[redacted]
dairyaustralia.com.au

24 May 2024

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

Public consultation submission: Neomycin reconsideration – proposed decisions on reconsideration

Dairy Australia welcomes this opportunity to provide a submission on the proposed decisions on the reconsideration of neomycin product registrations and label approvals.

Dairy Australia is the national services body for the Australian dairy industry. The Australian dairy industry is the third largest rural industry in Australia and a key sector of the agricultural economy, generating close to A$6.1 billion in farmgate value in the 2022/23 financial year[1].

Background

The 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 as detailed in the APVMA Special Gazette, 27th February 2024. The proposed decisions if implemented, will change the conditions of registration and/or cancel the registration of some veterinary chemical products of importance to dairy production in Australia.

The APVMA has published its reasons in the Neomycin Review Technical Report, which sets out the scientific evidence it relied on in support of its proposed decisions. The APVMA has invited public submissions regarding its proposed decisions.

This submission from Dairy Australia sets out the key issues, with supporting evidence, that our industry believes should be taken into consideration by the APVMA before their proposed decisions are finalised.

Industry position statement

Dairy Australia supports the continued registration of Mastalone Intramammary Suspension For Lactating Cows (CRIS# 49851) according to its current label directions. Mastalone is an important product in the treatment of mastitis as it is efficacious, broad-spectrum, and importantly is the only available intramammary lactating cow antibiotic which contains active constituents of ‘low’ importance to the development of antimicrobial resistance (AMR) in Australia[2].

Dairy Australia considers this product poses a low risk of unacceptable antibiotic residues in milk and meat products, and these risks are adequately managed by the antibiotic risk management procedures implemented across dairy supply chains.

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[1] Australian Dairy Industry In Focus 2023 (2024) Dairy Australia, [redacted]

[2] Australian Strategic and Technical Advisory Group on Antimicrobial Resistance. (2018, June). Importance Ratings and Summary of Antibacterial Uses in Human and Animal Health in Australia. Australain Government.

Dairy Australia considers this product poses a low risk to the domestic and international trade of dairy milk and meat products, and is unaware of any trade issues that have arisen specifically regarding the use of this product since it was first approved for use over 50 years ago.

General comments

Whilst not diminishing the importance to other livestock industries of other registered products containing neomycin as an active constituent, this submission focuses on the reconsideration of the registration of Mastalone Intramammary Suspension For Lactating Cows (CRIS# 49851).

Mastalone is an important veterinary chemical product which has been used by veterinarians and dairy farmers to treat clinical mastitis for over 50 years.

Clinical mastitis results from a bacterial infection of the mammary gland (in one or more quarters) causing inflammation and changes to the milk. Affected animals suffer acute pain and clots and/or blood in the milk, making it unsuitable for human consumption. The reduction in milk production can persist for the current and subsequent lactations. Some cows do not recover and must be culled from the herd.

Apart from the animal welfare implications, mastitis causes the highest economic loss from any disease of dairy cattle in Australia and whilst this disease cannot be completely eliminated, veterinarians and farmers are focused on minimizing its impact on their herds.

Mastalone has proven over several decades to be an efficacious treatment for clinical mastitis infections in lactating cows, using a combination of antimicrobial active constituents not included in other registered intramammary lactating cow preparations. The formulation contains antibiotic actives with activity against a broad range of both Gram-positive and Gram-negative mastitis pathogens[3].

All other registered intramammary lactating cow preparations contain beta-lactam antimicrobial active constituents from the Penicillin and Cephalosporin antimicrobial classes, which primarily target Gram-positive mastitis pathogens. These are bactericidal in nature with a 'medium' importance for the development of AMR in Australia[4].

Mastalone contains antimicrobial active constituents from the Aminoglycoside, Macrolide and Tetracycline antimicrobial classes, all of which have a 'low' importance for the development of AMR in Australia[4]. Mastalone will be an important alternative treatment should resistance to beta-lactam antibiotics become more widespread in mastitis pathogen populations.

In the proposed decisions and Neomycin Review Technical Report, the APVMA appears satisfied that Mastalone meets the safety (host, human and environment) and efficacy criteria required to allow this product's registration to be affirmed. However, the APVMA is not satisfied that the relevant particulars or conditions of the registration can be varied in such a way as to allow the registrations to be affirmed on the basis of residues and trade, primarily due to a lack of milk and meat residues data.

Residue Risks

Dairy Australia acknowledges that food safety/residue studies conducted according to International Cooperation on Harmonisation of Technical Requirements for Registration of Veterinary Medicinal Products (VICH) Guidelines have not been submitted in support of Mastalone. This is not surprising as the product was first registered over 50 years ago and pre-dates the VICH Guidelines.

Clinical studies are particularly useful for the pre-market assessment of products, where trial data collected from a small number of (usually heathy) animals is used to model the depletion of veterinary chemicals in

[3] A description of the coverage of the antibiotics included in Mastalone is provided in the 'General Directions' of the approved product label (#49851/106743)

[4] Australian Strategic and Technical Advisory Group on Antimicrobial Resistance. (2018, June). Importance Ratings and Summary of Antibacterial Uses in Human and Animal Health in Australia. Australain Government.

animals treated with the product, before it is registered for use. Post-registration, veterinary medicines are usually used in unhealthy animals of varying breed, age, weight, and stage of lactation.

In the case of Mastalone, which is registered and has been used to treat mastitis for many years, we are fortunate to have decades of both meat and milk residues data that can be used to assess the risk of unacceptable residues in the absence of clinical residue studies. This data has been collected in both commercial and government testing programs at various points of milk and meat supply chains.

Dairy Australia also acknowledges the extremely limited systemic absorption of neomycin when administered via the intramammary route[5].

Milk Residue Testing / Data

The Australian milk supply is tested for antibiotics at the farm, tanker and silo level using a range of commercial test kits. The antibiotic screening procedures implemented at each level of the supply chain form part of the food safety plan of every licensed dairy supply chain participant and are approved by State dairy food safety authorities (for domestic supply chains) and the Commonwealth Government (for export supply chains).

Whether for export or domestic markets, all milk entering the human food chain is tested with a broad-spectrum microbial inhibition test (MIT) at some point along the supply chain, usually using a Delvotest® T or Delvotest® SP-NT test[6]. These tests can detect neomycin in milk at levels well below the Australian, CODEX and EU MRLs (see Appendix 1). These tests and several other rapid immunoassay and MIT tests in use can also detect oxytetracycline and oleandomycin residues, providing assurance that unacceptable residues from the use of Mastalone would be detected.

In the unlikely event that milk returns a confirmed positive result (to a broad spectrum MIT test), the milk is removed from the supply chain under regulatory supervision, effectively eliminating the risk of residues to human health and/or trade. It is important to note that milk is removed based on the result of the confirmed MIT test – which detects neomycin at well below MRL.

Every instance is traced back to the farm and an investigation initiated to identify the cause of the positive detection. Analysis undertaken by Dairy Australia in 2015[7] of historic traceback reports showed that the majority of issues were caused by operator error (failing to observe the withhold period), with products containing cloxacillin being the most commonly implicated intramammary products. The use of Mastalone was recorded as a potential cause in 3.5% of the reports examined in this study (n=525), noting that this figure includes instances of operator error.

