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

4-07
8 August 2007

INITIAL / DRAFT ASSESSMENT REPORT

APPLICATION A608

MAXIMUM RESIDUE LIMITS – OXYTETRACYCLINE (ANTIBIOTIC)

DEADLINE FOR PUBLIC SUBMISSIONS: 6pm (Canberra time) 19 September 2007
SUBMISSIONS RECEIVED AFTER THIS DEADLINE WILL NOT BE CONSIDERED
(See 'Invitation for Public Submissions' for details)

For information on matters relating to this Assessment Report or the assessment process generally, please refer: http://www.foodstandards.gov.au/standardsdevelopment/

Executive Summary

Application A608 seeks to omit the Maximum Residue Limit (MRL) for the antibiotic oxytetracycline in salmonids of T*0.2 mg/kg and insert a more general MRL of T0.2 mg/kg for fish muscle in Standard 1.4.2 – Maximum Residue Limits of the *Australia New Zealand Food Standards Code* (the Code). It was also recommended that the '*' symbol indicating that the MRL is at the limit of analytical quantification (LOQ) be removed as analytical methods can now measure oxytetracycline residues in fish muscle at levels significantly lower than 0.2 mg/kg.

It is a routine Application from the Australian Pesticides and Veterinary Medicines Authority (APVMA), to update the Code in line with permits for use of oxytetracycline to treat bacterial infections in farmed fish.

The role of Food Standards Australia New Zealand (FSANZ) in the regulation of agricultural and veterinary chemicals is to protect public health and safety by ensuring that any potential residues in food are within appropriate safety limits. The dietary exposure assessment indicates that in relation to the current reference health standard, setting the MRL as proposed does not present any public health and safety concerns.

The *Agreement between the Government of Australia and the Government of New Zealand concerning a Joint Food Standards System* (the Treaty), excludes MRLs for agricultural and veterinary chemicals in food from the system setting joint food standards. Australia and New Zealand independently and separately develop MRLs for agricultural and veterinary chemicals in food.

FSANZ will make a Sanitary and Phytosanitary notification to the World Trade Organization (WTO). The proposed MRL for oxytetracycline in fish muscle is the same as the relevant international standard.

FSANZ decided, pursuant to section 36 of the *Food Standards Australia New Zealand Act 1991* (FSANZ Act), to omit to invite public submissions in relation to this Application prior to making a Draft Assessment. In making this decision, FSANZ was satisfied that the Application raised issues of minor significance or complexity only. Submissions are now invited on this Report to assist FSANZ make a Final Assessment.

Purpose
The purpose of this Application is to incorporate an MRL for fish muscle in the Code in line with permits for use of oxytetracycline in aquaculture in Australia. This will permit the sale of fish with residues up to the MRL and protect public health and safety by minimising residues in foods consistent with the effective treatment of oxytetracycline sensitive infections.

Preferred Approach

FSANZ recommends accepting Application A608 and amending Standard 1.4.2 – Maximum Residue Limits to change the current MRL of T*0.2 mg/kg in salmonids to a more general MRL of T0.2 mg/kg for oxytetracycline in fish muscle.

Reasons for Preferred Approach

This Application has been assessed against the requirements for Initial and Draft Assessments in sections 13 and 15 respectively, of the FSANZ Act. FSANZ recommends accepting this Application and the proposed draft variation to Standard 1.4.2 for the following reasons:

- MRLs serve to protect public health and safety by minimising residues in food consistent with the effective control of pests and diseases.

- The dietary exposure assessment indicates that setting the MRL as proposed does not present public health and safety concerns. Oxytetracycline (OTC) is not considered to present a significant risk in the development of antimicrobial resistance in the treatment of infections in humans. This is because OTC belongs to the tetracycline group of antibiotics which are classed as antibiotics of low importance in the Expert Advisory Group on Antimicrobial Resistance (EAGAR) Importance Ratings and Summary of Antibiotic Uses in Humans in Australia.

- The proposed variation will benefit stakeholders by maintaining public health and safety while permitting the legal sale of fish with oxytetracycline residues up to the MRL.

- The APVMA has assessed appropriate residue, animal transfer, processing and metabolism studies, in accordance with *The Manual of Requirements and Guidelines - MORAG - for Agricultural and Veterinary Chemicals 1 July 2005,* the outcome of the assessment supported the use of oxytetracycline in aquaculture and established an MRL for fish muscle as outlined in this Application.

- Office of Chemical Safety (OCS), part of the Therapeutic Goods Administration (TGA) has undertaken an appropriate toxicological assessment of oxytetracycline and has established an acceptable daily intake (ADI) of 0.03 mg/kg bw/day.

- FSANZ has undertaken a preliminary regulation impact assessment and concluded that the proposed draft variation is necessary, cost-effective and will benefit aquaculture producers and consumers.

- The proposed draft variation would provide certainty and consistency for aquaculture producers, importers and Australian, State and Territory enforcement agencies.

- The proposed changes are consistent with the FSANZ Act section 18 objectives.

Consultation

FSANZ decided, pursuant to section 36 of the FSANZ Act, not to invite public submissions in relation to Application A608 prior to making a Draft Assessment. In making this decision, FSANZ was satisfied that the Application raised issues of minor significance or complexity only.

Section 143 of the FSANZ Act provides that, subject to the *Administrative Appeals Tribunal Act 1975*, application may be made to the Administrative Appeals Tribunal for review of a decision made by FSANZ under section 36 of the FSANZ Act.

FSANZ is seeking public comment on this Initial / Draft Assessment Report to assist in assessing the Application. Comments on, but not limited to, the following would be useful:

- any impacts (costs/benefits) of the proposed change to the MRL;
- any further public health and safety considerations associated with the proposed MRL;
- any other affected parties to this Application.

Further details on making submissions are provided in the Invitation for Public Submissions section of this Report.

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INVITATION FOR PUBLIC SUBMISSIONS

Food Standards Australia New Zealand (FSANZ) invites public comment on this Initial / Draft Assessment Report based on regulation impact principles and the draft variation to the *Australia New Zealand Food Standards Code* (the Code) for the purpose of preparing an amendment to the Code for approval by the FSANZ Board.

Written submissions are invited from interested individuals and organisations to assist FSANZ in preparing the Final Assessment of this Application. Submissions should, where possible, address the objectives of FSANZ as set out in section 18 of the *Food Standards Australia New Zealand Act 1991* (FSANZ Act). Information providing details of potential costs and benefits of the proposed change to the Code from stakeholders is highly desirable. Claims made in submissions should be supported wherever possible by referencing or including relevant studies, research findings, trials, surveys etc. Technical information should be in sufficient detail to allow independent scientific assessment.

