

# PHARMACOKINETICS AND PHARMACODYNAMICS (PK/PD) OF FLORFENICOL ADMINISTERED ORALLY AGAINST COMMON SWINE PATHOGENS

David Burch<sup>1</sup>, Ulrich Klein<sup>2</sup>

<sup>1</sup>Octagon Services Ltd, Old Windsor, Berkshire, UK; <sup>2</sup>Novartis Animal Health Inc., Basel, Switzerland

## Introduction:

Florfenicol has become one of the commonly-used, effective treatments of a variety of porcine pathogens such as *Actinobacillus pleuropneumoniae*, *Pasteurella multocida*, *Haemophilus parasuis* and *Streptococcus suis*. It is available in a variety of formulations such as an injectable, feed premix and soluble product for inclusion in drinking water.

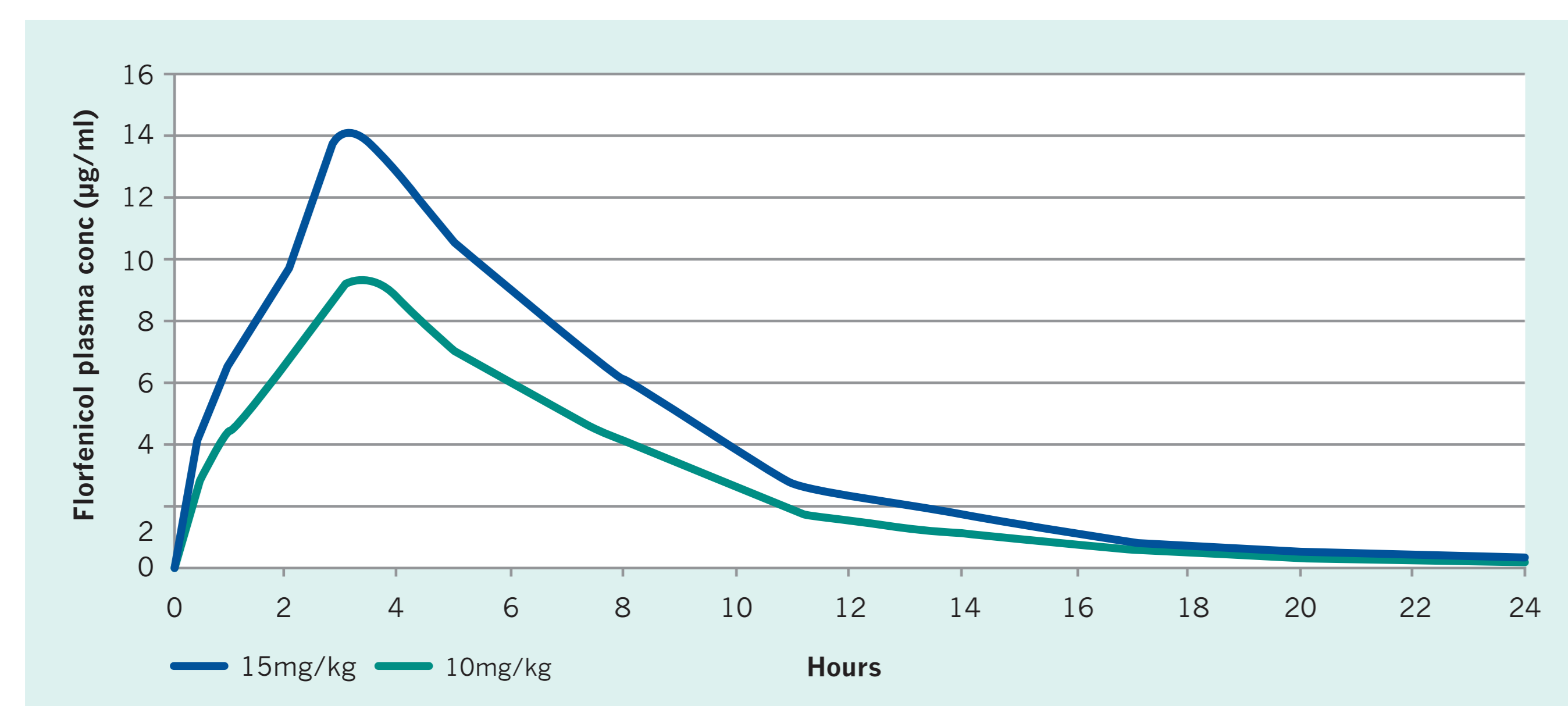
## Objective:

The objective of this review was to compare the pharmacokinetics (PK) of florfenicol (Florvio™ – Novartis Animal Health Inc.) in plasma following administration orally by gavage and via the drinking water with its pharmacodynamics (PD) related to common swine pathogens.