The Australian Milk Residue Analysis (AMRA) survey is a national residue monitoring program for agricultural and veterinary chemicals and environmental contaminants in bovine milk. The survey supports the export requirements of the Australian Government Department of Agriculture, Fisheries and Forestry (DAFF) under the Export Control (Milk and Milk Products) Rules 2021. The Survey is funded through DAFF, who also approve the sampling plan. Dairy Food Safety Victoria (DFSV) co-ordinates the Survey. One thousand tankers are sampled annually and the samples tested for a range of chemical residues, including antibiotics. No neomycin, oxytetracycline or oleandomycin residues have been detected in the AMRA survey over the last 25 years, providing evidence that the residue and trade risks of antibiotic residues in milk from Mastalone are being adequately managed based on current supply and use arrangements.

Meat Residue Testing / Data

Meat derived from slaughtered dairy cattle is included in the red meat supply chain and as such, is subject to the same regulatory oversight and quality assurance requirements as exists for beef cattle.

The National Residue Survey (NRS) operates within the Commonwealth Government and involves the annual testing of around 5,000 Australian cattle tissue samples for a range of pesticides, veterinary

[5] Neomycin Review Technical Report (2024). APVMA, Pharmacokinetics and metabolism–Absorption, pp 5
[6] Delvotest is a registered trademark of DSM Food Specialties B.V. 2023
[7] Unpublished data (Dairy Australia)

medicines, and environmental contaminants. Although tissues from dairy cattle are not differentiated from those of beef cattle in the figures reported, the results over the last 10 years show very high compliance with Australian MRLs for the antibiotics included in Mastalone. There were no detections above the Australian MRL for neomycin and oleandomycin from approximately 10,696 tissue samples tested over this time. There were three detections above the Australian MRL detected for oxytetracycline, noting that both neomycin and oxytetracycline are also administered to beef and dairy cattle in a range of other registered injectable and oral veterinary chemical products on the market.

Meat and tissue residues detected above the Australian MRL are subject to a traceback investigation to identify the circumstances which led to the residue detection. These reports are collated and analysed by State regulators with a view to mitigating systemic risks. To our knowledge Mastalone has not been identified as posing a particular risk to the meat supply chain. This is not surprising as the very low absorption of neomycin from the udder into edible animal tissues, combined with the current 30-day meat withholding period ensures the meat residue risks posed by the use of Mastalone are minimal.

Trade Risks

Antibiotics are an important tool used by dairy farmers to protect the health and welfare of their livestock, and the dairy industry is particularly focused on managing the risks to trade associated with their use.

Industry participants and regulators work together to implement the Antibiotic Management and Monitoring Policy[8] which documents the risk management processes undertaken at each level of the supply chain to manage antibiotic residue risks to food safety and trade, including the following:

- Product risk assessment/evaluation and registration to enable supply and use (by the APVMA);
- Veterinary prescription required/oversight of veterinary chemical product supplies;
- Farm QA requirements regarding using products as per veterinary directions/product label;
- Farm QA requirements to identify and manage treated animals & separate treated milk;
- Farm random vat residue testing programs;
- Tanker screening for antibiotic residues;
- Silo screening for antibiotic residues; and
- Product testing programs (QC).

It should be noted that the APVMA's risk assessment of products prior to registration is but one of the strategies used to manage the risks posed by the use of antibiotics. Taken in this context, the APVMA should be satisfied that the registration of Mastalone and its use according to the approved label does not unduly prejudice trade or commerce between Australia and places outside Australia

This policy, and trade issues more generally, are discussed through various dairy industry committees involving dairy companies, industry bodies, domestic and export regulators, including:

- Industry Working Group (IWG) convened by Dairy Australia meeting two to three times per year, and
- Dairy Export Industry Consultative Committee (DEICC) convened by DAFF meeting two times per year.

Issues raised through these Committees and from other sources are entered into the dairy industry's Issues Management Framework, which is administered by Dairy Australia on behalf of the Australian dairy industry. Although antibiotic residues are a well-recognised risk to trade, to our knowledge the use of Mastalone specifically has not been identified as a risk to trade in the Issues Management Framework.

More recently some customers are taking an interest in the types of antibiotics being used in milk production and their potential for the development of AMR. Dairy Australia considers that there is minimal likelihood of Mastalone becoming a commercial trade risk due to antimicrobial resistance concerns, based on the 'low' AMR importance rating of the product's active constituents, as determined by ASTAG.

[8] Australian Dairy Regulators' Forum (2021) Antibiotic management and monitoring policy. Dairy Australia,

Should APVMA's evaluation team require any further details about the information provided in this submission please contact:

[redacted]

Appendix 1: Comparison of the limits of detection (LODs) for commonly used broad-spectrum MIT tests used in antibiotic screening programs for Australian milk.

Antimicrobial actives	**Regulatory limits**			**Broad-spectrum (MIT) tests Limits of detection (ppb)**	
	AU MRL	**EU MRL**	**CODEX MRL**	Delvotest SP-NT	Delvotest T
Beta-lactams					
Ampicillin	10	4	NE	4	3-4
Amoxycillin	10	4	4	2-3	4
Benzyl penicillin G	1.5	4	4	1-2	2
Cloxacillin	10	30	NE	12	5-6
Beta-lactam Cephalosporins					
Cephalonium	20	20	NE	5-10	3-5
Ceftiofur	100	100	100	25-50	80
Cephapirin	10	60	NE	5	5-6
Cefuroxime	100	50	NE	30-80	50
Tetracyclines					
Oxytetracycline	100	100	NE	250-500	80-100
Macrolides					
Erythromycin	40	40	NE	40-80	150-160
Tilmicosin	25	50	NE	50-100	60
Tylosin	50	50	100	30	35
Sulfonamides					
Sulfadimidine	*	100#	25	50-100	75-100
Sulfadiazine	100	100#	NE	25-50	40-50
Sulfadoxine	100	100#	NE	100-200	65
Aminoglycosides					
Dihydrostreptomycin	200	200	200	>1000	800
Streptomycin	200	200	200	>1000	400
Neomycin	1500	1500	1500	100-200	60-110
Other					
Novobiocin	100	50	NE	1000	NS
Trimethoprim	50	50	NE	50-100	110-130

* No MRL specified in Food Standards Code

NE = No MRL Established

NS = No value specified

combined value for all sulfonamide

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23 May 2024

Proposed Regulatory Decision for the Reconsideration of Neomycin

To whom it may concern

The SunPork Group

The SunPork Group of companies is wholly Australian-owned by the Cameron, Hall and McLean families and is Australia's largest pig farming integrator. SunPork produces 1.1 million pigs per year representing 20% of Australia's pork and 140 million meals worldwide, including seven million kilograms of exports. SunPork employs over 1500 people and is a critical employer in regional Australian towns across four states of Australia including Kingaroy, Dalby, Goondiwindi, Millmerran, Pittsworth, Toowoomba, Grong Grong, Murray Bridge, Gawler and the Bendigo region.

SunPork is committed to the responsible, ethical, science-based care of animals to safeguard their comfort, health and welfare. Our farms are serviced by a team of four pig health veterinarians, two pig nutritionists and supported by animal welfare, production, sustainability and data scientists. All farms are quality-assured under the Australian Pig Industry Quality Assurance (APIQ✓) Program. All personnel involved in the care of animals on our farms must possess or be working to achieve the pork industry skillset which includes (but is not limited to) competencies in pig health and ill health, pig welfare and biosecurity.

