Commonwealth of Australia

Gazette

Agricultural and veterinary chemicals

APVMA Special Gazette, 27 February 2024

Published by the Australian Pesticides and Veterinary Medicines Authority

Australian Government

Australian Pesticides and Veterinary Medicines Authority

The *Agricultural and Veterinary Chemical Code Act 1994* (the Act) commenced on 15 March 1995. The Agricultural and Veterinary Chemicals Code (the Agvet Code) scheduled to the Act requires notices to be published in the *Gazette* containing details of the registration of agricultural and veterinary chemical products and other approvals granted by the Australian Pesticides and Veterinary Medicines Authority. The Agvet Code and related legislation also requires certain other notices to be published in the *Gazette*. A reference to Agvet Codes in this publication is a reference to the Agvet Code in each state and territory jurisdiction.

ISSN 1837-7629

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General information

The APVMA Gazette is published fortnightly and contains details of the registration of agricultural and veterinary chemicals products and other approvals granted by the APVMA, notices as required by the Agricultural and Veterinary Chemicals Code (the Agvet Code) and related legislation and a range of regulatory material issued by the APVMA.

Pursuant to section 8J(1) of the Agvet Code, the APVMA has decided that it is unnecessary to publish details of applications made for the purpose of notifying minor variations to registration details. The APVMA will however report notifications activity in quarterly statistical reports.

Distribution and subscription

The APVMA Gazette is published in electronic format only and is available from the APVMA website.

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APVMA contacts

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Privacy

For information on how the APVMA manages personal information when you contact us, see our Privacy Policy.

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Neomycin reconsideration – proposed decisions on reconsideration

1) The Australian Pesticides and Veterinary Medicines Authority (APVMA) is proposing to make regulatory decisions in relation to the reconsideration of neomycin product registrations and label approvals for oral, intramammary and injectable preparations being conducted under Part 2, Division 4 of the Agricultural and Veterinary Chemicals Code scheduled to the *Agricultural and Veterinary Chemicals Code Act 1994* (Agvet Code).

2) This notice is issued under section 34AB of the Agvet Code and relates to the reconsideration of neomycin product registrations and label approvals listed in Attachment A of this notice. This reconsideration extends to compliance with any requirement prescribed by the regulation for those registrations and approvals listed in Attachment A.

3) The Draft Statement of Reasons for the proposed course of action is included as Attachment B of this notice.

4) The information on which the reasons are based is set out in Attachment C of this notice.

5) Pursuant to section 34A(1) of the Agvet Code, the APVMA proposes to:

    a. vary the relevant particulars of the chemical product registrations listed in Table 1 in Attachment A of this notice in the manner set out in paragraphs 10), 18), 25) and 34) of the statement of reasons in Attachment B to allow affirmation under section 34(A)1 of the Agvet Code; and

    b. vary the relevant particulars of the label approvals listed in Table 1 in Attachment A of this notice in the manner set out in paragraph 49) of the statement of reasons in Attachment B, as reflected in the proposed sample labels in Attachment D, to allow affirmation under section 34(A)1 of the Agvet Code.

6) Pursuant to section 34AA(1) of the Agvet Code, the APVMA proposes to:

    a. cancel the chemical product registrations listed in Table 2 in Attachment A of this notice, as the APVMA is not satisfied that the relevant particulars or conditions of the registrations can be varied in such a way as to allow the registrations to be affirmed; and

    b. cancel the label approvals listed in Table 2 in Attachment A of this notice, as the APVMA is not satisfied that the relevant particulars or conditions of the approvals can be varied in such a way as to allow the approvals to be affirmed.

Written submissions are invited

7) The APVMA invites written submissions on the proposed course of action. All submissions will be considered by the APVMA prior to finalisation of this reconsideration.

8) Submissions or requests for further information can be sent to:

Chemical Review
Australian Pesticides and Veterinary Medicines Authority
GPO Box 3262
Sydney NSW 2001

Phone: +61 2 6770 2400
Email: chemicalreview@apvma.gov.au

Please note: Submissions will be published on the APVMA website, unless you have asked for the submission to remain confidential (see public submission coversheet).

- Please lodge your submission with a public submission coversheet, which provides options for how your submission will be published.

- Note that all submissions received are subject to legislative requirements, including the *Freedom of Information Act 1982*, the *Privacy Act 1988* and the Agvet Code. In providing your submission to the APVMA, you agree to the APVMA publicly disclosing your submission in whole or summary form. The APVMA confirms that if your submission includes confidential commercial information or protected information as defined in the Agvet Code, such information will be subject to the relevant provisions of the Agvet Code including relevant limitations on use and disclosure by the APVMA.

9) The closing date for submissions is 26 May 2024.

Sheila Logan
Executive Director, Risk Assessment Capability

With the delegated authority under sections 11, 32 and 44 of the *Agricultural and Veterinary Chemicals (Administration) Act 1992*

Date: 27 February 2024

Attachments

Note: The below Attachments form part of this Notice.

- Attachment A: Product registration(s) and approved label(s) placed under reconsideration
- Attachment B: Draft Statement of Reasons
- Attachment C: Information on which the reasons are based.
- Attachment D: Proposed varied labels for neomycin chemical products

Attachment A: Product registration(s) and label approval(s) placed under reconsideration

Table 1: Product registration(s) and associated label approval(s) placed under reconsideration that the APVMA is proposing to vary to allow affirmation

Type	Approval or registration number	Name	Holder	Label approval number(s) associated with the product	Proposed varied sample label associated with the product
Product	36026	Scourban Oral Anti-Diarrhohoeal Suspension	Elanco Australasia Pty Ltd	36026/129926, 36026/100547, 36026/56642, 36026/1201, 36026/01	Label 1
Product	36237	Jurox Neomycin Sulfate Injection	Jurox Pty Ltd	36237/50976, 36237/0305, 36237/02	Label 2
Product	37241	Neomycin Penicillin 100/200 Aqueous Suspension for Intramuscular Injection	Intervet Australia Pty Ltd	37241/0410, 37241/1006, 37241/0405, 37241/0504, 37241/0301	Label 3
Product	46414	Neo-Sulcan Scour Tablets	Jurox Pty Ltd	46414/132536, 46414/0410, 46414/0101	Label 4
Product	49788	Scour-X Oral Anti-Diarrhoeal Suspension	Ausrichter Pty Ltd	49788/0101, 49788/01	Label 5

Table 2: Product registration(s) and associated label approval(s) placed under reconsideration that the APVMA is proposing to cancel

Type	Approval or registration number	Name	Holder	Label approval number(s) associated with the product
Product	38696	Special Formula 17900 Forte-V Lactating Intramammary Antibiotic Suspension	Zoetis Australia Pty Ltd	38696/60502, 38696/0809, 38696/0402, 38696/0899
Product	49851	Mastalone Intramammary Suspension for Lactating Cows	Zoetis Australia Pty Ltd	49851/106743, 49851/0709, 49851/01
Product	52782	CCD Neomycin (Neomycin Sulphate Water Soluble Powder)	CCD Animal Health Pty Ltd	52782/0705, 52782/1003, 52782/1100
Product	67805	Abbeyneo Antibiotic Feed Additive	Abbey Laboratories Pty Ltd	67805/140221

Attachment B: Statement of Reasons

1) The APVMA has reconsidered chemical product registrations containing neomycin and associated label approvals under Part 2, Division 4 of the Code scheduled to the *Agricultural and Veterinary Chemicals Code Act 1994* (Agvet Code) to determine whether the:

   a) chemical products meet the safety criteria (section 5A of the Agvet Code), the efficacy criteria (section 5B of the Agvet Code), and the trade criteria (section 5C of the Agvet Code), and

   b) labels meet the labelling criteria (section 5D of the Agvet Code), and

   c) chemical products and labels comply with the requirements prescribed by the *Agricultural and Veterinary Chemicals Code Regulations 1995* (Agvet Regulations).

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Material findings of fact and reasons for the proposed decisions

Chemical products

2) Section 34(1)(b) and (d) of the Agvet Code provides that the APVMA must affirm the registration for a chemical product if, and only if, it is satisfied that the product:

   a) meets the safety criteria (section 5A),

   b) meets the efficacy criteria (section 5B),

   c) meets the trade criteria (section 5C), and

   d) complies with any requirement prescribed by the regulations.

3) Section 34(2) of the Agvet Code provides that subsection 34(1) applies only to the extent that the APVMA decides to reconsider matters covered by the subsection.

4) The APVMA has decided to reconsider all matters covered by subsection 34(1) in relation to the reconsideration of oral, intramammary and injectable chemical products containing neomycin.

   a) For chemical products containing a combination of active constituents, the APVMA has decided to reconsider the matters covered by subsections 34(1)(b) and (d) only to the extent that they relate to the fact that the chemical product contains the active constituent neomycin.

      I. The following additional active constituents are present in various neomycin products: calcium, dihydrostreptomycin, glycine, hyoscine, pectin, kaolin, magnesium, novobiocin, oleandomycin, oxytetracycline, procaine penicillin, potassium, sodium, streptomycin, sulfadimidine, sulfadiazine, vitamin B12 (riboflavin) and vitamin B1 (thiamine).

      II. The impact of the additional active constituents on products under reconsideration will be based on previous product specific assessments.

Consideration of whether registered chemical products meet the safety criteria

5) Section 5A(1) of the Agvet Code provides that a chemical product meets the safety criteria if use of the product, in accordance with any instructions approved or to be approved by the APVMA for the constituent or product or contained in an established standard:

   a) is not, or would not be, an undue hazard to the safety of people exposed to it during its handling or people using anything containing its residues (section 5A(1)(a))

   b) is not, or would not be, likely to have an effect that is harmful to human beings (section 5A(1)(b))

   c) is not, or would not be, likely to have an unintended effect that is harmful to animals, plants or things or to the environment (section 5A(1)(c)).

6) For the purposes of being satisfied that neomycin chemical products meet the safety criteria, the APVMA has had regard to the criteria set out in section 5A(3)(a) of the Agvet Code as follows:

a) Section 5A(3)(a)(i) of the Agvet Code – the toxicity of the product and its residues, including metabolites and degradation products, in relation to relevant organisms and ecosystems, including human beings:

I. The APVMA has considered the following in having regard to the toxicity of neomycin chemical products and their residues:

- information on the toxicity of the constituent neomycin and its residues, including the neomycin health-based guidance values, as set out in the *Neomycin Review Technical Report*.
- the impact of formulation excipients and where relevant additional active constituents, on the toxicity of the chemical products to relevant organisms and ecosystems, including human beings.
- the impact of use of products on target animal safety.

II. The APVMA is satisfied that an Acceptable Daily Intake (ADI) of 0.06 mg/kg bw/day is considered to be adequately protective of human health, as set out in the *Neomycin Review Technical Report*

III. The APVMA is satisfied that applying a margin of exposure of 100 to a point of departure 6 mg/kg bw/day is adequately protective for use of neomycin chemical products by occupational handlers, as set out in the *Neomycin Review Technical Report.*

IV. The APVMA is satisfied that there is no requirement to establish an acute reference dose (ARfD).

V. The APVMA is satisfied that exposure to neomycin below the regulatory levels set out in the *Neomycin Review Technical Report*, is not likely to have an unintended effect that is harmful to animals, plants or things or to the environment.

VI. The APVMA is satisfied that there is sufficient information to assess the impact of formulation excipients on the toxicity of neomycin chemical products and their residues, in relation to relevant organisms and ecosystems including human beings, where formulation specific food-safety (marker-residue depletion) information is available.

VII. The APVMA is **not satisfied** that there is sufficient data to assess the impact of formulation excipients on the toxicity of neomycin chemical products and their residues, in relation to relevant organisms and ecosystems including human beings, where formulation specific food-safety (marker-residue depletion) information is not available as detailed in the *Neomycin Review Technical Report*.

VIII. The APVMA is satisfied that there is sufficient information to assess target animal safety with regards to the use of products.

b) Section 5A(3)(a)(ii) of the Agvet Code – the relevant poison classification of the product under the law in force in this jurisdiction.

I. Neomycin is listed in Schedule 4 of the Standard for the Uniform Scheduling of Medicines and Poisons for all product types.

II. The APVMA is satisfied that the current neomycin poison classification remains appropriate based on the assessment of available toxicology data as outlined in the *Neomycin Review Technical Report*.

c) Section 5A(3)(a)(iii) of the Agvet Code – how the product is formulated.