The processes of FSANZ are open to public scrutiny, and any submissions received will ordinarily be placed on the public register of FSANZ and made available for inspection. If you wish any information contained in a submission to remain confidential to FSANZ, you should clearly identify the sensitive information and provide justification for treating it as confidential commercial information. Section 114 of the FSANZ Act requires FSANZ to treat in-confidence, trade secrets relating to food and any other information relating to food, the commercial value of which would be, or could reasonably be expected to be, destroyed or diminished by disclosure.

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

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

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

Submissions need to be received by FSANZ by 6pm (Canberra time) 19 September 2007.

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

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

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

INTRODUCTION

This Application was received from the APVMA on 16 May 2007 seeking a variation to Standard 1.4.2 – Maximum Residue Limits of the Code. The proposed variation to the Standard would extend the current oxytetracycline MRL of T*0.2 mg/kg in salmonids to T0.2 mg/kg in fish muscle in the Code. This would bring the MRL in the Code in line with APVMA permits for use of oxytetracycline containing products.

FSANZ's role in the regulation of agricultural and veterinary chemicals is to protect public health and safety by ensuring that any potential residues in food are within appropriate safety limits.

FSANZ will not agree to adopt MRLs into the Code where dietary exposure to residues of a chemical presents a risk to public health and safety. In assessing this risk, the APVMA and FSANZ conduct dietary exposure assessments in accordance with internationally accepted practices and procedures.

MRLs in the Code apply in relation to the sale of food under State and Territory food legislation and the inspection of imported foods by the Australian Quarantine and Inspection Service.

The MRL is the highest concentration of a chemical residue that is legally permitted or accepted in a food. The MRL does not indicate the amount of chemical that is always present in a treated food but it does indicate the highest residue that could possibly result from the registered conditions of use. The concentration is expressed in milligrams of the chemical per kilogram (mg/kg) of the food.

MRLs assist in indicating whether an agricultural or veterinary chemical product has been used according to its registered use and if the MRL is exceeded then this indicates a likely misuse of the chemical product.

MRLs are also used as standards for international trade in food. In addition, MRLs, while not direct public health limits, act to protect public health and safety by minimising residues in food consistent with the effective control of pests and diseases.

1. Background

1.1 Current Standard

The APVMA has approved the use of oxytetracycline to treat infections in farmed fish caused by oxytetracycline sensitive organisms and notified FSANZ of the need to amend the current MRL entry for oxytetracycline in the Code from T*0.2 mg/kg for salmonids to T0.2 mg/kg for fish muscle.

Salmonids refers to members of the fish family 'Salmonidae', this includes salmon, trout and chars. Other farmed fish are not members of the salmonid family and as permits have been issued for oxytetracycline use on non-salmonid fish, there is a need to amend the current MRLs to reflect these permits.

The APVMA recommendation for the MRL entry for oxytetracycline in fish muscle is consistent with the Joint Food and Agriculture Organization / World Health Organization Expert Committee on Food Additives (JECFA) food commodity classification system and the limit is consistent with the international Codex Standard.

It was also recommended that the '*' symbol indicating that the MRL is at the limit of analytical quantification (LOQ) be removed as analytical methods can now measure oxytetracycline residues in fish muscle at levels significantly lower than 0.2 mg/kg. It was recommended that the temporary status of the MRL should be retained as this denotes that the MRL has been established to apply to residues arising from the temporary use of oxytetracycline in fish. A 'T' in front of an MRL indicates that the MRL is temporary, a TMRL.

Currently there are oxytetracycline MRLs in Standard 1.4.2 of the Code for kidney of cattle, goats, pigs and sheep; liver of cattle, goats, pigs and sheep; meat (mammalian); milks; poultry, edible offal of; and poultry meat and TMRLs for honey and salmonids.

1.2 Use of Agricultural and Veterinary Chemicals

In Australia, the APVMA is responsible for assessing and registering agricultural and veterinary chemical products, and regulating them up to the point of sale. Following the sale of such products, the use of the chemicals is regulated by State and Territory 'control of use' legislation.

Before registering a product, the APVMA independently evaluates its safety and performance, making sure that the health and safety of people, animals and the environment are protected.

When a chemical product is registered for use or a permit for use granted, the APVMA includes MRLs in the APVMA MRL Standard. These MRLs are then adopted into control of use legislation in some jurisdictions and assist States and Territories in regulating the use of agricultural and veterinary chemicals.

There are currently no products containing antibiotics registered for use against bacterial infections in farmed fish. The absence of any such antimicrobial agents for use in aquaculture systems has been identified as a significant risk to industry sustainability. Significant outbreaks of bacterial disease have already occurred in finfish in aquaculture in Australia, including *Streptococcus iniae*, *Vibrio* spp., *Aeromonas* spp. and rickettsia-like organisms. The APVMA has approved the use of oxytetracycline under permit to treat infections caused by susceptible organisms.

1.3 Maximum Residue Limit Applications

After registering agricultural or veterinary chemical products, based on scientific evaluations, the APVMA makes applications to FSANZ to adopt MRLs in Standard 1.4.2 of the Code. FSANZ reviews information provided by the APVMA and validates whether dietary exposure is within appropriate safety limits. If satisfied that the residues are within safety limits and subject to adequate resolution of any issues raised during public consultation, FSANZ will agree to incorporate the proposed MRLs into Standard 1.4.2.

FSANZ notifies the Australia and New Zealand Food Regulation Ministerial Council (Ministerial Council) when variations to the Code are approved. If the Ministerial Council does not request a review of the draft variations to Standard 1.4.2, the MRLs are automatically adopted by reference into the food laws of the Australian States and Territories.

Appropriate toxicology, residue, animal transfer, processing and metabolism studies were provided to the APVMA in accordance with *The Manual of Requirements and Guidelines - MORAG - for Agricultural and Veterinary Chemicals 1 July 2005* to support the proposed oxytetracycline MRL for fish muscle of T0.2 mg/kg outlined in this Application.

A report on oxytetracycline is available on request from the relevant Project Coordinator at FSANZ on +61 2 6271 2222.