The SunPork Group recognises the importance of preserving antimicrobials for therapeutic use in humans and animals and is committed to antimicrobial stewardship. Antimicrobial stewardship is considered an important component of our Animal Care Program. **Since 2016, through its antimicrobial stewardship program, SunPork has reduced antimicrobial use by 76% across eight million pigs produced.** Where antimicrobials are used, this is based on diagnostic evidence. Antimicrobials are used only at prescribed dosages known to be effective using peer reviewed guidelines including the Antimicrobial Prescribing Guidelines for Pigs (Cutler et al, 2020). Antimicrobials are applied strictly under veterinary oversight and are only used to treat and control bacterial infections.

Proposed Regulatory Decision for the Reconsideration of Neomycin

The SunPork Group strongly opposes the proposed regulatory reconsideration and requests:

1. A clear understanding of the rationale for the Australian Pesticides and Veterinary Medicines Authority (APVMA) determination.
2. An extension to existing timeframes to allow proper consultation and consideration of the process with key stakeholders including the pork industry.

SunPork Pty Ltd
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3. Guidance on next steps to retain/obtain label registration for use in food producing species, specifically pigs, and associated time to facilitate of the following products:
    - Scour-X Oral Anti-Diarrhoeal Suspension (APVMA #36026)
    - Scourban Oral Anti-Diarrhoeal Suspension (APVMA #36026)
    - Jurox Neomycin Sulfate Injection (APVMA #36237)
    - Abbeyneo Antibiotic Feed Additive (APVMA #67805)
    - CCD Neomycin (Neomycin Sulphate Water Soluble Powder) (APVMA #52782)
4. Sufficient time to allow processes required to retain/obtain label registrations, to be undertaken by product registrants.

In making this representation, SunPork draws the attention of the APVMA to the below supporting statements:

1. Neomycin is the primary treatment choice in the strategic treatment of specific bacterial enteric infections caused by *Escherichia coli* and *Salmonella* in piglets and growing pigs.
2. In accordance with the Antimicrobial Prescribing Guidelines for Pigs (Cutler et al, 2020), the foreword for which is provided by Co-Chair of the Australian Strategic and Technical Advisory Group on Antimicrobial Resistance and former Australian Chief Veterinary Officer Dr Mark Schipp, Neomycin is the preferred first line of treatment for the following conditions of pigs:
    - Enterotoxigenic (non-haemolytic) *Escherichia coli* – a common cause of high morbidity, high mortality enteric disease in young piglets
    - Enterotoxigenic or enterotoxaemic (haemoloytic) *Escherichia coli* – a common cause of enteric and neurological disease and sudden death in young and newly weaned piglets
    - Salmonellae – a cause of enteric disease and sudden death in growing pigs
3. These uses are supported by scientific evidence of high susceptibility to Neomycin including in 96% of porcine *Salmonella* and >75% of *Escherichia coli* (Murray et al, 1986; DVFA, 2018).
4. Neomycin is rated a low importance antimicrobial by the Australian Government Importance Ratings and Summary of Antibacterial Uses in Human and Animal Health in Australia (ASTAG, 2018). In the absence of Neomycin, alternative or second line active agents that would be used to treat *Escherchia coli* and *Salmonella* infections include Trimethoprim plus Sulfonamide and Apramycin. Both Trimethoprim plus Sufonamide and Apramycin are rated as being of medium importance by ASTAG. Use of these alternatives therefore represents a shift to use of a more important antimicrobial and a shift away from industry antimicrobial stewardship, public health and One Health imperatives.

SunPork Pty Ltd
[redacted]
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5. In respect to chemical residues, SunPork notes that over the past 11 years there has only been one residue from 2750 pig samples that has exceeded the maximum residue limit (MRL). This suggests that residue detections are not a plausible cause for the review in respect to use in pigs.

6. In describing use of Neomycin in the management of pig health, SunPork acknowledges that current use patterns in pigs of some Neomycin products are not registered and represent off-label usage. Hence they may not have been considered by the APVMA in the review process it has undertaken on Neomycin product registrations. SunPork also acknowledges that off-label use patterns may preferably need to become on-label use patterns in relation to the reconsiderations being made. Australian Pork Limited, SunPork and the Australian Pig Veterinarians Special Interest Group of the Australian Veterinary Association welcome the opportunity to discuss the use of Neomycin in pigs and matters relating to retaining/obtaining appropriate registration further with the APVMA.

SunPork emphasises the very real compromise to pig health, welfare, antimicrobial stewardship and One Health imperatives that the APVMA reconsideration of Neomycin registrations poses. SunPork seeks to better understand the rationale behind this reconsideration and to find a pathway forward that addresses its concerns.

We strongly request that the APVMA partner with the pork industry and registrants in this matter, in the provision of guidance and time to progress a resolution that addresses APVMA concerns without precluding access to Neomycin, acknowledging that it is a preferred, efficacious treatment for the conditions prescribed in this submission.

[redacted]

References

Australian Strategic and Technical Advisory Group on Antimicrobial Resistance (ASTAG) (2018). Importance Ratings and Summary of Antibacterial Uses in Human and Animal Health in Australia (Version 1), Australian Government, Canberra.

Cutler, R. Gleeson, B. Page, S. Norris, J. Browning, G. (2020). Antimicrobial prescribing guidelines for pigs , Australian Veterinary Association Ltd and Animal Medicines Australia, Canberra

Danish Veterinary and Food Administration (DVFA) (2018). Evidence-based Prudent Use Guidelines for Antimicrobial Treatment of Pigs, Ministry of Environment and Food, Denmark.

Murray CJ, Ratcliff RM, Cameron PA, et al. (1986). The Resistance of Antimicrobial Agents in Salmonella from Veterinary Sources in Australia from 1975 to 1982. Australian Veterinary Journal;63:286-292.

From: [redacted]

Dear [redacted]

Thank you for the latest response to the information (Evaluation of Medical Products EMEA /MRL/816/02 – FINAl) This report is in the public domain and only requires an acknowledgement of the source. It may be used by the APVMA. This supports the current approval of Scour- X from a residue standpoint.
It would seem appropriate that a longer WHP for meat and offal of 28 days, and a use restriction of the administration of Scour- X in pre- ruminant calves with a label change. This would negate the need for additional residue data.

The information in the report is material in that it indicates that in UK and EU, Neomycin remains registered and approved for oral treatment of calves. The question of residues following the oral administration of Neomycin is not an issue. Therefore, if an adequate withholding period follows treatment and slaughter there is no issue.

Attached is a product Data Sheet for product BIMAMIX Oral Suspension for Calves ; Sulfadiazine + Neomycin :registration Ireland 12597/4047 ; registration UK VM501146/4022
The product data sheet for BIMAMIX Oral Suspension for Calves indicates in 'Pharmaceutical Particulars :

" Neomycin is poorly absorbed from the gastrointestinal tract , has a short half-life and is nearly all excreted unchanged from the gastrointestinal tract"

More importantly there is a significant error in the information in the document :

APVMA
Neomycin
Review Technical Report
February 2024

Residues and Trade p 26
Products 36026 and 49788

".....registered products 36036 and 49788 (2.16 mg/kg (neomycin) twice daily for a minimum of 5 days)"

The registered and approved dosage for product no 49788 (Scour – X) is once daily for a minimum of 5 (five days) 2.16 mg neomycin / day

That is 50% of the daily dose of Neomycin for product 36026 and for the UK registered product

BIMAMIX dose is 2.16 mg/kg x 2 daily ie 4.32 mg / kg daily.