I. The APVMA has considered the existing registration records in having regard to how the injectable, intramammary and oral chemical products containing neomycin are formulated. Chemical products containing neomycin are formulated as follows:

- injectable solution
- oral powder, pre-mix (feed additive or as an additive to animal drinking water)
- oral solution/suspension
- oral tablet
- intramammary preparation

II. The APVMA is satisfied that how each product is formulated is acceptable and appropriate for the use of the product.

d) Section 5A(3)(a)(iv) of the Agvet Code – the composition and form of the constituents of the product.

I. The APVMA has considered the existing registration records in having regard to the composition and form of the constituents in chemical products containing neomycin, including the Declaration of Composition for the source of active constituent and the manufacturer's specification of other constituents.

II. The APVMA is satisfied that the composition and form of the neomycin active constituents, formulation excipients, and, where relevant in specific neomycin chemical products, the additional active constituents listed in paragraph 4)a)I. remain appropriate based on previous assessments and the approved use of the products.

e) Section 5A(3)(a)(v) of the Agvet Code – any conditions to which its registration is, or would be, subject.

I. Product registrations are currently subject to the conditions prescribed in items 1, 2, 3, 4, 5, 6 and 7 of the table in regulation 17C(2) of the Agvet Regulations.

II. Under section 23(1)(b), the APVMA may also impose conditions on the approval or registration as the APVMA thinks appropriate.

- Each product is subject to a shelf-life condition imposed by the APVMA under section 23(1)(b). For each product, the condition states that the product can only be supplied if label includes an expiry date no greater than the shelf life of the product. The shelf life is determined by the APVMA for each product based on an assessment of product specific information and storage conditions.
- The APVMA is **not satisfied** that the conditions applied to each product remain appropriate, where the conditions do not include the storage conditions for which the expiry date applies or

where products are subject to an interim shelf-life condition, as further discussed in paragraph 7)d)I. and the *Neomycin Review Technical Report*.

f) Section 5A(3)(a)(vi) of the Agvet Code – any relevant particulars that are, or would be, entered in the Register for the product:

I. The APVMA has considered the relevant particulars on the Record for each registered chemical product containing neomycin including: distinguishing number, instructions for the use, the distinguishing name, the constituents, the concentration of each constituent, the composition and purity of each active constituent, the formulation type, the net contents, the holder of the registration, the name of each manufacturer, the address of each site at which the chemical product is manufactured, the nominated agent (if relevant) and the date of entry of these particulars.

II. The APVMA is **not satisfied** that the instructions for use on neomycin products would not pose an undue hazard to the safety of people exposed to it during its handling or people using anything containing its residues for the following reason:

- The instructions for use of chemical products containing neomycin may result in exposure of occupational handlers at levels that exceed the margin considered adequately protective to the user, as set out in the Neomycin *Review Technical Report.*

III. The APVMA is **not satisfied** that the instructions for use of some neomycin chemical products would not be likely to have an effect that is harmful to human beings through residues in food for the following reasons:

- There is insufficient information to assess the level of neomycin residues expected from the use of chemical products containing neomycin in accordance with instructions in the following situations:
    - injectable formulations containing 200 mg/mL neomycin sulfate as the only active constituent for use in cattle, sheep and pigs
    - feed or drinking water additive powder for use in cattle, pigs and poultry
    - oral tablets and oral liquid (drench) for use in calves
    - intramammary preparations in lactating cattle.
- There is insufficient information to establish appropriate withholding periods for neomycin chemical products and this may result in unacceptable levels of residues in food producing animals and their products, as set out in the *Neomycin Review Technical Report*.

IV. The APVMA **is not satisfied** that use of neomycin chemical products in accordance with instructions for use would not have an unintended effect that is harmful to target animals.

- The instructions for use, specifically in relation to restraints, contraindications, dosage regime, administration directions and precaution statements do not adequately outline the risk that the use of neomycin chemical products may cause ototoxicity and nephrotoxicity in target animals, as described in the *Neomycin Review Technical Report*.

V. The APVMA **is not satisfied** that the use of neomycin chemical products in accordance with instructions would not be likely to have an unintended effect that is harmful to non-target species. The instructions for use, specifically in relation to environmental protection, do not adequately address risks to non-target species, as detailed in the *Neomycin Review Technical Report.*

VI. The APVMA is **not satisfied** that the name of the active constituent and associated concentration of the active constituent as recorded in the register is accurate when expressed as 'neomycin sulfate', as opposed to 'neomycin (as neomycin sulfate)'.

VII. The APVMA is satisfied that all other relevant particulars that are entered in the Register for neomycin chemical products remain appropriate.

g) Section 5A(3)(a)(via) of the Agvet Code – whether the product conforms, or would conform, to any standard made for the product under section 6E to the extent that the standard relates to matters covered by subsection (1).

I. There are no standards made under section 6E which are relevant to the safety of chemical products containing neomycin.

h) Section 5A(3)(a)(vii) of the Agvet Code – any matters prescribed by the regulations.

I. Regulation 8AB(1)(a) of the Agvet Regulations prescribes the method of analysis (if any) of the chemical composition and form of the constituents of the chemical product.

- The APVMA has considered the existing registration records in having regard to the method of analysis of the chemical composition and form of the constituents of neomycin chemical products. The APVMA is satisfied of the method of analysis.

II. Regulations 8AB(1)(b) and (c) of the Agvet Regulations prescribe, respectively, that for a product manufactured in Australia—whether each step in the manufacture of the product complies, or will comply, with the manufacturing principles and the Australian GMP Code, and for a product manufactured outside Australia—whether each step in the manufacture of the product complies, or will comply, with a standard that the APVMA has determined is comparable to the manufacturing principles and the Australian GMP Code.

- The APVMA has considered existing registration records regarding whether each step in the manufacture of the products complies with the manufacturing principles and the Australian GMP Code (for products manufactured in Australia) or with a standard that the APVMA has determined is comparable to the manufacturing principles and the Australian GMP Code (for products manufactured outside Australia).

- The APVMA is satisfied that each of the veterinary chemical products containing neomycin comply with the requirements of regulations 8AB(1)(b) and (c) of the Agvet Regulations.

III. Regulations 8AB(1)(d), I and (f) of the Agvet Regulations do not apply based on the use patterns of neomycin products.

7) Under section 5A(3)(b) of the Agvet Code, the APVMA may have regard to one or more of the following matters in determining whether a chemical product meets the safety criteria:

a) Section 5A(3)(b)(i) of the Agvet Code – the acceptable daily intake of each constituent contained in the product.

I. The APVMA has considered the toxicity of neomycin, as set out in the *Neomycin Review Technical Report*, and is satisfied the acceptable daily intake of 0.06 mg/kg bw/day remains appropriate.

b) Section 5A(3)(b)(ii) of the Agvet Code – any dietary exposure assessment prepared under subsection 82(4) of the *Food Standards Australia New Zealand Act 1991* as a result of any proposed variation notified under section 82(3) of that Act in relation to the product, and any comments on the assessment given to the APVMA under section 82(4) of that Act.

I. There has not been a dietary exposure assessment prepared under subsection 82(4) of the *Food Standards Australia New Zealand Act 1991*.

c) Section 5A(3)(b)(iii) of the Agvet Code – whether any trials or laboratory experiments have been carried out to determine the residues of the product and, if so, the results of those trials or experiments and whether those results show that the residues of the product will not be greater than limits that the APVMA has approved or approves.

I. The APVMA is **not satisfied** that sufficient trials or laboratory experiments have been carried out to determine the residues of the products expected from use in the following situations, as detailed in the *Neomycin Review Technical Report*:

- injectable formulations containing 200 mg/mL neomycin sulfate as the only active constituent for use in cattle, sheep and pigs
- feed or drinking water additive powder for use in cattle, pigs and poultry
- oral tablets and oral liquid/suspension (drench) for use in calves
- intramammary preparations in lactating cattle.

II. The APVMA is satisfied that sufficient trials or laboratory experiments have been carried out for the APVMA to approve an appropriate maximum residues limit (MRL) for the use of neomycin injectable formulations containing 100 mg/mL neomycin (as the sulfate) and 200 mg/mL procaine penicillin for use in cattle, sheep and pigs, and that these results show the residues of neomycin chemical products will not be greater than the proposed maximum limits, as detailed in the *Neomycin Review Technical Report.*

d) Section 5A(3)(b)(iv) of the Agvet Code – the stability of the product.

I. As outlined in the *Neomycin Review Technical Report*, the APVMA is **not satisfied** of:

- the stability of all products when stored as directed, specifically when subjected to cold temperatures and light
- the stability of products that are currently subject to an interim shelf-life condition of registration, where supporting stability data has not been provided to confirm the validity of this provisional shelf-life and enable approval of a final shelf-life.

e) Section 5A(3)(b)(v) of the Agvet Code – the specifications for containers for the product.

I. There were no concerns identified in relation to the specifications for containers for neomycin chemical products.

f) Section 5A(3)(b)(vi) of the Agvet Code – such other matters as it thinks relevant.

I. The APVMA has considered the possible development of antimicrobial resistance to neomycin, stemming from the use patterns addressed in this reconsideration, and the significance of the development of antimicrobial resistance to neomycin to human health.

II. The APVMA is **not satisfied** the current instructions for use adequately address concerns in relation to reducing the potential development of antimicrobial resistance, as detailed in the *Neomycin Review Technical Report*.

8) The APVMA is therefore **not satisfied** that the use of chemical products containing neomycin meets the safety criteria as defined in section 5A of the Agvet Code.

Consideration of whether registered chemical products can be varied to meet the safety criteria

9) Section 34A(1) of the Agvet Code provides that if the APVMA is not satisfied under section 34(1) but is satisfied that the relevant particulars or conditions of the registration can be varied in such a way as to allow the registration to be affirmed, the APVMA must vary the relevant particulars or conditions.

10) The APVMA has considered whether registered chemical products can be varied in such a way as to meet the safety criteria set out in Section 5A(1) as follows:

a) To address concerns raised in paragraphs 6)a) and 7)c) when considering the criteria in sections 5A(3)(a)(i) and 5A(3)(b)(iii) of the Agvet Code in relation to the residues that are expected from use of neomycin chemical products in food producing situations:

I. The APVMA proposes to vary the products listed in Table 1 of Attachment A as follows:

- For product formulations where the risk to food-safety could not be adequately assessed due to insufficient residues data, as set out in the *Neomycin Review Technical Report* and paragraph 7)c)I of this statement of reasons, remove use on calves, cattle, sheep, pigs, poultry and lactating cattle.

- For products approved for use on horses, add the restraint *'DO NOT USE in horses that may be used for human consumption.'* and remove the withholding periods for horse meat.

II. The APVMA is **not satisfied** that products in Table 2 of Attachment A can be varied to address the food-safety concerns, as there is insufficient product specific food-safety (marker-residue depletion) information for all uses of these products, as outlined in the *Neomycin Review Technical Report*.

b) To address concerns raised in paragraph 6)f) when considering the criteria in section 5A(3)(a)(vi) of the Agvet Code in relation to any relevant particulars that are, or would be, entered in the Register for the product:

I. The APVMA is **not satisfied** that the instructions for use of the registered chemical products containing neomycin listed in Table 2 in Attachment A of this notice can be varied in such a way as to meet the safety criteria, as there is insufficient product specific food-safety (marker-residue

depletion) information to assess the risks associated with all uses of these products and their subsequent residues in target animals, as set out in the *Neomycin Review Technical Report*.