1.4 Proposed Variation to Standard 1.4.2 - Maximum Residue Limits

The amendment under consideration in Application A608 is to omit the MRL for the antibiotic oxytetracycline in salmonids of T*0.2 mg/kg and insert an MRL of T0.2 mg/kg for fish muscle in the Code. Accepting the proposed variation would mean extending the current permission to include all fish and allow the sale of fish with oxytetracycline residues up to the MRL. The requested MRL and dietary exposure estimate are outlined in the table below.

A guide to the table with notes on terms used and a list of acronyms appearing in MRL application reports are provided in Attachment 2.

Requested MRLs			**Dietary Exposure Estimates**
Oxytetracycline Oxytetracycline belongs to the tetracycline class of antibiotics. This class has human analogues. In Australia OTC is only used in animals (including bees). The APVMA has advised that the use relates to permits to treat bacterial infections in fish intended for human consumption. It is incorporated into medicated feed that is administered to fish to treat infections caused by oxytetracycline sensitive organisms. Tetracyclines effect antimicrobial activity by binding to the 30S ribosomal subunit of susceptible organisms. This interferes with the binding of aminoacyl *t*RNA to the messenger RNA/ribosome complex, which interferes with bacterial protein synthesis in growing or multiplying organisms.			NEDI = 4% of ADI
Salmonids	Omit	T*0.2	
Fish muscle	Insert	T0.2	

In considering issues associated with MRLs, it should be noted that MRLs and variations to MRLs in the Code do not permit or prohibit the use of agricultural and veterinary chemicals. Other Australian Government, State and Territory legislation regulates use of agricultural and veterinary chemicals.

1.5 Acute Dietary Exposure

Neither the Office of Chemical Safety (OCS) nor JECFA have established an acute reference dose (ARfD) for oxytetracycline, therefore no estimate of the national acute dietary exposure (National Estimated Short Term Intake or NESTI) has been conducted. These terms are explained in the risk assessment section of this report and in Attachment 2.

1.6 Antimicrobial Resistance

The National Health and Medical Research Council established the Expert Advisory Group on Antimicrobial Resistance (EAGAR) to provide advice to government and regulatory agencies on antimicrobial resistance and measures to reduce the risks of antimicrobial resistance. EAGAR's interest in the development of antimicrobial resistance focuses on antimicrobials of high and medium importance in the treatment of human infections.

Oxytetracycline belongs to the tetracycline group of antibiotics. Other antibiotics in this group such as demeclocycline, doxycycline, minocycline and tetracycline are used in human therapeutics and are classed as antibiotics of low importance in the EAGAR Importance Ratings and Summary of Antibiotic Uses in Humans in Australia.

As part of its Application to vary the oxytetracycline MRL for salmonids in the Code, the APVMA provided information on the use of oxytetracycline in aquaculture systems to EAGAR. As oxytetracycline is part of the tetracycline group of antibiotics that is of low importance in the treatment of human infections and is only used in animals in Australia, EAGAR considers its endorsement of the recommended MRL is not required.

Based on the above and taking into consideration the results of the dietary exposure assessment FSANZ concludes that there are no anticipated antimicrobial resistance concerns arising from this Application. The proposed variation poses no adverse consequences to human health.

1.7 Australia and New Zealand Joint Food Standards

The Treaty excludes MRLs for agricultural and veterinary chemicals in food from the system setting joint food standards. Australia and New Zealand independently and separately develop MRLs for agricultural and veterinary chemicals in food.

The Trans Tasman Mutual Recognition Arrangement (TTMRA) between Australia and New Zealand commenced on 1 May 1998. The following provisions apply under the TTMRA.

- Food produced or imported into Australia that complies with Standard 1.4.2 of the Code can be legally sold in New Zealand.

- Food produced or imported into New Zealand that complies with the New Zealand (Maximum Residue Limits of Agricultural Compounds) Food Standards, 2007 can be legally sold in Australia.

New Zealand MRLs are discussed further in section 10.3 of this report.

2. The Issue / Problem

Including MRLs in the Code has the effect of allowing legally treated produce to be sold legally, where any residues do not exceed MRLs. Changes to Australian MRLs reflect the changing patterns of agricultural and veterinary chemicals available to farmers. These changes include both the development of new products and crop or animal uses, and the withdrawal of older products following review.

3. Objectives

In assessing this Application FSANZ aims to ensure that the proposed MRL does not present a risk to public health and safety and that the sale of legally treated food is permitted. The APVMA has allowed the use of oxytetracycline under permit in accordance with its legislation, and now seeks to have the relevant MRL amendment included in the Code through this Application to vary Standard 1.4.2.

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

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

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

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

The proposed draft variation to Standard 1.4.2 is consistent with the FSANZ Act section 10 objectives of food regulatory measures.

4. Key Assessment Questions

The primary role of FSANZ in developing food regulatory measures for agricultural and veterinary chemicals is to ensure that the potential residues in treated food do not present public health and safety concerns.

Before an agricultural or veterinary chemical is registered, the *Agricultural and Veterinary Chemicals Code Act 1994* (*Ag Vet Code Act*) requires the APVMA to be satisfied that there will not be any appreciable risk to the consumer, to the person handling, applying or administering the chemical, to the environment, to the target crop or animal or to trade in an agricultural commodity.

In assessing the public health and safety implications of chemical residues, FSANZ considers the dietary exposure to chemical residues from potentially treated foods in the diet by comparing the dietary exposure with the relevant health standard. FSANZ will not approve MRLs for inclusion in the Code where the dietary exposure to the residues of a chemical could represent a risk to public health and safety. In assessing this risk, FSANZ reviews dietary exposure assessments conducted by the APVMA in accordance with internationally accepted practices and procedures.

The three steps undertaken in conducting a dietary exposure assessment are:

- determination of the residues of a chemical in a treated food;
- determination of the acceptable reference health standard/s for a chemical in food (i.e. the ADI and/or the ARfD); and
- calculating the dietary exposure to a chemical from relevant foods, using food consumption data from national nutrition surveys and comparing this to the acceptable reference health standard.

RISK ASSESSMENT

5. Safety Assessment

5.1 Determination of the Residues of a Chemical in a Treated Food

The APVMA assesses a range of data when considering the proposed use of a chemical product on a food. These data enable the APVMA to determine what the likely residues of a chemical will be on a treated food. These data also enable the APVMA to determine what the maximum residues will be on a treated food if the chemical product is used as proposed and from this, the APVMA determines an MRL.

