.2.1.2 Nivalenol (NIV)

No data are currently available on human health effects of NIV.

4.2.1.3 T-2 toxin (T2)

T2 has been implicated in a condition called alimentary toxic aleukia (ATA), incidents of which were reported in the former USSR during the period 1931-1947 following consumption of mouldy over-wintered wheat (JECFA, 2001c). Moulds were reported to be *F. poae* and *F. sporotrichioides*. The symptoms included necrotic lesions of the oral cavity, oesophagus and stomach and pronounced leucopenia (low white blood cell count) and resulted in high mortality rates.

An outbreak occurred in China of 97 cases following consumption of rice infected by *F. heterosporum* and *F. graminearum* (Wang *et al.*, 1993). Symptoms included nausea, dizziness, vomiting, abdominal distention and pain, chills and diarrhea. Onset of disease occurred approximately 10-30 minutes after consumption of rice. T2 was detected in three rice samples at levels of 0.18-0.42 mg/kg. No analyses were conducted for other mycotoxins.

IARC categorised T2 in 1993 as not classifiable as to its carcinogenicity to humans (Group 3; IARC, 1993).

4.2.1.4 HT-2 toxin (HT2)

No reports were found linking exposure to HT2 to human disease. However, HT2 is a major metabolite of T2 and the two toxins are generally considered together when being evaluated (JECFA, 2001c; SCF,2001).

4.2.2 Toxicity

4.2.2.1 Acute toxicity

As outlined above, trichothecenes have been implicated in a number of outbreaks of acute human toxicosis.

Table 14 summarises LD_{50} information for the major trichothecenes.

Table 14: Acute toxicity (LD_{50}) of trichothecenes in experimental animals

Trichothecene	Species	Route of administration	LD_{50} (mg/kg body weight)
DON	Mouse	Oral	46-78
DON	Mouse	Intraperitoneal, subcutaneous	43-77
DON	Chicken	Oral	140
DON	Duck	Subcutaneous	27
NIV	Mouse	Oral	39
NIV	Mouse	Intraperitoneal, subcutaneous, intravenous	5-10
NIV	Rat	Oral	19.5
NIV	Rat	Subcutaneous	0.9
T2	Mouse	Oral	10
T2	Mouse	Intraperitoneal, subcutaneous, intravenous	0.4-14
T2	Rat	Intraperitoneal, subcutaneous, intravenous, intramuscular	0.47-2.2
T2	Guinea pig	Intraperitoneal, subcutaneous, intravenous	1-2
T2	Rabbit	Intramuscular	1.1
T2	Chicken	Oral	1.8-6.3
T2	Pig	Intravenous	1.2
HT2	Mouse	Intraperitoneal, subcutaneous	6.5-10
HT2	Rat	Subcutaneous	1
HT2	Chicken	Oral	7.2

Short term animal exposure to DON is characterised by reduced feed consumption and vomiting (hence the alternative name, vomitoxin) (JECFA, 2001b).

4.2.2.2 Chronic toxicity

The main toxic effect of trichothecenes is their ability to bind to ribosomes and inhibit protein synthesis (SCF, 2002). Trichothecenes have an inhibitory effect on RNA and DNA synthesis and exert toxic effects on cell membranes. Trichothecenes are also immunotoxic, although effects on the immune system are strongly dose dependent and they may be immunostimulatory at low concentrations (Pestka *et al*., 2004).

4.2.3 Toxicological assessment

JECFA have established a Provisional Maximum Tolerable Daily Intake (PMTDI) for DON of 1 μg/kg body weight/day, based on a NOEL of 100 μg/kg body weight/day in a 2-year

mouse feeding study (JECFA, 2001b). Although it was recognised that DON can cause acute human illness, JECFA concluded that there was insufficient information to establish an acute exposure limit.

The EU Scientific Committee on Food came to the same conclusions in establishing a temporary TDI (t-TDI) for DON (SCF, 1999). This t-TDI was subsequently upgraded to a full TDI (SCF, 2002).

The EU Scientific Committee on Food noted that only LOAELs were available from long-term studies on NIV and used a lowest LOAEL of 0.7 mg/kg body weight/day, for growth retardation and leucopenia in mice, and a safety of 1000 to derive a temporary TDI (t-TDI) for NIV of 0.7 μg/kg body weight/day (SCF, 2000a).

JECFA concluded that the toxic effects of T2 and HT2 could not be differentiated and included HT2 in the PMTDI established for T2 (JECFA, 2001c). JECFA concluded that the single long term study available was not suitable for establishing a tolerable intake and based their assessment on critical effects (immunotoxicity and haematotoxicity) in several short-term studies on pigs. The lowest LOEL of 0.029 mg/kg body weight/day for changes in white and red blood cell counts was considered to be close to a NOEL, due to the subtlety and reversible of effects seen. A safety factor of 500 was applied to derive a PMTDI of 0.06 μg/kg body weight/day for T2 and HT2 (JECFA, 2001c).

The EU Scientific Committee on Food came to the same conclusions in establishing a temporary TDI (t-TDI) for T2 and HT2 combined of 0.06 μg/kg body weight/day (SCF, 2001).

4.3 Exposure Assessment

4.3.1 Trichothecenes in New Zealand cereal grains

Table 15 summarised published information on trichothecenes in New Zealand grain crops. Trichothecene mycotoxins are common contaminants in New Zealand-grown cereals, particularly those grown in the North Island.

Table 15: Trichothecenes in New Zealand cereal grains

Crop	Year	Location	Mycotoxin	Proportion positive	Maximum Concentration (mg/kg)		Reference
					DON	NIV	
Maize	1984	Manawatu	DON DAS T2	11/20 6/20# 13/20§	0.3		Hussein *et al*., 1989
Maize	1987-1989	Waikato Manawatu Gisborne	NIV/DON NIV/DON NIV/DON	38/38 19/19 16/34	3.5 1.7 0.97	1.9 1.95 3.6	Lauren *et al*., 1991
Maize	1992-1994	Waikato, Bay of Plenty, Manawatu, Gisborne	NIV/DON	605/616	8.5	7.0	Lauren *et al*., 1996
Wheat	1986-1989	Waikato Manawatu Gisborne	NIV/DON NIV/DON NIV/DON	48/48 30/36 3/6	11.95 2.31	1.27 0.78 0.09	Lauren *et al*., 1991
Wheat	1998-2000	Wairarapa, Manawatu, Rangatikei	NIV DON	12/15 14/15	3.25	0.57	Cromey *et al*., 2002
Wheat	1998-2000	Wairarapa, Manawatu, Rangatikei	NIV* DON*	12/54 12/54	1.82	0.93	Cromey *et al*., 2002
Barley	1987-1989	Waikato Manawatu Gisborne	NIV/DON NIV/DON NIV/DON	17/18 14/23 2/3	1.0 0.09 0.08	0.53 0.22 0.03	Lauren *et al*., 1991
Oats	1989	Gisborne	NIV/DON	2/3	0.08	0.61	Lauren *et al*., 1991

NIV = nivalenol DON = deoxynivalenol T2 = T2 toxin DAS = diacetoxyscirpenol
# DAS concentrations in the range 0.01-0.9 mg/kg were reported
§ T2 Concentrations in the range 0.005-0.2 mg/kg were reported
* Results were only reported for samples with combined NIV + DON levels greater than 0.5 mg/kg

Maximum levels of DON and NIV were particularly high in the study of Lauren *et al*. (1996). It was noted that during the study period the weather was generally cooler than average, with 1991/92 particularly being characterized by a cold, wet summer and late harvest.

Lauren *et al.* (1991) also examined 102 samples of wheat, 41 samples of barley and 26 samples of oats from South Island sites (Canterbury, South Otago and Southland). While results for these sites were not given in detail, the authors noted that:

- The incidence of trichothecenes in South Island grain crops was low (20%).
- Only DON and NIV-type trichothecenes were detected.
- The level of contamination never exceeded 0.1 mg/kg.

4.3.2 Trichothecenes in the New Zealand food supply

Lauren and Veitch (1996) carried out a survey of NIV and DON in maize-based foods available in New Zealand. Results are summarised in Table 16.

Table 16: Trichothecenes in New Zealand foods

Food	Number of samples	Number of samples positive (range, mg/kg)	
		NIV*	DON*
Breakfast cereals	20	3 (0.07-0.08)	2 (0.10-0.11)
Extruded snack foods	20	1 (0.05)	ND
Maize meal products (flours, grits)	17	6 (0.06-0.65)	8 (0.05-0.41)
Breads	16	2 (0.06-0.20)	2 (0.04-0.05)
Masa flour products (corn chips, taco shells)	24	2 (0.03-0.05)	1 (0.09)
Snack bars	13	3 (0.03-0.06)	ND
Maize oil	8	ND	ND
Miscellaneous products (corn syrup, brewing sugar)	6	ND	ND
Total	**124**	**17 (13.7%)**	**13 (10.5%)**

NIV = nivalenol DON = deoxynivalenol ND = not detected at detection limit of 0.05 mg/kg

* Where samples were analysed in duplicate, with one result being positive and the other not detected, results have been reported here as the mean, with not detected results assigned a concentration of zero. Hence, some results reported here are below the limit of detection for single results.

The majority of food samples tested did not contain detectable amounts of DON or NIV and concentrations, when detected, were generally lower than those detected in New Zealand-grown maize. Both food processing and introduction of imported maize may have an influence on trichothecene levels in processed foods.

4.3.3 Trichothecenes in Australian cereal grains

Relatively little information was available on trichothecenes in Australian grain.

Blaney *et al*. (1987) examined wheat from southern Queensland – a wheat growing region that was considered to be more likely to suffer rain damage and fungal infection. In 1983, 1291 samples of wheat were examined with 62 found to contain greater than 0.2% of 'pink grain' – an indicator of fungal infection. In 1984 and 1985, only general purpose (GP) graded wheat was examined (60 and 80 samples respectively). Eleven lines of wheat from the 1983 harvest and two from the 1984 harvest, containing elevated proportions of pink grains, were analysed and found to contain DON in the range 0.02 to 11.7 mg/kg. The remaining wheat samples were pooled on the basis of grade and receiving depot to give 37 pooled wheat samples across the three harvest years (1983, 1984 and 1985). DON was detected in 31/37 pooled wheat samples at concentrations ranging from a trace (<0.01 mg/kg) to 1.7 mg/kg. The highest DON levels were consistently found in GP grade wheat. Australian wheat imported into New Zealand is predominantly Australian Standard White (ASW), with lesser amount of Prime Hard (PH).

Following a wet harvest in 1983, Tobin (1988) sampled 12 wheat lines from the Northern Rivers area of New South Wales and found 11 samples were positive for DON, with an average concentration of 1.8 mg/kg and a maximum concentration of 6.7 mg/kg. Tobin also analysed grain responsible for vomiting and feed refusal in pigs and found DON at a level of

3.7 mg/kg. Three samples of triticale were taken from a single crop over a three week period when harvesting had been disrupted by rain. The samples contained 1.1, 11.2 and 9.0 mg DON/kg respectively. Samples of barley exhibiting *Fusarium* head blight were taken from farms where DON-positive wheat samples had been obtained. No toxin was detected in the barley samples.

4.3.4 Overseas context

JECFA (2001b; c) have consolidated a large amount of information on DON, T2 and HT2 in food commodities. Summary results are included in Table 17.

Table 17: Worldwide data on occurrence of trichothecenes in cereal crops

Commodity	Mycotoxin	Number of countries	Number of individual samples represented	Weighted mean (Maximum; mg/kg)*	Percentage of samples < LOD or LOQ*
Barley	DON	11	1,778	0.72 (34)	41
Barley	T2	6	372	0.0046 (0.31)	91
Barley	HT2	4	364	0.0044 (0.29)	92
Maize	DON	17	5,719	0.18 (19)	52
Maize	T2	9	1,239	0.0032 (2.4)	97
Maize	HT2	5	292	0.0029 (0.23)	98
Oats	DON	7	834	0.09 (2.6)	32
Oats	T2	4	758	0.021 (0.53)	71
Oats	HT2	4	758	0.035 (2.0)	67
Popcorn	DON	2	50	0.31 (4.5)	92
Rice	DON	4	203	0.15 (9.5)	80
Rice	T2	2	125	0.0007 (0.019)	95
Rice	HT2	1	26	ND	
Rye	DON	4	295	0.07 (1.3)	51
Rye	T2	3	83	0.0002 (0.017)	99
Rye	HT2	3	87	0.00001 (0.023)	99
Sorghum	DON	1	15	ND	100
Triticale	DON	1	10	0.09 (0.20)	20
Wheat	DON	18	14,200	0.39 (30)	38
Wheat	T2	10	2,564	0.0016 (0.8)	96
Wheat	HT2	3	1,740	0.0019 (0.31)	90
Other cereals	DON	2	254	0.05 (2.3)	55

* In calculating means, results below the LOD/LOQ were assigned a concentration of zero

There have also been a number of reports of trichothecene occurrence in processed foods, which were not summarised by JECFA (2001b, c).

Papadopoulou-Bouraoui *et al*. (2004) found DON in 87% of 313 European retail beer samples, with contamination in the range 4-57 µg/l. Molto *et al*. (2000) analysed Argentinean beer for a range of trichothecenes. DON was detected in 44% of beer samples, with toxin levels in the range 4-221 µg/l. No other trichothecenes were detected. Suga *et al.* (2005) detected DON in Japanese domestic beer samples in the range 0.5-1.4 µg/kg. HT2 and NIV

were detected in malt, but not in beer. Ruprich and Ostry (1995) detected DON in 77% of 77 Czech beer samples, with concentrations in the range 7-70 μg/l.

Schollenberger *et al*. (2005a) analysed 101 commercially available German bread samples. DON was the most commonly detected trichothecene, detected in 92% of bread samples with a median concentration of 134 μg/kg (range 15-690 μg/kg) in positive samples. NIV, T2, HT2 and 3-acetyl-DON were also detected, but less frequently (1-8% of samples) and at lower levels (median concentrations in the range 4-25 μg/kg). DON levels were associated with a greater proportion of wheat in wheat-rye mixes and median DON levels in bread from organically grown cereals were lower than breads from conventionally grown cereals.

Cirillo *et al.* (2003) found DON in 84% of 2002 Italian processed foods, including breads, pasta, breakfast cereals, biscuits and baby foods. Concentrations were in the range 7-930 μg/kg. Pacin *et al.* (1997) examined Argentinean wheat, wheat flour and bakery products for the presence of DON. The prevalence of contamination was essentially the same between the raw wheat and the bakery products (approximately 93%), although the average concentration in the wheat (1800 μg/kg) was significantly higher than that in the flour (1300 μg/kg) and the bakery products (460 μg/kg).

A survey of retail corn-based foods did not detect trichothecenes (DON, NIV) in sweet corn, corn oil, popcorn and a range of corn-containing pre-prepared meal. Trichothecenes were detected in some samples of polenta, cornflour, taco shells/tortilla chips and breakfast cereals (FSA, 2005).

Schollenberger *et al*. (2005b) detected trichothecenes in several non-cereal foods, including potato products, pumpkin seeds, sunflower seeds and hazelnuts, with T2 and HT2 being the main toxins detected. A survey of 'ethnic' foods available in the UK detected trichothecenes in a range of retail foods including rice, wheat noodles, bread (chapattis, nan), chilli powder, curry powder, ginger, garlic, curry paste and chilli sauce (MAFF, 1994b).

El-Banna *et al*. (1983) demonstrated that DON in chicken feed ration (4-5 mg/kg) was not transferred to the eggs or tissues of chickens receiving the feed. Similarly, DON and its de-epoxy derivative were not detected in eggs from hens fed a DON-contaminated maize-based diet (11.9 mg DON/kg) for 16 weeks (Valenta and Danicke, 2005). Sypecka *et al*. (2004) reported some transmission of DON to the eggs of hens fed naturally-contaminated wheat (up to 10 mg/kg of feed), although rates of transmission were extremely low.

Beasley and Lambert (1990) reviewed information on metabolism of trichothecenes by animals. The toxins are rapidly eliminated and residues in animals tissues were either not detected or only detected at very low levels. Withdrawal of contaminated feed results in rapid clearance of residues from tissues.

While making direct comparisons is somewhat problematic, DON contamination levels in New Zealand cereals are not inconsistent with those encountered overseas.

4.3.5 New Zealand estimates of dietary exposure

Based on the food concentration data of Lauren and Veitch (1996; see Table 16), Thomson (1996) estimated dietary exposure of New Zealanders to DON and NIV at 5.6 ng/kg body weight/day for each mycotoxin. This estimate was based solely on consumption of maize products. Maize is not a highly consumed food in New Zealand (3.2 g/person/day; ANZFA, 2001b) and the exposure estimates of Thomson are likely to be underestimates.

No estimates for T2 and HT2 exposure in New Zealand were found.

4.3.6 Overseas estimates of dietary exposure

A summary of exposure estimates for DON, NIV, T2 and HT2 is given in Table 18.

Table 18: Overseas estimates of dietary exposure to trichothecenes (DON, NIV, T2, HT2)

Country	Population group	Mean exposure (µg/kg body weight/day)	Reference
Deoxynivalenol (DON) TDI = 1.0 µg/kg body weight/day			
African diet	Adult, 60 kg	0.78	JECFA, 2001b
Latin American diet	Adult, 60 kg	1.2	JECFA, 2001b
European diet	Adult, 60 kg	1.4	JECFA, 2001b
Middle Eastern diet	Adult, 60 kg	2.4	JECFA, 2001b
Far Eastern diet	Adult, 60 kg	1.6	JECFA, 2001b
France	Adult, 15+ years Child, 3-14 years	0.28 0.45	Leblanc *et al*., 2005
Austria	Total population, 75 kg	0.29-0.66	SCOOP, 2003
Belgium	Adolescent, 13-18 years, 60 kg	0.25-1.26	SCOOP, 2003
Denmark	Total population, 70 kg	0.17-0.21	SCOOP, 2003
Finland	Adult, 77.1 kg	0.14-0.25	SCOOP, 2003
France	Adult, 66.4 kg Male, 73.9 kg Female, 60.1 kg Child, 31.6 kg	0.46-0.89 0.44-0.88 0.48-0.90 0.73-1.51	SCOOP, 2003
Germany	Total population, 70 kg Infant, 4 months, 10 kg	0.27-0.38 0.51-0.60	SCOOP, 2003
Netherlands	Total population, 65.8 kg Child, 1-4 years, 13.8 kg Child, 1-6 years, 17.1 kg	0.34 0.85 0.76	SCOOP, 2003
Norway	Male, 81 kg Female, 66 kg Infant, 6 months, 8 kg	0.34-0.61 0.30-0.53 0.29-0.44	SCOOP, 2003
Portugal	Total population, 65 kg	0.36-1.00	SCOOP, 2003
Sweden	Adult, 75 kg	0.08-0.13	SCOOP, 2003

Country	Population group	Mean exposure (µg/kg body weight/day)	Reference
United Kingdom (consumers only)	Male, 16-64 years, 70.1 kg Female, 16-64 years, 70.1 kg Child, 1.5-4.5 years, 14.5 kg Infant, 6-12 months, 8.7 kg Male, 65+ years, 70.8 kg Female, 65+ years, 70.8 kg Child, 4-6 years, 20.5 kg Child, 7-10 years, 30.9 kg Adolescent, 11-14 years, 48 kg Adolescent, 15-18 years, 63.8 kg	0.18 0.14 0.48 0.37 0.17 0.14 0.50 0.40 0.28 0.21	SCOOP, 2003
Nivalenol (NIV) t-TDI = 0.70 µg/kg body weight/day			
Austria	Total population, 75 kg	0.08-0.33	SCOOP, 2003
Denmark	Total population, 70 kg	0.03-0.05	SCOOP, 2003
Finland	Adult, 77.1 kg	0.03-0.16	SCOOP, 2003
France	Adult, 66.4 kg Male, 73.9 kg Female, 60.1 kg Child, 31.6 kg	0.06-0.14 0.06-0.15 0.06-0.12 0.09-0.21	SCOOP, 2003
Norway	Male, 81 kg Female, 66 kg	0.06-0.22 0.05-0.19	SCOOP, 2003
Sweden	Adult, 75 kg	0.006-0.022	SCOOP, 2003
United Kingdom (consumers only)	Male, 16-64 years, 70.1 kg Female, 16-64 years, 70.1 kg Child, 1.5-4.5 years, 14.5 kg Infant, 6-12 months, 8.7 kg Male, 65+ years, 70.8 kg Female, 65+ years, 70.8 kg Child, 4-6 years, 20.5 kg Child, 7-10 years, 30.9 kg Adolescent, 11-14 years, 48 kg Adolescent, 15-18 years, 63.8 kg	0.025 0.017 0.064 0.062 0.027 0.021 0.064 0.050 0.034 0.026	SCOOP, 2003
T2 toxin t-TDI = 0.06 µg/kg body weight/day (combined with HT2)			
Austria	Total population, 75 kg	0.043-0.296	SCOOP, 2003
Denmark	Total population, 70 kg	0.050-0.069	SCOOP, 2003
Finland	Adult, 77.1 kg	0.018-0.075	SCOOP, 2003
France	Adult, 66.4 kg Male, 73.9 kg Female, 60.1 kg Child, 31.6 kg	0.045-0.047 0.043-0.044 0.045-0.047 0.060-0.067	SCOOP, 2003
Italy	Total population, 70 kg	0.011-0.012	
Norway	Male, 81 kg Female, 66 kg	0.005-0.034 0.005-0.030	SCOOP, 2003

Country	Population group	Mean exposure (µg/kg body weight/day)	Reference
United Kingdom (consumers only)	Male, 16-64 years, 70.1 kg Female, 16-64 years, 70.1 kg Child, 1.5-4.5 years, 14.5 kg Infant, 6-12 months, 8.7 kg Male, 65+ years, 70.8 kg Female, 65+ years, 70.8 kg Child, 4-6 years, 20.5 kg Child, 7-10 years, 30.9 kg Adolescent, 11-14 years, 48 kg Adolescent, 15-18 years, 63.8 kg	0.011 0.006 0.014 0.012 0.008 0.005 0.015 0.001 0.009 0.008	SCOOP, 2003
HT2 toxin t-TDI = 0.06 µg/kg body weight/day (combined with T2)			
Austria	Total population, 75 kg	0.11-0.37	SCOOP, 2003
Finland	Adult, 77.1 kg	0.019-0.079	SCOOP, 2003
France	Adult, 66.4 kg Male, 73.9 kg Female, 60.1 kg Child, 31.6 kg	0-0.030 0-0.030 0-0.028 0-0.044	SCOOP, 2003
Norway	Male, 81 kg Female, 66 kg	0.030-0.038 0.026-0.034	SCOOP, 2003
United Kingdom (consumers only)	Male, 16-64 years, 70.1 kg Female, 16-64 years, 70.1 kg Child, 1.5-4.5 years, 14.5 kg Infant, 6-12 months, 8.7 kg Male, 65+ years, 70.8 kg Female, 65+ years, 70.8 kg Child, 4-6 years, 20.5 kg Child, 7-10 years, 30.9 kg Adolescent, 11-14 years, 48 kg Adolescent, 15-18 years, 63.8 kg	0.012 0.006 0.018 0.016 0.009 0.006 0.019 0.015 0.010 0.009	SCOOP, 2003

TDI = Tolerable Daily Intake
t-TDI = temporary Tolerable Daily Intake

The European scientific co-operation (SCOOP, 2003) consolidated national European data on levels of trichothecenes in foods and estimates of dietary exposure. In most cases, the mean estimates of dietary exposure were within the tolerable daily intake (TDI) for DON and NIV. Exposure to T2 and HT2 exceeded the TDI in several countries. In most cases bread, or wheat or flour, was the main contributor to exposure to DON and NIV, although in the UK estimates breakfast cereals often made a greater contribution than bread. For T2 and HT2 toxins, rye, durum (pasta) wheat, oats and beer (barley) were also major contributors in some countries.

