

Antimicrobial Stewardship Framework

A GUIDELINE FOR VETERINARIANS AND THE EGG INDUSTRY

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In submitting this report, the researcher
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Foreword

This project was conducted to examine the importance of antimicrobial stewardship (AMS), as distinct from prudent antimicrobial use, and to develop a set of relevant guidelines for industry use. The guidelines highlight the core principles of judicious use of antimicrobial agents and underline the need to meet industry best practice, and provide a range of tools and background information in support of AMS.

This project was funded from industry revenue which is matched by funds provided by the Australian Government.

This report is an addition to Australian Eggs Limited's range of peer reviewed research publications and an output of our R&D program, which aims to support improved efficiency, sustainability, product quality, education and technology transfer in the Australian egg industry.

Most of our publications are available for viewing or downloading through our website: www.australianeggs.org.au

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Abbreviations

AMR	Antimicrobial resistance
AMS	Antimicrobial stewardship
APVMA	Australian Pesticides and Veterinary Medicines Authority
ASTAG	Australian Strategic and Technical Advisory Group on AMR
AVA	Australian Veterinary Association
AVPA	Australasian Veterinary Poultry Association
CRAU	US Certified Responsible Antibiotic Use
DAFF	The former Australian Government Department of Agriculture, Fisheries and Forestry (now the Department of Agriculture)
FVE	Federation of Veterinarians of Europe
GSP	Good Stewardship Practice
IDSA	Infectious Diseases Society of America
MIC	Minimum inhibitory concentration
MRL	Maximum residue limits
PubCRIS	APVMA Public Chemicals Registration Information System
SLD	Spotty Liver Disease
WHO	World Health Organisation
WHP	Withholding period

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1 Introduction

In view of the global concern at the increasing public health incidence of antimicrobial resistance (AMR) and the adoption by the Australian Government of Australia's first National Antimicrobial Resistance Strategy (Australian Government 2015), it is increasingly important to ensure that all uses of antimicrobial agents are necessary and meet what would be considered industry best practice.

The National AMR Strategy is designed to address all uses of antimicrobials, whether in humans in hospital, aged care facilities or the community, and in animals, including livestock and companion animal species. The strategy contains the following seven objectives:

1 Increase awareness and understanding of antimicrobial resistance... through effective communication, education and training...

2 Implement effective antimicrobial stewardship practices...

3 Develop nationally coordinated One Health surveillance of antimicrobial resistance and antimicrobial usage...

4 Improve infection prevention and control measures...

5 Agree to a national research agenda...

6 Strengthen international partnerships and collaboration...

7 Establish and support clear governance arrangements... to ensure leadership, engagement and accountability for actions to combat antimicrobial resistance.

Objective 2 – antimicrobial stewardship; objective 3 – surveillance of antimicrobial resistance and use; and objective 4 – infection prevention and control measures, are particularly important and relevant to the Antimicrobial Stewardship Framework for the egg industry.

A recent global review of AMR conducted on behalf of the UK Government revealed that antimicrobial use in food producing animals in Australia was amongst the lowest in the world (O'Neill 2015). While the data in the O'Neill report combined use in all livestock species, the results are consistent with low antimicrobial use in Australian poultry production.

The long standing conservative approach to antimicrobial registration and use in Australia has led to the fortunate position that antimicrobial resistance of public health importance is either absent or at very low levels in samples obtained from Australian poultry (Abraham et al. 2014; Barlow & Gobius 2008; Barton et al. 2003; DAFF 2007; Miflin et al. 2007; Obeng et al. 2012, 2013, 2014; Page 2012), including eggs (Pande et al. 2015).

Despite the favourable antimicrobial resistance situation in Australian poultry, it remains essential to ensure that the antimicrobial agents that are available for use are preserved by ensuring that birds remain healthy and do not require antimicrobial treatment, and that when treatment is necessary the use of antimicrobials maximises treatment effectiveness while minimising adverse effects on resistance. Antimicrobial stewardship is the process by which the effectiveness of antimicrobials can be preserved, and a framework for antimicrobial stewardship is described in this document.

2 What is antimicrobial stewardship (AMS)?

The discipline of **antimicrobial stewardship** needs to be distinguished from **prudent antimicrobial use**, the subject of innumerable guidelines and codes of practice written and introduced over many decades.

Prudent use is defined by the World Health Organisation (WHO) as “usage of antimicrobials which maximizes therapeutic effect and minimizes the development of antimicrobial resistance” (WHO 2001). The Federation of Veterinarians of Europe (FVE 1999) adds that “Prudent use ... is an integral part of good veterinary practices. It is an attitude to maximise therapeutic efficacy and minimise selection of resistant micro-organisms. Prudent use principles are a guide for optimal use of antibiotics. They should not be interpreted so restrictively as to replace professional judgement of practitioners or to compromise animal health or welfare. In all cases, animals should receive prompt and effective treatment as deemed necessary by the prescribing or supervising veterinarian”.

The Australian poultry veterinarian community has a long history of abiding by prudent use principles. The ‘AVPA Code of Practice for the Use of Antibiotics in the Poultry Industry’ has been the guiding principle for antibiotic use in the Australian industry for over 30 years and has served the industry very well.

Antimicrobial stewardship has at its core the need to review, measure and monitor progress towards the common goal as stated by WHO and FVE above.

The most widespread definition of antimicrobial stewardship in the medical world is that of the Infectious Diseases Society of America (IDSA) (Dellit et al. 2007):

coordinated interventions designed to improve and measure the appropriate use of [antibiotic] agents by promoting the selection of the optimal [antibiotic] drug regimen including dosing, duration of therapy, and route of administration.

A similar definition in the veterinary literature (Guardabassi & Prescott 2015) describes antimicrobial stewardship as:

*the multifaceted and dynamic approaches required to sustain the clinical efficacy of antimicrobials by **optimizing drug use**, choice, dosing, duration, and route of administration, while **minimizing the emergence of resistance** and other adverse effects.*

Further distinguishing antimicrobial stewardship from prudent use, the main focus of egg industry antimicrobial stewardship is captured by the following statement:

*Antimicrobial Stewardship promotes planning about how to **NOT** use antibiotics rather than using them judiciously.*

If antimicrobials are needed, then the maxim ‘as little as possible, as much as necessary’ is a guiding principle. At the heart of antimicrobial reduction is the implementation of other infection prevention and control strategies into the veterinary Antimicrobial Stewardship Framework.

The ultimate goal of antimicrobial stewardship is ‘to provide effective antimicrobial therapy whilst safeguarding their effectiveness for future generations’.

3 The 5R framework of antimicrobial stewardship

The antimicrobial framework that captures the definition and goal is summarised in the infographic on page 9.

Three key elements of the framework include:

- The introduction of the term Good Stewardship Practice or GSP (Weese et al. 2016, Prescott & Boerlin 2016) to describe what is necessary when implementing an antimicrobial stewardship plan. It should be noted that GSP is a commitment to a global good (AMR reduction), can be individualised to each situation, can commence slowly and build progressively, and is not labour or cost intensive.
- The 5R core elements of antimicrobial stewardship:
 - Responsibility
 - Review
 - Reduce
 - Refine
 - Replace.
- Cycles of continuous improvement.

3.1 Responsibility

The appropriate use of antimicrobials is a shared responsibility between the prescribing veterinarian, who accepts responsibility for the decision to use an antimicrobial agent, and the egg producer, who is responsible for good animal care practices and following all directions for use and implementing associated management changes. This approach safeguards the health and welfare of the flock whilst minimising the likelihood of any immediate or longer-term adverse impacts on the individual animal, other livestock, or on public health.

Everybody in each egg farming enterprise, from senior management to casual employees, should recognise the importance of preserving the effectiveness of antibiotics, and willingly become an antimicrobial steward. Enterprise management should make AMS a priority, support the formation of an AMS team and the development and implementation of the AMS plan.

It is the responsibility of the consulting veterinarian to ensure that all veterinary products that are or could be used are used judiciously. Under Australian law, a veterinarian, who has to be able to demonstrate 'due care and supervision' of the health of a flock, must be able to demonstrate 'professional intervention' into the ordering, storage, supply and use of antibiotics, including withholding periods.

3.2 Review

Antimicrobial stewardship initiatives should be reviewed regularly, and a process of continuous improvement adopted to evaluate compliance with initiatives, and ensure that antimicrobial use practices reflect contemporary best practice.

The current status of flock health and welfare and antibiotic use should be reviewed progressively, areas for improvement identified, objectives of GSP described, and progress and outcomes of the AMS plan monitored and measured.

There are a limited number of antimicrobial agents available for use in pullets, laying hens and spent hens, with registered antimicrobial agents presented in Appendix 2 and importance ratings for human use set out in Appendix 1.

