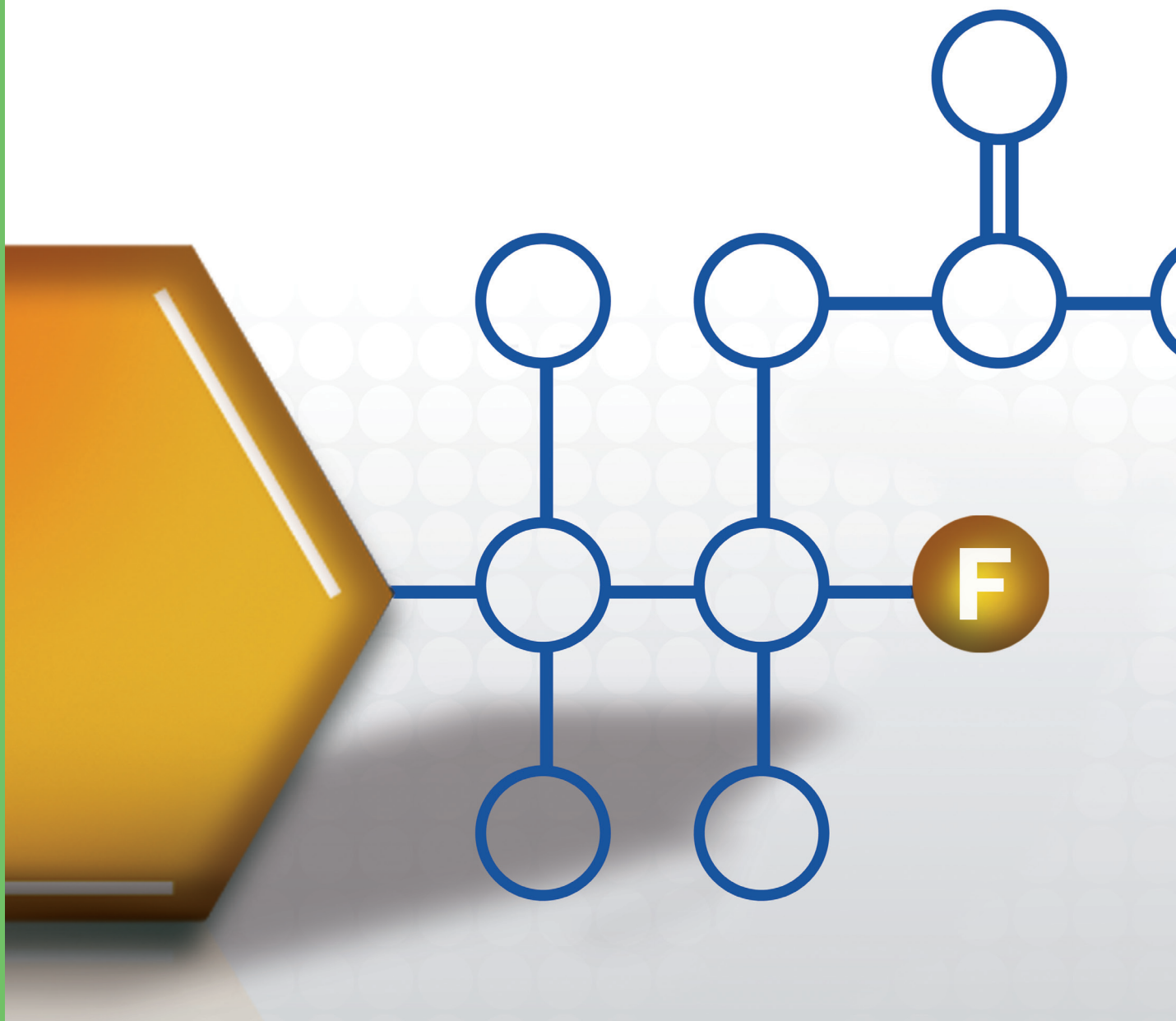


# SELECT NEWS

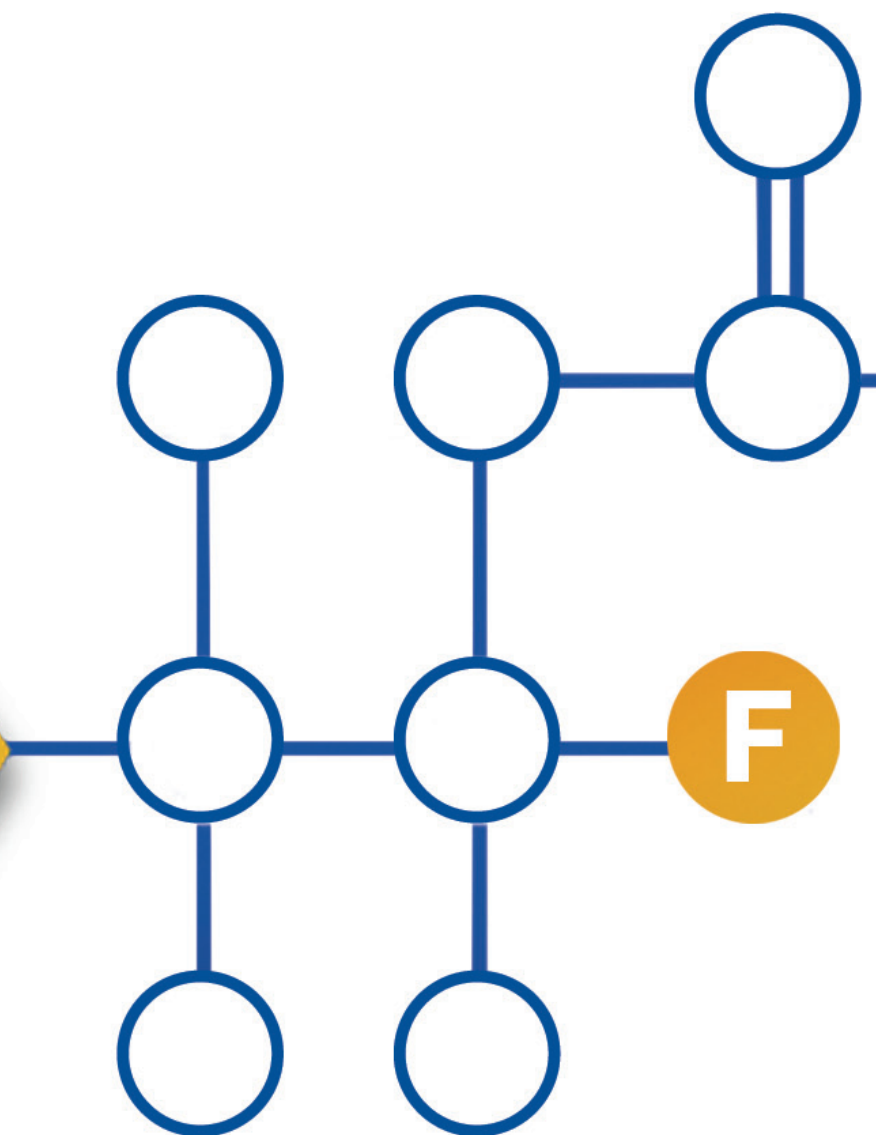
**Florfenicol** Monograph:  
Injectable & Oral Therapy for **Swine**



## Did you know that...?

**Florfenicol** is one of the **most powerful antibiotics** currently available in **veterinary medicine** with one of the **lowest levels of resistance in Europe**.







