



# Evaluation of practices used to reduce the incidence of bovine respiratory disease in Australian feedlots

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## Introduction

Bovine respiratory disease (BRD) has been identified as the most significant infectious disease of feedlot cattle in eastern Australia (Project DAN.64). BRD causes economic loss due to medication costs, mortalities, excessive feed inputs associated with increased time on feed, reduced sale prices and associated labour costs. BRD is a complex multifactorial condition with a number of animal, environmental and management risk factors predisposing cattle to illness. A range of microorganisms are implicated in BRD with at least four viral and three bacterial species involved singly or in combination.

The viruses most commonly associated with BRD in Australia are bovine herpesvirus 1 (BHV 1), bovine viral diarrhoea virus (BVDV or bovine pestivirus), bovine parainfluenza 3 virus (PI3), and bovine respiratory syncytial virus (BRSV). More recently, coronavirus has been identified as a potential viral contributor to BRD in Australia (Hick et al., 2012). A number of bacterial species have also been recognised as important to the BRD complex; these include *Mannheimia haemolytica*, *Pasteurella multocida*, and *Histophilus somni*.

Though one or more of the pathogens listed above can be isolated from clinical cases of BRD, there is no evidence that infection alone causes serious illness. This indicates that, in addition to specific infectious agents, other factors are crucial for the development of BRD under field conditions.

These can be categorised as environmental, animal, and management risk factors. These risk factors are likely to exert their effects through a number of pathways including reductions in systemic and possibly local immunity. For example, stressors such as weaning, handling at saleyards, transport, dehydration, weather conditions, dietary changes, comingling, and pen competition might reduce the effectiveness of the immune system, allowing infection with pathogens to lead to the development of BRD.

The purpose of this document is to summarise the evidence supporting the practices currently utilised by the Australian feedlot sector to reduce the incidence of BRD. Predisposing factors largely beyond the control of most feedlots, such as weather and exposure to respiratory viruses,

are discussed separately (listed in Table 1), but these factors can generate indirect responses that are discussed under the preventative practices categories.

The current practices are classified as either animal preparation practices (Table 2) or feedlot management practices (Table 3). Under these headings the evidence supporting each practice has been categorised as follows:

1. **Australian Evidence:** A practice that is supported by published peer reviewed research conducted in Australia. Typically, the supporting evidence would be published in a scientific journal but could also include studies submitted for higher degrees.
2. **Overseas Evidence:** A practice that is supported by published peer reviewed research conducted overseas. This distinction has been made as there are some intrinsic differences between the industries in different countries and continents that might not enable direct application of the findings from this evidence to the Australian feedlot sector.
3. **Registration Evidence:** A practice supported by research done in Australia and submitted to the Australian Pesticides and Veterinary Medicines Authority (APVMA) for product registration. These studies frequently use small numbers in experimental settings and are not subject to broader review and publication.
4. **Anecdotal Evidence:** The reliability of this evidence is variable. It can be based on controlled research that has not been published or observations of population data.
5. **Minimal Evidence or Untested:** This might include practices that have been adopted in the past but the basis for this adoption is now unknown. This classification also includes practices that have not been subjected to scientific evaluation.

Table 1. Predisposing factors for bovine respiratory disease in Australian feedlots and their supporting evidence

Predisposing factor	Evidence	Comments
Predisposing factors with robust supporting evidence		
Season and weather	Australian & Nth American	
Dust concentration	US studies	Evidence from cattle in a commercial feedlot and evidence from sheep & goat exposure that might translate to cattle.
Gender	Australian & Nth American	Trend for greater BRD risk in steers
Breed	Australian & Overseas	BRD predisposition of Bos taurus > Bos indicus and Hereford > other Bos taurus
Serological increase to respiratory viruses	Australian epidemiological study	Increasing BRD risk with exposure to increasing number of viruses
Predisposing factors with minimal supporting evidence or untested		
Rainfall/mud	Untested	

Table 2. Animal preparation practices utilised to minimise BRD in Australian feedlots and their supporting evidence

Animal preparation practice	Evidence	Comments
Animal preparation practices with robust supporting evidence		
Yard weaning	Australian	
Reducing transport time	Australian & Overseas	
Distance travelled (as opposed to time in transport)	Australian & Overseas	Australian epidemiological study & US multivariate analysis of survey data.
Animal preparation practices with equivocal supporting evidence		
Pre-vaccination with Bovilis MH	Australian	Registration data with epidemiological support
Pre-vaccination with Pestigard	Australian	Epidemiological data
Animal preparation practices with minimal supporting evidence or untested		
Pre-vaccination with Bovishield		Untested
Truck design/exhaust fumes	Nth American	Conference proceedings with limited published support.
Hydration status on arrival at feedlot	Overseas	Poorly defined indirect data
Higher pre-feedlot growth rate		Untested

Table 3. Feedlot management practices currently utilised to minimise BRD in Australian feedlots and their supporting evidence

Feedlot management practice	Evidence	Comments
Feedlot management practices with robust supporting evidence		
Reduction in purchase groups per pen & avoiding saleyard purchases	Australian & Overseas	
Shared water troughs between pens	Australian	Epidemiological data consistent with viral serological increase results
Reducing time to fill a pen with a complete batch of cattle	Australian	Epidemiological data
Mass medication with antibiotics at feedlot entry	Australian & Overseas	
Introductory diet	Overseas	
Feed delivery management	Overseas	Australian meta-analysis using data from North America
Dietary vitamin E	Overseas	
Hormonal growth promotant	Overseas	HGP's have no effect on the incidence of BRD
Concurrent disease	Overseas	Lactic acidosis associated with increased risk of BRD
Feedlot management practices with equivocal research outcomes		
Removal of cattle persistently infected with BVDV	Overseas & Anecdotal	Equivocal research outcomes
Pen area allocation	Australian	Epidemiological data
Bunk space	Australian	Epidemiological data
Dietary trace element supplementation > NRC recommendation	Australian analysis of US data	
Injection of trace elements at feedlot entry supplemental to NRC recommended dietary trace elements	Nth American	
In-feed antibiotics	Overseas	
Feedlot management practices with minimal evidence or untested		
Vaccination with modified live BHV 1 at feedlot entry	Registration	
Mixing cattle during the feeding period	Overseas	Indirect evidence based on metabolic measures of stress.
Large BW range within a pen (ie > 100 kg)	No Evidence	
Liquid supplements in receival pens (i.e. urea/molasses)	No Evidence	
Staffing levels i.e. pen riders per 10,000 head	No Evidence	
Low stress cattle handling	No Evidence	
Electrolytes in the water on arrival	No Evidence	
Reducing time between feedlot arrival and induction	No Evidence	
Feedlot management practices known not to reduce the incidence of BRD		
Injection with vitamins A, D & E at feedlot entry	Australian	Found not to be effective in Australian published study.
Urea-molasses liquid supplement in starter pens	Australian	Found not to be effective in Australian published study.
Artificial dietary sweeteners (Sucram)	Overseas	

## Predisposing Factors – Robust Supporting Data

- Season and Weather – Australian and north American data.

The peak incidence of BRD usually occurs in autumn and early winter in Australia and the USA (Irwin et al., 1979). Whereas the association between season and BRD incidence in the USA could be confounded by the influx of light weight calves in autumn, feedlot cattle numbers do not consistently vary with season in eastern Australia. A large Australian epidemiological study, The National Bovine Respiratory Disease Initiative (NBRDI; Barnes et al., 2014), found strong associations between season of feedlot entry and the incidence of BRD. Relative to spring, risk of BRD was increased in winter (OR = 1.6, 95% CI = 1.0 to 2.3,  $P = 0.03$ ) and markedly increased in summer (OR = 2.4, 95% CI = 1.4 to 3.8,  $P = 0.001$ ) and autumn (OR = 2.1, 95% CI = 1.2 to 3.2,  $P = 0.004$ ). These analyses do not differentiate between northern (Qld and northern NSW) and southern feedlots. Observational data suggest that BRD incidence is highest in autumn and winter in southern Australia with a low summer incidence, but that incidence can be high during summer in northern feedlots.

Rapid and severe temperature changes and greater weather extremes in the USA contribute to higher BRD morbidity and mortality rates compared with Australia (Irwin et al., 1979). This observation prompted Australian reviewers to propose that rapid change in temperature, rather than temperature per se, is responsible for an increase in the incidence of BRD (Cusack et al., 2003), which is supported by US studies (Alexander et al., 1989; MacVean et al., 1986). Further, a more recent US study (Cernicchiaro et al., 2012) found that several weather factors (maximum wind speed, mean wind chill temperature, and temperature change, with lag periods of 3 to 4 days and 5 to 7 days before disease occurrence) were associated ( $P < 0.05$ ) with increased daily BRD incidence, with the effects more marked in low BW cattle. An Australian study showed a stronger correlation between minimum temperature and BRD incidence ( $r = 0.54$ ,  $P = 0.002$ ) than temperature range and BRD incidence ( $r = 0.25$ ,  $P = 0.05$ ) during the winter months (Cusack et al., 2007).