3.2.1 Measurement – quantity of use

Each antimicrobial use should be recorded by the AMS team and the records periodically analysed to determine the quantity of each antimicrobial agent (as mg or kg of antimicrobial active ingredient) used per year (or other unit of time).

A case study of antimicrobial use and dose determination is set out in Appendix 8.

The calculation of quantity of use can be derived from the information set out in the following table.



- 1 **Good Stewardship Practice (GSP)** – Embedded thinking and action to improve antimicrobial use and reduce antimicrobial resistance selection and impact.
- 2 **Responsibility** – High level commitment with everybody taking and sharing responsibility for antimicrobial use.
- 3 The 3Rs of responsible use: **Reduce** use, **Refine** use and **Replace** use – wherever possible.
- 4 **Review** current antimicrobial use and infection control practices, **Develop** objectives to improve current practice, **Implement** the stewardship plan, **Review** and measure.
- 5 Every cycle of **5R antimicrobial stewardship** leads to best practice in prevention & control and antimicrobial use.

In-feed medication

Antimicrobial use (mg)	=	Inclusion rate in feed (ppm [=mg/kg])	×	Feed consumed/day (kg)	×	Duration (days)
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In-water medication

Antimicrobial use (mg)	=	flock mass (bird no. × av. weight) (kg)	×	Daily dose (mg/kg/day)	×	Duration (days)
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It is clear from this table that if one of the AMS objectives is to reduce antimicrobial use, then the shorter the treatment period, the less the antimicrobial use. In addition, the fewer the number of birds treated, the less antimicrobial agent used. Segregating birds for treatment in place of treating an entire flock of birds can reduce antimicrobial use considerably. An AMS team question could be 'can birds be selected or segregated for targeted treatment'?

3.2.2 Measurement – quality of use: appropriate use

While it is generally not difficult to measure the quantity of antimicrobial agents used (as it is purely a mathematical computation of information from accurate treatment records), the ability to measure the quality of use can be challenging. However, it can be argued that achieving a high level of quality use of antimicrobials is an important AMS goal.

One approach to measuring quality of use is set out in the following table (National Centre for Antimicrobial Stewardship and Australian Commission on Safety and Quality in Health Care 2016) (adapted for veterinary use).

The basic principle of assessment of quality is whether or not the prescription or use of antimicrobials was compliant with the most appropriate local or national antimicrobial use labels, regulations and guidelines.

In order to be able to assess quality of use, it is necessary that the indication or reason for antimicrobial use is recorded and there must be an antimicrobial use regulation or guideline available as the reference standard for quality determination. Australian Veterinary Association (AVA) Guidelines on Antimicrobial Use in Poultry are expected to be available in 2019 and will aid the assessment of quality of use.

APPROPRIATE		
1	Optimal	Antimicrobial prescription follows label directions or endorsed guidelines, including antimicrobial choice. Body weight is known, indication is recorded, correct antimicrobial agent is used, dosage, administration route, duration and withholding period are complied with.
2	Adequate	Antimicrobial prescription is legal but does not optimally follow label directions or endorsed guidelines (e.g. is off-label), including antimicrobial choice, dosage, route or duration, however, use is still a reasonable alternative choice for the likely causative or cultured pathogens. Withholding period may not be established for the antimicrobial used.
INAPPROPRIATE		
3	Suboptimal	Antimicrobial prescription including antimicrobial choice, dosage, route and duration, is an unreasonable choice for the likely causative or cultured pathogen, or failure to appropriately substantiate with microbiological results.
4	Inadequate	Antimicrobial prescription including antimicrobial choice, dosage, route or duration is unlikely to treat the likely causative or cultured pathogens; OR an antimicrobial is not indicated for the documented or presumed indication; OR there may be the potential risk of toxicity; OR use is contra-indicated for the class of poultry being treated; OR record-keeping is not sufficient.



3.3 Reduce

Wherever possible, means of reducing the use of antimicrobials should be implemented. Infection control and prevention measures underpin animal health and welfare, and are supported by meticulous hygiene and sanitation, precision nutrition, genetics, biosecurity, vaccination, and expert animal husbandry, which when combined ensure infectious disease incidence (and the need for antimicrobials) is minimised.

An emerging challenge to antibiotic reduction strategies is the increased popularity of free range egg production with inherent difficulties in providing reliable and effective biosecurity. Exposure to pathogens from wild birds and other carriers can lead to introduction of disease. Diseases such as Spotty Liver Disease (SLD) are also more likely to occur in free range operations and control can necessitate the strategic use of antibiotics (Courtice et al. 2018). For SLD and other diseases of free range systems, the development and effective use of vaccines offers a potential control measure to incorporate into the AMS plan.

3.3.1 Vaccination

Vaccination can protect birds from bacterial diseases as well as protozoal and viral diseases that compromise immunity and predispose to secondary bacterial infection. There are many advantages in incorporating a vaccination program into a poultry health management plan. A well-managed vaccination program must also include a comprehensive serological monitoring program to ensure its effectiveness. All major bacterial, most viral infectious diseases (avian influenza is an exception), and the most important protozoal (coccidiosis) infectious diseases of commercial poultry in Australia have a vaccine available for their control. A list of Australian poultry vaccines is provided in Appendix 3.

3.3.2 Biosecurity

Biosecurity can be defined as the sum of management and physical preventive measures designed to reduce the risk of the introduction, development and spread of diseases to, from and within an animal population (EFSA 2017).

Egg producers are already very familiar with the enormous benefits and critical importance of biosecurity. Australian Eggs Limited has a number of reference documents to assist with implementing and managing biosecurity on-farm (Australian Eggs Limited 2017). Proper implementation of biosecurity protocols maintains good health and welfare of poultry on farms, and reduces financial losses by decreasing the frequency and magnitude of infectious disease outbreaks (Scott et al. 2018). Biosecurity is a vital component of antimicrobial stewardship as reduced occurrence of infectious disease translates directly to less need for antimicrobial use.

The following tables are extracted from National Farm Biosecurity Technical Manual for Egg Production (April 2015).

3.3.3 Objectives of biosecurity

To prevent the introduction of infectious disease agents to chickens



To prevent the spread of disease agents from an infected area to an uninfected area



To minimise the incidence and spread of microorganisms of public health significance

3.3.4 Major routes for pathogen transmission

Poultry	Introduction of new birds; transfer of birds from rearing area to production area; dead bird disposal; spent layer hen depopulation; movement of eggs and egg product between establishments.
Other Animals	Wild birds, especially water fowl; feral and domestic animals, including other livestock and pets; insects; rodents; domestic and aviary birds.
People	Farm personnel and family members living on site; contractors, maintenance personnel, neighbours, service personnel and visitors; disease can be transmitted by hands, footwear, clothing and poor personal hygiene.
Equipment	Transport cages, husbandry equipment, packing materials such as egg flats.
Vehicles	Dirt/manure/contaminants carried on cars, trucks and tractors.
Air	Transmission as an aerosol or dust.
Water Supply	Water supplies may become contaminated by water fowl, other animal species or run off.
Feed	Finished feed may be contaminated by the raw materials used, during transport, or by exposure to rodents and birds at the site of production or on the recipient property.
Litter and Waste	Transport of litter material on and off the farm site as well as storage of used litter on site may be a biosecurity risk; transport of egg waste and dead birds, and the composting or burial of egg waste and dead birds on the site may be a biosecurity risk.

3.4 Refine

Refined use means the right diagnosis, the right drug, at the right time, at the right dose, the right route, and for the right length of time. Information about each use of an antimicrobial agent should be recorded so that total use can be evaluated, and future use fine-tuned. Antimicrobial agents registered for use in pullet and laying hens are presented in Appendix 2 and a use decision making flow chart is set out in Appendix 5.

3.4.1 Detection and diagnosis

Disease detection and diagnosis can be difficult and often disease has progressed substantially before any evidence is observed. Small changes in flock behaviour (e.g. changes in feeding, drinking, laying patterns or vocalisation) can be early indicators of disease. Obtaining the early opinion of an experienced poultry veterinarian is very important in order to obtain an earlier, more accurate diagnosis. Early detection and diagnosis permit faster interventions, and improve the chances of successful treatment outcomes and reduction in potential antimicrobial resistance development.

A number of remote and automatic techniques are being developed to monitor bird behaviour and movement to detect patterns and changes consistent with emerging ill-health. Some recent examples are set out in Appendix 7.