The MRL is the maximum level of a chemical that may be in a food and it is not the level that is usually present in a treated food. However, incorporating the MRL into food legislation means that the residues of a chemical are minimised (i.e. must not exceed the MRL), irrespective of whether the dietary exposure assessment indicates that higher residues would not represent a risk to public health and safety.

5.2 Determining the Acceptable Reference Health Standard for a Chemical in Food

OCS assesses the toxicology of agricultural and veterinary chemicals and establishes the ADI and where applicable, the ARfD for a chemical. The Australian ADI was adopted from the figure established by JECFA. As neither OCS nor JECFA have established an ARfD for oxytetracycline, a NESTI has not been calculated.

Both the APVMA and FSANZ use these reference health standards in dietary exposure assessments.

The ADI is the daily intake of an agricultural or veterinary chemical, which, during the consumer's entire lifetime, appears to be without appreciable risk to the health of the consumer. This is on the basis of all the known facts at the time of the evaluation of the chemical. It is expressed in milligrams of the chemical per kilogram of body weight.

The ARfD of a chemical is the estimate of the amount of a substance in food, expressed on a body weight basis that can be ingested over a short period of time, usually during one meal or one day, without appreciable health risk to the consumer, on the basis of all the known facts at the time of evaluation.

5.3 Calculating Dietary Exposure

The APVMA and FSANZ undertake chronic dietary exposure assessments for all agricultural and veterinary chemicals and undertake acute dietary exposure assessments where OCS or the Joint Food and Agriculture Organization / World Health Organization Meeting on Pesticide Residues (JMPR) or JECFA (in the case of antibiotics) have established an ARfD.

The APVMA and FSANZ have agreed that all dietary exposure assessments for agricultural and veterinary chemicals undertaken by the APVMA will be based on food consumption data for raw commodities, derived from individual dietary records from the latest National Nutrition Survey (NNS). The Australian Bureau of Statistics with the then Australian Government Department of Health and Aged Care undertook the latest NNS over a 13-month period (1995 to early 1996). The sample of 13,858 respondents aged 2 years and older was a representative sample of the Australian population and, as such, a diversity of food consumption patterns was reported.

5.3.1 Chronic Dietary Exposure Assessment

The National Estimated Daily Intake (NEDI) represents an estimate of chronic dietary exposure. Chemical residue data, as opposed to the MRL, are the preferred concentration data to use if they are available, as they provide a more realistic estimate of dietary exposure. The NEDI calculation may incorporate more specific data including food consumption data for particular sub-groups of the population. The NEDI calculation may take into account such factors as the proportion of the crop or commodity treated; residues in edible portions and the effects of processing and cooking on residue levels; and may use median residue levels from supervised trials rather than the MRL to represent agricultural or veterinary chemical residue levels. Monitoring and surveillance data or data from total diet studies may also be used, such as the 19th and 20th Australian Total Diet Surveys (ATDS).

FSANZ is currently planning the next ATDS (now the Australian Total Diet Study). The study will analyse the levels of various agricultural and veterinary chemicals in food and estimate the potential dietary exposure of population groups in Australia to those chemicals.

In conducting chronic dietary exposure assessments, the APVMA and FSANZ consider the residues that could result from the permitted uses of a chemical product on foods. Where data are not available on the specific residues in a treated food then a cautious approach is taken and the MRL is used.

The use of the MRL in dietary exposure estimates may result in considerable overestimates of exposure because it assumes that the entire national crop is treated with a pesticide and that the entire national crop contains residues equivalent to the MRL. In reality, only a portion of a specific commodity is treated with an agricultural or veterinary chemical; most treated crops contain residues well below the MRL at harvest; and residues are usually reduced during storage, preparation, commercial processing and cooking. It is also unlikely that every food for which an MRL is proposed will have been treated with the same compound over the lifetime of consumers.

The residues that are likely to occur in all foods are multiplied by the mean daily consumption of these foods derived from individual dietary records from the latest NNS. These calculations provide information on the level of a chemical that is consumed for each food and take into account the consumption of processed foods e.g. apple pie and bread. The estimated exposure for each food is added together to provide the total dietary exposure to a chemical from all foods with MRLs.

The estimated dietary exposure is then divided by the average Australian's bodyweight to provide the amount of chemical consumed per day per kg of human bodyweight. This is compared to the ADI. It is therefore the overall dietary exposure to a chemical that is compared to the ADI - not the MRL. FSANZ considers that the chronic dietary exposure to the residues of a chemical is acceptable where the best estimate of exposure does not exceed the ADI.

Further, where these calculations use the MRL they are considered to be overestimates of dietary exposure because they assume that:

- the chemical will be used on all commodities for which there is a registered use;
- treatment occurs at the maximum application rate;
- the maximum number of permitted treatments have been applied;
- the minimum withholding period has been applied; and
- this will result in residues at the maximum residue limit.

In agriculture and animal husbandry this is not the case, but for the purposes of undertaking a risk assessment, it is important to be conservative in the absence of reliable data to refine the dietary exposure estimates further.

5.3.2 Acute Dietary Exposure Assessment

The NESTI is used to estimate acute dietary exposure. Acute (short term) dietary exposure assessments are undertaken when an ARfD has been determined for a chemical. Acute dietary exposures are normally only estimated for raw unprocessed commodities (fruit and vegetables) but may include consideration of meat, offal, cereal, milk or dairy product consumption on a case-by-case basis.

The NESTI is calculated in a similar way to the chronic dietary exposure. The residues of a chemical in a specific food are multiplied by the 97.5th percentile food consumption of that food, a variability factor is applied, the exposure divided by a mean body weight for the population group being assessed and this result is compared to the ARfD. NESTIs are calculated from ARfDs set by OCS and JMPR or JECFA, the consumption data from the 1995 NNS and the MRL when the data on the actual residues in foods are not available. FSANZ considers that the acute dietary exposure to the residues of a chemical is acceptable where the best estimate of acute dietary exposure does not exceed the ARfD.

6. Risk Assessment Summary

The APVMA assesses a range of data when considering the proposed use of a chemical product on a food commodity. These data enable the APVMA to determine what the likely residues of a chemical will be on a treated food commodity. These data also enable the APVMA to determine what the maximum residues will be on a treated food if the chemical product is used as proposed and from this, the APVMA determines an MRL.

For this Application, the APVMA has assessed appropriate toxicology, residue, animal transfer, processing and metabolism studies, in accordance with *The Manual of Requirements and Guidelines - MORAG - for Agricultural and Veterinary Chemicals 1 July 2005.* The outcomes of this assessment supported the use of oxytetracycline in farmed fish and recommended an MRL for fish muscle of T0.2 mg/kg.

