EXPLANATORY STATEMENT

APPLICATION A535

MAXIMUM RESIDUE LIMITS – NEOMYCIN (ANTIBIOTIC)

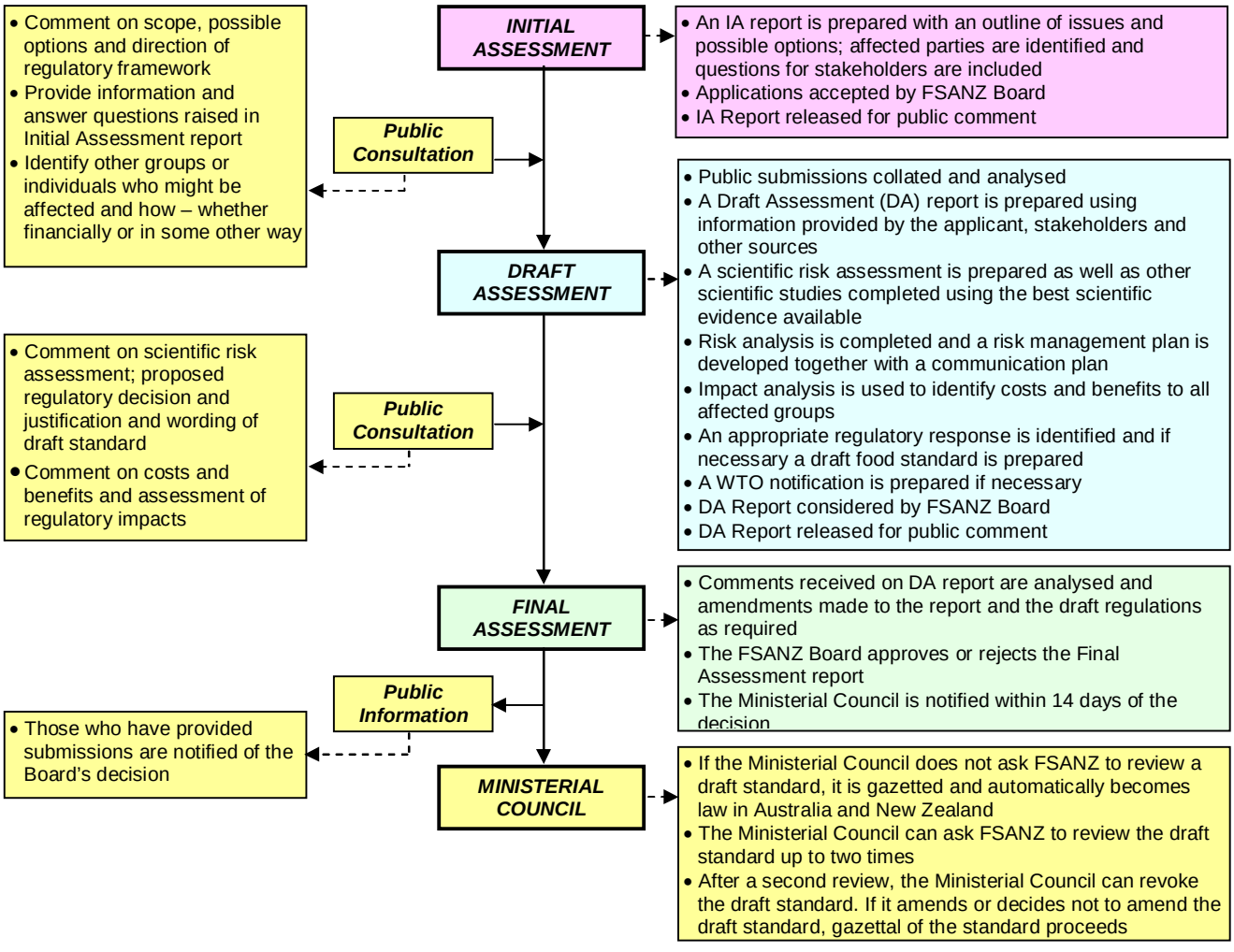
FOOD STANDARDS AUSTRALIA NEW ZEALAND (FSANZ)

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

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

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

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



Final Assessment Stage (s.36)

FSANZ has now completed the assessment of the Application A535 and held a single round of public consultation under section 36 of the FSANZ Act. This Final Assessment Report and its recommendations have been approved by the FSANZ Board and notified to the Ministerial Council.

If the Ministerial Council does not request FSANZ to review the draft amendments to the Code, an amendment to the Code is published in the *Commonwealth Gazette* and the *New Zealand Gazette* and adopted by reference and without amendment under Australian State and Territory food law.

Further Information

Further information on this Application and the assessment process should be addressed to the FSANZ Standards Management Officer at 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
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Assessment reports are available for viewing and downloading from the FSANZ website www.foodstandards.gov.au or alternatively paper copies of reports can be requested from FSANZ's Information Officer at info@foodstandards.gov.au including other general enquiries and requests for information.

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Executive Summary and Statement of Reasons

This Application (A535) seeks the establishment of Maximum Residue Limits (MRLs) for mammalian commodities for the antibiotic, neomycin into the *Australia New Zealand Food Standards Code* (the Code). It is an application from the Australian Pesticides and Veterinary Medicines Authority (APVMA) to update the Code in order to reflect the current registration status of agricultural and veterinary chemicals in use in Australia.

The *Agreement between the Commonwealth of Australia and the Government of New Zealand to establish a system for the development of joint food standards* (the Treaty), excluded MRLs for agricultural and veterinary chemicals in food from the joint Australia New Zealand food standards setting system. Australia and New Zealand independently and separately develop MRLs for agricultural and veterinary chemicals in food.

The dietary exposure assessment indicates that the residues associated with the proposed MRLs do not represent an unacceptable risk to public health and safety.

FSANZ made a Sanitary and Phytosanitary notification to the World Trade Organization (WTO). No WTO member made a submission on this Application.

Statement of Reasons

FSANZ recommends progressing this Application for the following reasons:

- The dietary exposure assessment indicates that the residues associated with the proposed MRLs for neomycin do not represent an unacceptable risk to public health and safety.

- The proposed MRLs in this Application are not the result of changes to the usage pattern for neomycin. The data before APVMA indicates that the present MRLs, based on the usage of neomycin, should be reviewed due to residues in kidney exceeding its current MRL. The requested changes will benefit all stakeholders by maintaining public confidence in the health and safety of this chemical while permitting the legal sale of products treated with neomycin.

- APVMA has assessed appropriate toxicology, residue, animal transfer, processing and metabolism studies, in accordance with the *Guidelines for Registering Agricultural and Veterinary Chemicals, the Ag and Vet Requirements Series, 1997*, to support the use of neomycin.

- The Office of Chemical Safety (OCS) of the Therapeutic Goods Administration (TGA) of the Australian Government Department of Health and Ageing has undertaken an appropriate toxicological assessment of the neomycin and has established relevant ADI.

- The Expert Advisory Group on Antimicrobial Resistance (EAGAR) has evaluated the impact of the potential residues of neomycin in the food supply and has supported the proposed MRLs in this Application.

- FSANZ has undertaken a regulation impact assessment process. That process concluded that the amendment to the Code is necessary, cost effective and of benefit to both producers and consumers.

- None of FSANZ's section 10 objectives of food regulatory measures are compromised by the proposed changes.

1. Introduction

This Application was received from APVMA on 30 March 2004 seeking amendments to Standard 1.4.2 of the Code. The proposed amendments to the Standard would align MRLs in the Code for the antibiotic neomycin with the MRLs in APVMA's MRL Standard.

1.1 Summary of the proposed MRLs for neomycin

The MRL amendments under consideration in this Application for neomycin are as follows:

Chemical Food	**MRL** **(mg/kg)**	
Neomycin		
Edible offal (mammalian)	Omit	*0.5
Fats mammalian [except milk fats]	Omit	*0.02
	Substitute	T0.5
Kidney of cattle, goats, pigs and sheep	Insert	T10
Liver of cattle, goats, pigs and sheep	Insert	T0.5
Meat (mammalian)	Omit	*0.5
	Substitute	T0.5
Milk	Omit	0.5
Milks	Insert	T1.5

Neomycin is an aminoglycoside antibiotic; it is used is to treat bacterial enteritis (scours) in cattle and pigs. Aminoglycosides are mostly bactericidal antibiotics with activity limited to aerobic bacteria and mycoplasma. This chemical has limited use in human medicine, as there are a number of alternative antibiotics available. The data before APVMA indicates that the present MRLs, based on the usage of neomycin, should be reviewed due to concerns about residues in kidney exceeding the current MRL. Both the New South Wales and Victorian Departments of Agriculture have indicated an on-going problem with neomycin residues in kidney exceeding the MRL following therapeutic use on culled cows and also on calves. Some of the above cases were the result of parenteral use. However, none of the residues found by the States in kidney exceeded the Codex MRL of 10 mg/kg.