3.4.2 Core principles of judicious use

Refined antimicrobial use can be ensured by following core principles of judicious use that offer guidance throughout the process of treatment decision making and monitoring:

1. Pre-treatment principles
2. Diagnosis
3. Drug selection
4. Drug use
5. Post-treatment guidelines.

Full details of the core principles are provided in Appendix 4. Investigation of treatment failure is an important component of judicious use and an investigation outline is presented in Appendix 6.

3.5 Replace

The use of antimicrobials should be replaced whenever available evidence supports the efficacy, safety and low or absent potential to select for AMR of the alternative.

There has been substantial interest for almost two decades to find alternatives to antibiotics for use in poultry and other livestock species. Enzymes, organic acids, prebiotics, probiotics, phytochemicals (chemicals obtained from plants), essential oils, competitive exclusion organisms, antibodies,

immunomodulators, bacteriophages, predatory bacteria, antimicrobial peptides, clays (including zeolites), minerals and other approaches have been investigated.

A wide range of these alternative products is now commercially available and is being incorporated into mainstream poultry farming operations. Most of these alternatives are intended as gut health modulators, but there are alternatives for respiratory and other systemic infections, primarily vaccines.

Vaccination is a fundamental component of mainstream flock health programs in modern poultry farming. A wide range of vaccines is available for viral, bacterial and protozoal pathogens and should be considered as a primary alternative to antimicrobials for bacterial pathogens.

One important task of the antimicrobial stewardship team is to identify those alternatives with sufficient evidence to be considered as safe and efficacious replacements for antimicrobial use.





4 Implementation

SUMMARY	
Stage 1	Stage 2
<ul style="list-style-type: none"> ■ Responsibility – senior management recognise the value of AMS and appoint a leader for the AMS plan ■ Stocktake of current practices ■ Review of practices against 3R prudent use principles – including assessment of quantity and quality of use (REDUCE, REPLACE, REFINE) 	<ul style="list-style-type: none"> ■ Develop objectives ■ Implement AMS plan ■ Review of Stage 2: measure outcomes

4.1 How to develop an AMS plan

Egg producers have already developed experience in maintaining high levels of bird health and welfare, and appropriate antibiotic use. The following steps summarise what can readily be done to implement the AMS plan. It is important from the start to take an inclusive and participatory approach, to build ownership and commitment to the AMS plan and its implementation.

4.1.1 Stage 1

- The first and most important task is for the business's management to recognise the value and benefits of preserving antibiotics (for animal and human use) and making antimicrobial stewardship a policy – this is adoption of the first core principle – **RESPONSIBILITY**. All those associated with the business also need to share this responsibility for animal health, welfare and need to protect antibiotics.
- An antimicrobial stewardship leader needs to be appointed, who reports to senior management or the owner, and can form a team and coordinate the AMS activities. This team should include a veterinary consultant or advisor, possibly as team leader.
- The second task is to **REVIEW** the current situation on antibiotic use. Which antibiotics are used, what is the reason for use, how much of each antibiotic is used? Is there an antibiotic prudent use guideline? Is there a flock health plan and is it current?

- Task three is to critically examine the current situation and identify any possible ways in which it can be improved. The next 3Rs, **REDUCE**, **REPLACE** and **REFINE** should be used to help with this analysis of current practice and help guide future practice.
- Examples of possible areas for improvement include:
 - is current use of antibiotics consistent with the Australasian Veterinary Poultry Association (AVPA) Code of Practice for the use of antibiotics in the poultry industry?
 - are there peaks of seasonal poor health that can be prevented, thereby reducing the need for antibiotics?
 - are vaccines or other non-antibiotic interventions available and used optimally?
 - are there breaches in biosecurity that can be improved?
 - are facilities and equipment in need of repair or replacement to improve disease control?
 - do production systems need to be reviewed to reduce between-flock cross-infection?

4.1.2 Stage 2 – develop objectives

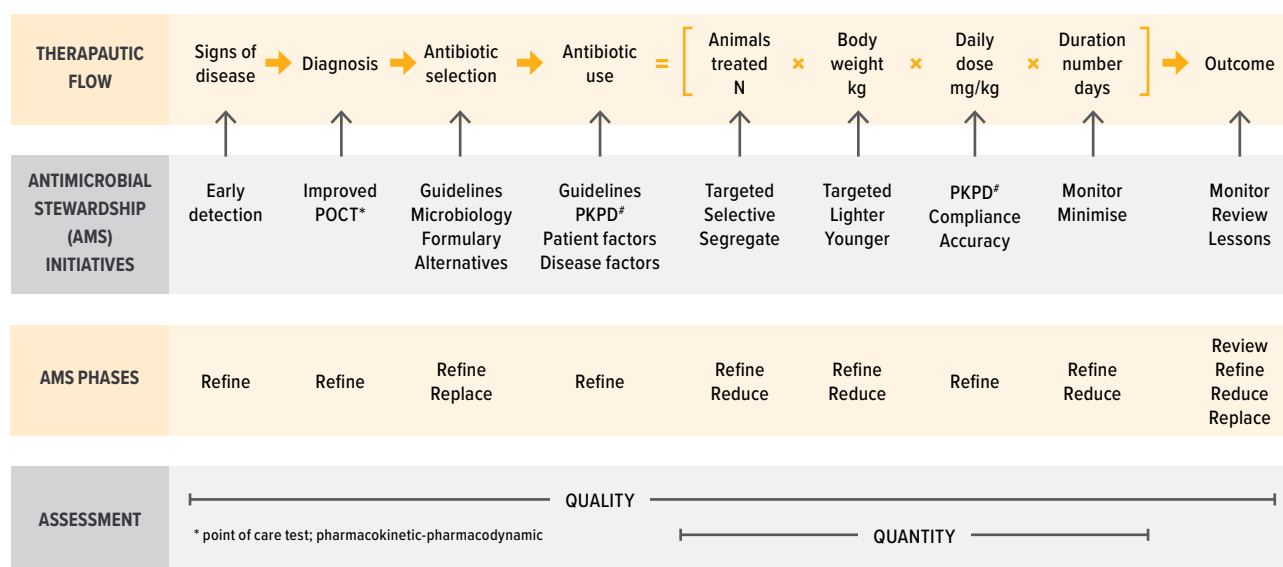
- Once an area or areas of improvement have been identified it is then possible to describe the first objective of the AMS plan. For example, the first objective might be to reduce the risk or likelihood of fowl cholera by vaccination and thereby reduce associated antibiotic use.

- With an objective described and with agreement of the team and management that this is appropriate, new responsibilities are assigned and the plan is implemented.
- After a suitable time period, initially this might be at 6 and 12 months, progress towards achieving the objective can be assessed – continuous **REVIEW** is an important feature of AMS and should always be accompanied by action, either continuation of the original plan or modification based on new information that becomes available.

4.2 Measuring outcomes

Antimicrobial stewardship plans have two approaches to measuring outcomes – **QUANTITATIVE** (how much antibiotic is being used) and **QUALITATIVE** (does each use of antibiotics meet the quality criteria). The assessment of outcomes should also ask if use of antibiotics is necessary and how much use can be reduced, replaced and refined.

The following figure summarises where antimicrobial stewardship initiatives can help improve bird health, maximise antimicrobial effectiveness and minimise antimicrobial resistance.



5 Antimicrobial stewardship verification strategy

Verification of the implementation of each AMS plan is important for both transparency and to demonstrate commitment to the principles of antimicrobial stewardship.

As recommended by the US Centers for Disease Control and Prevention (Sanchez et al. 2016), self-audit of AMS plans is completely acceptable and encouraged.

However, once the AMS plan has successfully completed its initial introductory pilot phase, practical lessons have been learned leading to changes in the AMS plan, and experience with AMS has been gained, then external auditing by an independent auditor should be considered a priority.

An excellent model for AMS plan auditing is that described by the US Certified Responsible Antibiotic Use (CRAU) standard, which could be readily adapted for use by the Australian egg industry –

http://www.schoolfoodfocus.org/wp-content/uploads/dlm_uploads/2016/05/CRAU-Rationale-and-Standard_FIN.pdf.