The findings from Cusack et al. (2007) do not preclude the possibility that temperature range is strongly correlated with the incidence of BRD in Australian feedlots during autumn. The NBRDI (Barnes et al., 2014) did not find consistent evidence of a substantial effect on BRD incidence of either mean maximum daily temperature in wk 1 after induction, mean minimum daily temperature in wk 1, mean daily temperature range in wk 1, total rainfall in wk 1, or mean daily maximum wind speed in wk 1. It is possible that more complex interactions of the individual measures of temperature, wind speed and rainfall, perhaps in combination with humidity, during seasons of higher BRD incidence and for the duration of the feeding period, could affect BRD incidence and further research into these potential effects is therefore warranted. In addition, the lag periods of 3 to 4 days and 5 to 7 days between the weather characteristic of interest and the occurrence of BRD throughout the feeding period should be investigated in future Australian research.

- Dust concentration – Direct evidence in cattle in a commercial feedlot and indirect supporting evidence from North America using experimental exposure of small ruminants to dust.

Feedlot dust can contain viable microbes and, more importantly, endotoxin (Purdy et al., 2002). MacVean et al. (1986) found that the incidence of BRD in the period from 16 to 30 days on feed was associated with the concentration of airborne particles 2 to 3.3  $\mu\text{m}$  in diameter, and a 15 d lag from peak exposure to peak disease generated the closest correlation.

Repeated exposure of sheep to feedlot dust containing endotoxin for 4 h periods induced temporary pyrexia and leukocytosis, and generalised alveolar septal thickening and hypercellularity (Purdy et al., 2002). Repeated exposure of goats to feedlot dust resulted in a mild, acute exudative bronchointerstitial pneumonia (Purdy et al., 2002).

- Gender – Australian and North American data.

In North America, Snowden et al. (2006), found steers were more likely to be diagnosed with BRD than heifers. Cusack et al. (2007) found an association ( $P = 0.03$ ) between gender and mortality due to BRD, with steers in this sample being slightly more likely to die during the feeding period compared with heifers. More recently, Croft et al. (2014) found the incidence of BRD was greater in steers ( $P < 0.001$ ) in an Australian feedlot, and this finding was supported by the NBRDI (Barnes et al., 2014) where heifers were found to probably be at reduced risk of BRD compared with steers (OR: 0.7, CI = 0.4 to 1.1,  $P = 0.06$ ). In summary, there is evidence that BRD incidence will be slightly greater in steers than heifers in Australian feedlots. With a negligible proportion of entire male cattle entering feedlots in Australia this finding is not confounded by the stress of castration encountered in many North American studies.

- Recognising Hereford cattle as having a higher BRD risk – Australian data supported by North American data.

Breed can be related to the incidence of BRD (Cusack et al., 2007). British breeds of cattle were more likely to develop clinical BRD than *Bos indicus* breeds. Compared to the base population, the development of clinical BRD over time was 10 times higher in Herefords, 6 times higher in Murray Greys, and 5 times higher in Angus feedlot cattle. Barnes et al. (2014) also found Herefords were at increased risk of BRD (OR = 2, 95% CI = 1.5 to 2.6,  $P < 0.001$ ). A relationship between breed and BRD incidence is supported by North American studies (Muggli-Cockett, 1992; Snowden et al., 2005), with greater susceptibility of the Hereford breed identified by Snowden et al. (2006).

- Increase in serum antibody concentration to the respiratory viruses, BHV 1, PI3, BRSV and BVDV during the first 42 days in the feedlot – Australian epidemiological study.

Barnes et al. (2014) found an association between serological antibody concentration increase between feedlot entry and day 42 to the respiratory viruses, BHV 1, PI3, BRSV and BVDV, either singly (OR = 1.4, 95% CI = 1.2 to 1.6,  $P < 0.001$ ; OR = 1.4, 95% CI = 1.2

to 1.7,  $P < 0.001$ ; OR = 1.4, 95% CI = 1.3 to 1.7,  $P < 0.001$ ; OR = 1.3, 95% CI = 1.1 to 1.6,  $P = 0.001$  respectively) or in combination. Using an enzyme linked immunosorbent assay (ELISA), serological results were categorised based on optical densities on a graduated scale from 1 to 5. Seroconversion was defined as a change in category from zero on feedlot entry to at least 2 at the six week follow up sample. Serological increase was defined as an increase from feedlot entry to the follow up sample of 2 categories or more from initial category values of 1, 2, or 3. The small proportion of cattle seronegative to the listed respiratory viruses at feedlot entry resulted in considerably smaller sample sizes for seroconversion compared with serological increase, with results consistent with those for serological increase but not as statistically strong.

The risk of BRD increased with the number of these respiratory viruses to which serological increase occurred (serological increase to one virus, OR = 1.3, 95% CI = 1.1 to 1.6,  $P = 0.003$ ; serological increase to two viruses, OR = 1.9, 95% CI = 1.5 to 2.3,  $P < 0.001$ ; serological increase to three viruses, OR = 2.1, 95% CI = 1.6 to 2.6,  $P < 0.001$ ; serological increase to four viruses, OR = 1.8, 95% CI = 1.1 to 2.7,  $P = 0.006$ ). Thus, the risk of BRD increased with increasing exposure to respiratory viruses of cattle with low initial respiratory virus antibody titres during the first 6 weeks in the feedlot.

The effects of serological increase outlined above are consistent with the observation that mixing at least 28 d before feedlot entry had a protective effect against BRD (Barnes et al., 2014; reported below). It is likely that this reduction in the risk of BRD was due to some extent to removing the risk of BRD associated with respiratory virus exposure of cattle with low antibody titres to these viruses in the feedlot. Further, the relationship between exposure to an increasing number of respiratory viruses and increasing risk of BRD in the Barnes et al. (2014) study might provide an explanation for additional associations identified by this study, possibly involving greater transmission of respiratory viruses through close contact between cattle eg. water troughs shared between pens (discussed below).

## Predisposing Factors – Untested

- Rainfall/mud

## Animal Preparation

### Practices with robust supporting evidence

- Yard weaning – Australian and North American data

Fell et al. (1998) examined the effects of different weaning procedures and vaccination regimens in the preparation of cattle for feedlots on subsequent health outcomes over a three year period. Vaccines were administered at least one month before feedlot delivery to ensure that vaccinated animals had developed immunity by the time they arrived at the feedlot.

This study examined the performance and health outcomes for groups of cattle that were weaned in one of three ways:

1. Paddock weaning – no supplemental feeding or handling for 21 days (PW, control group);
2. Yard weaning with good quality hay or silage with minimal handling for 10 days (YW);
3. Yard weaning with good quality hay or silage with novel training procedures to increase capacity to adapt to the feedlot (YW-T).

British breed calves from two herds (one experimental and one commercial) were weaned at 7 to 9 months of age. Following weaning the calves were held on pasture for 6 to 9 months and then transferred to a commercial feedlot. At the feedlot the study cattle were mixed in a pen with cattle procured using standard feedlot practices. Within these experimental treatments a variety of experimental vaccines were applied to groups with similar numbers of controls.

Calves YW and YW-T had greater mean daily gains and reduced morbidity compared to PW. A similar, but lesser, effect was observed with vaccination with YW compared with PW, with average daily gain and morbidity for YW-T being intermediate. The effect of vaccination was somewhat complicated with a variety of vaccines and regimens applied over the course of the three experiments, which might have reduced the

effectiveness of this treatment. While training in combination with YW showed some benefit it was not as beneficial as YW alone. This finding led the authors to conclude that the establishment of social groups within weaning groups is a critical component for improving health outcomes and productivity of feedlot cattle.

In summary, management of weaning alone or in combination with vaccination at least one month before feedlot delivery yielded an economic benefit in reduced disease incidence and increased weight gain during the feedlot phase. Barnes et al. (2014) showed yard weaning alone had a direct effect of reducing the risk of BRD (OR = 0.7, 95% CI = 0.5 to 1.0,  $P = 0.02$ ) which is in keeping with the equivocal effect of vaccination in the DAN.069 study (Fell et al., 1998) reported above. Further, a US study (Step et al., 2008) showed that weaning without vaccination 45 d before feedlot delivery had similar benefits to weaning with vaccination, using a modified live viral vaccine (against BHV 1, BVDV types 1 and 2, PI3, BRSV) and a *Mannheimia haemolytica* toxoid, 45 d before feedlot delivery. The lack of an effect of prior vaccination in the calves weaned and held for 45 days occurred despite the administration of corresponding vaccines to all calves at feedlot entry.