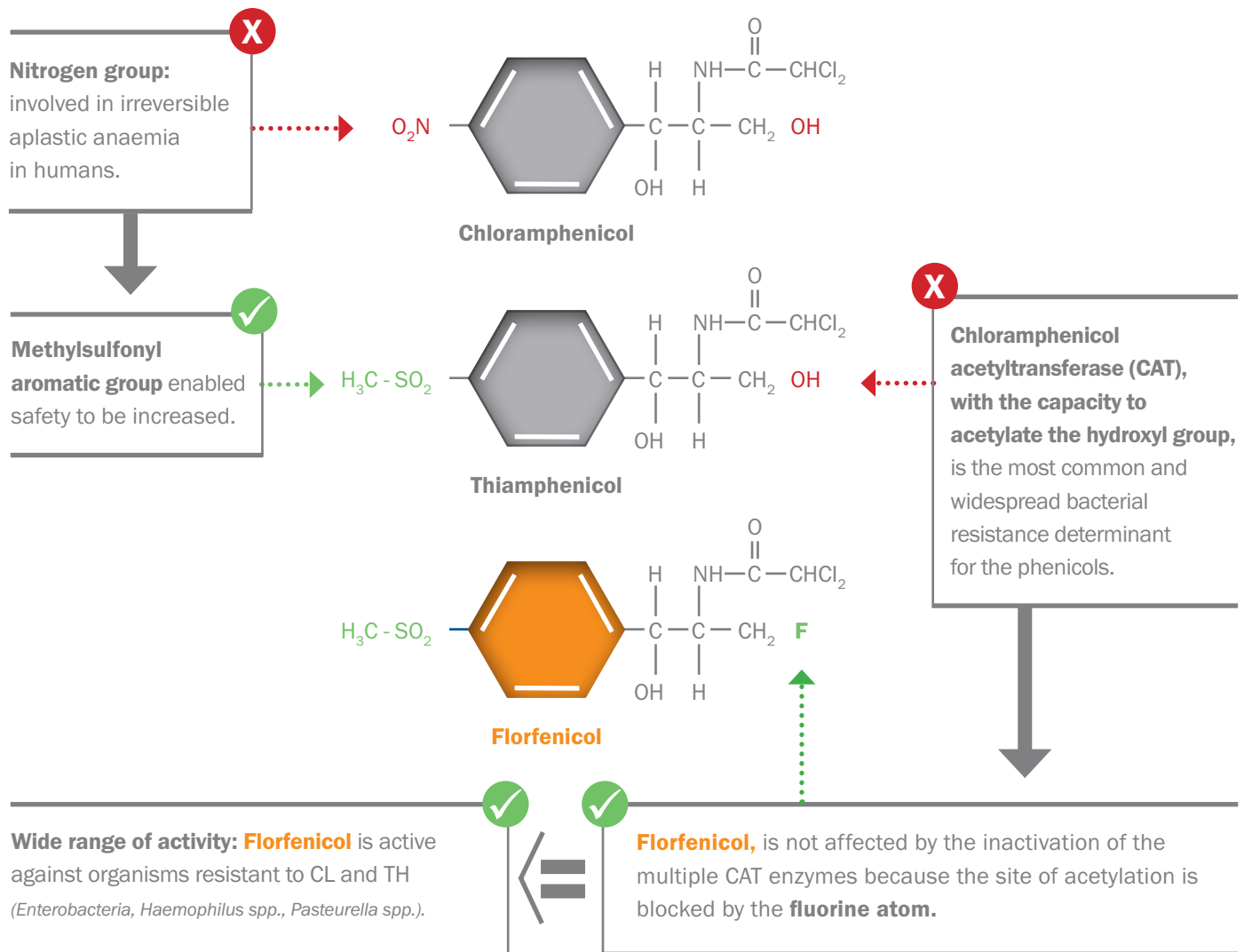
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## 1 Florfenicol structure and therapeutic implications

**Florfenicol** is a synthetic antibiotic that belongs to the family of amphenicols and specifically is a fluorinated derivative of thiamphenicol. Its pharmacological profile is similar to its two predecessors chloramphenicol (CL) and thiamphenicol (TH), but with major improvements thanks to differential structural characteristics:

**Figure 1.** Molecular structure of chloramphenicol, thiamphenicol and **Florfenicol**.



**Florfenicol** is currently one of the most popular antibiotics in veterinary medicine for treating a wide variety of infectious diseases, due to its:

- ✓ wide range of action, and
- ✓ high sensitivity of most common pathogens in swine production

## 2 Pharmacokinetics

### - Digestive and intramuscular absorption:

Excellent bioavailability, around 100%<sup>1,3</sup>.

### - Plasma protein binding:

**Florfenicol** binds to plasma proteins between 17 – 20%<sup>2</sup>.

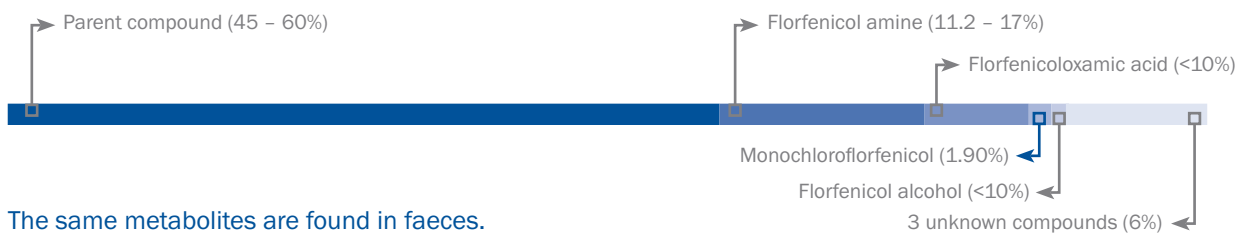
### - Distribution:

**Florfenicol** is rapidly distributed to all tissues (including target tissues like lungs), reaching active concentrations in the organs and tissues similar to concentrations observed in serum<sup>3</sup>.