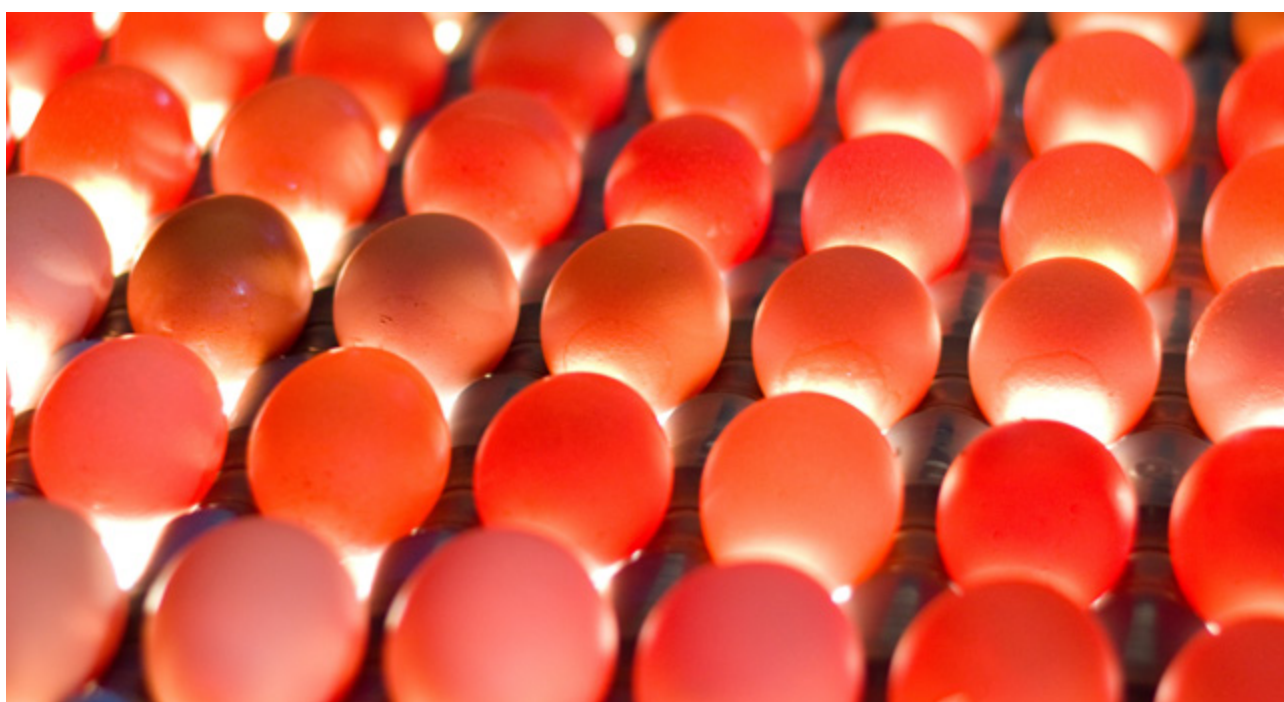
The CRAU standard sets out background and purpose, objectives, management principles, and responsible antibiotic use criteria.

Assurance of compliance with the CRAU standard (or AMS plan in the current situation) requires third-party certification through inspection and audit.

Supporting compliance verification are audit guidelines and an audit checklist –

<https://www.ams.usda.gov/services/auditing/crau>.

The audit list can serve as an excellent starting point for self-audit of the AMS plan.





6 References

Abraham, S., M. D. Groves, D. J. Trott, T. A. Chapman, B. Turner, M. Hornitzky and D. Jordan (2014).

“*Salmonella enterica* isolated from infections in Australian livestock remain susceptible to critical antimicrobials.” *Int J Antimicrob Agents* 43(2): 126-130.

ASTAG (Australian Strategic and Technical Advisory Group on AMR) (2018). Importance Ratings and Summary of Antibacterial Uses in Human and Animal Health in Australia, Version 1.0 (2018). Canberra, Commonwealth of Australia.

Australian Eggs (2017). National-Farm-Biosecurity-Technical-Manual-for-Egg-Production-2015.pdf. <https://www.australianeggs.org.au/for-farmers/biosecurity/#item-728>

Australian Government Department of Health and Australian Government Department of Agriculture (2015). National Antimicrobial Resistance Strategy 2015–2019. Canberra, Commonwealth of Australia.

Australian Veterinary Poultry Association (2001). AVPA Code of Practice for the Use of Antibiotics in the Poultry Industry. Australasian Veterinary Poultry Association.

Barlow, R. and K. Gobius (2008). Pilot survey for antimicrobial resistant (AMR) bacteria in Australian food. Cannon Hill, Queensland, Food Science Australia.

Barton, M. D., R. Pratt and W. S. Hart (2003). “Antibiotic resistance in animals.” *Commun Dis Intell Q Rep* 27 Suppl: S121-126.

Courtice, J. M., L. K. Mahdi, P. J. Groves and M. Kotiw (2018). “Spotty Liver Disease: A review of an ongoing challenge in commercial free-range egg production.” *Veterinary Microbiology Online Manuscript*.

DAFF (2007). Pilot Surveillance Program for Antimicrobial Resistance in Bacteria of Animal Origin. November 2003 to July 2004. Canberra, ACT, Australian Government Department of Agriculture, Fisheries and Forestry (DAFF).

- Dellit, T. H., R. C. Owens, J. E. McGowan, Jr., D. N. Gerding, R. A. Weinstein, J. P. Burke, W. C. Huskins, D. L. Paterson, N. O. Fishman, C. F. Carpenter, P. J. Brennan, M. Billeter and T. M. Hooton (2007). "Infectious Diseases Society of America and the Society for Healthcare Epidemiology of America guidelines for developing an institutional program to enhance antimicrobial stewardship." *Clin Infect Dis* 44(2): 159-177.
- EMA (European Medicines Agency) and EFSA (European Food Safety Authority) (2017). "EMA and EFSA Joint Scientific Opinion on measures to reduce the need to use antimicrobial agents in animal husbandry in the European Union, and the resulting impacts on food safety (RONAFA)." *EFSA Journal* 15(1) (4666): 245pp.
- FVE (1999). Antibiotic Resistance & Prudent Use of Antibiotics in Veterinary Medicine. Brussels, Federation of Veterinarians of Europe.
- Guardabassi, L. and J. F. Prescott (2015). "Antimicrobial Stewardship in Small Animal Veterinary Practice: From Theory to Practice." *Vet Clin North Am Small Anim Pract* 45(2): 361-376.
- Miflin, J. K., J. M. Templeton and P. J. Blackall (2007). "Antibiotic resistance in *Campylobacter jejuni* and *Campylobacter coli* isolated from poultry in the South-East Queensland region." *J Antimicrob Chemother* 59(4): 775-778.
- National Centre for Antimicrobial Stewardship and Australian Commission on Safety and Quality in Health Care (2016). Antimicrobial prescribing and infections in Australian residential aged care facilities: Results of the 2015 Aged Care National Antimicrobial Prescribing Survey pilot. Sydney, ACSQHC.
- O'Neill, J. (2015). Review on antimicrobial resistance. Antimicrobials in agriculture and the environment. Reducing unnecessary use and waste. December 2015.
- Obeng, A. S., H. Rickard, M. Sexton, Y. Pang, H. Peng and M. Barton (2012). "Antimicrobial susceptibilities and resistance genes in *Campylobacter* strains isolated from poultry and pigs in Australia." *J Appl Microbiol* 113(2): 294-307.
- Obeng, A. S., H. Rickard, O. Ndi, M. Sexton and M. Barton (2013). "Comparison of antimicrobial resistance patterns in enterococci from intensive and free range chickens in Australia." *Avian Pathology* 42(1): 45-54.
- Obeng, A. S., H. Rickard, O. Ndi, M. Sexton and M. Barton (2014). "Prevalence of antimicrobial resistance in enterococci and *Escherichia coli* in meat chicken flocks during a production cycle and egg layer pullets during rearing." *International Journal of Poultry Science* 13: 489-503.
- Page, S. W. (2012). "Does antibiotic use in farmed animals pose a risk to human health? – No." *Med J Aust* 196(5): 303.
- Pande, V. V., V. C. Gole, A. R. McWhorter, S. Abraham and K. K. Chousalkar (2015). "Antimicrobial resistance of non-typhoidal *Salmonella* isolates from egg layer flocks and egg shells." *International Journal of Food Microbiology* 203: 23-26.
- Prescott, J. F. and P. Boerlin (2016). "Antimicrobial use in companion animals and Good Stewardship Practice." *Veterinary Record* 179(19): 486-488.
- Sanchez, G. V., K. E. Fleming-Dutra, R. M. Roberts and L. A. Hicks (2016). "Core Elements of Outpatient Antibiotic Stewardship." *MMWR Recomm Rep* 65(RR-6): 1-12.
- Scott, A. B., M. Singh, P. Groves, M. Hernandez-Jover, B. Barnes, K. Glass, B. Moloney, A. Black and J. A. Toribio (2018). "Biosecurity practices on Australian commercial layer and meat chicken farms: Performance and perceptions of farmers." *PLoS One* 13(4): e0195582.
- Weese, J. S., S. W. Page and J. F. Prescott (2013). *Antimicrobial Stewardship in Animals. Antimicrobial Therapy in Veterinary Medicine* (fifth edition). S. Giguere, J. F. Prescott and P. M. Dowling. Ames, Iowa, John Wiley & Sons, Inc: 117-132.
- WHO (2001). WHO Global Strategy for Containment of Antimicrobial Resistance. Geneva, World Health Organisation.
- WHO (2017). Critically important antimicrobials for human medicine (5th revision). Geneva, World Health Organisation.