II. The APVMA proposes to vary the relevant particulars of chemical products containing neomycin listed in Table 1 in Attachment A as follows, as detailed in the *Neomycin Review Technical Report*:

- In relation to the exposure of occupational handlers from use of oral (liquid), oral (tablet), and injectable products, add the safety direction *'Wash hands after use*'.
- In relation to the exposure through residues in food:
  - For product formulations where the risk to food-safety could not be adequately assessed due to insufficient residues information, as set out in the *Neomycin Review Technical Report*, remove use on calves, cattle, sheep, pigs, poultry and lactating cattle.
  - For the injectable neomycin product approved for use on cattle, pigs and sheep:
    - add the withholding period *'MILK: DO NOT USE in lactating or pregnant cows or ewes where milk may be used or processed for human consumption.'* As the residues in milk resulting from use of the product could not be assessed
    - add the restraint *'RE-TREATMENT INTERVAL: DO NOT RE-TREAT cattle for 12 months after the last dose in one course of treatment. DO NOT RE-TREAT sheep for 4 months after the last dose in one course of treatment. DO NOT RE-TREAT pigs for 10 weeks after the last dose in one course of treatment'*
    - add the withholding period: *'MEAT: DO NOT USE less than 42 days for cattle, 35 days for sheep and 100 days for pigs before slaughter for human consumption.'*
  - For all neomycin chemical products approved for use on horses, add the restraint *'DO NOT USE in horses that may be used for human consumption.'* And remove the withholding periods for horse meat.
- In relation to target animal safety:
  - For all neomycin products, add the contraindication *'Not to be used in target animals with compromised renal function, gastrointestinal inflammation and those being treated with other potentially nephrotoxic drugs.'*
  - For all injectable neomycin products, add the dosage and administration instruction *'Treatment should not be repeated at less than 24-hour intervals'* to reduce the risk of nephrotoxicity in target animals.
  - For parenteral (injectable) products, add the precautions statement *'Neomycin exhibits concentration-dependent killing and a post-antibiotic effect. Repeated daily administration or overdosage with neomycin can cause renal damage and deafness. Care should be taken in animals with known or suspected impaired renal function. Care should be taken in animals being treated with other potentially nephrotoxic substances, such as NSAIDs. Where practical, it is recommended to weigh young animals to ensure accurate dosage calculation based on bodyweight.'*

- For oral products, add the precautions statement *'Neomycin exhibits concentration dependent killing and a post-antibiotic effect. Overdosage with neomycin can cause renal damage and deafness. Care should be taken in animals with known or suspected impaired renal function. While this is unlikely at therapeutic doses, care should be taken in animals being treated with other potentially nephrotoxic substances, such as NSAIDs. Where practical, it is recommended to weigh young animals to ensure accurate dosage calculation based on bodyweight.'*

- For all neomycin chemicals products that recommend a minimum duration of treatment of 5 days for salmonellosis, add the instructions: *'If no improvement in symptoms is seen after 5 days, the diagnosis should be reestablished.'*

- In relation to environmental exposure, for products with pack sizes greater than 1 kg or 1 L, add to the instructions for use *'DO NOT contaminate wetlands or water courses with this product or used containers.'* to mitigate risks to non-target organisms.

- For products where the active constituent is expressed in the Register as 'neomycin sulfate':

  - vary the name of the active constituent recorded in the Register to 'neomycin (as neomycin sulfate)'

  - vary the concentration of the active constituent recorded in the Register to accurately reflect the amount of neomycin in the product.

c) To address concerns raised in paragraphs 6)e) and 7)d) when considering criteria in sections 5A(3)(a)(v) and 5A(3)(b)(iv) of the Agvet Code in relation to conditions to which registrations are subject and the stability of products, as detailed in the *Neomycin Review Technical Report*:

I. The APVMA proposes to vary the shelf-life condition of registrations to include the storage conditions for which the expiry date applies. Specifically, add the respective storage temperatures of between 2 ˚C and 8 ˚C (refrigerate), below 25 ˚C (air conditioning) or below 30 ˚C (room temperature).

II. The APVMA proposes to vary the storage instructions for use as follows:

- For liquid products in Table 1 of Attachment A, add the storge instruction *'Do not freeze.'*

- For all products in Table 1 of Attachment A, add the storage instruction *'Protect from light.'*

III. For products which have an interim shelf life, the APVMA proposes to impose the following condition of registration under section 23(1)(b) of the Agvet Code:

- *'Within 2 years of the publication of the section 34AC notice of the neomycin final regulatory decision, you are required to provide real time stability data to enable the APVMA to determine and establish an appropriate shelf life.'*

d) To address concerns raised in paragraph 7)f) when considering criteria in sections 5A(3)(b)(vi) of the Agvet Code in relation to such other matters as the APVMA thinks relevant:

I. The APVMA proposes to vary the instructions for use all products in Table 1 of Attachment A to reduce the likelihood of the development of antimicrobial resistance as follows, as detailed in the *Neomycin Review Technical Report*:

- add the statement of claims *'Indiscriminate use of [Name of Product] may contribute to the development of antibiotic resistance'*
- add the general directions *'Prudent Use: Veterinarians must assess the clinical need for antimicrobials prior to prescription and must communicate the risk of antimicrobial resistance in humans and the need for prudent use in animals. Culture and sensitivity tests should be performed when appropriate to determine susceptibility of the causative organism(s). Empirical therapy may be instituted before results of susceptibility studies are known; however, once these results become available, the antibiotic treatment should be adjusted accordingly.'*
- add the restraint *'DO NOT prescribe [Name of Product], prior to investigating the use of non-antibiotic options. If [Name of Product] is indicated and selected for use, prudent prescribing practices (appropriate dose, duration and frequency) should be followed to minimise treatment failure while limiting the possible emergence of antimicrobial resistance.'*

11) The APVMA is satisfied that the relevant particulars and conditions of the registered chemical products listed in Table 1 in Attachment A of this notice can be varied as set out in paragraph 10), to meet the safety criteria.

12) The APVMA is **not satisfied** that the relevant particulars or conditions of the registered chemical products in Table 2 in Attachment A of this notice can be varied to meet the safety criteria.

Consideration of whether registered chemical products meet the efficacy criteria

13) Section 5B(1) of the Agvet Code provides that a chemical product meets the efficacy criteria if use of the product, in accordance with instructions approved, or to be approved, by the APVMA for the product or contained in an established standard, is, or would be, effective according to criteria determined by the APVMA by legislative instrument.

a) Neomycin products are not contained in an established standard.

b) The criteria for veterinary chemical products are listed in Part 3 of the *Agricultural and Veterinary Chemicals Code (Efficacy Criteria) Determination 2014*, including:

I. criteria based on type of product, as set out in clause 5; and

II. criteria based on demonstrated effectiveness, as set out in clause 6.

14) Section 5B(2) of the Agvet Code provides that for the purposes of being satisfied as to whether a chemical product meets the efficacy criteria, the APVMA must have regard to the following:

a) Section 5B(2)(a) – whether any trials or laboratory experiments have been carried out to determine the efficacy of the product and, if so, the results of those trials or experiments.

I. The APVMA has considered the assessments of previously submitted information for the registration and variation of chemical products containing neomycin.

II. The APVMA is satisfied that this information continues to support the efficacy of neomycin chemical products for the use pattern on the currently approved labels, and for variations to instructions for use that are within existing use patterns.

III. The variations to the instructions for use proposed to satisfy the safety criteria (as set out in paragraph 9) are within existing use patterns, except for the increase to a 24-hour retreatment interval for injectable products that currently have an administration interval of every 8-12 hours.

IV. The APVMA is **not satisfied** that trials or laboratory experiments have been carried out to support the efficacy of injectable products if the re-treatment interval is increased from 8–12 hours to 24 hours to address target animal safety, as outlined in paragraph 10)b)II and in the *Neomycin Review Technical Report*.

b) Section 5B(2)(b) – any conditions to which its registration is, or would be, subject.

I. The APVMA has considered the conditions of registration which apply to chemical products containing neomycin. The APVMA is satisfied that the current conditions of registration are appropriate in relation to the efficacy of the chemical products, and that no additional conditions of registration are required to satisfy the efficacy criteria.

c) Section 5B(2)(c) – any relevant particulars that are, or would be, entered in the Register for the product.

I. The APVMA has considered the relevant particulars that are entered in the Register for chemical products containing neomycin with regards to efficacy.

II. The APVMA satisfied that the relevant particulars entered into the Register with regards to efficacy remain appropriate for the use patterns on the currently approved labels, and for variations to instructions for use that are within existing use patterns.

III. The variations to the instructions for use proposed to satisfy the safety criteria (as set out in paragraph 9) are within existing use patterns, except for the increase to a 24-hour retreatment interval for injectable products that currently have an administration interval of every 8–12 hours.

IV. The APVMA **is not satisfied** that the relevant particulars entered in the Register for use of injectable products on horses are appropriate if the re-treatment interval needs to be increased from 8–12 hours to 24 hours to address target animal safety, as outlined in paragraph 10)b)II and in the *Neomycin Review Technical Report*.

d) Section 5B(2)(ca) – whether the product conforms, or would conform, to any standard made for the product under section 6E to the extent that the standard relates to matters covered by subsection (1);

I. There are no standards made under section 6E which are relevant to the efficacy of chemical products containing neomycin.

e) Section 5B(2)(d) any matters prescribed by the regulations.

I. There are no regulations which are relevant to the efficacy of chemical products containing neomycin.

15) The APVMA is **not satisfied** that the use of injectable chemical products containing neomycin on horses will meet the efficacy criteria as set out in section 5B of the Agvet Code, if products are varied as proposed increase the retreatment interval from 8–12 hours to 24 hours.

16) The APVMA is satisfied that chemical products, except for the situation outlined in paragraph 15) above, meet the efficacy criteria as set out in section 5B of the Agvet Code, based on the criteria for demonstrated effectiveness for veterinary chemical products determined by the APVMA by legislative instrument.

Consideration of whether registered chemical products can be varied to meet the efficacy criteria

17) Section 34A(1) of the Agvet Code provides that if the APVMA is not satisfied under section 34(1) but is satisfied that the relevant particulars or conditions of the registration can be varied in such a way as to allow the registration to be affirmed, the APVMA must vary the relevant particulars or conditions.

18) The APVMA has considered whether registered chemical products can be varied in such a way as to meet the efficacy criteria set out in section 5B of the Agvet Code as follows:

a) To address concerns identified in paragraphs 14)a) and 14)c), when considering criteria in sections 5B(2)(a) and 5B(2)(c) of the Agvet Code, the APVMA proposes to remove the use on horse from neomycin injectable chemical products that current have a re-treatment interval of less than 24 hours.

19) The APVMA is satisfied that the relevant particulars or conditions of the registered chemical products containing neomycin in the situation outlined in paragraph 15) above can be varied to meet the efficacy criteria as set out in section 5B of the Agvet Code.

Consideration of whether registered chemical products meet the trade criteria

20) Section 5C(1) of the Agvet Code provides that a product meets the trade criteria if use of the product, in accordance with instructions approved, or to be approved, by the APVMA or contained in an established standard, does not, or would not, unduly prejudice trade or commerce between Australia and places outside Australia.

21) Section 5C(3) of the Agvet Code provides that for the purposes of the operation of this Code in relation to a particular chemical product, the APVMA is required to have regard to the matters set out in subsections (1) and (2) only to the extent prescribed by the regulations; or if there are no such regulations—to the extent that the APVMA thinks the matters are relevant.

a) Regulation 8AD(2) of the Agvet Regulations provides that if it can be reasonably expected that a chemical product will be used in relation to a crop or animal, a product of which might be provided to a place outside Australia; or a crop that will be fed to animals a product of which might be provided to a place outside Australia then the APVMA must have full regard to the matters set out in section 5C(1) and (2) of the Agvet Code.

I. Chemical products containing neomycin are approved for use on cattle, sheep, pigs, poultry, horses, dogs and cats in the form of injectable, oral and intramammary formulations. Cattle, sheep, pigs, poultry, eggs and cattle dairy products are considered major export commodities. It is therefore reasonably expected that a product of these animals (cattle, sheep, pigs and poultry) might be provided to a place outside of Australia.

22) For the purposes of being satisfied that the neomycin chemical products meet the trade criteria as described in section 5C(1) of the Agvet Code, the APVMA has considered the criteria set out in section 5C(2) for the use patterns listed in paragraph 21) and has determined as follows:

a) Section 5C(2)(a) – any conditions to which its registration is, or would be, subject.

I. The APVMA is satisfied that the conditions of registration currently applied to chemical products containing neomycin remain appropriate with regards to the risk to trade or commerce between Australia and places outside Australia.

b) Section 5C(2)(b) – any relevant particulars that are, or would be, entered in the Register for the product.

I. The relevant particulars entered in the Register for each registered product containing neomycin have been reviewed, including the instructions for use for the chemical products.

II. The instructions for the use of injectable chemical products containing neomycin on cattle, pigs, sheep and dairy cattle in the form of an injectable may result in residues of neomycin in major export commodities that exceed residue tolerance requirements for importing countries, as set out in the *Neomycin Review Technical Report*.

III. The instructions for the use of oral chemical products containing neomycin in calves in the form of an oral solution or oral tablet may result in residues of neomycin in major export commodities that exceed residue tolerance requirements for importing countries, as set out in the *Neomycin Review Technical Report*.

IV. The instructions for the use of oral chemical products containing neomycin in poultry, pigs and cattle in the form of a feed additive may result in residues of neomycin in major export commodities that exceed residue tolerance requirements for importing countries, as set out in the *Neomycin Review Technical Report*.

V. The instructions for the use of oral chemical products containing neomycin in poultry in the form of an additive added to animal drinking water may result in residues of neomycin in poultry and eggs that exceed residue tolerance requirements for importing countries, as set out in the *Neomycin Review Technical Report*.