- Reducing time taken for transport of cattle to the feedlot – indirect Australian and overseas data and Australian epidemiological data.

With transport duration greater than 24 h, increasing transport time was associated with higher BRD incidence in US cattle (Johnson, 1985). While no controlled studies in Australia have specifically investigated the relationship between increased transport times and subsequent BRD outcomes, one study was conducted to assess metabolic changes in cattle subjected to transportation. Stanger et al. (2005) examined the immune status of *Bos indicus* steers after 72 h of road transportation. The comparison of immunological functions

before and after transport indicated a degree of dysfunction for six days post-transport. The authors concluded this could increase susceptibility to infectious agents for six days after transport, though this aspect was not tested in the study. In keeping with this, a Polish study (Urban-Chmiel, 2006) found transport duration of 72 h (1700 km) resulted in significantly reduced ( $P < 0.05$ ) leukocyte viability with samples exposed to leukotoxin from *M. haemolytica*.

Most of the stress of transport of less than 24 h duration was suggested by Cole et al. (1988) to be related to the loading and unloading process. However, Barnes et al. (2014) found that cattle transported for 6 h or more within 24 h of feedlot entry were at slightly increased risk of BRD (OR = 1.2, 95% CI = 1.0 to 1.5,  $P = 0.02$ ) compared with cattle transported for less than 6 h within 24 h of feedlot entry.

The effects of the time cattle are held in saleyards or holding yards before transport to the feedlot have not been evaluated.

- Distance traveled (as opposed to time in transport) – Inadequately defined European data and robust US data.

Mormede et al. (1982) found a higher incidence of BRD in cattle held overnight in a holding yard, and transported a longer distance (300 km), compared with cattle transported a short distance, from the same property of origin, directly to a European feedlot. The study design does not allow the separation of the effects on BRD incidence of transport distance from transport duration. Another possible confounding factor in the higher incidence of BRD is the increased handling due to being held overnight in holding yards. Conversely, Ribble et al. (1995) found the distance 45,243 calves were transported to a feedlot over a 4 yr period was not correlated with the incidence of BRD. However, a more recent US study (Sanderson, et al., 2008) found an increase in BRD morbidity with increased transport distance (Incidence Rate Ratio [IRR] = 1.001,  $P < 0.001$ ), with the data indicating a 10% increase in initial BRD morbidity risk for each 160 km increase in transport distance. This finding is further supported by another US study (Cernicchiaro et al., 2012) where distance travelled (mean = 698 km, median = 552 km, range = 0 to 3,087 km)

was associated ( $P < 0.05$ ) with BRD morbidity and overall mortality, and negatively associated with hot carcass weight and mean daily gain.

### Practices with equivocal evidence

- Pre-vaccination against *Mannheimia haemolytica* with Bovilis MH™ (Intervet) vaccine – Controlled experiment registration data with epidemiological support.

There have been no controlled studies published regarding the effectiveness of pre-vaccination against *Mannheimia haemolytica* with the commercially available vaccine Bovilis MH™ (Intervet). Efficacy was demonstrated by CSIRO for registration of the vaccine with the Australian Pesticides and Veterinary Medicines Authority (APVMA) using a pen study with experimental challenge ( $n = 8$ ). A field experiment was also conducted at 3 sites ( $n = 100$  at each site), with no significant difference in morbidity or mortality found in response to two injections of vaccine at a 4 wk interval. However, the incidence of BRD at all three sites was reported as being very low for the duration of the experiment, making the detection of vaccination effects unlikely. Barnes et al. (2014) found a modest protective effect against BRD with the use of this vaccine (OR = 0.8, 95% CI = 0.6 to 1.0,  $P = 0.02$ ). Note that the 95% credible interval includes 1 (no effect) but there is a 98% probability that the point estimate is less than 1, even though the protective effect is not strong. However, this epidemiological study (Barnes, et al., 2014) was unable to separate data where only one injection of Bovilis MH™ was given at feedlot entry, and it is therefore likely that the protective effect of two injections of the vaccine at a 4 wk interval with the second being given no later than feedlot entry could be greater than the quoted odds ratio suggests.

- Pre-vaccination against Bovine Viral Diarrhoea Virus with Pestigard™ vaccine (two vaccine injections) – epidemiological data.

The role of BVDV in the pathogenesis of BRD has been subject to much conjecture due to a lack of evidence implicating it as a primary BRD pathogen. BVDV might facilitate colonisation of the lungs by other pathogens (Richer et al., 1988). Experimental infection of immunocompetent, seronegative calves with BVDV type 1d induced primary BRD, in the absence of concurrent infection with other BRD pathogens (Baule et al., 2001), suggesting a possible

primary role for the virus in the pathogenesis of BRD. It appears, therefore, that BVDV might enhance the development of BRD by immunosuppression and as a primary respiratory pathogen. Barnes et al. (2014) found a modest protective effect from on-farm vaccination with two injections of Pestigard™ at a 4 to 6 wk interval on feedlot BRD risk (OR = 0.8, 95% CI = 0.5 to 1.1,  $P = 0.05$ ). Considering that the 95% credible interval includes 1 (no effect) this is not a strong effect, but alternatively, there is a 95% probability that the point estimate is less than 1, ie. that the vaccine exerts a modest protective effect.

### Practices with minimal evidence or untested

- Pre-vaccination against *Mannheimia haemolytica* with Bovishield™ vaccine

There are no controlled published studies on the use of Bovishield™ vaccine in commercial feedlots in either Australia or North America.

- Truck design/exhaust fumes – North American unpublished data (conference proceedings), and a peer reviewed study

Exposure to exhaust fumes was found to reduce subsequent feedlot growth rate (Cole, et al., 1989). When the exhaust stack on a prime-mover was lower than the top of the trailer, calves that travelled on the top deck tended to have lower subsequent feedlot growth rates than calves that travelled on the lower deck. Further, calves from the top deck had higher feedlot growth rates than calves from the bottom deck when the exhaust stack was higher than the trailer. An expectation of an increase in the incidence of BRD in calves exposed to exhaust fumes is based on this recorded effect on growth rate. A more recent study (White et al., 2009), that assessed the effects of location within the transport vehicle on ADG and health, supported the previous finding that animals located closer to the front of the trailer had lower growth rates. Again the assumption was that the findings were due to exposure to exhaust fumes. Both of these studies have been published as conference proceedings and not subjected to peer review.

Wahrmund et al. (2012) found that cattle transported in the front of the lower deck, and the rear of the upper deck, had higher ( $P < 0.02$ ) total morbidity than those from the other compartments. This might be interpreted as BRD

risk being increased by inadequate air circulation in the case of the cattle transported in the front of the lower deck, and wind chill in the case of the cattle transported in the rear of the upper deck. However, the authors note that findings across studies are inconsistent. Further, care must be taken with the extrapolation of U.S. transport findings to Australia considering the much higher minimum temperatures in Australia and the greater ventilation of Australian cattle crates due to their more open design.

- Hydration status on arrival at the feedlot – Inadequately defined European data with a supporting US study.

Mormede et al. (1982) found a higher BRD incidence in cattle transported for longer distances that were dehydrated, but the effects of hydration status were not isolated from the effects of transport distance and duration. Dehydration can be a result of prolonged transport and might be one of the mechanisms by which transport could increase the incidence of BRD. There is further support for this from a US study (Cernicchiaro et al., 2012) where the association between distance travelled and BRD morbidity ( $P < 0.05$ ) resulted in a more dramatic increase in BRD during summer once the distance travelled exceeded a threshold of 500 to 750 km. These effects and their relative contributions to BRD incidence have not been adequately defined.

- Higher pre-feedlot growth rate – Untested.

## Feedlot Management

### Practices with robust supporting evidence

- Reduction in purchase groups per pen and avoiding purchase of cattle out of saleyards – Evidence from North America and Australia with the effect of timing of mixing clarified by an Australian study.

