Bundesamt für Verbraucherschutz und Lebensmittelsicherheit

GERM-Vet German Resistance Monitoring

# Use of Cephalosporins in Veterinary Medicine
## Results Of the German National Antibiotic Resistance Monitoring (GE*RM*-Vet)

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### Objectives

Cephalosporins (3rd and 4th generation) are classified from WHO as "highest priority critically important antimicrobials" and from OIE as "critically important antimicrobials". Nevertheless, they are important to treat bacterial infections in veterinary medicine. Since 2001, an annual representative German-wide study (GE*RM*-Vet) monitors bacterial isolates from diseased animals for resistances against a set of five different cephalosporins (amongst other antimicrobials).

### Conclusions:

An intelligent and rational application of antimicrobial agents is needed to minimise the development and the spread of antimicrobial resistant bacteria and their resistance genes as far as possible. Depending on the affiliation to animal and bacterial species we see large differences in resistance rates and a very different impact on resistance situation in veterinary medicine. This representative antimicrobial resistance monitoring serves as a valid tool in risk management. With these representative and quantitative data, we are able to monitor and estimate the development of antimicrobial resistance in veterinary pathogens to 3rd and 4th generation cephalosporins.

### Results:

***S. aureus*, mastitis**

Basically low resistance rates were detected for *S. aureus* from diary cattle. Higher rates were only seen against penicillins (14-20%) and aminopenicillins (14-18%), against cephalosporins they were very low (0-3%). Since 2008 MRSA isolates were rarely observed. $MIC_{90}$-values range on a similar level over the sample period.

***E. coli*, mastitis**

*E. coli* strains from diary cattle also showed low resistance rates below 19%. The newer cephalosporins showed a good effectiveness with low $MIC_{90}$-values (data not shown). $MIC_{90}$-values range on a similar level over the sample period. Very few ESBL-positive isolates were found.

***E. coli*, enteritis**

High resistance rates were shown for *E. coli* against aminopenicillins (up to 80%) for calves as for isolates from piglets as well. $MIC_{90}$-values of cephalosporins of the 3rd and 4th generation are high for bacterial strains isolated from calves (for all tested cephalosporins >32 mg/L). The rate for ESBL positive *E. coli* isolates from calves seems to be still increasing from 7% in 2006 to 34% in 2014 (Fig. 5). $MIC_{90}$-values of cephalosporins for bacterial strains isolated from piglets were lower than those isolated from calves.

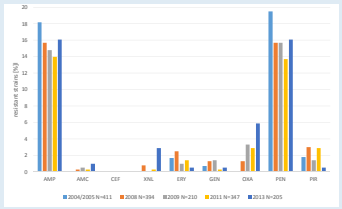

**Figure 1.** Resistance level [%] of *S. aureus* strains (N= 1.567) from diary cattle with acute mastitis, Germany 2002-2013.

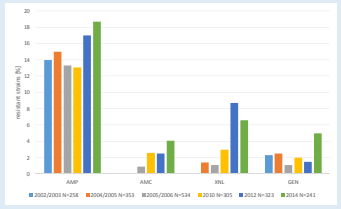

**Figure 2.** Resistance level [%] of *E. coli*-strains (N = 2.014) from diary cattle with acute mastitis, Germany 2002-2014.

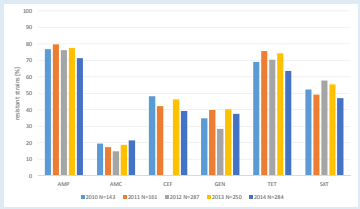

**Figure 3.** Resistance level [%] of *E. coli* strains from calf (N=1.125) with enteritis, Germany 2010-2014 (CEF not tested in 2012) .

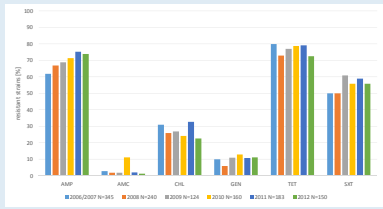

**Figure 4.** Resistance level [%] of *E. coli* strains from piglets (N=1.202) with enteritis, Germany 2006-2012 (CEF not tested in 2012) .

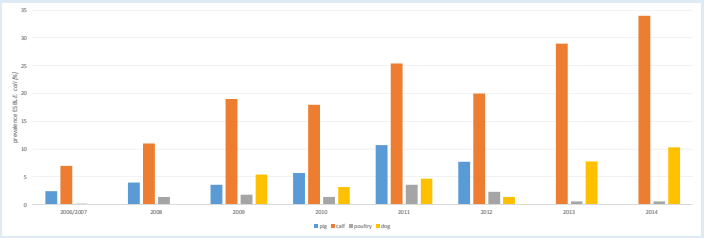

**Figure 5.** prevalence [%] of phenotypically ESBL-producing *E. coli*-strains from different animal species, Germany 2006-2014.

| | 2010 | 2011 | 2012 | 2013 | 2014 |
|---|---|---|---|---|---|
| | calf | | | | |
| **FOT** | >32 | >32 | >32 | >32 | >32 |
| **CEQ** | >32 | >32 | >32 | >32 | >32 |
| **XNL** | >32 | >32 | >32 | >32 | >64 |
| **ENR** | >16 | >16 | >16 | >16 | >16 |
| N= | 143 | 161 | 287 | 250 | 284 |