VI. The instructions for the use of intramammary chemical products containing neomycin in lactating cattle in the form of an intramammary solution may result in residues of neomycin in lactating cattle and dairy products that exceed residue tolerance requirements for importing countries, as set out in the *Neomycin Review Technical Report*.

VII. The APVMA is **not satisfied** that the instructions for use entered in the Register for chemical products containing neomycin, approved for use on food producing species including cattle, sheep, pigs and poultry would not unduly prejudice trade or commerce between Australia and places outside Australia.

c) Section 5C(2)(ba), whether the product conforms, or would conform, to any standard made for the product under section 6E to the extent that the standard relates to matters covered by subsection (1);

I. There are no standards made under section 6E that are relevant to the risk to trade or commerce between Australia and places outside Australia.

d) Section 5C(2)(c), any matters prescribed by the regulations.

I. The APVMA has had regard to Regulation 8AD, as outlined in paragraph 21) above, in considering the risk to trade or commerce between Australia and places outside Australia posed by the use of chemical products containing neomycin.

23) The APVMA is **not satisfied** that the use of chemical products containing neomycin, in accordance with instructions for use for approved for major export commodities, does not, or would not, unduly prejudice trade or commerce between Australia and places outside Australia.

Consideration of whether registered chemical products can be varied to meet the trade criteria

24) Section 34A(1) provides that if the APVMA is not satisfied under section 34(1) but is satisfied that the relevant particulars or conditions of the registration can be varied in such a way as to allow the registration to be affirmed, the APVMA must vary the relevant particulars or conditions.

25) The APVMA has considered whether the instructions for use for registered neomycin products can be varied in such a way as to meet the trade criteria set out in Section 5C(1) as follows:

a) To address concerns identified in paragraph 22)b), when considering the criteria in section 5C(2)(b) of the Agvet Code, in relation to the any relevant particulars (specifically, instructions for use) that are entered in the Register:

I. The APVMA is **not satisfied** that the instructions for use of the registered chemical products containing neomycin listed in Table 2 in Attachment A of this notice can be varied in such a way as to meet the trade criteria, as there is insufficient product-specific information to assess the risks associated with all uses of these products and their subsequent residues in target animals, as set out in the *Neomycin Review Technical Report*.

II. The APVMA proposes to vary the instructions for use of chemical products containing neomycin listed in Table 1 in Attachment A as follows, as detailed in the *Neomycin Review Technical Report*:

- Remove the uses on calves, cattle, pigs, poultry and sheep for where the risk to trade or commerce between Australia and places outside Australia could not be adequately assessed due to insufficient product-specific relevant laboratory studies or trials.

- For the injectable neomycin product approved for use on cattle, pigs and sheep, include the following trade advice statement:

    - *'EXPORT SLAUGHTER INTERVAL (ESI): DO NOT USE less than 57 days for cattle, 56 days for sheep and 100 days for pigs before slaughter for export. Before using this product, confirm the current ESI from the manufacturer on 1800 033461 or the APVMA website (apvma.gov.au/residues).'*

26) The APVMA is satisfied that the relevant particulars or conditions of chemical products containing neomycin listed in Table 1 in Attachment A of this notice can be varied in the ways set out in paragraph 25)a)II above, so that the chemical products containing neomycin meet the trade criteria.

27) The APVMA is **not satisfied** that the relevant particulars or conditions of the registered chemical products containing neomycin in Table 2 in Attachment A of this notice can be varied in such a way as to meet the trade criteria.

Consideration of whether registered chemical products comply with any requirement prescribed by the regulations

28) Regulation 16 of the Agvet Regulations prescribes the particulars of a chemical product which must be recorded in the Register pursuant to section 20(1)(c) of the Agvet Code:

a) The APVMA has had regard to the particulars recorded in the Register for each chemical product containing neomycin.

b) The APVMA is **not satisfied** that all particulars prescribed by regulation 16 of the Agvet Regulations and recorded in the Register for neomycin chemical products remain appropriate.

I. The APVMA is **not satisfied** that the name of the active constituent and associated concentration of the active constituent as recorded in the register is accurate when expressed as 'neomycin sulfate', as opposed to 'neomycin (as neomycin sulfate)'.

29) Regulation 17C of the Agvet Regulations prescribes conditions to which the registration of a chemical product is subject.

a) The APVMA is satisfied that holders of neomycin chemical products can comply with the conditions prescribed by regulation 17C of the Agvet Regulations.

30) Regulation 18 of the Agvet Regulations prescribes conditions of registration relating to the containers for chemical products.

a) The APVMA is satisfied that neomycin chemical products comply with the conditions prescribed by regulation 18 of the Agvet Regulations.

31) Regulation 42 of the Agvet Regulations prescribes standards for chemical products to which chemical products must conform in accordance with section 87 of the Agvet Code.

a) Under regulation 42(3)(e) a veterinary chemical product or a constituent in a veterinary product must comply with a standard specified in the British Pharmacopoeia; or the British Pharmacopoeia (Veterinary); or the European Pharmacopoeia; or the United States Pharmacopeia if the APVMA has not otherwise specified a standard.

b) The APVMA is satisfied that constituents in neomycin chemical products conform to a standard prescribed by Regulation 42(3)(e) of the Agvet Regulations.

32) The APVMA is **not satisfied** that neomycin chemical products meet the all the requirements prescribed by the regulations.

Consideration of whether registered chemical products can be varied to comply with any requirement prescribed by the regulations

33) Section 34A(1) provides that if the APVMA is not satisfied under section 34(1) but is satisfied that the relevant particulars or conditions of the registration can be varied in such a way as to allow the registration to be affirmed, the APVMA must vary the relevant particulars or conditions.

34) The APVMA has considered whether the particulars prescribed by regulation 16 of the Agvet Regulations and recorded in the Register for neomycin chemical products can be varied in such a way so that neomycin chemical product comply with the requirements prescribed by regulations as follows:

a) The APVMA proposes to vary the name of the active constituent recorded in the Register from 'neomycin sulfate' to 'neomycin (as neomycin sulfate)'.

b) The APVMA proposed to vary the concentration of the active constituent recorded in the Register to accurately reflect the amount of neomycin in the product.

35) The APVMA is satisfied that the particulars prescribed by regulation 16 of the Agvet Regulations and recorded in the Register for neomycin chemical products listed in Table 1 in Attachment A can be varied in the ways set out in paragraph 34) above.

Conclusion of consideration of registered chemical products

36) Section 34A(1) of the Agvet Code provides that if the APVMA is not satisfied under section 34(1) but is satisfied that the relevant particulars or conditions of the registration can be varied in such a way as to allow the registration to be affirmed, the APVMA must vary the relevant particulars or conditions.

37) The APVMA is satisfied that the relevant particulars or conditions of registered neomycin chemical products listed in Table 1 in Attachment A of this notice can be varied to meet the safety criteria, efficacy criteria, trade criteria any requirement prescribed by the regulations. Therefore, APVMA proposes to vary the relevant particulars and conditions as follows:

a) Vary the instructions for use for products listed in Table 1 of Attachment A, as set out in the *Neomycin Review Technical Report* and paragraphs 10), 18) and 25) of this statement of reasons.

b) For products where the active constituent is expressed in the Register as 'neomycin sulfate', vary the name and concentration of the active constituent, as set out in paragraphs 10)b)II. and 34).

c) Vary the shelf-life condition of registrations to include the storage conditions for which the expiry date applies. Specifically, add the respective storage temperatures of between 2 ˚C and 8 ˚C (refrigerate), below 25 ˚C (air conditioning) or below 30 ˚C (room temperature).

d) For products which have an interim shelf life, impose the following condition of registration under section 23(1)(b) of the Agvet Code – '*Within 2 years of the publication of the section 34AC notice of the neomycin final regulatory decision, you are required to provide real time stability data to enable the APVMA to determine and establish an appropriate shelf life.'*

38) The APVMA is **not satisfied** that the relevant particulars or conditions of the neomycin chemical products registrations listed in Table 2 in Attachment A of this notice can be varied in such a way as to allow the registration to be affirmed for the following reasons:

a) The APVMA is **not satisfied** that the safety and trade risks associated with current approved uses of these chemical products can be adequately assessed due to insufficient product-specific residues information, as set out in the *Neomycin Review Technical Report* and paragraphs 10) and 25) of this statement of reasons.

b) The APVMA is **not satisfied** that the relevant particulars or conditions of these chemical products can be varied meet the to satisfy the safety and trade criteria.

39) Section 34AA(1) provides that if the APVMA does not affirm the registration, it must suspend or cancel the registration.

Labels for chemical products

40) Section 34(1)(c) and (d) of the Agvet Code provides that the APVMA must affirm the approval of a product label if, and only if, it is satisfied that the label:

a) meets the labelling criteria

b) complies with any requirement prescribed by the regulations.

41) Subsection 34(2) of the Agvet Code provides that subsection 34(1) applies only to the extent that the APVMA decides to reconsider matters covered by this subsection.

42) The APVMA has decided to reconsider all matters covered by subsection 34(1) in relation for label approvals of oral, intramammary and injectable chemical products containing neomycin.

a) For chemical products containing a combination of active constituents, the APVMA has decided to reconsider the matters covered by subsections 34(1)(c) and (d) only to the extent that they relate to the fact that the chemical product contains the active constituent neomycin.

I. The following additional active constituents are present in various neomycin products: calcium, dihydrostreptomycin, glycine, hyoscine, pectin, kaolin, magnesium, novobiocin, oleandomycin, oxytetracycline, procaine penicillin, potassium, sodium, streptomycin, sulfadimidine, sulfadiazine, vitamin B12 (riboflavin) and vitamin B1 (thiamine).

II. The impact of the additional active constituent on relevant chemical product registrations will be considered based on previous assessments of those active constituents.

Consideration of whether approved labels for chemical products meet the labelling criteria and comply with any requirement prescribed by the regulations

43) Section 5D(1) of the Agvet Code provides that a label for containers for a chemical product ‘meets the labelling criteria’ if the label contains adequate instructions relating to the following as are appropriate:

a) the circumstances in which the product should be used (5D(1)(a));

b) how the product should be used (5D(1)(b));

c) the times when the product should be used (5D(1)(c));

d) the frequency of the use of the product (5D(1)(d));

e) the withholding period after the use of the product (5D(1)(e));

f) the re-entry period after the use of the product (5D(1)(f));

g) the disposal of the product when it is no longer required (5D(1)(g));

h) the disposal of containers of the product (5D(1)(h));

i) the safe handling of the product and first aid in the event of an accident caused by the handling of the product (5D(1)(i));

j) any matters prescribed by the regulations (5D(1)(j). In this regard, regulation 8AE(1) of the Agvet Regulations prescribes the following:

I. Regulation 8AE(1)(a) – for a chemical product that is a veterinary chemical product, the duration of the treatment.

II. Regulation 8AE(1)(b) – the prevention of undue prejudice to trade or commerce between Australia and places outside of Australia.

III. Regulation 8AE(1)(c) – the appropriate signal words (if any) required by the current Poisons Standard.

IV. Regulation 8AE(1)(d) – for a chemical product that is a date-controlled product, the storage of containers for the product.

V. Regulation 8AE(1)(e) – any other matter determined by the APVMA CEO under regulation 8AE(2).

44) Regulation 17 of the Agvet Regulations prescribes the particulars of a label approval which must be recorded in the relevant APVMA file pursuant to sections 21(a), 6(2)(c) and 21(c)(iva) of the Agvet Code.

45) Regulations 18B to 18J (inclusive) of the Agvet Regulations prescribe the conditions of approval to which label approvals are subject.

46) Section 5D(2) of the Agvet Code provides that for the purposes of being satisfied as to whether the current approved labels for containers for neomycin chemical products meet the labelling criteria, the APVMA must have regard to the criteria set out in section 5D(2). The APVMA has considered these criteria as follows:

a) Section 5D(2)(a) of the Agvet Code – any conditions to which its approval is, or would be, subject.

I. The APVMA is satisfied that the label approvals comply with the conditions to which they are subject, as prescribed by regulations 18B to 18J (inclusive) of the Agvet Regulations, and that no further conditions of approval are required.

b) Section 5D(2)(b) of the Agvet Code – any relevant particulars and instructions that are, or would be, entered in the relevant APVMA file for the label.

I. In relation to the relevant particulars that are entered in the APVMA file for the label:

- The APVMA is not satisfied that the name of the active constituent and the proportion of the active constituent entered into the APVMA file for the labels are accurate when expressed as ‘neomycin sulfate’, as opposed to ‘neomycin (as neomycin sulfate)’.