OCS has undertaken an appropriate toxicological assessment of the chemical products and has established an ADI of 0.03 mg/kg bw/day for oxytetracycline. The Australian ADI was adopted from the figure established by JECFA. As neither OCS nor JECFA have established an ARfD for oxytetracycline, a NESTI has not been calculated.

FSANZ has reviewed the dietary exposure assessment submitted by the APVMA as part of its Application and concluded that the residues associated with the proposed MRL do not present any public health and safety concerns. This was determined by comparing estimates of dietary exposure to oxytetracycline (calculated using food consumption data and MRLs for all foods for which its use is permitted during production), with the ADI. The NEDI for oxytetracycline is 4% of the ADI. The additional safety factors inherent in calculation of the ADI mean that there is negligible risk to public health and safety when estimated exposures are below this reference health standard.

The NEDI calculation is a conservative overestimate of dietary exposure to potential residues in food. In reality, only a portion of specific commodities for which use of oxytetracycline is permitted would be treated with it during production. Also, most treated commodities contain residues well below the MRL before they appear on the market; and residues are usually reduced during storage, washing, preparation, commercial processing and cooking. It is also unlikely that every food for which an MRL is proposed or permitted will have been treated with the same pesticide during production and eaten over the lifetime of consumers.

The MRL is the maximum level of a chemical that may be in a food and it is not the level that is usually present in a treated food. However, incorporating the MRL into food legislation means that the residues of a chemical are minimised (i.e. must not exceed the MRL), irrespective of whether the dietary exposure assessment indicates that higher residues would not represent an unacceptable risk to public health and safety.

FSANZ considers that this Application raises no safety concerns from a dietary exposure or microbiological perspective.

RISK MANAGEMENT

7. Options

7.1 Option 1 – no change to the existing oxytetracycline TMRL for salmonids

Under this option, the *status quo* would be maintained and there would be no change to the existing oxytetracycline TMRL of T*0.2 mg/kg in salmonids in the Code.

7.2 Option 2 – vary the Code in Schedule 1 of Standard 1.4.2 - Maximum Residue Limits to extend the existing permission to fish muscle as proposed

Under this option, the oxytetracycline MRL of T*0.2 mg/kg in salmonids would be omitted and the proposed MRL of T0.2 mg/kg in fish muscle would be approved for inclusion in the Code.

8. Impact Analysis

The impact analysis represents likely impacts based on available information. The impact analysis is designed to assist in the process of identifying the affected parties, any alternative options consistent with the objective of the proposed changes, and the potential impacts of any regulatory or non-regulatory provisions. Information from public submissions is needed to make a final assessment of the proposed change.

8.1 Affected Parties

The parties affected by proposed MRL amendment include:

- domestic and international consumers;
- producers and processors of domestic and export fish and fish products;
- importers of fish and fish products; and
- Australian Government, State and Territory agencies involved in monitoring and regulating the use of agricultural and veterinary chemicals in food and the potential resulting residues.

8.2 Benefit Cost Analysis

8.2.1 Option 1 – no change to the existing oxytetracycline TMRL for salmonids

8.2.1.1 Benefits

- For consumers there are unlikely to be any discernable benefits;

- for producers and processors of domestic and export fish commodities this option would not result in any discernable benefits;

- for importers this option would not result in any discernable benefits; and

- for Australian Government, State and Territory agencies this option would not result in any discernable benefits.

8.2.1.2 Costs

- For consumers there are unlikely to be any discernable costs as the unavailability of some fish or fish products from certain suppliers is likely to be seen as typical fluctuation in the food supply;

FSANZ invites comment on whether these costs are likely to be discernable by consumers.

- for producers and processors of domestic and export fish and fish products the absence of an MRL may give rise to the concern that legal use of chemical products may result in the production of fish and fish products that may not be legally sold under food legislation. Primary producers do not produce food or use antibiotics to comply with MRLs. They use antibiotics to treat and control disease in accordance with the prescribed label conditions, and expect that the resulting residues will be acceptable and that legally treated food can be legally sold;

- for importers this option would not result in any discernable costs; and

- for Australian Government, State and Territory agencies, this option would give rise to uncertainty, inefficiency and confusion in the enforcement of regulations.

8.2.2 Option 2 – vary the Code in Schedule 1 of Standard 1.4.2 - Maximum Residue Limits to extend the existing permission to fish muscle as proposed

8.2.2.1 Benefits

- Maintaining consumer confidence in the food supply in relation to residues of veterinary chemicals in foods and potential flow on benefits resulting from the price and availability of fish and fish products if producers and processors can legally sell food containing residues consistent with the proposed extended permission;

FSANZ invites comment on whether these benefits are likely to be discernable by consumers.

- producers and processors would legally be able to sell fish and fish products containing residues up to the proposed MRL also, compliance costs would potentially be minimised;

- fish and fish products with residues consistent with the proposed MRL could be legally imported; and

- for Australian Government, State and Territory agencies, an MRL in line with the permitted use would create certainty and allow efficient enforcement of regulations.

8.2.2.2 Costs

- For consumers there are unlikely to be any discernable costs;

- for producers and processors of domestic and export fish and fish products, this option is unlikely to result in any discernable costs, as changes in use patterns are made as required, proper use resulting in compliance with proposed MRLs already;

- for importers, this option would not result in any discernable costs; and

- for Australian Government, State and Territory agencies, this option would not result in any discernable costs, although there may be minimal impacts associated with slight changes to residue monitoring programs.

8.3 Comparison of Options

In assessing applications, FSANZ considers the impact of various regulatory (and non-regulatory) options on all sectors of the community, including consumers, food industries and governments in Australia. For Application A608, there are no options other than a variation to Standard 1.4.2.

FSANZ preferred approach is to adopt option 2 – to vary the Code in Schedule 1 of Standard 1.4.2 - Maximum Residue Limits to extend the existing permission for oxytetracycline residues in salmonids to permit an MRL of 0.2 mg/kg of this antibiotic in fish muscle as proposed for the following reasons:

- There are no public health and safety concerns associated with the proposed MRL amendment (this benefit also applies to option 1).

- The change would minimise potential costs to producers and processors of fish and fish products and rural and regional communities in terms of confidence in legally being able to sell legally treated fish.

- The change would minimise residues consistent with the effective use of veterinary medicine to treat diseases.