No reference in the Review Technical Report as printed is made to the continued registration and approval of BIMAMIX in UK and Ireland and the approval the Pharmaceutical Particulars

Please consider the additional information . I have already lodged a public submission and provide this extra updated information through your processes.

Regards,

[redacted]

[redacted]

Thank you for your written submission in relation to the neomycin proposed regulatory decision. The APVMA has access to the cited report (Evaluation of Medical Products EMEA /MRL/816/02-FINAL) and will consider the information in your written submission and the cited report prior to making a final regulatory decision. However, please be advised that the APVMA may be unable to rely on any commercially confidential information cited in the European report for regulatory purposes without permission from the data owner.

Further, please note that submissions can be published on the APVMA website if we have received permission to do so. We request that you lodge a public submission coversheet for your submission, which provides options for how your submission will be published (available at: https://www.apvma.gov.au/news-forms-and-publications/forms/public-submission-coversheet).

Please be advised that the public consultation period for the neomycin proposed regulatory decision is open until 26 May 2024. If you have any further information you wish to provide the APVMA, written submissions are invited until this date.

[redacted]

and sea, waters, environment and community. We pay our respects to the Traditional Custodians of the lands we live and work on, their culture, and their Elders past and present.

Classification: OFFICIAL

[redacted]

I last week attended the Australian Cattle Veterinarians Association Conference (at Wodonga) with the opportunity to further discuss the use of Scour – X in calves and the impact of the withdrawal of Neomycin as a treatment for diarrhoea in calves particularly the issue of residues in meat following oral treatment with Neomycin with many veterinarians. From these numerous conversations about the use of Scour-X, in the field by expert dairy veterinarians several points stood out.

1. Scour – X use is limited to dairy bred female calves; the management of dairy calves post – calving: males calves are sent for slaughter as ' bobby calves' (7- 15 days of age) and receive no treatment. The females are retained to be' grown out ', bred and added to the milking herd .
2. Only female calves retained on dairy farms are treated, they do not enter the food chain
3. Surveys are published by the Dept. of Agriculture indicate sampling of beef carcass meat do not indicate residues to Neomycin are an issue.

A report from The European agency for the Evaluation of Medical Products EMEA /MRL/816/02-FINAL indicates

> " A recent study in calves dosed orally with 14 C Neomycin has provided direct evidence to support the view that a high percentage of neomycin remains in the gastrointestinal tract . The absorption in this species was minimal(1 to 11%) about 90% was recovered in faeces and 70 to 80 was present as parent neomycin as indicated by mass spectrometric analysis"
>
> It can be concluded from this study that meat residues do not and will not occur when neomycin is orally dose to calves.

Scour – X should remain available for veterinary prescription. A further addition could be " Product to be used only on dairy heifer calves" as a further restriction on use of product.

Regards,

[redacted]

[redacted]

[redacted]

The Neomycin Review Technical Report (available at https://www.apvma.gov.au/chemicals-and-products/chemical-review/listing/neomycin/neomycin-review-technical-report) includes a summary of the residues risk assessment for neomycin products formulated as oral suspensions, including Scour-X Oral Anti Diarrhoeal Suspension (product 49788). The data considered in this assessment has been referenced. As noted, residues data specific for the product formulation and label use pattern (including treatment regime) would be required to enable a contemporary residues and trade assessment.

We would be happy to organise a meeting with staff from our chemical review and residues teams to discuss this assessment. Please advise by return email to chemicalreview@apvma.gov.au if you would like a meeting organised.

Consultation of the proposed regulatory decision is also open until 26 May 2024. The APVMA will consider all information received during the consultation period prior making a final regulatory decision.

The legislative basis for the review of decisions made by the APVMA are set out in section 166 of the Agvet Code (internal review of decisions) and section 167 of the Agvet Code (review of decisions by Administrative Appeals Tribunal). If, after consideration of the information received in the consultation period, the APVMA decides to vary relevant particulars or conditions under subsection 34A(1) or suspend or cancel approvals or registrations under section 34AA, these decisions would qualify as reviewable decisions.

Kind regards,

[redacted]

chemicalreview@apvma.gov.au | www.apvma.gov.au

The APVMA acknowledges the Traditional Custodians of Australia and their continuing connection to land and sea, waters, environment and community. We pay our respects to the Traditional Custodians of the lands we live and work on, their culture, and their Elders past and present.

[redacted]

Subject: RE: Neomycin Reconsideration – Section 34AB Notice of Proposed Decision

[redacted]

[redacted]

In response to advice regarding the product Scour- X Oral Anti Diarrhoeal Suspension and APVMA's proposal to delete, from Scour- X product registration, approval of use for calves.

The reason given for the proposal to delete the approval for registration in calves is that 'insufficient ' residue data available . Please define ' insufficient'.

When Scour -X was initially submitted for registration to the NRA, residues data was submitted for Scour – X by Jurox Pty Ltd (since been acquired by Zoetis) the data was accepted by the NRA.

The initial advice regarding this matter should be subject to independent review for competency . I would appreciate your guidance on who APVMA would propose to evaluate this decision.

Regards,

[redacted]

[redacted]

Subject: Neomycin Reconsideration – Section 34AB Notice of Proposed Decision [SEC=OFFICIAL]

OFFICIAL

[redacted]

Neomycin Reconsideration – Section 34AB Notice of Proposed Decision

Please find attached a notice under section 34AB of the Schedule to the *Agricultural and Veterinary Chemicals Code Act 1994* in relation to the neomycin reconsideration undertaken by the APVMA under Part 2 Division 2 of that Act.

Written submissions

We invite you to provide us with written submissions in relation to this reconsideration. The closing date for these submissions is 26 May 2024.

When making your submission we would be grateful is you could include reasons for your comments, supporting them, if possible, with relevant scientific information and indicating the source of the information you have used.

We also draw your attention to the Note included in the attached notice advising that submissions will be published on the APVMA website, unless you have asked for the submission to remain confidential in the public submission coversheet accompanying your submission.

Assessment outcomes

A summary of the underlying risk assessments and the product-specific assessment outcomes has been published in the Neomycin Review Technical Report.

As outlined in the Section 34AB Notice of Proposed Decision and the neomycin Review Technical Report, the use of Scour-X Oral Anti-Diarrhoeal Suspension (APVMA No. 49788) in calves was not supported due to insufficient residues data.

To enable a contemporary residues and trade assessment for this product, the APVMA would need residue trial data specific for this product formulation and label use patterns. The test product used in the studies would need to be representative of the commercial formulation and the maximum label dose rate should be administered to the target species. The residue trials should be depletion trials and the label withholding period should be addressed by one of the sampling time points. Further information on residue trial design can be found in APVMA guidance for Food safety studies for veterinary drugs used in food-producing animals.

Please advise by return email to chemicalreview@apvma.gov.au if you would like to meet with the APVMA to discuss these product-specific assessment outcomes.

If you have any questions or would like further information, please contact the chemical review team by phone (02) 6770 2400 or email chemicalreview@apvma.gov.au.