There is no change to the dose rates, methods of use for neomycin or the withholding period. The current method of uses include:

- cattle – injection, orally and topically;
- pigs – injection or orally; and
- sheep – injection only.

1.2 The ADI for neomycin

OCS has considered and established an ADI of 0.06 mg/kg BW/ Day from the figure established by the Joint FAO/WHO Expert Committee on Food Additives (JECFA).

FSANZ does not establish ADIs for agricultural and veterinary chemicals. Further information on establishing ADIs can be found on the website of OCS at: http://www.tga.gov.au/chemicals/ocs/ or by contacting OCS on +61 2 (02) 6270 4300.

1.3 Limit of Quantification

It is proposed to omit the current MRL for neomycin for edible offal, which is at the limit of quantification (LOQ). The LOQ is the lowest concentration of an agricultural or veterinary chemical 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 and is indicated by an * in the above 'Summary of proposed MRLs for neomycin'. The proposed deletion of this MRL is associated with the APVMA's review of neomycin.

1.4 MRLs for Permits

The proposed MRLs in this Application are temporary and are indicated by a 'T' in the above 'Summary of proposed MRLs for neomycin'. These MRLs are associated with the APVMA's review of neomycin.

FSANZ does not issue permits or grant permission for the temporary use of agricultural and veterinary chemicals. Further information on MRLs for permits can be found on the website of APVMA at http://www.apvma.gov.au/ or by contacting APVMA on +61 2 6272 5158.

1.5 The National Estimated Dietary Intake

The National Estimated Dietary Intake (NEDI) for neomycin is equivalent to 25% of the ADI. This calculation is considered to be a gross overestimate of the actual consumption of neomycin as it assumes all slaughtered animals were treated and contain residues at the MRL. This calculation used summary food consumption figures derived from the National Nutrition Survey 1995 data. It is concluded that the chronic dietary exposure is less than the ADI and there is no unacceptable risk to public health and safety.

1.6 Acute dietary exposure

Neither the OCS nor the JECFA, have set an acute reference dose for neomycin.

1.7 Expert Advisory Group on Antimicrobial Resistance

The National Health and Medical Research Council established EAGAR to provide advice to government and regulatory agencies on antibiotic resistance and especially measures to reduce the risks of antibiotic resistance.

As part of its application, APVMA has supplied a letter from EAGAR in which EAGAR state that they support the proposed MRLs as a temporary measure only, until the APVMA's review of this chemical is completed.

1.8 Antibiotics as allergens

APVMA assesses the potential allergenicity of antibiotic residues in food commodities. While evidence for residues of antibiotics in foods causing allergic reactions is sparse, there is some evidence for rare occurrences of allergic reactions to the β-lactam antibiotics. For this reason β-lactam antibiotics are only used as therapeutic treatments for individual animals and not as a mass medication.

Neomycin belongs to the aminoglycoside group of antibiotics and not to the β-lactam group of antibiotics. Therefore, allergic reactions to the residues of this chemical in food are not expected to occur. No submissions were received providing data or addressing the specific occurrence of hypersensitivity to residues of neomycin in mammalian commodities.

2. Regulatory Problem

2.1 Current Regulations

APVMA has approved the MRLs of neomycin for mammalian commodities in this Application, and has made consequent amendments to the APVMA MRL Standard. APVMA's approval of MRLs for neomycin now means that there is a discrepancy between the residues of neomycin in the APVMA MRL Standard and the MRLs for this chemical in the Code.

3. Objective

The objective of this Application is to ensure that the residues of neomycin associated with the proposed MRLs do not represent an unacceptable risk to public health and safety and that the proposed MRLs permit the legal sale of food that has been legally treated. APVMA has already established MRLs under its legislation, and now seeks, by way of this Application to include the amendments in the Code.

3.1 Consideration of issues under section 10 of the *Food Standards Australia New Zealand Act 1991*

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

3.1.1 The protection of public health and safety

OCS has considered and established an ADI for neomycin. APVMA and FSANZ carry out estimations of dietary exposure to agricultural and veterinary chemicals and compare them to the ADI. Based on dietary exposure assessments, the residues associated with the proposed MRLs in this Application do not represent an unacceptable risk to public health and safety.

3.1.2 The provision of adequate information relating to food to enable consumers to make informed choices

This is not relevant for this Application.

3.1.3 The prevention of misleading or deceptive information

This is not relevant for this Application.

In addition to these objectives, subsection 10(2) requires FSANZ to have regard to a number of matters set out in paragraphs 10(2)(a) to (d). Each of these matters is discussed below.

3.1.4 The need for standards to be based on risk analysis using the best available scientific evidence

FSANZ considers proposed MRLs in accordance with the best available scientific evidence. The procedures adopted by FSANZ, the TGA and APVMA are based on a comprehensive examination of detailed scientific information. That includes a rigorous toxicological assessment and dietary exposure assessments undertaken in accordance with international protocols.

3.1.5 The promotion of consistency between domestic and international food standards

This is addressed in section 9.1.

3.1.6 The desirability of an efficient and internationally competitive food industry

The inclusion of the requested MRLs would assist in permitting the legal sale of legally treated food. Varying the Code to include the proposed MRLs would promote trade and commerce and allow food industries to continue to be efficient and competitive.

3.1.7 The promotion of fair trading in food

As the MRLs in the Code apply to all food whether produced domestically or imported, the inclusion of the MRLs would benefit all producers equally.

3.1.8 Any written guidelines formulated by the Ministerial Council for the purposes of this paragraph and notified to FSANZ

To date the Ministerial Council has not made a written notification to FSANZ of any policy guidelines that are relevant to this Application.

4. Background

4.1 The use of agricultural and veterinary chemicals

In Australia, APVMA is responsible for registering agricultural and veterinary chemical products, granting permits for use of chemical products and regulating the sale of agricultural and veterinary chemical products. Following the sale of these products, the use of the chemicals is then regulated by State and Territory 'control of use' legislation.

Before registering such a product, APVMA must be satisfied that the use of the product will not result in residues that would be an undue risk to the safety of people, including people using anything containing its residues.

When a chemical product is registered for use or a permit for use granted, APVMA includes MRLs in its 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.

4.2 Maximum Residue Limit applications

After registering the agricultural or veterinary chemical products, based on their scientific evaluations, APVMA makes applications to FSANZ to adopt the MRLs in Standard 1.4.2 of the Code. FSANZ reviews the information provided by APVMA and validates whether the dietary exposure is within agreed safety limits.

If satisfied that the residues do not represent an unacceptable risk to public health and safety and subject to adequate resolution of any issues raised during public consultation, FSANZ will then agree to adopt the proposed MRLs into Standard 1.4.2 of the Code.

FSANZ then notifies the Ministerial Council of the proposed adoption of the variation into the Code. If the Ministerial Council does not request FSANZ to review its decision, the MRLs are automatically adopted by reference under the food laws of the Australian States and Territories, after gazettal by FSANZ.

The inclusion of the MRLs in the Code has the effect of allowing legally treated produce to be legally sold, provided that the residues in the treated produce do not exceed the MRL. 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 uses, and the withdrawal of older products following review.

Appropriate toxicology, residue, animal transfer, processing and metabolism studies were provided to APVMA in accordance with the *Guidelines for Registering Agricultural and Veterinary Chemicals, the Ag and Vet Requirements Series, 1997* to support the MRLs in the commodities as outlined in this Application.

Full evaluation reports for individual chemicals are available upon request from the relevant Project Coordinator at FSANZ on +61 2 6271 2222.