## Materials and methods:

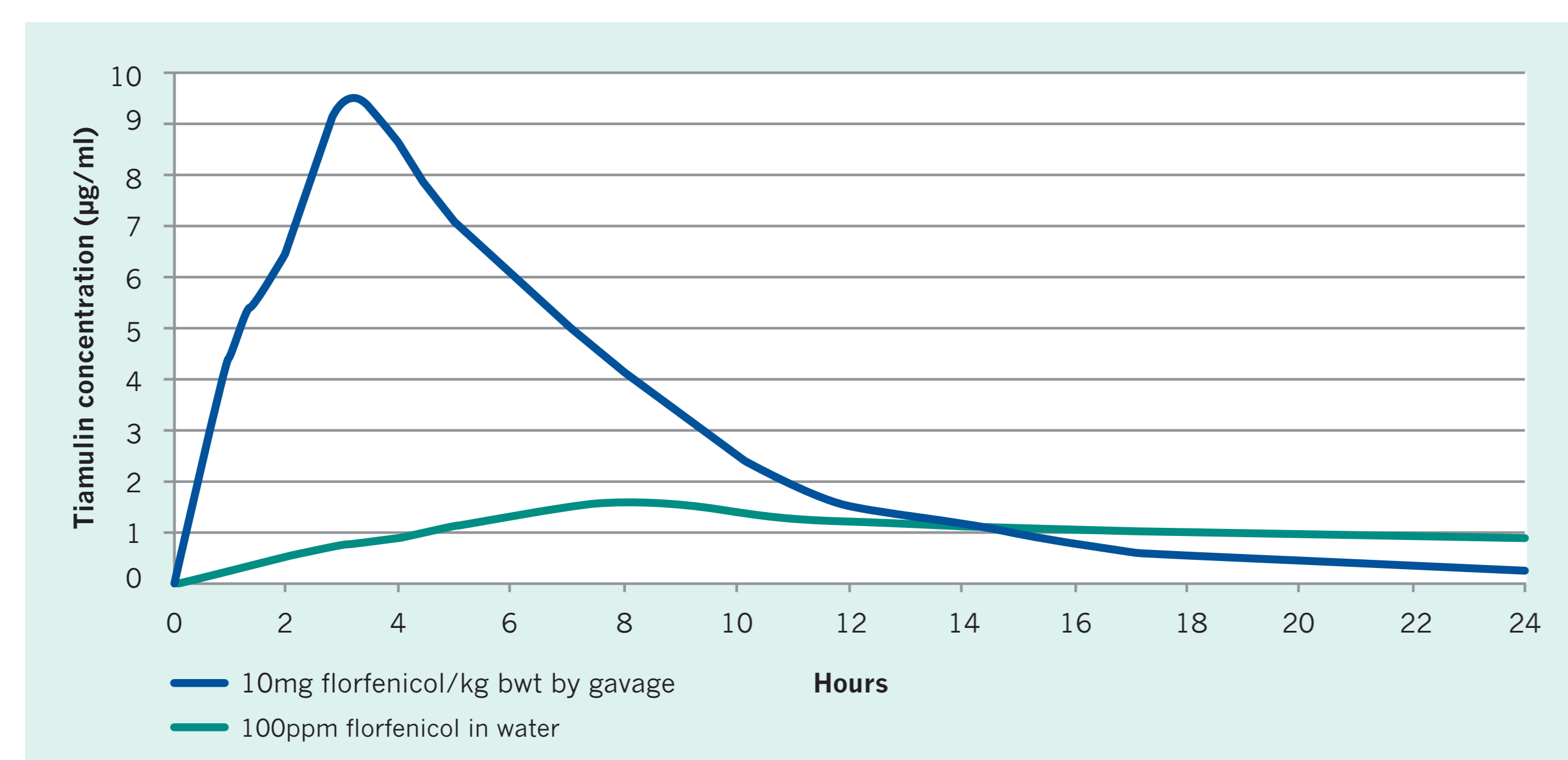
### Pharmacokinetics:

The PK of florfenicol administered by capsule (Voorspoels *et al.*, 1999) at 15mg/kg bwt showed the product was very well absorbed (see Figure 1) giving a reported concentration maximum ( $C_{max}$ ) of 14.8µg/ml and area under the curve (AUC 24h) of 100.5µg.h/ml. A predicted absorption curve based on 10mg florfenicol/kg bwt was also included, as this was the recommended dose rate when given in feed with an estimated AUC 24h of 67.3µg.h/ml.