### - Excretion

The principal route of excretion is renal:

**Figure 2.** Urine metabolites distribution<sup>4</sup>:



**In general, it is considered that there are no significant differences in the bioavailability between the oral and intramuscular route<sup>3</sup>.**

## SELECTAN<sup>®</sup>

### Pharmacokinetic particulars:

**Injectable:** After initial intramuscular administration of **Florfenicol**, maximum serum concentrations between 1.9 and 3.1 µg/ml are reached after 2.2 hours, and deplete with a terminal mean half-life of 35.5 hours. After a second intramuscular administration, maximum serum concentrations between 2.0 and 8.1 µg/ml are reached after 1.7 hours<sup>5</sup>.

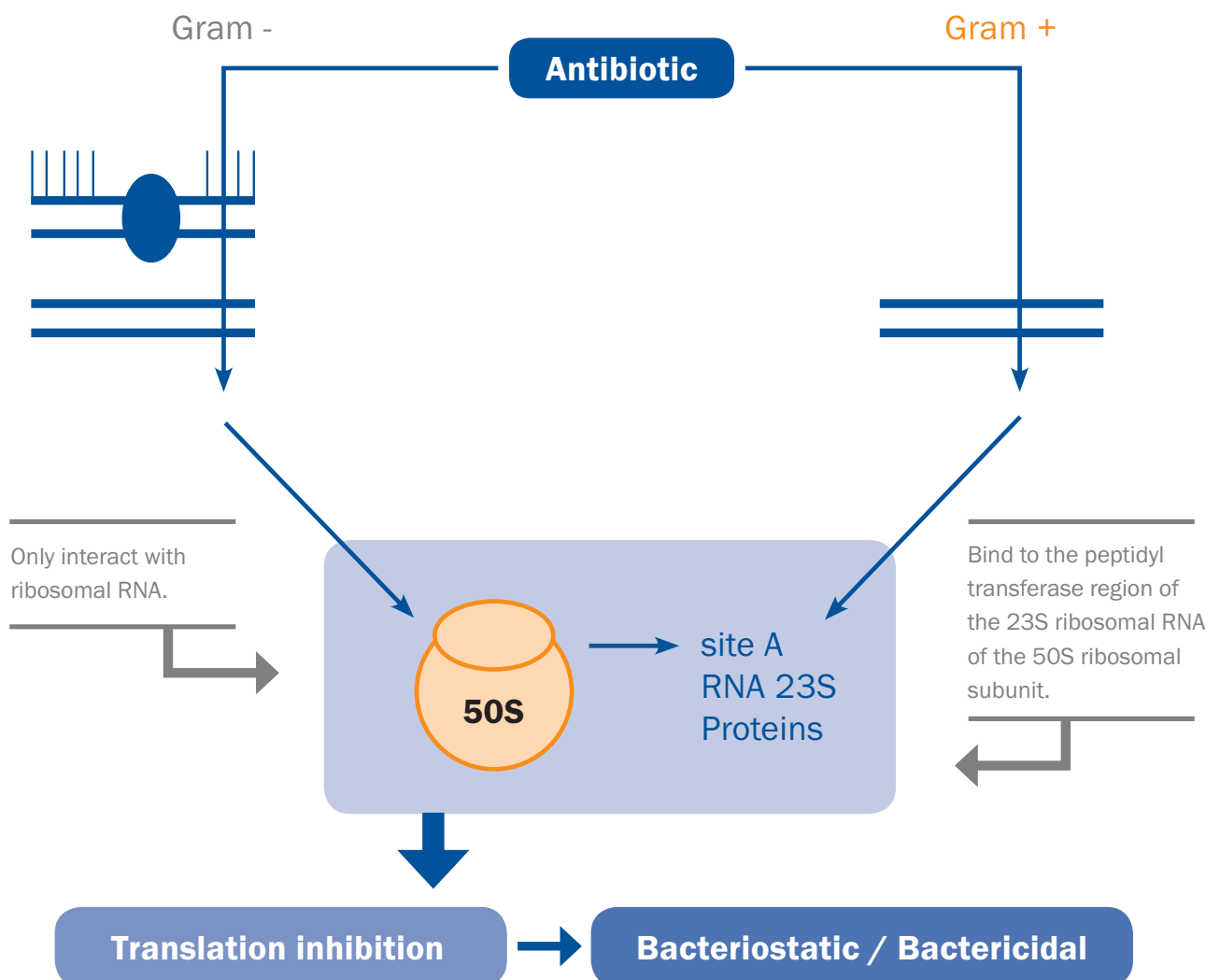
**Oral:** When administered *ad libitum* in medicated drinking water, **Florfenicol** concentrations in serum remained above 1 µg/ml, well above the targeted MIC value for the labelled swine pathogens, throughout the full five day treatment period<sup>6</sup>.