Estimates of exposure to DON and NIV are generally much higher than the tentative estimate made for New Zealand (Thomson, 1996). This will, at least in part, be due to the fact that the New Zealand estimate was based solely on contamination in maize – a food that is not eaten in large amounts in New Zealand.

4.4 Risk Characterisation

4.4.1 Adverse health effects in New Zealand

No cases of trichothecene intoxication have been reported in New Zealand.

DON has been implicated in oesophageal and gastric cancer overseas. These cancers are moderately common in New Zealand, with approximately 200 and 350 new registrations per year, respectively (2000 year, NZHIS, 2004). However, it should be noted that the link between trichothecene exposure and cancer is not proven and IARC concluded that there was inadequate evidence for carcinogenicity of DON and NIV in humans and animals (Group 3; IARC, 1993). It was also concluded that there was no data available to assess the carcinogenicity of T2 toxin in humans and limited evidence for its carcinogenicity in animals (Group 3; IARC, 1993).

4.4.2 Adverse health effects overseas

4.4.2.1 Epidemiological studies

Ecological studies have been carried out in the Transkei (now part of South Africa) and China on the relationship between trichothecenes and oesophageal cancer (see IARC, 1993 for summaries), but results were generally inconclusive.

4.4.2.2 Risk assessments and other activity overseas

JECFA

DON, T2 and HT2 have been assessed by the Joint FAO/WHO Expert Committee on Food Additives (JECFA, 2001b;c).

The assessment of DON recognised that DON is capable of causing outbreaks of acute illness in humans, but that animal studies did not suggest that DON was a carcinogenic hazard. JECFA recommended that the combined effects of different trichothecenes should be investigated and that, as the trichothecenes have similar toxic properties, toxic equivalency factors should be developed. It was recommended that further information was required in most areas (epidemiology, genotoxicity, exposure, effect of processing, and prevention of *Fusarium* plant diseases).

The assessment of T2 and HT2 concluded that there was substantial evidence for the immunotoxicity and haematotoxicity of T2, but that there was a need to reduce the uncertainty around its carcinogenicity. Further information was also felt to be necessary on levels in foods and dietary exposure outside of Europe.

SCF

The EU Scientific Committee on Food have produced Opinions for DON, NIV, T2 and HT2 (SCF, 1999; 2000a; 2001; 2002).

SCF concluded that for DON general toxicity and immunotoxicity were the critical effects, with no indication of carcinogenicity. The Committee also suggested that further information of the relationship between DON, 3-acetyl-DON and 15-acetyl-DON were important, to determine whether these compound should be assessed separately or grouped with DON for assessment.

SCF concluded that for NIV general toxicity and immunotoxicity/haematotoxicity were the critical effects. However, further long-term toxicological studies and exposure estimates are required for NIV.

SCF concluded that for T2 general toxicity, haematotoxicity and immunotoxicity were the critical effects. It was suggested that further information on metabolism and toxicokinetics, as well as exposure, were required.

SCF also considered DON, NIV, T2 and HT2 jointly and concluded that dose additivity, but also antagonism were observed for combinations of trichothecenes and concluded that the available data did not support establishment of a group TDI.

4.5 Risk Management Information

4.5.1 Relevant food controls: New Zealand

4.5.1.1 Establishment of regulatory limits

Trichothecenes are not currently regulated in New Zealand.

4.5.2 Relevant food controls: overseas

4.5.2.1 Establishment of regulatory limits

Table 19 summarises the reported regulatory positions on trichothecenes (van Egmond and Jonker, 2003). It should be noted that the limits reported here include a mixture of regulatory maximum permitted limits and guideline levels.

Table 19: Regulatory limits for trichothecenes in various countries (food regulations only)

Country	Commodity description	Trichothecene	Regulatory limit (mg/kg)
Armenia	All foods	T2	0.1
	Wheat	DON	0.7
	Barley	DON	1.0
Belarus	Wheat	DON	0.7
	Barley	DON	1.0
	Infant foods	DON	Not allowed
	Grain, flour, groats	T2	Unknown
	Infant food	T2	Not allowed
Bulgaria	Processed cereal products	DON	1.0
	Cereals, subject to further treatment	DON	2.0
	Maize and maize products	DON	1.0
	Processed cereal products	T2	0.1
Canada	Domestic, uncleaned soft wheat	DON	2.0
	Soft wheat flour (adult food)	DON	1.2
	Soft wheat flour (infant food)	DON	0.6
China	Wheat and wheat flour, maize and maize flour	DON	1.0
Cuba	Imported cereals	DON	0.3
Czech Republic	Corn, rice, maize	DON	2.0
	Flour	DON	1.0
Estonia	Wheat and wheat products	DON	0.7
	Barley and barley products	DON	1.0
	Cereal and cereal products	T2	0.1
European Union	Cereal products, as consumed	DON	0.5
	Flour, used as raw material	DON	0.75
Hungary	Milled cereal products	DON	1.0
	Edible bran	DON	1.2
	Milled cereal products	T2	0.3
Iran	Wheat, barley, maize, rice	DON	1.0
Japan	Wheat and wheat products	DON	1.1
Latvia	Cereals	DON	1.0
	Cereals	T2	0.1
Moldova	Wheat and wheat flour	DON	0.7
	Barley and barley flour	DON	1.0
	Cereals and cereal flour	T2	0.1
Russian Federation	Wheat	DON	0.7
	Barley	DON	1.0
	Barley	T2	0.1
Singapore	Cereal and grain products	DON	Not given
	Wheat, maize, rice	T2	0.02
	Wheat, rice for production of children's food	T2	0.0005
	Maize for production of children's food	T2	0.001
Switzerland	Cereal grains	DON	1.0

Country	Commodity description	Trichothecene	Regulatory limit (mg/kg)
Ukraine	Wheat of other than strong, hard varieties, flour, bread	DON	0.5
	Grain-based and fruit-vegetable-dairy mix baby foods	DON	0.2
	Wheat of strong, hard varieties	DON	1.0
	Grains, flour, etc.	T2	0.1
USA	Finished wheat products for human consumption	DON	1.0
Uruguay	Wheat flour and by-products	DON	1.0

From van Egmond and Jonkers (2003)

While trichothecene concentrations in food are not currently regulated in New Zealand, it is interesting to note that many of the maximum concentrations reported for New Zealand cereals in Table 14 for DON would exceed most regulatory limits reported in Table 19.

4.5.2.2 Codes of practice and related initiatives

Codex have produced a Code of Practice for prevention and reduction of mycotoxin contamination in cereals, with specific annexes relating to OTA, zearalenone, fumonisins and trichothecenes (http://www.codexalimentarius.net/download/standards/406/CXC_051e.pdf). Recommended practices cover planting, preharvest, harvest, storage and transport.

The Code also discusses a HACCP approach to control of mycotoxin contamination of grains. The Food and Agriculture Organization of the United Nations (FAO) in collaboration with the International Atomic Energy Agency (IAEA) have produced a manual on the application of HACCP in mycotoxin prevention and control (ftp://ftp.fao.org/docrep/fao/005/y1390e/y1390e00.pdf). European efforts in this area are ongoing through a collaborative effort known as the Mycotoxin Prevention Cluster, with a specific project aimed at prevention of *Fusarium* mycotoxins entering the animals and human food chains (http://www.mycotoxin-prevention.com/Project2.htm). This project has five major tasks:

- Development of critical control systems;
- Pre-harvest biocontrol;
- Post harvest control;
- Decontamination using microbial inoculants for prevention of entry into animal production systems; and
- Decontamination using physicochemical means.

4.5.2.3 Management of trichothecene formation in crops

Preharvest measures to control *Fusarium* infection can also reduce the formation of trichothecenes (JECFA, 2001b). Control measures include culture techniques, breeding and growing of resistant cultivars and use of fungicides or biological control agents (JECFA, 2001b).

Cultural control measures include:

- Crop rotation, particularly rotation involving non-host crops. Maize-wheat rotation can lead to increased incidence of *Fusarium* diseases, such as head blight (Cromey, 2002a);
- Removal or ploughing in of crop debris, which may serve as a reservoir for inoculum;
- Effective weed control to remove a potential reservoir for inoculum;
- Irrigation to reduce water stress and severity of disease, although overhead irrigation has been shown to increase the severity of disease (JECFA, 2001b).

Differences in cultivar susceptibility to *Fusarium* has been recognised for over 100 years. However, few reports of complete immunity exist (JECFA, 2001b).

Fungicides vary considerably in their ability to control *Fusarium* species and to inhibit trichothecene production. Edwards *et al*. (2001) demonstrated that, while tebuconazole and metconazole were effective in reducing infection and DON levels, azoxystrobin had less effect on infection and resulted in a slight increase in DON levels relative to controls. Similar results have been reported for fungicide treatment of wheat in New Zealand (Cromey *et al*., 2002b).

4.5.3 Influence of processing on trichothecene levels

The influence of various food processing procedures on trichothecene levels has been reviewed (Hazel and Patel, 2004).

Infected grains may be shriveled and lower in weight than healthy grain. While some studies have reported as much as a 74% decrease in DON levels after sorting, infected grains may be indistinguishable from healthy grains and routine grain cleaning can result in reductions of no better than 20% (Scott *et al*., 1984).

4.5.3.1 Wet milling

Wet milling of maize to produce starch and glucose syrups results in concentration of water-soluble trichothecenes in the steep water. Lauren and Ringrose (1997) conducted wet milling trials on naturally-contaminated maize and found levels of DON and NIV in solid fractions (germ, fibre and gluten) 5-10 times lower than in the grain entering the wet milling process.

4.5.3.2 Dry milling

Dry milling of maize and wheat results in highest levels of trichothecenes in germ and bran fractions and reduced levels, relative to the whole grain, in the starchy endosperm (Hazel and Patel, 2004). However, for wheat, the distribution of trichothecenes between milling fractions has been reported to depend on the degree of fungal penetration into the grain, which in turn is dependent on the susceptibility of the cultivar to infection (Nowicki *et al*., 1988).

4.5.3.3 Cooking

Breadbaking is a major use for wheat and the fermentation processes involved can result in metabolism of many compounds. Investigations on the influence of breadbaking on the DON content of wheat have shown equivocal results, ranging from significant increases in DON levels (Young *et al*., 1984) to decreases of up to 60% (see Hazel and Patel, 2004 for a review). Yeast in liquid culture does not metabolise DON (Boswald *et al.*, 1995), however, there is some evidence that *Lactobacilli*, also involved in the fermentation process, may metabolise trichothecenes (El-Nezami *et al*.,2002).

DON has been shown to be stable at extrusion temperatures. Accerbi *et al*. (1999) demonstrated a modest reduction in DON levels upon extrusion, but a more dramatic reduction when extrusion was combined with soaking of grain in sodium bisulphate. Sodium bisulphate removes DON by formation of sulphonate salts. These salts are stable under acid conditions, but may revert to parent DON under alkaline conditions (Cazzaniga *et al*., 2001).

4.5.3.4 Brewing

The brewing process involves both steps with the potential to decrease trichothecene levels (steeping) and steps with the potential to increase trichothecene levels (germination, mashing). It has been concluded that the overall brewing process has little impact on trichothecene levels (Scott, 1996).

While the initial stages of grain treatment (seed cleaning, milling) are likely to result in some decrease in trichothecene levels of grain products, a range of food processing steps (cooking, fermentation, extrusion) cannot be viewed as likely to have a consistent impact on the trichothecene levels of contaminated grain. Boiling in water will usually result in a significant decrease in trichothecene levels, due to the water solubility of these compounds. For example boiling of pasta has been reported to result in loss of 50% of DON content (Nowicki *et al.,* 1988). The limited impact of food processing on trichothecene levels has been confirmed by a recent UK survey of cereal products at retail, with 298 of 377 containing detectable trichothecenes (FSA, 2003).

4.6 Conclusions

4.6.1 Description of risks to New Zealand consumers

Trichothecene mycotoxins have been associated with outbreaks of acute human illness, including outbreaks with high rates of mortality (alimentary toxic aleukia). The critical toxicological effects are similar for all trichothecenes (general toxicity, immunotoxicity, haematotoxicity). While some epidemiological studies have attempted to relate trichothecene exposure to oesophageal cancer, gastric cancer and endemic osteoarthritis, the evidence is inconclusive. Test on laboratory animals generally do not suggest that the trichothecenes are carcinogenic.

While no cases of trichothecene intoxication have been documented in New Zealand, the symptoms of acute intoxication mean that cases are likely to be ascribed to microbial sources.

Fusarium species have been found in a range of New Zealand cereal crops and production of trichothecene mycotoxins by these fungal species has been demonstrated. A survey of maize-based consumer foods in New Zealand found occasional occurrence of DON and NIV. While some early New Zealand surveys reported detection of T2 toxin, later work did not report detection of the toxin or its major causative organism (*F. sporotrichioides*). Although no regulatory limits for trichothecenes are in place in New Zealand, concentration of DON detected in New Zealand grown cereals would occasionally exceed regulatory limits adopted in other countries.

International estimates of trichothecene exposure have generally identified wheat and wheat products as the major contributors to exposure. Wheat is the most commonly consumed cereal in New Zealand, with most New Zealand-produced wheat grown in the South Island. Available survey data suggest that the prevalence and concentration of trichothecenes in South Island cereals is generally low (Lauren *et al*., 1991; Sayer and Lauren, 1991). The balance of the wheat consumed in New Zealand is from Australia and is from ASW (Australian Standard White) or Prime Hard grade. The limited information available suggests that trichothecene contamination is rare in Australian wheat, other than the General Purpose grade (Blaney *et al*., 1987).

While there is a lack of data on trichothecenes in New Zealand wheat, oat and barley-based foods, it appears likely that the exposure of New Zealanders to trichothecenes will be similar to or less than that of European countries and less than internationally determined Tolerable Daily Intakes.

4.6.2 Commentary on risk management options

Trichothecenes are not currently regulated in New Zealand. Agronomic research conducted in New Zealand demonstrates a good awareness of the deleterious effects of *Fusarium* infection and the connection between *Fusarium* infection and trichothecene production.

4.6.3 Data gaps

New Zealand specific information on trichothecenes in New Zealand wheat-based and barley-based (beer) foods would help to confirm the circumstantial evidence suggesting that contamination in these products is likely to be low. It is also important to confirm that T2 toxin (and HT2 toxin) are not issues in the New Zealand context.

5 FUMONISINS

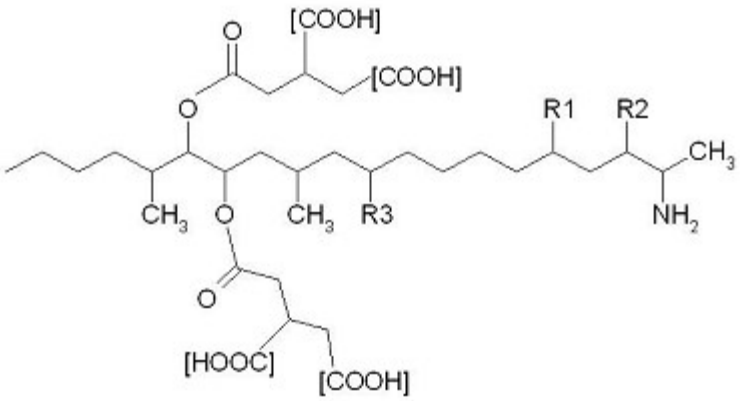
5.1 Hazard Identification

Fumonisins are mycotoxins produced predominantly by *Fusarium verticillioides* (*F. moniliforme*) and *F. proliferatum.* These fungal species are endemic in maize worldwide, but are rarely found in other crops (Pitt and Tomaska, 2001). The fungi grow optimally at about 25ºC and will grow at temperatures up to 32-37ºC (Pitt and Tomaska, 2001). While at least six fumonisins are known, fumonisin B_1 and B_2 (FB_1, FB_2) are the most important.

5.1.1 Structure and nomenclature

Fumonisins consist of a 20 carbon aliphatic chain with two ester linked hydrophilic polyol side chains. Structural details for FB_1 – FB_4 are shown in Figure 5.

Figure 5: Structure of major fumonisins



Fumonisin B_1: R1= OH; R2= OH; R3= OH; Fumonisin B_2: R1= H; R2= OH; R3= OH; Fumonisin B_3: R1= OH; R2= OH; R3= H; Fumonisin B_4: R1= H; R2= OH; R3= H

Fumonisins C_1-C_4 are identical to the corresponding B fumonisin, except the aliphatic carbon chain does not have the terminal methyl group on the right hand end (Soriano and Dragacci, 2004).

5.1.2 Occurrence

F. verticillioides and *F. proliferatum* are amongst the most common fungi associated with maize worldwide and can be recovered from most maize kernels, even when the kernels appear healthy (WHO, 2000). *F. verticillioides* is considered to be the major cause of *Fusarium* kernel rot in maize, a significant plant disease occurring in warm, dry weather (JECFA, 2001d). *Fusarium* kernel rot, and associated fumonisin synthesis, is also strongly associated with insect damage of kernels, as this provides an entry point for the fungus (WHO, 2000). Thin kernel pericarp (greater susceptibility to insect injury), propensity to kernel splitting, and previous infection with other *Fusarium* species, such as *F. graminearum*, all increase the risk of *F. verticillioides* infection and fumonisin formation (WHO, 2000).

F. verticillioides is widespread in the tropics and humid temperate zones, but is uncommon in cooler temperate zones (Pitt and Hocking, 1997). Surveys of *Fusarium* species in New

Zealand maize are supportive of this observation, as the fungus is only rarely isolated (Sayer, 1991; Sayer and Lauren, 1991; Hussein *et al*., 2002). *F. proliferatum* has not been reported in New Zealand maize.

Although fumonisin-producing fungi appear to be relatively rare in New Zealand, Mirocha *et al.* (1992) found FB_1 in New Zealand pasture grasses, at concentration in the range 1-9 mg/kg. The pastures analysed were associated with an idiopathic disease of wapiti (elk) and wapiti hybrids grazed on the pastures.

5.2 Hazard Characterisation: Adverse Health Effects

Incidents of human toxicosis have been associated with fumonisin contaminated foods. However, it should be noted that in most cases the implicated food may contain more than one known mycotoxin and may potentially contain other, as yet uncharacterized, toxins.

5.2.1 Conditions

An outbreak of acute mycotoxicosis occurred in southern India in 1995 due to consumption of rain-damaged, mouldy sorghum and maize. FB_1 was the most common mycotoxin in both crops, with concentration up to 8 mg/kg in sorghum and 65 mg/kg in maize. However, a relatively high concentration of aflatoxin B_1 was also detected in the maize (Shetty and Bhat, 1997). Cases exhibited gastrointestinal symptoms, including abdominal pain, borborygmi (rumbling stomach) and diarrhoea. Similar symptoms were observed in laying hens and 1-day-old cockerels fed contaminated maize and fed their normal diet with addition of 8 or 16 mg/kg of FB_1 (JECFA, 2001d).