Australian cattle maintained as a group from weaning until feedlot entry adapted more rapidly to the feedlot diet and had higher growth rates over the first 37 d compared with cattle purchased through saleyards from a variety of sources (Fell et al., 1998). It is not possible to separate the effects of mixing in this study from the potential effects of exposure to saleyards. However, in the Canadian Bruce County Project, morbidity and mortality from BRD were greater with mixing of calves from different sources and assembly of calves from widely separated geographic locations (Martin et al., 1982). More recently, O'Connor et al. (2005) found a strong relationship between commingling and BRD (OR = 3, 95% CI = 2.5 to 3.6), and Sanderson et al. (2008) also found an increase in BRD morbidity (Incidence Rate Ratio [IRR] = 2.0,  $P < 0.001$ ) with cattle from multiple sources. In an Australian study, Croft et al. (2014) found BRD incidence was higher in cattle purchased from saleyards compared with cattle purchased out of paddocks (12.4% versus 5.7%,  $P < 0.001$ ).

Barnes et al. (2014) showed that the timing of mixing determines the effect on the incidence of BRD. Mixing at least 28 days before feedlot entry involving a saleyard transaction was associated with a reduction in the incidence of BRD (OR dependent on subsequent mixing = 0.6 to 0.8). Conversely, mixing between 27 and 13 days before feedlot entry via a saleyard was associated with an increase in BRD incidence (OR = 1.9, 95% CI = 1.3 to 2.7,  $P = 0.001$ ). With both these times of saleyard transit there was no evidence of a large direct effect, indicating that the effects were mediated through mixing rather than direct saleyard effects. Cattle that were mixed through a saleyard 12 days or less before feedlot entry had a markedly increased risk of BRD (OR = 2.6, 95% CI = 1.6 to 4.1,  $P < 0.001$ ). The direct effect of saleyard exposure within 12 days of feedlot entry

was attenuated but important (OR = 1.6, 95% CI = 0.9 to 2.6,  $P = 0.05$ ), indicating that there were negative effects specific to saleyard exposure in this period in addition to the effects of mixing. The variable effects of the timing of mixing and saleyard exposure might be explained to some extent by immunological responses occurring with earlier mixing conferring a threshold of antibody concentrations to the major respiratory viruses. In addition, a longer period between saleyard passage and mixing prior to feedlot entry provides additional time for the cattle to recover from the effects of these stressors. It is logical that recovery time would enhance the potential immunological benefits of prior exposure to respiratory viruses.

- Water troughs shared between pens – Australian epidemiological data.

The sharing of water troughs between pens (Barnes et al., 2014) was associated with an increased risk of BRD (OR = 3.6, 95% CI = 1.3 to 8.8,  $P = 0.006$ ). Subset analysis supported this result, indicating that the observed increase in BRD risk was unlikely to be due to confounding by feedlot. Two case control studies done by Barnes et al. (2014) found shared water troughs increased the risk of BRD (OR = 3.1, 95% CI = 1.0 to 7.5,  $P = 0.03$ ; OR = 3.3, 95% CI = 1.1 to 7.7,  $P = 0.02$ ).

- Reducing time to fill a pen with a complete batch of cattle – Australian epidemiological data

Barnes et al. (2014) found that cohort fill duration, that is, the time taken to fill a pen with a complete batch of cattle, greater than 1 d, was associated with an increased risk of BRD compared with cohort fill duration of only 1 d (OR = 1.9, 95% CI = 1.2 to 2.8,  $P = 0.005$ ). This effect was mediated primarily through mixing (direct effect OR = 1.2, 95% CI = 0.6 to 2.2,  $P = 0.288$ ) with greater mixing occurring with pens that took longer to fill.

- Mass medication with antibiotics at feedlot entry – Australian data with numerous supporting North American studies.

An Australian study examined the effects on cattle destined for the domestic market of mass

medication at feedlot entry with long acting oxytetracycline and tilmicosin (Cusack, 2004). Cattle mass medicated with tilmicosin had significantly fewer treatments for all illnesses ( $P = 0.0004$ ) and BRD specifically ( $P = 0.0001$ ), compared with cattle not given antibiotic at feedlot entry and compared with cattle mass medicated with oxytetracycline ( $P = 0.004$ ). There was no significant difference in treatments for all diseases ( $P = 0.47$ ) and treatments for BRD ( $P = 0.26$ ) between oxytetracycline treated cattle and cattle not given antibiotic at feedlot entry. The cattle treated with tilmicosin at feedlot entry had a significantly higher mean daily BW gain ( $1.67$  v  $1.59$   $\text{kg} \cdot \text{animal}^{-1} \cdot \text{d}^{-1}$ ), than cattle not medicated with antibiotic at feedlot entry ( $P = 0.03$ ) and cattle medicated with oxytetracycline at feedlot entry ( $P = 0.05$ ). Unpublished financial analysis of this study showed mass medication was profitable, even with a relatively low incidence of BRD, mainly due to the higher growth rate of the tilmicosin medicated cattle. Field observations show the lower BW cattle fed for the Australian domestic market have a higher incidence of BRD than the higher BW cattle fed for the Japanese market. This would presumably affect the response to mass medication of cattle in the different weight ranges, and therefore, the profitability of the practice. Further research into responses to antibiotic mass medication of cattle over a range of feedlot entry weights under a variety of Australian feedlot production systems is warranted.

North American studies have illustrated reductions in the incidence of BRD in response to mass medication with injectable antimicrobials. Positive responses to mass medication have been found following administration to all cattle at feedlot entry of benzathine penicillin (King et al., 1955), long acting oxytetracycline (Lofgreen, 1983; Harland et al., 1991; Van Donkersgoed et al., 1994), sulfadimethoxine (Lofgreen, 1983), and tilmicosin (Schumann et al., 1990; Schumann et al., 1991; Galyean et al., 1995; McClary and Vogel, 1999); selective administration on the basis of rectal temperature at feedlot entry of tilmicosin (Galyean et al., 1995); administration of long acting oxytetracycline to all cattle in a pen once BRD incidence exceeded 5% (no time frame reported, Janzen and McManus, 1980); and delayed administration of tilmicosin to all

cattle in a pen (Schumann et al., 1991; McClary and Vogel, 1999). In addition to a reduction in BRD morbidity, 4 of these experiments (Janzen and McManus, 1980; Schumann et al., 1990; Schumann et al., 1991; Galyean et al., 1995) also showed a positive growth rate response to treatment.

Van Donkersgoed (1992) used meta-analysis to examine the effect of antimicrobial mass medication on morbidity, mortality and growth rate as these related to BRD. Of 107 field trials, only ten were randomised controlled field trials deemed suitable for meta-analysis. The results indicated that parenteral mass medication with long acting oxytetracycline or tilmicosin on feedlot arrival would significantly reduce BRD morbidity in feedlot cattle. However, the author concluded that data on the effects of mass medication on mortality and performance were unreliable, there were insufficient data on the most effective treatment regimens, and there were no valid data on the efficacy of mass medication delivered in feed or water for prevention of BRD. Subsequently, Hellwig et al. (1999) found mass medication with injectable tilmicosin at feedlot arrival was superior to chlortetracycline added to the ration in terms of BRD morbidity and treatment costs. However, this was a small study ( $N = 88$ ) presented as a research report without peer review.

Tulathromycin is the most recent antibiotic to become available for the treatment and prevention of BRD in Australia. As yet there are no published Australian studies on the efficacy of mass medication with tulathromycin, but North American studies have shown it to be more effective in reducing the incidence of BRD than tilmicosin (Kilgore et al., 2005; Rooney et al., 2005) or florfenicol (Rooney et al., 2005).

- Introductory diet – North American data.

There is a strong association between feeding corn silage during the first month in the feedlot and increased incidence of BRD (Martin et al., 1982). In the Bruce County Beef Project's analysis of introductory feeding practices, mortality due to BRD was 5 times higher in calves fed corn silage as a major portion of their diet during the first week in the feedlot than in calves that were not fed substantial amounts of corn silage until the fourth week. Feeding grain

with the silage appeared to reduce some of the negative effects of silage consumption. Inclusion of non-protein nitrogen in the introductory diet in addition to that in the silage was also associated with increased mortality. Although analyses of the diets were not provided in this study it appears that feeding excessive amounts of non-protein nitrogen with inadequate rumen degradable true protein and inadequate starch and sugars might be responsible for the observed increase in the incidence of BRD rather than silage feeding per se. The relationship between dietary crude protein and BRD incidence is unclear (Duff and Galyean, 2007). Crude protein is derived from dietary nitrogen concentration and does not adequately describe the characteristics of the protein provided by a diet. The relationship between protein and BRD incidence can only be accurately assessed by evaluating the relative contributions to diets of true protein, non-protein nitrogen, rumen degradable protein, rumen undegradable protein and unavailable protein (from acid detergent insoluble nitrogen).