4.3 Maximum Residue Limits

The MRL is the highest concentration of a chemical residue that is legally permitted or accepted in a food. The MRL does <u>not</u> 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 neomycin 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 the 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.

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

In considering the issues associated with MRLs it should be noted that MRLs and amendments to MRLs do not permit or prohibit the use of agricultural and veterinary chemicals. The approvals for the use of agricultural and veterinary chemicals and the control of the use of agricultural and veterinary chemicals are regulated by other Commonwealth, State and Territory legislation.

In summary, the MRLs in APVMA's MRL Standard are used in some jurisdictions to assist in regulating the use of agricultural and veterinary chemical products under State and Territory 'control-of-use' legislation. Whereas the 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.

4.4 Food Standards-setting in Australia and New Zealand

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

4.5 Trans Tasman Mutual Recognition Arrangement

Following the commencement of the Trans Tasman Mutual Recognition Arrangement (TTMRA) between Australia and New Zealand on 1 May 1998:

- food produced or imported into Australia, which complies with Standard 1.4.2 of the Code can be legally sold in New Zealand; and

- food produced or imported into New Zealand, which complies with the *New Zealand (Maximum Residue Limits of Agricultural Compounds) Mandatory Food Standard, 1999* can be legally sold in Australia.

5. Evaluation of Issues Raised in Public Comment

Submissions were received from:

- Sujeewa Croos
- New South Wales Food Authority (NSWFA)
- Mr Kevin Yip
- Food Technology Association of Victoria Inc (FTAV)
- Queensland Health

The submission from the Queensland Health supported this Application.

5.1 Evaluation of Issues Raised in the submission from Sujeewa Croos

5.1.1 Dietary Exposure and potential for resistance development

The submission from Sujeewa Croos raised concerns on the potential for microbial resistance occurring from the dietary exposure of residues of neomycin.

5.1.1.1 Evaluation

The use of antibiotics in Australia has been the subject of detailed consideration by the Joint Expert Technical Advisory Committee on Antibiotic Resistance (JETACAR). JETACAR has acknowledged that the use and overuse of antibiotics in human medicine is well recognised and is the major factor contributing to the development of antibiotic resistance. However, JETACAR also made a series of recommendations relating to the use of antibiotics in agriculture.

The Commonwealth Government responded to the JETACAR recommendations and has since established the Commonwealth Interdepartmental JETACAR Implementation Group to coordinate and implement the Government's response. FSANZ considers that this process is the means by which the issue of antibiotic use in agriculture can best be addressed.

Further, the National Health and Medical Research Council has established the Expert Advisory Group on Antimicrobial Resistance (EAGAR) to provide advice to governments and regulatory agencies on antimicrobial resistance.

As a part of all applications for proposed antibiotic MRLs FSANZ requests that APVMA provide a letter from EAGAR in which EAGAR state their position on the proposed antibiotic MRLs. In the case of neomycin EAGAR have stated that they support the proposed MRLs as a temporary measure only, until the APVMA's review of this chemical is completed.

This being the case, FSANZ considers that, based on this advice, the risk of antimicrobial resistance to the residues associated with the proposed MRLs do not represent an unacceptable risk to public health and safety.

5.1.2 Antibiotics as allergens

The submission from Sujeewa Croos raised concerns on the potential for hypersensitive reactions from dietary exposure to the potential residue of neomycin in food.

5.1.2.1 Evaluation

This chemical is an aminoglycoside antibiotic and there is no evidence, that FSANZ is aware of, in the scientific literature for occurrences of allergic reactions to the residues of aminoglycoside antibiotics from the consumption of residues of this chemical in foods, nor has any submission provided specific evidence relevant to this chemical.

Given the above, FSANZ considers that the residues of neomycin associated with the proposed MRLs do not represent an unacceptable risk to public health and safety, including hypersensitivity reactions.

5.2 Evaluation of Issues Raised in the submission from Food Technology Association of Victoria Inc

5.2.1 Time limits placed on MRLs for permits

FTAV enquired as to the time limits placed on permits for MRLs.

5.2.1.1 Evaluation

FSANZ does not issue permits or grant permission for the temporary use of agricultural and veterinary chemicals. These proposed MRLs have resulted from the review of neomycin by APVMA. FSANZ is unaware of any time limit placed on the APVMA's review of this chemical or any other agriculture and/or veterinary chemical.

5.2.2 Review of submissions by stakeholders

The FTAV submission stated:

> *The question is begged as to what use are responses to these requests if this additional material is not open to review by stakeholders?*

5.2.2.1 Evaluation

The purpose of inviting public submissions on applications and proposals to vary the Code is to provide FSANZ stakeholders the opportunity to submit details of the potential costs and benefits of the proposed changes to the Code or other scientific and/or technical information that could support a submission.

As submissions received did not provide evidence that this Application is not a matter of minor significance and/or would significantly adversely affect the interest of any person or body, FSANZ has not recommended to the FSANZ Board that another round of submissions be invited.

In the case of this Application, the FSANZ Board was satisfied that omitting to invite public submissions prior to making a draft assessment was warranted as this Application raises matters of minor significance or complexity. Furthermore, FSANZ considered that omitting to invite public submissions prior to making a Draft Assessment would not significantly adversely affect the interests of any person or body.

Further, if a stakeholder objects to the decision to omit to invite public submissions prior to making a draft assessment, section 63 of the FSANZ Act provides that subject to the *Administrative Appeals Act 1975*, application may be made to the Administrative Appeals Tribunal for review of a decision of FSANZ under section 36 of the FSANZ Act not to do something.

5.2.3 Antibiotics as allergens

This submission raised concerns on the potential for hypersensitive reactions from dietary exposure to the potential residue of neomycin in food.

5.2.3.1 Evaluation

This chemical is an aminoglycoside antibiotic and there is no evidence, that FSANZ is aware of, in the scientific literature for occurrences of allergic reactions to the residues of aminoglycoside antibiotics from the consumption of residues of this chemical in foods. The invitation for submissions was an opportunity for stakeholders to provide evidence of hypersensitivity to the consumption of mammalian commodities which may contain residues of neomycin. No submissions were received specifically addressing this matter.

Given the above, FSANZ considers that the residues of neomycin associated with the proposed MRLs do not represent an unacceptable risk to public health and safety, including hypersensitivity reactions.

5.2.4 Harmonisation of FSANZ and APVMA processes for establishing MRLs

The FTAV submission suggested that before any changes are made to MRLS that FSANZ, APVMA and NRA should act co-jointly and inform all and request information from all Australian stakeholders.

5.2.4.1 Evaluation

FSANZ is closely working with the Australian Government Departments of Agriculture, Fisheries and Forestry (DAFF), and Health and Ageing (DoHA) to investigate how to establish a harmonised MRL setting system. Ongoing discussions have indicated that a harmonised MRL setting system cannot be established without changes to FSANZ and/or APVMA legislation.

5.2.5 Proposed primary production standards

The submission from the FTAV stated that:

> *As FSANZ is reported as being responsible for all regulatory aspects of primary production then surely these types of chemicals and MRLs must be included in this FSANZ responsibility.*

5.2.5.1 Evaluation

It is not envisaged that the Primary Production and Processing Standards, once enacted, would give FSANZ the legislative power to regulate or enforce the use of agricultural and veterinary chemicals in Australia. However, FSANZ would continue to ensure that the potential residues in food associated with the proposed MRLs for inclusion in Standard 1.4.2 – Maximum Residue Limits would not represent an unacceptable risk to public health and safety.

APVMA would remain responsible for registering agricultural and veterinary chemical products, granting permits for use of chemical products and regulating the sale of agricultural and veterinary chemical products. Following the sale of these products, the use of the chemicals is then regulated by State and Territory 'control of use' legislation.

5.3 Evaluation of Issues Raised in the submission from New South Wales Food Authority

5.3.1 The MRLs in the Code applying to the milk at the point of sale, i.e. bulk milk ex-farm and packaged milk, while APVMA MRLs applies to milk of individual animals

NSWFA raised concerns about the establishment of MRLs at the point sale or at the farm gate.

5.3.1.1 Evaluation

The APVMA and JECFA both recommend MRLs based on residues in individual cow's milk. This method is adopted world-wide and is documented in both the EU and the USA. Hence, the APVMA's recommendations to FSANZ for milk MRLs have individual cows as the basis for its recommendations. This is the case for all milk MRLs. This approach does not account for residues in milk at the farm gate. It also does not take into account whether the treatment regime with a product is for whole-herd or partial-herd treatment.