High concentrations of FB_1 in the diet have been correlated with oesophageal and liver cancer, and neural tube defects (WHO, 2000; JECFA, 2001d). Studies in South Africa, China, Iran, Northern Italy, Kenya, Zimbabwe, USA, and Brazil found differences in the fumonisin content of staple foods between areas with high rates of oesophageal cancer and areas with low rates. However, populations in high incidence regions were often also exposed to higher levels of other mycotoxins, as well as suffering a range of micronutrient deficiencies (JECFA, 2001d).

Associations to liver cancer have been observed in China and South Africa, while associations to neural tube defects have been noted in South Africa, China and the USA (JECFA, 2001d).

5.2.2 Toxicity

5.2.2.1 Acute toxicity

No studies have been published on the acute toxicity of single doses of FB_1 in laboratory animals. Available evidence suggests that it is not acutely toxic (JECFA, 2001d).

5.2.2.2 Chronic toxicity

Short-term and chronic toxicity in experimental animals due to FB_1 is primarily due to its ability to interfere with synthesis of complex glycol-shingolipids, through inhibition of the enzyme ceramide synthase. This has effects on cellular processes such as cell growth, cell differentiation and morphology, endothelial cell permeability and apoptosis (cell death; SCF, 2000b). This mode of action is believed to explain most of the toxic effects exhibited by FB_1, including hepatotoxicity and nephrotoxicity and tumour formation in the liver and kidneys (JECFA, 2001d).

Two species-specific disease have been linked to FB_1 exposure:

- Equine leukoencephalomalacia (ELEM) affects horses, ponies, donkeys and mules, causing liquefaction of the brain. Fumonisin-contaminated feed has been implicated in the disease and the symptoms were reproduced by intravenous administration of FB_1 to horses (JECFA, 2001d)
- Porcine pulmonary oedema (PPO) is believed to be induced by cardiovascular dysfunction, followed by acute left-side heart failure. Hepatotoxicity occurs concurrently with PPO. PPO has been reproduced by intravenous administration of purified FB_1, but not by oral administration (JECFA, 2001d).

Ability of cells to avoid apoptotis is critical in the development of cancer and it has been hypothesized that the ability of FB_1 to induce apoptotis may select for cell resistant to apoptotis (Jones *et al*., 2001). It has also been suggested that compensatory cell proliferation, in response to apoptosis, will support an increased risk of tumour formation (Howard *et al.*, 2001).

5.2.3 Toxicological assessment

JECFA have evaluated fumonisins (JECFA, 2001d) and concluded that nephrotoxicity, observed in several species of rat was the most sensitive toxic effect for pure FB_1, with an NOEL of 0.2 mg/kg body weight/day. A group Provisional Maximum Tolerable Daily Intake (PMTDI) for FB_1, FB_2 and FB_3, singly or in combination, of 2 μg/kg body weight/day was assigned (safety factor of 100).

The EU Scientific Committee on Food came to identical conclusions (SCF, 2000b) in assigning a TDI for FB_1 of 2 μg/kg body weight/day, also taking into account data on equine leukoencephalomalacia (ELEM) with an NOAEL of 0.2 mg/kg body weight. The Committee also noted that there was not adequate evidence that FB_1 is genotoxic.

IARC considered the available information on FB_1 (IARC, 2002) and concluded that there was sufficient evidence for the carcinogenicity of FB_1 in experimental animals, but that there was inadequate evidence for its carcinogenicity in humans. FB_1 was classified as a possible human carcinogen (Group 2B).

5.3 Exposure Assessment

Although *F. verticillioides* and *F. proliferatum* are known to cause diseases in crops other than maize (sorghum, rice), fumonisin mycotoxins occurrence is most commonly reported in maize.

5.3.1 Fumonisins in the New Zealand food supply

There are no published data on fumonisin levels in susceptible foods in New Zealand. However the results of a small survey of New Zealand "corn meal" were cited in a review of worldwide data (Shephard *et al*., 1996). The twelve samples analysed were actually whole kernel corn and fumonisins were not detected, the detection limit being 0.05 mg/kg. More recently, 50 samples, mostly of imported corn (maize) products, have been analysed for fumonisins. Only one sample was found to contain fumonisin B1 (D Lauren, personal communication, 1998). Corn-based breakfast cereals and corn chips sold in New Zealand contain mostly imported maize with lower levels of New Zealand product (D Lauren, personal communication, 1998).

Although there are reports of fumonisins in sweet corn, for example in the Netherlands (Bresch *et al*., 1998), New Zealand sweet corn is not considered to be a problem as it is picked at a high moisture content at a stage before contamination with *Fusarium* moulds is likely.

5.3.2 Fumonisins in the Australian food supply

Available information on fumonisins (FB_1 unless otherwise stated) in Australian maize and maize-based foods is summarised in Table 20.

Table 20: FB_1 in Australian maize and maize-based foods

Food type	Number of samples	Number containing FB_1 (%)	FB_1 concentration	Reference
Maize	70	67 (96%)	0.3-40.6 mg/kg	Bryden *et al.*, 1998
Commercial maize	41	16 (39%) 20 (49%) 5 (12%)	≤1 mg/kg 1-5 mg/kg >5 mg/kg	Pitt and Tomaska, 2001
Cornflakes	2	0 (0%)		Pitt and Tomaska, 2001
Maize	10	2 (20%)	0.19-0.48 mg/kg	Tseng and Liu, 2001

It has been claimed that fumonisins have been found at very high levels in some samples of maize sourced from Australian food manufacturers known to export to New Zealand (Lauren and Veitch, 1996). High levels have also been detected in Australian maize used in horse feed which can result in equine leukoencephalomalacia (D Lauren, personal communication, 1998).

5.3.3 Overseas context

A large amount of data on the prevalence and concentrations of fumonisins B_1, B_2 and B_3 has been summarised (JECFA, 2001d). Fumonisins were detected in over 60% of all maize and maize-based foods tested. Prevalence was lower in sound than mouldy grain and concentrations were lower in processed foods than whole grain. The exposure assessment carried out by JECFA used concentration distribution data from a study in the Netherlands (de Nijs *et al*., 1998). De Nijs *et al*. (1998) consolidated data from surveys in Africa, Asia,

Europe and North and South America to produce a composite distribution with prevalence of 93%, median FB_1 level of 0.42 mg/kg and a mean FB_1 level of 1.36 mg/kg for all maize samples (positive and negative). The EU Scientific Co-operation collected information on fumonisins in various foods (SCOOP, 2003). For maize, 66% of samples were positive for FB_1 and 51% were positive for FB_2. Assuming that samples where the toxin was not detected contained true zero concentrations, the weighted average concentration of FB_1 in maize was 0.35 mg/kg.

While the vast majority of data available relate to fumonisins in maize and foods derived from maize, other foods have occasionally been analysed for fumonisins. Table 21 summarises data for studies of non-maize foods.

Table 21: Worldwide data on occurrence of fumonisins in non-maize food

Food	Country	Number of samples positive/total samples (%)	Range	Reference
Asparagus	Italy	Composite of 25 samples affected by crown rot	Stem 0.46 mg/kg FB_1 0.06 mg/kg FB_2 Results on dry weight basis	Logrieco *et al*., 1998
Asparagus	Germany	9/10 (90% of *F. proliferatum* infected spears)	0.036-4.5 mg/kg FB_1 Results on a dry weight basis	Seefelder *et al*., 2002
Asparagus	China	24/30 (80%)	0.024-0.67 mg/kg FB_1 0.017-0.138 mg/kg FB_2 Results on dry weight basis	Liu *et al*., 2005
Barley	UK	0/5 (0.0%)		Patel *et al*., 1997
Beans	Botswana	0/5		Siame *et al*., 1998
Beer	Canada	11/41 (27%)	0.4-103 µg/l FB_1 0.45-12 µg/l FB_2	Scott and Lawrence, 1995
Beer	Canada	22/46 (48%)	0.2-52.8 µg/l FB_1 0.4-11.5 µg/l FB_2	Scott *et al*., 1997
Beer	Spain	14/32 (44%)	4.8-85.5 µg/l Fumonisins	Torres *et al*., 1998
Beer	USA	25/29 (86%)	<0.3-13.5 µg/l Fumonisins	Hlywka and Bullerman, 1999
Milk (raw)	USA	1/165 (0.6%)	1.3 µg/l FB_1	Maragos and Richard, 1994
Milk (raw)	Denmark	0/42 (0.0%)		Sørensen and Elbæk, 2005
Oats	UK	0/5 (0.0%)		Patel *et al*., 1997
Peanuts	Botswana	0/15		Siame *et al*., 1998

Rice	UK	0/5 (0.0%)		Patel *et al*., 1997
Rice	USA	8/20 (40%)	0.5-4.3 mg/kg FB_1 ND-1.2 mg/kg FB_2 ND-0.6 mg/kg FB_3	Abbas *et al*., 1998
Rice	Korea	5/88 (5.7%)		Park *et al*., 2005
Sorghum (meal)	Botswana	2/2 (100%)	0.02-0.02 mg/kg FB_1	Doko *et al.,* 1996
Sorghum (grain)	Burundi	0/5 (0.0%)		Munimbazi and Bullerman, 1996
Sorghum (meal)	Burundi	1/1 (100%)	28.8 mg/kg FB_1	Munimbazi and Bullerman, 1996
Sorghum	India	Normal 2/43 (3.6%) Rain-affected 25/25 (100%)	0.15-0.51 mg/kg FB_1 0.07-7.9 mg/kg FB_1	Shetty and Bhat, 1997
Sorghum (mouldy)	India	20/20 (100%)	0.14-7.8 mg/kg FB_1	Bhat *et al*., 1997
Sorghum	Botswana	3/20 (15%)	0.02-0.06 mg/kg FB_1	Siame *et al*., 1998
Sorghum syrup	USA	1/35 (2.8%)	0.12 mg/kg FB_1	Trucksess *et al*., 2000
Soya	UK	0/5 (0.0%)		Patel *et al*., 1997
Wheat	UK	0/5 (0.0%)		Patel *et al*., 1997
Wheat (emmer, spelt, *T.monococcum*)	Italy	5/8 (63%)	0.02-0.07 mg/kg FB_1	Castoria *et al*., 2005

Little information is available concerning fumonisin residues in foods of animal origin. Malmauret *et al*. (2002) compared the contaminant content of organic and conventional foods and did not detect fumonisin in any of twelve samples (six organic, six conventional) of each of beef, pork, poultry and eggs. However, it is unknown what the contamination status of the animal feed was.

Leblanc *et al*. (2005) reported detection of FB_1 in 3/6 samples of poultry offal, at concentrations in the range 0.09-0.12 mg/kg.

Scott *et al.* (1994) studied transmission of FB_1 in four cows dosed either orally (1.0 and 5.0 mg FB_1/kg body weight) or intravenously (0.05 and 0.20 mg FB_1/kg body weight) with pure FB_1. No residues of FB_1 or its metabolite AP_1 were detected in milk. Richard *et al*. (1996) fed two Jersey cows a diet containing approximately 75 mg/kg of fumonisins for 14 days. The cows consumed an average of 3 mg FB_1/kg body weight/day. No FB_1 residues were detected in milk.

5.3.4 New Zealand estimates of dietary exposure

Both Thomson (1996) and Lake and Stanton (1998) discussed the potential for fumonisin exposure in New Zealand, but did not estimate dietary exposure due to the general lack of concentration data.

5.3.5 Overseas estimates of dietary exposure

National estimates of fumonisin exposure are summarised in Table 22.

Table 22: Overseas estimates of dietary exposure to fumonisins

Country	Population group	Estimated Fumonisin exposure (µg /kg body weight/day)		Reference
		Mean	High percentile (percentile)	
Africa	Adult, based on GEMS/Food regional diet	2.4 FB_1	7.3 FB_1 (90)	JECFA, 2001d
Argentina	Male, 1-5 years, 14 kg Male, 6-10 years, 25 kg Male, 11-14 years, 40 kg Male, 15-25 year, 61 kg Male, 26-55 years, 78 kg Male, 55+ years, 80 kg Female, 1-5 years, 14 kg Female, 6-10 years, 24 kg Female 11-14 years, 40 kg Female, 15-25 years, 56 kg Female, 25-55 years, 58 kg Female, 55+ years, 60 kg	0.6 FB_1 0.0 0.0 0.1 0.1 0.0 0.5 0.0 0.0 0.1 0.1 0.0		Solovey *et al*., 1999
Austria	Total population	0.077 FB_1	0.27 FB_1 (95)	SCOOP, 2003
Belgium	All, 13-18 years	0.016 FB_1	0.11 FB_1 (95)	SCOOP, 2003
Europe	Adult, based on GEMS/Food regional diet	0.2 FB_1	0.6 FB_1 (90)	JECFA, 2001d
Far East	Adult, based on GEMS/Food regional diet	0.7 FB_1		JECFA, 2001d
France	Total population Adult, male Adult, female Child, all	0.22 FB_1 0.23 FB_1 0.21 FB_1 0.36 FB_1		SCOOP, 2003
France	Child, 3-14 years Adult, 15+ years	0.046 FB_1 + FB_2 0.014 FB_1 + FB_2		Leblanc *et al*., 2005
Germany	Total population, >4 years	0.13 FB_1		SCOOP, 2003
Italy	Total population Consumers only	0.047 FB_1 0.52 FB_1		SCOOP, 2003
Latin America	Adult, based on GEMS/Food regional diet	1.0 FB_1	2.9 FB_1 (90)	JECFA, 2001d
Middle Eastern	Adult, based on GEMS/Food regional diet	1.1 FB_1	3.3 FB_1 (90)	JECFA, 2001d
Netherlands	Adult Child, 1-4 years Child, 1-6 years	0.003 FB_1 0.0 FB_1 0.0 FB_1		SCOOP, 2003
Norway	Population, male Consumers, male Population, female Consumers, female	0.0001 FB_1 0.0003 FB_1 0.0001 FB_1 0.0003 FB_1		SCOOP, 2003
Switzerland	Total population	0.03		JECFA, 2001d
UK	Total population	0.03		JECFA, 2001d

Country	Population group	Estimated Fumonisin exposure (µg /kg body weight/day)		Reference
USA	Maize consumers	0.08		Humphreys *et al*., 2000

It should be noted that no exposure estimates were available from developing countries, other than those formulated using the GEMS/Food regional diets. In parts of Africa and Central America maize will constitute a major part of the diet in these populations.

5.4 Risk Characterisation

5.4.1 Adverse health effects in New Zealand

No cases of fumonisin intoxication have been reported in New Zealand. FB_1 has been implicated in human oesophageal cancer. This cancer is moderately common in New Zealand, with approximately 200 new registrations per year (2000 year, NZHIS, 2004).

5.4.1.1 Risk assessments and other activities

Lake and Stanton (1998) reviewed fumonisins as a food safety issue in New Zealand and concluded that "the risk to New Zealanders from fumonisins is likely to be slight, this conclusion is based on circumstantial information. A limited survey to provide reliable data is recommended".

5.4.2 Adverse health effects overseas

5.4.2.2 Epidemiological studies

Ecological studies have been carried out in the Transkei (South Africa), China and Northern Italy on the relationship between fumonisins and oesophageal cancer (see IARC, 1993 or JECFA, 2001d for summaries). Interpretation of these studies is complicated by the fact that study populations were often exposed to multiple mycotoxins, as well as suffering from multiple nutritional deficiencies (JECFA, 2001d).

Transkei

Regions of the Transkei have very high rates of oesophageal cancer. People in these regions eat a diet based on maize porridge. Sydenham *et al*. (1990) analysed mouldy and apparently healthy corn from areas with high and low rates of oesophageal cancer. Mouldy corn from the low incidence area contained higher levels of trichothecenes, moniliformin and zearalenone, while mouldy corn from the high cancer incidence area had higher levels of fumonisins (FB_1, FB_2). Apparently healthy corn from the high incidence area also had higher levels of fumonisins than corn from the low incidence area. These observations were confirmed by Rheeder *et al*. (1992).

China

Maize is consumed as a staple in counties of Henan province. Oesophageal cancer rates have been reported to be 4-5 times higher in some counties than in others. Mouldy and apparently healthy maize from high incidence areas were found to have average FB_1 concentrations of

74 and 35.3 mg/kg respectively (Chu and Li, 1994). Yoshizawa *et al*. (1994) analysed maize samples from high (Linxian county) and low (Shangqiu county) areas for oesophageal cancer. Mean levels of fumonisins in positive samples were similar (FB_1 Linxian 0.87 mg/kg and Shangqiu 0.89 mg/kg, FB_2 Linxian 0.45 mg/kg and Shangqiu 0.33 mg/kg) although the prevalence of fumonisin contamination was almost twice as high in the high cancer incidence area (48%) than the low cancer incidence area (25%).

Ueno *et al*. (1997) compared the mycotoxin content of maize between an area with a high rate of primary liver cancer (Haimen) and an area with a low rate (Penlai). While the prevalence and concentrations of fumonisins were higher in maize in the high incidence area than the low incidence area, prevalence and concentrations of other mycotoxins (aflatoxin B_1, deoxynivalenol and nivalenol) were also higher in the high risk area for primary liver cancer.

Northern Italy

Pordenone province in Northeastern Italy has some of the highest rates of oral, pharyngeal and oesophageal cancer in Europe (WHO, 2000). A case-control study was carried out involving 282 upper digestive tract cancer patients and 505 hospital controls (Franceschi *et al*., 1990). Highly significant associations were found between frequent maize consumption and oral, pharyngeal and oesophageal cancers (odd ratios 3.3, 3.2 and 2.8 respectively), although the effect was only evident in individuals who reported heavy drinking.

Although fumonisin levels in maize were not measured as part of this study, significant levels of FB_1 have been reported in Italian polenta (0.15-3.76 mg/kg; WHO, 2000).

USA

Missimer *et al*. (2006) carried out a population based case-control study to investigate a possible connection between consumption of fumonisin-contaminated corn and an increased prevalence of neural tube defects (NTD) along the Texas-Mexico border. Fumonisin exposure, as assess by maternal serum sphinganine to sphingosine ratio or by maternal recollection of tortilla consumption, was associated with an increased odds ratio of having a NTD affected pregnancy. Odds ratios increased with increasing exposure, with the exception of the highest exposure class. The investigators suggested that at the high exposure level foetal death may have been more likely to occur.

5.4.2.2 Risk assessments and other activity overseas

JECFA

As previously stated in section 5.2.3, JECFA have allocated a group Provisional Maximum Tolerable Daily Intake for the total of FB_1, FB_2 and FB_3 of 2 μg/kg body weight/day.

JECFA recommended further research requirement in laboratory animals and also recommended that "the relationship between the intake of fumonisin and human disease in areas where nixtamalised maize-products comprise a large portion of the diet should be investigated. Particular emphasis should be placed on diseases of the liver and kidney and other diseases suspected of being associated with intake of fumonisin B_1, such as nasopharyngeal and oesophageal cancers and neural tube defects".

SCF

The EU Scientific Committee on Food have produced an Opinion for FB_1, recommending collection of data on the occurrence of FB_1 contamination of foodstuffs in Europe (SCF, 2000b). The Committee did not recommend monitoring for residues of FB_1 in animal products, as there was no indication of significant carry-over.

The Committee welcomed further studies on the kinetics of FB_1 in humans, including transplacental transfer in humans or non-human primates and studies giving further information on cardiovascular toxicity.

SCF did not give an opinion on fumonisins other than FB_1.

USA

Humphreys *et al*. (2001) carried out a quantitative risk assessment for FB_1 and FB_2 in US corn. Corn consumption was estimated from 3-day food consumption surveys, while the fumonisin content of corn was estimated from FDA surveillance data. The investigators examined two management approaches, limiting corn consumption and limiting fumonisin contamination. The model used demonstrated that limiting corn consumption was a more effective means of avoiding fumonisin toxicity than limiting the fumonisin level in the corn.

Nordic countries (Denmark, Norway, Sweden, Finland, Iceland)

The Nordic evaluation concluded that there was insufficient information to carry out a complete risk assessment, but recommended that human dietary exposure to fumonisins should be less than 1 μg/kg body weight/day (Petersen and Thorup, 2001). Surveillance reported in this study reported detection of FB_1 and FB_2 in a range of corn-based foods, but not in corn starch, corn-on-the-cob or sweet corn, with concentrations in the range 0.001-1.03 mg FB_1/kg and 0.007-0.243 mg FB_2/kg.

5.5 Risk Management Information

5.5.1 Relevant food controls: New Zealand

5.5.1.1 Establishment of regulatory limits

Fumonisins are not currently regulated in New Zealand.

5.5.2 Relevant food controls: overseas

5.5.2.1 Establishment of regulatory limits

Table 23 summarises the reported regulatory positions on fumonisins for eight countries (van Egmond and Jonkers, 2003). It should be noted that the limits reported here include a mixture of regulatory maximum permitted limits and guideline levels.