Lofgreen (1983) reported a reduction in morbidity and mortality when newly arrived calves were fed grass hay only, but this feeding practice resulted in a decrease in growth rate. If hay was provided for longer than 3 d in the receiving pen, it tended to inhibit intake of mixed ration, thereby reducing energy intake in newly arrived cattle (Johnson, 1985). Cattle purchased in saleyards and introduced to diets containing 20 to 30% high moisture barley were 4.9 times more likely to be treated for BRD, and 6.7 times more likely to die from BRD, than cattle assembled on their farm of origin and started on a diet containing 10% high moisture barley (Wilson et al., 1985), but this study does not isolate the effects of saleyard purchase from diet. Cattle with low blood glucose concentrations on arrival at the feedlot had a greater chance of subsequently developing severe BRD, and morbidity and mortality were reduced in calves fed a diet containing 55% concentrate rather than good quality hay at the saleyards before transport to the feedlot (Cope, 1978). Conversely, Rivera et al. (2005) found a slight increase in BRD morbidity with diets with increasing concentrates over a range from zero to 75% concentrate [morbidity, % = 49.59

– (0.0675 x roughage, %);  $P = 0.003$ ]. However, higher roughage diets were associated with lower ADG ( $P < 0.001$ ), and lower BRD morbidity with such diets did not offset the financial loss due to lower growth rate. Although rumen pH was not measured in these studies, the effects of higher grain diets on the incidence of BRD might be mediated by the development of lactic acidosis (Buczinski et al., 2015; Chako et al., 2015), a disorder which is influenced by feed milling and delivery in addition to diet formulation. It is possible that diets with at least 50% concentrates can reduce the incidence of BRD in cattle newly arrived at the feedlot provided they do not result in lactic acidosis. The appropriate formulation of the initial diet for cattle on arrival at feedlots requires further research. The potential for inappropriately processed or limit fed higher concentrate introductory diets to have adverse health effects due to lactic acidosis should be measured in research on the relationship between introductory diet and BRD by monitoring rumen pH, total volatile fatty acid yield, and lactate concentration.

In summary, published studies indicate that introductory diets should not provide a high proportion of crude protein as non-protein nitrogen, particularly where fermentable carbohydrate is limiting. Further, it appears that higher concentrate introductory diets are appropriate provided their milling and delivery does not cause lactic acidosis. Formulation targets for introductory diets to minimise the incidence of BRD are yet to be established, and research to determine them will require full description of dietary protein and monitoring of rumen fermentation characteristics.

- Feed Delivery Management – North American data.

Lactic acidosis has been shown to increase the risk of BRD (Buczinski et al., 2015; Chako et al., 2015) and the likelihood of death in diagnosed cases (Buczinski et al., 2015). These are most likely related to endotoxaemia (Plaizier, 2008; Ghozo, 2006; Andersen, 2003) and bacteraemia (Steele et al., 2011; Plaizier, 2008) arising from a loss of structural integrity and therefore barrier function in the rumen (Steele et al., 2011; Penner et al., 2010) and large intestine (Gressley et al., 2011). The effects of ruminal acidosis are logically exacerbated

in cattle that have been deprived of feed for greater than 24 h prior to feedlot delivery because feed deprivation itself compromises gastrointestinal tract barrier function (Zhang et al., 2013; Gabel and Aschenbach, 2002). Thus, feed management that achieves high stable intakes during the adaptation period without inducing lactic acidosis appears to be important to immunocompetence and reducing the risk of BRD.

Holland et al. (2007) found that during a 21 d adaptation period, feeding *ad libitum* or feeding a higher concentrate starter diet (88%, programme fed) was associated with greater BRD morbidity compared with a lower concentrate starter diet (64%) or with limited maximum intakes of 2.1, 2.3 and 2.5 times initial maintenance energy requirement. Unfortunately, this study did not monitor rumen pH or blood lactate concentrations, but it is likely that ruminal acidosis occurred with the *ad libitum* and high concentrate diets, and that this increased the incidence of BRD via the pathways outlined above.

- Dietary Vitamin E – Australian meta-analysis of North American data.

Delivery of supplemental antioxidant vitamins to cattle placed in feedlots might be expected to improve health and performance outcomes by reducing the effects of oxidative stress to which these cattle are exposed (Chirase et al., 2004). Meta-analytic procedures were used by Cusack et al. (2008) to assess published experiments on the effects of vitamin E supplementation in feedlot cattle. The health outcome of morbidity, and the production outcomes of average daily gain (ADG) and gain to feed ratio (G:F), were analysed. The authors concluded that supplemental dietary vitamin E should be fed within the NRC (1996) recommended range and that higher dietary inclusion rates do not consistently reduce BRD morbidity and are not profitable.

- Implantation with Hormonal Growth Promotant – North American data.

Robust studies with large sample sizes from North America have shown that implantation of cattle newly arrived at the feedlot with a hormonal growth promotant does not increase the risk of BRD (Richeson et al., 2015; Poe et al., 2013). Further, Richeson et al. (2015) found there

was no effect of hormonal growth promotant implantation on antibody titres in response to vaccination. Thus, not only is the risk of BRD unaffected, the BRD preventative measure of vaccination appears to also be unaffected by the use of hormonal growth promotants.

- Concurrent Disease – North American data.

Lactic acidosis has been shown to increase the incidence of BRD (Buczinski et al., 2015; Chako et al., 2015) and the likelihood of death in diagnosed cases (Buczinski et al., 2015). This is discussed in more detail in the section on Feed Delivery Management above. The reviewer is unaware of studies into the correlation between other feedlot diseases and the incidence of BRD.

### Practices with equivocal research outcomes

- Removal of cattle persistently infected with BVDV

Whilst the prevalence of cattle entering the feedlot persistently infected with BVDV is low (0.3% in a US study; Loneragan et al., 2005), cattle in the same and adjoining pens have been found to have an increased risk of BRD (0.5 cases per 1000 head days vs 0.35 cases per 1000 head days; RR = 1.43, CI = 1.0 to 2.0,  $P = 0.04$ ). Conversely, O'Connor et al. (2005) found the presence of an animal persistently infected with BVDV did not increase the incidence of BRD in the same pen. However, the serological status of the pen-mates at the start of the feeding period was not determined in either the Loneragan (2003) experiment or the O'Connor (2005) experiment, so the susceptibility of the populations of interest to infection with BVDV was unknown.

Unpublished data (Batterham, Quirindi Feedlot Services; *personal communication*) showed that cattle in a pen with a persistently infected animal had a 2.3 times greater likelihood of being treated for BRD, but there was no effect on growth rate or feed conversion ratio. There was also no effect on the BRD treatment rate in adjacent pens. From these data, it was calculated that persistently infected animal identification and removal from cattle newly arrived at a feedlot would only be profitable where pen size is greater than 200 animals and the incidence of BRD exceeds 10% of mean feedlot occupancy on a monthly basis

- Pen area allocation (stocking density, pen density) – Australian epidemiological data

At pen area allocations greater than 11 m<sup>2</sup>/standard cattle unit, Barnes et al. (2014) found no substantial consistent effect of increasing area allocations (decreasing stocking density) on BRD incidence. However, estimates for the total effect of pen area allocation on the risk of BRD were imprecise probably because the distribution across categories (11 to < 14 m<sup>2</sup>, 14 to < 17 m<sup>2</sup>, 17 to < 25 m<sup>2</sup>, and ≥ 25 m<sup>2</sup>) was clustered by feedlot. These area allocations all exceed the recommended minimum and it is possible that effects of area allocation are limited or absent above the minimum. It is also possible that lower area allocations could have an effect on BRD incidence in regions with higher rainfall, and particularly higher winter rainfall in southern Australia. Further research is warranted to clarify this potential effect.

- Bunk space – Australian epidemiological data.

For bunk space categories of < 18 cm/hd, 18 to < 24 cm/hd, and ≥ 24 cm/hd, Barnes et al. (2014) found no effect of bunk space on BRD risk. This is an important finding because most of these bunk spaces are less than previous recommendations and it is therefore likely that the management of feed delivery is more important to feed intake, production and health, than the bunk spacing itself. Further, the common industry bunk space of 22 cm/hd is supported by this finding.

- Dietary Trace Element Supplementation Greater Than NRC Recommendation – North American data.

North American research into the effects of dietary supplementation with zinc and copper at concentrations greater than the National Research Council (NRC, 1996) recommendation can be summarised as follows (study designs and results in Table 4).

- Dietary organic sources of Cu do not enhance immunity, health or production compared with inorganic sources and expenditure on these is therefore not justified.