- An MRL in line with the permitted use of oxytetracycline in aquaculture would assist enforcement.

Option 1 is an undesirable option.

- Potential costs to producers and processors of fish and fish products may result. Additional costs may impact negatively on their viability and in turn the viability of the rural and regional communities that depend upon the sale of fish commodities.

- A discrepancy between permitted use of the antibiotic and food legislation could have negative impacts on compliance costs for producers and processors of fish and fish products, perception problems in export markets and undermine the efficient enforcement of standards for chemical residues.

COMMUNICATION AND CONSULTATION STRATEGY

9. Communication

Applications by the APVMA to amend maximum residue limits in the Code do not normally generate public interest. FSANZ adopts a basic communication strategy, with a focus on alerting the community that a change to the Code is being contemplated.

FSANZ publishes the details of the Application and subsequent assessment reports on its website, notifies the community to the period of public consultation through newspaper advertisements, and issues media releases drawing attention to proposed Code amendments. Once the Code has been amended, FSANZ incorporates the changes in the website version of the Code and, through its email and telephone advice service, responds to industry enquiries.

Should the media show an interest in the antibiotic being assessed, FSANZ or the APVMA can provide background information and other advice, as required.

10. Consultation

FSANZ decided, pursuant to section 36 of the FSANZ Act, to omit to invite public submissions in relation to Application A608 prior to making a Draft Assessment. However, FSANZ now invites written submissions for the purpose of the Final Assessment under s.17(3)(c) of the FSANZ Act and will have regard to any submissions received.

FSANZ made its decision under section 36 because it was satisfied that Application A608 raised issues of minor significance or complexity only.

Section 143 of the FSANZ Act provides that, subject to the *Administrative Appeals Tribunal Act 1975*, an application for review of the decision to omit to invite public submissions prior to making a Draft Assessment, may be made to the Administrative Appeals Tribunal.

FSANZ is seeking public comment on this Initial / Draft Assessment Report to assist in assessing the Application. Comments on, but not limited to, the following would be useful:

- any impacts (costs/benefits) of the proposed MRL;
- any public health and safety considerations with the proposed MRL;
- likely costs and benefits in relation to the importation of food if the proposed MRL is advanced; and
- any other affected parties to this Application.

10.1 World Trade Organization

As a member of the WTO, Australia is obligated to notify WTO member nations where proposed mandatory regulatory measures are inconsistent with any existing or imminent international standards and the proposed measure may have a significant effect on trade.

MRLs prescribed in the Code constitute a mandatory requirement applying to all food products of a particular class whether produced domestically or imported. Food products exceeding the relevant MRL set out in the Code cannot legally be supplied in Australia.

Agricultural and veterinary chemicals are used differently in different countries around the world as pests, diseases and environmental factors differ and because permissions for products differ. This means that residues in imported foods may be different from those in domestically produced foods.

Application A608 requests deleting the existing MRL for oxytetracycline residues in salmonids and incorporating a more general MRL of T0.2 mg/kg in fish muscle in the Code. In the European Union, the European Agency for the Evaluation of Medicinal Products currently permits oxytetracycline residues of 100 µg/kg (0.1 mg/kg) in muscle of all food producing species. Oxytetracycline is approved for use in aquaculture in the United States and a tolerance of 2 ppm (2 mg/kg) for residues of oxytetracycline in finfish and lobster muscle has been codified. The APVMA has advised that Japan has established an MRL of 0.2 mg/kg for fish. These variations indicate that oxytetracycline residues in fish may have an effect on trade of fish and derivative food products between WTO members.

This Application will be notified as a Sanitary and Phytosanitary (SPS) measure in accordance with the WTO Agreement on the Application of SPS Measures, as the primary objective of the measure is to support the regulation of the use of agricultural and veterinary chemical products to protect human, animal and plant health and the environment.

10.2 Codex Alimentarius Commission MRLs

Codex standards are used as the relevant international standard or basis as to whether a new or changed standard requires a WTO notification. The following table lists MRLs proposed in Application A608 where there is a corresponding MRL in the international Codex standard.

Chemical Food	**Proposed MRL** **mg/kg**	**Codex MRL** **mg/kg**
Oxytetracycline Fish muscle	T0.2	0.2

10.3 New Zealand (Maximum Residue Limits of Agricultural Compounds) Food Standards 2007

All imported and domestically produced food sold in New Zealand (except for food imported from Australia) must comply with the New Zealand (Maximum Residue Limits of Agricultural Compounds) Food Standards 2007 (the New Zealand MRL Standards).

Under the New Zealand MRL Standards, agricultural chemical residues in food must comply with the specific MRLs listed in the Standards. The New Zealand MRL Standards also include a provision for residues of up to 0.1 mg/kg for agricultural chemical / commodity combinations not specifically listed or, if the food is imported, it may comply with Codex MRLs. Further information about the New Zealand MRL Standards is available on the New Zealand Food Safety Authority website at: http://www.nzfsa.govt.nz/acvm/registers-lists/nz-mrl/index.htm

MRLs in the Code and in the New Zealand MRL Standards may vary for a number of legitimate reasons including differing use patterns for chemical products as a result of varying pest and disease pressures and varying climatic conditions.

The following table lists the proposed variations to MRLs in Application A608 and includes the corresponding MRL that has been established in the New Zealand MRL Standards. Notwithstanding the provision for residues of up to 0.1 mg/kg in the New Zealand MRL Standards, New Zealand has established an MRL of 0.1 mg/kg for oxytetracycline in fish meat.

Chemical Food	**Proposed MRL** **mg/kg**	**NZ MRL** **mg/kg**
Oxytetracycline Fish muscle	T0.2	Fish meat 0.1

CONCLUSION

11. Conclusion and Preferred Option

This Application has been assessed against the requirements for Initial and Draft Assessments in sections 13 and 15 respectively, of the FSANZ Act. FSANZ recommends accepting this Application and the proposed draft variation to Standard 1.4.2. – Maximum Residue Limits.

The preferred approach is to adopt option 2 to vary the oxytetracycline MRL in Schedule 1 of Standard 1.4.2 – Maximum Residue Limits as proposed.

Preferred Approach

FSANZ recommends accepting Application A608 and amending Standard 1.4.2 – Maximum Residue Limits to change the current MRL of T*0.2 mg/kg in salmonids to a more general MRL of T0.2 mg/kg for oxytetracycline in fish muscle.