Table 23: Regulatory limits for fumonisins in various countries (food regulations only)

Country	Commodity description	Fumonisin	Regulatory limit (µg/kg)
Bulgaria	Maize and processed products thereof	$FB_1 + FB_2$	1000
Cuba	Maize, rice	FB_1	1000
France	Cereals and cereal products	FB_1	1000 (Target) 3000 (Maximum)
Iran	Maize	$FB_1 + FB_2$	1000
Singapore	Corn and corn products	FB_1	Not given
Switzerland	Maize	$FB_1 + FB_2$	1000
Taiwan	Maize products	FB_1	Not stated
USA	Degermed, dry milled corn products	$FB_1 + FB_2 + FB_3$	2000 (Guide)

From van Egmond and Jonker (2003)

5.5.2.2 Codes of practice and related initiatives

Codex have produced a Code of Practice for prevention and reduction of mycotoxin contamination in cereals, with specific annexes relating to OTA, zearalenone, fumonisins and trichothecenes (http://www.codexalimentarius.net/download/standards/406/CXC_051e.pdf). Recommended practices cover planting, preharvest, harvest, storage and transport.

The fumonisin specific annex identifies time of harvest as a critical factor in preventing fumonisin formation in maize, with recommendations that maize be harvested in cooler months.

The Code also discusses a HACCP approach to control of mycotoxin contamination of grains. The Food and Agriculture Organization of the United Nations (FAO) in collaboration with the International Atomic Energy Agency (IAEA) have produced a manual on the application of HACCP in mycotoxin prevention and control

(ftp://ftp.fao.org/docrep/fao/005/y1390e/y1390e00.pdf). European efforts in this area are ongoing through a collaborative effort known as the Mycotoxin Prevention Cluster, with a specific project aimed at prevention of *Fusarium* mycotoxins entering the animals and human food chains (http://www.mycotoxin-prevention.com/Project2.htm). This project has five major tasks:

- Development of critical control systems;
- Pre-harvest biocontrol;
- Post harvest control;
- Decontamination using microbial inoculants for prevention of entry into animal production systems; and
- Decontamination using physicochemical means.

5.5.2.3 Management of fumonisin formation in crops

Preharvest measures to control *Fusarium* infection can also reduce the formation of fumonisins (JECFA, 2001d). Control measures include culture techniques, breeding and growing of resistant cultivars and use of fungicides or biological control agents (JECFA, 2001d).

Cultural control measures include:

- Crop rotation, particularly rotation involving non-host crops. Maize-wheat rotation can lead to increased incidence of *Fusarium* diseases, such as head blight;
- Removal or ploughing in of crop debris, which may serve as a reservoir for inoculum;
- Effective weed control to remove a potential reservoir for inoculum;
- Irrigation to reduce water stress and the severity of disease, although overhead irrigation has been shown to increase the severity of disease (JECFA, 2001d).

Differences in cultivar susceptibility to *Fusarium* has been demonstrated. However, there appears to be a strong cultivar-location interaction and when maize cultivars that accumulated low amounts of fumonisin were grown in other areas they accumulated increased amount of fumonisin (Duvick, 2001). A number of factors may contribute to cultivar resistance to fumonisin accumulation, including:

- Inhibition of fungal invasion (kernel hardness, silk composition, inhibitory compounds, etc.);
- Presence of fumonisin degrading enzymes;
- Mechanical barriers or engineered resistance to insect attack (Duvick, 2001).

Maize hybrid have been produced by genetic modification techniques to introduce an endotoxin originally found in *Bacillus thuringiensis*. These 'Bt-maize' hybrids have been shown to accumulate lower amounts of fumonisin than conventional equivalents under conditions of natural and manual insect infestation (Munkvold *et al*., 1999; Hammond *et al*., 2004)

5.5.2.3 Control of fumonisins post-harvest

Fumonisin formation post-harvest can be controlled by:

- Prevention of fungal growth and fumonisin production. Fungal species are unable to grow at water activities below 0.65-0.7 (approximately 14-15% grain moisture). Drying of freshly-harvested grain is an effective means of controlling fungal growth and consequent fumonisin production (JECFA, 2001d). Application of propionates controlled growth of *Fusarium* isolates, although the degree of control depended on the form and concentration of the propionate, the grain water activity, the storage temperature and the *Fusarium* isolate (Marin *et al*., 1999). However, none of the treatments had any effect on FB_1 production by *F. verticillioides*, while for *F. proliferatum* FB_1 production generally decreased with increasing concentration of propionate.
- Segregation of high risk material. Maize screenings (broken grains and non-grain material) may contain significantly higher concentrations of fumonisin than whole grains (JECFA, 2001d).
- Chemical and physical decontamination. Ammoniation under conditions of high temperature or pressure has been shown to reduce the concentration of fumonisins in maize by 79%, leaving no mutagenic activity (Park *et al*., 1992). Reaction with fructose (to block the amine group) has been shown to eliminate the toxicity of FB_1 to rats (Lu *et al*., 1997). Irradiation of maize with 15 kGy of gamma-irradiation sterilized the grain, but only reduced fumonisin levels by approximately 20% (Visconti *et al*., 1996).

5.5.3 Influence of processing on fumonisin levels

5.5.3.1 Dry milling

Katta *et al.* (1997) monitored the *Fusarium* and fumonisin content of milling fractions from dry milling of naturally fumonisin-contaminated maize. Mill streams of significance for human food (cornmeal, flour and grits) showed greatly reduced concentrations of FB_1 compared to the whole grain, while the bran fraction showed elevated FB_1 concentration compared to the whole grain. This is consistent with FB_1 contamination being associated with the surface and near-surface regions of the grain. Brera *et al.* (2004) found similar results, with the concentration of fumonisin in the flour at approximately 9% of the concentration in the whole grain, while concentrations in bran were approximately 160% of the levels in whole grain.

5.5.3.2 Wet milling

Bennett *et al*. (1996) demonstrated that starch produced by wet milling of fumonisin-contaminated maize (initial contamination level 13.9 mg FB_1/kg) was free of detectable FB_1. The steep water and process water contained 22% of the recoverable toxin, while the germ, fibre and gluten all contained fumonisins at concentrations lower than the whole grain.

5.5.3.3 Nixtamalisation

Nixtamalisation or 'masa-type' processes involves alkaline cooking and heating of maize for the production of tortillas and related products (Saunders *et al*., 2001). The initial stage of the

process involves cooking the maize in a lime solution and overnight steeping. This product is then washed and drained to produce nixtamal, before grinding to produce masa, and sheeting, cutting and cooking to produce tortillas or chips. The initial nixtamalisation process has been shown to reduce fumonisin contamination by 40-80% (Dombrink-Kurtzman *et al.*, 2000; Saunders *et al*., 2001; Voss *et al*., 2001). Some of the fumonisin is converted to hydrolysed fumonisin, which is almost as toxic as the parent toxin, however, overall toxin levels are substantially reduced. The subsequent processing steps (masa production, tortilla production) have negligible impact on fumonisin levels (Saunders *et al*., 2001).

5.5.3.4 Cooking, canning and extrusion

Fumonisins are quite heat stable. Significant reductions in fumonisin levels can be achieved by increasing the temperature and/or time of heating. However, the increases necessary to achieve substantial reductions are generally beyond normal commercial processing parameters (Saunders *et al*., 2001). Castelo *et al*. (1998) demonstrated decreases of 10-15% of fumonisin levels during canning (121ºC) of corn products, but no significant loss of fumonisins during baking of corn muffins at 204ºC for 20 minutes. Roasting of cornmeal at 218ºC for 15 minutes resulted in almost complete loss of fumonisins, presumably due to the significantly higher internal temperatures reached in the food.

Piñeiro *et al*. (1999) reported a 70-80% reduction in fumonisin levels during frying of polenta or autoclaving of cornmeal.

The influence of extrusion on fumonisins has been reviewed by Castells *et al*. (2005). Various studies have reported decreases in fumonisin concentration following extrusion of maize flour or meal in the range 26-99%. Fumonisin inactivation is increased at higher temperatures and at slower screw speeds.

5.5.3.5 Fermentation

Naturally fumonisin-contaminated corn was yeast fermented for ethanol production (Bothast *et al*., 1992). Fermentation caused little degradation of FB_1, with most of the toxin from the original grain being recovered from the distillers' grains, thin stillage and distillers' solubles fractions. No toxin was detected in the ethanol or centrifuge solids.

Detection of fumonisins in beer (see Table 26) also suggests that fumonisins are resistant to fermentative degradation.

5.6 Conclusions

5.6.1 Description of risks to New Zealand consumers

There is consistent epidemiological evidence to suggest that dietary exposure to fumonisins can cause adverse health outcomes in humans. The most likely human health endpoints are liver and oesophageal cancers and neural tube defects, although overt nephrotoxicity appears to be the most sensitive endpoint in laboratory animals. Acute mycotoxicosis resulting in general gastrointestinal symptoms has also been reported.

While *Fusarium* species capable of fumonisin production (*F. verticillioides, F. proliferatum*) have occasionally been found in New Zealand cereal crops (Sayer and Lauren, 1991; Sayer, 1991; Lauren and Di Menna, 1999), these fungal species appear to be relatively rare in New Zealand crops. Limited surveillance of New Zealand maize did not detect fumonisins, although fumonisins have been detected on imported corn.

The available evidence suggests that New Zealanders will primarily be exposed to fumonisins through consumption of imported corn. As New Zealanders are generally low level consumers of maize products the risk due to fumonisin exposure in New Zealand is likely to be low. Some of the processes used on maize (extrusion, nixtamalisation) will tend to further decrease the fumonisin content of the food in New Zealand.

While indications are that New Zealanders exposure to fumonisins will be very low, there is insufficient New Zealand specific information on the fumonisin content of available foods to define the level of risk.

5.6.2 Commentary on risk management options

Fumonisins are not currently regulated in New Zealand. Agronomic research conducted in New Zealand demonstrates a good awareness of the deleterious effects of *Fusarium* infection, but without specific reference to fumonisins. This is little evidence to suggest that fumonisin-producing *Fusarium* species occur commonly in New Zealand.

5.6.3 Data gaps

General information on the fumonisin content of the New Zealand food supply.

6 ZEARALENONE

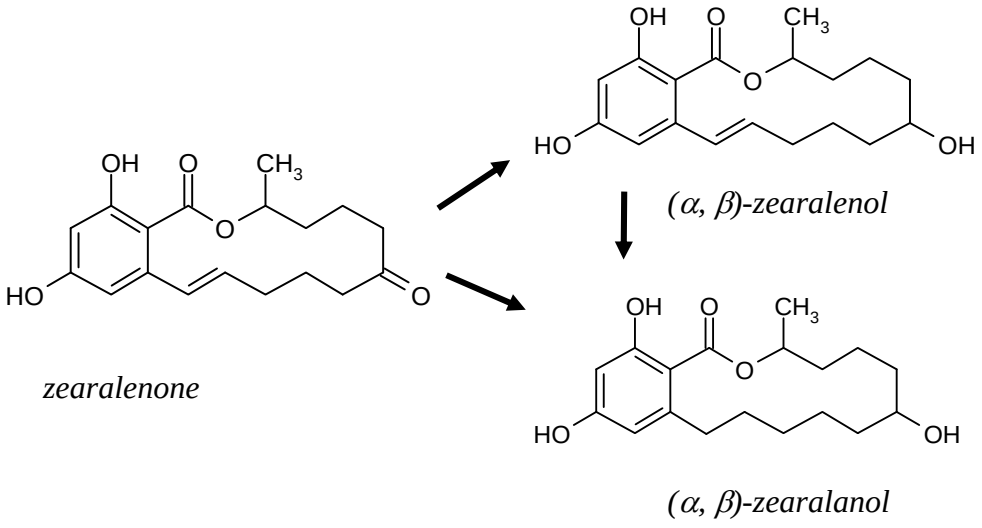
6.1 Hazard identification

Zearalenone is a nonsteroidal estrogenic mycotoxin produced by several *Fusarium* species that proliferate in poorly stored grains, oilseeds and hay. *Fusarium* infection tends to develop during prolonged cool, wet, growing and harvest seasons (Krska, 1999). Zearalenone occurs in both temperate and warm regions of the world in cereal crops such as corn or maize, barley, oats, wheat, rice and sorghum but also in bread and bananas. The highest incidence rates have been in North America, and central and northern Europe although the occurrence of zearalenone has also been reported in Egypt, South Africa, Italy South America and New Zealand (Krska, 1999). Zearalenone is stable during storage and milling and processing or cooking of food and does not degrade at high temperatures. In mammals, zearalenone is metabolised to the stereoisomers, α- and β- zearalenol and α- and β- zearalenol (Figure 6). The α- isomer of zearalanol, zeranol, has been used as a growth promoter in beef cattle and feedlot lambs in the United States and Canada (Kuiper-Goodman *et al*., 1987; IARC, 1993) but is not registered for veterinary use in New Zealand (NZFSA, 2006).

6.1.1 Structure and nomenclature

The IUPAC chemical name for zearalenone, with the molecular formula $C_{18}H_{22}O_5$, is (3S,11*E*)-3,4,5,6,9,10-Hexahydro-14,16-dihydroxy-3-methyl-1*H*-2-benzoxacyclotetradecin-1,7(8*H*)-dione although it may also be known as 6-(10-hydroxy-6-oxo-*trans*1-undecenyl)-β-resorcyclic-μ-lactone. Zearalenone shows some structural similarities to the female sex hormone, 17β-estradiol, with two distally located oxygen-containing groups. The chemical structure of zearalenone and the mammalian metabolites zearalenol and zearalanol are shown in Figure 6.

Figure 6: Structure of zearalenone and its major metabolites



6.1.2 Occurrence

Fusarium taxonomy is complex and some early identifications have been questioned. Zearalenone is now regarded as being produced by *F. graminearum, F. culmorum, F. cerealis, F. equiseti, F. crookwellense* and *F. semitectum* (CAC, 2000; Yiannikouris and Jouany, 2002). Other species have been reported to produce zearalenone, however, they appear to be less important with respect to formation of zearalenone in crops (Pitt and Hocking, 1997). All these *Fusarium* species been detected in New Zealand food crops, except *F. cerealis*, with *F.graminearum* seemingly the most prevalent species in the North Island and *F. culmorum* the most prevalent species in the South Island (Table 13).

6.2 Hazard Characterisation: Adverse Health Effects

6.2.1 Conditions

Zearalenone has been implicated in several incidents of adverse human health effects but on the present evidence base, the impact on human health is speculative.

Elevated levels of zearalenone have been measured in cancerous and abnormal endometrial tissue compared with normal endometrial tissue from 49 women (Tomaszewski *et al.,* 1998) suggesting a possible link between zearalenone and human endometrial tissue growth. However, in this study, zearalenone was not detected in a further 13 abnormal cases so there is some inconsistency with the observations.

Zearalenone or zearalanol was suspected to be a causative agent of precocious puberty after being found in the blood of Puerto Rican girls aged between six months to eight years with early sexual development and who had been exposed to contaminated food (Sàenz de Rodriguez, 1984).

Early breast development has also been reported from Hungary where zearalenone was detected in the serum of 5 out of 36 affected subjects and in foods consumed by the subjects (Szuets *et al.,* 1997), implicating zearalenone as a possible causative agent.

Zearalenone was found together with other *Fusarium* mycotoxins in a condition known as "scabby grain toxicosis" reported in China but the significance of this finding is not clear (Peraica *et al*., 1999).

6.2.2 Toxicity

6.2.2.1 Acute toxicity

There have been no reports of acute human toxicity caused by zearalenone.

Zearalenone has low acute toxicity after either oral or interperitoneal administration in mice, rats and guinea pigs, with LD_{50} values ranging from >500 to >20,000 (JECFA 2000, SCF 2000c).

6.2.2.2 Chronic toxicity

The health concerns of exposure to zearalenone relate to its estrogenic activity via estrogen receptor binding. Estrogenicity in the order of 1-50% of the endogenous hormone 17β-estradiol has been reported from receptor binding, cell proliferation and *in vivo* assays (Kiang *et al.,* 1978, IEH, 2000, Soto *et al.,* 1995, Welshons *et al.,* 1990, Hobson *et al.,* 1977). Estrogen mimicking environmental compounds have been implicated in a range of possible human health effects including reproductive effects (sperm count and quality, cryptorchidism, hypospadias, precocious puberty), neurobehavioural and increased incidence of hormonal cancers. Two global reviews (WHO, 2002; IUPAC/SCOPE, 2003) have concluded that there is no conclusive evidence that low level exposure to such compounds causes human disease.

Zearalenone was found to be negative in genotoxicity tests except for chromosomal aberrations at very high concentrations (JECFA 2000, SCF 2000c).

6.2.3 Toxicological assessment

JECFA (2000) established a Provisional Maximum Tolerable Daily Intake for zearalenone of 0.5 μg/kg body weight/day based on a dose that had no observed hormonal effects in pigs, the most sensitive species, and a safety factor of 100.

SCF (2000c) used the same animal NOEL, but applied a larger safety factor of 200 to derive a temporary Tolerable Daily Intake (t-TDI) of 0.2 μg/kg body weight/day.

IARC evaluation assigned zearalenone to Group 3 (not classifiable as to their carcinogenicity to humans) because of inadequate evidence in humans and limited evidence in experimental animals (IARC, 1993).

6.3 Exposure Assessment

6.3.1 Zearalenone in New Zealand cereals

In New Zealand, the climate is generally favourable for the growth of *Fusarium* species. Zearalenone has been found in several investigations: a preliminary investigation of wheat (Agnew *et al.*, 1986), a small study of maize (Hussein *et al.*, 1989), and a large survey of the occurrence of *Fusarium* mycotoxins in cereals grown in New Zealand in 1986-1989 (Lauren *et al.,* 1991).

Lauren *et al*. (1991) reported finding zearalenone in the majority of maize samples (76%), but at concentrations less than 0.5 mg/kg. In the same study, wheat, barley and oats from six regions in New Zealand showed contamination rates of 32%, 18% and 34% respectively with maximum concentrations of 0.46, 0.17 and 0.09 mg/kg.

Samples of commercially grown hybrids of maize taken at harvest from several North Island sites from 1992 to 1994 were analysed for *Fusarium* mycotoxins including zearalenone (Lauren *et al.*, 1996). Results are summarised in Table 24. Two factors contributing to higher contamination levels were the late harvesting of crops and the use of hybrids that were more susceptible to accumulation of zearalenone.

Table 24: Distribution of zearalenone contamination of New Zealand maize

Year	No. samples	% of samples with zearalenone (mg/kg)				
		<0.4	0.4 – 1.0	1.0 – 2.0	>2.0	Max. level
1992	178	67	17	8	7	10.5
1993	162	81	14	3	2	2.7
1994	176	93	3	2	2	6.1

6.3.2 Zearalenone in the New Zealand food supply

A preliminary survey of maize-based foods, mainly cornflakes, was conducted by HortResearch (The Horticulture and Food Research Institute of New Zealand Ltd.) for samples collected in 1993. The range in seven samples (five positives) was from 0.16 to 0.30 mg/kg with a mean concentration of 0.22 mg/kg.

A more extensive survey in 1995 examined 124 maize-based foods and found a much lower incidence of contamination (7.2%) (Lauren and Veitch, 1996). Results are presented in Table 25.

Table 25: Zearalenone New Zealand maize-based foods

Food category	No. samples	No. positives	Mean[1] (mg/kg)	Range (mg/kg)
Breakfast Foods	20	5	0.084	0.05-0.12
Extruded snack foods	20	1	0.14	0.14
Flours; grits	17	2	0.22	0.12-0.30
Breads	16	2	0.10	0.06-0.14
Masa flour products	24	0	-	< 0.05
Corn (maize) oils & snack bars	21	0	-	< 0.05
Corn syrups & liquid brewing sugar	6	0	-	< 0.05

1 mean of positive values

6.3.3 Zearalenone in Australian cereals

Zearalenone intoxication of pigs fed contaminated maize and sorghum has been reported in Australia, with maximum levels of 8 mg/kg detected in the maize (Blaney *et al*., 1984). Williams *et al.* (1988) reported using wheat naturally contaminated with *Fusarium graminearum* containing 4 mg zearalenone/kg and 23 mg DON/kg in pig feeding trails.

Blaney *et al*. (1987) examined wheat from southern Queensland – a wheat growing region that was considered to be more likely to suffer rain damage and fungal infection. In 1983, 1291 samples of wheat were examined with 62 found to contain greater than 0.2% of 'pink grain' – an indicator of fungal infection. In 1984 and 1985, only general purpose (GP) graded wheat was examined (60 and 80 samples respectively). Eleven lines of wheat from the 1983 harvest and two from the 1984 harvest, containing elevated proportions of pink grains, were analysed and found to contain zearalenone in the range <0.01 to 0.43 mg/kg. The remaining wheat samples were pooled on the basis of grade and receiving depot to give 37 pooled wheat samples across the three harvest years (1983, 1984 and 1985). Zearalenone was detected in

4/37 pooled wheat samples at concentrations in the range 0.01 to 0.10 mg/kg. All four samples were GP grade wheat. It should be noted that Australian wheat imported into New Zealand is predominantly Australian Standard White (ASW), with lesser amount of Prime Hard (PH).

6.3.4 Zearalenone in the Australian food supply

Bryden *et al*. (1995) detected zearalenone in 14 of 40 retail food samples, including breakfast cereals, snack foods, popcorn, cornflour, maize meal and corn kernels. Results were in the range 0.01-0.068 mg/kg, with a mean for positive results of 0.023 mg/kg.