The establishment of different MRLs based on the point of sale for the Code and the farm gate for the APVMA MRL Standard is not within the terms of reference of this application. FSANZ suggested that the NSW Food Authority may wish to pursue this matter further through the Food Regulation Standing Committee and/or the Technical Advisory Group.

5.3.2 Violations of the existing milk MRL of 0.5 mg/kg.

NSWFA raised concerns that neomycin residues detected in milk have not exceeded the MRLs.

5.3.2.1 Evaluation

Neomycin residues in milk have not been the trigger for the proposed MRLs in this application. Residues of this chemical in cattle kidney exceeding the MRL have occurred in recent years, triggering the impending review of neomycin. In undertaking a preliminary review of neomycin, APVMA considered that both tissue and milk MRLs were not supported by the data available to APVMA and JECFA. Therefore, the proposed MRLs are for the interim period of the review, so that violations would not occur.

The usage pattern, including routes of administration, dosage rates and withholding periods for neomycin relevant to the proposed MRLs remain unchanged.

FSANZ has validated the APVMA's chronic estimated dietary exposure from the proposed MRLs for neomycin, which includes the increased MRL for milk. The dietary exposure indicates that there will be no unacceptable risk to public health and safety. Also, the proposed milk MRL would ensure that during the APVMA's review of neomycin that potential violations of the existing MRL of 0.5 mg/kg would not occur.

5.3.3 The dairy industry has a policy of minimising antibiotic use

In its submission the NSWFA stated that: *The dairy industry has a policy of minimising antibiotic use.*

5.3.3.1 Evaluation

FSANZ does not regulate nor enforce the use of agricultural and veterinary chemicals in Australia and has no legislative power of control to do so. Nor does FSANZ have any statutory role in questioning the merits of, or enforcement, of the use of agricultural or veterinary chemicals. Therefore, FSANZ cannot comment on the policies of industry groups pertaining to their use of agricultural and/or veterinary chemicals.

5.3.4 Minimising the exposure to residues of neomycin

This submission raised concerns minimising the exposure to the potential residues of neomycin in food. This matter is addressed in section 5.1.1 of this Report.

5.4 Evaluation of Issues Raised in the submission from Mr Kevin Yip

5.4.1 Limit of Detection

The submission from Mr Yip raised concerns about the limit of quantification (LOQ) of neomycin in food.

5.4.1.1 Evaluation

It should be noted that none of the proposed MRLs in this Application are at the limit of quantification and FSANZ does not have the responsibility to establish the limit of detections nor the LOQ for residues of agricultural and/or veterinary chemicals in food.

The LOQ is the lowest concentration of an agricultural or veterinary chemical 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. The inclusion of the MRLs at the LOQ means that no detectable residues of the relevant chemical should occur. FSANZ incorporates MRLs at the LOQ in the Code to assist in identifying a practical benchmark for enforcement and to allow for future developments in methods of detection that could lead to a lowering of this limit.

5.4.2 Antibiotics as allergens

This submission raised concerns on the potential for hypersensitive reactions from dietary exposure to the potential residue of neomycin in food. This matter is addressed in section 5.2.3 of this Report.

5.4.3 International recognised acceptable daily intakes

This submission suggested that this Application be put on hold until the OCS of the Australian Government Department of Health and Ageing has published the result of the toxicological assessment of neomycin for establishing an acceptable daily intake.

5.4.3.1 Evaluation

OCS has considered and established an ADI of 0.06 mg/kg BW/ Day from the figure established by JECFA.

5.4.4 Options available to FSANZ for the proposed MRLs

In his submission Mr Yip had concerns about the usage of neomycin.

5.4.4.1 Evaluation

FSANZ does not regulate nor enforce the use of agricultural and veterinary chemicals in Australia and has no legislative power of control to do so, nor does FSANZ have any statutory role in questioning the merits of or enforcement of the use of agricultural or veterinary chemicals. This application has resulted from the review by APVMA of the occurrence of residues of neomycin. However, it should be noted that there is no change to the usage pattern of this chemical.

FSANZ's preferred approach is to adopt the changes to MRLs in the Code to include new or increase some existing MRLs and to delete or decrease some existing MRLs. FSANZ prefers this approach because:

- the residues associated with the MRL amendments would not result in an unacceptable risk to public health and safety;
- the changes would minimise the potential costs to primary producers and rural and regional communities in terms of legally being able to sell legally treated food;
- the changes would minimise residues consistent with the effective use of agricultural and veterinary chemicals to control pests and diseases; and
- the changes would remove discrepancies between agricultural and food legislation and assist enforcement.

6. Regulatory Options

6.1 Option 1 – status quo – no change to the existing MRLs in the Code

Under this option, the status quo would be maintained and there would be no changes in the existing MRLs to the Code.

6.2 Option 2(a) – adopt the change to MRLs to delete or decrease some existing MRLs

Under this option, only those variations that were reductions and deletions would be approved for inclusion into the Code. The proposed increases and inclusions of new MRLs would not be approved.

6.3 Option 2(b) – adopt the changes to MRLs to include new or increase some existing MRLs

Under this option, only those variations that were increases and additions of MRLs would be approved for inclusion into the Code. The proposed decreases and deletions of MRLs would not be approved.

Option 2 has been arranged into two sub-options because the impacts of each sub-option are different. Splitting the option into two sub-options also allows a more detailed impact analysis. However, FSANZ cannot legally separate these two sub-options and may only accept or reject the Application.

7. Affected Parties

The parties affected by proposed MRL amendments include:

- consumers, including domestic and overseas customers;
- growers and producers of domestic and export food commodities;
- importers of agricultural produce and foods; 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. 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 application, and the potential impacts of any regulatory or non-regulatory provisions.

8.1 Option 1 – status quo – no change to the existing MRLs in the Code

8.1.1 Benefits

- for consumers the major benefit would be the maintenance of the existing confidence in the food supply in relation to residues of neomycin;
- for producers of domestic and export meat commodities, the adoption of this option would not result in any discernable benefits;
- for importers, the adoption of this option would not result in any discernable benefits; and
- for Australian Government, State and Territory agencies, the adoption of this option would not result in any discernable benefits.

8.1.2 Costs

- for consumers there are unlikely to be any discernable costs as the unavailability of some meat commodities from certain producers is likely to be seen as typical seasonal fluctuations in the food supply;

- for producers of domestic and export meat commodities, the adoption of this option would result in costs resulting from not being able to legally sell food containing residues consistent with increased MRLs or MRL additions for neomycin. Primary producers do not produce meat commodities or use neomycin to comply with MRLs. They use neomycin to treat diseases in accordance with the prescribed label conditions, and expect that the resulting residues will be acceptable and that the legally treated meat commodities can be legally sold. If the legal use of neomycin results in the production of meat commodities that cannot be legally sold under food legislation then primary producers will incur substantial losses. Major losses for primary producers would in turn impact negatively upon rural and regional communities;

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

- for Australian Government, State and Territory agencies, the adoption of this option would create discrepancies between agricultural and food legislation thereby creating uncertainty, inefficiency and confusion in the enforcement of regulations.

8.2 Option 2(a) – adopt the changes to MRLs to delete and decrease some existing MRLs

8.2.1 Benefits

- for consumers the major benefit would be the maintenance of the existing confidence in the food supply in relation to residues of neomycin;

- for producers of domestic and export meat commodities, the adoption of this option would not result in any discernable benefits;

- for importers, the adoption of this option would not result in any discernable benefits; and

- for Australian Government, State and Territory agencies, the adoption of this option would foster community confidence that regulatory authorities are maintaining the standards to minimise residues in the food supply.

8.2.2 Costs

- for consumers there are unlikely to be any discernable costs as the unavailability of some food from certain importers is likely to be seen as typical seasonal fluctuations in the food supply;

- for producers of domestic and export meat commodities, the adoption of this option is unlikely to result in any costs, as reductions in MRLs are adopted where this is practically achievable, with little or no impact on production costs;

- for importers, the adoption of this option may result in costs, as meat commodities may not be able to be imported if these commodities contained residues consistent with the MRLs for neomycin proposed for deletion or reduction.

