

## ADVERSE REACTIONS FOLLOWING THE USE OF ECONOR<sup>®</sup> IN PIGS: 5) THE EFFECT OF ENDOTOXIN IN ECONOR<sup>®</sup>-MEDICATED SUSECPTIBLE PIGS

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### Introduction

Adverse reactions (ADRs) to the use of valnemulin (Econor<sup>®</sup>) were reproduced in herds in Denmark in which pigs were subject to heavy infection pressure. Infections with Gram-negative bacteria, such as *Actinobacillus pleuropneumoniae* were particularly prevalent. In these herds, higher numbers of *E. coli* and *Bacteroides* spp. were found in the faeces of pigs with ADRs compared with unaffected medicated pigs (Table 1). The response of pigs from an ADR-susceptible herd to an artificial endotoxin challenge (see for example Norimatsu et al, 1995) was thus compared with that in local pigs, in a study carried out in France.

### Materials and Methods

Faeces samples were taken at slaughter from 2 herds in which ADRs had been reproduced. Eight pigs exhibiting typical signs of ADR (pyrexia, depression, ataxia with or without oedema), as well as 6 unaffected medicated and 8 unmedicated pigs were samples. Faeces were stored frozen at -20°C and viable counts performed for total aerobes, total anaerobes, *E. coli*, *Bacteroides fragilis* group, *Clostridium perfringens*, and lactic acid bacteria. In the endotoxin challenge study, groups of 6 French and 12 pigs from the ADR-susceptible herd in Denmark were medicated with Econor in feed at a dose of 4mg/kg bodyweight or left unmedicated. After 3.5 days all pigs were challenged by an IV injection of *E.coli* O55:B5 lipopolysaccharide (Signa, St. Louis, Missouri) at a dose of 4ug/kg. Four French and 4 Danish pigs remained unmedicated and unchallenged as controls. Pigs were examined, rectal temperatures taken, and clinical scores computed before the challenge, 1, 2, 4, 6, 8 & 10 hours after the challenge, and daily thereafter. Blood samples were taken before and 1, 4, 8, 24 & 48 hours after challenge, and examined for haematology and biochemical parameters as well as for the cytokines TNF $\alpha$ , IL1 and IL6. Pigs were killed 1 week after the challenge.

### Results

The results of microbiological examinations of faeces from the Danish farms are shown in Table 1. Samples from ADR cases had significantly higher mean *E. coli* (p<0.05) and *B. fragilis* (p<0.01) counts than samples from medicated animals with no ADR.

In the challenge study, the Danish pigs were on arrival somewhat heterogeneous in weight, in poorer condition, and less active than their French counterparts, although by the end of the study their performance was

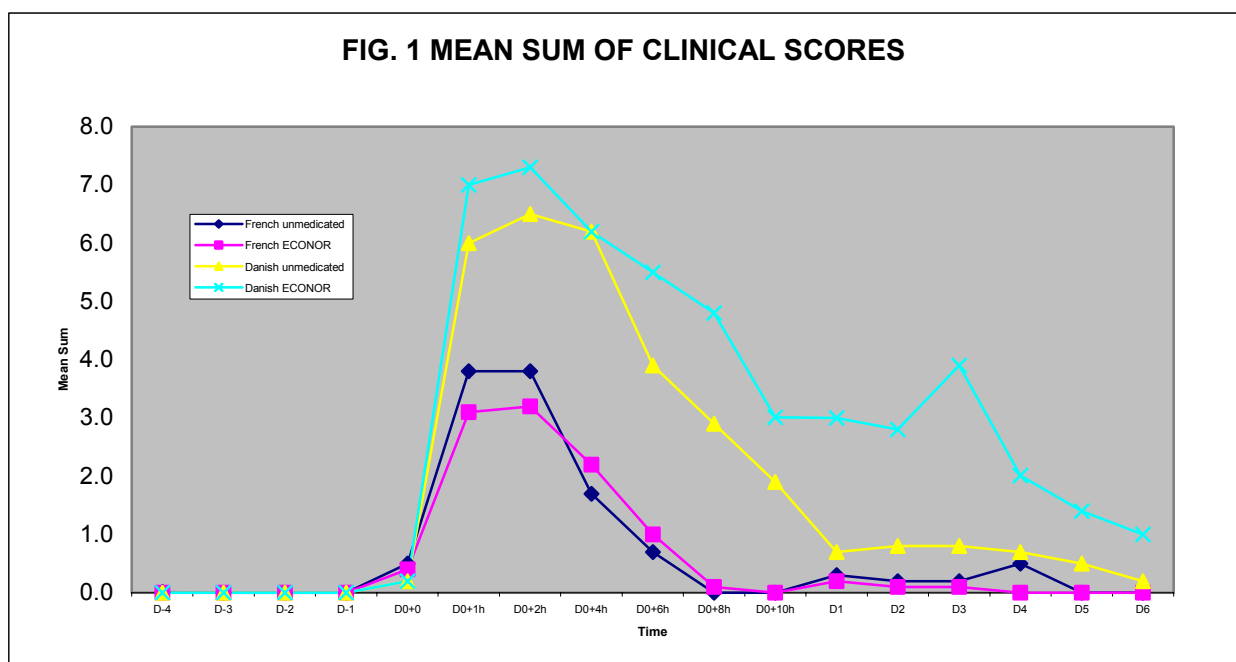
similar. Analysis of feed showed that the average intake of valnemulin was between 3.7 and 4.3 mg/kg.

After the challenge, pigs from the French source reacted as expected with increases in rectal temperature, depression, and increased respiratory rate and, in some cases, ataxia and looseness of faeces. Econor-medicated or unmedicated pigs reacted similarly. Their condition returned to normal after 8 to 10 hours.

By contrast the Danish pigs reacted more strongly and for longer than the French pigs. Unmedicated pigs had returned to normal only after 24 hours. Econor-medicated pigs reacted even more strongly and had not returned to normal 48 hours after the challenge. There was tendency for clinical score to rise again on Day 3, resembling the ADRs seen in the field in Denmark. Figure 1 illustrates these results.

Table 1 Summarised mean viable counts in faeces from Danish ADR trials

	Mean (log cfu/g) and (coefficient of variation) for each group			
	Total aerobes	Total anaerobes	E.coli	B.fragilis
ECO+ ADR+	7.97 (13%)	8.93 (5%)	6.18 (44%)	6.53 (19%)
ECO+ ADR-	7.25 (16%)	8.90 (4%)	3.14 (62%)	4.73 (19%)
ECO- ADR-	7.66 (11%)	8.79 (9%)	5.81 (37%)	5.67 (19%)



### **Discussion and Conclusions**

Although bacterial counts were significantly higher in pigs with ADR than in apparently non-susceptible pigs, they were similar to those in unmedicated pigs. This suggests that susceptibility to ADR in Econor-medicated pigs is associated with high *E. coli* and *B. fragilis* counts, but Econor administration *per se* did not significantly affect viable counts. The exaggerated reaction of pigs from the “susceptible” herd to endotoxin challenge suggests that exposure to Gram-negative bacterial toxin may be a mechanism for the observed effect.

### **Reference**

Schmidt H & Banting A, 2000. Proc 16<sup>th</sup> IPVS Congress, Melbourne, Australia: 99