6.3.5 Overseas context

Internationally, there have been many reports of the occurrence of zearalenone in food and feeds from a wide range of countries with the highest prevalence of the toxin occurring in cereals, namely, barley, corn or maize, oats, rice, sorghum and wheat. For reviews see Price and Fenwick (1985), Pohland and Wood (1987), Kuiper-Goodman *et al.* (1987), JECFA (2000) and SCOOP (2003). The highest concentrations are generally found in corn or maize and lower concentrations in barley, oats, rice and wheat. Zearalenone is also found in grain products such as flour, pasta, pizza, malt, infant foods and breakfast cereals.

A collation of the prevalence of zearalenone in foods from temperate climates is shown in Table 26. Although this list is not exhaustive, it provides a wide range of data for comparison with concentrations reported in New Zealand foods (Table 25). Not included are the occasional occurrences in beans, oilseeds, spices and nuts (JECFA, 2000). Where multiple entries are available, a weighted average has been calculated from the mean concentration and corresponding number of positive results. The means cited are calculated from positive samples only.

The prevalence and concentrations reported in New Zealand wheat, barley, maize, oats and corn are moderately high compared with international levels.

Table 26: Worldwide data on occurrence of zearalenone in food

Food	Country	Incidence +ve/total samples	Mean (mg/kg)	Maximum (mg/kg)	Reference
Barley	Canada	3/210 5/7 41/180	0.013 0.17 ≤0.0003	0.021 NR NR	JECFA, 2000
	Czechoslovakia	58%	NR	0.26	JECFA, 2000
	Finland	2/30 5/20	0.026 0.031	0.030 0.053	JECFA, 2000 SCOOP, 2003
	Germany	NR 0/14 24/46	0.003-0.036 0 0.024	0.31 0 0.32	JECFA, 2000
	Japan	7/17 13/18 29/31 1/1	4.16 0.024 0.024 0.004	15.3 0.097 0.39 0.004	JECFA, 2000 JECFA, 2000

Food	Country	Incidence +ve/total samples	Mean (mg/kg)	Maximum (mg/kg)	Reference
	Korea	0/30 20/39 21/28 10/30	0 0.29 0.11 0.036	0 1.42 1.28 0.17	JECFA, 2000 Park *et al.*,2002
	Netherlands	6/7	0.007	0.009	JECFA, 2000
	Sweden, Norway	23/329	0.018	NR	JECFA, 2000
	USA	1/1	<0.019	<0.019	JECFA, 2000
Corn/maize	Argentina	677/2271	0.16	2.0	JECFA, 2000
	Austria	83/198	0.088	0.34	SCOOP, 2003
	Brazil	15/364	NR	9.8	JECFA, 2000
	Brazil	65/214	0.16	0.72	Vargas *et al.*,2001
	Bulgaria	0/264	0	0	JECFA, 2000
	Canada	374/2225 2/19 0/6	2.74 NR 0	141.0 NR 0	JECFA, 2000
	China	17/47 5/5	0.044 NR	0.17 NR	JECFA, 2000
	Czechoslovakia	7%	0.11	NR	JECFA, 2000
	France	246/280	0.13	1.82	SCOOP, 2003
	Germany	6/7	0.012	0.035	JECFA, 2000
	Hungary	17%	0.03	0.079	JECFA, 2000
	Italy	14/15	0.046	0.15	JECFA, 2000
	Italy	45/48	0.67	6.49	SCOOP, 2003
	Korea	9/61	0.14	0.39	JECFA, 2000
	Korea	4/18	0.005	0.006	Park *et al.*,2002
	Netherlands	1/1	0.68	NR	JECFA, 2000
	UK	128/139	0.12	0.58	SCOOP, 2003
	USA	NR 16/628 37/351	0.90 NR 0.50	NR 0.50 NR	JECFA, 2000
	Yugoslavia	3/100	5.1	10.0	JECFA, 2000
Cornflour	Canada	15/154	0.025	0.18	JECFA, 2000
	Iran	19/19	0.38	0.89	Oveisi *et al.*, 2005
	Italy	16/53	0.045	0.099	SCOOP, 2003
	Korea	9/47	0.022	0.084	Park *et al.*,2002
	UK	4/8	0.012	0.017	SCOOP 2003
	USA	3/11	0.038	0.10	JECFA, 2000
Cornflakes	Canada	1/1	0.01	0.01	JECFA, 2000
	Norway	33/50	0.005	0.014	SCOOP, 2003
	UK	7/15	0.046	0.17	SCOOP, 2003
Corn cereals	USA	7/8	0.012	0.020	JECFA, 2000
	Canada	0/60	0	0	JECFA, 2000
Corn snacks	Canada	1/1	0.025	0.025	JECFA, 2000
	Iran	19/19	0.83	1.47	Oveisi *et al.*, 2005
	UK	27/54	0.038	0.086	SCOOP 2003
	USA	1/14	0.01	0.01	JECFA, 2000
Oats	Austria	3/192	0.027	0.030	SCOOP, 2003
	Canada	0/NR	0	0	JECFA, 2000
	Finland	3/21 30/30	0.063 0.64	0.086 1.31	JECFA, 2000 SCOOP 2003
	Germany	4/14	0.007	0.011	JECFA, 2000
	Netherlands	3/4	0.017	0.029	JECFA, 2000

Food	Country	Incidence +ve/total samples	Mean (mg/kg)	Maximum (mg/kg)	Reference
	Sweden, Norway Norway	14/233 8/22	0.026 0.0003	NR 0.002	JECFA, 2000 SCOOP, 2003
	UK	0/4	0	<0.008	SCOOP, 2003
	USA	1/1	0.018	0.018	JECFA, 2000
Rice	India	0/30	0	0	JECFA, 2000
	Germany	0/3	0	0	SCOOP 2003
	Russia	0/280	0	0	JECFA, 2000
	Papua, New Guinea	1/1	3.06	3.06	JECFA, 2000
	UK	0/100	0	0	SCOOP, 2003
	Uruguay	3/42	NR	>0.2	Piñeiro *et al*., 1996
Rye	Canada	0/1	0	0	JECFA, 2000
	Denmark	2/30	0.001	0.002	Rasmussen *et al.*, 2003
	Germany	17/37 2/3	0.016 0.013	0.10 0.024	JECFA, 2000 SCOOP 2003
	Finland	0/12	0	0	SCOOP 2003
	Korea	3/5	0.002	0.004	JECFA, 2000
	Netherlands	1/4	0.011	NR	JECFA, 2000
	Sweden, Norway Norway	0/31 0/4	0 0	0 0	JECFA, 2000 SCOOP 2003
Wheat	Brazil	0/12	0	0	JECFA, 2000
	Canada	19/193	0.011	0.033	JECFA, 2000
	China	13/36	<0.01	NR	JECFA, 2000
	Denmark	10/30	0.001	0.002	Rasmussen *et al.*, 2003
	Germany	208/500 1/5	0.085 0.072	8.04 0.072	JECFA, 2000 SCOOP, 2003
	Finland	2/40 1/39	0.022 0.001	0.032 0.001	JECFA, 2000 SCOOP, 2003
	France	72/72	0.011	0.052	SCOOP, 2003
	India	0/30	0	0	JECFA, 2000
	Japan	9/26	0.38	1.69	JECFA, 2000
	Korea	2/10	0.008	0.040	JECFA, 2000
	Netherlands	7/13	0.045	0.17	JECFA, 2000
	Russia	5/191	NR	NR	JECFA, 2000
	Sweden, Norway Norway	7/101 9/35	0.005 0.003	NR 0.013	JECFA, 2000 SCOOP 2003
	Taiwan	9/22	0.016	0.032	JECFA, 2000
	UK	14/41	0.007	NR	JECFA, 2000
	Uruguay	5/106	NR	>0.2	Piñeiro *et al*., 1996
	USA	19/42	NR	11.1	JECFA, 2000
Wheat flour	China	0/4	0	0	JECFA, 2000
	Germany	1/4	0.013	0.013	SCOOP 2003
	Japan	3/27	0.003	0.006	JECFA, 2000
	USA	2/17	0.013	0.014	JECFA, 2000
Bread - white	UK	1/40	0.016	0.016	SCOOP, 2003

Food	Country	Incidence +ve/total samples	Mean (mg/kg)	Maximum (mg/kg)	Reference
Dried fruit and vegetables	Egypt	0/6	0	0	JECFA, 2000
	Korea	0/37	0	0	Park *et al.*,2002
	Uruguay	7/253	NR	>0.2	Piñeiro *et al*., 1996
Meat products	Uruguay	0/58	0	0	Piñeiro *et al*., 1996
	Canada	0/34	0	0	JECFA, 2000
Infant foods	Canada	9/60 59/181	0.004 0.013	NR 0.035	JECFA, 2000 Lombaert *et al.*,2003
	Germany	4/171	0.011	0.014	SCOOP 2003
	Japan	0/27	0	0	JECFA, 2000
	UK	2/34	0.012	0.012	SCOOP, 2003

NR = no result available,

High levels of zearalenone have been reported in African beer (up to 4.6 mg/kg; JECFA, 2000), however, studies carried out in Korea and Canada, analysing local and imported beers, did not detect any residues of zearalenone or its metabolites (Shim *et al*., 1997; Scott *et al*., 1993).

Very high levels of zearalenone have also been reported for moldy bananas from India (17 mg/kg) and tomatoes from Egypt (80 mg/kg) (JECFA, 2000). However, these results do not appear to be representative of contamination in the products in general.

Zearalenone and its metabolites (α- and β-zearalenol) can be transmitted to the milk of cows, sheep and pigs, although these observations come from studies where animals were fed elevated levels of zearalenone and residues have not been detected in a single study of normal retail milk samples (country of survey not stated; JECFA, 2000). In contrast, El-Hoshy (1999) reported detection of zearalenone in 20% of randomly sampled Egyptian raw milk samples (range 0.003-0.010 mg/kg) and 15% of pasteurised milk samples (range 0.001-0.007 mg/kg). Zearalenone was also detected in condensed milk, milk powder, and hard and soft cheeses.

Sypecka *et al*. (2004) fed hens a diet naturally contaminated with zearalenone at 0.5 mg/kg. No residues of zearalenone or its metabolites were detected in eggs. Dänicke *et al*. (2002) also did not find zearalenone or its metabolites in eggs or muscle of hens fed contaminated maize with a zearalenone content of 1.58 mg/kg.

Zearalenone and its metabolites are able to be transmitted to organ and muscle meats, with the liver being the main organ of accumulation (JECFA, 2000). Chickens fed 100 mg zearalenone/kg for eight days had 0.059-0.103 mg zearalenone/kg in muscle and up to 0.68 mg zearalenone/kg in liver (JECFA, 2000). El-Hoshy (1999) found residues of zearalenone in 20% of fresh and 24% of frozen meat samples and in 25%, 25%, 15% and 20% of minced meat, sausage, beef burger and luncheon samples from Egypt. Mean zearalenone levels were typically 0.005-0.009 mg/kg.

Since grain feeding of ruminant animals is not usual in New Zealand, domestic meat and milk supplies are unlikely to be a significant source for the New Zealand consumer. Feeding of contaminated grain to poultry may result in some transmission of zearalenone residues into

human foods, although evidence suggests that any incurred residues are likely to be at very low concentrations.

6.3.6 New Zealand estimates of dietary exposure

Thomson *et al*. (2003) have estimated the exposure of New Zealanders to zearalenone from consumption of maize-based foods. Estimates were made by combining food consumption information from simulated diets formulated for the 1997/98 NZTDS (Brinsdon, 2004) with zearalenone concentrations for mixed grain breads, corn-based breakfast cereals and corn-based snack foods from the study of Lauren and Veitch (1996). Average zearalenone concentrations were calculated by assuming that some level of zearalenone was present in all samples and assuming that the level in samples reported as 'not detected' was equal to half of the limit of detection. Average concentration is a reasonable approach given the concern of chronic rather than acute toxicity. Details of the exposure estimation are outlined in Table 27.

Table 27: Estimated average dietary exposure to zearalenone for five New Zealand population age-sex groups

Age-sex group	Food	Consumption (g/day)	Zearalenone concentration (mg/kg)	Exposure (µg/kg bw/day)
Adult male	Mixed grain bread	25	0.034	0.010
	Breakfast cereal	2.9	0.040	0.0015
	Total			**0.010**
Adult female	Mixed grain bread	17	0.034	0.0083
	Breakfast cereal	4.3	0.040	0.0024
	Total			**0.011**
Young male	Mixed grain bread	29	0.034	0.013
	Breakfast cereal	4.4	0.040	0.0023
	Total			**0.015**
Vegetarian	Mixed grain bread	62	0.034	0.030
female	Breakfast cereal	4.3	0.040	0.0024
	Total			**0.032**
Child	Mixed grain bread	20	0.034	0.029
	Breakfast cereal	3.6	0.040	0.006
	Corn-based snack foods	6.4	0.030	0.008
	Total			**0.044**

Body weights: adult male = 82 kg, adult female = 70 kg, young male = 78 kg (Russell *et al*., 1999), vegetarian female = 70kg (assumed to be the same as an adult female), child = 23kg (MoH, 2003).

Since New Zealand wheat, barley and oats have all been reported to contain zearalenone on occasions (see section 6.3.1), these estimates of exposure will be underestimated to some extent.

6.3.7 Overseas estimates of dietary exposure

A summary of overseas exposure estimates for zearalenone is given in Table 28.

Table 28: Overseas estimates of dietary exposure to zearalenone

Country	Population group	Mean exposure (µg/kg body weight/day)	Reference
***t*-TDI = 0.2 or 0.5 µg/kg body weight/day**			
African diet	Adult, 60 kg	0.041	JECFA, 2000
European diet	Adult, 60 kg	0.025	JECFA, 2000
Far Eastern diet	Adult, 60 kg	0.056	JECFA, 2000
Latin American diet	Adult, 60 kg	0.036	JECFA, 2000
Middle Eastern diet	Adult, 60 kg	0.059	JECFA, 2000
Austria	Adults, 75 kg	0.028	SCOOP, 2003
Canada	Adults, 60 kg	<0.016	JECFA, 2000
Denmark		0.02	SCF, 2000c
Finland	Adult, 77.1 kg	0.027	SCOOP, 2003
France	Adult, 66.4 kg Male, 73.9 kg Female, 60.1 kg Child, 3-15 yrs, 31.6 kg	0.027 0.029 0.024 0.042	SCOOP, 2003
France	Adult, 15+ years	0.033	Leblanc *et al*., 2005
France	Child, 3-14 years	0.066	Leblanc *et al*., 2005
Italy	Adults, 70kg	0.0008	SCOOP, 2003
Netherlands	Adults, 65.8 kg Child, 1-4 years, 13.8 kg Child, 1-6 years, 17.1 kg	0.021 0.046 0.050	SCOOP, 2003
Norway	Male, 81 kg Female, 66 kg Infant, 6 months, 8 kg	0.008 0.007 0.012-1.51	SCOOP, 2003
Norway		0.02	SCF, 2000c
Portugal	Total population, 65 kg	0.004	SCOOP, 2003
United Kingdom	Adult male, 70.1 kg Adult female, 70.1 kg Infant, 6-12 mths, 8.7 kg Child, 4-6 yrs, 20.5 kg	0.014 0.013 0.050 0.055	SCOOP, 2003
USA		0.03	SCF, 2000c

The New Zealand average exposure estimates of 0.01 µg/kg bw/day for adults are comparable with average intake estimates for Norway and the UK and similar, but perhaps slightly lower than those for a number of other temperate western countries (Austria, Canada, Denmark, Finland, France and the Netherlands).

The higher intake by children compared with adults, and the level of exposure of New Zealand children, is consistent with findings for British, French and Dutch children (SCOOP, 2003). Whilst maize and maize products were significant sources of zearalenone for consumers in the UK and Italy, wheat bread was a significant contributor to intake of zearalenone for adults (and children) from Austria, France and Germany. The exclusion of wheat products in the New Zealand estimate may result in an underestimation of average intake.

6.4 Risk Characterisation

6.4.1 Adverse health effects in New Zealand

No cases of human adverse health effects attributable to zearalenone exposure have been reported in New Zealand.

6.4.1.1 Risk assessment and other activities

In a risk assessment covering a range of natural and synthetic dietary estrogenic compounds, zearalenone was shown to be the most estrogenic compound (Thomson *et al*., 2003). However, a lack of information on blood levels resulting from dietary exposure precluded an assessment of zearalenone's contribution to total dietary estrogenic exposure.

6.4.2 Adverse health effects overseas

A causative role of zearalenone in human health outcomes has not been established.

3.4.2.3 Risk assessments and other activity overseas

JECFA

JECFA concluded that hormonal effects were the most critical for zearalenone (JECFA, 2000). Hepatocellular adenomas and pituitary cancers observed in long-term rodent studies were concluded to be a consequence of the estrogenic activity of zearalenone, rather than any overt genotoxicity.

SCF

The EU Scientific Committee on Food considered zearalenone, as part of a wider consideration of *Fusarium* toxins (SCF, 2000). The Committee concurred with the conclusions reached by JECFA, but suggested that further work was required on no hormonal effect levels in pigs, on the potential genotoxicity of zearalenone, on blood levels in humans with known dietary intake, and on differences in metabolism between species.

Canada

Kuiper-Goodman *et al*. (1987) reported the outcomes of a risk assessment for zearalenone. A safety limit was calculated, based on estrogenicity (0.1 μg/kg body weight/day) and based on tumourigenicity in rats and mice (0.05 μg/kg body weight/day for an excess risk level of one in 10^6). The authors recommended that, on the basis of the risk assessment, no immediate regulatory action was necessary, but that zearalenone exposure should be kept as low as technologically possible. It was also recommended that data on zearalenone contamination of non-maize foods be collected and that further information on genotoxicity and comparative metabolism be sought.

Codex

Codex, through the 32st meeting of the Codex Committee on Food Additives and Contaminants (CAC, 2000), reviewed a position paper on zearalenone (prepared by Norway) and concluded that:

- The best way to protect consumers from the toxic effects of zearalenone is to reduce fungal infection of cereals and consequent toxin production,
- Codex should continue work on development of a Code of Practice for reducing levels of mycotoxins in cereals, and
- There was still a requirement to establish maximum zearalenone limits for risk products intended for high risk consumers.

6.5 Risk Management Information

6.5.1 Relevant food controls: New Zealand

6.5.1.1 Establishment of regulatory limits

Zearalenone is not currently regulated in New Zealand.

6.5.2 Relevant food controls: overseas

6.5.2.1 Establishment of regulatory limits

In 2003, at least 17 countries reported having regulatory limits for zearalenone in food (van Egmond and Jonkers, 2003). Table 29 summarises the reported regulatory positions on zearalenone for different foods in different countries.

Table 29: Regulatory limits for zearalenone in various countries (food regulations only)

Country	Commodity description	Regulatory limit (mg/kg)
Armenia	All foods	1.0
Austria	Wheat, rye, durum wheat	0.06
Belarus	Barley, wheat, maize	1.0
Bulgaria	Processed cereal products	0.1
Colombia	sorghum	1.0

Country	Commodity description	Regulatory limit (mg/kg)
Egypt	Wheat, barley, maize, cereal flours and products, confectionery products, legume vegetables, fats, oils	1.0
France	Cereal and cereal products Vegetable oils	0.05 0.2
Hungary	Milled cereal product, cereal constituent of muesli	0.1
Indonesia	Maize	Not detectable
Iran	Barley Maize, rice, wheat	0.4 0.2
Italy	Baby food Cereals and cereal products	0.02 0.1
Mexico	Wheat and wheat flour, barley and barley flour, maize and maize flour	1.0
Morocco	Cereals, vegetable oils	0.2
Russian Federation	Wheat, barley, maize, corn	1.0
Serbia and Montenegro	Corn	1.0
Ukraine	Grain-based baby foods Grains, beans, sunflower press, flour, bread, all nuts, all seeds, vegetable oil, wheat middlings	0.04 1.0
Uruguay	Corn, barley	0.2

From van Egmond and Jonkers (2003)

6.5.2.2 Codes of practice and related initiatives

Codex have produced a Code of Practice for prevention and reduction of mycotoxin contamination in cereals, with specific annexes relating to OTA, zearalenone, fumonisins and trichothecenes (http://www.codexalimentarius.net/download/standards/406/CXC_051e.pdf). Recommended practices cover planting, preharvest, harvest, storage and transport.

The zearalenone specific annex identifies monitoring of establishment of *Fusarium* infection during cereal flowering and winnowing of grain at harvest or later, to remove small, shriveled grains as specific GAP measures.

The Code also discusses a HACCP approach to control of mycotoxin contamination of grains. The Food and Agriculture Organization of the United Nations (FAO) in collaboration with the International Atomic Energy Agency (IAEA) have produced a manual on the application of HACCP in mycotoxin prevention and control (ftp://ftp.fao.org/docrep/fao/005/y1390e/y1390e00.pdf). European efforts in this area are ongoing through a collaborative effort known as the Mycotoxin Prevention Cluster, with a specific project aimed at prevention of *Fusarium* mycotoxins entering the animals and human food chains (http://www.mycotoxin-prevention.com/Project2.htm). This project has five major tasks:

- Development of critical control systems;
- Pre-harvest biocontrol;
- Post harvest control;

- Decontamination using microbial inoculants for prevention of entry into animal production systems; and
- Decontamination using physicochemical means.

6.5.2.3 Management of zearalenone formation in crops

Preharvest measures to control *Fusarium* infection can also reduce the formation of zearalenone (JECFA, 2000). Zearalenone production appears to be favoured by wet, cool weather. Control measures include culture techniques, breeding and growing of resistant cultivars and use of fungicides or biological control agents (JECFA, 2000).