**Figure 1. PK of florfenicol after a single administration at 15mg/kg bwt and predictive curve at 10mg/kg bwt (after Voorspoels *et al.*, 1999)**

When florfenicol was administered in drinking water (Gutierrez *et al.*, 2011) for 3 days at 100 and 150ppm (normally the approximate equivalent dose to 10 & 15mg/kg bwt) a much lower plasma concentration than expected was achieved (see Figure 2). The reported AUC 24h for day 1, 2 & 3 at 100ppm florfenicol was 28.3, 25.7 and 21.6µg.h/ml and 29.8, 27.6 and 22.9µg.h/ml at 150ppm florfenicol.



**Figure 2. Comparison of florfenicol plasma concentrations following oral gavage at 10mg/kg bwt and 100ppm administered in the drinking water (after Voorspoels *et al.*, 1999; Gutierrez *et al.*, 2011).**

This was surprising, as there was comparatively little difference between the 100ppm and 150ppm florfenicol treated pigs AUC24hs (6.2%). The AUCs were far lower than the single oral dose with a mean at 100ppm of 25.2µg.h/ml (37.4% of a 10mg/kg bwt dose by oral gavage) and a mean at 150ppm of 26.8µg.h/ml (26.6% of the 15mg/kg bwt oral dose). It was associated with a marked drop in water intake. The mean concentration steady state ( $C_{ss}$ ) for 100ppm in drinking water over 3 days was estimated at 1.05µg/ml and at 150ppm 1.12µg/ml.

### Pharmacodynamics:

The PD for florfenicol (Zolynas *et al.*, 2003) against a range of swine pathogens is summarised in Table 1.

