Critical appraisal – Randomised controlled trial questions – Thiry et al 2014

Introduction	
Are the aims clearly stated?	Yes The objective of the present study was to confirm the efficacy and the safety of the florfenicol-flunixin formulation for the treatment of naturally occurring BRD in juvenile calves less than six weeks of age in comparison to florfenicol.
Methods	
Is the study design suitable for the aims?	Yes
Which population was studied?	210 pre-ruminating calves (bodyweight 31-78.6kg, age 12-41 days) of a number of beef breeds split into 2 groups: Antibiotics and flunixin (N=106), Antibiotics alone (N=104) Farms in France, Spain and Belgium
Were the treatments randomly allocated? If yes, how was the randomisation done?	Yes Computer-generated randomisation code
Were the groups comparable prior to intervention?	Yes in terms of body temperature >/=40.3^{o}C and had a depression and respiratory score of >/= 2.
Was the person who administered the interventions blinded?	Not clear
Is it clear what measurements were carried out in the study?	Rectal temperature Depression score Respiratory Score Done at 6hours, then daily until day 4, from day 4-10 clinical scoring done and RT taken if depression

	score >/= 1 or respiratory score >/=2
Were the correct measurements chosen? Do they reflect (or are they strongly related to) the outcome of interest?	Yes Yes
Were previously established validated methods used to make the measurements? (e.g. Glasgow pain score, International Units etc)	Yes for body temperature. Subjective clinical scores
What outcomes were measured?	Rectal temperature at 6 hours Treatment success (depression score =0, respiratory score </=1, RT < 40^{o}C) or failure (depression score>1, respiratory score >2, RT > 40^{o}C) at day 4 and cumulatively at day 10.
Are the outcomes clinically relevant?	Yes
Were the outcomes assessed blind?	Yes
Are the statistical methods described?	Yes
Was the statistical significance level stated?	Yes
Was the sample size justified?	yes
Was ethical approval obtained?	Yes This study was conducted in accordance with the Veterinary International Conference on Harmonisation (VICH) guideline on good clinical

	practices (EMEA/CVMP 2000).
Are the methods described in enough detail that you could repeat them?	Yes
Results	
Were the basic data adequately described?	Not in enough detail to be able to repeat the basic analysis
Do the numbers add up? Are all subjects accounted for?	Yes
Was the statistical significance (p value) stated in the results? Is this consistent with the methods? (It should be stated in the sample size or power calculation)	Yes Yes
Were any side effects of the intervention reported if applicable?	Injection site reactions Pain on injection
What were the main findings/key results?	The means of change in rectal temperature from time 0 hour to time six hours was−1.36°C in the florfenicol-flunixin group and −0.6°C in the florfenicol group. The means of relative change (%) in rectal temperature (±SD) between groups significantly different (P<0.0001). By 6 hours, a decrease in the severity of depression was observed in both treatment groups with a significantly greater improvement observed in the florfenicol-flunixin group than in the florfenicol group (P<0.0001). By day 4, florfenicol-flunixin group had 99 successes (93.4%) and the florfenicol group had 93 successes (90.3%). Hence the florfenicol-flunixin formulation was significantly non-inferior to florfenicol for the initial treatment success on day

	four. By day 10 florfenicol-flunixin group had 71 successes (67%) and the florfenicol group had 62 successes (60.2%). Hence the florfenicol-flunixin formulation was significantly non-inferior to florfenicol for the cumulative treatment success on day 10. The incidence of injection site reactions for florfenicol-flunixin group was 16.8% and 15.5% for the florfenicol group.
Discussion and conclusion	
What do the main findings/key results mean?	Flunixin helps reduce rectal temperature and may contribute to improving clinical status
Are the negative findings discussed? How are the negative findings interpreted?	Yes .
Does the discussion reflect the results?	Yes
Interpretation	
What are the clinical implications of this study? Are the subjects in the study similar to those in the BET/your own?	Flunixin reduce the body temperature of clinical score of calves with respiratory disease. Yes
General	
Who funded this study?	Not stated but 3 authors were employees of a company that produces the drugs tested.