- The APVMA is satisfied that, excluding the name of the active constituent, the associated proportion of the active constituent, and the instructions contained on the label (as discussed below), all other particulars that are recorded in the relevant APVMA file remain appropriate.

II. In relation to the instructions on circumstances in which the product should be used (s5D(1)(a)):

- The APVMA is satisfied that the target species listed on approved labels remain appropriate for the injectable products containing 100 mg/mL neomycin (as the sulfate) and 200 mg/mL procaine penicillin.

- The APVMA is **not satisfied** that the target species listed on the approved labels of all other products are appropriate, as detailed in paragraphs 10), 18) and 25) of this statement of reasons and the *Neomycin Review Technical Report*. Specifically, the uses on cattle (including calves and lactating cows), sheep, poultry and pigs where the food-safety and trade risks could not be adequately assessed, and use of injectable products on horses where there is insufficient information to support continued efficacy if the re-treatment interval is increased from 8–12 hours to 24 hours to address target animal safety concerns.

- The APVMA is **not satisfied** that the instructions for use are adequate, unless the approved label contains the instructions and restraints detailed in paragraph 10) and 25) of this statement of reasons and in the *Neomycin Review Technical Report*.

III. In relation to the instructions on how the product should be used (s5D(1)(b)):

- The APVMA is **not satisfied** that the instructions on how products should be used contained on approved labels, including environmental protection statements, precautions and dosage and administration instructions, remail adequate to address the environmental safety and target animal safety risks, as detailed in the *Neomycin Review Technical Report*.

IV. In relation to the instructions on the times when the product should be used (s5D(1)l):

- The APVMA is satisfied that the instructions on the times where products should be used contained on approved labels remain appropriate for registered neomycin products.

V. In relation to the instructions on the frequency of the use of the product (s5D(1)(d)).

- The APVMA is **not satisfied** that the instructions on the frequency of use of products (specifically, the dosage intervals and re-treatment intervals) on approved labels are acceptable for injectable neomycin chemical products due to unacceptable risks to animal safety and food safety, as detailed in the *Neomycin Review Technical Repor*t.

- The APVMA is satisfied that the instructions on the frequency of use on approved labels, other than those of injectable products, are acceptable, as detailed in the *Neomycin Review Technical Report*.

VI. In relation to the instructions on the withholding period after the use of the product (s5D(1)(e)):

- The APVMA is **not satisfied** that withholding periods contained on approved labels are adequate to mitigate unacceptable risks to safety in all situations for neomycin products, as detailed in the Neomycin *Review Technical Report*.

VII. In relation to the instructions on the re-entry period after the use of the product (s5D(1)(f)):

- Re-entry periods are not required on the labels of neomycin chemical products.

VIII. In relation to the instructions on the disposal of the product when it is no longer required (s5D(1)(g):

- The APVMA is **not satisfied** that the instructions contained on all labels for the disposal of the product when it is no longer required are adequate or consistent with the best practice guide in the *Veterinary Labelling Code*.

IX. In relation to the instructions on the disposal of containers for the product (s5D(1)(h):

- The APVMA is **not satisfied** that disposal instructions for containers for neomycin chemical products presented in packages of greater than 1 L or 1 kg of are adequate or consistent with best practice guide in the *Veterinary Labelling Code*.

X. In relation to the instructions on the safe handling of the product and first aid in the event of an accident caused by the handling of the product (s5D(1)(i).

- The APVMA is satisfied that the first aid instructions contained on the approved label of neomycin products under reconsideration remain appropriate.

- The APVMA is **not satisfied** that the safety handling instructions for neomycin included on current labels, are adequate as detailed in the *Neomycin Review Technical Report*.

XI. Any matters prescribed by the regulations (s5D(1)(j).

- Regulation 8AE(1)(a) of the Agvet Regulations – for a chemical product that is a veterinary chemical product, the duration of the treatment.
    - The APVMA is satisfied that the instructions for the duration of the treatment using veterinary chemical products containing neomycin remain appropriate.

- Regulation 8AE(1)(b) of the Agvet Regulations – the prevention of undue prejudice to trade or commerce between Australia and places outside of Australia.
    - The APVMA is **not satisfied** that there are adequate instructions to prevent undue prejudice to trade or commerce between Australia and places outside of Australia on current label approvals that permit the use of neomycin on major export commodities, as detailed in the *Neomycin Review Technical Report* and paragraphs 22)b) of this statement of reasons.

- Regulation 8AE(1)(c) of the Agvet Regulations – the appropriate signal words (if any) required by the current Poisons Standard.
    - The following signal words are required on labels to meet the current Poisons Standard:
        - As an S4 veterinary product, ‘PRESCRIPTION ANIMAL REMEDY’
    - The following additional cautionary statements are required:
        - KEEP OUT OF REACH OF CHILDREN
        - As a poison only for the treatment of animals, the signal heading must include the statement ‘FOR ANIMAL TREATMENT ONLY’
    - The APVMA is satisfied that the appropriate signal words required by the current Poisons Standard are included on approved labels.

- Regulation 8AE(1)(d) of the Agvet Regulations – for a chemical product that is a date-controlled product, the storage of containers for the product.
    - In regulation 4 of the Agvet Regulations, a date-controlled chemical product is defined as each veterinary chemical product and an agricultural chemical product specified in Schedule 1 to the Agvet Regulations.
    - The APVMA is **not satisfied** that the instructions for storage of containers for chemical products containing neomycin remain appropriate if they do not address cold storage or exposure to light.
- Regulation 8AE(1)(e) of the Agvet Regulations – any other matter determined by the APVMA CEO under regulation 8AE(2).
    - There are no other matters determined by the APVMA CEO under regulation 8AE(2) in relation to neomycin label approvals.

c) Section 5D(2)(c) of the Agvet Code – whether the label conforms, or would conform, to any standard made for the label under section 6E to the extent that the standard relates to matters covered by subsection (1).

I. There is no standard made for neomycin label approvals under section 6E.

d) Section 5D(2)(d) of the Agvet Code – any matters prescribed by the regulations.

I. Regulation 17 of the Agvet regulations prescribes particulars to be included for labels.

- The APVMA is **not satisfied** that the prescribed particulars defined by regulation 17(1)(c) and 17(1)(d) on current labels will be correct for products where the active constituent is currently referred to as 'neomycin sulfate'. As outlined in the *Neomycin Review Technical Report,* the active constituent is neomycin and the active constituent should be correctly expressed in terms of 'neomycin (as neomycin sulfate)'.
- The APVMA is satisfied that other prescribed particulars on labels are correct.

II. Regulation 18E requires that if a labelling standard has not been made by the APVMA and the product is a veterinary chemical product, then the label must comply with the requirements of the *Veterinary Labelling Code*.

III. The APVMA has reviewed the current label approvals for neomycin veterinary products and is **not satisfied** that the approved labels have adequate instruction to comply with the current *Veterinary Labelling Code.*

IV. The APVMA is satisfied that neomycin labels approvals are compliant with all other matters prescribed by the regulations; specifically, the conditions to which label approvals are subject as prescribed by regulations 18B to 18J (inclusive).

47) The APVMA is **not satisfied** that current approved labels for containers for neomycin chemical products contain adequate instructions relating to the matters set out in paragraph 43) above.

Consideration of whether approved labels for chemical products can be varied as to meet the labelling criteria and comply with any requirement prescribed by the regulations

48) Section 34A(1) provides that if the APVMA is not satisfied under section 34(1) but is satisfied that the relevant particulars or conditions of the approval can be varied in such a way as to allow the approval to be affirmed, the APVMA must vary the relevant particulars or conditions.

49) The APVMA has considered whether the labels approved for containers for neomycin chemical products can be varied in such a way as to meet the labelling criteria and comply with any requirement prescribed by the regulations as follows:

a) To address concerns identified in paragraph 46)b), when considering the criteria in paragraph 5D(2)(b) of the Agvet Code:

I. In relation to the concerns identified in paragraph 46)b)I. and 46)d)I. in relation to the relevant particulars that are entered in the APVMA file for the label; specifically, the name of the active constituent and the proportion of the active constituent:

- The APVMA proposes to vary the name of the active constituent recorded in the APVMA file to 'neomycin (as neomycin sulfate)'.

- The APVMA proposes to vary the proportion the active constituent recorded in the APVMA file to accurately reflect the amount of neomycin in the product.

II. In relation to the concerns identified in paragraph 46)b)II. regarding the instructions for the circumstances in which a product should be used (s5D(1)(a)):

- The APVMA is **not satisfied** that label approvals listed in Table 2 in Attachment A can be varied in such a way that there will be adequate instructions in relation to the circumstances in which the products should be used, as the APVMA is **not satisfied** that the safety and trade risks can be adequately assessed due to insufficient product-specific residues data for all uses of these products, as set out in the *Neomycin Review Technical Report* and paragraphs 10) and 25) of this statement of reasons.

- The APVMA is satisfied that the label approvals listed in Table 1 in Attachment A of this notice can be varied to remove uses on cattle (including calves), sheep, poultry and pigs where the food-safety and trade risks could not be adequately assessed, and use of injectable products on horses where there is insufficient information to support continued efficacy if the re-treatment interval is increased, as set out in the *Neomycin Review Technical Report* and paragraphs 10), 18) and 25) of this statement of reasons.

- The APVMA proposes to further vary the instructions for the circumstances in which a product is to be used for the labels listed in Table 1 in Attachment A of this notice as follows, as set out in paragraph 10) and 25) of this statement of reasons and reflected in the proposed labels in Attachment D of this notice:

  - For the labels of all neomycin products:

    - add the statement of claims *'Indiscriminate use of [Name of Product] may contribute to the development of antibiotic resistance.'*

- add the general directions '*Prudent Use: Veterinarians must assess the clinical need for antimicrobials prior to prescription and must communicate the risk of AMR in humans and the need for prudent use in animals. Culture and sensitivity tests should be performed when appropriate to determine susceptibility of the causative organism(s). Empirical therapy may be instituted before results of susceptibility studies are known; however, once these results become available, the antibiotic treatment should be adjusted accordingly'.*

- add the restraint *'DO NOT prescribe [Name of Product], prior to investigating the use of non-antibiotic options. If [Name of Product] is indicated and selected for use, prudent prescribing practices (appropriate dose, duration and frequency) should be followed to minimise treatment failure while limiting the possible emergence of antimicrobial resistance.'*

- add the contraindication *'Not to be used in animals with compromised renal function, gastrointestinal inflammation and those being treated with other potentially nephrotoxic drugs.'*

  - For the labels of neomycin products approved for use on horses, add the restraint *'DO NOT USE in horses that may be used for human consumption.'*

III. In relation to the concerns identified in paragraph 46)b)III. regarding the instructions for how the product should be used (s5D(1)(b)), the APVMA proposes to vary the approved labels listed in Table 1 in Attachment A of this notice as follows, as set out in the *Neomycin Review Technical Report* and reflected in the proposed labels in Attachment D of this notice:

- On labels for containers greater than 1 kg or 1 L, add the environmental protections statement *'DO NOT contaminate wetlands or water courses with this product or used containers.'*

- For parenteral (injectable products), add the precaution statement *'Neomycin exhibits concentration-dependent killing and a post-antibiotic effect. Repeated daily administration or overdosage with neomycin can cause renal damage and deafness. Care should be taken in animals with known or suspected impaired renal function. Care should be taken in animals being treated with other potentially nephrotoxic substances, such as NSAIDs. Where practical, it is recommended to weigh young animals to ensure accurate dosage calculation based on bodyweight.'*

- For oral products, add the precaution statement *'Neomycin exhibits concentration dependent killing and a post-antibiotic effect. Overdosage with neomycin can cause renal damage and deafness. Care should be taken in animals with known or suspected impaired renal function. While this is unlikely at therapeutic doses, care should be taken in animals being treated with other potentially nephrotoxic substances, such as NSAIDs. Where practical, it is recommended to weigh young animals to ensure accurate dosage calculation based on bodyweight.'*

- On all labels that recommend a minimum duration of treatment of 5 days for salmonellosis, add the dosage and administration instructions *'If no improvement in symptoms is seen after 5 days, the diagnosis should be reestablished.'*

IV. In relation to the concern identified in paragraph 46)b)V. regarding the instructions for the frequency of the use of the product (s5D(1)(d)), the APVMA proposes to vary the relevant label

approvals listed in Table 1 in Attachment A of this notice as follows, as set out in the *Neomycin Review Technical Report* and reflected in the proposed labels in Attachment D of this notice:

- For all injectable neomycin products, add the dosage and administration instruction *'Treatment should not be repeated at less than 24-hour intervals'* to reduce the risk of nephrotoxicity in target animals.