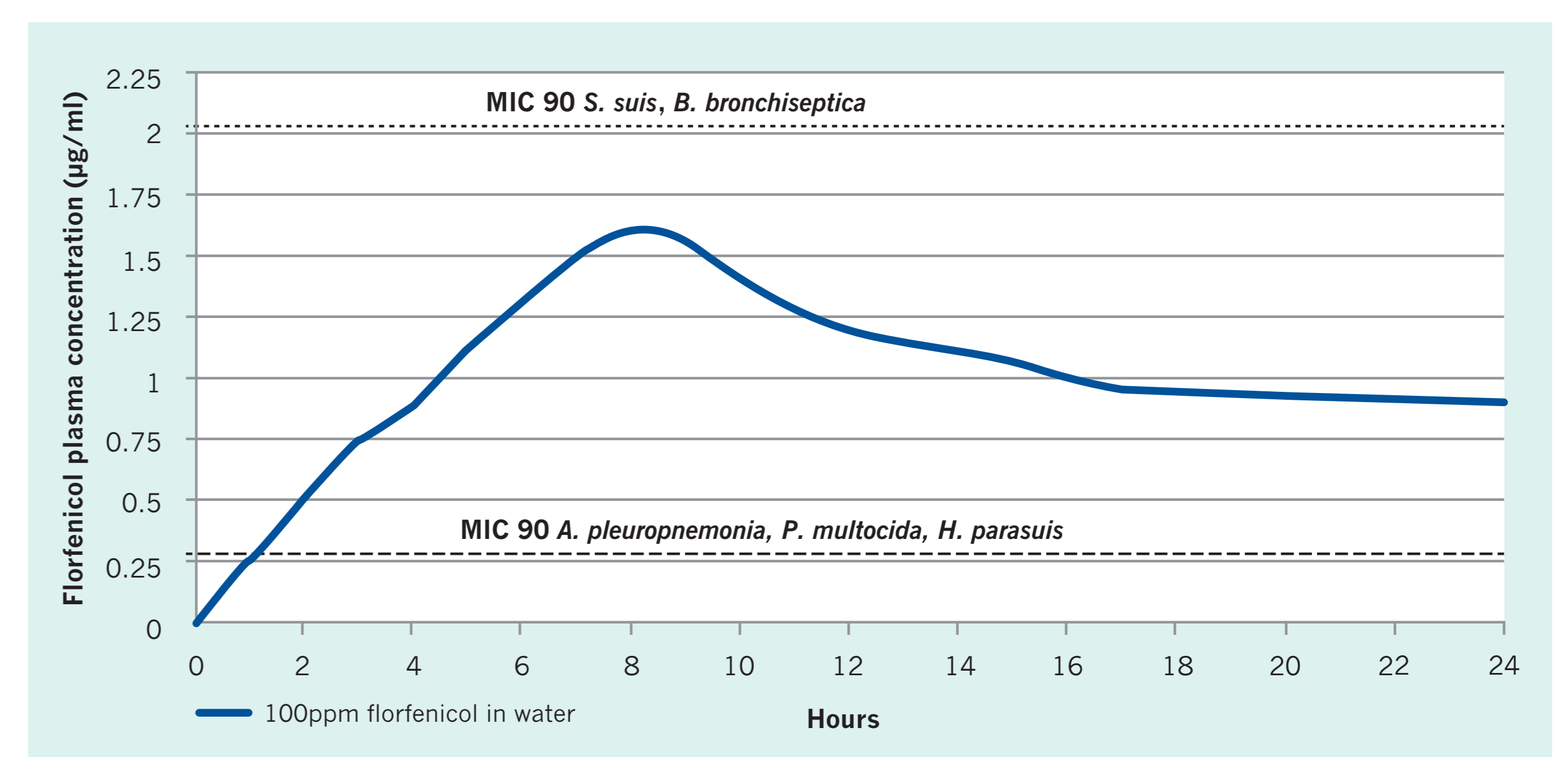
Organism	No of isolates	MIC <sub>50</sub> (µg/ml)	MIC <sub>90</sub> (µg/ml)	MIC range
<i>A. pleuropneumoniae</i>	100	0.25	0.5	0.25-1.0
<i>P. multocida</i>	107	0.5	0.5	0.25-0.5
<i>Haemophilus parasuis</i>	36	0.25	0.5	0.12-1.0
<i>Streptococcus suis</i>	62	2.0	2.0	1.0-2.0
<i>Bordetella bronchiseptica</i>	49	2.0	2.0	0.5-2.0
<i>Salmonella spp</i>	36	4.0	4.0	2.0-4.0
<i>Mycoplasma hyopneumoniae</i>	14	2	8	0.5-8.0
<i>Mycoplasma hyorhinis</i>	24	2	4	0.5-8.0

**Table 1. Florfenicol activity against a range of swine pathogens (Zolynas *et al.*, 2003)**

Florfenicol showed a high level of activity against *A. pleuropneumoniae* and *H. parasuis* with MIC<sub>50</sub>s and MIC<sub>90</sub>s of 0.25 and 0.5µg/ml, respectively; for *P. multocida*, the MIC<sub>50</sub> and MIC<sub>90</sub> was both 0.5µg/ml, and for *S. suis* and *B. bronchiseptica* both were 2.0µg/ml, respectively.

### Pharmacokinetic / Pharmacodynamic relationship

The PK/PD relationship of florfenicol in plasma following administration in the drinking water at 100ppm was compared with the MIC<sub>90</sub> of *A. pleuropneumoniae*, *H. parasuis*, *P. multocida* and *S. suis* (see Figure 3).



**Figure 3. PK/PD relationship of florfenicol administered at 100ppm in water with the MIC<sub>90</sub> of various pig pathogens**

## Results and conclusions:

Florfenicol administered at 100ppm in the drinking water reached concentrations well in excess of the MIC<sub>90</sub> for *A. pleuropneumoniae*, *H. parasuis* and *P. multocida* but not the MIC<sub>50</sub> or MIC<sub>90</sub> for *S. suis* or *B. bronchiseptica*.

## References:

- Voorspoels *et al.*, 1999. Vet. Record, 145, 397-399.
- Gutierrez *et al.*, 2011. J. Anim. Sci. 89, 2926-2931.
- Zolynas, *et al.*, 2003. Proc. AASV Meeting, Orlando, Florida, USA, pp 211-214.

# FLORVIO