

**4 FEBRUARY 2000**

## **ANIMAL REMEDIES BOARD UPDATE ON ANTIBIOTIC RESISTANCE ACTIONS**

At the Animal Remedies Board meeting of 15 December 1999, after consideration of the public submissions on the issue, it was decided that the Board's previous decision be reaffirmed. The submissions were referred to the Registrar to take into account the specific comments of submitters.

At the meeting on 20 October 1999 plans were made to progress the management of the antibiotic resistance issue, with the two principle actions being:

1. work with the Ministry of Health to establish the terms of reference for a joint antibiotic resistance management programme, including a joint ministerial committee with an overview of the issue; and
2. progress a managed review of all existing veterinary antibiotic products.

The following is an update of the activity undertaken under each of the action areas.

### **JOINT ANTIBIOTIC RESISTANCE MANAGEMENT PROGRAMME**

The Ministry of Health and MAF has met to discuss the development of an antibiotic resistance management programme. Within the context of that programme they are considering the terms of reference and make-up of the joint ministerial committee. It is agreed that, after brief consideration, the role of such a committee should at least include:

- improving co-ordination between the health and agricultural sectors to promote the best use of antimicrobials in animal and human health;
- advising on the terms of reference and components of the resistance management programme that would be necessary and sufficient (both from a technical and resource management perspective) to define and monitor the resistance problem in New Zealand.
- consider the analysis of information generated in the resistance management programme; and
- providing advice on the implementation of controls measures considered necessary in light of analysis of surveillance findings.

However, there are a number of technical resource management issues that still need to be addressed.

MAF and Ministry of Health agree that the role of the Ministerial committee and the nature of the resistance management programme itself must be clarified before the matter can be presented to Ministers and a committee with the appropriate expertise and experience can be established.

The Ministries intend to have a proposal for the resistance management programme at a stage of development that can be considered by Ministers by March 2000. In the meantime, MAF will progress with the review of licensed veterinary antibiotic

products according to the attached rationale. Ministry of Health will continue to promote responsible use of antibiotics by the medical profession.

## **REVIEW OF VETERINARY ANTIBIOTIC PRODUCTS**

In order to implement a review of antibiotics, the ACVM Group has prepared the attached description of the review and the decision rationale that will be used in regard to changes in licensing of antibiotic trade name products.

### **Implementation**

The licensees of products containing antibiotics have been sent this rationale and invited to take part in the review in order to clarify the significance of their product in relation to antibiotic resistance.

They have also been advised that if the review indicates that human health concerns relating to their product are significant:

- licensing for growth promotion use in particular will be discontinued, except where the criteria in the report can be met.
- the licensee will be required to provide data to support claims for prophylactic or therapeutic uses where this is lacking.
- immediate action will be taken with regard to suspension of licences when the public health concern is known to be significant at the outset of the review. Otherwise, licences will be maintained during the review in light of the animal welfare impacts.

Consideration of antibiotic resistance will become part of the licensing process for new applications for antibiotic products. It will be promulgated as a specific ACVM Registration Standard.

The ACVM Group will proceed with the review of products in the following order based on the urgency recommended by the Antibiotic Resistance Steering Group. Assessment will be undertaken on antibiotic families rather than on individual products. Antibiotic-containing products licensed for growth promotion will be considered first in each antibiotic family. Review of other products in each family will follow within the same timeframe.

The first group of products to be reviewed reflects the findings of the Expert Panel with regard to either confirmed or plausible mechanisms of transfer of antibiotic resistance or direct development of resistance.

#### **1. Fluoroquinolones**

The sole fluoroquinolone licensed for use in water for food-producing animals has had its licence suspended until the product can be reviewed. Suspension was considered necessary for this product because of the importance of the product for human use and the confirmed examples of antibiotic resistance. It is expected that the review will be completed by April 2000.

#### **2. Avoparcin, Virginiamycin, Avilamycin**

The licensees of these products have been advised of the review. It is expected that the review of these products will be completed by June 2000.