7 Appendices – Tools and background information to support antimicrobial stewardship

7.1 Appendix 1 – Antimicrobial agent importance rating

ASTAG (2018) importance rating definitions

High

These are essential antibacterials for treatment of human infections where there are few or no alternatives for many infections. They have also been called ‘critical’, ‘last resort’ or ‘last line’ antibacterials.

Medium

There are other alternatives available but less than for those classified as Low.

Low

There are a reasonable number of alternative agents in different classes available to treat most infections even if antibacterial resistance develops.

WHO 2017 importance rating criteria

Criterion 1 (C1): The antimicrobial class is the sole, or one of limited available therapies, to treat serious bacterial infections in people.

Criterion 2 (C2): The antimicrobial class is used to treat infections in people caused by either:

(1) bacteria that may be transmitted to humans from non-human sources; or (2) bacteria that may acquire resistance genes from non-human sources.

Critically important

Antimicrobial classes that meet both C1 and C2 are termed critically important for human medicine.

Highly important

Antimicrobial classes that meet either C1 or C2 are termed highly important for human medicine.

Important

Antimicrobial classes used in humans that meet neither C1 nor C2 are termed important for human medicine.



SUMMARY TABLE

CRITICALLY IMPORTANT ANTIMICROBIALS FOR HUMAN MEDICINE

WHO 5th revision (2017)

[underlined] antimicrobial classes have a member approved for use in poultry]*(antibiotics in italics shows the specific antibiotics approved for use in poultry in Australia)*

CRITICALLY IMPORTANT ANTIMICROBIALS (CIA)	HIGHLY IMPORTANT ANTIMICROBIALS (HIA)	IMPORTANT ANTIMICROBIALS (IA)	ANIMAL USE ONLY ANTIMICROBIALS (NHU)
1. <u>Aminoglycosides</u> (<i>neomycin</i>) 2. Ansamycins 3. Carbapenems and other penems 4. Cephalosporins (3rd and 4th generation) [HPCIA] 5. Glycopeptides [HPCIA] 6. Glycylcyclines 7. Lipopeptides 8. <u>Macrolides</u> (<i>tylosin</i> , <i>erythromycin</i>) and ketolides [HPCIA] 9. Monobactams 10. Oxazolidinones 11. <u>Penicillins</u> (natural, aminopenicillins (<i>amoxicillin</i>), and antipseudomonal) 12. Phosphonic acid derivatives 13. Polymyxins [HPCIA] 14. Quinolones [HPCIA] 15. TB. Drugs used solely to treat tuberculosis or other mycobacterial diseases	16. Amidinopenicillins 17. Amphenicols 18. Cephalosporins (1st and 2nd generation) and cephamycins 19. <u>Lincosamides</u> (<i>lincomycin</i>) 20. Penicillins (antistaphylococcal) 21. Pseudomonic acids 22. Riminofenazines 23. Steroid antibacterials 24. <u>Streptogramins</u> (<i>virginiamycin</i>) 25. <u>Sulfonamides, dihydrofolate reductase inhibitors and combinations</u> 26. Sulfones 27. <u>Tetracyclines</u> (<i>oxytetracycline</i> , <i>chlortetracycline</i>)	28. <u>Aminocyclitols</u> (<i>apramycin</i> , <i>spectinomycin</i>) 29. <u>Cyclic polypeptides</u> (<i>bacitracin</i>) 30. Nitrofurantoin 31. Nitroimidazoles 32. <u>Pleuromutilins</u> (tiamulin)	33. <u>Polyether ionophores</u> (<i>monensin</i> , <i>salinomycin</i> , <i>narasin</i> , <i>maduramicin</i> , <i>semduramicin</i> , <i>lasalocid</i>) 34. <u>Phosphoglycolipids</u> (<i>flavophospholipol</i>) 35. Quinoxalines 36. <u>Everninomicins</u> (<u>orthosomycins</u>) (<i>avilamycin</i>) 37. Aminocoumarin 38. Arsenical

HPCIA: Highest Priority Critically Important Antimicrobials

Quinolones

Third and fourth generation cephalosporins

Macrolides and ketolides

Glycopeptides

Polymyxins

7.2 Appendix 2 – Antimicrobial agents approved for use in Australian layer hens

ANTIMICROBIAL AGENT	CLASS	IMPORTANCE ASTAG 2018	IMPORTANCE WHO 2017	TARGET BIRD	WHP eggs (days) [@]
Bacitracin	Polypeptide	low	4	Hens & pullets	nil
Chlortetracycline	Tetracycline	low	3	Hens & pullets	nil
Flavophospholipol	Glycophospholipid	nhu	5	Hens & pullets	nil
Lincomycin	Lincosamide	med	3	Hens & pullets	nil
Neomycin (feed)	Aminoglycoside	low	2	Hens & pullets	nil
Spectinomycin	Aminocyclitol	med	4	Hens & pullets	nil
Amoxicillin	Penicillin	low	2	Pullets	DNU*
Lasalocid	Ionophore	nhu	5	Pullets	(14) DNU
Monensin	Ionophore	nhu	5	Pullets	DNU
Neomycin (water)	Aminoglycoside	low	2	Pullets	(14) DNU
Salinomycin	Ionophore	nhu	5	Pullets	(7) DNU
Sulfadimidine	Sulfonamide	low	3	Pullets	DNU
Trimethoprim + Sulfadimidine	Diaminopyrimidine + Sulfonamide	med	3	Pullets	DNU
Tylosin	Macrolide	low	1	Pullets	DNU
Trimethoprim + Sulfadiazine	Diaminopyrimidine + Sulfonamide	med	3	Pullets#	DNU

Note: Not all registered antimicrobial agents are used or available for use.

Importance: Importance for human medicine:

ASTAG 2018: nhu=no human use.

WHO 2017: 1=HPCIA; 2=CIA; 3=HIA; 4=IA; 5=NHU.

ASTAG (2018). Importance Ratings and Summary of Antibacterial Uses in Human and Animal Health in Australia, Version 1.0 (2018). Canberra, Commonwealth of Australia.

WHO (2017). Critically important antimicrobials for human medicine (5th revision). Geneva, World Health Organisation.

Target bird: Pullets – rearing hens prior to point of lay; Pullets# – check label, only some products can be used in pullets, Hens – hens in lay.

WHP (withholding period) eggs: DNU – do not use in egg laying birds; numbers in brackets are the WHP in days to cease treatment before pullets go into lay; **DNU*** – WHP in pullets is under review; @ always read label carefully and follow label directions for use.

7.3 Appendix 3 – Vaccines registered by APVMA for use in poultry

VACCINES APPROVED FOR USE IN POULTRY IN AUSTRALIA*	
Immunogen	Type
Avian encephalomyelitis virus*	Virus
Avian influenza virus type A, H5N2*	Virus
Avibacterium paragallinarum#	Bacteria
Campylobacter hepaticus#%	Bacteria
Chicken anaemia virus*	Virus
Egg drop syndrome 76 virus*	Virus
Eimeria acervulina*	Protozoa
Eimeria brunetti*	Protozoa
Eimeria maxima*	Protozoa
Eimeria mitis*	Protozoa
Eimeria necatrix*	Protozoa
Eimeria praecox*	Protozoa
Eimeria tenella*	Protozoa
Erysipelothrix rhusiopathiae#	Bacteria
Escherichia coli*#	Bacteria
Fowl adenovirus*	Virus
Fowl pox vaccine*	Virus
Herpes virus of turkeys (HVT)*	Virus
Infectious bronchitis virus (IB)*	Virus
Infectious bursal disease virus (IBD)*	Virus
Infectious laryngotracheitis virus (ILT)*	Virus
Marek's disease virus*#	Virus
Mycoplasma gallisepticum (MG)*#	Bacteria
Mycoplasma synoviae (MS)*	Bacteria
Newcastle disease virus (ND)*	Virus
Ornithobacterium rhinotracheale#	Bacteria
Pasteurella multocida*#	Bacteria
Riemerella anatipestifer#	Bacteria
Salmonella Typhimurium*#	Bacteria

*APVMA PubCRIS and #Permit databases accessed 15 October 2018.

