JETACAR RECOMMENDATIONS – OUTCOMES FOR THE POULTRY INDUSTRY

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Summary

International and domestic concerns by the medical profession and scientific community that essential antibiotics were becoming ineffectual due to microbial resistance resulted in the establishment of the Joint Expert Technical Advisory Committee on Antibiotic Resistance (JETACAR) in late 1997. The purpose of JETACAR was to evaluate the Australian situation on the use of antibiotics in food-producing animals and the development of antibiotic-resistant bacteria in humans. JETACAR produced a report in October 1999 containing 22 recommendations for development of appropriate future management plans for antibiotic use, particularly in food-producing animals. While the poultry industry has been developing health programmes to reduce dependency on antibiotic use for many years, necrotic enteritis of meat chickens will require alternative methods of control if currently used antibiotics become unavailable or too expensive.

I. INTRODUCTION

The development and spread of antibiotic-resistant-bacteria in humans and the consequential difficulty in controlling some bacterial infections particularly in hospitals have become increasingly frequent topics for scientific discussion and media reports in recent years. Some segments of the medical profession fear that the situation is so serious that there will be a return to the "pre-antibiotic era" (prior to the 1940s) when bacterial infections commonly resulted in death of humans. While it is likely that antibiotic resistance has occurred mainly due to the use, overuse or improper use of antibiotics in man and the failure by the medical profession to control the spread of antibiotic-resistant bacteria, there are some in the scientific community that have targeted the use of antibiotics in animals, particularly food-producing livestock, as a possible cause of the antibiotic resistance problem in human medicine.

It was in this context that in December 1997 the Federal Minister for Health and Family Services and the Federal Minister for Primary Industries and Energy agreed to establish the Joint Expert Technical Advisory Committee on Antibiotic Resistance on The Use of Antibiotics in Food-Producing Animals: Antibiotic-Resistant Bacteria in Animals and Humans (JETACAR).

II. JETACAR OPERATION

JETACAR consisted of invited experts from public health, human medicine, veterinary medicine, molecular biology and primary industries which guaranteed a diversity of viewpoints.

The Terms of Reference given to the Committee were first, to review the scientific evidence on the link between the use of antibiotics in food-producing animals, the emergence and selection of antibiotic-resistant bacteria and their spread to humans; and secondly to develop evidence-based recommendations for the appropriate future management of antibiotic use in food-producing animals.

The Committee met on seven occasions between April 1998 and June 1999, communicated electronically between meetings, considered numerous recent international
reviews on the topic, commissioned a review of the scientific literature on antibiotic resistance in four key bacterial pathogens, listed the current regulatory controls on antibiotics in Australia, compiled data on current use patterns in animals and man in Australia, discussed the current status of antibiotic resistance in Australia and addressed some of the benefits of antibiotic use in animals. As part of the information gathering process, 23 of 52 key stakeholders invited to provide scientific data and practical advice made submissions to the Committee and subsequently comments from 35 stakeholders on the draft Report were considered before the Report was finalised.

JETACAR produced a lengthy Report containing 22 recommendations in October 1999 (JETACAR, 1999).

III. JETACAR RECOMMENDATIONS

The JETACAR recommendations can be broadly grouped into seven categories, namely Regulatory Controls (1-9), Monitoring and Surveillance (10 and 11), Infection Prevention Strategies and Hygienic Measures (12-14), Education (15-17), Further Research (18), Communication (19 and 20) and Co-ordination of the Resistance Management Programme (21 and 22).

Below is a precis of recommendations and comments on the possible outcomes for the poultry industry.

(a) Recommendation 1

That antibiotics used as growth promotants or with similar use patterns not be registered unless they are efficacious, are not used as systemic therapeutic antibiotics in humans or animals and are not likely to impair the efficacy of other antibiotics through the development of resistant strains of organisms.

This recommendation reaffirms in general the recommendations of the Swann (1969) and the World Health Organisation (WHO Berlin, 1997) Reports and has been applied since the early 1970s by the National Registration Authority for Agricultural and Veterinary Chemicals (NRA) and the Working Party on Antibiotics of the Therapeutic Goods Administration (WPA) when registering antibiotics, including growth promotants (Table 1), for animal use in Australia.

Table 1. Antibiotics registered as growth promotants in Australia.