- It is unclear if organic sources of Mn and Co improve immunity, health or production, compared with inorganic sources of Mn and Co, in isolation from the effects of Zn, and expenditure on these is therefore not justified.
- Compared with inorganic dietary sources of Zn, organic sources of Zn do not consistently improve feedlot production, but, immunoenhancement can result which can occasionally translate into reduced morbidity during the early feeding period. Therefore, it is possible that reduced morbidity could be achieved with the inclusion of an organic Zn source during the adaptation phase (21 to 28d) to provide a dietary concentration of 45 mg/kg DM in addition to the basal inclusion of 30 mg/kg DM from the cheaper inorganic ZnSO<sub>4</sub>. This would provide total Zn at the rate recommended by NRC (1996) for stressed cattle (75 to 100 mg/kg DM) during the adaptation phase, with a reduction to the NRC (1996) recommendation of 30 mg/kg DM for non-stressed cattle thereafter. Of the inorganic salts, the more soluble ZnSO<sub>4</sub> is preferred. Further research is required to verify that this variable dietary inclusion is cost effective, and the randomised study designs listed in the table below could readily be evaluated with meta-analysis to further clarify the health and production effects of organic trace elements compared with inorganic trace elements.

Table 4. The effects of organic trace elements versus inorganic trace elements on health and production of feedlot cattle

Reference	Trace Element/s and Supplemental Dietary Concentration	Sample Size (n) & entry BW, kg	Study Duration, d	Production (ADG, FCR)	Immune Response	Morbidity
Kegley et al., 2012	Randomised block design (RBD). Organic source of Zn @ 360 mg/hd/d as Zn-aa-complex, Cu @ 125 mg/hd/d as Cu-aa-complex, Mn @ 200 mg/hd/d as Mn-aa-complex, Co @ 12mg/hd/d as CoGlu <sup>a</sup> (Availla-4 <sup>TM</sup> , Zinpro); versus Inorganic source of these trace elements at the same rate as ZnSO <sub>4</sub> , CuSO <sub>4</sub> , MnSO <sub>4</sub> , CoCO <sub>3</sub> .	n = 144 (N of 77 str & 211 bulls banded @ induction) BW = 238	42	↑Organic total LWG (P = 0.04); ↑Organic ADG (P = 0.04)	↑Inorganic Ab response to BHV1 vaccination in naïve calves (P = 0.03).	No difference (morbidity = 63%)
Sharman et al., 2008	RBD Organic source of Zn @ 360 mg/hd/d as Zn-aa-complex, Cu @ 125 mg/hd/d as Cu-aa-complex, Mn @ 200 mg/hd/d as Mn-aa-complex, Co @ 12.5 mg/hd/d as CoGlu (Availla-4 <sup>TM</sup> , Zinpro); versus Inorganic source of these trace elements at the same rate as ZnSO <sub>4</sub> , CuSO <sub>4</sub> , MnSO <sub>4</sub> , CoCO <sub>3</sub> .	n = 108 BW = 230	27 (Full feeding period of 224)	No differences	Indirect: ↑SOD <sup>b</sup> with organic (P < 0.03; n = 24 in the subsample); no differences in IgA, IgG or IgM in the absence of stimulation.	No difference, but % repulls & mortality tended (P < 0.08) to be higher with aa complex source
Dorton et al., 2007	RBD Controls with no supplemental trace elements; versus organic source of Zn @ 360 mg/hd/d as Zn-aa-complex, Cu @ 125 mg/hd/d as Cu-aa-complex, Mn @ 200 mg/hd/d as Mn-aa-complex, Co @ 12.5 mg/hd/d as CoGlu (Availla-4 <sup>TM</sup> , Zinpro); versus Inorganic source of these trace elements at the same rate as ZnSO <sub>4</sub> , CuSO <sub>4</sub> , MnSO <sub>4</sub> , CoCO <sub>3</sub> . *After 30d on the same treatments during the preconditioning phase (Dorton et al., 2006). During the finishing phase (d 29 to 84) NRC recommended trace elements fed except for Zn with controls with no supplemental Zn; versus Zn @ 30 mg/kg DM as ZnSO <sub>4</sub> ; versus Zn @ 30 mg/kg DM as Zn-aa-complex.	n = 125 BW = 250	28 (receival phase); Measurement @ d 84 during finishing phase *After 30d on the same treatments before feedlot arrival (Dorton et al., 2006)	Not reported	No differences in BHV1 Ab, SOD, INF-γ, pig red blood cell Ab (total Ig, IgG, IgM);  At end of receival phase ↑total IgM with organic trace elements.  During finishing phase ↑ovalbumin Ab with Zn-aa	Not reported

Reference	Trace Element/s and Supplemental Dietary Concentration	Sample Size (n) & entry BW, kg	Study Duration, d	Production (ADG, FCR)	Immune Response	Morbidity
Nunnery et al., 2007	Exp. 1 RBD Controls with no supplemental trace elements Versus 75 mg/kg diet DM as Zn SO <sub>4</sub> , ZnMet, or Zn propionate	n = 24 BW = 223	35 & 168	No differences	No differences humoral immunity	No differences
Nunnery et al., 2007	Exp. 2 RBD Controls with no supplemental trace elements Versus 75 mg/kg diet DM as Zn SO <sub>4</sub> , ZnMet, or Zn propionate	n = 6 BW = 291	21	No differences	No differences ovalbumin IgG response	
Dorton et al., 2006	RBD Controls with no supplemental trace elements; versus organic source of Zn @ 360 mg/hd/d as Zn-aa-complex, Cu @ 125 mg/hd/d as Cu-aa-complex, Mn @ 200 mg/hd/d as Mn-aa-complex, Co @ 12.5 mg/hd/d as CoGlu (Availa-4™, Zinpro); versus Inorganic source of these trace elements at the same rate as ZnSO <sub>4</sub> , CuSO <sub>4</sub> , MnSO <sub>4</sub> , CoCO <sub>3</sub> .	n = 125 BW = 239	30	No differences	NA	No differences
Salyer et al., 2004	Randomised 2x2 factorial Inorganic Cu @ 10 mg/kg DM as CuSO <sub>4</sub> + inorganic Zn @ 75 mg/kg DM as ZnSO <sub>4</sub> ; Inorganic Cu @ 10 mg/kg DM as CuSO <sub>4</sub> + organic Zn @ 75 mg/kg DM as Zn-polysaccharide; Organic Cu @ 10 mg/kg DM as Cu-polysaccharide + inorganic Zn @ 75 mg/kg DM as ZnSO <sub>4</sub> ; Organic Cu @ 10 mg/kg DM as Cu-polysaccharide + organic Zn @ 75 mg/kg DM as Zn-polysaccharide.	Exp 1. Health n = 54; Prod'n n = 6; BW = 208 Exp 2. n = 6 BW = 272	Exp.1 = 35 Exp. 2 = 21	No differences	↑ovalbumin Ab d14, d21 with Zn-polysaccharide v ZnSO <sub>4</sub> & ↑ovalbumin Ab d14, d21 with CuSO <sub>4</sub> v Cu-polysaccharide	No differences
Kessler et al., 2001	RBD Controls with no supplemental Zn (Exp. 1 - Zn = 25 mg/kg DM, Exp. 2 - Zn = 38mg/kg DM); versus supplemental Zn @ 360 mg/hd/d as ZnSO <sub>4</sub> ; versus supplemental Zn @ 360 mg/hd/d as Zn-aa-complex	Exp.1 n = 28 bulls & strs BW = 240 Exp.2 n = 25 hfrs BW = 176	Exp.1 = 28 Exp.2 = 140	Exp.1 ADG no differences over 28d, but ↑ADG d15-28 with Zn-aa Exp.2 No differences	No differences in WBC, BHV1 Ab, BVDV Ab, Exp.1 BRSV Ab. Exp.2 ↑Ab response to 2 <sup>nd</sup> BRSV vaccination with Zn-aa	Exp.1 No differences; Exp.2 No morbidity