- For the labels of injectable neomycin products approved for use on cattle, sheep and pigs, add the restraint *'RE-TREATMENT INTERVAL: DO NOT RE-TREAT cattle for 12 months after the last dose in one course of treatment. DO NOT RE-TREAT sheep for 4 months after the last dose in one course of treatment. DO NOT RE-TREAT pigs for 10 weeks after the last dose in one course of treatment.'*

V. In relation to the concerns identified in paragraph 46)b)VI. regarding the instructions for the withholding period after the use of the product (s5D(1)(e)), the APVMA proposes to vary the labels listed in Table 1 in Attachment A as follows, as set out in the *Neomycin Review Technical Report* and reflected in the proposed labels in Attachment D of this notice:

- For the labels of injectable neomycin product approved for use on cattle, pigs and sheep, add the withholding period *'MEAT: DO NOT USE less than 42 days for cattle, 35 days for sheep and 100 days for pigs before slaughter for human consumption.'* and *'MILK: DO NOT USE in lactating or pregnant cows or ewes where milk may be used or processed for human consumption.'*

- For the labels of all neomycin chemical products approved for use on horses, remove the withholding periods for horse meat.

VI. In relation to the concerns identified in paragraph 46)b)VIII and 46)b)IX regarding the disposal of the product when it is no longer required (s5D(1)(g)) and disposal of containers for the product (s5D(1)(h)), respectively, the APVMA proposes to vary the relevant label approvals listed in Table 1 in Attachment A to include the following disposal instructions, as set out in the *Neomycin Review Technical Report* and reflected in the proposed labels in Attachment D of this notice:

- For small containers (up to 1 Kg or 1 L) – *'Dispose of container by wrapping with paper and putting in garbage.'*

- For injectable products – *'Discarded needles/sharps should immediately be placed in a designated and appropriately labelled 'sharps' container.'*

- For oral products greater than 1 L – *'Triple-rinse container and dispose of rinsate in compliance with relevant local, state or territory government regulations. Do not dispose of undiluted chemicals on-site. If recycling, replace cap and return clean container to recycler or designated collection point. If not recycling, break, crush, or puncture container and deliver to an approved waste management facility. If an approved waste management facility is not available, dispose of in compliance with relevant local, state or territory government regulations. Do not burn empty containers or product.'*

VII. In relation to the concerns identified in paragraph 46)b)X. regarding the safe handling of the product (s5D(1)(i)), the APVMA proposes to vary the relevant label approvals listed in Table 1 in Attachment A to include the following safety instructions, as set out in the *Neomycin Review Technical Report* and reflected in the proposed labels in Attachment D of this notice:

- For oral (liquid), oral (tablet) and injectable formulations containing neomycin, add the safety direction *'Wash hands after use.'*

VIII. In relation to concerns identified in paragraph 46)b)XI. regarding any matters prescribed by the regulations (s5D(1)(j)):

- For the prevention of undue prejudice to trade or commerce between Australia and places outside of Australia (Regulation 8AE(1)(b)), the APVMA proposes to vary the approved labels listed in Table 1 in Attachment A of this notice as follows, as set out in the *Neomycin Review Technical Report* and reflected in the proposed labels in Attachment D of this notice:
  - Remove the uses on calves, cattle, sheep, pigs, poultry from the labels where the risk to trade could not be adequately assessed due to insufficient product-specific information, as set out in the *Neomycin Review Technical Report*.
  - For the label of the injectable neomycin product approved for use on cattle, pigs and sheep, add the following trade advice statement:
    - *'EXPORT SLAUGHTER INTERVAL (ESI): DO NOT USE less than 57 days for cattle, 56 days for sheep and 100 days for pigs before slaughter for export. Before using this product, confirm the current ESI from the manufacturer on 1800 033461 or the APVMA website (apvma.gov.au/residues).'*
- For the storage of containers for products that are date-controlled chemical products (Regulation 8AE(1)(d)), the APVMA proposed to vary the approved labels listed in Table 1 in Attachment A of this notice as follows, as set out in the *Neomycin Review Technical Report* and reflected in the proposed labels in Attachment D of this notice:
  - For liquid neomycin products, add the storge instruction *'Do not freeze.'*
  - For all neomycin products, add the storage instruction *'Protect from light.'*

IX. For the label approvals listed in Table 1 in Attachment A of this notice, the APVMA is proposing to make the variations outlined above so that it can be satisfied that the instructions regarding the matters listed in section 5D(1) of the Agvet Code are adequate.

b) In relation to the concerns identified when considering the criteria in section 5D(2)(d) of the Agvet Code regarding compliance with the *Veterinary Labelling Code*, the APVMA is satisfied that label approvals listed in Table 1 in Attachment A will meet the relevant *Veterinary Labelling Code* if they are varied in the ways set out above, and in the additional ways set out below, as reflected in the proposed labels in Attachment D of this notice.

I. For antibiotic products, the class or group (by mode of action) of the active constituents should be identified under product claims. Therefore, the APVMA proposes to:

- Add the statement *'Neomycin belongs to aminoglycosides class of antibiotics.'* to the label of the product that contain neomycin as the only antibiotic active constituent.
- Add the statement *'Neomycin belongs to aminoglycosides and procaine penicillin belongs to penicillins class of antibiotics.'* to the label of the product that contains a combination of active constituents neomycin and penicillin.

- Add the statement *'Sulfadimidine is a synthetic antimicrobial agent that contain the sulfonamide group. Sulfadiazine belongs to sulfonamide class of antibiotics. Streptomycin and neomycin belong to aminoglycosides class of antibiotics.'* to the label of the product that contains the active constituents sulfadimidine, sulfadiazine, streptomycin and neomycin.

- Add the statement *'Sulfadimidine is a synthetic antimicrobial agent that contain the sulfonamide group. Sulfadiazine belongs to sulfonamide class of antibiotics. Neomycin belongs to aminoglycosides class of antibiotics.'* to the label of the products that contain the active constituents sulfadimidine, sulfadiazine and neomycin.

II. For the labels of neomycin products where safety directions have been added to mitigate occupational safety risks, as set out in paragraphs 10)b)II., add the signal heading 'READ SAFETY DIRECTIONS BEFORE OPENING OR USING'.

III. For the labels of neomycin products where the active constituent statement is expressed as the concentration of *'neomycin sulfate'*, amend the active constituent statement to include the concentration of '*neomycin (as neomycin sulfate)'*, as per varied relevant particulars.

50) Section 34A(3) of the Agvet Code provides that if the variation would affect instructions for use on a label, the APVMA must not make the variation until it has consulted each co-ordinator designated for a jurisdiction and taken into account any recommendations made by the co-ordinators.

a) The APVMA will consult with each co-ordinator designated for a jurisdiction and take into account any recommendations made by the co-ordinators prior to making any variations that would affect instructions for use on a label, noting the proposals set out in this statement of reasons may be amended after consideration of all consultation submissions.

51) The APVMA is satisfied that the relevant particulars of the label approvals listed in Table 1 in Attachment A can be varied in the ways set out in paragraph 49), so that the labels contain adequate instructions so as to meet the labelling criteria relating to the components set out in paragraph 43) and comply with any requirement prescribed by the regulations.

52) The APVMA is **not satisfied** that the relevant particulars or conditions of the label approvals in Table 2 in Attachment A can be varied so that labels contain adequate instructions so as to meet the labelling criteria relating to the components set out in paragraph 43) as there is insufficient relevant residues data to assess risks to trade and safety and as a result all uses of products in Table 2 in Attachment A are not supported.

Conclusion on consideration of approved labels for chemical products

53) Section 34A(1) of the Agvet Code provides that if the APVMA is not satisfied under section 34(1) but is satisfied that the relevant particulars or conditions of the approval can be varied in such a way as to allow the approval to be affirmed, the APVMA must vary the relevant particulars or conditions.

54) The APVMA is satisfied that the relevant particulars of the label approvals listed in Table 1 in Attachment A can be varied to meet the labelling criteria and comply with any requirement prescribed by the regulations, as set out in paragraph 49) of this statement of reasons and as reflected in the proposed labels in Attachment D of this notice.

55) The APVMA is **not satisfied** that the relevant particulars or conditions of the neomycin the label approvals listed in Table 2 in Attachment A can be varied in such a way as to allow the approval to be affirmed for the following reasons:

a) The APVMA is **not satisfied** that the label approvals can be varied in such a way that there will be adequate instructions in relation to the circumstances in which these products should be used, as set out in paragraph 49)a)II of this statement of reasons.

56) Section 34AA(1) provides that if the APVMA does not affirm the approval, it must suspend or cancel the approval.

Overall Conclusions

57) For the purposes of sections 34(1), 34A(1) and 34AA(1) of the Agvet Code, and having regard to the matters set out above, the APVMA has determined that:

a) Regarding neomycin chemical product registrations, the APVMA is:

I. **not satisfied** that the neomycin chemical product registrations meet the safety criteria, efficacy criteria, trade criteria and any requirement prescribed by the regulations

II. satisfied that the particulars of neomycin chemical product registrations listed in Table 1 in Attachment A can be varied in such a way (as set out in paragraphs 10), 18), 25) and 34) of the statement of reasons) to allow the chemical product registrations to be affirmed

III. **not satisfied** that the particulars of neomycin chemical product registrations listed in Table 2 in Attachment A can be varied in such a way to allow the chemical product registrations to be affirmed, for the reasons set out in paragraphs 38) of the statement of reasons.

b) Regarding neomycin label approvals, the APVMA is:

I. **not satisfied** that the labels approvals for containers for neomycin chemical products meet the labelling criteria and comply with any requirement prescribed by the regulations

II. satisfied that the particulars of neomycin label approvals listed Table 1 in Attachment A can be varied in such a way (as set out in paragraph 49) of the statement of reasons and as reflected in the proposed labels in Attachment D) to allow the label approvals to be affirmed

III. **not satisfied** that the particulars or conditions of neomycin label approvals listed in Table 2 in Attachment A can be varied in such a way to allow the label approvals to be affirmed, for the reasons as set out in paragraph 55) of the statement of reasons.

58) Consequently, pursuant to section 34A(1) of the Agvet Code, the APVMA proposes to:

a) vary the relevant particulars and conditions of the chemical product registrations listed in Table 1 in Attachment A, in a manner set out in paragraphs 10), 18), 25) and 34) of the statement of reasons, to allow affirmation under section 34(1) of the Agvet Code; and

b) vary the relevant particulars of the label approvals listed in Table 1 in Attachment A in the manner set out in paragraph 49) of the statement of reasons, and as reflected in the proposed labels in Attachment D of this notice, to allow affirmation under section 34(1) of the Agvet Code.

59) Further, pursuant to section 34AA(1) of the Agvet Code, the APVMA proposes to:

a) cancel the neomycin chemical product registrations listed in Table 2 in Attachment A, as the APVMA is not satisfied that the relevant particulars or conditions of the registrations can be varied in such a way as to allow the registrations to be affirmed; and

b) cancel the neomycin label approvals listed in Table 2 in Attachment A, as the APVMA is not satisfied that the relevant particulars or conditions of the approvals can be varied in such a way as to allow the approvals to be affirmed.

Preliminary consideration of a phase-out period

60) The APVMA has considered whether a phase-out period could be applied to existing neomycin registrations and approvals in the event of a final decision to suspend, cancel or vary neomycin registrations and approvals.

61) If, having considered all submissions received in response to this section 34AB notice, the APVMA proceeds to suspend or cancel any neomycin chemical product registrations or label approvals, this will be done in accordance with the Agvet Code. Division 5 of Part 2 of the Agvet Code includes requirements regarding the giving of notice of suspensions and cancellations and the inclusion of instructions relating to possession, custody or use of the constituent or product (section 45A). This Division also includes provision in relation to permits taken to have been issued to possess, have custody of or use the constituent or product, or product as labelled if notice of suspension or cancellation is given to a holder or other person under paragraph 45A(1)(a) (section 45B).

62) If, having considered all submissions received in response to this section 34AB notice, the APVMA proceeds to vary any neomycin label approvals, a determination can be made under section 81(3) of the Agvet Code to permit the supply of registered chemical products with labels that were approved at an earlier time for a period allowed by the APVMA.