[redacted]

[redacted]

chemicalreview@apvma.gov.au | www.apvma.gov.au

The APVMA acknowledges the Traditional Custodians of Australia and their continuing connection to land and sea, waters, environment and community. We pay our respects to the Traditional Custodians of the lands we live and work on, their culture, and their Elders past and present.

[redacted]

[redacted]

22 April 2024

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

Via email: chemicalreview@apvma.gov.au

Dear APVMA,

RE: NEOMYCIN CHEMICAL REVIEW

The Australia Chicken Meat Federation (ACMF) extends its gratitude to the Australian Pesticides and Veterinary Medicines Authority (APVMA) for affording us the opportunity to review the proposed regulatory decision concerning products containing neomycin.

Ensuring the safety of products utilised in animal health management is paramount to the Australian chicken meat industry. We commend the comprehensive chemical re-evaluation undertaken by the APVMA. ACMF's response pertains specifically to the re-evaluation of neomycin-containing products utilised within the poultry industry, notably CCD Neomycin and Abbeyneo Antibiotic Feed Additive (referred to herein as Abbeyneo).

Whilst it remains an imperative of the industry to ensure we have access to sufficient tools to respond to poultry health aliments in a timely and effective manner, it is equally important that these tools are used judiciously.

The industry remains unwavering in its commitment to investing, both materially and financially, in ensuring the judicious use of antimicrobials. This commitment is evidenced through routine monitoring of stewardship practices, resistance patterns, and the ongoing development or evaluation of suitable alternatives.

ACMF views the APVMA's decision to cancel registrations for products containing neomycin as a precautionary measure aimed at safeguarding public health and the environment. Consultation within our industry has led to a similar conclusion. ACMF firmly believes that deregistering CCD Neomycin and Abbeyneo represents a sensible step in fortifying our industry's and Australia's dedication to responsible antimicrobial usage, particularly considering the availability of viable alternatives.

In conclusion, the ACMF supports the APVMA's decision to deregister CCD Neomycin and Abbeyneo. We believe this action demonstrates our industry's commitment to public health, environmental sustainability, and responsible antimicrobial use.

Should you require further information, please feel free to contact the ACMF Office.

[redacted]

[redacted]

16.5.2024

Re: Mastalone registration and use in the Dairy Industry

I am a practicing Large Animal Veterinarian in the Dairy industry and been so for the past 30 years operating in the Southwest of Western Australia principally in the Busselton, Capel and Scott River regions.

During my time in practice I have seen a decline in the number & range of intra-mammary preparations available to us the Veterinarian & Farmers that we service.

It is my understanding that:

1. Neomycin, Oxytetracycline have been rated as low importance by ASTAG?
2. Not aware of any antibiotic residue issues with Neomycin.
3. Neomycin removed in partnership with Penicillin as an injectable antibiotic.

Discussion:

Currently Mastalone is the only Lactational Intra-mammary preparation that I am aware of that has Neomycin &/or Oxytetracycline. By removing Neomycin as an intra-mammary by default also removes Oxytetracycline + Prednisolone – a very important combination for treating clinical cases that are not responsive to other treatment regimes.

Currently we have 4 high class treatment options that I see as valuable in treating lactational mastitis:

1. Cloxacillin
2. Amoxicillin & Clavulanic acid
3. Cephalosporins
4. Mastalone – Neomycin, Oxytetracycline hydrochloride, Oleandomycin, Prednisolone

[redacted]

There are a number of my clients that only use Mastalone for the treatment of lactational mastitis, if not used as a routine by other clients then it is the fallback for the treatment of cows that are refractory to the first three options.

In my experience invitro testing [culture and sensitivity testing] can have a poor correlation to mastitis clearance rates obtained in the field.

It is my understanding that Neomycin in combination with Penicillin or by itself as an injectable antibiotic could be more open to abuse by Prescribers, Horse owners, Pig producers etc. I cannot understand why an lactating intramammary which has a very specific use that cannot be used more widely in different industries should be targeted with the same fate.

I don't see the need for Neomycin to be included in Dry Cow therapies as there are very good options in Cloxacillin & Cephalosporin preparations.

In my opinion it would be detrimental to the dairy industry & animal welfare if Mastalone is removed from the market as there are no alternatives to take its place.

Yours Sincerely,

[redacted]

[redacted]

21/05/2024

Re: APVMA regulatory decision regarding Neomycin.

To whom it may concern,

I wish to write to you to oppose the cancellation of the intramammary products containing neomycin (Special Formula 17900 Forte-V Lactating Intramammary Antibiotic Suspension, and Mastalone Intramammary Suspension for Lactating Cows). I am a cattle Veterinarian and have been using these products from Zoetis for the last seven years.

It is in my professional opinion that these intramammary products are of high significant value to the South Australian Dairy farmers that are under my veterinary care. From my experience in the cattle industry, these medications can target and treat mastitis cases much more effectively than other forms of intramammary medication. Removing these products will negatively impact not just south Australian dairy farmers but dairy farmers throughout Australia. As a veterinarian, there is already a limited amount of intramammary products available on the market in Australia so removing these two products would drastically limit treatment choices and hence would make appropriate antimicrobial stewardship decisions more difficult.

I have a firm belief that these intramammary products are more effective at treating mastitis than the intramammary cloxacillin alternatives. I agree with Zoetis that there have been no indications of safety, efficacy, residue or trade issues. Please reconsider the cancellation of Mastalone and Special Formula 17900 Forte-V Lactating Intramammary Antibiotic Suspension

Thank you.

[redacted]

Neomycin proposed regulatory decision

Submission of the Australian Veterinary Association Ltd

22 April 2024

www.ava.com.au

The Australian Veterinary Association (AVA)

The Australian Veterinary Association (AVA) is the national organisation representing veterinarians in Australia. Our members come from all fields within the veterinary profession. Clinical practitioners work with companion animals, horses, farm animals, such as cattle and sheep, and wildlife. Government veterinarians work with our animal health, public health and quarantine systems while other members work in industry for pharmaceutical and other commercial enterprises. We have members who work in research and teaching in a range of scientific disciplines. Veterinary students are also members of the Association.

Discussion

The AVA thanks the Australian Pesticides and Veterinary Medicines Authority for the opportunity to comment on the proposed regulatory decision for the reconsideration of neomycin.

We have strong concerns about the proposal to cancel the registration of Mastalone® Intramammary Suspension for Lactating Cows, because of the impact this will have on the treatment of dairy cows, and on antimicrobial stewardship by veterinary practitioners.

The product Mastalone® is widely used by dairy veterinarians and is a main stay of mastitis treatment.

Mastalone® contains three LOW importance antimicrobials, according to the ratings by the Australian Strategic and Technical Advisory Group on Antimicrobial Resistance (ASTAG).

These are: oxytetracycline, oleandomycin and neomycin.

It is the only low importance lactating cow intramammary available in Australia; all alternatives contain antimicrobials rated of MEDIUM importance by ASTAG.

If the product is no longer available, this will:

(a) reduce the therapeutic armoury of veterinarians; and

(b) force veterinarians to use medium importance intramammary treatments instead, which is not a good outcome from an antimicrobial stewardship perspective.

The AVA is not aware of any evidence of residue issues that would justify cancellation of this product.

Recommendation

- On behalf of our members the AVA recommends that the registration of Mastalone® Intramammary Suspension for Lactating Cows is not cancelled, so that it may remain as an intramammary treatment option.