Cultural control measures include:
- Crop rotation, particularly rotation involving non-host crops. Maize-wheat rotation can lead to increased incidence of *Fusarium* diseases, such as head blight;
- Removal or ploughing in of crop debris, which may serve as a reservoir for inoculum;
- Effective weed control to remove a potential reservoir for inoculum;
- Irrigation to reduce water stress and the severity of disease, although overhead irrigation has been shown to increase the severity of disease.

6.5.2.3 Control of zearalenone post-harvest

Zearalenone can be formed in crops during storage , as well as in the field (JECFA, 2000). Formation during storage is assisted by elevated grain moisture levels due to incorrect harvest time or improper grain drying.

Storage of grain under modified atmospheres (20-60% carbon dioxide with 5 or 20% oxygen) resulted in complete inhibition of zearalenone production. However, lower carbon dioxide concentrations were required to achieve complete inhibition at lower oxygen levels (Paster *et al*. (1991).

Gamma-irradiation of wheat or flour at dose levels of 6 kGy completely eliminated fungal flora. Irradiation at 4 kGy resulted in a decrease in *Fusarium* toxin levels, while irradiation at 8kGy resulted in elimination of toxins (Aziz *et al*., 1997).

6.5.3 Influence of processing on fumonisin levels

6.5.3.1 Dry milling

In studies on naturally contaminated yellow corn, cleaning prior to milling only removed 3-10% of zearalenone. Highest zearalenone levels were found in the mill fractions associated with the outer grain layers (germ, degermer fines, bran meal and hulls) while the starchy milling fractions (grits, meal, flour) contained only 10-22% of the total zearalenone (Bennett *et al*., 1976).

When wheat containing 2.05 mg zearalenone/kg was experimentally milled, break and reduction flour contained decreased concentrations of zearalenone (0.7-1.1 mg/kg), while concentrations were higher in bran, middlings and shorts (2.6-4.8 mg/kg) (Lee *et al.*, 1987). L'vova *et al*. (1998) reported that milling of zearalenone-contaminated wheat resulted in 83% of the mycotoxin being found in the bran, while only 17% was found in the flour.

Feedmilling of barley results in approximately 85% of zearalenone being removed with the screenings and hull fractions. Only 3% of initial zearalenone passed into the barley groats (L'vova *et al*., 1998).

6.5.3.2 Wet milling

Lauren and Ringrose (1997) the wet milling fractions of maize for zearalenone contamination. The aqueous fractions (light steep liquid and corn steep liquor) contained detectable amounts of zearalenone. Zearalenone concentrations in the solid products of the wet milling process (germ, fibre, gluten) were 2-3 times those in the raw maize. Elevated levels of zearalenone were also found in animal feed products and maize oil.

6.5.3.3 Cooking

Breadmaking reduces zearalenone levels by 23-34% compared to the feed flour (L'vova *et al*., 1998). Instant noodle manufacture reduced zearalenone levels by 48-62% (Ryu *et al*., 2002), while biscuit production reduced levels by 16-27% (Ryu *et al*., 2002).

While no studies of the impact of maize nixtamalisation (alkaline cooking) on zearalenone levels were identified, Lauren and Smith (2001) demonstrated that heating of zearalenone-contaminated maize for up to 12 days at 110ºC, following sodium bicarbonate treatment, had no impact on zearalenone content.

Roasting of zearalenone contaminated wheat or barley produced reduction in zearalenone levels by 90% following heating at 220ºC for 25 minutes (Yumbe-Guevara *et al*., 2003).

Extrusion cooking of corn grits at temperatures in the range 120-160ºC resulted in reductions in zearalenone concentrations in the range 66-83%. The moisture content of the grits (18-26%) had no significant effect on zearalenone reduction (Ryu *et al*., 1999).

6.5.3.4 Fermentation

Fermentation of corn with *Saccharomyces uvarum* for 5 days at 32ºC resulted in little destruction of zearalenone (Bennett *et al*., 1981). Additional evidence for the ability of zearalenone to survive the fermentation process comes from its occurrence in native beers from southern Africa (JECFA, 2000).

Ethanol produced from fermentation and distillation of contaminated maize did not contained detectable zearalenone (Bennett *et al*., 1981).

6.6 Conclusions

6.6.1 Description of risks to New Zealand consumers

The link between zearalenone exposure and human health effects is currently speculative. Although zearalenone has been clearly demonstrated to have significant estrogenic activity, the significance of this activity at dietary concentrations in uncertain.

There is clear evidence of the presence of *Fusarium* fungi that are known to produce the mycotoxin zearalenone, occurring in both the North and South Islands of New Zealand. The work of Lauren and Veitch (1996) demonstrated the presence of zearalenone in New Zealand corn based foods. International data show that the prevalence and concentrations of zearalenone in food are highly variable. The results available suggest that the prevalence and concentrations reported in the New Zealand foods are moderately high compared with that reported for temperate countries (JECFA, 2000; SCOOP 2003; Vargas *et al* (2001); Park *et al*, (2002); Rasmussen *et al*,2003) .

Initial estimates of dietary exposure to zearalenone in New Zealand suggest that exposure to well below internationally agreed tolerable daily intake levels. However, it should be noted that exposure estimates in New Zealand are based solely on the presence of the toxin in maize-based foods. Wheat-based foods are consumed in much higher amounts in New Zealand and occurrence of zearalenone has been reported in New Zealand-grown wheat (Lauren *et al*., 1991).

6.6.2 Commentary on risk management options

New Zealand does not currently regulate the level of zearalenone in food, in contrast to a number of other countries. The concentrations found in New Zealand foods (Lauren and Veitch, 1996) were below any of these regulatory limits with the exception of a corn meal that would exceed the limit specified by Italy and Uruguay for cereal products and corn respectively.

New Zealand does not currently exercise direct risk management measures to control the entry of zearalenone into the human food chain. Control of zearalenone is likely to occur as a consequence of GAP and GMP practices, designed to achieve other quality and safety objectives.

6.6.3 Data gaps

The major data gap at present is the establishment of a definitive link between zearalenone exposure and adverse human health effects, although expert bodies such as JECFA and SCF feel that there is sufficient evidence to recommend that exposure be kept as low as possible and further work be undertaken to elucidate the toxicity to humans.

In New Zealand information on zearalenone contamination in wheat, wheat-based products and infant cereals is currently limited .

7 ERGOT ALKALOIDS

7.1 Hazard Identification

Ergot refers to fungal structures from *Claviceps* species replacing grain kernels with large discoloured sclerotia (see Figure 7). *Claviceps* spp. produce a number of alkaloids, however 'ergot alkaloids' refers specifically to those containing the clavine or ergoline ring system. Ergot alkaloids are mainly produced by *C. purpurea* and, to a lesser extent, *C. fusiformis* (CAST, 2003).

Figure 7: Rye heads showing ergot sclerotia

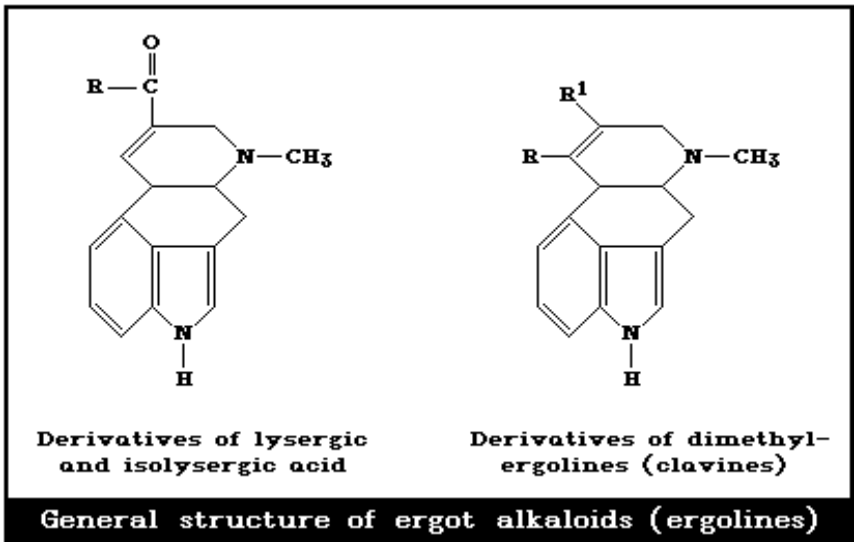
7.1.1 Structure and nomenclature

Ergot alkaloids are derivatives of lysergic acid and can be divided into three main groups:

- Group I: Derivatives of lysergic acid (ergotamine, alpha-ergocryptinine, ergocristine, ergosine, ergocornine, ergometrine);
- Group II: Derivatives of isolysergic acid (ergocristinine, ergometrinine, ergosinine, ergocorninine, alpha-ergocryptinine, ergotamine);
- Group III: Derivatives of dimethylergolin (clavines; agrocalvine, elymoclavine, chanoclavine, penniclavine, setoclavine)

The basic skeletal structures for the ergoline and clavinet ergot alkaloids are shown in Figure 8.

Figure 8: Structure of ergot alkaloids



Reproduced from WHO (1990)

7.1.2 Occurrence

Sclerotia are compact hyphal structures that develop in the colonies of many fungal genera (WHO, 1990). Sclerotia formed by *Claviceps* spp. are unique in terms of size (up to several centimetres in length), colouration, and content of highly biologically active alkaloids.

Host plants for *Claviceps* species mainly belong to the grass family. *C. purpurea* has a particularly wide host range. The cereals most commonly colonised by *C. purpurea* are rye, wheat, triticale, barley, oats and sorghum. The ergot of *C. purpurea* contains group I and II ergolines. *C. fusiformis* is a parasite of pearl millet in Africa and East Asia and its ergot contains mainly group III ergolines (WHO, 1990).

Ergot alkaloids have been isolated from *Aspergillus, Rhizopus* and *Penicillium* fungi and from some higher plants (WHO, 1990). However, it is not known whether these sources represent human exposure routes.

Incidence of *C. purpurea* appears to be related to high humidity and low maximum temperatures in midsummer (Webster, 1980). These conditions probably cause an extension of the period during which cereals are susceptible to infection.

In New Zealand, *C. purpurea* has been reported on barley, rye and wheat, as well as a large number of non-food crops (Pennycook, 1989). In the middle of the last century in New Zealand, ergot was reported to be rarely found on wheat, oats or two-row malting barley (Neill, 1941). Six-row barley was reported to be heavily ergotised in some areas, while rye was little grown in New Zealand. Two- and six-row barley refer to the number of rows of barley grains that make up the plant head (see http://dev.gramene.org/species/hordeum/barley_intro.html for more detail).

7.2 Hazard Characterisation: Adverse Health Effects

7.2.1 Conditions

Ergotism has been known to man for centuries and numerous epidemics occurred in Europe between the 9th and 18th centuries, where it was known as St. Anthony's fire (WHO, 1990). Two types of disease may occur:

- Gangrenous ergotism. The affected part (arm or leg) shrinks, becoming mummified and dry, with the gangrene gradually spreading. The gangrenous form of ergotism is probably caused by the vasoconstrictive properties of Group I and II alkaloids (ergotamine-like). Symptoms include edema, pruritis, necrotic extremities, prickling sensations and severe muscular pain (CAST, 2003).
- Convulsive ergotism. The whole body is attacked by general convulsions, returning at intervals of a few days. The convulsive form of ergotism appears to be caused by Group III alkaloids produced by *C. fusiformis*. Symptoms include tingling under the skin, pruritis, numbness of extremities, muscle cramps, convulsions and hallucinations (CAST, 2003).

7.2.2 Toxicity

7.2.2.1 Acute toxicity

No information was available on the acute toxicity of individual ergot alkaloids or of the ergot complex (WHO, 1990).

7.2.2.2 Chronic toxicity

Limited experimental studies have been carried out on animals and usually involve feeding of whole ergot, rather than individual ergolines (WHO, 1990). Study results reported include:

- Cattle. Feed containing more than 10 g ergot/kg (1%) commonly produced lameness in cattle, sometimes leading to gangrene. Cattle fed 1 mg ergotamine tartrate/kg body weight became ill in 1-2 days and four of six died within 10 days. Symptoms included anorexia, hyperventilation, cold extremities, salivation and tongue necrosis. Post-mortem examination found extensive intestinal inflammation (WHO, 1990).
- Sheep. Four lambs were fed 0.12 to 0.75 g ergot/kg body weight for two months. Lambs on higher doses became ill within 2-6 days, with symptoms including diarrhea,

edema of the hind legs and tail and lameness. Post-mortem examination found inflammation and necrosis of the forestomach and intestinal mucosa (WHO, 1990).

- Swine. A diet containing 40 g ergot/kg (4%) was well tolerated. Depression of growth rate was observed with diets containing 100 g ergot/kg (10%) (WHO, 1990). Diets containing 0, 1 or 10g ergot/kg (0.05, 0.6 or 4.66 mg total alkaloids /kg) fed *ad libitum* to 12 pigs produced no symptoms of ergot poisoning or carryover of alkaloids into meat. Reduced feed intake and reduced body weight gain were observed at the highest dose level (Mainka *et al*., 2005a).
- Primates. Male rhesus monkeys were dosed with either ergot from *C. fusiformis* or ergoline extract from the ergot, for up to one month. No effect was observed exception for animals receiving intraperitoneal doses of 5.4-11.1 mg ergoline/kg body weight. Within 10 minutes of dosing animals exhibited symptoms of drowsiness, hyperexcitation, redness of face, and loss of response to thermal and tactile stimuli in the hind limbs and tail (WHO, 1990).

Poultry appear to be relatively unaffected by ergot exposure. Mainka *et al*. (2005b) confirmed this observation in a study of the impact of ergot contaminated feed on the performance and health of piglets and chickens. The critical level of ergot alkaloid exposure for piglets was in the range 5.6 to 11.1 mg total alkaloid/kg diet, with feed intake and live weight gains significantly decreased. In chickens, inflammation of the proximal duodenum was observed at dose levels of 2.8 and 11.1 mg total alkaloid/kg diet, but live performance was unaffected.

7.2.3 Toxicological assessment

The EU Scientific Panel on Contaminants in the Food Chain have carried out an assessment of the risks of ergot in animal feed (SPCFC,2005). In addition to conclusions relevant to animal health and welfare, they concluded that levels of ergot alkaloids in animal tissues was unlikely to be a significant source of human exposure.

7.3 Exposure Assessment

7.3.1 Ergot in the New Zealand food supply

No information was identified on the incidence or concentrations of ergot or ergot alkaloids in New Zealand cereals.

7.3.2 Ergot in the Australian food supply

No information was identified on the incidence or concentrations of ergot or ergot alkaloids in Australian cereals. The lack of any such information was confirmed by an ANZFA toxicological review (http://www.foodstandards.gov.au/_srcfiles/P158_FAR.pdf).

Considerable information is available on sorghum ergot, caused by *C. africana* and *C. sorghi*, but it is uncertain whether this plant disease has any relevance for human health.

7.3.3 Overseas context

Little information on the incidence and levels of ergot or ergot alkaloids in foods is available. Information found is summarised in Table 30.

Table 30: Worldwide data on occurrence of ergot or ergot alkaloids in foods

Country	Year	Food	What measured	Incidence (percentage; mean of positives µg/kg)	Reference
Canada	1985-1991	Rye flour	Total alkaloids*	118/128 (92%; 239 µg/kg)	Scott *et al*. (1992)
Canada	1985-1991	Wheat flour	Total alkaloids*	68/93 (73%; 31 µg/kg)	Scott *et al*. (1992)
Canada	1985-1991	Bran/bran cereal	Total alkaloids*	29/35 (83%; 37 µg/kg)	Scott *et al*. (1992)
Canada	1985-1991	Triticale flour	Total alkaloids*	24/26 (92%; 89 µg/kg)	Scott *et al*. (1992)
Canada	1986-1991	Rye bread/ crackers/ crispbread	Total alkaloids*	52/114 (46%; 45 µg/kg)	Scott *et al*. (1992)
Canada	1997-1999	Infant cereal foods	Ergot alkaloids#	41/162 (25%; 27 µg/kg))	Lombaert *et al*. (2003)
Switzerland		Wheat flour Wheat flour (coarse) Wheat flour (more coarse) Rye flour 'Bioproducts'	Total ergolines	Mean = 4.2 µg/kg 30.7 µg/kg 103.4 µg/kg 139.7 µg/kg 10.2-22.7 µg/kg	Baumann *et al*. (1985)
Uruguay	1993-1995	Wheat	Total alkaloids	10/26 (38%)	Piñeiro *et al*., 1996)

* The study also provided information on concentrations of individual alkaloids. Those data are summarised in Table 31.
# Includes ergosine, ergotamine, ergocornine, egocryptine and ergocristine

Lorenz (1979) reported results from North America that showed 0.00-0.25% ergot on wheat, 0.04-0.18% ergot on barley, 0.00-0.01% ergot on oats and 0.06-0.92% ergot on triticale. No data were presented for rye.

7.3.3.1 Alkaloid content of ergot

Ergot sclerotia may contain up to 1% of total ergot alkaloids (WHO, 1990), although lower levels have been reported for sclerotia of cereals (0.09 to 0.21%, SPCFC, 2005).

Young (1981a) examined individual sclerotia from Canadian wheat and found total alkaloid contents in the range 0.013-0.307%, with an average of 0.163%. The average alkaloid content of sclerotia from rye was slightly higher at 0.249% (range 0.011-0.452%; Young, 1981b).

Bhat *et al*. (1976) reported figures for South-East Asia for rye (0.07%), wheat (0.092%) and total alkaloids.

Table 31 summarises available information on the alkaloid composition of ergot contamination in foods, although it should be noted that the alkaloid composition will vary from sclerotia to sclerotia, even within a single plant (Young, 1981a; 1981b).

Table 31: Alkaloid composition of ergot in foods

Country	Food	Percentage alkaloid (%)						Reference
		Ergonovine	Ergosine	Ergotamine	Ergocornine	Ergocryptine	Ergocristine	
Canada	Rye flour	7.1	13.0	26.4	9.2	10.5	33.9	Scott *et al.* (1992)
Canada	Wheat flour	9.3	10.6	24.0	7.4	10.3	38.5	Scott *et al.* (1992)
Canada	Bran/bran cereal	12.5	6.8	17.7	10.1	12.0	40.9	Scott *et al.* (1992)
Canada	Triticale	9.7	6.8	19.7	9.3	9.3	45.2	Scott *et al.* (1992)
Canada	Rye bread/ crackers/ crispbread	7.5	20.6	35.1	10.5	6.1	20.2	Scott *et al.* (1992)
Canada	Canadian Western Red Spring wheat (slightly ergot contaminated)	4.4	12.1	25.3	1.6	12.1	45.1	Fajardo *et al.* (1995)
Canada	Canadian Western Red Spring wheat (Heavily ergot contaminated)	6.0	10.4	19.2	11.6	13.2	40.0	Fajardo *et al.* (1995)
USA	Barley*	-	3.8	49.0	6.9	9.9	27.7	Porter *et al.* (1987)
USA	Wheat*	-	2.0	9.6	6.6	4.7	75.8	Porter *et al.* (1987)

* Total proportions of lesser alkaloids (ergonine, ergovaline, ergostine and ergoptine) were also determined for these samples at less than 4% for barley and less than 1.5% for wheat.

7.3.4 New Zealand estimates of dietary exposure

No estimates of dietary exposure to ergot or ergot alkaloids have been reported for the New Zealand population. Exposure of New Zealanders to ergot is likely to be largely due to its presence in wheat.

Rye is not a highly consumed food in New Zealand (2.4 g/person/day; ANZFA, 2001b). For the year ending September 2005 New Zealand imported approximately 459 tonnes of rye flour, principally from Australia. While information on rye grown in New Zealand could not be found, food balance sheets maintained by the Food and Agriculture Organization of the United Nations (FAO; http://faostat.fao.org/) does not report domestic production of rye in New Zealand.

7.3.5 Overseas estimates of dietary exposure

Few estimates of dietary exposure to ergot or ergot alkaloids have been found in the literature. Baumann *et al*. (1985) estimated dietary intake of total ergolines (ergot alkaloids) by the Swiss population to be 5.1 µg/person/day (0.07µg/kg body weight/day for a 70 kg adult).

ANZFA (now FSANZ) reported results from a study by the Denmark National Food Agency that estimated average population dietary exposure to ergot alkaloids at 5.7 µg/person/day (0.08 µg/kg body weight/day for a 70 kg adult; http://www.foodstandards.gov.au/_srcfiles/P158_FAR.pdf).

7.4 Risk Characterisation

7.4.1 Adverse health effects in New Zealand

No cases of human adverse health effects attributable to ergot exposure have been reported in New Zealand.

7.4.2 Adverse health effects overseas

While outbreaks of ergotism occurred on a regular basis during the middle ages, such outbreaks have been reasonably rare in recent times. Two documented outbreaks of ergotism occurred during the second half of the twentieth century and are summarised in the following sections.

7.4.2.1 Ethiopia

An outbreak of ergotism occurred in the Wollo region of Ethiopia in 1978 (Demeke *et al*., 1979; King, 1979). Locally grown barley became heavily contaminated with wild oats (70%). Ergometrine was detected in sclerotia from the crop. A total of 93 cases of ergotism were reported in addition to 47 deaths reported to be due to ergotism (case fatality rate = 47/140 = 34%). Examination of 44 cases revealed dry gangrene of one or more limbs (7.5%), feeble or absent peripheral pulses (36.5%), swelling of limbs (11.2%), desquamation of skin (12.8%) and loss of one or more limbs (21.5%).