Any MRL deletions or reductions have the potential to restrict the importation of meat commodities and could potentially result in higher food costs and a reduced product range available to consumers, as meat commodities that exceed the new, lower MRLs could not be legally imported or sold to consumers. To identify any restrictions and possible trade impacts, Codex MRLs are addressed in section 11.5.3 and data on imported foods are addressed in section 11.5.4; and

- for Australian Government, State and Territory agencies, the adoption of this option would not result in any discernable costs, although there would need to be an awareness of changes in the standards for residues in meat commodities.

8.3 Option 2(b) – adopt the changes to MRLs to include new and increase some existing MRLs

8.3.1 Benefits

- for consumers, the major benefit would be potential flow on benefits resulting from the price and availability of meat commodities if growers can legally sell food containing residues consistent with increased MRLs or MRL additions;

- for producers of domestic and export meat commodities, the benefits of this option would result from being able to legally sell meat commodities containing residues consistent with increased MRLs or MRL additions;

- Other benefits include the consistency between agricultural and food legislation thereby minimising compliance costs to primary producers;

- for importers, the adoption of this option would result in the benefit that meat commodities could be legally imported if it contained residues consistent with increased MRLs or MRL additions; and

- for Australian Government, State and Territory agencies, the benefits of this option would include the removal of discrepancies between agricultural and food legislation thereby creating certainty and allowing efficient enforcement of regulations.

8.3.2 Costs

- for consumers there are no discernable costs;

- for producers of domestic and export meat commodities, the adoption of this option would not result in any discernable costs;

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

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

9. Consultation

9.1 World Trade Organization Notification

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.

This Application contains variations to MRLs which are addressed in the international Codex standard. MRLs in this Application also relate to chemicals used in the production of heavily traded agricultural commodities that may indirectly have a significant effect on trade of derivative food products between WTO members.

FSANZ made a Sanitary and Phytosanitary notification to the WTO for this Application in accordance with the WTO SPS agreement because 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. No WTO member has made a submission on this Application.

9.1.1 Codex MRLs

The standards of the Codex Alimentarius Commission are used as the relevant international standard or basis as to whether a new or changed standard requires a WTO notification. The Codex Alimentarius Commission has recently adopted the following MRLs for neomycin:

Neomycin Food	**Codex MRL (mg/kg)**
Fat (all species)	0.5
Kidney (all species)	10
Liver (all species)	0.5
Milk (cattle)	0.5
Muscle (all species)	0.5

Further, the recent recommendation by JECFA of an MRL for 1.5 mg/kg for milk is under consideration by Codex.

9.1.2 Imported Foods

Agricultural and veterinary chemicals are used differently in countries other than in Australia because of different pests or diseases or because different products may be used. This means that residues in imported food may still be safe for human consumption, may be different from those in domestically produced food.

The proposed deletions of the MRLs for mammalian edible offal, affects all mammalian offal other than the kidney and liver of cattle, goats, pigs and sheep. The proposed kidney and liver MRLs are equal to or greater than the MRL proposed for deletion.
However, the proposed deletion of the mammalian edible offal MRL may affect imported food containing offal other than kidney and liver of cattle, goats, pigs and sheep.

These imported products may be complying with existing MRLs even though these existing MRLs are no longer required for domestically produced food. This is because imported food may contain residues consistent with the MRL proposed for deletion.

To assist in identifying possible impacts where imported food may be affected, FSANZ has compiled the following table that states the imported quantity of mammalian edible offal for the years 2001 and 2002.

Food	**2001 Tonnes**	**2002 Tonnes**
Edible offal (mammalian)	5127	5088

FSANZ requested comments as to any possible ramifications for imports from the proposed deletion of the mammalian edible offal MRLs. No submissions were received which addressed the importation of edible offal (mammalian).

10. Conclusion and Recommendation

The dietary exposure assessments indicate that the residues associated with the proposed MRLs for neomycin do not represent an unacceptable risk to public health and safety. APVMA has already registered this chemical product and rejection of the MRLs would result in legally treated food not being able to be legally sold. Therefore, accepting the requested changes will benefit all stakeholders by maintaining public health and safety while permitting the legal sale of food treated with agricultural and veterinary chemicals to control pests and diseases and improve agricultural productivity. It is recommended that both options 2a and 2b be adopted

11. Implementation and Review

The use of neomycin and its MRLs are to be reviewed as part of APVMA's Existing Chemical Review Program. Further information on the APVMA's review process can be found at the APVMA website at http://www.apvma.gov.au/chemrev/chemrev2.shtml.

In addition, regulatory agencies involved in the regulation of chemical products continue to monitor health, agricultural and environmental issues associated with the use of chemical products.

The 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 surveys such as the Australian Total Diet Survey.

These monitoring programs and the continual review of the use of agricultural and veterinary chemicals mean that considerable scope exists to review MRLs on a continual basis.
At this time it is proposed that the proposed MRL amendments should come into effect upon gazettal and continue to be monitored by the same means as other residues in food.

ATTACHMENTS

1. Draft variation to the *Australia New Zealand Food Standards Code*
2. Notes on Terms
3. Background to Dietary Exposure Assessments
4. Summary of Submissions Received

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] *omitting from* Schedule 1 *the food and associated MRLs for the following chemical –*

NEOMYCIN	
INHIBITORY SUBSTANCE, IDENTIFIED AS NEOMYCIN	
EDIBLE OFFAL (MAMMALIAN)	*0.5
MILK	0.5

[1.2] *inserting in* Schedule 1 *the foods and associated MRLs for the following chemical –*

NEOMYCIN	
INHIBITORY SUBSTANCE, IDENTIFIED AS NEOMYCIN	
KIDNEY OF CATTLE, GOATS, PIGS AND SHEEP	T10
LIVER OF CATTLE, GOATS, PIGS AND SHEEP	T0.5
MILKS	T1.5

[1.3] *omitting from* Schedule 1 *under the entries for the following chemical, the maximum residue limit for the food, substituting –*

NEOMYCIN	
INHIBITORY SUBSTANCE, IDENTIFIED AS NEOMYCIN	
FATS (MAMMALIAN) [EXCEPT MILK FATS]	T0.5
MEAT (MAMMALIAN)	T0.5

Attachment 2

Notes on Terms

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 more realistic estimate of dietary exposure and is the preferred calculation. It may incorporate more refined food consumption data including that for specific 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 the above data is 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 OCS and Joint FAO/WHO Meeting on Pesticide Residues, the consumption data from the 1995 National Nutrition Survey (NNS) and the MRL when the 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 supervised trials median residue (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.

Attachment 3

Background To Dietary Exposure Assessments

Before an agricultural or veterinary chemical is registered, the *Agricultural and Veterinary Chemicals Code, 1994* (*Ag Vet Code Act*) requires 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.

FSANZ's primary role in developing food regulatory measures for agricultural and veterinary chemicals is to ensure that the potential residues in treated food do not represent an unacceptable risk to public health and safety. In assessing the public health and safety implications of chemical residues, FSANZ considers the dietary exposure to chemical residues from all 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 an unacceptable risk to public health and safety. In assessing this risk, FSANZ conducts dietary exposure assessments in accordance with internationally accepted practices and procedures.

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

- determination of the residues of a chemical in a treated food;
- determination of the acceptable health standard for a chemical in food (i.e. the acceptable daily intake and/or the acute reference dose); and
- calculating the dietary exposure to a chemical from all foods, using food consumption data from nutrition surveys and comparing this to the acceptable health standard.

Determination of the residues of a chemical in a treated food

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

Determination of the acceptable 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.

Both APVMA and FSANZ use these 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.

Calculating the dietary exposure

APVMA and FSANZ undertake chronic dietary exposure assessments for all agricultural and veterinary chemicals and undertake acute dietary exposure assessments where either the OCS or Joint FAO/WHO Meeting on Pesticide Residues has established an ARfD.

APVMA and FSANZ have recently agreed that all dietary exposure assessments for agricultural and veterinary chemicals undertaken by APVMA will be based on food consumption data for raw commodities, derived from individual dietary records from the latest 1995 National Nutrition Survey (NNS). The Australian Bureau of Statistics with the then Australian Government Department of Health and Aged Care undertook the NNS survey 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 were reported.