[redacted]

20th May 2024

Chemical Review
Australian Pesticides and Veterinary Medicines Authority
GPO Box 3262
Sydney, NSW 2001
chemicalreview@apvma.gov.au

RE: Review of Neomycin

To whom it may concern,

Aurora Dairies Pty Ltd is the largest dairy farming entity in Australia, managing and operating 55 farms across South Australia, Victoria, Tasmania and New Zealand. We manage over 50,000 cows and produce 320 million litres of milk annually, supplying various factories and markets.

Mastalone ® (containing neomycin) manufactured and distributed in Australia by Zoetis, is a critical drug that we use daily under veterinary direction to control and treat mastitis – the most important animal disease in our business and the dairy industry more broadly. Should this product be removed from the market, it will further restrict our treatment options for this disease and will have serious implications for the quality of the milk that we produce.

We encourage you to rescind your proposal to change label approvals for intramammary use of neomycin for the following reasons:

1. **Efficacy**
    - Mastalone is the only non-beta lactam intramammary product available for treating mastitis in dairy cows during lactation, crucial for addressing pathogens resistant to other treatments.
    - Its efficacy is well-documented, supported by years of use and in-vitro sensitivity data against common mastitis pathogens. This is reaffirmed by our on-farm experience.
    - Surveys in the dairy industry over previous decades show high efficacy of tetracycline and neomycin, with very low levels of bacterial resistance.
    - It is a critical drug that supports our initiatives to produce high-quality and safe food as articulated in our animal welfare, milk quality and sustainability strategies.

2. **Antimicrobial Resistance**
    - Mastalone® contains neomycin, oleandomycin, and oxytetracycline, rated as Low Importance by the Australian Strategic and Technical Advisory Group on Antimicrobial Resistance (ASTAG) which indicates minimal risk of contributing to significant antimicrobial resistance issues.
    - We are not aware of any instances of neomycin resistance being present on any of our farms.

[redacted]

Proudly Dairy.

3. **Trade and Residues**
    - Over 11 years, only 3 out of 10,696 residue samples showed oxytetracycline above the MRL, likely due to the use of injectable oxytetracyclines in the cattle industry rather than use of Mastalone®.
    - To be best of our knowledge, no residues of oleandomycin or neomycin have been found in tissue samples over this period and we therefore regard the risk of neomycin residues as being close to non-existent. Aurora Dairies has never been responsible for neomycin residues in milk or meat and have robust systems in place to manage this risk.
    - Aurora Dairies considers that the removal of a highly efficacious, cost effective and low risk product such as Mastalone® from the market will not result in less antibiotic use, but rather increased use of other potentially less effective and higher residue risk products – contrary to the APVMA's objective.

4. **Industry Importance:**
    - Mastalone® is crucial for maintaining animal health and dairy production efficiency. We frequently use it as a last line of treatment when other products have failed, and it therefore helps reduce culling and animal wastage due to mastitis.
    - Cancelling Mastalone's registration poses welfare implications and risks to dairy production.
    - Over the last 10 years the number of available products to effectively treat mastitis has reduced, and R&D pipelines are limited in the development of future options due to the size of the Australian market and the development and regulatory costs involved in achieving registration.

Thank you for your consideration.

[redacted]

[redacted]

Proudly Dairy.

[redacted]

Good Morning
I am a veterinarian working in a mixed practice which includes some dairy farmers.
I find Mastalone a very useful intramammary treatment in those refractive cases.
Therefore I and my clients would be disappointed if this preparation was to be discontinued. We have already lost Special Formula forte. Sometimes a combination of drugs in the one preparation is the best treatment we can dispense for a timely recovery.

[redacted]

Sent from my iPad

Australian Pork Limited

[redacted]

24 May 2024

Chemical Review
Australian Pesticides and Veterinary Medicines Authority
GPO Box 3262
Sydney NSW 2001
chemicalreview@apvma.gov.au

Submitted via online form

To whom it may concern,

RE: Proposed Regulatory Decision for the Reconsideration of Neomycin

On behalf of the Australian pork industry, we would like to thank you for the opportunity to provide a submission for consideration.

About Australian Pork Ltd

Australian Pork Ltd (APL) is the peak national representative body for Australian pork producers. It is a producer-owned company combining marketing, export development, research and innovation and strategic policy development to assist in securing a profitable and sustainable future for the Australian pork industry.

The domestic pork industry is a vital part of Australia's food supply chain, with pork the second most consumed meat in Australia and all fresh pork consumed in Australia domestically sourced. In 2022/23, the Australian pork industry produced 453,426 metric tonnes of pork. The largest volume of production is sourced from Queensland, Victoria and South Australia from an Australian domestic commercial sow herd, as at 1 July 2023, of 285,538 sows.

The Australian pork industry contributes around $6 billion in gross domestic product to the economy and supports a diverse range of careers across the food supply chain. The industry is domestically focused with around 90% of our production supporting food security for Australians. The value of the 10% exported in 2022/23 was around $182 million.

Approximately 34,600 jobs are supported by the industry nationally, predominantly in regional Australia, supporting the economic and social prosperity of communities and the wellbeing of individuals. The Australian pork industry's workforce is skilled, specialised and generally engaged on a permanent basis.

APL holds a number of roles on behalf of the Australian pork industry. APL is:

- The pork Research, Development and Extension organisation leading climate research and extension in partnership with the Australian government and the research community,
- The marketing arm of the Australian pork industry managing national campaigns such as "Get some pork on your fork" and the Valuable Provenance campaign raising awareness of how to support the growth of high-quality smallgoods made from Australian pork,
- The peak body for the Australian pork industry, representing pork within the National Farmers' Federation and other representative frameworks,
- Leading the pork industry's Sustainability Framework implementation,
- Part of the sector-wide collaborative effort to develop an Australian Agricultural Sustainability Framework, coordinated by the National Farmers' Federation on behalf of the Federal Department of Agriculture, and
- The industry signatory to the Emergency Animal Disease Response Deed (EADRA).

Pork industry Antimicrobial Stewardship

The pork industry is committed to the responsible care of pigs to safeguard their comfort, health and welfare. 91% of our commercial herds are quality-assured under the Australian Pig Industry Quality Assurance (APIQ) Program. The highly skilled staff who are involved in the care of animals on our farms must be highly competent in pig health, pig welfare and biosecurity. Antimicrobials are applied when deemed necessary under strict veterinary oversight and are only used to treat and control bacterial infections.

The Pork industry recognises the importance of preserving antimicrobials for therapeutic use in humans and animals and the industry is committed to good antimicrobial stewardship. APL, along with Australian Veterinary Association (AVA), Australian Department of Agriculture and Water Resources through the Australian Biosecurity Response and Reform Program (ABRR) and Animal Medicine Australia had developed the Antimicrobial Prescribing Guidelines for Pigs (Cutler et al, 2020). This was a proactive step, the first of its kind for an Australian livestock industry.

The industry also conducted three rounds of Antimicrobial resistance (AMR) surveys and all results indicated low or no resistance to those antimicrobials deemed critically important to human health.