### 3 Mechanism of action

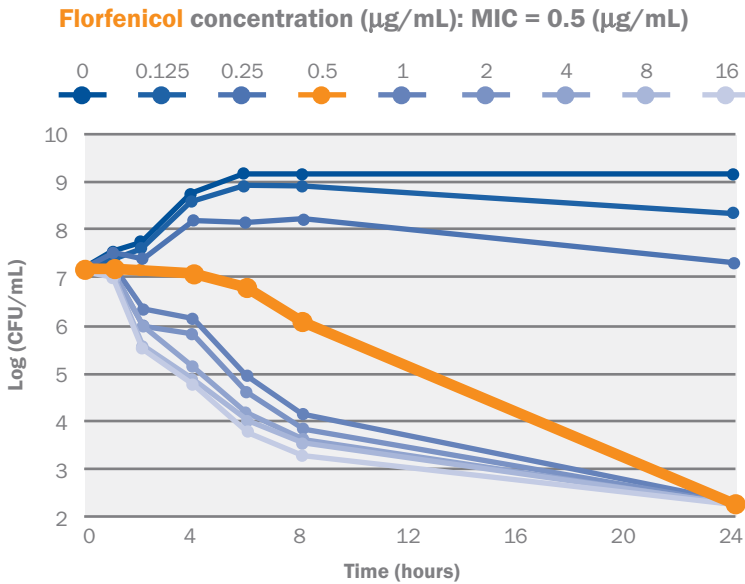
**Florfenicol**'s mechanism of action is the inhibition of protein synthesis by bacterial peptidyl transferase, by binding to 50S subunit of ribosomes (Figure 3)<sup>15</sup>.

By preventing the replication of the organism, **Florfenicol** was initially classified as a bacteriostatic drug. However, several studies *in vitro* against different bacteria have demonstrated bactericidal activity when **Florfenicol** is at concentrations similar to the MIC (Graphs 1 and 2)<sup>7</sup>.

**Figure 3.** Mechanism of action of phenicols in the microorganism.

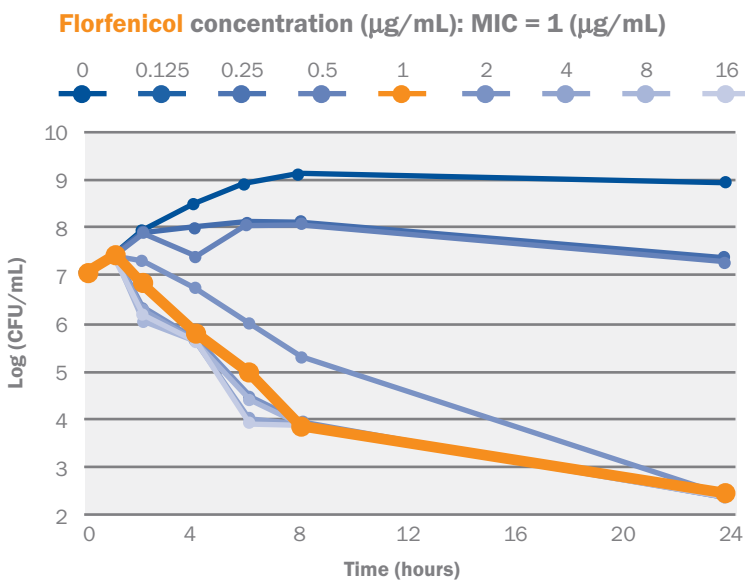


**Graph 1.** Time-kill curve of **Florfenicol** versus *Actinobacillus pleuropneumoniae* isolated from pigs.



The MIC (0.5  $\mu\text{g/mL}$ ) and all higher concentrations resulted in a drop in bacterial count of more than 5 logs after 24 hours of exposure.