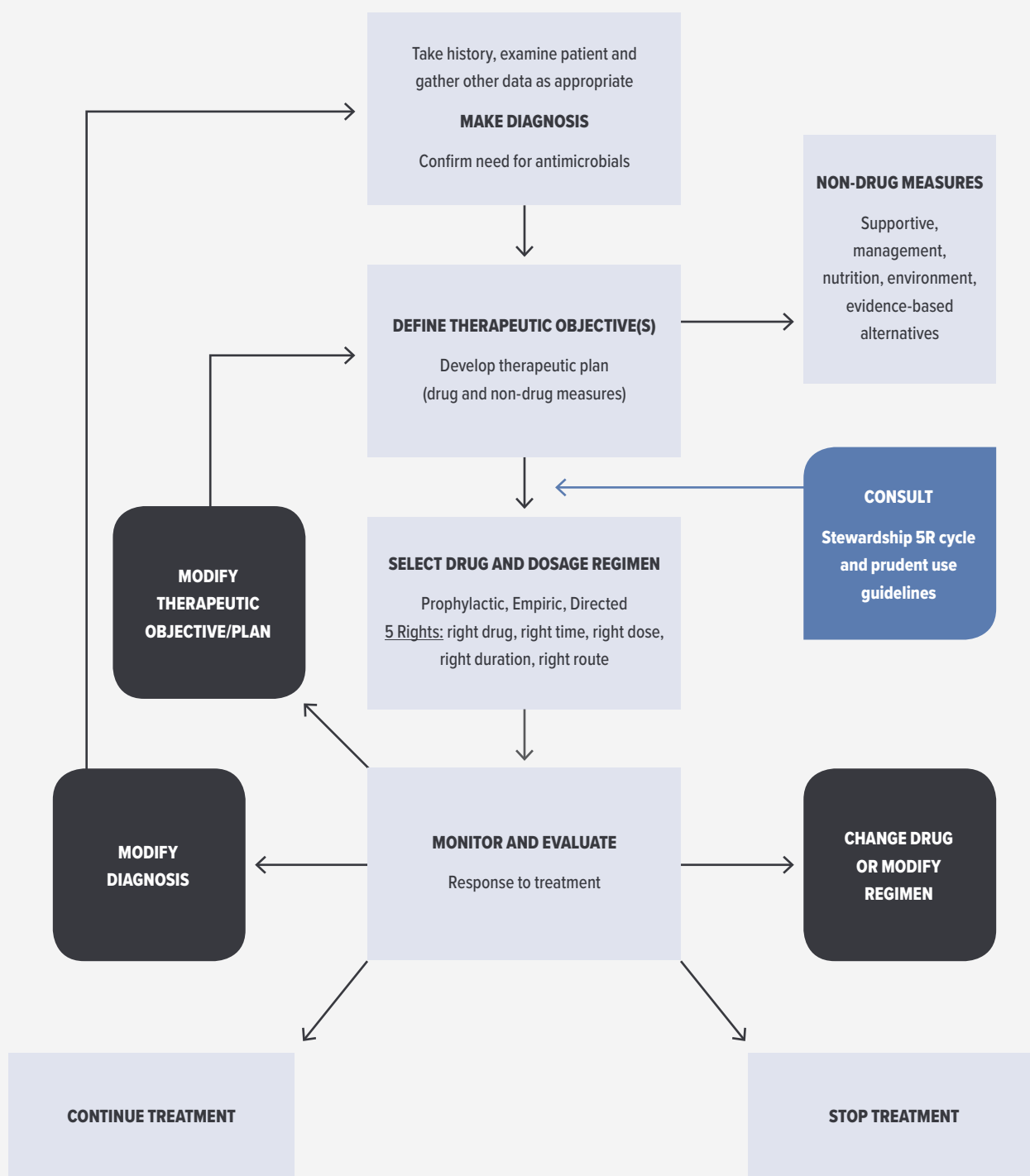
% *Campylobacter hepaticus* vaccine to protect from Spotty Liver under development.

7.4 Appendix 4 – Core principles of judicious use of antimicrobial agents

#	CATEGORY	PRINCIPLES
1	PRETREATMENT PRINCIPLES	Disease prevention <ul style="list-style-type: none"> ■ Appropriate (best practice) biosecurity, husbandry, hygiene, routine health monitoring, vaccination, nutrition, housing, and environmental controls. ■ Codes of Practice, Quality Assurance Programmes, Herd Health Surveillance Programmes and Education Programmes should promote the responsible and prudent use of antimicrobial agents.
2		Professional intervention All uses (labelled and extra-label) of antimicrobials meet all the requirements of a valid veterinarian-client-patient relationship.
3		Alternatives to antimicrobial agents Efficacious, scientific evidence-based alternatives to antimicrobial agents can be an important adjunct to good husbandry practices.
4	DIAGNOSIS	Accurate diagnosis <ul style="list-style-type: none"> ■ Diagnosis of a bacterial infection (clinical diagnosis complemented with point of care tests, laboratory diagnosis and epidemiological information as appropriate).
5	THERAPEUTIC OBJECTIVE AND PLAN	Therapeutic objective and plan Develop outcome objectives (e.g. clinical or microbiological cure) and implementation plan (including consideration of therapeutic choices, supportive therapy, host, environment, infectious agent and other factors).
6	DRUG SELECTION	Justification of antimicrobial use <ul style="list-style-type: none"> ■ Other therapeutic options should be considered prior to antimicrobial therapy. ■ Antimicrobials are a complement to good husbandry practices and should never be used to compensate for or mask poor farm or veterinary practices. ■ Informed professional judgment balancing the risks (especially the risk of AMR selection and dissemination) and benefits to humans, animals and the environment.
7		Guidelines for antimicrobial use Disease-specific guidelines for antimicrobial selection and use should be consulted.
8		Critically important antimicrobial agents Antimicrobial agents, including those considered important in treating refractory infections in human or veterinary medicine, should be used in animals only after careful review and reasonable justification.
9		Culture and sensitivity testing Utilise culture and susceptibility (or equivalent) testing when clinically relevant to aid in the selection of antimicrobials, especially if initial treatment has failed.
10		Spectrum of activity Use narrow-spectrum in preference to broad-spectrum antimicrobials whenever appropriate.
11		Extra-label (off-label) antimicrobial therapy <ul style="list-style-type: none"> ■ Must be prescribed only in accordance with prevailing laws and regulations. ■ Should be confined to situations where medications used according to label instructions have been ineffective and where there is scientific evidence, including residue data if appropriate, supporting the off-label use pattern.

#	CATEGORY	PRINCIPLES
12	DRUG USE	Dosage regimens Regimens for therapeutic antimicrobial use should be optimised using current pharmacological (pharmacokinetic-pharmacodynamic [PK/PD]) information.
13		Duration of treatment Therapeutic exposure to antimicrobials should be minimised by treating only for as long as needed to meet the therapeutic objective.
14		Labelling and instructions Written instructions about the drug use regimen must be given to the end user by the veterinarian with clear details of method of administration, dose rate, frequency and duration of treatment, precautions and withholding period.
15		Target animals Limit therapeutic antimicrobial treatment to ill or at-risk animals, treating the fewest animals possible.
16		Record keeping Accurate records of diagnosis (indication), treatment and outcome should be kept to allow therapeutic regimens to be evaluated by the prescriber and permit benchmarking as a guide continuous improvement.
17		Compliance Encourage and ensure that instructions for drug use are implemented appropriately.
18		Monitor response to treatment <ul style="list-style-type: none"> Report to relevant authorities any reasonable suspicion of an adverse reaction to the medicine in either treated animals or farm staff having contact with the medicine, including any unexpected failure to respond to the medication. Each treated case that fails to respond as expected should be thoroughly investigated.
19	POST-TREATMENT CONSIDERATIONS	Environmental contamination Minimise environmental contamination with antimicrobials and resistance determinants whenever possible.
20		Surveillance of antimicrobial resistance Susceptibility surveillance should be undertaken periodically, and the results provided to the prescriber, supervising veterinarians and other relevant parties.
21		Continuous evaluation Veterinarians should continuously evaluate their prescribing practices, based on such information as the main indications and types of antimicrobials used in different animal species and evaluated in relation to available data on antimicrobial resistance and current use guidelines.

7.5 Appendix 5 – Decision making flow chart



7.6 Appendix 6 – Investigation of treatment failure

Whenever the response to treatment of poultry with confirmed or presumed bacterial infections is less than expected it is important to investigate to determine the cause. It is only when the actual cause or likely causes are identified that appropriate changes to treatment can be made. A systematic investigation of apparent treatment failure is essential as there are many possible causes of apparent treatment failure, as set out in the following table. Resistance of the causal agent to antimicrobials is just one of many microbial factors that require consideration.