### **3. Macrolides**

The licensees of these products have been advised of the review. It is expected that the review of these products will be completed by December 2000.

The second group of products to be reviewed are those for which animal health is a concern.

#### **1. Bacitracin**

The licensees of these products have been advised of the review. It is expected that the review of these products will be completed by December 2000.

While a mechanism of transfer of antibiotic resistance was identified for bacitracin with regard to cross-resistance with vancomycin, the likelihood of the transfer occurring is slight. In addition, bacitracin itself is not an antibiotic used in human health. Therefore, the urgency of review is less than that of the three antibiotic families above. However, the Expert Panel considered that the growth promotion use of bacitracin jeopardises the use of this antibiotic for prophylaxis and therapy in animals. Consequently, to protect the value of this antibiotic for the prevention and control of specific diseases, products containing bacitracin that are licensed for growth promotant use will be reviewed.

#### **2. Ionophors**

The ACVM Group believes that these antibiotics can be reviewed to confirm that they are not of significance with regard to antibiotic resistance as they are not used in human health and there is no known mechanism of antibiotic resistance. Licensees of ionophors will be encouraged to focus their claims on the prophylactic and therapeutic uses of these products. It is expected to be completed by December 2000.

#### **3. Flavophospholipol, Olaquinox, Quinoxalines**

These are not commonly used products. They are not used in human health and there is no known mechanism of antibiotic resistance. The timetable for review of these products is uncertain, given the magnitude of the review.

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Concerns have been raised that by grouping the fluoroquinolones and avoparcin in the same paragraph, in the press release of 20 October 1999; it could be interpreted that fluoroquinolones were registered for growth promotion and disease prevention purposes.

No fluoroquinolone is registered in New Zealand for growth promotion or disease prevention.

The sole oral fluoroquinolone registered for use in food producing animals is approved only for individual animal therapeutic use.

The proprietor of the only licensed oral fluoroquinolone registered for use in food animals has clarified its advice to the Animal Remedies Board. It is not intending to withdraw its licence. Consequently the Animal Remedies Board is dealing with the issue, so as to preclude the use of oral fluoroquinolones in food producing animals.

The proprietors of avoparcin containing products have been contacted, and advised of the policy decisions of the Animal Remedies Board, that priority be given to reassessment of avoparcin products.

20 October 1999

## **Animal Remedies Board Adopts ‘Prudent’ Approach to Antibiotic Use in Food Animals**

The Animal Remedies Board has adopted policy recommendations relating to the use of antibiotics as growth promotants and for prevention of disease in food animals in New Zealand.

The Board considered recommendations from its Antibiotic Resistance Steering Group which comprised representatives of consumer groups, livestock producers, veterinarians, the pharmaceutical industry, Animal Remedies Board, Ministry of Agriculture and Forestry, Ministry of Research Science and Technology and the Environmental Risk Management Authority.

There is concern in some quarters that the use of antibiotics in food animals – particularly as growth promotants or as prophylactics (i.e. for disease prevention rather than treatment) – could increase the risk of antibiotic resistance among people who eat the meat of those animals. The Steering Group noted that current information is limited, but research in the area of antibiotic resistance is daily adding clarification to the problem.

The Board agreed with the Steering Group’s view that there was a need for a full risk assessment of the possible connection between the use of antibiotics in food animals and human antibiotic resistances but that ‘...delays should not hinder prudent regulatory action in the meantime.’

The full policy decisions are attached.

Among the key points of the Board’s proposed policy was the need for integrated human and animal health information and the need for liaison and co-ordination among relevant agencies. It has recommended that a Ministerial inter-departmental committee including representatives from the Ministry of Agriculture and Forestry and the Ministry of Health be set up to take a holistic view of the issue of antibiotic resistance.

The Board also endorsed the Steering Committee’s recommendations for new criteria in assessing applications to register antibiotics for growth promotant use and for prophylactic use. The guidelines outline issues that should be considered when assessing an application, including the implications for public health and animal welfare.