**Graph 2.** Time-kill curve of **Florfenicol** versus *Pasteurella multocida* isolated from pigs.



The MIC (1  $\mu\text{g/mL}$ ) and all higher concentrations resulted in a drop in bacterial count of more than 3 logs by 8 hours and more than 5 logs by 24 hours. Half the MIC (0.5  $\mu\text{g/mL}$ ) resulted in a drop of 3 logs by 24 hours of exposure (based on this graph, the MIC is probably closer to 0.5  $\mu\text{g/mL}$ ).

**Definitions:**

**MIC (Minimum Inhibitory Concentration):** The lowest concentration of antimicrobial substance that prevents visible growth of microorganisms after 18 and 24 hours of culturing.

**MBC (Minimum Bactericidal Concentration):** The lowest concentration of antimicrobial substance capable of killing 99.9% of inoculated microorganisms after 18 and 24 hours of culturing.

**Florfenicol** is a time-dependent bactericidal antibiotic with a marked concentration dependence against several major veterinary pathogens<sup>7</sup>.

## 4 Spectrum of action

**Florfenicol** is a broad-spectrum antibiotic with activity against a variety of Gram-positive and Gram-negative bacteria that cause respiratory and enteric diseases in pigs (Table 1 and Table 2). It has also been shown to have a broader spectrum than chloramphenicol and even its other analogue, thiamphenicol<sup>8</sup>.

**Table 1.** Main indications of **Florfenicol** (susceptible organisms) against pathogenic agents in pigs<sup>8</sup>.

GRAM +	GRAM -	Other
<ul style="list-style-type: none"> <li>• <i>Streptococcus spp.</i></li> <li>• <i>Staphylococcus spp.</i></li> </ul>	<ul style="list-style-type: none"> <li>• <i>Actinobacillus pleuropneumoniae</i></li> <li>• <i>Pasteurella spp.</i></li> <li>• <i>Haemophilus spp.</i></li> <li>• <i>Bordetella bronchiseptica</i></li> <li>• Enterobacteriaceae (<i>Escherichia coli</i>, <i>Salmonella spp.</i>)</li> </ul>	<ul style="list-style-type: none"> <li>• <i>Mycoplasma spp.</i></li> </ul>

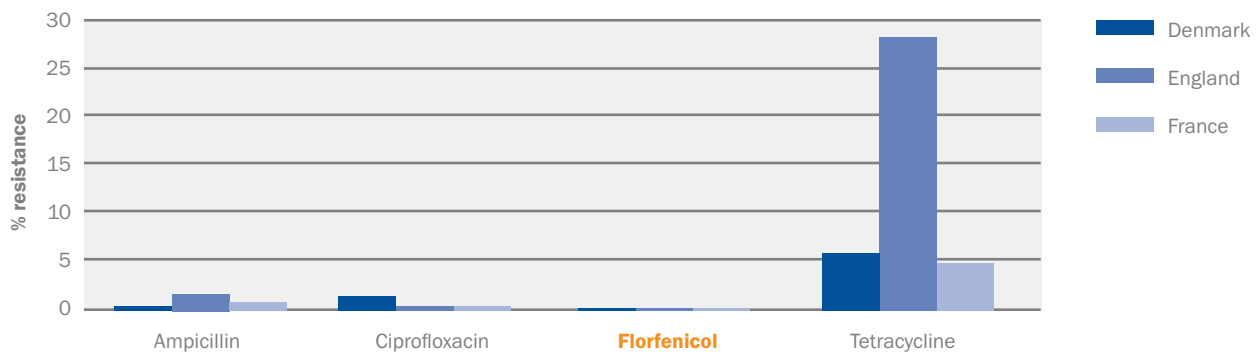
**Table 2.** Activity (MIC<sub>90</sub> µg/mL) of **Florfenicol** against selected bacteria in swine<sup>7, 8, 9</sup>.

