



# Recent scientific data on resistance development of tiamulin and other antibiotics in mycoplasma

## Introduction

**An excellent paper has recently been produced by Gautier-Bouchardon, A.V. and others on the comparative antimicrobial resistance development of tiamulin with other antibiotics against *Mycoplasma gallisepticum*, *Mycoplasma synoviae* and *Mycoplasma iowae*. It confirms tiamulin is much slower at developing resistance than enrofloxacin, tylosin and erythromycin.**

## Study design

Stock solutions of sub inhibitory concentrations of Erythromycin (ERY), Oxytetracycline HCL (OTC), Tylosin tartate (TYLO), Enrofloxacin (ENRO) and Tiamulin fumarate acid (TIAM) were made, in which the avian mycoplasmas were cultured. A drug free culture and an inoculated microtube served as controls. For each passage experiment, growth of mycoplasma was monitored by a colour change in the highest concentration of antibiotic after 5 days of cultivation. The resistant Mycoplasma was chosen for the next passage.

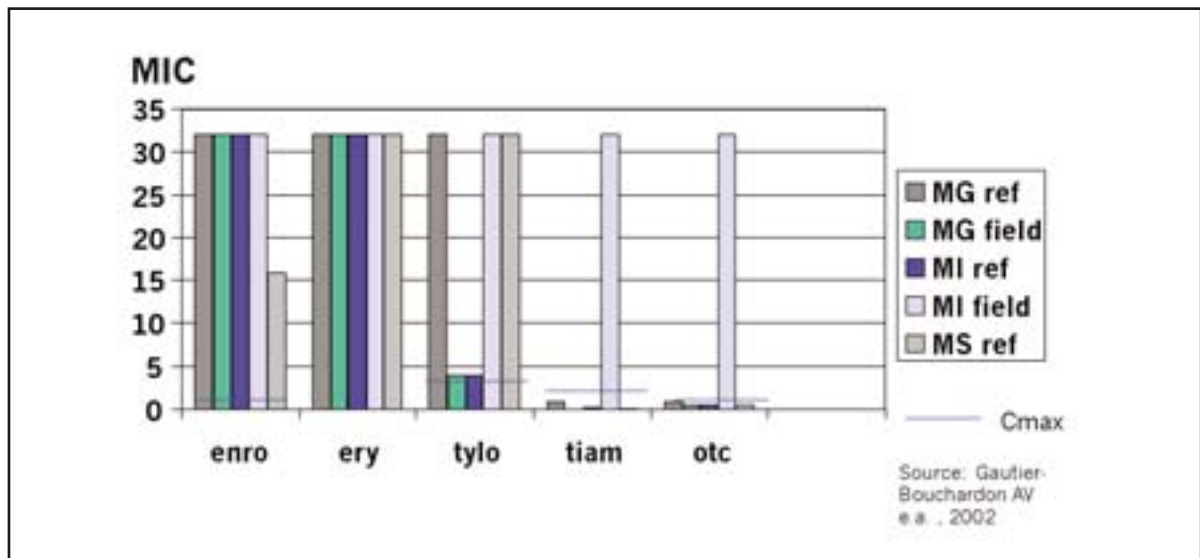
The drug concentrations were gradually increased. This process was repeated for the number of times necessary to observe growth in an antibiotic dose of at least 1 mg/ml or for up to 10 passages. After these passages, MICs were determined for the selected mutants. Sensitivity and resistance of strains was determined on the NCCLS values for the respective antibiotics for rapidly growing bacteria. Before selection, strains were susceptible to all the antibiotics tested, except the reference strain of *M. synoviae*, which was resistant to erythromycin and presented a reduced susceptibility to enrofloxacin.

## Results

Resistance development for the various pathogens and antibiotics is given in the table below.

	<i>M. gallisepticum</i>	<i>M. synoviae</i>	<i>M. iowae</i>
Erythromycin	High level resistance within 2- 6 passages		
Tylosin			
Enrofloxacin	Gradual resistance development		
Oxytetracycline	No resistance	No resistance	Gradual Resistance
Tiamulin	No resistance	No resistance	Gradual Resistance

Graph 1. Maximum MIC of MG, MS and MI after 10 passages in antibiotic media



The maximum MICs of Mycoplasma reference strains and field strains for various antibiotics after 10 passages through antibiotic containing media are given in the graph below. For reference, the Cmax of the various antibiotics are given as well. Cmax of erythromycin was not available.

### Conclusions

1. Whatever the antibiotic used for the selection, the two *M. iowae* strains were able to grow in high antibiotic concentrations more rapidly than *M. gallisepticum* or *M. synoviae*.
2. Whatever the Mycoplasma strain used, high resistances to Erythromycin and Tylosin were reached rapidly, whereas the rise of in resistance to Enrofloxacin was more gradual.
3. No resistance developed of *M. synoviae* and *M. gallisepticum* for Tiamulin, with MICs rising to maximum 1 mcg/ml after 10 cycles of exposure to Tiamulin.
4. Oxytetracycline resistance did not develop for *M. synoviae* and *M. gallisepticum* and there was a moderate 1-8-fold decrease of the original susceptibility.

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**Further information on the Tiamutin® (tiamulin) range of products is available from the Poultry Products Manager at Novartis Animal Health operations in over 50 countries worldwide.**

### Reference

A.V. Gautier-Bouchardon, A.K. Reinhardt, M. Kobisch, I. Kempf. In vitro development of resistance to enrofloxacin, erythromycin, tylosin, tiamulin and oxytetracycline in *Mycoplasma gallisepticum*, *Mycoplasma iowae* and *Mycoplasma synoviae*. Veterinary Microbiology 99, (2002) 47-58.