EVALUATION OF PRACTICES USED TO REDUCE THE INCIDENCE OF BOVINE RESPIRATORY DISEASE IN AUSTRALIAN FEEDLOTS

Reference	Trace Element/s and Supplemental Dietary Concentration	Sample Size (n) & entry BW, kg	Study Duration, d	Production (ADG, FCR)	Immune Response	Morbidity
Kessler et al., 2003	RBD Control with Zn concentration not stated; versus 45 mg/kg DM as Zn-proteinate; versus 45 mg/kg DM as Zn polysaccharide; versus 45 mg/kg DM as ZnO.	n = 15 BW = 146	284	No differences	NA	NA
Malcolm-Callis et al., 2000 (Exp.3)	RBD Zn: 30 mg/kg DM as ZnSO <sub>4</sub> , Zn-aa, Zn polysaccharide	n = 84, BW = 252	126 with measurement at 28, 56, 84 & 112 d	No differences	NA	NA
George et al., 1997	2 RBD's. 106 mg/kg DM as ZnO, 58 mg/kg DM as MnO, 37 mg/kg DM as CuSO <sub>4</sub> , 7 mg/kg Co as CoCO <sub>3</sub> ; versus same dietary concentrations of trace elements as ZnMet <sup>c</sup> , MnMet, CuLys <sup>d</sup> , CoGlu; versus organic trace element complexes fed at 3X the basal concentrations, reduced to 1X for the remainder of the feeding period.	Exp 1. n = 66 BW = 214; Exp. 2 n = 39 BW = 200	42 with measurement at 14 & 28 d	No differences	↑PHA <sup>c</sup> skin swelling @ 21d with 3X/1X organic (P < 0.05); PI3 secondary Ab titre @ 14 & 28d with 1X organic (P < 0.01); ↑BHV1 Ab titre @ 14 & 28d with 1x organic (P < 0.05)	17.2% ↓ in BRD with organic 3X/1X (P < 0.05)
Galyean et al., 1995	4 x 2 Factorial Design. Basal: 30 mg/kg DM as ZnO, 3.25 mg/kg DM as CuO; versus Basal + 5 mg/kg DM as CuLys; versus Low ZnMet = basal + 35 mg/kg DM as ZnMet; versus Low ZnMet + 5 mg/kg DM as Cu Lys; versus High ZnSO <sub>4</sub> = Basal + 70 mg/kg DM as ZnSO <sub>4</sub> ; versus High ZnSO <sub>4</sub> + 5 mg/kg DM as Cu Lys; versus High ZnMet = Basal + 70 mg/kg DM as ZnMet; versus High ZnMet + 5 mg/kg DM as CuLys.	n = 72 BW = 241 to 249 across treatments(NSD)	161 with 28 d measurement (CuLys discontinued)	161 d: Zn no effect; CuLys ↓ ADG (P < 0.02)	NA	Trend for ↓ by high Zn as either ZnSO <sub>4</sub> or ZnMet cf. Basal and Low ZnMet diets (P < 0.07).
Ward et al., 1993	RBD with a 3 x 2 Factorial Design: Cu ± Mo and S. Control diet with 6.2 mg/kg DM Cu: versus control + 5 mg/kg DM as CuSO <sub>4</sub> ± 5 mg/kg DM Mo and 2 g/kg DM S; versus control + 5 mg/kg DM as CuLys ± 5 mg/kg DM Mo and 2 g/kg DM S.	n = 21 BW = 218	98 with measurement at 21 d intervals	No differences over 98 d; ↑ADG CuSO <sub>4</sub> first 21d (P < 0.01)	No differences	Not reported.

Reference	Trace Element/s and Supplemental Dietary Concentration	Sample Size (n) & entry BW, kg	Study Duration, d	Production (ADG, FCR)	Immune Response	Morbidity
Chirase et al., 1991 (Exp. 3)	RBD Control diet with Zn = 96 mg/kg DM; versus control + ZnO for a total dietary Zn concentration of 163 mg/kg DM Zn; versus control + ZnMet for total dietary Zn concentration of 171 mg/kg DM.	n = 11 BW = 260	28 after BHV1 challenge with measurement of DMI, BW and rectal T <sub>b</sub> daily	No differences between Zn sources, ZnMet DMI higher (P < 0.01) than control d1 after BHV1	No difference in rectal temperature between sources or cf control	NA.
Spears et al., 1991	RBD Control diet with Zn = 26.4 mg/kg DM; versus control + 25 mg/kg DM as ZnMet; versus control + 25 mg/kg DM as ZnO.	n = 30 BW = 214	28	No differences between Zn sources and controls over 28 d	No differences between Zn sources and control in PI3 Ab d14; ZnMet BHV1 titre d14 higher (P < 0.07) cf control but not significantly different to ZnO	Morbidity low and no differences
Wittenberg et al., 1990	RBD with blocking for BW & liver Cu concentration + Cu binding Mo added at 10 mg/kg DM Control diet Exp.A with Cu = 4.1 mg/kg DM Control diet Exp.B with Cu = 7.2 mg/kg DM versus control + 10 mg/kg as CuSO <sub>4</sub> ; versus control + 10 mg/kg as CuProteiniate.	n = 12 Exp.A BW = 331.8 Exp.B BW = 236.1	Exp.A = 105 Exp.B = 84	No differences between Cu sources with CuPro ↑ADG cf Cu depleted control (P < 0.05)	NA	NA
Greene et al., 1988	RBD Control diet with Zn = 81 mg/kg DM; versus control + 360 mg/d as ZnMet; versus control + 360 mg/d as ZnO.	n = 15 BW = 330	112	No differences	NA	NA

<sup>a</sup>CoGlu = cobalt glucoheptonate; <sup>b</sup>SOD = superoxide dismutase, an enzyme important to the prevention of cell membrane damage as part of the inflammatory response; <sup>c</sup>Znmet = zinc methionine; <sup>d</sup>CuLys = copper lysine; <sup>e</sup>PHA = phytohaemagglutinin, an antigen injected intradermally to assess in vivo cell mediated immune function.

- Injection of Trace Elements at Feedlot Entry Supplemental to Dietary Trace Elements Equal to or Greater Than NRC Recommendation – North American data.

Trace element injections have been shown to rapidly increase animal plasma trace element concentrations for less than 24 h (Bohman et al., 1984). It has been proposed that elevated plasma concentrations of trace elements during the early receiving period could reduce the incidence of BRD even with cattle fed diets providing NRC recommended trace element concentrations because of low feed intake in cattle newly arrived at the feedlot (Richeson and Kegley, 2011). The effects of trace mineral injections on BRD incidence have been variable with most showing no effect. Richeson and Kegley (2011) found a trace mineral injection at a dose rate of 1 ml / 45.5 kg, containing 20 mg/ml zinc, 20 mg/ml manganese, 10 mg/ml copper and 5 mg/ml selenium reduced ( $P = 0.02$ ) the incidence of BRD compared with controls fed at least NRC recommended dietary concentrations of these elements. However, the same experiment found no significant effect on BRD incidence with a similar trace element injection at the same dose rate, containing 48 mg/ml zinc, 10 mg/ml manganese, 16 mg/ml copper, and 5 mg/ml selenium. Previously, Clark et al. (2006) found no effect ( $P = 0.86$ ) on BRD incidence from treating cattle newly arrived at the feedlot with a trace mineral injection at a dose rate of 1 ml / 53 kg, containing 40 mg/ml zinc, 10 mg/ml manganese, 15 mg/ml copper, and 5 mg/ml selenium. Whilst studies using injectable products can use the individual animal as the unit of interest with statistical blocking to account for pen effects, the above studies have low statistical power due to the use of pen as the unit of interest ( $n = 5$  to 9). Large commercial studies using the individual animal as the unit of interest could clarify the effects of injectable trace elements on BRD incidence. However, considering the short duration of increased plasma trace element concentrations achieved with injectable trace elements, and a peak BRD incidence curve extending over a period of approximately 3 to 6 weeks, strategies to achieve higher, stable feed intakes during the adaptation period might be expected to negate any potential positive effects from injectable trace element products.

- Supplemental yeast or yeast products – North American data.

Ponce et al. (2012) found that the addition to the receiving diet of 1.8 g•animal<sup>-1</sup>•d<sup>-1</sup> of enzymatically hydrolysed yeast extract (Celmanax™) tended ( $P = 0.09$ ) to reduce BRD morbidity. Whilst Finck et al. (2014) found an indirect immunological response to lipopolysaccharide challenge in cattle supplemented with 5 g•animal<sup>-1</sup>•d<sup>-1</sup> of live yeast (*Saccharomyces cerevisiae subsp. boulardii*) or 5 g•animal<sup>-1</sup>•d<sup>-1</sup> of cell wall from the same yeast species, this did not translate into a reduction ( $P = 0.36$ ) in BRD morbidity. This is consistent with the earlier finding by Keyser et al. (2007), that supplemental yeast (*Saccharomyces cerevisiae subsp. boulardii*; Proternative Stress Formula™) fed at a rate of 0.5 g•animal<sup>-1</sup>•d<sup>-1</sup>, in addition to 1 g/animal of the same product as an oral paste at induction, did not reduce BRD morbidity.