Organism	MIC <sub>90</sub>
• <i>Actinobacillus pleuropneumoniae</i>	0.5
• <i>Pasteurella multocida</i>	0.5
• <i>Streptococcus suis</i>	2
• <i>Bordetella bronchiseptica</i>	8
• <i>Haemophilus parasuis</i>	0.5
• <i>Mycoplasma hyopneumoniae</i>	2

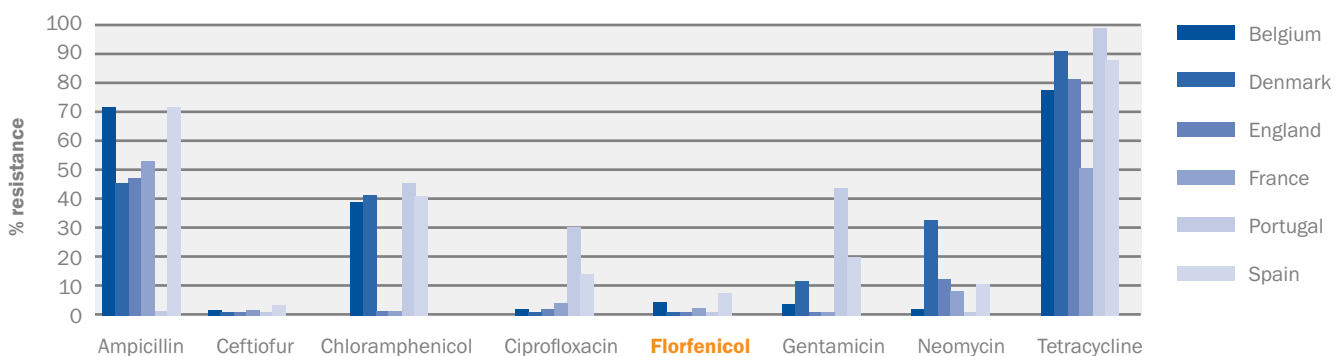
### - *In vitro* sensitivity of main microorganisms in swine

- ✓ **Florfenicol** shows high *in vitro* activity against many bacteria isolated from pigs (Table 2).
- ✓ The low MIC levels observed for several years by government agencies and European scientists show that there has been no significant development of resistance in these bacteria since the introduction of **Florfenicol** in veterinary medicine<sup>11,12</sup>.
- ✓ **Florfenicol** is one of the antibiotics which has a lower resistance level, especially when compared with most popular antibiotics such as tetracycline and penicillins (Graphs 3, 4 and 5)<sup>11, 13</sup>.

**Graph 3.** Occurrence of antimicrobial resistance of *Actinobacillus pleuropneumoniae* isolated from pigs in different European countries 2004.

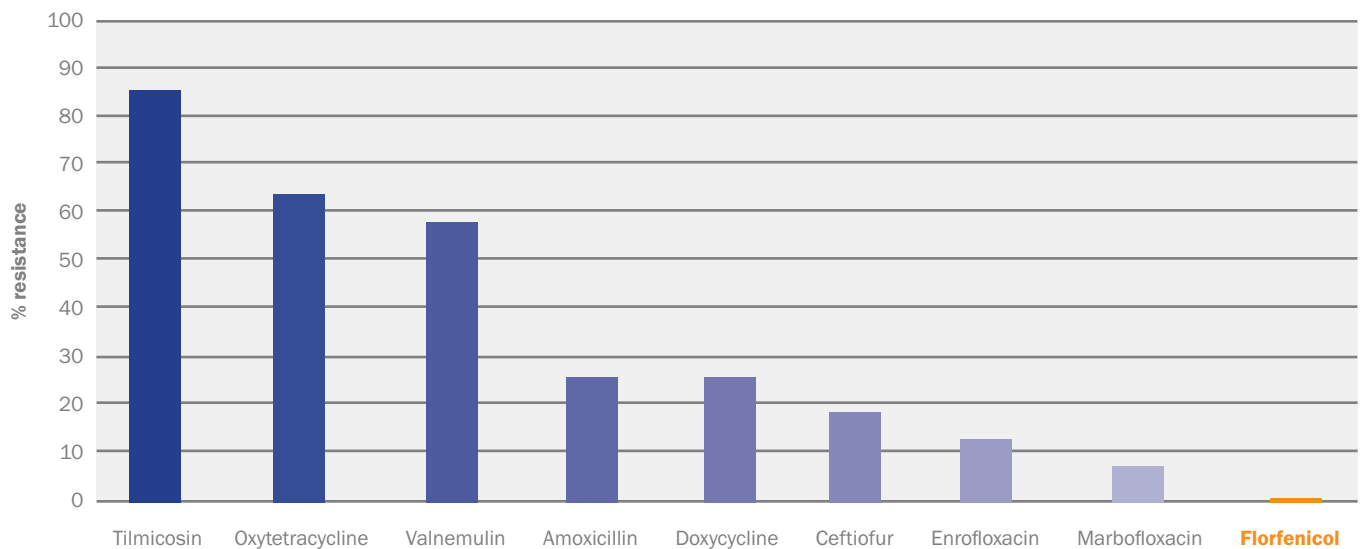


**Graph 4.** Occurrence of antimicrobial resistance of *Escherichia coli* isolated from diseased pigs in different European countries 2004.