Chronic Dietary Exposure Assessment

The National Estimated Daily Intake (NEDI) represents a realistic estimate of chronic dietary exposure <u>if the chemical residue data are available</u> and is the preferred calculation. It may incorporate more refined food consumption data including that for specific 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 pesticide residue levels. When adequate information is available, monitoring and surveillance data or total diet studies may also be used such as the Australian Total Diet Survey (ATDS).

Where the data is 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 crop is treated with a pesticide; 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 pesticide over the lifetime of consumers.

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

The residues that are likely to occur in all foods are then multiplied by the daily consumption of these foods derived from individual dietary records from the latest 1995 National Nutrition Survey (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. These calculations for each food are added together to provide the total dietary exposure to a chemical from all foods.

This figure 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 this 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 crops 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 agricultural 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.

Attachment 4

Summary of Submissions Received

Submitter	Comments raised
Sujeewa Croos	Supported the deletions of the MRLs. Did not support the increase of the MRLs
Food Technology Association of Victoria	Did not support the Application.
New South Wales Food Authority	Did not support the increase of the MRL for milks.
Queensland Health	Supported the Application
Kevin Yip	Did not support the Application.

Attachment 5

FIRST REVIEW REPORT

EXECUTIVE SUMMARY

Application A535 seeks the establishment of maximum residue limits (MRLs) for mammalian commodities for the antibiotic, neomycin, into the *Australia New Zealand Food Standards Code* (the Code). It is an application from the Australian Pesticides and Veterinary Medicines Authority (APVMA) to update the Code in order to reflect the current registration status of agricultural and veterinary chemicals in use in Australia.

It is proposed to omit the current MRL for neomycin for edible offal, which is at the limit of quantification (LOQ)[1] designated as an asterisk (*) in the table below and establish temporary MRLs for kidney and liver of cattle, goats, sheep and pigs and in mammalian fats (except milk fats) and meat (mammalian). In addition, an increase is proposed from 0.5 to T1.5 mg/kg for neomycin residues in milk.

Therefore, the MRL amendments under consideration in this Application for neomycin are as follows:

Chemical Food	**MRL** **(mg/kg)**	
Neomycin		
Edible offal (mammalian)	Omit	*0.5
Fats mammalian [except milk fats]	Omit	*0.02
	Substitute	T0.5
Kidney of cattle, goats, pigs and sheep	Insert	T10
Liver of cattle, goats, pigs and sheep	Insert	T0.5
Meat (mammalian)	Omit	*0.5
	Substitute	T0.5
Milk	Omit	0.5
Milks	Insert	T1.5

On 15 April 2005, FSANZ was requested by the Australia and New Zealand Food Regulation Ministerial Council (Ministerial Council) to conduct a Review of the decision taken at FSANZ14 (December 2004) in relation to Application A535 on the basis that public health and safety are not protected.

The Ministerial Council provided the following information concerning the grounds on which the request for the first review is based:

[1] The LOQ is the lowest concentration of an agricultural or veterinary chemical 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 and is indicated by an * in the above Table

- the current MRL for Neomycin of 0.5 mg/kg is considered safe and should be achievable through good agricultural practices;

- a 20-fold increase is being proposed and further studies are needed to show that this higher level is safe;

- an MRL of 10 mg/kg provides levels in animal kidneys that are actively antibacterial;

- at this level concerns about antibiotic resistance including the views of the Expert Advisory group on Antimicrobial Resistance (EAGAR) need to be resolved; and

- potential increases in allergic reactions in sensitised individuals require further investigation.

FSANZ response to the issues raised by the Ministerial Council

FSANZ has thoroughly considered the issues raised by the Ministerial Council and considers that there are no public health and safety issues if the MRLs for neomycin are approved for the following reasons:

- FSANZ does not base its decisions on whether the MRLs are appropriate to reflect good agricultural practice (GAP), as this is the key role of the APVMA.

- The proposed MRL for kidney at 10 mg/kg was established and confirmed by the same rigorous risk assessment as used for liver and meat residues. Therefore there is no scientific basis on public health and safety grounds to accept the liver and meat MRLs and reject the kidney MRL.

- While the proposed MRL for kidney of cattle, goats, pigs and sheep is 10 mg/kg this does not mean that residues will be present at that level. The MRL is intended to account for the highest possible residue that could result from the use and not the level that will always be present. It should be noted that residues would only be expected in treated animals and not all animals.

- Based on dietary exposure assessments, the residues associated with the proposed MRLs in this application do not represent an unacceptable risk to public health and safety and account for < 25% of the ADI.

- FSANZ has not assessed whether residues at 10 mg/kg in kidneys would have antibacterial action, as this is not of material concern in assessing the safety of residues. However APVMA has advised FSANZ that neomycin residues in kidney are in a bound form and are not free to exert antibacterial action.

- As part of its Application, APVMA has supplied a letter from the Expert Advisory group on Antimicrobial Resistance (EAGAR)[2] in which EAGAR state that the proposed MRLs are supported, until the APVMA's review of this chemical is completed. EAGAR reconfirmed their original conclusion at a recent meeting on 20 June 2005, where FSANZ specifically asked their advice on all the issues raised by the Ministerial Council.

- Neomycin belongs to the aminoglycoside group of antibiotics and not to the β-lactam group of antibiotics. Therefore, allergic reactions to the residues of this chemical in food are not expected to occur (Joint Expert Committee on Food Additives (JECFA), WHO Food Additive Series 34 – Neomycin). There is no information available indicating that the residues have exhibited allergenic potential, including from countries where neomycin is used more widely than in Australia.

- Although allergic reactions due to antibiotic residues in food may seem to be a possibility in individuals who have previously been sensitized, an examination of the data shows that it is highly unlikely. The Office of Chemical safety (OCS) of the Therapeutic Goods Administration (TGA) of the Australian Government Department of Health and Ageing is not aware of any reports in the medical literature of hypersensitivity reactions due to neomycin residues in food.

- The proposed MRLs are temporary (T) until the APVMA completes its review of neomycin.

FSANZ Decision

FSANZ has undertaken an assessment and review of the proposed MRLs for neomycin as requested by the Ministerial Council for neomycin and reaffirms that the MRLs are appropriate for the following reasons:

- FSANZ supports the APVMA proposals to omit the current MRL for neomycin for edible offal, which is at the LOQ and establish temporary (T) MRLs for kidney of cattle, goats, sheep and pigs (T10 mg/kg), liver of cattle, goats, sheep and pigs (T0.5 mg/kg), mammalian fats (except milk fats) (T0.5 mg/kg) and meat (mammalian) (T0.5 mg/kg). In addition, an increase is proposed from 0.5 to T1.5 mg/kg for neomycin residues in milk;

- all MRLs are temporary, pending finalisation of the review being conducted by the APVMA;

- a detailed dietary risk assessment has been undertaken by FSANZ and it was concluded that there are no public health and safety concerns;

- advice from the Expert Advisory Group on Antimicrobial Resistance (EAGAR) re-confirms that the proposed MRLs are supported until the APVMA's review of neomycin is complete; and

[2] This is an expert advisory group established by the Australian Government to provide specialist advice to regulatory agencies on issues in relation to antimicrobial resistance.

- following an assessment of the grounds in which the Ministerial Council requested a review, FSANZ re-affirms its approval of the current drafting for Standard 1.4.2 in relation to the proposed changes to MRLs for neomycin in a range of commodities.

1. Objectives of Review

On 15 April 2005, the Ministerial Council requested a First Review of Application A535 and the draft variations to Standard 1.4.2 – Maximum Residue Limits (Australia Only) of the Code. The Ministerial Council is seeking this review on the grounds that it does not protect public health and safety.

Application A535 seeks the establishment of maximum residue limits (MRLs) for mammalian commodities for the antibiotic, neomycin, into the Code. It is an application from APVMA to update the Code in order to reflect the current registration status of agricultural and veterinary chemicals in use in Australia.