63) While the APVMA has not yet made any final decision to suspend, cancel or vary any neomycin registrations, the preliminary view of the APVMA is that, in the event that a decision to cancel, suspend or vary is made, any section 45B permit could have the maximum duration of 12 months and any determination under section 81(3) of the Agvet Code could allow supply of relevant chemical products with the earlier approved label also for a 12 month period.

Attachment C: Information on which the reasons are based

The information on which the reasons in the draft statement of reasons is based is set out below:

1) Information provided in response to notices issued under section 32(1) of the Agvet Code including notices issued on 31 January 2007, 1 July 2015 and 13 September 2023.

2) Submissions received in response to publication of the Neomycin: Target animal safety risk assessment report,

3) APVMA records for approval of relevant active constituents and registration of the relevant products, including information submitted at the time of approval and registration.

4) Other information as detailed in the following assessment reports:

    a. *Neomycin Review Technical Report* (APVMA 2024, available at apvma.gov.au/chemicals-and-products/chemical-review/listing/neomycin/neomycin-review-technical-report)

    b. Neomycin: Target animal safety risk assessment report (APVMA 2017, available at apvma.gov.au/node/26381)

5) The relevant provisions of the Agvet Code and instruments under that Code, in particular those set out below:

Table A1: *Agricultural and Veterinary Chemicals Code Act 1994*

Section	Section heading
3	Definitions
5A	Definition of *meets the safety criteria*
5B	Definition of *meets the efficacy criteria*
5C	Definition of *meets the trade criteria*
5D	Definition of *meets the labelling criteria*
6E	The APVMA may make standards
19	How approval of active constituent takes place
20	How registration of chemical product takes place
21	How approval of label takes place
23	Conditions of approval or registration
31	The APVMA may reconsider an approval or registration
33	The APVMA may require information, reports, results or samples
34	Reconsideration by the APVMA
34A	Varying relevant particulars or conditions to allow affirmation
34AA	Suspension or cancellation
34AB	Notice of proposed decision

Table A2: Agricultural and Veterinary Chemicals Code Regulations 1995

Section	Section heading
8AA	Safety criteria – active constituents
8AB	Safety criteria – chemical products
8AD	Trade criteria
8AE	Labelling criteria
15	Particulars of approved active constituents to be recorded
16	Particulars of registered chemical products to be recorded
17	Particulars for label
17C	Conditions of approval or registration – active constituents and chemical products
18	Conditions of registration of chemical products – containers
18E	Labelling standards and requirements

Table A3: Other legislative instruments under the *Agricultural and Veterinary Chemicals Code Act 1994*

Legislative instruments
Agricultural and Veterinary Chemical Code (Efficacy Criteria) Determination 2014
Agricultural and Veterinary Chemicals Code (Conditions of Approval or Registration) Order 2021
Agricultural and Veterinary Chemicals Code (Agricultural Active Constituents) Standards 2022

6) The Veterinary Labelling Code, available at apvma.gov.au.

7) Therapeutic Goods (Poisons Standard – October 2023) Instrument 2023 (i.e. the Standard for the Uniform Scheduling of Medicines and Poisons)

Attachment D: Proposed varied labels for neomycin chemical products

Label 1: 36026

Signal heading:	PRESCRIPTION ANIMAL REMEDY KEEP OUT OF REACH OF CHILDREN READ SAFETY DIRECTIONS BEFORE OPENING OR USING FOR ANIMAL TREATMENT ONLY
Product name:	SCOURBAN ORAL ANTI-DIARRHOHOEAL SUSPENSION
Constituent statement:	1065 mg/30 mL SULFADIMIDINE 1065 mg/30 mL SULFADIAZINE 182 mg/30 mL STREPTOMYCIN (AS STREPTOMYCIN SULFATE) 159.6 mg/30 mL PECTIN 133 mg/30 mL SODIUM (AS SODIUM CHLORIDE) 57 mg/30 mL POTASSIUM (AS POTASSIUM CHLORIDE) 36.5 mg/30 mL NEOMYCIN (AS NEOMYCIN SULFATE) 5.9 mg/30 mL CALCIUM (AS CALCIUM GLUCONATE) 1.77 mg/30 mL MAGNESIUM (AS MAGNESIUM SULFATE) 0.95 mg/30 mL HYOSCINE (AS HYOSCINE HYDROBROMIDE) 627 mg/30 mL GLYCINE Also Contains: 3.1 g/30 mL KAOLIN CLAY
Statement of claims:	An aid in the prevention and treatment of bacterial diarrhoea in horses, dogs and cats. For the treatment of gastroenteritis and scour/pneumonia complex caused by sensitive bacterial organisms. For restoring electrolyte loss, reducing intestinal motility and elimination of bacterial toxins. Sulfadimidine is a synthetic antimicrobial agent that contain the sulfonamide group. Sulfadiazine belongs to sulfonamide class of antibiotics. Streptomycin and neomycin belong to aminoglycosides class of antibiotics. Indiscriminate use of Scourban oral anti-diarrhoeal suspension may contribute to the development of antibiotic resistance.
Net contents:	100 mL 500 mL 2 L 5 L
Directions for use:	
Restraints:	DO NOT USE in horses that may be used for human consumption. DO NOT prescribe SCOURBAN ORAL ANTI-DIARRHOHOEAL SUSPENSION, prior to investigating the use of non-antibiotic options. If SCOURBAN ORAL ANTI-DIARRHOHOEAL SUSPENSION is indicated and selected for use, prudent prescribing practices (appropriate dose, duration and frequency) should be followed to minimise treatment failure while limiting the possible emergence of antimicrobial resistance.
Contraindications:	This product is contraindicated for use in animals with a known sulfonamide sensitivity, liver damage or blood dyscrasias. Not to be used in animals with compromised renal function, gastrointestinal inflammation and those being treated with other potentially nephrotoxic drugs.
Precautions:	Neomycin exhibits concentration dependent killing and a post-antibiotic effect. Overdosage with neomycin can cause renal damage and deafness. Care should be taken in animals with known or suspected impaired renal function. While this is unlikely at therapeutic doses, care should be taken in animals being treated with other potentially nephrotoxic substances, such as NSAIDs. Where practical, it is recommended to weigh young animals to ensure accurate dosage calculation based on bodyweight.

Dosage and administration	SHAKE WELL BEFORE USE For oral use only. Treat twice daily. Small animals: (Dogs and cats): 2 mL/3 kg bw Horses: 30 mL/25 kg bw IF NO IMPROVEMENT IS SEEN AFTER 5 DAYS, THE DIAGNOSIS SHOULD BE RE-ESTABLISHED.
General directions:	When treating salmonellosis and bacterial pneumonias continue treatment for a minimum of 5 days. Prudent Use: Veterinarian must assess the clinical need for antimicrobials prior to prescription and must communicate the risk of antimicrobial resistance (AMR) in humans and the need for prudent use in animals. Culture and sensitivity tests may be performed when appropriate to determine susceptibility of the causative organism(s). Empirical therapy may be instituted before results of susceptibility studies are known; however, once these results become available, the antibiotic treatment should be adjusted accordingly. NOT TO BE USED FOR ANY PURPOSE, OR IN ANY MANNER, CONTRARY TO THIS LABEL.
Withholding period:	
Trade advice:	
Safety directions:	Wash hands after use.
First aid instructions:	If poisoning occurs contact a doctor or Poisons Information Centre: Phone Australia 131 126.
First aid warning	
Additional user safety:	Additional information is listed in the Safety Data Sheet.
Environmental statements:	Do not contaminate wetlands or water courses with this product or used containers.
Disposal:	(100 mL, 500 mL) packs: Dispose of container by wrapping with paper and putting in garbage. (2 L, 5 L) packs: Triple-rinse container and dispose of rinsate in compliance with relevant local, state or territory government regulations. Do not dispose of undiluted chemicals on-site. If recycling, replace cap and return clean container to recycler or designated collection point. If not recycling, break, crush, or puncture container and deliver to an approved waste management facility. If an approved waste management facility is not available, dispose of in compliance with relevant local, state or territory government regulations. Do not burn empty containers or product.
Storage:	Store below 25 °C (air conditioning). Do not freeze. Protect from light.

Label 2: 36237

Signal heading:	PRESCRIPTION ANIMAL REMEDY KEEP OUT OF REACH OF CHILDREN READ SAFETY DIRECTIONS BEFORE OPENING OR USING FOR ANIMAL TREATMENT ONLY
Product name:	JUROX NEOMYCIN SULFATE INJECTION
Constituent statement:	135 mg/mL NEOMYCIN (AS NEOMYCIN SULFATE)
Statement of claims:	For the treatment of infections due to Neomycin sensitive organisms in dogs and cats. Neomycin belongs to aminoglycosides class of antibiotics. Indiscriminate use of Jurox neomycin sulfate injection may contribute to the development of antibiotic resistance.
Net contents:	100 mL
Directions for use:	
Restraints:	DO NOT prescribe JUROX NEOMYCIN SULFATE INJECTION, prior to investigating the use of non-antibiotic options. If JUROX NEOMYCIN SULFATE INJECTION is indicated and selected for use, prudent prescribing practices (appropriate dose, duration and frequency) should be followed to minimise treatment failure while limiting the possible emergence of antimicrobial resistance.
Contraindications:	Not to be used in animals with compromised renal function, gastrointestinal inflammation and those being treated with other potentially nephrotoxic drugs.
Precautions:	Neomycin exhibits concentration-dependent killing and a post-antibiotic effect. Repeated daily administration or overdosage with neomycin can cause renal damage and deafness. Care should be taken in animals with known or suspected impaired renal function. Care should be taken in animals being treated with other potentially nephrotoxic substances, such as NSAIDs. Where practical, it is recommended to weigh young animals to ensure accurate dosage calculation based on bodyweight.
Dosage and administration	DISCARD THE UNUSED PORTION WITHIN 29 DAYS AFTER FIRST BROACHING WHEN STORED BETWEEN 2 °C AND 8 °C. Dogs and cats: 10 mg/kg bodyweight once daily. Treatment should not be repeated at less than 24-hour intervals.
General directions:	Prudent Use: Veterinarian must assess the clinical need for antimicrobials prior to prescription and must communicate the risk of AMR in humans and the need for prudent use in animals. Culture and sensitivity tests may be performed when appropriate to determine susceptibility of the causative organism(s). Empirical therapy may be instituted before results of susceptibility studies are known; however, once these results become available, the antibiotic treatment should be adjusted accordingly. NOT TO BE USED FOR ANY PURPOSE, OR IN ANY MANNER, CONTRARY TO THIS LABEL UNLESS AUTHORISED UNDER APPROPRIATE LEGISLATION.
Withholding period:	
Trade advice:	
Safety directions:	Wash hands after use.
First aid instructions:	If poisoning occurs contact a doctor or Poisons Information Centre: Phone Australia 131 126.
First aid warning	
Additional user safety:	
Environmental statements:	
Disposal:	Dispose of container by wrapping with paper and putting in garbage. Discarded needles/sharps should immediately be placed in a designated and appropriately labelled 'sharps' container.
Storage:	Store below 30 °C (room temperature). Do not freeze. Store in a dry place. Store upright. Protect from light.