**Florfenicol** is a valuable alternative to traditional antibiotics in preventing and treating many respiratory and digestive diseases affecting pigs<sup>12</sup>.

**Graph 5.** Sensitivity of *Pasteurella multocida* strains to **Florfenicol**<sup>13</sup>.



#### - Key facts on resistances<sup>14</sup>:

The development of antimicrobial resistance is an increasing problem in human and veterinary medicine that can be caused by many factors, including:

- ✓ Target site mutations
- ✓ Over-expression of antimicrobial efflux pumps
- ✓ Acquisition of transferable resistance determinants

These resistance mechanisms determine resistance emergence during clinical use of an antimicrobial drug.

#### **Florfenicol** low resistance rates are consistent with<sup>14</sup>:

- ✓ The ribosomal RNA is the binding site of **Florfenicol** → Several nucleotide mutations would need to occur in order to mutate most ribosomes in a bacterium and cause blockage of **Florfenicol** binding
- ✓ **Florfenicol** is relatively resistant to constitutive antimicrobial efflux pumps in target pathogens.

## 5 Conclusions

### Florfenicol:

- ✓ One of the most **powerful antibiotics** exclusively for **veterinary use**.
- ✓ **Broad spectrum** antibiotic with **bactericidal** effect against the most common swine pathogens.
- ✓ **Highly effective** and valuable alternative to traditional antibiotics.
- ✓ One of the **lowest** levels of **resistance** in Europe.

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The low rate of resistance development, the low prevalence of transferable resistance determinants among swine respiratory pathogens, and the limited use of phenicols in human and veterinary medicine explain the **continued high degree of Florfenicol susceptibility** among **swine respiratory isolates**.

## SELECTAN® ORAL

### SELECTAN® Florfenicol



**SELECTAN®** Florfenicol, in injectable solution. **COMPOSITION PER ML:** Florfenicol 300 mg. **INDICATIONS:** Diseases caused by florfenicol susceptible bacteria: **-Swine:** Treatment of acute outbreaks of respiratory disease caused by *Actinobacillus pleuropneumoniae* and *Pasteurella multocida*. **-Cattle:** Treatment of respiratory infections due to *Mannheimia haemolytica*, *Pasteurella multocida* and *Histophilus somni*. **ADMINISTRATION ROUTE:** Intramuscular. **DOSAGE:** **-Swine:** 1 ml/20 kg b.w., equivalent to 15 mg of florfenicol/kg b.w., into neck muscles, administered twice at 48 hours intervals. The volume administered per injection site should not exceed 3 ml. **-Cattle:** 1 ml/15 kg b.w., equivalent to 20 mg of florfenicol/kg b.w., administered twice at 48 hours intervals. The volume administered per injection site should not exceed 10 ml. **WITHDRAWAL PERIOD:** **Meat:** **-Swine:** 18 days. **-Cattle:** 30 days. **Special precautions for storage:** Not require any special storage conditions. **PACKAGING:** 50, 100 and 250 ml plastic bottles. Reg. N°: 1802 ESP.

**SELECTAN® ORAL** 23 mg/ml Concentrate for use in Drinking Water. Florfenicol. **COMPOSITION PER ML:** Florfenicol 23 mg. **INDICATIONS:** **Swine:** Treatment and prevention at the group level where clinical signs are present of swine respiratory disease associated with *Actinobacillus pleuropneumoniae* and *Pasteurella multocida* susceptible to florfenicol. **AMOUNTS TO BE ADMINISTERED AND ADMINISTRATION ROUTE:** Oral route in drinking water. **Swine:** 10 mg florfenicol per kg body weight per day for 5 consecutive days. This dose is equivalent to 0.44 ml of the product per kg body weight per day. In order to obtain the correct dosage water uptake has to be monitored and the concentration of florfenicol has to be adjusted accordingly. **WITHDRAWAL PERIOD:** Meat and offal: 20 days. **SPECIAL PRECAUTIONS FOR STORAGE:** Do not store above 25°C. **PACKAGING:** 5 L plastic barrels. For animal treatment only. Reg. N°: 2286 ESP.

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