The MRL amendments under consideration in this Application for neomycin are as follows:

Chemical Food	**MRL** **(mg/kg)**	
Neomycin		
Edible offal (mammalian)	Omit	*0.5
Fats mammalian [except milk fats]	Omit	*0.02
	Substitute	T0.5
Kidney of cattle, goats, pigs and sheep	Insert	T10
Liver of cattle, goats, pigs and sheep	Insert	T0.5
Meat (mammalian)	Omit	*0.5
	Substitute	T0.5
Milk	Omit	0.5
Milks	Insert	T1.5

It is proposed to omit the current MRL for neomycin for edible offal, which is at the limit of quantification (LOQ)[3] and establish temporary (T) MRLs for kidney and liver of cattle, goats, sheep and pigs and in mammalian fats (except milk fats) and meat (mammalian). In addition, an increase is proposed from 0.5 to T1.5 mg/kg for neomycin residues in milk.

The objective of this Review is to reconsider the draft variation to Standard 1.4.2 in light of the Ministerial Council's concerns as outlined in Section 2.

2. Review on grounds requested by the Ministerial Council

The First Review was requested on the grounds that the proposed increase in the MRL for Neomycin does not protect public health and safety in that:

- the current MRL for Neomycin of 0.5 mg/kg is considered safe and should be achievable through good agricultural practices;

[3] The LOQ is the lowest concentration of an agricultural or veterinary chemical 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 and is indicated by an * in the above

- a 20-fold increase is being proposed and further studies are needed to show that this higher level is safe;

- an MRL of 10 mg/kg provides levels in animal kidneys that are actively antibacterial;

- at this level concerns about antibiotic resistance including the views of EAGAR need to be resolved; and

- potential increases in allergic reactions in sensitised individuals require further investigation.

Following a request for a formal review, FSANZ had three months to complete the review. In this particular case, the Review was required to be completed by 15 July 2005.

2.1 FSANZ evaluation of Public health and safety issues raised by the Jurisdictions

2.1.1 The current MRL for neomycin of 0.5 mg/kg is considered safe and should be achievable through good agricultural practices.

The APVMA currently consider that the proposed MRLs are appropriate and reflect current GAP.

The proposed increases in MRLs are temporary, as an interim measure to cover the occurrence of residues resulting from approved uses, while the APVMA reviews the use of neomycin. The current MRLs for liver and meat have been evaluated as safe and are maintained at the same residue limits, although they now have a temporary status. The proposed MRL for kidney at 10 mg/kg was established and confirmed by the same rigorous risk assessment as used for liver and meat residues. Therefore there is no scientific basis on public health and safety grounds to accept the liver and meat MRLs and reject the kidney MRL.

2.1.2 A 20 fold increase is being proposed and further studies are needed to show that this higher level is safe

The Office of Chemical safety (OCS) of the TGA has considered and established an Acceptable Daily Intake (ADI) for neomycin (see http://www.tga.gov.au/docs/pdf/adi.pdf). APVMA and FSANZ carry out estimations of dietary exposure to agricultural and veterinary chemicals and compare them to the ADI. Based on dietary exposure assessments, the residues associated with the proposed MRLs in this application do not represent an unacceptable risk to public health and safety and account for < 25% of the ADI.

2.1.3 An MRL of 10 mg/kg provides levels in animal kidneys that are actively antibacterial

While the proposed MRL for kidney of cattle, goats, pigs and sheep is 10 mg/kg this does not mean that residues will be present at that level. The MRL is intended to account for the highest possible residue that could result from the use and not the level that will always be present. It should be noted that residues would only be expected in treated animals and not all animals.

FSANZ has not assessed whether residues at 10 mg/kg in kidneys would have antibacterial action, as this is not of material concern in assessing the safety of residues. However APVMA has advised FSANZ that neomycin residues in kidney are in a bound form and are not free to exert antibacterial action. After ingestion the bound neomycin residues are released in the human gut but much is adsorbed onto intestinal contents and inactivated. An *in vitro* study indicates 83 to 98% of neomycin is bound to faecal matter (the Joint FAO/WHO Expert Committee on Food Additives (JECFA), WHO Food Additive Series 34 – Neomycin) http://www.inchem.org/documents/jecfa/jecmono/v34je07.htm.

Concentrations of neomycin are also diluted in the gut contents. The formula used to calculate the microbiological ADI[4] takes this into account, and with appropriate safety factors ensures that residues ingested at the MRL will not reach the Minimum Inhibitory Concentration (MIC) in the human bowel (colon). The MIC is the minimum concentration of the antibacterial agent in a given culture medium below which bacterial growth is not inhibited. When the proposed MRLs for neomycin were compared to the microbiological ADI, rather than the toxicological ADI[5], overall dietary exposure was <10% of the ADI.

Therefore concentrations resulting from consumption of residues in kidney will not exceed either the toxicological or the microbiological ADI. APVMA also advises that both JECFA and the European Agency for Evaluation of Medicinal Products (EMEA) have reported evidence that neomycin administered to humans at 30 mg/kg bw/day (equal to 1.8g/day for a 60 kg adult) produced no effect on human gut flora. As a comparison, a consumer would have to ingest in excess of 180 kg kidney/day at the MRL of 10 mg/kg to reach a level where effects on the human gut flora might be observed.

2.1.4 At this level[6] concerns about antibiotic resistance including the views of the Expert Advisory group on Antimicrobial Resistance (EAGAR) need to be resolved.

As part of its application, APVMA has supplied a letter from EAGAR in which EAGAR state that the proposed MRLs are supported, until the APVMA's review of this chemical is completed (refer to Section 2.2).

2.1.5 Potential increases in allergic reactions in sensitised individuals require further investigation

Neomycin belongs to the aminoglycoside group of antibiotics and not to the β-lactam group of antibiotics. Therefore, allergic reactions to the residues of this chemical in food are not expected to occur (Joint Expert Committee on Food Additives (JECFA), WHO Food Additive Series 34 – Neomycin). There is no information available indicating that the residues have exhibited allergenic potential, including from countries where neomycin is used more widely than in Australia.

[4] The microbiological ADI is a new health reference level which incorporates the microbiological effects of antibiotic residues, which also takes into consideration the possibility of selection of antibiotic resistant micro organisms.
[5] Established by the Office of Chemical Safety of the TGA
[6] This relates to a change from an MRL of 0.5 mg/kg in edible offal (mammalian) to a temporary MRL of 10 mg/kg in kidney of cattle, goats, pigs and sheep.

APVMA bases its evaluation of the issue of allergenicity on information evaluated by OCS who provides APVMA with a toxicology report, which includes any available information on immunotoxicity derived from appropriate tests and sources. APVMA also sources information from other evaluations, such as JECFA. Any significant issues that arise concerning specific immunotoxicological effects of antibiotics are dealt with in APVMA reports. Through this process FSANZ can be assured that all potential immunotoxic effects of antibiotics are evaluated.

Information from OCS indicates no evidence of primary sensitisation through oral exposure to the low level of antibiotic residues in food. This indicates that, in most instances, primary sensitisation will have resulted from human therapeutic use, which is at substantially higher levels than those incurred through consumption of neomycin residues in food. In these cases any information regarding potential allergenicity would be known from studies related to use in humans.

Although allergic reactions due to antibiotic residues in food may seem to be a possibility in individuals who have previously been sensitized, an examination of the data shows that it is highly unlikely. The OCS is not aware of any reports in the medical literature of hypersensitivity reactions due to neomycin residues in food.

2.2 Advice from EAGAR meeting on 20 June 2005

The National Health and Medical Research Council established EAGAR to provide advice to government and regulatory agencies on antibiotic resistance and especially measures to reduce the risks of antibiotic resistance. As part of its Application, APVMA has supplied a letter from EAGAR in which EAGAR stated that it supported the proposed MRLs as a temporary measure only, until the APVMA's review of this chemical was completed.

In light of the issues raised by the Ministerial Council, FSANZ raised these specific issues with EAGAR at its meeting on 20 June 2005. EAGAR reconfirmed its original conclusion that it supported the proposed MRLs as a temporary measure only, until the APVMA's review of this chemical is completed. EAGAR did not agree that further studies were needed to show that the increase in the MRL for kidneys was safe, as the safety has already been adequately established and discussed extensively by EAGAR at a previous meeting (**Attachment 2**).