<table>
<thead>
<tr>
<th>Antibiotics Class</th>
<th>Growth Promotant</th>
<th>Registered Animal Species</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arsenical</td>
<td>3-nitro-arsionic acid</td>
<td>Pigs, Poultry</td>
</tr>
<tr>
<td>Bambermycin</td>
<td>flavophospholipol</td>
<td>Cattle, Pigs, Poultry</td>
</tr>
<tr>
<td>Glycopeptide</td>
<td>avoparcin</td>
<td>Cattle, Pigs, Meat Poultry</td>
</tr>
<tr>
<td>Macrolide</td>
<td>tylosin</td>
<td>Pigs</td>
</tr>
<tr>
<td></td>
<td>oleandomycin</td>
<td>Cattle</td>
</tr>
<tr>
<td></td>
<td>kitasamycin</td>
<td>Pigs</td>
</tr>
<tr>
<td>Polyether (ionophore)</td>
<td>lasalocid</td>
<td>Cattle</td>
</tr>
<tr>
<td></td>
<td>monensin</td>
<td>Cattle</td>
</tr>
<tr>
<td></td>
<td>narasin</td>
<td>Cattle</td>
</tr>
<tr>
<td></td>
<td>salinomycin</td>
<td>Pigs, Cattle</td>
</tr>
<tr>
<td>Polypeptide</td>
<td>bacitracin</td>
<td>Meat Poultry</td>
</tr>
<tr>
<td>Quinoxaline</td>
<td>olaquindox</td>
<td>Pigs</td>
</tr>
<tr>
<td>Streptogramin</td>
<td>virginiamycin</td>
<td>Pigs, Meat Poultry</td>
</tr>
</tbody>
</table>

Source: JETACAR REPORT 1999
(b) **Recommendation 2**

*That antibiotics currently registered as growth promotants, that do not now appear to fulfil the criteria in Recommendation 1, undergo a review by the NRA with a priority on glycopeptides (avoparcin), streptogramins (virginiamycin) and macrolides (tylosin, kitasamycin, oleandomycin).*

Avoparcin was already undergoing a review prior to the JETACAR Report because of purported links to the development of bacterial resistance to vancomycin, which is now considered a critical antibiotic for human use. Avoparcin has never been registered in northern America, its use was suspended in Europe in 1998 and the manufacturer (Roche) has recently withdrawn it from sale in Australia.

Virginiamycin was listed because the streptogramin quinupristin/dalfopristin is now considered a likely critical antibiotic for treatment of vancomycin-resistant enterococci (VRE) and multiresistant *Staphylococcus aureus* (MRSA) in humans.

If antibiotics fail a NRA Review, JETACAR accepted the principle that industries must be given a phaseout period in which to develop alternative health programmes.

(c) **Recommendation 3 (and 11)**

*That importers of antibiotics be licensed, that more accurate records of antibiotics imported be compiled and that audit trails be developed from importer to end-user to better define use patterns of antibiotics in animals in Australia.*

All antibiotics used in Australia are imported. Currently permits to import antibiotics are issued by the Therapeutic Goods Administration (TGA) and data are collated by both the TGA and the NRA. For example, data collected between 1992 and 1997 indicate that 64% of antibiotics imported were for animal use and that antibiotics with growth promotant claims constituted the majority of the antibiotic active ingredient imported.

The intent of this recommendation is to improve the existing process and to extend data collection past the importer. The poultry, feed and chemical industries could currently provide some components of this information.

(d) **Recommendations 4 and 5**

*That the NRA apply a Risk Analysis of Microbial Resistance Safety (Special Data Requirements for New Antibiotic Applications) for all new applications, major extensions of use and reviews of currently registered antibiotics.*

This process will formalise and make the existing process more transparent and accountable. In addition post-registration antibiotic resistance monitoring has been included as a requirement.

It is possible that this upgraded process will result in fewer antibiotics being registered for food-producing animals. Already some antibiotics registered overseas for use in poultry, e.g. fluoroquinolones, cephalosporins, nitrofurans, chloramphenicol, gentamicin and colistin, are not registered for use in poultry in Australia. It is also likely that the cost of antibiotics to the poultry industry will increase as a result.

(e) **Recommendation 6**

*That all antibiotics be classified as prescription drugs.*
Currently most of the antibiotic active ingredient used in food-producing animals in Australia (particularly for growth promotion and for some prophylactic use patterns) does not require veterinary intervention. This is in contrast to the situation where antibiotics are used in individual animals or humans. In this case, a veterinary or medical prescription is required.