APL has a range of concerns regarding the proposed regulatory reconsideration and requests that prior to proceeding any further with the reconsideration of Neomycin, that the APVMA:

1. Demonstrates a clear understanding of the rationale for this reconsideration.

2. Provides an extension to existing timeframes to allow more thorough consultation and consideration of the needs and proposed options with key stakeholders including the pork industry.
3. Provides guidance on next steps to retain/obtain label registration for use in food producing species, specifically pigs, and associated time to facilitate access to the following products:
    - Scour-X Oral Anti-Diarrhoeal Suspension (APVMA #36026)
    - Scourban Oral Anti-Diarrhoeal Suspension (APVMA #36026)
    - Jurox Neomycin Sulfate Injection (APVMA #36237)
    - Abbeyneo Antibiotic Feed Additive (APVMA #67805)
    - CCD Neomycin (Neomycin Sulphate Water Soluble Powder) (APVMA #52782)
4. Provides sufficient time to allow processes required to retain/obtain label registrations, to be undertaken by product registrants.

In making this representation, APL would like to draw the attention of APVMA to the key supporting statements:

1. Neomycin is the primary treatment choice in the strategic treatment of specific bacterial enteric infections caused by *Escherichia coli* and *Salmonella* in piglets and growing pigs.
2. In accordance with the Antimicrobial Prescribing Guidelines for Pigs (Cutler et al, 2020), the foreword for which is provided by Co-Chair of the Australian Strategic and Technical Advisory Group on Antimicrobial Resistance and former Australian Chief Veterinary Officer Dr Mark Schipp, Neomycin is the preferred first line of treatment for the following conditions of pigs:
    - Enterotoxigenic (non-haemolytic) *Escherichia coli* – a common cause of high morbidity, high mortality enteric disease in young piglets.
    - Enterotoxigenic or enterotoxaemic (haemoloytic) *Escherichia coli* – a common cause of enteric and neurological disease and sudden death in young and newly weaned piglets.
    - Salmonellae – a cause of enteric disease and sudden death in growing pigs.
3. These uses are supported by scientific evidence of high susceptibility to Neomycin including in 96% of porcine *Salmonella* and >75% of *Escherichia coli* (Murray et al., 1986; DVFA, 2018).
4. Neomycin is rated a low importance antimicrobial by the Australian Government Importance Ratings and Summary of Antibacterial Uses in Human and Animal Health in Australia (ASTAG, 2018). In the absence of Neomycin, alternative or second line active agents that would be used to treat *Escherichia coli* and *Salmonella* infections include Trimethoprim plus Sulfonamide and Apramycin. Both Trimethoprim plus Sufonamide and Apramycin are rated as being of medium importance by ASTAG. Use of these alternatives therefore represents a shift to use of a more important antimicrobial and a shift away from industry antimicrobial stewardship, public health and One Health imperatives.

5. In respect to chemical residues, over the past 11 years there has only been one residue result, from 2750 pig samples, that has exceeded the maximum residue limit (MRL). This suggests that residue detections are not a plausible cause for the review in respect to use of the product in pigs.

APL must stress the very real risk of compromise to pig health, welfare, antimicrobial stewardship and One Health imperatives that the APVMA reconsideration of Neomycin registrations poses. APL seeks to better understand the rationale behind this reconsideration and to find a pathway forward that addresses our industry's concerns.

We request that the APVMA partner with the pork industry and registrants in this matter, in the provision of guidance and time to progress a resolution that addresses APVMA concerns without precluding access to Neomycin, acknowledging that it is a preferred, efficacious treatment for the conditions prescribed in this submission.

We would be happy to share further information to support our farming businesses, please contact the APL General Manager of Policy and Industry Relations [redacted]

Yours sincerely,

[redacted]

Chief Executive Officer

References

Cutler, R. Gleeson, B. Page, S. Norris, J. Browning, G. (2020). Antimicrobial prescribing guidelines for pigs, Australian Veterinary Association Ltd and Animal Medicines Australia, Canberra

Murray CJ, Ratcliff RM, Cameron PA, et al. (1986). The Resistance of Antimicrobial Agents in *Salmonella* from Veterinary Sources in Australia from 1975 to 1982. Australian Veterinary Journal; vol. 63: p286-292.

Danish Veterinary and Food Administration (DVFA) (2018). Evidence-based Prudent Use Guidelines for Antimicrobial Treatment of Pigs, Ministry of Environment and Food, Denmark.

Australian Strategic and Technical Advisory Group on Antimicrobial Resistance (ASTAG) (2018). Importance Ratings and Summary of Antibacterial Uses in Human and Animal Health in Australia (Version 1), Australian Government, Canber

Australian Dairy Farmers

[redacted]

24 May 2024

Chemical Review
Australian Pesticides and Veterinary Medicines Authority
GPO Box 3262 Sydney NSW 2001
Email: chemicalreview@apvma.gov.au

[redacted]

Public consultation: Neomycin – proposed decisions on reconsideration

Australian Dairy Farmers (ADF) welcomes the opportunity to provide a submission on the proposed decisions on the reconsideration of neomycin product registrations and label approvals.

The ADF is the national industry representative body (IRB) for dairy farmers across Australia. The Australian dairy industry is the third largest rural industry in Australia and a key sector of the agricultural and Australian economy, generating close to A$6.1 billion in farmgate value in the 2022/23 financial year[1].

As the recognized national representative body for dairy farmers across the six dairy producing States, ADF's mission is to improve the productivity and sustainability of dairy farmers in Australia. Critical to this mission is to maintain and improve Australia's animal health and welfare systems. ADF is comprised of State dairy farming representative organisations, and dairy farmers themselves, from all of the dairy producing States of Australia.

Mastalone® Intramammary Suspension For Lactating Cows (CRIS# 49851) is considered by ADF to be a vital tool for dairy farmers to treat clinical mastitis. Mastitis is a painful disease, causing significant animal welfare concerns and economic losses on every dairy farm. Timely and appropriate treatment is essential for the welfare of the affected animal(s).

Mastalone® contains antibiotic active constituents (Oxytetracycline, Oleandomycin and Neomycin) that are not available in other registered intramammary products, are of low importance to the development of antimicrobial resistance[2] and cover a broader spectrum of mastitis pathogens than alternative products. It provides an important alternative product to other intramammary lactating cow products, which contain only beta-lactam antibiotic active constituents.

ADF is aware of the Australian Pesticides and Veterinary Medicines Authority's (APVMA) responsibility to assess the efficacy, safety and risks to trade of all products captured within the scope of the APVMA's review of neomycin.

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[1] Australian Dairy Industry In Focus 2023 (2024) Dairy Australia, [redacted]

[2] Australian Strategic and Technical Advisory Group on Antimicrobial Resistance. (2018, June). Importance Ratings and Summary of Antibacterial Uses in Human and Animal Health in Australia. Australain Government.

ADF is extremely concerned that the APVMA proposes to cancel the registration of Mastalone®, primarily due to a lack of data to enable the APVMA to assess risks to trade from chemical residues.

ADF considers there is a very real risk of an inappropriate and perverse regulatory outcome if Mastalone® were deregistered. By removing registration of a tried and tested, broad-spectrum, low risk product, the availability of a poorer selection of products covering a narrower spectrum of pathogens at arguably higher risk may result. This may lead to inferior animal-welfare outcomes in Australia's third largest agricultural sector.

In appealing for ongoing access to Mastalone as a vital tool for farmers, ADF makes the following points:

- Mastalone® has been used for over 50 years by dairy farmers in Australia when treating severe cases of mastitis or as a second-line treatment where others have failed.
- The industry has a long history of monitoring for, and successfully managing the risks of antimicrobial residues in milk and meat products traded domestically and around the world.
- Individual farmers place high importance on adhering to risk-management procedures, particularly when drug treatments are involved.
- Through industry's established chemical residue risk management procedures, ADF is unaware of Mastalone® being identified as posing a risk to the health of consumers of dairy products or to trade in such products.