3. Background

Neomycin is an aminoglycoside antibiotic; it is used is to treat bacterial enteritis (scours) in cattle and pigs. Aminoglycosides are mostly bactericidal antibiotics with activity limited to aerobic bacteria and mycoplasma. This chemical has limited use in human medicine, as there are a number of alternative antibiotics available. The data before APVMA indicates that the present MRLs, based on the usage of neomycin, should be reviewed due to concerns about residues in kidney exceeding the current MRL. Both the New South Wales and Victorian Departments of Agriculture have indicated an on-going problem with neomycin residues in kidney exceeding the MRL following therapeutic use on culled cows and also on calves. Some of the above cases were the result of parenteral use. However, none of the residues found by the States in kidney exceeded the Codex MRL of 10 mg/kg.

There is no change to the dose rates, methods of use for neomycin or the withholding period. The current method of uses include:

- cattle – injection, orally and topically;
- pigs – injection or orally; and
- sheep – injection only.

4. Conclusions from the Final Assessment Report

The dietary exposure assessments indicate that the residues associated with the proposed MRLs for neomycin do not represent an unacceptable risk to public health and safety. APVMA has already registered this chemical product and rejection of the MRLs would result in legally treated food not being able to be legally sold. Therefore, accepting the requested changes will benefit all stakeholders by maintaining public health and safety while permitting the legal sale of food treated with agricultural and veterinary chemicals to control pests and diseases, and improve agricultural productivity and animal welfare.

The use of neomycin and its MRLs are to be reviewed as part of APVMA's Existing Chemical Review Program. Further information on the APVMA's review process can be found at the APVMA website at http://www.apvma.gov.au/chemrev/chemrev2.shtml.

In addition, regulatory agencies involved in the regulation of chemical products continue to monitor health, agricultural and environmental issues associated with the use of chemical products.

The 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 surveys such as the Australian Total Diet Survey.

These monitoring programs and the continual review of the use of agricultural and veterinary chemicals mean that considerable scope exists to review MRLs on a continual basis.
At this time it is proposed that the proposed MRL amendments should come into effect upon gazettal and continue to be monitored by the same means as other residues in food.

4.1 Impact of Regulatory options

The following options were identified for Application A535:

4.1.1 Option 1 – status quo – no change to the existing MRLs in the Code

Under this option, the status quo would be maintained and there would be no changes in the existing MRLs to the Code.

4.1.2 Option 2(a) – adopt the change to MRLs to delete or decrease some existing MRLs

Under this option, only those variations that were reductions and deletions would be approved for inclusion into the Code. The proposed increases and inclusions of new MRLs would not be approved.

4.1.3 Option 2(b) – adopt the changes to MRLs to include new or increase some existing MRLs

Under this option, only those variations that were increases and additions of MRLs would be approved for inclusion into the Code. The proposed decreases and deletions of MRLs would not be approved.

FSANZ's preferred approach was to adopt Options 2(a) and 2(b) – to adopt the change to MRLs in the Code to include new or increase some existing MRLs and to delete or decrease some existing MRLs. FSANZ preferred this approach because:

- the residues associated with the MRL amendments would not result in an unacceptable risk to public health and safety (this benefit also applies to Option 1);
- the changes would minimise the potential costs to primary producers and rural and regional communities in terms of legally being able to sell legally treated food;
- the changes would minimise residues consistent with the effective use of agricultural and veterinary chemicals to control pests and diseases; and
- the changes would remove discrepancies between agricultural and food legislation and assist enforcement.

4.2 Consultation

FSANZ undertook one round of public consultation in relation to this Application. A total of 5 submissions were received. Issues raised in the public submissions consisted of the following:

- the potential for development of antimicrobial resistance;
- antibiotics as allergens;
- time limits placed on MRLs for permits;
- Limit of Quantification;
- stakeholders reviewing the submissions;
- harmonisation of the FSANZ and APVMA processes for establishing MRLs;
- establishing MRLs and control of agricultural and veterinary chemicals under the proposed primary production standards;
- end point for MRLs i.e. where is the MRL to be established, the point of sale or the farm gate;
- violations of the existing milk MRL for neomycin;
- use of antibiotics;
- minimising the dietary exposure to residues of neomycin; and
- internationally recognised acceptable daily intakes.

FSANZ made a comprehensive assessment of all the above issues, which is contained in the Final Assessment Report.

4.3 Statement of Reasons

FSANZ agreed at FSANZ14 to progressing this Application for the following reasons:

- The dietary exposure assessment indicates that the residues associated with the proposed MRLs for neomycin do not represent an unacceptable risk to public health and safety.

- The proposed MRLs in this Application are not the result of changes to the usage pattern for neomycin. The data before APVMA indicates that the present MRLs, based on the usage of neomycin, should be reviewed due to residues in kidney exceeding its current MRL. The requested changes will benefit all stakeholders by maintaining public confidence in the health and safety of this chemical while permitting the legal sale of products treated with neomycin.

- APVMA has assessed appropriate toxicology, residue, animal transfer, processing and metabolism studies, in accordance with the *Guidelines for Registering Agricultural and Veterinary Chemicals, the Ag and Vet Requirements Series, 1997*, to support the use of neomycin.

- The Office of Chemical Safety (OCS) of the Therapeutic Goods Administration (TGA) of the Australian Government Department of Health and Ageing has undertaken an appropriate toxicological assessment of the neomycin and has established relevant ADI.

- The Expert Advisory Group on Antimicrobial Resistance (EAGAR) has evaluated the impact of the potential residues of neomycin in the food supply and has supported the proposed MRLs in this Application.

- FSANZ has undertaken a regulation impact assessment process. That process concluded that the amendment to the Code is necessary, cost effective and of benefit to both producers and consumers.

- None of FSANZ's section 10 objectives of food regulatory measures are compromised by the proposed changes.

The proposed drafting to amend the Code is shown in **Attachment 1**.

5. Review Options

There are three options proposed for consideration under this Review:

1. reaffirm approval of the draft variation to Standard 1.4.2; or

2. reaffirm approval of the draft variation to Standard 1.4.2 subject to any amendments FSANZ considers necessary; or

3. withdraw approval of the draft variation to Standards 1.4.2 as notified to the Council.

No additional data has been presented to the Board to justify a consideration under option 2 and 3.

The recommended option is Option 1.

6. Conclusion

Following an assessment of the grounds in which the Ministerial Council requested a review, FSANZ reaffirms that the MRLs for neomycin are appropriate for the following reasons:

- FSANZ supports the APVMA proposals to omit the current MRL for neomycin for edible offal, which is at the LOQ and establish temporary (T) MRLs for kidney of cattle, goats, sheep and pigs (T10 mg/kg), liver of cattle, goats, sheep and pigs (T0.5 mg/kg), mammalian fats (except milk fats) (T0.5 mg/kg) and meat (mammalian) (T0.5 mg/kg). In addition, an increase is proposed from 0.5 to T1.5 mg/kg for neomycin residues in milk.

- All MRLs are temporary, pending finalisation of the review being conducted by the APVMA.

- A detailed dietary risk assessment has been undertaken by FSANZ and it was concluded that there are no public health and safety concerns.

- Advice from EAGAR re-confirms that the proposed MRLs are supported until the APVMA's review of neomycin is complete.

Appendix

1. Draft variation or standard to the *Australia New Zealand Food Standards Code*

Appendix 1

Draft Variations 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] *omitting from* Schedule 1 *the food and associated MRLs for the following chemical –*

NEOMYCIN	
INHIBITORY SUBSTANCE, IDENTIFIED AS NEOMYCIN	
EDIBLE OFFAL (MAMMALIAN)	*0.5
MILK	0.5

[1.2] *inserting in* Schedule 1 *the foods and associated MRLs for the following chemical –*

NEOMYCIN	
INHIBITORY SUBSTANCE, IDENTIFIED AS NEOMYCIN	
KIDNEY OF CATTLE, GOATS, PIGS AND SHEEP	T10
LIVER OF CATTLE, GOATS, PIGS AND SHEEP	T0.5
MILKS	T1.5

[1.3] *omitting from* Schedule 1 *under the entries for the following chemical, the maximum residue limit for the food, substituting –*

NEOMYCIN	
INHIBITORY SUBSTANCE, IDENTIFIED AS NEOMYCIN	
FATS (MAMMALIAN) [EXCEPT MILK FATS]	T0.5
MEAT (MAMMALIAN)	T0.5