The intent of this recommendation is to make the veterinary profession more responsible for the use of antibiotics in food-producing animals. Since the poultry industry is already well serviced by veterinarians, appropriate availability and cost should not be affected by this recommendation.

(f) Recommendations 7 and 8

That the Agricultural Resource Management Council of Australia and New Zealand (ARMCA NZ) harmonise legislation on Control of Use of antibiotics between states.

The current situation where a veterinarian can prescribe some antibiotics for specific uses in some states but not others (Table 2) does not appear to have any rational scientific basis.

Table 2. Legislation to control use of antibiotics in food-producing animals by veterinary script*

<table>
<thead>
<tr>
<th></th>
<th>QLD</th>
<th>NSW</th>
<th>VIC</th>
<th>SA</th>
<th>WA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Use of unregistered products</td>
<td>Yes</td>
<td>No</td>
<td>Unscheduled ingredients only</td>
<td>Yes</td>
<td>Scheduled ingredients only</td>
</tr>
<tr>
<td>Use of human medicines</td>
<td>Yes</td>
<td>No</td>
<td>Single animals only</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Use of products compounded by veterinarian</td>
<td>Yes</td>
<td>No</td>
<td>Unscheduled ingredients only</td>
<td>No</td>
<td>Yes</td>
</tr>
<tr>
<td>Varying dose or treatment regime</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Use on off-label species</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes unless prohibited</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>Use contrary to label prohibitions</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
</tr>
</tbody>
</table>

* Lee Cook, Personal Communication 1999

(g) Recommendation 10

That a formal antibiotic resistance monitoring system be established in food-producing industries.

The Chicken Meat Committee of the Rural Industries Research and Development Corporation has been proactive in supporting a project entitled “Antibiotic Resistance in Bacteria isolated from Poultry” supervised by Dr. Mary Barton at the University of Adelaide, partly to develop technical methods that could be useful for future monitoring programmes.
The mechanism and funding of the proposed monitoring system will need discussion, but the poultry industry has an existing precedent in the chemical residue monitoring programme undertaken by the National Residue Survey (NRS) of the National Office of Food Safety of the Commonwealth Department of Agriculture, Fisheries and Forestry (AFFA).

It is likely that the cost of antibiotic use by the poultry industry will increase due to this requirement to conduct resistance monitoring.

(h) **Recommendation 12**

*That Hazard Analysis Critical Control Point (HACCP) Programmes be implemented as a means of reducing the contamination of food products with foodborne organisms, including antibiotic-resistant organisms, and that these programmes include on-farm infection control.*

The Australian Standard for Hygienic Production of Poultry Meat for Human Consumption (ARMCANZ, 1997), which is based on HACCP principles and which now includes a requirement for microbiological testing, forms the basis for processing of poultry meat in Australia. Poultry companies are being required by retail customers to implement audited food safety programmes, including on-farm HACCP programmes. ARMCANZ has endorsed a poultry national biosecurity plan that includes food safety elements and the Australian Animal Health Council (Turner, 1999) is currently developing this plan in conjunction with industry.

Hence the poultry industry is already undertaking substantial measures to provide safe food, but the chicken meat industry may need to formalise and promulgate a HACCP programme for livestock production. Such a programme will need to address procedures to limit the development and transfer of antibiotic-resistance bacteria.

(i) **Recommendation 13 (and 18)**

*That alternatives to antibiotics be researched and developed to control bacterial diseases and improve feed utilisation.*

Long term uses of antibiotics in feed for prevention of disease (prophylaxis) and feed enhancement (growth promotion) are particularly being targeted by the medical profession and microbiologists.

The Australian poultry industry has a proven record of developing vaccines to control bacterial diseases such as fowl cholera (*Pasteurella multocida*), infectious coryza (*Haemophilus paragallinarum*), duck infectious serositis (*Riemerella anatipestifer*), chronic respiratory disease (*Mycoplasma gallisepticum*), infectious synovitis (*Mycoplasma synoviae*), turkey erysipelas (*Erysipelothrix rhusiopathiae*) and paratyphoid (*Salmonella typhimurium*). Necrotic enteritis caused by *Clostridium perfringens* is the only disease of poultry which is still controlled by in-feed antibiotic programmes based on avoparcin, virginiamycin or bacitracin.