11.1 Reasons for Preferred Approach

This Application has been assessed against the requirements for Initial and Draft Assessments in sections 13 and 15 respectively, of the FSANZ Act. FSANZ recommends accepting this Application and the proposed draft variation to Standard 1.4.2 for the following reasons:

- MRLs serve to protect public health and safety by minimising residues in food consistent with the effective control of pests and diseases.

- The dietary exposure assessment indicates that setting the MRL as proposed does not present public health and safety concerns. Oxytetracycline (OTC) is not considered to present a significant risk in the development of antimicrobial resistance in the treatment of infections in humans. This is because OTC belongs to the tetracycline group of antibiotics which are classed as antibiotics of low importance in the Expert Advisory Group on Antimicrobial Resistance (EAGAR) Importance Ratings and Summary of Antibiotic Uses in Humans in Australia.

- The proposed variation will benefit stakeholders by maintaining public health and safety while permitting the legal sale of fish with oxytetracycline residues up to the MRL.

- The APVMA has assessed appropriate residue, animal transfer, processing and metabolism studies, in accordance with *The Manual of Requirements and Guidelines - MORAG - for Agricultural and Veterinary Chemicals 1 July 2005,* the outcome of the assessment supported the use of oxytetracycline in aquaculture and established an MRL for fish muscle as outlined in this Application.

- OCS has undertaken an appropriate toxicological assessment of oxytetracycline, and has established an ADI of 0.03 mg/kg bw/day.

- FSANZ has undertaken a preliminary regulation impact assessment and concluded that the proposed draft variation is necessary, cost-effective and will benefit producers and consumers.

- The proposed draft variation would provide certainty and consistency for aquaculture producers, importers and Australian, State and Territory enforcement agencies.

- The proposed changes are consistent with the FSANZ Act section 18 objectives.

12. Implementation and Review

The use of chemical products and MRLs are under constant review as part of the APVMA Existing Chemical Review Program. In addition, regulatory agencies continue to monitor health, agricultural and environmental issues associated with chemical product use. Residues in food are also monitored through:

- State and Territory residue monitoring programs;

- Australian Government programs such as the National Residue Survey; and

- dietary exposure studies such as the Australian Total Diet Study.

These monitoring programs and the continual review of the use of agricultural and veterinary chemicals mean that there is considerable scope to review MRLs.

It is proposed that the MRL amendment in this Application should take effect on gazettal and that the MRL be subject to existing monitoring arrangements.

ATTACHMENTS

1. Draft Variation to the *Australia New Zealand Food Standards Code*
2. A Guide to the Table Outlining the Requested Variation to Standard 1.4.2 – Maximum Residue Limits of the *Australia New Zealand Food Standards Code* and Estimated Dietary Exposure to the Relevant Chemical

Attachment 1

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

To commence: on gazettal

[1] ***Standard 1.4.2*** *of the Australia New Zealand Food Standards Code is varied by –*

[1.1] o*mitting from* Schedule 1 *the food and associated MRL for the following chemical –*

OXYTETRACYCLINE INHIBITORY SUBSTANCE, IDENTIFIED AS OXYTETRACYCLINE	
SALMONIDS	T*0.2

[1.2] *inserting in alphabetical order in* Schedule 1*, the food and associated MRL for the following chemical –*

OXYTETRACYCLINE INHIBITORY SUBSTANCE, IDENTIFIED AS OXYTETRACYCLINE	
FISH MUSCLE	T0.2

Attachment 2

A Guide to the Table Outlining the Requested Variation to Standard 1.4.2 – Maximum Residue Limits of the *Australia New Zealand Food Standards Code* and Estimated Dietary Exposure to the Relevant Chemical

NOTES ON TERMS USED IN THE TABLE AND RISK ASSESSMENT

ADI – Acceptable Daily Intake - The ADI is the daily intake of an agricultural or veterinary chemical, which, during the consumer's entire lifetime, appears to be without appreciable risk to the health of the consumer. This is based on all the known facts at the time of the evaluation of the chemical. The ADI is expressed in milligrams of the chemical per kilogram of body weight.

ARfD – Acute Reference Dose - The ARfD is the estimate of the amount of a substance in food, expressed on a body weight basis, that can be ingested over a short period of time, usually during one meal or one day, without appreciable health risk to the consumer, on the basis of all the known facts at the time of evaluation.

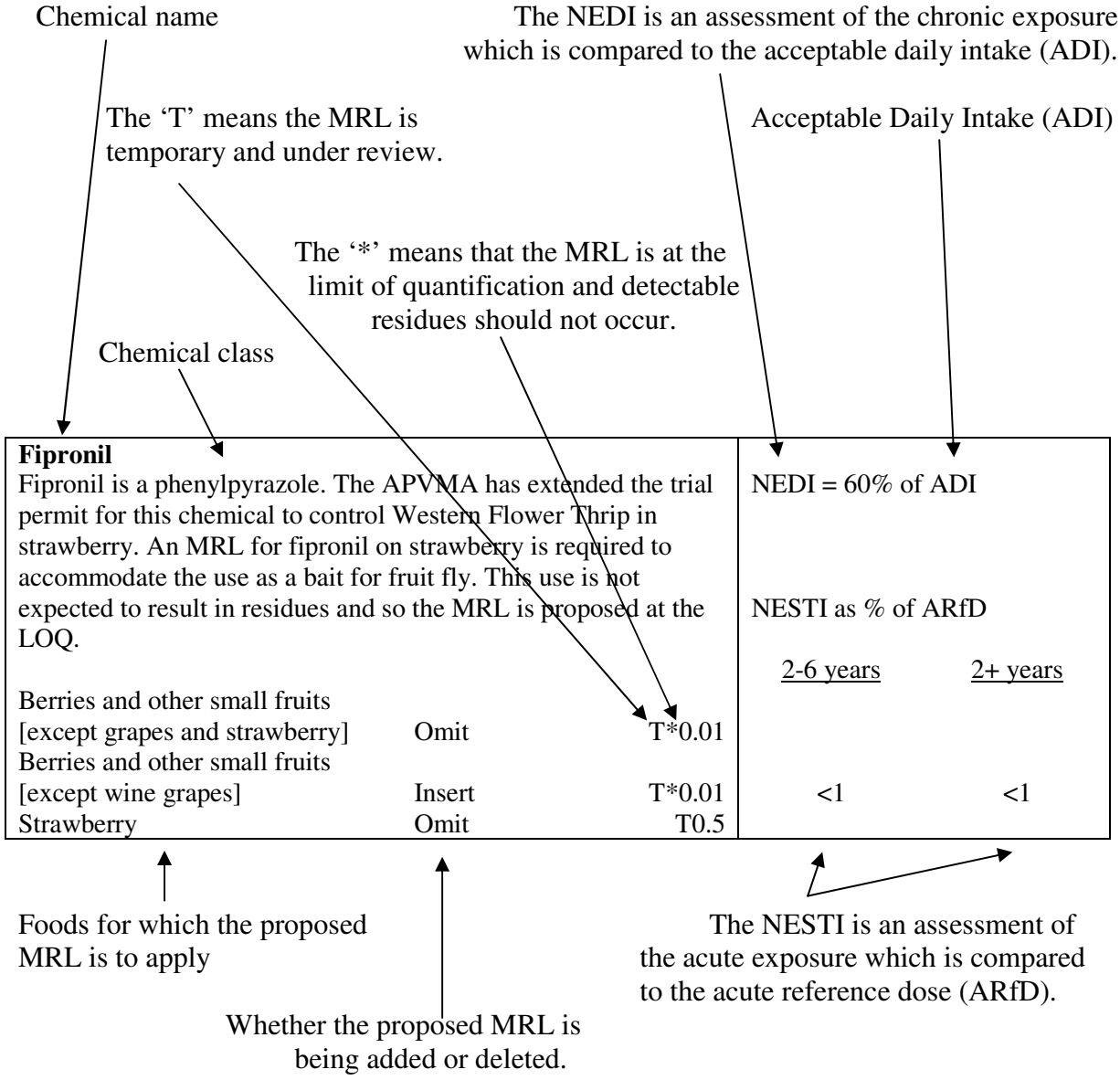
LOQ - Limit of Quantification - The LOQ is the lowest concentration of a pesticide residue that can be identified and quantitatively measured in a specified food, agricultural commodity or animal feed with an acceptable degree of certainty by a regulatory method of analysis.