TWELVE MAJOR FACTORS ASSOCIATED WITH APPARENT TREATMENT FAILURE IN POULTRY	
Diagnosis <ul style="list-style-type: none"> Condition not of bacterial origin – non-infectious (e.g. feed contaminant), other infectious agent (e.g. fungal, viral or protozoal infection) 	Pharmacology <ul style="list-style-type: none"> Inappropriate drug selection Inappropriate dosage regimen (inadequate dose rate, route, frequency, duration) Pharmacokinetic issues (esp. changes in absorption, distribution and clearance) Impaired perfusion and penetration (blood brain barrier, abscess, oedema, etc.) Interaction with concurrent medication
Therapeutic goals <ul style="list-style-type: none"> Unrealistic objective (bacterial eradication vs disease control) 	Supportive therapy <ul style="list-style-type: none"> Omission of concurrent supportive measures (e.g. warmth, nutrition, hydration)
Pathophysiology <ul style="list-style-type: none"> Progression of underlying disease Poor management of mixed infection (e.g. mixed aerobic and anaerobic infection) 	Microbial factors <ul style="list-style-type: none"> Toxin elaboration Antimicrobial drug resistance (AMR) Reinfection Bacterial dormancy/persistence (e.g. non-growth phase) Bacterial L-forms Phenotypic tolerance (e.g. small colony variants) Inoculum effects – dense bacterial loads in infected tissue Biofilm formation Superinfection (bacteria or fungal) Poor correlation of in vitro susceptibility and clinical outcome
Host factors <ul style="list-style-type: none"> Predisposing factors uncorrected Comorbidities (concurrent infections and other conditions, e.g. coccidiosis) Impaired immune function Nutritional deficits 	Epidemiology <ul style="list-style-type: none"> External bacterial challenge continues unabated
Pharmaceutical factors <ul style="list-style-type: none"> Substandard product (expired, inappropriate storage) 	Toxicology <ul style="list-style-type: none"> Apparent failure due to adverse drug reaction, not infection control failure
Treatment <ul style="list-style-type: none"> Poor compliance (e.g. treatments not administered) Misadministration (e.g. animal avoided treatment, erratic consumption of medicated water or feed) 	Investigation Failure <ul style="list-style-type: none"> Inappropriate samples collected Non-representative animal(s) investigated (e.g. post mortem of untreated animal)

While it might be tempting to conclude that apparent treatment failure is due to AMR, this cause is infrequently found following investigation. If the cause is incorrectly assumed to be due to the presence of AMR in the implicated pathogens, then treatment choices will be modified unnecessarily with the possible use of antibacterial agents that are less appropriate or may have increased likelihood of selecting AMR – both unintended adverse consequences.

7.7 Appendix 7 – Examples of refined approaches to early detection of infectious disease applicable to poultry

<p>De Montis, A. et al. (2013). "Analysis of poultry eating and drinking behavior by software eYeNamic." <i>Journal of Agricultural Engineering Research</i> 44(2): 166-173.</p>	<p>Constant presence of at least one operator in livestock buildings for broilers would allow a perfect control of animal behaviour and, especially, deviations in feeding and drinking patterns, in the perspective of a high welfare status. However, as nowadays it is impossible for a farmer to be present in the farm all day long, automatic monitoring systems are required. The purpose of this paper is to introduce a system (eYeNamic) for automatic monitoring and analyzing broilers' behavior in a farm. eYeNamic is a camera system introduced and produced by Fancom BV, a company operating in the field of automation of livestock facilities. It includes three cameras located on the ridge of the broiler house and able to monitor chickens' behaviour twenty-four hours a day. Through eYeNamic it is possible to process the images and to obtain a measure of animals' distribution and activity, which can be conceived as valuable indicators of animal welfare. The study presented in this paper was divided into several phases: data collection, images visualization, observation of the distribution and activity of the chickens, and statistical analysis of the observations. The analysis of correlation between the number of 14 days old broilers near the feeding line (manual counted) and the average occupation density measured with eYeNamic indicates that the best conditions have occurred with a 50 cm by 75 cm area around each feeding pan. With reference to the drinking line, the best response was found in an area 50 cm wide and the whole drinking line long. For the activity behavior, there was no significant correlation between activity and number of chickens eating from all the pans: this confirms that broilers while eating reduce their activity. It was concluded from this study that eYeNamic is a good system to observe animal behavior and, especially, to take care of their drinking and eating behaviour. A satisfactory correspondence between eYeNamic remote and human observations depends on a correct definition of animals' eating behaviour. In our case, this correspondence is established for the manual labeling, only if a broiler maintains its whole head inside the pan for a period lasting 20 seconds. In many cases the simple closeness to the pan or drinking line does not guarantee that a broiler is eating or drinking.</p>
<p>Neethirajan, S. (2017). "Recent advances in wearable sensors for animal health management." <i>Sensing and Bio-Sensing Research</i> 12: 15-29.</p>	<p>Biosensors, as an application for animal health management, are an emerging market that is quickly gaining recognition in the global market. Globally, a number of sensors being produced for animal health management are at various stages of commercialization. Some technologies for producing an accurate health status and disease diagnosis are applicable only for humans, with few modifications or testing in animal models. Now, these innovative technologies are being considered for their future use in livestock development and welfare. Precision livestock farming techniques, which include a wide span of technologies, are being applied, along with advanced technologies like microfluidics, sound analyzers, image-detection techniques, sweat and salivary sensing, serodiagnosis, and others. However, there is a need to integrate all the available sensors and create an efficient online monitoring system so that animal health status can be monitored in real time, without delay. This review paper discusses the scope of different wearable technologies for animals, nano biosensors and advanced molecular biology diagnostic techniques for the detection of various infectious diseases of cattle, along with the efforts to enlist and compare these technologies with respect to their drawbacks and advantages in the domain of animal health management. The paper considers all recent developments in the field of biosensors and their applications for animal health to provide insight regarding the appropriate approach to be used in the future of enhanced animal welfare.</p>
<p>Larsen, H.; Cronin, G.M.; Gebhardt-Henrich, S.G.; Smith, C.L.; Hemsworth, P.H.; Rault, J.-L. Individual Ranging Behaviour Patterns in Commercial Free-Range Layers as Observed through RFID Tracking. <i>Animals</i> 2017, <i>7</i>, 21.</p>	<p>Understanding of how free-range laying hens on commercial farms utilize the outdoor space provided is limited. In order to optimise use of the range, it is important to understand whether hens vary in their ranging behaviour, both between and within individual hens. In our study, we used individual tracking technology to assess how hens in two commercial free-range flocks used the range and whether they varied in their use of the range. We assessed use of three areas at increasing distance from the shed; the veranda [0–2.4 m], close range [2.4–11.4 m], and far range [≥11.4 m]. Most hens accessed the range every day (68.6% in Flock A, and 82.2% in Flock B), and most hens that ranged accessed all three areas (73.7% in Flock A, and 84.5% in Flock B). Hens spent half of their time outside in the veranda adjacent to the shed. We found that some hens within the flocks would range consistently (similar duration and frequency) daily, whereas others would range inconsistently. Hens that were more consistent in their ranging behaviour spent more time on the range overall than those that were inconsistent. These different patterns of range use should be taken into account to assess the implications of ranging for laying hens.</p>