**Table 1.** $MIC_{90}$-values [mg/L] of *E. coli* -strains from calf (N=1.125) with enteritis, Germany 2010-2014.

| | 2006/ 2007 | 2008 | 2009 | 2010 | 2011 | 2012 |
|---|---|---|---|---|---|---|
| | piglet | | | | | |
| **FOT** | 0.12 | 0.12 | 0,12 | 0.12 | 0.12 | 0.5 |
| **CEQ** | 0.12 | 0.3212 | 0,12 | 0.12 | 0.12 | 0.5 |
| **XNL** | 0.5 | 0,5 | 0,5 | 0.5 | 0.5 | 1 |
| **ENR** | 0.5 | 1 | 1 | 0.5 | 0.5 | 8 |
| N= | 345 | 240 | 124 | 160 | 183 | 150 |

**Table 2.** $MIC_{90}$-values [mg/L] of *E. coli* -strains from pig (N=1.202) with enteritis, Germany 2006-2012.

***E. coli*, poultry**

Cephalosporins are not approved for veterinary use in poultry. Nevertheless, we see high $MIC_{90}$ values for broilers, although the ESBL rates for *E. coli* are still between 0.6 and 2.3%.

| | 2010 | | 2011 | | 2012 | | 2013 | | 2014 | |
|---|---|---|---|---|---|---|---|---|---|---|
| | turkey | broiler | turkey | broiler | turkey | broiler | turkey | broiler | turkey | broiler |
| **FOT** | 0.12 | 4 | 0.12 | 0.5 | 0.12 | 16 | 0.12 | 0.12 | 0.12 | 0.12 |
| **CEQ** | 0.12 | 0.25 | 0.12 | 0.25 | 0.12 | 32 | 0.06 | 0.12 | 0.12 | 0.06 |
| **XNL** | 0.5 | 4 | 0.5 | 0.5 | 0.5 | 16 | 0.5 | 0.5 | 0.5 | 0.5 |
| **COL** | 4 | 1 | 8 | 1 | 8 | 1 | 1 | 1 | 2 | 1 |
| N= | 95 | 42 | 125 | 74 | 159 | 35 | 109 | 38 | 110 | 31 |

**Table 3.** $MIC_{90}$-values [mg/L] of *E. coli* strains from turkeys (N=598) and broilers (N=220), Germany 2010-2014.

***E. coli*, pets**

Recently increasing $MIC_{90}$ values for *E. coli* and cephalosporins have been detected. Particularly bacterial strains isolated from infections of the gastrointestinal tract (GIT) are affected.

| | 2010 | | 2011 | | 2012 | | 2013 | | 2014 | |
|---|---|---|---|---|---|---|---|---|---|---|
| | GIT | UGT | GIT | UGT | GIT | UGT | GIT | UGT | GIT | UGT |
| **FOT** | 0.12 | 0.12 | 0.12 | 0.12 | >32 | 8 | >32 | 0.12 | 32 | 32 |
| **CEQ** | 0.12 | 0.12 | 0.06 | 0.12 | >32 | 4 | 32 | 0.5 | 32 | 32 |
| **XNL** | 0.5 | 0.5 | 0.5 | 0.5 | >64 | 8 | >64 | 1 | 64 | 32 |
| **ENR** | 0.25 | 16 | 16 | 16 | >16 | >16 | >16 | 16 | 2 | 2 |
| N= | 27 | 23 | 21 | 32 | 18 | 33 | 17 | 37 | 65 | 32 |

**Table 4.** $MIC_{90}$-values [mg/L] of *E. coli* strains from pets (Gastrointestinal-tract, GIT; N=148, Urogenital-tract, UGT; N=157), Germany 2010-2014.

### Methods:

Based on a statistically valid sampling plan the bacterial isolates were investigated by using the broth microdilution method according to CLSI document VET01-A4. The MIC values were assessed with their corresponding clinical veterinary breakpoints (CLSI VET01-S). If no breakpoints were available, $MIC_{90}$ values were used for classification.

**Abbreviations:**
**AMP** ampicillin, **AMC** amoxicillin/clavulanic acid, **CEF** cephalothin, **CEQ** cefquinome, **ERY** erythromycin, **ENR** enrofloxacin, **FOT** cefotaxime, **GEN** gentamicin, **OXA** oxacillin, **PEN** penicillin G, **PIR** pirlimycin, **TET** tetracyclin, **SXT** trimethoprim/sulfamathoxazole, **XNL** ceftiofur

**Acknowledgment:**
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**References**
[1] CLSI document VET01-A4. Performance standards for antimicrobial disk and dilution susceptibility tests for bacteria isolated from animals; approved standard. Clinical and Laboratory Standards Institute, Wayne, PA, USA (2013).
[2] CLSI document VET01-S Performance standards for antimicrobial disk and dilution susceptibility tests for bacteria isolated from animals; Third informational supplement. Clinical and Laboratory Standards Institute, Wayne, PA, USA (2013).

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