Label 3: 37241

Signal heading:	PRESCRIPTION ANIMAL REMEDY KEEP OUT OF REACH OF CHILDREN READ SAFETY DIRECTIONS BEFORE OPENING OR USING FOR ANIMAL TREATMENT ONLY
Product name:	NEOMYCIN PENICILLIN 100/200 AQUEOUS SUSPENSION FOR INTRAMUSCULAR INJECTION
Constituent statement:	100 mg/mL NEOMYCIN (AS NEOMYCIN SULFATE) 200 mg/mL PROCAINE PENICILLIN
Statement of claims:	For infections caused by penicillin-neomycin sensitive organisms in horses, cattle, sheep, pigs, dogs and cats. For urinary infections, pasteurellosis, mastitis, metritis and as an ancillary treatment against enteric infections. Penicillin has been shown *in vitro* to be effective against Gram positive aerobic bacteria such as *Staphylococcus aureus*, *Streptococci* spp., most *Actinomyces* spp. (Corynebacteria) and *Erysipelothrix* spp. Sensitive Gram positive anaerobic bacteria include most clostridia. Penicillin has also been shown *in vitro* to be effective against certain Gram negative bacteria including *Pasteurella multocida* and *Actinobacillus (Haemophilus) pleuropneumoniae*. Neomycin has been shown *in vitro* to be effective against Gram negative organisms such as *E. coli*, *Pasteurella* spp., *Salmonella* spp. and *Klebsiella* spp. as well as some Gram positive bacteria and *Leptospira* spp. Synergism between penicillin and neomycin combined produces a greater activity than the use of either antibiotic by itself. Neomycin belongs to aminoglycosides and procaine penicillin belongs to penicillins class of antibiotics. Indiscriminate use of NEOMYCIN PENICILLIN 100/200 AQUEOUS SUSPENSION FOR INTRAMUSCULAR INJECTION may contribute to the development of antibiotic resistance.
Net contents:	100 mL 250 mL
Directions for use:	
Restraints:	DO NOT USE in horses that may be used for human consumption. RE-TREATMENT INTERVAL: DO NOT RE-TREAT cattle for 12 months after the last dose in one course of treatment. DO NOT RE-TREAT sheep for 4 months after the last dose in one course of treatment. DO NOT RE-TREAT pigs for 10 weeks after the last dose in one course of treatment. DO NOT prescribe NEOMYCIN PENICILLIN 100/200 AQUEOUS SUSPENSION FOR INTRAMUSCULAR INJECTION, prior to investigating the use of non-antibiotic options. If NEOMYCIN PENICILLIN 100/200 AQUEOUS SUSPENSION FOR INTRAMUSCULAR INJECTION is indicated and selected for use, prudent prescribing practices (appropriate dose, duration and frequency) should be followed to minimise treatment failure while limiting the possible emergence of antimicrobial resistance.
Contraindications:	NEOMYCIN-PENICILLIN 100/200 AQUEOUS SUSPENSION FOR INTRAMUSCULAR INJECTION should not be administered to animals known to be allergic to penicillin or neomycin. Not to be used in animals with compromised renal function, gastrointestinal inflammation and those being treated with other potentially nephrotoxic drugs.
Precautions:	Neomycin exhibits concentration-dependent killing and a post-antibiotic effect. Repeated daily administration or overdosage with neomycin can cause renal damage and deafness. Care should be taken in animals with known or suspected impaired renal function. Care should be taken in animals being treated with other potentially nephrotoxic substances, such as NSAIDs. Where practical, it is recommended to weigh young animals to ensure accurate dosage calculation based on bodyweight. Occasional allergies to penicillin in animals have been observed but these are very rare. Persons who are allergic to penicillins or neomycin should avoid direct contact with the product. The administration of products containing procaine benzylpenicillin may occasionally cause transient pyrexia, vomiting, shivering, listlessness and incoordination in pigs. Additionally in pregnant sows and gilts, abortion has been reported in a few cases. Local reaction (swelling) may occur at the injection site in horses for up to a week after administration. Doses exceeding 15 mL should be divided between 2 injection sites.

Dosage and administration	SHAKE WELL BEFORE USE. USE THE CONTENTS OF THE VIAL WITHIN 28 DAYS OF INITIAL BROACHING AND DISCARD ANY UNUSED PORTION. NEOMYCIN-PENICILLIN 100/200 AQUEOUS SUSPENSION FOR INTRAMUSCULAR INJECTION should be given by intramuscular injection to large animals. Dogs and cats may be injected by either the subcutaneous or intramuscular routes. The following dose rates are advised: Horse and Cattle: 25 mL/500 kg (1 mL/20 kg) IM Pigs and Sheep: 2 mL/40 kg (1 mL/20 kg) IM Dogs and Cats: 1 mL/10 kg IM or SC Injections may be repeated at 24-hour intervals for a maximum of 3 days. Repeat injections should be given at a different site. The usual aseptic precautions should be taken when administering the injections. Treatment should not be repeated at less than 24-hour intervals.
General directions:	Prudent Use: Veterinarian must assess the clinical need for antimicrobials prior to prescription and must communicate the risk of AMR in humans and the need for prudent use in animals. Culture and sensitivity tests may be performed when appropriate to determine susceptibility of the causative organism(s). Empirical therapy may be instituted before results of susceptibility studies are known; however, once these results become available, the antibiotic treatment should be adjusted accordingly. NOT TO BE USED FOR ANY PURPOSE, OR IN ANY MANNER, CONTRARY TO THIS LABEL.
Withholding period:	MEAT: DO NOT USE less than 42 days for cattle, 35 days for sheep and 100 days for pigs before slaughter for human consumption. MILK: DO NOT USE in lactating or pregnant cows or ewes where milk may be used or processed for human consumption. Any variation by the prescribing veterinarian to the approved dose, frequency, duration, route, disease or target species may require extending the approved withholding period.
Trade advice:	EXPORT SLAUGHTER INTERVAL (ESI): DO NOT USE less than 57 days for cattle, 56 days for sheep and 100 days for pigs before slaughter for export. Before using this product, confirm the current ESI from the manufacturer on 1800 033461 or the APVMA website (apvma.gov.au/residues).
Safety directions:	Wash hands after use.
First aid instructions:	If poisoning occurs, contact a doctor or Poisons Information Centre: Phone Australia 131 126.
First aid warning	
Additional user safety:	
Environmental statements:	
Disposal:	Dispose of container by wrapping with paper and putting in garbage. Discarded needles and sharps should immediately be placed in a designated and appropriately labelled 'sharps' container.
Storage:	Store between 2 °C and 8 °C (Refrigerate). Do not freeze. Protect from light.

Label 4: 46414

Signal heading:	PRESCRIPTION ANIMAL REMEDY KEEP OUT OF REACH OF CHILDREN READ SAFETY DIRECTIONS BEFORE OPENING OR USING FOR ANIMAL TREATMENT ONLY
Product name:	NEO-SULCAN SCOUR TABLETS
Constituent statement:	Each tablet contains: 750 mg SULFADIMIDINE 750 mg SULFADIAZINE 169 mg NEOMYCIN (AS NEOMYCIN SULFATE) 3 mg RIBOFLAVIN 2 mg THIAMINE HYDROCHLORIDE 1.52 mg HYOSCINE (AS METHOBROMIDE)
Statement of claims:	For the treatment of scours and enteritis of bacterial origin sensitive to neomycin or sulphonamides horses. Sulfadimidine is a synthetic antimicrobial agent that contain the sulfonamide group. Sulfadiazine belongs to sulfonamide class of antibiotics. Neomycin belongs to aminoglycosides class of antibiotics. Indiscriminate use of NEO-SULCAN SCOUR TABLETS may contribute to the development of antibiotic resistance.
Net contents:	40 tablets
Directions for use:	
Restraints:	DO NOT USE in horses that may be used for human consumption. DO NOT prescribe NEO-SULCAN SCOUR TABLETS, prior to investigating the use of non-antibiotic options. If NEO-SULCAN SCOUR TABLETS is indicated and selected for use, prudent prescribing practices (appropriate dose, duration and frequency) should be followed to minimise treatment failure while limiting the possible emergence of antimicrobial resistance.
Contraindications:	Not to be used in animals with compromised renal function, gastrointestinal inflammation and those being treated with other potentially nephrotoxic drugs.
Precautions:	Neomycin exhibits concentration dependent killing and a post-antibiotic effect. Overdosage with neomycin can cause renal damage and deafness. Care should be taken in animals with known or suspected impaired renal function. While this is unlikely at therapeutic doses, care should be taken in animals being treated with other potentially nephrotoxic substances, such as NSAIDs. Where practical, it is recommended to weigh young animals to ensure accurate dosage calculation based on bodyweight.
Dosage and administration	Horses: 1 TABLET per 35 kg bodyweight administered orally twice daily. Repeat treatment daily until 2 days after symptoms have subsided except in cases of salmonellosis where treatment should continue for a minimum of 5 consecutive days. IF NO IMPROVEMENT IS SEEN AFTER 5 DAYS, THE DIAGNOSIS SHOULD BE RE-ESTABLISHED.
General directions:	Prudent Use: Veterinarian must assess the clinical need for antimicrobials prior to prescription and must communicate the risk of AMR in humans and the need for prudent use in animals. Culture and sensitivity tests may be performed when appropriate to determine susceptibility of the causative organism(s). Empirical therapy may be instituted before results of susceptibility studies are known; however, once these results become available, the antibiotic treatment should be adjusted accordingly. NOT TO BE USED FOR ANY PURPOSE, OR IN ANY MANNER, CONTRARY TO THIS LABEL.
Withholding period:	
Trade advice:	
Safety directions:	Wash hands after use.
First aid instructions:	If poisoning occurs contact a doctor or Poisons Information Centre: Phone Australia 131 126.
First aid warning	
Additional user safety:	
Environmental statements:	

Disposal:	Dispose of container by wrapping with paper and putting in garbage.
Storage:	Store below 30 °C (room temperature). Protect from light.

Label 5: 49788

Signal heading:	PRESCRIPTION ANIMAL REMEDY KEEP OUT OF REACH OF CHILDREN READ SAFETY DIRECTIONS BEFORE OPENING OR USING FOR ANIMAL TREATMENT ONLY
Product name:	SCOUR-X ORAL ANTI-DIARRHOEAL SUSPENSION
Constituent statement:	Each 30 mL contains: 1278 mg SULFADIAZINE 852 mg SULFADIMIDINE 36.5 mg/30 mL NEOMYCIN (AS NEOMYCIN SULFATE) 0.91 mg HYOSCINE (AS METHOBROMIDE) 4.5 mg THIAMINE HYDROCHLORIDE 6.6 mg RIBOFLAVINE 213 mg PECTIN 3.1 g KAOLIN (light)
Statement of claims:	For the treatment of Neomycin or sulphonamide sensitive bacterial enteritis in horses, dogs and cats. Sulfadimidine is a synthetic antimicrobial agent that contain the sulfonamide group. Sulfadiazine belongs to sulfonamide class of antibiotics. Neomycin belongs to aminoglycosides class of antibiotics. Indiscriminate use of SCOUR-X ORAL ANTI-DIARRHOEAL SUSPENSION may contribute to the development of antibiotic resistance.
Net contents:	2 L
Directions for use:	
Restraints:	DO NOT USE in horses that may be used for human consumption. DO NOT prescribe SCOUR-X ORAL ANTI-DIARRHOEAL SUSPENSION, prior to investigating the use of non-antibiotic options. If SCOUR-X ORAL ANTI-DIARRHOEAL SUSPENSION is indicated and selected for use, prudent prescribing practices (appropriate dose, duration and frequency) should be followed to minimise treatment failure while limiting the possible emergence of antimicrobial resistance.
Contraindications:	Not to be used in animals with compromised renal function, gastrointestinal inflammation and those being treated with other potentially nephrotoxic drugs.
Precautions:	Neomycin exhibits concentration dependent killing and a post-antibiotic effect. Overdosage with neomycin can cause renal damage and deafness. Care should be taken in animals with known or suspected impaired renal function. While this is unlikely at therapeutic doses, care should be taken in animals being treated with other potentially nephrotoxic substances, such as NSAIDs. Where practical, it is recommended to weigh young animals to ensure accurate dosage calculation based on bodyweight.
Dosage and administration	SHAKE WELL BEFORE USE Horses: 30 mL per 25 kg body weight orally daily for 3 to 5 days. Dogs and cats: 2 mL per 3 kg body weight orally daily for 3 to 5 days. Repeat treatment daily until 2 days after symptoms have subsided except in cases of salmonellosis where treatment should continue for a minimum of 5 consecutive days. IF NO IMPROVEMENT IS SEEN AFTER 5 DAYS, THE DIAGNOSIS SHOULD BE RE-ESTABLISHED
General directions:	Prudent Use: Veterinarian must assess the clinical need for antimicrobials prior to prescription and must communicate the risk of AMR in humans and the need for prudent use in animals. Culture and sensitivity tests may be performed when appropriate to determine susceptibility of the causative organism(s). Empirical therapy may be instituted before results of susceptibility studies are known; however, once these results become available, the antibiotic treatment should be adjusted accordingly. NOT TO BE USED FOR ANY PURPOSE, OR IN ANY MANNER, CONTRARY TO THIS LABEL.
Withholding period:	
Trade advice:	
Safety directions:	Wash hands after use.
First aid instructions:	If poisoning occurs contact a doctor or Poisons Information Centre: Phone Australia 131 126.

First aid warning	
Additional user safety:	
Environmental statements:	Do not contaminate wetlands or water courses with this product or used containers.
Disposal:	Triple-rinse container and dispose of rinsate in compliance with relevant local, state or territory government regulations. Do not dispose of undiluted chemicals on-site. If recycling, replace cap and return clean container to recycler or designated collection point. If not recycling, break, crush, or puncture container and deliver to an approved waste management facility. If an approved waste management facility is not available, dispose of in compliance with relevant local, state or territory government regulations. Do not burn empty containers or product.
Storage:	STORE below 30 °C (room temperature). Do not freeze. Protect from light.