These criteria will be implemented as soon as practicable, and will be re-evaluated regularly in light of any new knowledge that becomes available.

The Board considered, among other antimicrobials, fluoroquinolones and avoparcin used for growth promotion or disease prevention in food animals. It has been advised that the fluoroquinolone product in question is likely to be voluntarily removed from the market and that future products are not likely to be able to meet the new criteria for licensing. (Avoparcin products will also be re-assessed and are not likely to meet the licensing criteria.)

However, the Board noted that, when considering whether to withdraw a product licence, thought must be given to ensure that a product that is essential for the health and welfare of animals is not inadvertently or precipitately withdrawn from the market. In Sweden, the withdrawal of antibiotic growth promotants resulted in a significant increase in mortality rate in pigs the following year.

The Board's policy is open for public consultation until 10 December 1999. The Board will decide at its next meeting on 15 December 1999 whether its policy requires refinement as a result of submissions.

The policy, along with the recommendations and report of the Steering Committee and Expert Panel, are available on the MAF website (<http://www.maf.govt.nz/ACVM/>) or by contacting:

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Animal Remedies Board  
P O Box 2526  
Wellington  
Phone: (04) 460-8750

Media inquiries to:

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## **ANIMAL REMEDIES BOARD POLICY DECISIONS - 20 October 1999**

The Animal Remedies Board's decisions in regard to the regulatory control of in-feed antibiotic growth promotants in New Zealand are:

1. In recognition of the urgent need for inter-agency co-ordination of activities related to antibiotic resistance in animal and human health, the Board recommends the establishment of a joint ministerial committee to ensure co-operation, co-ordination and ongoing review of policies and criteria for regulatory control of in-feed antibiotics.
2. The Board supports the development of standards, guidelines and codes of practice for the use of agricultural antibiotics by veterinarians and industry, and will provide endorsement of codes considered appropriate to manage antibiotic resistance.
3. The Board considers that the following matters must be addressed in the licensing of new antibiotic products for growth promotion and re-assessment of existing products:
  - The implications for public health of the concurrent use of a functionally related product in human medicine in New Zealand or Australia;
  - The implications for public health of the subsequent introduction of a functionally related product in human medicine in New Zealand or Australia;
  - The implications for public health for products that produce resistance or cross-resistance to systemic antibiotics used in human medicine;
  - Product use should be compatible with a zero withholding period;
  - The impact of the product on animal welfare;
  - The impact of the use of the product on the concurrent availability of the same or functionally related product as a therapeutic agent for animal disease;
  - The efficacy of the product; and
  - The impact of the product on international trade in primary produce.
4. In addition to the above, the Board considers that the following matters must be addressed in the licensing of new antibiotic products for prophylactic use and re-assessment of existing products:
  - The impact of the use of the drug in animals on the use of a functionally related product in human medicine for the treatment of serious disease in people for which there is no suitable alternative. Such drugs include: fluoroquinolones, glycopeptides, streptogramins and third generation cephalosporins;
  - Efficacy of the drug and establishment of optimum dose and treatment duration; and
  - The impact of resistance selection on animal and human health.
5. That re-assessment of existing growth promotant and prophylactic antibiotic products, requiring the above matters to be addressed for continued licensing, should occur as soon as possible, with priority given to re-assessment of avoparcin products.

Where licensing solely for growth promotion cannot be supported following re-assessment, consideration must be made of the use of that product for disease prevention and treatment purposes to ensure that a product, essential for the health and welfare of the animals, is not inadvertently and precipitately removed from the market.
6. The Board notes the voluntary withdrawal of the existing oral fluoroquinolone animal remedy for food-producing animals, and that similar products in the future are unlikely to meet the criteria established by the Board for licensing.

7. That the current moratorium on the licensing of any new antimicrobial growth promotants will continue until appropriate modification of Regulations are able to be made to allow re-assessment of existing products and licensing of new products. The moratorium will be reviewed at the next meeting of the Animal Remedies Board. During the period until the next Animal Remedies Board meeting, the Board will accept public comment on the need to refine the policies detailed above.