Dairy Australia is providing a separate submission to provide more detail on the industry's risk management procedures for antibiotic residues, which are endorsed by ADF.

ADF and its representative member State dairy farmer organisations do not consider the ongoing label-compliant use of Mastalone® as posing a risk to the domestic or international trade of dairy products, and so support the on-going registration of this vital intramammary product.

[redacted]

[redacted]

[redacted]

Chemical Review
Australian Pesticides and Veterinary Medicines Authority
GPO Box 3262
Sydney NSW 2001
chemicalreview@apvma.gov.au

24 May 2024

Proposed Regulatory Decision for the Reconsideration of Neomycin

To whom it may concern

Rivalea Australia

JBS Australia is the largest meat and food processor in Australia with more than 15,000 tam members and a strong portfolio of leading beef, lamb, pork, salmon and value-added branded products. JBS globally is the largest animal protein business and one of the largest food companies in the world, with operations in North America, South America, Europe, Australia and New Zealand. JBS Australia's Pork Division includes the Rivalea pig breeding and progeny raising enterprise. Rivalea Australia employs over 1000 people and is a critical employer in regional Australian towns across New South Wales and Victoria. The company operates across a number of farming, processing and distribution sites.

Rivalea Australia is committed to the responsible, ethical, science-based care of animals to safeguard their comfort, health and welfare. Our farms are serviced by a team of three pig health veterinarians, two pig nutritionists and supported by animal welfare, production, sustainability and data scientists. All farms are quality-assured under the Australian Pig Industry Quality Assurance (APIQ✓) Program. All personnel involved in the care of animals on our farms must possess or be working to achieve the pork industry skillset which includes (but is not limited to) competencies in pig health and ill health, pig welfare and biosecurity.

Rivalea Australia recognises the importance of preserving antimicrobials for therapeutic use in humans and animals and is committed to antimicrobial stewardship. Antimicrobial stewardship is considered an important component of our Animal Care Program. Rivalea Australia continues to monitor antimicrobial usage and through its antimicrobial stewardship program, is committed to reducing antimicrobial use. Where antimicrobials are used, this is based on diagnostic evidence. Antimicrobials are used only at prescribed dosages known to be effective using peer reviewed guidelines including the Antimicrobial Prescribing Guidelines for Pigs (Cutler et al, 2020). Antimicrobials are applied strictly under veterinary oversight and are only used to treat and control bacterial infections.

Proposed Regulatory Decision for the Reconsideration of Neomycin

Rivalea Australia strongly opposes the proposed regulatory reconsideration and requests:

1. A clear understanding of the rationale for the Australian Pesticides and Veterinary Medicines Authority (APVMA) determination.
2. An extension to existing timeframes to allow proper consultation and consideration of the process with key stakeholders including the pork industry.

[redacted]

3. Guidance on next steps to retain/obtain label registration for use in food producing species, specifically pigs, and associated time to facilitate of the following products:
    - Scour-X Oral Anti-Diarrhoeal Suspension (APVMA #36026)
    - Scourban Oral Anti-Diarrhoeal Suspension (APVMA #36026)
    - Jurox Neomycin Sulfate Injection (APVMA #36237)
    - Abbeyneo Antibiotic Feed Additive (APVMA #67805)
    - CCD Neomycin (Neomycin Sulphate Water Soluble Powder) (APVMA #52782)
4. Sufficient time to allow processes required to retain/obtain label registrations, to be undertaken by product registrants.

In making this representation, Rivalea Australia draws the attention of the APVMA to the below supporting statements:

1. Neomycin is the primary treatment choice in the strategic treatment of specific bacterial enteric infections caused by *Escherichia coli* and *Salmonella* in piglets and growing pigs.
2. In accordance with the Antimicrobial Prescribing Guidelines for Pigs (Cutler et al, 2020), the foreword for which is provided by Co-Chair of the Australian Strategic and Technical Advisory Group on Antimicrobial Resistance and former Australian Chief Veterinary Officer Dr Mark Schipp, Neomycin is the preferred first line of treatment for the following conditions of pigs:
    - Enterotoxigenic (non-haemolytic) *Escherichia coli* – a common cause of high morbidity, high mortality enteric disease in young piglets
    - Enterotoxigenic or enterotoxaemic (haemoloytic) *Escherichia coli* – a common cause of enteric and neurological disease and sudden death in young and newly weaned piglets
    - Salmonellae – a cause of enteric disease and sudden death in growing pigs
3. These uses are supported by scientific evidence of high susceptibility to Neomycin including in 96% of porcine *Salmonella* and >75% of *Escherichia coli* (Murray et al, 1986; DVFA, 2018).
4. Neomycin is rated a low importance antimicrobial by the Australian Government Importance Ratings and Summary of Antibacterial Uses in Human and Animal Health in Australia (ASTAG, 2018). In the absence of Neomycin, alternative or second line active agents that would be used to treat *Escherchia coli* and *Salmonella* infections include Trimethoprim plus Sulfonamide and Apramycin. Both Trimethoprim plus Sufonamide and Apramycin are rated as being of medium importance by ASTAG. Use of these alternatives therefore represents a shift to use of a more important antimicrobial and a shift away from industry antimicrobial stewardship, public health and One Health imperatives.

5. In respect to chemical residues, Rivalea Australia notes that over the past 11 years there has only been one residue from 2750 pig samples that has exceeded the maximum residue limit (MRL). This suggests that residue detections are not a plausible cause for the review in respect to use in pigs.

6. In describing use of Neomycin in the management of pig health, Rivalea Australia acknowledges that current use patterns in pigs of some Neomycin products are not registered and represent off-label usage. Hence they may not have been considered by the APVMA in the review process it has undertaken on Neomycin product registrations. Rivalea Australia also acknowledges that off-label use patterns may preferably need to become on-label use patterns in relation to the reconsiderations being made. Australian Pork Limited, Rivalea Australia and the Australian Pig Veterinarians Special Interest Group of the Australian Veterinary Association welcome the opportunity to discuss the use of Neomycin in pigs and matters relating to retaining/obtaining appropriate registration further with the APVMA.

Rivalea Australia emphasises the very real compromise to pig health, welfare, antimicrobial stewardship and One Health imperatives that the APVMA reconsideration of Neomycin registrations poses. Rivalea Australia seeks to better understand the rationale behind this reconsideration and to find a pathway forward that addresses its concerns.

We strongly request that the APVMA partner with the pork industry and registrants in this matter, in the provision of guidance and time to progress a resolution that addresses APVMA concerns without precluding access to Neomycin, acknowledging that it is a preferred, efficacious treatment for the conditions prescribed in this submission.

Yours sincerely

[redacted]

References

Australian Strategic and Technical Advisory Group on Antimicrobial Resistance (ASTAG) (2018). Importance Ratings and Summary of Antibacterial Uses in Human and Animal Health in Australia (Version 1), Australian Government, Canberra.

Cutler, R. Gleeson, B. Page, S. Norris, J. Browning, G. (2020). Antimicrobial prescribing guidelines for pigs , Australian Veterinary Association Ltd and Animal Medicines Australia, Canberra

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