No estimate of the level of exposure to ergot was made.

7.4.2.2 India

Several outbreaks of illness associated with consumption of ergot-contaminated bajra (pearl millet) in the state of Rajasthan have been reported since 1958, with the most recent occurring in 1975 (Krishnamachari and Bhat, 1976). In total, 78 persons from 21 villages reported symptoms of nausea, vomiting and giddiness. Symptoms developed within 1-2 hours of consuming the contaminated meal and lasted for 24-48 hours. Contamination was due to *C. fusiformis* and resulted in ergot levels in grain of 15-174 g/kg, equating to ergoline levels of 15-199 mg/kg. Although there were insufficient data to determine a no effect level, the authors concluded that an exposure of 28 µg ergoline/kg body weight would be non-toxic.

7.4.2.3 Risk assessments and other activity overseas

ANZFA/FSANZ

FSANZ (then ANZFA) carried out a risk assessment of ergot, as part of their larger review of standards for non-metal contaminants:
(http://www.foodstandards.gov.au/_srcfiles/P158_FAR.pdf)

The risk assessment made a conservative exposure assessment, based on a 95th percentile consumption level for wheat and a proposed regulatory limit for ergot of 0.05% in cereal grains, yielding an estimate of 3 µg total alkaloids/kg body weight/day. It was concluded that this level of exposure was well below the no effect level reported by Krishnamachari and Bhat (1976; 28 µg/kg body weight).

It is worth noting that the no effect level was derived for clavine-type alkaloids, while alkaloids likely to occur in Australian and New Zealand foods are much more likely to be of the ergometrine type. Also, as noted in section 7.4.2.2, the level of Krishnamachari and Bhat (1976) of 28 µg/kg body weight is not a true no effect level.

SPCFC (EU Scientific Panel on Contaminants in the Food Chain)

While the focus of this risk assessment was animal health, several points pertinent to human risk assessment were made:

- The alkaloid content of sclerotia is sufficiently variable that no relationship between the amount of ergot and the total alkaloid concentration can be established.
- The available data do not allow identifying marker ergot alkaloids that could be monitored in all feed (food) materials as indicators for ergot contamination.
- The limited available data do not allow an estimate of carry-over rates to animal products (edible tissues, milk and eggs), however, there is no evidence that ergot alkaloids accumulate in edible tissues (muscle meats, offals).
- Levels of alkaloids measured in animal tissues indicate that these are unlikely to be an important source of human exposure.

7.5 Risk Management Information

7.5.1 Relevant food controls: New Zealand

7.5.1.1 Establishment of regulatory limits

Standard 1.4.1 of the Joint Australia New Zealand Food Standards Code defines a maximum limit (ML) for ergot in cereal grains of 500 mg/kg (0.05%).

7.5.2 Relevant food controls: overseas

7.5.2.1 Establishment of regulatory limits

In 2003, only three countries (Canada, Australia and New Zealand) reported having regulatory limits for ergot in food (van Egmond and Jonkers, 2003). The joint New Zealand and Australian regulatory limit is summarised in section 7.5.1.1. In Canada the ergot content of grains is regulated by the Canadian Grain Commission, with limits for various grades of wheat in the range 0.01-0.10%, rye (0.05-0.33%) and barley (0.05% to no limit) (http://www.grainscanada.gc.ca/views/ergot/ergot99-e.htm).

7.5.2.2 Management of ergot formation in crops

Open-pollinated crops , such as rye, are much more susceptible to infection by *Claviceps* spp. than close-pollinated crops, such as wheat (CAST, 2003). Increased use of hybrid (male sterile) wheat may increase the risk of infection in this crop.

Grass weeds in proximity to cereal crops may act as reservoirs for *Claviceps* infection. Management practices for the control of ergot in grain crops, summarised by the UK Home-Grown Cereals Authority (HGCA) include:

- Crop rotation between cereal and non-cereal crops.
- Use of clean (non-ergot contaminated) seed.
- Avoid growing susceptible crops or varieties in ergot problem areas.
- Control grass weed that may act as hosts for *Claviceps.*
- Harvest any heavily contaminated areas separately and decontaminate or dispose of affected grain.

From: http://www.hgca.com/research/topicsheets/topicsheet56.html

7.5.2.3 Control of ergot post-harvest

Ergot sclerotia are considerably more fragile than the grains of the infected plants. The sclerotia tend to break up during harvest and about half of the ergot will be lost during harvest and threshing (Lorenz, 1979). Intact sclerotia are generally larger than cereal grains and will be removed by the grain cleaning procedures at mills, including sieves and separators. Lorenz (1979) reported that up to 82% of ergot can be removed by grain cleaning.

The lower density of sclerotia can be used to separate them from grain by flotation in solutions such as 20% sodium chloride or 32% potassium chloride (Lorenz, 1979) or by use of an air-screen cleaner (Adam *et al.*, 2004).

7.5.3 Influence of processing on fumonisin levels

7.5.3.1 Dry milling

Shuey *et al*. (1973) milled wheat containing 0.3-15.0% added ergot. For low ergot contamination levels (0.3% of grain weight) approximately 93% of the ergot was found in the bran and shorts (mainly made up of fine ground bran and germ), with only 7% in the flour. For high contamination wheat (15.0% ergot) 87% was in the bran and shorts, with the remaining 13% in the flour. Fajardo *et al*. (1995) carried out milling trials on Canadian wheat containing 0.004% or 0.03% naturally-occurring ergot. Analysis of mill streams for individual ergot alkaloids gave results qualitatively similar to those of Shuey *et al*. (1973), with highest alkaloid concentrations in non-flour fractions.

Wheat ergot levels of 0.3% were not visibly noticeable in the resultant flour. However, flour made from wheat with 1.5 or 3.0% ergot had the appearance of having been mixed with ground pepper (Lorenz, 1979).

7.5.3.2 Breadbaking and cooking

Consistent results showing a reduction in naturally-occurring ergot alkaloid concentrations in food products produced by baking or other cooking processes have been achieved.

Scott and Lawrence (1982) reported reductions of 59-100% in levels of individual ergot alkaloids during baking of whole wheat bread and reductions of 50-85% in baking of rye bread. Fajardo *et al*. (1995) reported alkaloid reduction in the crust of remix bread of 25-55%. Higher concentrations of ergot alkaloids were detected in the crumb, which was ascribed to the lower baking temperatures encountered in the crumb compared to the crust.

Baking of pancakes made from triticale flour, naturally contaminated with ergot, resulted in decreases of levels of individual alkaloids in the range 25-74% (Scott and Lawrence, 1982).

Production of noodles from ergot contaminated flour resulted in a decrease in alkaloid levels of 11-46%. Cooking resulted in a further slight decrease in ergot alkaloid levels (Fajardo *et al*., 1995). Similar results were obtained with spaghetti manufacture and cooking.

7.6 Conclusions

7.6.1 Description of risks to New Zealand consumers

Ergot is known to cause serious human disease. However, outbreaks of ergotism have become increasingly rare in modern times. There have been no documented cases of human ergotism in New Zealand.

Infection of cereals by *Claviceps purpurea* has been reported in New Zealand, although a report in the 1940s stated that its occurrence was rare in wheat, oats and two-row barley. Rye is the cereal most often affected by ergot. There appears to be very little rye grown in New Zealand. Rye flour is imported, predominantly from Australia and, to a lesser extent, Germany. However, there is no recent information on the occurrence of ergot in New Zealand grown or imported cereals. The majority of cereals imported into New Zealand come from Australia, but no information on ergot in Australian crops was found.

Harvesting and cleaning of grain prior to milling will remove the majority of the ergot present in the crop and further processing (e.g. breadbaking) will tend to decrease ergot levels further.

Exposure of New Zealanders to ergot and the alkaloids contained within the ergot sclerotia is likely to be very low. Good Agricultural Practice and modern grain handling practices are likely to provide a high level of risk management.

7.6.2 Commentary on risk management options

Under the Food Standards Code the maximum limit for ergot in cereal grains is set at 500 mg/kg (0.05%). While this standard would provide a high level of consumer protection, there is no evidence to suggest that the Standard is being actively enforced.

7.6.3 Data gaps

Data on the occurrence of ergot and ergot alkaloids in New Zealand and Australian cereals is not available.

8 PATULIN

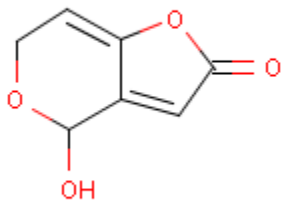
8.1 Hazard Identification

Patulin, 4-hydroxy-4H-furo[3,2c]pyran-2(6H)-one is a bicyclic lactone metabolite of several species of *Penicillium, Byssochlamys* and *Aspergillus* moulds. Of the fungi producing patulin *Penicillium expansum* is probably the most commonly encountered species and is often isolated from decaying apples.

8.1.1 Structure and nomenclature

The chemical structure of patulin is shown in Figure 98.

Figure 9: Structure of patulin



8.1.2 Occurrence

Patulin in commercial apple products is principally due to soft rot caused by *Penicillium expansum* (Pitt and Hocking, 1997). The toxin is produced over the temperature range 0-25ºC, with optimum production at 25ºC. Production of patulin by *P. expansum* requires a minimum water activity of 0.95 and an acidic environment (pH 3.2-3.8). Patulin is also relatively heat stable.

Production of patulin by *P. griseofulvum, P. roqueforti,* and *P. funiculosum* has been reported (Pitt and Hocking, 1997), as well as *P. claviforme, P. urticae* and *P.patulum* (Drusch and Ragab, 2003).

Isolates of *Byssochlamys nivea* and *B. fulva* have been shown to produce patulin under experimental conditions, but there are no reports of production of patulin in commercial fruit juices due to *Byssochlamys* infection (Pitt and Hocking, 1997).

Patulin has been shown to be produced by isolates of *Aspergillus clavatus* (Pitt and Hocking, 1997) and *A. giganteus* (Drusch and Ragab, 2003).

8.2 Hazard Characterisation: Adverse Health Effects

No reports were located of adverse health effects in humans due to patulin exposure. Patulin was trialled as an antibiotic for use against the common cold in the 1940s. The authors of the study reported that no ill effects were observed, but the report is unclear as to the clinical tests applied (Hopkins, 1943).

8.2.1 Toxicity

8.2.1.1 Acute toxicity

The acute oral toxicity of patulin, as assessed by LD_{50}, has been determined in the mouse (17-48 mg/kg body weight), the rat (28-118 mg/kg body weight) and the hamster (32 mg/kg body weight) (JECFA, 1995b). Toxic signs include agitation, convulsions, dyspnea, pulmonary congestion and edema, and ulceration, hyperaemia and distension of the gastrointestinal tract.

8.2.1.2 Chronic toxicity

JECFA reviewed toxicological information on patulin in 1995 (JECFA, 1995b). In short-term animal toxicology studies, patulin caused gastrointestinal hyperaemia (increased blood supply to part of the body, without haemorrhage), distension, haemorrhage and ulceration.

A 13 week toxicity study in rats showed a compound-related impairment of kidney function and villous hyperaemia of the duodenum, with a NOEL of 0.8 mg/kg body weight/day. In reproductive toxicity studies no reproductive or teratogenic effects were observed, but patulin was embryotoxic at high doses. Doses at which embryotoxicity was observed were high enough to cause overt maternal toxicity.

Although experimental data are variable, JECFA assessed patulin to be genotoxic, but not carcinogenic.

Patulin exhibited immunosuppressive properties in both *in vitro* and *in vivo* studies, but the dose levels required for these effects to be observed were higher than the NOEL observed in short and long-term studies (JECFA, 1995b).

In a long-term carcinogenicity and toxicity study in rats a NOEL for the most sensitive endpoint (decrease in body weight gain in males) of 0.1 mg/kg body weight was observed when animals were dosed three times per week. At the highest dose level of 1.5 mg/kg body weight there was a significantly increased mortality in both male and female treated rats (Becci *et al*., 1981).

8.2.2 Toxicological assessment

JECFA have evaluated patulin (JECFA, 1990; 1995b) and concluded that the most sensitive toxicological endpoint was body weight gain in a long-term rat study with a NOEL of 0.1 mg/kg body weight three times per week (equates to 42 µg/kg body weight/day). A safety factor of 100 was applied to derive a Provisional Maximum Tolerable Daily Intake of 0.4 µg/kg body weight/day.

The EU Scientific Committee on Food issued a minute statement on patulin agreeing with the JECFA and IARC assessments and endorsing the PMTDI derived by JECFA (http://europa.eu.int/comm/food/food/chemicalsafety/contaminants/out55_en.pdf).

The US Food and Drug Administration independently reviewed the available toxicological data, but concurred with the JECFA decision to establish a PTDI of 0.43 µg/kg body weight/day (http://www.cfsan.fda.gov/~dms/patubckg.html).

IARC have reviewed information on the carcinogenicity of patulin and concluded that there was inadequate evidence for the carcinogenicity of patulin in experimental animals and that no evaluation could be made of the carcinogenicity of patulin to humans (Group 3; IARC, 1986).

8.3 Exposure Assessment

8.3.1 Patulin in New Zealand apple-based foods

Two surveys have been carried out to determine the prevalence and concentrations of patulin in apple products available for retail purchase in New Zealand (Wilson, 1981; Stanton, 1998). Results are summarised in Table 32.

Table 32: Patulin in New Zealand apple products

Food	Number of samples	Number positive (%)	Range of positive results (µg/kg)	Reference
Apple juice	20	3 (15%)	106-216	Wilson, 1981
Apple and apple-based juice	35	6 (17%)	10-58	Stanton, 1998
Apple and apple-based juice concentrates	7	7 (100%)	12-95	Stanton, 1998
Apple drinks and alcoholic beverages	6	0 (0%)		Stanton, 1998
Apple-based foods	37	0 (0%)		Stanton, 1998

New Zealand production of apple juice is dominated by one manufacturer (Enzafoods New Zealand Limited; http://www.enzafoods.co.nz/). However, apple juice available to the consumer will include product from a number of other smaller manufacturers. New Zealand also imports significant quantities of apple juice (approximately 8,000 tonnes in the year to the end of September 2005), with over 80% of imports from China and approximately 10% from each of Australia and South Africa. Routine regulatory testing of imported apple juice for patulin is not carried out.

8.3.2 Patulin in Australian apple-based foods

Patulin is a common contaminant of apple juice and apple-based products in Australia.

Watkins *et al*. (1990) examined 113 samples of apple juice, purchased in Victoria and representing 29 different brands, for the presence of patulin. Patulin was detected in 74 samples (65%), representing 23 different brands, at concentrations in the range 6-629 µg/l.

Burda (1992) examined apple, pear and mixed fruit products marketed in New South Wales. Patulin was detected in 148 of 258 juice and juice concentrate samples (57%), at concentrations in the range 5-1130 µg/l, and 18 of 70 non-juice apple-based samples (26%; sauces, purees, pulps and jellies), with concentrations in the range 5-32 µg/kg.

The 1996 Australian Market basket survey examined nine infant strained apple samples for the presence of patulin (Hardy, 1998). All samples were negative for the presence of patulin.

8.3.3 Overseas context

Table 33 summarises results of a number of international surveys of patulin in apple-based products.

Table 33: Worldwide data on occurrence of patulin in food

Country	Product	Samples positive/Total samples (%)	Range of positive results (µg/l or µg/kg)	Reference
Belgium	Apple juices Cider	Imported 12/14 (86) Domestic 23/29 (79) Imported 1/2 (50) Domestic 2/5 (40)	2.5-10.6 2.9-38.8 6.1 2.8	Tangni *et al.*, 2003
Brazil	Apple juice Other juices Fruit	1/30 (3) 0/57 (0) 0/38 (0)	17	De Sylos and Rodriguez-Amaya, 1999
Germany	Apple juice Other fruit juices Apple pulp Other fruit pulp and syrup	13/14 (93) 5/5 (100) 0/1 (0) 1/2 (50)	0.7-26 0.1-5.2 0.8	Rychlik and Schieberle, 1999
Europe	Apple juice Apple juice concentrate Cider Pear juice Grape juice Other juices Apple puree Other purees Baby food	2659/4633 (57) 1128/1175 (96) 126/339 (37) 17/100 (17) 128/324 (40) 5/174 (3) 7/97 (7) 0/50 (0) 43/312 (14)	0.03-1150 5-1227 2-1604 0.03-91 3-750 2-32.4 0.2-86 0.2-68	SCOOP, 2002
Italy	Apple products	11/44 (25)	1.4-74.2	Ritieni, 2003

Country	Product	Samples positive/Total samples (%)	Range of positive results (µg/l or µg/kg)	Reference
Italy	Apple juice Pear juice Other juices Fruit purees Apple Apple vinegar	Conventional 16/33 (48) Organic 12/24 (50) Conventional 1/7 (14) Organic 4/8 (50) Conventional 8/45 (18) Organic 6/12 (50) Conventional 1/15 (7) Organic 9/25 (36) Conventional 7/13 (54) Organic 3/9 (33) Conventional 0/2 (0) Organic 2/6 (33)	0.5-53.4 0.5-69.3 1.1 0.5-61 0.5-1.7 0.5-13.5 0.7 0.5-13.0 0.5-81.7 0.5-50.8 0.5-4.2	Piemontese *et al*., 2005
Japan	Apple juice	15/76 (20)	1-45	Ito *et al*., 2004
Japan	Apple and mixed juices	Imported 6/45 (13) Domestic 3/143 (2)	6-10 6-15	Watanabe and Shimizu, 2005
South Africa	Apple and mixed juices Whole fruit products Infant fruit juices Infant fruit purees	8/31 (26) 2/12 (17) 6/10 (60) 0/7 (0)	5-45 10 5-20	Leggott and Shephard, 2001
Spain	Apple juice Apple food for children	82/100 (82) 0/12 (0)	0.5-170	Prieta *et al*., 1994
Sweden	Blueberry soup Peach/pear juice Apple juice	0/42 (0) 0/19 (0) 5/39 (13)	 NR	Thuvander *et al*., 2001
Turkey	Apple juice	215/215 (100)	7-375	Gokmen and Acar, 1998
Turkey	Apple juice	27/45 (60)	19.1-732.8	Yurdun *et al*., 2001
UK	Apple juice	17/62 (27)	10-94	MAFF, 1993
UK	Baby juices/drinks Jam and jelly spreads Chutneys Apple purees and sauces Pie fillings Dried fruit Other dried fruit products Baby apple desserts Baby apple purees Baby cereal/savoury Baby foods, dried	1/11 (9) 0/14 (0) 0/9 (0) 0/13 (0) 0/10 (0) 0/8 (0) 0/5 (0) 0/9 (0) 0.3 (0) 0/4 (0) 0/10 (0)	10	MAFF, 1994c
UK	Apple juice, cloudy Apple juice, clear	38/113 (34) 27/78 (35)	10-497 NR	MAFF, 1994d
UK	Apple juice	64/185 (35)	10-490	MAFF, 1995b
UK	Fruit juices Tomato products	0/128 (0) 0/26 (0)		MAFF, 1995c
UK	Apple juice	62/173 (36)	10-184	MAFF, 1996c

Country	Product	Samples positive/Total samples (%)	Range of positive results (µg/l or µg/kg)	Reference
UK	Apple juice, from concentrate	38/101 (38)	5-30	MAFF, 1999c
	Apple juice, directly produced	110/199 (55)	5-171	

NR = not reported

All overseas studies confirm that patulin is a frequent contaminant of apple juice and apple products. Some European studies have reported detection of patulin in other fruit juices (e.g. pear, grape). Occurrence of patulin in New Zealand apple products is within the range of overseas observations.

8.3.4 New Zealand estimates of dietary exposure

Stanton (1998) estimated dietary exposure to patulin for five age-gender groups using median patulin concentration data from New Zealand and food consumption data from the Australian Market Basket Survey. It is interesting to not the relatively small differences between average consumption levels for apple juice and extreme (95th percentile) consumption levels. Results are summarised in Table 34.

Table 34: Estimated dietary exposure to patulin in New Zealand

Age group	Weight (kg)	Consumption of Apple Juices (g/person/day)		Estimated patulin intakes (µg/kg bw/day)	
		Average	Extreme*	Average	Extreme*
Infant, 9 months	9.2	32.0	37.9	0.017	0.020
Toddler, 2 years	12.4	123.9	144.7	0.050	0.059
Boy/girl, 12 years	40	74.4	112.5	0.009	0.014
Adult male	77	59.4	96.1	0.004	0.006
Adult female	59	47.7	79.2	0.004	0.007

PMTDI = 0.4 µg/kg bw/day (400 ng/kg bw/day)
* 95th percentile

Estimated patulin dietary exposure in New Zealand is well below the PMTDI of 0.4 µg/kg body weight/day.

8.3.5 Overseas estimates of dietary exposure

Table 35 summarises a number of estimates of dietary exposure to patulin that have been derived overseas.