Live yeast products have been found to increase productivity in dairy cows through enhanced fibre digestion in the rumen (Finck et al., 2014). It therefore follows that positive effects in beef feedlot cattle are more likely in higher fibre diets, and within these, in starter diets with still higher fibre fractions. Further research is therefore warranted with live yeast products with higher fibre feedlot diets during the early feeding period, using larger sample sizes. The effect of mannan oligosaccharides (MOS) from yeast cell walls in binding pathogens such as *E. coli* and *Salmonella* spp., and the effect of this on the gross outcome of morbidity, and specifically BRD morbidity, requires further research.

- In feed Antibiotics – US data.

Van Donkersgoed (1992) was unable to assess the effects of in-feed antibiotics on the incidence of BRD due to a lack of randomised studies with appropriate controls.

Subsequently, Gallo and Berg (1995) found feeding 700 mg/hd/d CTC and sulfamethazine for the first 56 days on feed significantly reduced BRD morbidity ( $P = 0.001$ ) but did not reduce BRD mortality ( $P = 0.58$ ). Kreikemeier et al. (1996) reported in a non peer reviewed research report that showed feeding chlortetracycline for 5 days from d 1 at the rate of 22 mg/kg BW reduced ( $P = 0.01$ ) total morbidity (BRD

morbidity not quoted). Conversely, Duff et al. (2000) found more recently that feeding chlortetracycline for 5 days from d 1 at the rate of 22 mg/kg BW had no significant effect on BRD morbidity, and Stanford (2015) found in a small pen study with 240 animals run over 2 years, that chlortetracycline fed at 350 mg head<sup>-1</sup> d<sup>-1</sup> with 350 mg head<sup>-1</sup> d<sup>-1</sup> sulfamethazine, or chlortetracycline fed at 11 mg/kg BW, or chlortetracycline fed at 350 mg head<sup>-1</sup> d<sup>-1</sup>, had no effect on BRD incidence.

Studies to determine the efficacy of in-feed antibiotics in the prevention of BRD in Australian feedlots are warranted. However, the current Provisional Russian Export Slaughter Interval for oxytetracycline and chlortetracycline of 90 days practically precludes the use of these antibiotics delivered either mixed with feed or parenterally, where any part of the carcass is marketed to Russia.

#### Practices with minimal evidence or untested

- Vaccination against infectious bovine rhinotracheitis (IBR) at feedlot entry with a modified live BHV 1 vaccine – Australian data used to register the vaccine Rhinogard™ (Zoetis).

Seven trials with a live attenuated Australian strain of BHV 1 administered intranasally resulted in a significant improvement in growth rate and feed conversion ratio ( $P < 0.05$ ) without a significant reduction in the percentage of cattle treated for all feedlot diseases ( $P > 0.05$ ) during the first 30 d on feed (Young, unpublished registration data submitted to the APVMA). It is possible vaccination might have had a significant effect on the incidence of BRD, or more specifically, IBR, had these diagnoses been recorded. Field observations by feedlot veterinarians support the effectiveness of vaccination at feedlot entry with Rhinogard™ in the prevention of IBR. The onset of activity of this modified live vaccine is rapid, with local production of immunoglobulin A in the upper airways conferring protection against the development of IBR. Infectious bovine rhinotracheitis is caused by a single organism, BHV 1, and there is a vaccine that is effective against this organism. It is therefore a preventable disease and should be viewed separately to the pneumonia of BRD.

- Mixing cattle during the feeding period – Limited indirect North American data.

Gupta et al. (2005) found steers mixed and relocated at 2 wk intervals had increased plasma cortisol, albumin, urea and non-esterified fatty acids. There was also a trend ( $P = 0.10$ ) for lower growth rate in the mixed and relocated steers. However, this study only had 6 steers in each pen. This small number of animals in each pen would presumably reduce the effects of social stress compared with commercial feedlot pens, considering the observation of Taylor et al. (1997), that social hierarchy becomes unstable with more than approximately 100 animals in a pen.

- Large BW range within a pen (ie > 100 kg) – Untested.
- Liquid supplements in receival pens (ie urea/molasses) – Untested.
- Staffing levels i.e. pen riders per 10,000 head – Untested.
- Low stress cattle handling – Untested.
- Electrolytes in the water on arrival – Untested.
- Reducing time between feedlot arrival and induction – Untested.

#### Practices that we know do not reduce the risk of bovine respiratory disease

- Vitamins A, D & E at feedlot entry – Australian data.

Cusack et al. (2008) examined the effects of injectable vitamins A, D and E at feedlot entry on health and growth rate. Two thousand, four hundred and sixty five cattle were allocated systematically at feedlot entry to: a commercial vitamin A, D and E preparation at the label dose rate; commercial vitamin A, D and E at twice the label dose rate; a formulation with no vitamin D, a lower concentration of vitamin A and a higher concentration of vitamin E; and the oil based carrier alone at volumes corresponding to the above treatments. Comparisons of growth rate, disease and mortality were made between the groups at the conclusion of the feeding period. There were no differences between cattle administered vitamin A, D and E at feedlot entry and the controls in growth rate ( $P = 0.11$ ), all diseases ( $P = 0.99$ ), BRD ( $P = 0.60$ ) or mortalities ( $P = 0.95$ ). Cattle treated with the higher

vitamin E and lower vitamin A preparation had a higher ( $P = 0.02$ ) incidence of anorexia than the other groups. The routine injection of cattle with vitamins A, D and E at feedlot entry is unlikely to result in improvements in health and growth rate where cattle are provided with these vitamins in their diets at concentrations equal to the recommendations by the National Research Council (1996). In addition, a meta-analytic review by Cusack et al. (2008), found that the available data do not support the use of supplemental vitamin E administered as an injection (morbidity risk ratio = 1.17,  $P = 0.165$ ), and these results are further supported by Barnes et al. (2014) where injection of cattle with vitamin A, D and E at induction had no effect on the risk of BRD (OR = 1.1, 95% CI = 0.6 to 1.9,  $P = 0.36$ ).

- Liquid Supplements in Starter Pens - Australian data.

Croft et al. (2014) found that the feeding of a mean of 2.1L urea-molasses supplement (5% urea, CP = 32.6%, ME = 8.96 MJ/kg DM, product DM = 70%; Bundaberg Molasses, Oakey, Qld) to cattle in starter pens had no effect on ADG ( $P = 0.65$ ), BRD morbidity ( $P = 0.27$ ) or BRD mortality ( $P = 0.75$ ).

- Artificial Dietary Sweeteners – US data.

It is widely accepted that rapidly achieving high, stable feed intake in newly arrived cattle, in the absence of lactic acidosis, is important to immunocompetence. The effect of the artificial dietary sweetener, Sucram, on dry matter intake and BRD morbidity, plus production outcomes, was investigated on this premise. Feeding the saccharin-based dietary sweetener, Sucram, at rates of 100, 200 or 300 g/tonne DM had no effect on the incidence of BRD (Ponce, et al., 2014; McMeniman et al., 2006).

## Recommendations

In summary, we have substantial evidence to recommend the following BRD prevention practices as of May 2016. These measures are listed in approximate order of the likely extent of their effects on reducing the incidence of BRD.

- Avoid placement of cattle in the feedlot if purchased through saleyards within the previous 12 days and if backgrounding paddocks are available do not place the cattle in the feedlot for at least 28 days to confer a protective effect against BRD.
- With cattle placed directly in the feedlot, reduce the number of purchase groups per pen.
- Fill pens as quickly as practical, ideally within 1 day.
- Minimise the distance cattle are transported to the feedlot and the time taken for delivery.
- Yard weaning.
- Mass medication of high risk cattle where the other preventative measures have not been possible.
- When constructing new pens or replacing water troughs, provide separate water troughs for each pen.
- Avoid high concentrations of non-protein nitrogen in starter diets.
- Prevent lactic acidosis through the management of diet formulation, feed milling and feed delivery.
- Provide dietary vitamin E at the upper range of the National Research Council recommendation of 60 IU/kg diet DM, but no greater.
- Provide dietary zinc at a basal concentration of 30 mg/kg diet DM for the duration of the feeding period and provide additional zinc in an organic form at 45 mg/kg diet DM for the first 28 days, to achieve a total dietary zinc concentration during the adaptation phase of 75 mg/kg DM.
- Vaccination with modified live BHV 1 vaccine at feedlot entry.
- Two injections of Bovilis MH at 4 wk intervals before feedlot delivery.
- Two injections of Pestigard at 4 wk intervals before feedlot delivery.

These recommendations will be added to and refined over time as more research findings are published. A study is currently being done in Australia to assess the effects on BRD incidence of local backgrounding (4 to 12 weeks) with or without vaccination against *M. haemolytica* and/or BVDV.

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