NEDI - National Estimated Dietary Intake - The NEDI represents a realistic estimate of chronic dietary exposure and is the preferred calculation. It may incorporate more specific food consumption data including that for particular sub-groups of the population. The NEDI calculation may take into account such factors as the proportion of the crop or commodity treated; residues in edible portions; the effects of processing and cooking on residue levels; and may use median residue levels from supervised trials other than the MRL to represent pesticide residue levels. In most cases the NEDI is still an overestimation because more specific residue data are often not available and in these cases the MRL is used.

NESTI - National Estimated Short Term Intake - The NESTI is used to estimate acute dietary exposure. Acute (short term) dietary exposure assessments are undertaken when an ARfD has been determined for a chemical. Acute dietary exposures are normally only estimated based on consumption of raw unprocessed commodities (fruit and vegetables) but may include consideration of meat, offal, cereal, milk or dairy product consumption on a case-by-case basis. FSANZ has used ARfDs set by the TGA and Joint FAO/WHO Meeting on Pesticide Residues, the consumption data from the 1995 NNS and the MRL when the supervised trials median residue (STMR) is not available to calculate the NESTIs.

The NESTI calculation incorporates the large portion (97.5 percentile) food consumption data and can take into account such factors as the highest residue on a composite sample of an edible portion; the STMR, representing typical residue in an edible portion resulting from the maximum permitted pesticide use pattern; processing factors which affect changes from the raw commodity to the consumed food and the variability factor.

The following are examples of entries and the proposed MRLs listed are not part of this Application.



Fipronil			NEDI = 60% of ADI	
Fipronil is a phenylpyrazole. The APVMA has extended the trial permit for this chemical to control Western Flower Thrip in strawberry. An MRL for fipronil on strawberry is required to accommodate the use as a bait for fruit fly. This use is not expected to result in residues and so the MRL is proposed at the LOQ.			NESTI as % of ARfD	
			2-6 years	2+ years
Berries and other small fruits [except grapes and strawberry]	Omit	T*0.01		
Berries and other small fruits [except wine grapes]	Insert	T*0.01	<1	<1
Strawberry	Omit	T0.5		

There is more information on the NEDI, NESTI ADI and ARfD above and in the Risk Assessment section of this report. FSANZ considers that the chronic dietary exposure to the residues of a chemical is acceptable where the best estimate of this exposure does not exceed the ADI. And that the acute dietary exposure to the residues of a chemical is acceptable where the best estimate of acute dietary exposure does not exceed the ARfD.

Information about the use of the chemical is provided so consumers can see the reason why the residues may occur in food.

Data from the 19th and 20th Australian Total Diet Surveys (ATDS) are provided when available because they provide an indication of the typical exposure to chemicals in table ready foods. The ATDS results are more realistic because analysed concentrations of the chemical in foods are used; the NEDI and NESTI calculations are theoretical calculations that conservatively overestimate exposure.

Chlorpyrifos Chlorpyrifos is an acaricide, nematicide and insecticide. The APVMA has approved an extension of use for the control of pests in coffee crops.	NEDI = 83% of ADI 20th ATDS = <1% of ADI for all population groups assessed 19th ATDS = 3% of ADI for toddlers 2 years, 1% of ADI for boys 12 years and <1% of ADI for other population groups assessed NESTI as % of ARfD 2-6 years 2+ years 8 <1
Coffee beans Insert T0.5	

Small variations may be noted in the exposure assessment between different ATDSs. These variations are minor and typically result because of the different range of foods in the individual studies.

Acronyms:

1.	**ADI**	Acceptable Daily Intake
2.	**APVMA**	Australian Pesticides and Veterinary Medicines Authority
3.	**ARfD**	Acute Reference Dose
4.	**ATDS**	Australian Total Diet Survey
5.	**the Code**	*Australia New Zealand Food Standards Code*
6.	**DIAMOND**	Dietary Modelling of Nutritional Data
7.	**FSANZ**	Food Standards Australia New Zealand
8.	**JECFA**	Joint FAO/WHO Expert Committee on Food Additives
9.	**JMPR**	Joint FAO/WHO Meeting on Pesticide Residues
10.	**LOQ**	Limit of Analytical Quantification
11.	**MRL**	Maximum Residue Limit
12.	**NEDI**	National Estimated Daily Intake
13.	**NESTI**	National Estimated Short Term Intake
14.	**NNS**	National Nutrition Survey of Australia 1995
15.	**OCS**	Office of Chemical Safety
16.	**TMRL**	Temporary MRL
17.	**TGA**	Therapeutic Goods Administration