Table 35: Overseas estimates of dietary exposure to patulin

Country	Foods included	Population group*	Mean estimated dietary exposure (µg/kg bw/day)	Reference
Austria	Apple juice, grape juice	Child, 3-19 years Adult, 25+ years Elderly, 74+ years	Mean = 0.015-0.023 P95 = 0.043- 0.083 Mean = 0.002-0.007 P95 = 0.016-0.036 Mean = 0.003-0.012 P95 = 0.017-0.042	SCOOP, 2002
Belgium	Apple juice, grape juice	Teenagers, 14-18 years	Mean = 0.0007-0.001 P95 = 0.004-0.009	SCOOP, 2002
Belgium	Apple juice, cider	Child, 10 kg bw Adult, 60 kg bw	0.03 0.18	Tangni *et al.*, 2003
France	Apple juice, apple puree, cider	All children All adults	Mean = 0.005 P95 = 0.023 Mean = 0.001 P95 = 0.006	SCOOP, 2002
France	Alcoholic beverages, soft drinks, compote and stewed fruit, fruits, cakes	Child, 3-14 years Adult, 15+ years	Mean = 0.03 P95 = 0.11 Mean = 0.018 P95 = 0.057	Leblanc *et al.*, 2005
Germany	Apple, pear and grape juices, apple puree and compote, canned tomato	Child, 1-6 years Child, 6-14 years Adult, 14+ years	Mean = 0.025-0.051 P95 = 0.026-0.176 Mean = 0.010 P95 = 0.029 Mean = 0.002 P95 = 0.006	SCOOP, 2002
Italy	Fruit juice (apple, pear), baby food, preserved fruit, apple, pear, peach	All population	Mean = 0.093 P95 = 0.39	SCOOP, 2002
Italy	Apple, pear and other juices, fruit purees, apples, apple vinegar	Child, 1-10 years Adolescent, 10-18 years Adults, 18-64 years Elderly, 65+ years	Conventional 0.003 Organic 0.014 Conventional 0.0009 Organic 0.004 Conventional 0.0003 Organic 0.001 Conventional 0.0002 Organic 0.0009	Piemontese *et al.*, 2005
Norway	Apple juice, apple nectar, apple cider	Average person	0.001	SCOOP, 2002
Portugal	Apple juice, pear juice	Total population	0.294	SCOOP, 2002
Spain	Fruit juices	Total population	0.0001-0.0003	SCOOP, 2002
Sweden	Fruit soups, juices	Child, 7-14 years	Mean = 0.005-0.008 P95 = 0.013-0.024	Thuvander *et al.*, 2001
Sweden	Purees and soups, apple juice, mixed juices	Child, 7-14 years Adult, 15-74 years Adult, 19-74 years	Mean = 0.005 P95 = 0.012 Mean = 0.002 P95 = 0.006 Mean = 0.001 P95 = 0.001	SCOOP, 2002

Country	Foods included	Population group*	Mean estimated dietary exposure (µg/kg bw/day)	Reference
United Kingdom#	Apple juice	Toddler, 1.5-4.5 years Child, 4-18 years Adult, 16-64 years	Mean = 0.12 P95 = 0.36 Mean = 0.04 P95 = 0.13 Mean = 0.011 P95 = 0.032	SCOOP, 2002

P95 = 95th percentile

* Some studies presented estimates for 'total population' and 'consumers'. Estimates presented here are for 'total population' unless specifically identified as otherwise

Exposure estimates were only provided for consumers

The 1994 Australian Market Basket Survey (AMBS) determined patulin in apple juice and in fruit leathers (Marro, 1996). Patulin was not detected in the fruit leathers, but the mean estimated dietary exposure due to apple juice consumption was in the range 0.009 (adult males/females) to 0.117 (toddlers) µg/kg body weight/day. The 95th percentile estimated dietary exposures were in the range 0.015 (adult male) to 0.137 (toddlers) µg/kg body weight/day.

The 1996 AMBS analysed strained infant apple for the presence of patulin (Hardy, 1998). Patulin was not detected in any sample.

New Zealand estimates of dietary exposure (Stanton, 1998) are generally similar to or lower than overseas estimates.

8.4 Risk Characterisation

Human intoxication due to patulin ingestion has not been reported and patulin exposure has not been implicated in any human disease states. Patulin was trialled as an antibiotic for use against the common cold in the 1940s. The authors of the study reported that no ill effects were observed, but the report is unclear as to the clinical tests applied (Hopkins, 1943).

8.5 Risk Management Information

8.5.1 Relevant food controls: New Zealand

8.5.1.1 Establishment of regulatory limits

Patulin is not currently regulated in New Zealand.

8.5.1.2 Industry quality assurance procedures

The majority of New Zealand's domestically produced apple juice is processed by ENZAfoods New Zealand Ltd (http://www.enzafoods.co.nz/). ENZAfoods process have been covered by ISO9001 accreditation and HACCP plans since 1993, including daily monitoring of product for patulin.

8.5.2 Relevant food controls: overseas

8.5.2.1 Establishment of regulatory limits

Table 36 summarises the reported regulatory positions on patulin (van Egmond and Jonker, 2003).

Table 36: Regulatory limits for patulin in various countries (food regulations only)

Country	Commodity description	Regulatory limit (µg/kg)
Armenia	Tomato paste, apple	5
Belarus	Mushrooms, fruits, vegetables	50
Bulgaria	Fruit juices and nectars, fruit concentrates	50
China	Semi-finished products (juice or paste) Fruit juice or jam, fruit wine, canned products, hawthorn strip (cake)	100 50
Codex Alimentarius	Apple juice and apple ingredients in other beverages	50
Cuba	Fruits	50
Czech Republic*	Child nourishment Baby nourishment Foodstuff type A Foodstuff type B	30 20 50 100
Estonia	Fresh or frozen fruits and vegetables, including berries and mushrooms, tinned apples, tomatoes and seabuck thorns, apple and seabuck thorn jam, juices, drinks, concentrates and nectars; salted, pickled, leavened or otherwise processed fruits, vegetables and mushrooms	50
European Union	Fruit juices and nectars, in particular, apple juice, and fruit juice ingredients in other beverages Concentrated fruit juice after reconstitution Spirit drinks, cider and other fermented drinks derived from apples or containing apple juice Solid apple products, including apple compote, apple puree intended for direct consumption Apple juice and solid apple products for infants and young children Other baby food	50 50 50 25 10 10
Hungary	Products of fruits and vegetables	50
Iran	Fruit juices, nectars and fruit drinks	50
Israel	Apple juice	50
Korea, Republic of	Apple juice, apple juice concentrate	50
Latvia	Apple, tomato juice	50
Lithuania	Juice	25
Moldova	Juices, canned vegetables, fruits	50
Morocco	Apple juice	50
Poland	Apple juice, apple products	30

	Commodity description	Regulatory limit (µg/kg)
Romania	Fruit juice	50
Russian Federation	Bottled, canned or potted vegetables, fruit, berries; juices, beverages or concentrate of vegetables, berries (canned); jams, confitures, syrups, fruit and berries mashed with sugar, fruit or berry concentrates with sugar	50
Serbia and Montenegro	Apple juice	50
Singapore	Apple and apple juice	50
Slovakia	Milk, meat, poultry, flour and its products, rice, vegetables, potatoes Infant formulae Food for children Other foodstuffs	50 20 30 100
South Africa	All foodstuffs	50
Switzerland	Fruit juices	50
Taiwan	Apple juice	NS
Turkey	Fruit juice	50
Ukraine	Vegetable and fruit-berry preserves and mixes for babyfood, fish preserves for babyfood Vegetables, including potatoes, fruit and grapes, berries; vegetable, fruit, berry preserves in cans and jars	20 50
USA	Apple juice, apple juice concentrate, and apple juice component of a food that contains apple juice as an ingredient	50
Uruguay	Fruit juice	50

From van Egmond and Jonker (2003)

* Type A and B foodstuffs not specified

The most commonly adopted regulatory limit for patulin in apple juice is 50 µg/kg. This is also the maximum level proposed by Codex (Standard 235-2003; http://www.codexalimentarius.net/download/standards/10095/CXS_235e.pdf).

8.5.2.2 Codex Code of Practice

Codex have formulated a Code of Practice (CoP) for the prevention and reduction of patulin in apple juice and apple juice ingredients (CAC/RCP 50-2003; http://www.codexalimentarius.net/download/standards/405/CXC_050e.pdf). The CoP makes recommendation on practice based on Good Agricultural Practice (GAP) and Good Manufacturing Practice (GMP). Recommendations based on GAP cover the areas of preharvest, harvesting and transportation of fruit, post-harvest handling and storage practices of fruit for the fresh fruit market, and post-storage grading of fruit for the fresh market or juice manufacture. Recommendations based on GMP cover the areas of transportation, checking and pressing of fruit, packaging and final processing of juice, quality assessment of juice.

8.5.3 Influence of processing on patulin levels

Moake *et al*. (2005) identified three areas of the juice production process where there was potential to decrease the level of patulin contamination:

- The quality of the fruit and processing prior to pressing, including storage;
- Juice clarification; and
- Pasteurisation and further processing.

Several studies have made specific estimates of patulin reduction during food processing. Normally fungal growth and patulin production is associated with damaged fruit and reductions in patulin contamination can be achieved through exclusion of damaged fruit from further processing or removal of damaged portions of the fruit. Lovett *et al*. (1975) showed that removal of obviously rotten portions of apples resulted in removal of 93-99% of patulin in the resulting apple juice. Beretta *et al*. (2000) compared the patulin content of rotten and apparently sound areas of individual apples. The concentration of patulin in the rotten areas was 5-3000 times higher than in the apparently sound portion of the apple. This difference increased if the peel was excluded from the sound material.

Jackson *et al.* (2003) detected patulin in cider pressed from fresh ground-harvested apples (range 40.2 – 374 μg/l), but not in cider pressed from fresh tree-picked apples. Tree-picked apples were stored for 4-6 weeks at 0-2ºC, subsamples were either culled (damaged and rotten fruit removed) or not culled. Patulin was not detected in cider pressed from culled, stored apples, but was detected in unculled, stored apples at levels in the range 1.0-64.0 μg/l (Jackson *et al*., 2003). Washing of ground-harvested apples, with either potable water or chlorine solutions (100 or 200 ppm) resulted in reductions in the patulin content of the resulting ciders of between 10 and 100%. In some experiments chlorine washing was more effective, but in other experiments chlorine washes were no more effective than a potable water wash (Jackson *et al*., 2003). Sydenham *et al*. (1997) demonstrated that the patulin level of fruit stored in uncontrolled conditions increased over the course of 33 days. Washing the fruit in water decreased the contamination level, white sorting and removal of rotten or damaged fruit decreased the contamination level further (by approximately 40% after 7 days and by approximately 80% at day 33).

Moodley *et al* (2002) examined the impact of different packaging materials (polyethylene or polypropylene) and modified atmospheres on the fungal growth and patulin production. Polypropylene did not inhibit fungal growth of patulin production. Polyethylene packaging significantly inhibited fungal growth and patulin production. This effect was further enhanced by increasing carbon dioxide to nitrogen ratios.

Bissesseur *et al*. (2001) examined the impact of various clarification methods (filtration, centrifugation, fining with bentonite, enzymic treatment with pectinase) on the patulin level of juice produced from artificially contaminated apple pulp. Clarification techniques, in combination with pressing, resulted in reduction of toxin levels of between 70 and 90%, with centrifugation being most effective and filtration being least effective. However, pressing alone was responsible for a 50% reduction in patulin levels. Examination of combinations of clarification methods showed that pressing, followed by centrifugation and fining was most effective in reducing the patulin level of the final juice.

Activated carbon was examined for its ability to absorb patulin from apple juice (Leggott *et al*., 2001). Activated carbon was able to remove up to 80% of the patulin present. Removal was lee in a high Brix apple juice (20º) than a low Brix apple juice (12º). Temperature had relatively little effect on patulin removal.

Moake *et al*. (2005) have reviewed studies that considered the impact of pasteurisation on the level of patulin contamination. While patulin is unstable at high pH, it is relatively stable to thermal degradation at the acidic pH usual in fruit juices.

Production of alcoholic cider from patulin-contaminated apple juice has been shown to result in degradation of patulin to non-detectable levels (Moss and Long, 2002). Three commercial strains of *Saccharomyces cerevisiae* were shown to degrade patulin during active fermentation, but not when growing aerobically.

8.6 Conclusions

8.6.1 Description of risks to New Zealand consumers

Patulin has not been linked to actual cases of adverse health effects in human. It has been administered to humans as a potential antibiotic for use against the common cold.

Stanton (1998) detected patulin in New Zealand apple juices at frequencies and concentrations consistent with those found overseas. Estimates of dietary exposure in New Zealand were similar to or less than estimates made in other developed countries.

The major apple juice manufacture in New Zealand (ENZAfoods) have quality assurance systems in place to control patulin contamination. However, a significant amount of apple juice available in New Zealand will be from small manufacturers or imported, principally from China. Little is known about patulin control systems in apple juice from these sources.

While patulin in apple juice may indicate poor manufacturing practice (e.g. use of ground harvested apples for juice manufacture), there is little evidence to indicate that it constitutes a human health risk.

8.6.2 Commentary on risk management options

Patulin contamination of apple juice is largely controllable by good manufacturing practice (GMP) and there is good evidence that GMP is employed by the major New Zealand manufacturer. However, there is currently no risk management applied to the large amount of imported apple juice. Application of a regulatory limit is the most obvious management measure for this product.

8.6.3 Data gaps

Internationally, there is a need for further information on associations or lack of associations between patulin exposure and human disease. Information on patulin in New Zealand consumer products is now dated and makes no distinctions between the various sources of apple juice.

9 RANKING RISKS ASSOCIATED WITH DIETARY MYCOTOXIN EXPOSURE IN NEW ZEALAND

While it is not possible to attribute individual cases of human disease in New Zealand, information is available from which to consider the relative importance of risks due to various mycotoxins in New Zealand. Such a ranking exercise needs to consider:

- The likely adverse health effects due to exposure to each mycotoxin, and the seriousness of those effects.
- The weight of evidence for a causative role of the mycotoxin in the adverse health effect observed.
- The exposure level or dose at which the mycotoxin can exert its toxic effects. A surrogate for this exposure level is the tolerable daily intake or equivalent for each mycotoxin.
- The proximity of New Zealand exposure estimates to tolerable limits and the need for sufficient data to make those estimates realistic. This would include information on imported foods.

Table 37 summarises information reviewed in this risk profile relevant to risk ranking.

While the information in Table 37 contains considerable uncertainties the following general comments can be made:

- There is consistent evidence to support a causal link between chronic aflatoxin exposure and serious human disease (primary liver cancer). Exposure levels in New Zealand are likely to represent a very low level of risk, although better information on the contribution of maize to dietary aflatoxin exposure would decrease the uncertainty around this conclusion.
- There is some evidence to support a link between human kidney disease and exposure to ochratoxin A. However, further work is required to establish a causal relationship. Dietary exposure to ochratoxin A in New Zealand may approach tolerable daily intake levels and further investigation, particularly of the occurrence of ochratoxin A in bread and other wheat products, would help to clarify the situation.
- This is little evidence that T2/HT2 toxins occur in New Zealand or Australian cereal crops. Confirmation of this observation would allow attention to be focused on other issues.
- There is very good evidence that trichothecenes are able to cause outbreaks of gastrointestinal disease in humans. Current New Zealand exposure estimates appear unreasonably low compared to estimates made in Europe, where crop contamination levels appear to be similar. Some European exposure estimates approach the tolerable daily intakes and it would seem prudent to continue some New Zealand focus on this issue, particularly the potential for trichothecene contamination of wheat and wheat-based products.
- While there is an increasing body of information linking fumonisin exposure to serious human diseases, there is virtually no information on the exposure of New Zealanders to these mycotoxins. While the fungal species that produce fumonisins have only rarely been reported in New Zealand, our considerable level of cereals imports mean that potential for dietary exposure still exists.
- Evidence linking zearalenone exposure to human disease states is fragmentary and inconsistent. However, the exposure of New Zealanders to zearalenone may be significant when compared to tolerable daily intakes. Further investigation of the role

of wheat-based foods in zearalenone dietary exposure in New Zealand would help to clarify this issue.

- Ergotism represents a serious and real human health risk. However, in the context of current agricultural and food manufacturing practices, the dietary risk appears to be extremely low.
- While toxicological experiments have raised concerns about patulin exposure, there is no evidence linking patulin exposure to human disease. However, high levels of patulin contamination are indicative of poor manufacturing practice and a level of ongoing monitoring is probably justified.

Ranking of risk across different mycotoxins will involve a degree of subjectivity, as there is not absolute measure for the relative seriousness of different health effects. However, the proximity of estimates of OTA exposure to critical exposure limits suggests that improved estimates of New Zealand exposure should be ranked highly.

The seriousness of the health outcomes resulting from aflatoxin exposure and the relatively high weight of evidence supporting a casual role suggest that further work on sources of dietary exposure (e.g. maize) should also be ranked highly.

Table 37: Risk ranking information for mycotoxins in the New Zealand food supply

Mycotoxin	Human health effects	Animal health effects	Weight of evidence$	Critical exposure limit (µg/kg body weight/day)	New Zealand dietary exposure µg/kg body weight/day	Major contributing foods
Aflatoxins	Primary liver cancer	Hepatocellular and/or cholangiocellular liver tumours	Medium-high	0.01*	0.0001#	Peanuts, maize
Ochratoxin A	Nephrotoxicity	Nephrotoxicity	Medium-low	0.0012-0.014	0.0024§	Bread, cereals, dried fruit, wine
Deoxynivalenol	Gastrointestinal symptoms	General toxicity, haematotoxicity, immunotoxicity	High	1.0	0.006# (0.1-0.8)¥	Maize, wheat, beer
Nivalenol	-	General toxicity, haematotoxicity, immunotoxicity	High	0.7	0.006# (0.01-0.2)¥	Maize, wheat, beer
T2/HT2 toxin	Gastrointestinal symptoms, haematotoxicity	General toxicity, haematotoxicity, immunotoxicity	High	0.06	- (0.0-0.08)¥	Maize, wheat, beer
Fumonisins	Gastrointestinal symptoms, oesophageal cancer, liver cancer, neural tube defects	Nephrotoxicity, carcinogenicity	Medium	2.0	- (0.0001-0.2)¥	Maize
Zearalenone	Early puberty, hormone-dependent cancers	Hormonal effects	Low	0.2-0.5	0.01-0.04#	Maize, wheat

Mycotoxin	Human health effects	Animal health effects	Weight of evidence$	Critical exposure limit (µg/kg body weight/day)	New Zealand dietary exposure µg/kg body weight/day	Major contributing foods
Ergot alkaloids	Ergotism (gangrenous or convulsive)		High	28¤	(0.07-0.08)¥	Rye, wheat, barley, triticale
Patulin	-	Reduced weight gain, immunotoxicity	Low	0.4	0.004-0.05	Apple juice and apple products

$ The weight of evidence assessment is subjective, but is based on the strength and consistency of associations between mycotoxin exposure and specified human disease. The consistency between human and animal disease associations is also considered. A definitive cause and effect relationship between the toxin and human disease (e.g. ergotism) is classified as a high weight of evidence, while failure to identify a human disease state (e.g. patulin) is classified as a low weight of evidence.
* No tolerable exposure limit has been set for aflatoxin. Using the JECFA estimate for cancer potency, this exposure level would result in 1 excess cancer per million of population. Although a 'one in a million' cancer risk should not be considered to represent an acceptable level of protection for New Zealand it has been used as a benchmark level of risk by the US Environmental Protection Agency for assessing environmental carcinogens.
# The available New Zealand estimate of exposure may be an underestimate, as not all potentially contaminated foods were considered.
§ Exposure estimate not based on New Zealand data.
¥ Range of typical exposures from temperate developed countries
¤ The basis for this no effect level is not well defined and is derived from a study of human toxicity due to *C. fusiformis* infection of pearl millet. The relevance of these data to *C. purpurea* infection and the different range of alkaloids produced by *C. purpurea* is uncertain.

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APPENDIX 1: FUNGAL SPECIES PRODUCING MYCOTOXINS DISCUSSED IN THIS DOCUMENT

Genus	Species	Major mycotoxin(s) produced	Other mycotoxin(s) reported
Aspergillus	*flavus*	AFB_1, AFB_2	
	parasiticus	AFB_1, AFB_2, AFG_1, AFG_2	
	nomius	AFB_1, AFB_2, AFG_1, AFG_2	
	ochraceus	OTA	
	carbonarius	OTA	
	niger	OTA	
Penicillium	*verrucosum*	OTA	
	expansum	PAT	
Fusarium	*graminearum*	DON, NIV, ZEA	
	culmorum	DON, NIV, ZEA	
	crookwellense	NIV, ZEA	
	equiseti	ZEA, T2, HT2	
	cerealis	ZEA	
	semitectum	ZEA	T2
	poae	T2, HT2, NIV	
	sporotrichioides	T2, HT2	ZEA
	acuminatum	T2, HT2	ZEA
	verticillioides	FB_1, FB_2	FB_3
	proliferatum	FB_1, FB_2, FB_3	
Claviceps	*purpurea*	Ergot alkaloids (group I and II)	
	fusiformis	Ergot alkaloids (group III)	

AFB_1, AFB_2, AFG_1, AFG_2	aflatoxins B_1, B_2, G_1, G_2
OTA	ochratoxin A
PAT	patulin
DON	deoxynivalenol
NIV	nivalenol
T2	T-2 toxin
HT2	HT-2 toxin
ZEA	zearalenone
FB_1, FB_2, FB_3	fumonisin B_1, B_2, B_3