<p>Larsen, H., Hemsworth, P., Cronin, G., Gebhardt-Henrich, S., Smith, C., & Rault, J. (2018). Relationship between welfare and individual ranging behaviour in commercial free-range laying hens. <i>Animal</i>, 1-9. doi:10.1017/S1751731118000022</p>	<p>Laying hens housed in free-range systems have access to an outdoor range, and individual hens within a flock differ in their ranging behaviour. Whether there is a link between ranging and laying hen welfare remains unclear. We analysed the relationships between ranging by individual hens on a commercial free-range layer farm and behavioural, physiological and health measures of animal welfare. We hypothesised that hens that access the range more will be (1) less fearful in general and in response to novelty and humans, (2) have better health in terms of physical body condition and (3) have a reduced physiological stress response to behavioural tests of fear and health assessments than hens that use the range less. Using radio frequency identification tracking across two flocks, we recorded individual hens' frequency, duration and consistency of ranging. We also assessed how far hens ventured into the range based on three zones: 0 to 2.4, 2.4 to 11.4, or > 11.4 m from the shed. We assessed hen welfare using a variety of measures including: tonic immobility, open field, novel object, human approach, and human avoidance (HAV) behavioural tests; stress-induced plasma corticosterone response and faecal glucocorticoid metabolites; live weight, comb colour, and beak, plumage, footpad, and keel bone condition. Range use was positively correlated with plasma corticosterone response, faecal glucocorticoid metabolites, and greater flight distance during HAV. Hens that used the range more, moved towards rather than away from the novel object more often than hens that ranged less. Distance ranged from the shed was significantly associated with comb colour and beak condition, in that hens with darker combs and more intact beaks ranged further. Overall the findings suggest that there is no strong link between outdoor range usage and laying hen welfare. Alternatively, it may be that hens that differed in their ranging behaviour showed few differences in measures of welfare because free-range systems provide hens with adequate choice to cope with their environment. Further research into the relationship between individual range access and welfare is needed to test this possibility.</p>
<p>Morales, I. R., et al. (2016). "Early warning in egg production curves from commercial hens: A SVM approach." <i>Computers and Electronics in Agriculture</i> 121: 169-179.</p>	<p>Artificial Intelligence allows the improvement of our daily life, for instance, speech and handwritten text recognition, real time translation and weather forecasting are common used applications. In the livestock sector, machine learning algorithms have the potential for early detection and warning of problems, which represents a significant milestone in the poultry industry. Production problems generate economic loss that could be avoided by acting in a timely manner.</p> <p>In the current study, training and testing of support vector machines are addressed, for an early detection of problems in the production curve of commercial eggs, using farm's egg production data of 478,919 laying hens grouped in 24 flocks.</p> <p>Experiments using support vector machines with a 5 k-fold cross-validation were performed at different previous time intervals, to alert with up to 5 days of forecasting interval, whether a flock will experience a problem in production curve. Performance metrics such as accuracy, specificity, sensitivity, and positive predictive value were evaluated, reaching 0-day values of 0.9874, 0.9876, 0.9783 and 0.6518 respectively on unseen data (test-set).</p> <p>The optimal forecasting interval was from zero to three days, performance metrics decreases as the forecasting interval is increased. It should be emphasized that this technique was able to issue an alert a day in advance, achieving an accuracy of 0.9854, a specificity of 0.9865, a sensitivity of 0.9333 and a positive predictive value of 0.6135. This novel application embedded in a computer system of poultry management is able to provide significant improvements in early detection and warning of problems related to the production curve.</p>

7.8 Appendix 8 – Case study of water and feed medication dose rate calculation

Disease challenge

Bacterial diseases requiring antibiotic treatment in the layer industry are generally limited to cases of fowl cholera (*Pasteurella multocida*), spotty liver disease (*Campylobacter hepaticus*) and sporadic incidences of peritonitis due to non-specific pathogens like *E.coli*.

Farming enterprise

Most cases of bacterial disease in layers occur in free range farming enterprises due to higher levels of exposure of flocks to pathogens and the inability to maintain optimal biosecurity or maintain pathogen-free sites once infection and colonisation of a site has occurred. Barn facilities provide good biosecurity, but the ability to sanitise between batches can be compromised if the shedding, equipment or flooring is old or not well maintained. Cage facilities provide good opportunities for a good level of biosecurity to both prevent incursion of disease, and to eradicate through thorough cleaning and sanitation should a disease challenge occur. The bacterial diseases usually encountered are generally transmitted via the faecal-oral route so cleaning of the hens' immediate contact environment and maintaining separation between birds and their faeces provides good prevention against infection.

Antimicrobial options

There are very few choices of antimicrobials for use in layer hens (see Appendix 2) so the prescribing veterinarian is limited to using the available antimicrobials as per label directions or prescribing off-label use. Even for those antibiotics that are registered for use in layer hens, the registered dose rate is often inadequate due to minimum inhibitory concentration (MIC) creep making them less efficacious.

Off-label use

Off-label use of antimicrobials is the right of the prescribing veterinarian, but also the sole responsibility of the prescribing veterinarian to avoid residues greater than the approved maximum residue limits (MRL) in eggs. With no resources available to assist a veterinarian in calculating suitable withholding periods to avoid the presence of residues above the MRL, the written instruction of a withholding period can be no more than a professionally considered estimate.

Duration of treatment

Duration of treatment needs to be sufficient to ensure treatment objectives are met.

Route of administration

There are two options for administration of antimicrobials to a flock using mass medication methods – in-water and in-feed. Calculations need to be done to determine the correct amount of antimicrobial required to ensure the correct daily intake by whichever method of administration is selected. In-water medication has the advantage over in-feed medication due to the ability to introduce medication practically immediately whereas in-feed medication is delayed until medicated feed can be produced and delivered to the shed.

In-water medication requires knowledge of the daily water intake of the flock on a per bird basis and a per shed basis. Once the total weight of antimicrobial is calculated (see below), it then needs to be added to the day's estimate of water consumption. This is only feasible if the water system to the shed has been set up to provide medication through the water.

In-feed medication requires knowledge of the daily feed intake of the flock so that medication can be added to the feed to provide the daily medication requirements in the feed consumed. Unless good farm records are maintained, this figure is often unavailable. An estimate can be made of feed consumption based on the number of birds in the flock and historical feed deliveries.

Calculation of antimicrobial volume required

In-water – water intake over a 24-hour period is determined. Medication tank method: That volume of water is then held in a separate tank and the medication added and thoroughly mixed into the water. It is very important to ensure that the water inlet to the medication tank is turned off so that medicated water is not being diluted by incoming water. Only enough medication for a single day's treatment should be mixed. Venturi method: Venturi systems of medication addition must be calibrated to ensure accurate dilution of medication so that the daily allocation is consumed in a 24-hour period.

Example calculation

- Average bird weight 0.745 kg
- Water intake 100 ml/bird/day
- Medication required 60 mg/kg/day
- Medication period 5 days

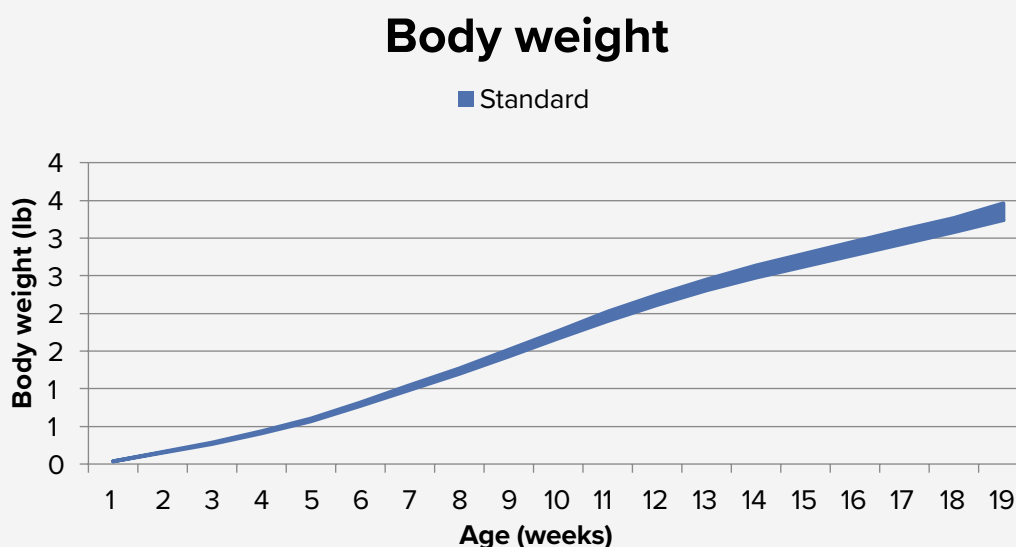


Figure 1 Breed standard bodyweight Hyline Brown layer (Specialised Breeders Australia, 2018)

Total medication required per bird per day = 0.745 kg x 60 mg/kg = 45 mg/bird

Mixing rate = 45 mg into 100 ml water = 450 mg/litre = 450 grams/1000 litres

Total kg of birds to be treated (hen weight in kg) = number of birds in shed x average body weight of flock (from weight records or breed standard – see Figure 1)

Total amount of antimicrobial required (grams) = (hen weight in kg) x prescribed dose rate (mg/kg)/1000 = 0.745 kg x 60 mg/kg/day x 5 days = 223 mg/bird (or 223 grams/1000 birds)

In-feed – It is important to discuss inclusion rates and addition methods with the feedmill manager to ensure there is even mixing of feed and no risk of contamination of feed produced after the production run of medicated feed.

Example calculation

- Feed intake 60 grams per day
- Medication dose is 20 mg/kg bodyweight per day
- Average weight of birds is 0.745 kg
- Medication period 14 days

Total medication required per bird per day = 20 mg/kg x 0.745 kg = 15 mg/day

Mixing rate = 15 mg into 60 grams of feed = 250 mg/kg of feed (or 250 ppm)

Total medication required = 15 mg/bird x 14 days = 210 mg/bird (or 210 grams /1000 birds)

References

Specialised Breeders Australia. (2018). Hyline Brown Performance Standards. Retrieved from <http://www.specialisedbreeders.com.au/hyline-brown>