The Chicken Meat Committee of the Rural Industries Research and Development Corporation has recently supported four projects related to development of possible alternatives to antibiotics for control of necrotic enteritis, including vaccines.

Alternatives such as organic acids, competitive exclusion products, probiotics, prebiotics, oligosaccharides, nucleotides, essential oils, enzymes, and plant extracts are being trialled in Europe where many in-feed antibiotics can no longer be used. The Australian chicken meat industry may be able to benefit from the experiences of European poultry companies.
(j) Recommendations 15-17

That Prudent Use Guidelines/Codes of Practice be developed, used, updated when required and promulgated by stakeholders of antibiotic use. Principles to control antibiotic resistance should be included.

The Australian Veterinary Poultry Association developed a Code of Practice for the Use of Schedule 4 Restricted Substances in the Poultry Industry in 1987 and this was updated in 1995. A further update, including more emphasis on the control of antibiotic resistance and extracts of the World Veterinary Association Prudent Use Guidelines (WVA et al., 1999), will be needed.

The poultry, feed and chemical industries should be made aware of the key principles in this updated Code.

IV. PERSPECTIVES

Some facts recognised by JETACAR that warrant mention include:

- The use and overuse of antibiotics in human medicine is the major factor contributing to the development of antibiotic resistance in man.
- Australia has one of the highest usage rates (25 defined daily doses per 1000 population per day) of antibiotics in humans in developed countries.
- Antibiotic-resistant bacteria and resistance genes can be spread internationally by people and food movements.
- The predominant VRE isolated to date in Australia are of a type (vanB Enterococcus faecium) that has not been associated with avoparcin use in animals.
- While avoparcin use in animals in Australia has remained relatively constant, the use of vancomycin in humans has increased by more than 300% since 1992 (annual import of 299 kg in 1992-94 compared with 868 kg in 1994-97).
- Australia does not have fluoroquinolone-resistant campylobacter or multiresistant Salmonella typhimurium DT104, that are of concern overseas, and fluoroquinolones are not registered for use in food-producing animals in Australia.
- Australian poultry flocks are free of Salmonella enteritidis, the major salmonella type infecting people in many overseas countries.
- The recorded quantity of antibiotics used in animals in Australia is substantially elevated by the inclusion of some chemicals that are mainly used as antiprotozoals, eg. coccidiostats and histomonostats.
- Australia already has one of the strictest registration processes in the world for the supply and use of antibiotics in animals.
- The results of antibiotic residue monitoring by the NRS in the last decade indicate excellent compliance with antibiotic withdrawal periods by the poultry industry, giving consumers considerable confidence that Australian poultry meat and eggs do not contain antibiotic residues.

V. CONCLUSIONS

The JETACAR recommendations are likely to accelerate a process that has been occurring for some years in the Australian poultry industry, namely less reliance on antibiotics to control bacterial diseases.

Other disease control measures including eradication, vaccination, hygiene, biosecurity, husbandry and nutritional programmes will need to continue to be applied to the
control of bacterial infections. Strategic, short term, scripted antibiotic regimes may be used as an adjunct in the future.

The range of antibiotics available to food-producing industries is likely to continue to constrict, due to registration and post-registration requirements becoming even more rigorous and costly. Less availability of antibiotics internationally due to fewer antibiotics being developed for animals is likely to be a factor in this process.

The poultry industry in Australia has always supported research on topics that are critical to the industry and this is already occurring for the development of alternatives to antibiotics to control necrotic enteritis.

Similarly the industry has always been industrious in transferring relevant technology and research findings from overseas. Once again there could be a need for this approach.

The industry will need to continue to demonstrate a willingness to self regulate the control of antibiotics to convince consumers and public health officials that the industry is adopting a responsible attitude to the control of antibiotic-resistant bacteria and antibiotic resistance genes.

While it is clear that overuse and improper use of antibiotics is the major reason for increasing antibiotic failure in humans, it is also clear that food-producing industries will increasingly need to justify the use of specific antibiotics and particular dosage regimes.

REFERENCES


JETACAR (1999). The Use of Antibiotics in Food-Producing Animals: Antibiotic-Resistant Bacteria in Animals and Humans. Department of Health and Aged Care and Department of Agriculture, Fisheries and Forestry – Australia, Canberra.


WHO, Geneva.