OPEN ACCESS Paper

Antimicrobial drug use in Austrian pig farms: plausibility check of electronic on-farm records and estimation of consumption

M. Trauffler, A. Griesbacher, K. Fuchs, J. Köfer

Electronic drug application records from farmers from 75 conventional pig farms were revised and checked for their plausibility. The registered drug amounts were verified by comparing the farmers' records with veterinarians' dispensary records. The antimicrobial consumption was evaluated from 2008 to 2011 and expressed in weight of active substance(s), number of used daily doses (nUDD), number of animal daily doses (nADD) and number of product-related daily doses (nPrDD). All results were referred to one year and animal bodyweight (kg biomass). The data plausibility proof revealed about 14 per cent of unrealistic drug amount entries in the farmers' records. The annual antimicrobial consumption was 33.9 mg/kg/year, 4.9 UDD_{kg}/kg/year, 1.9 ADD_{kg}/kg/year and 2.5 $PrDD_{kg}$/kg/year (average). Most of the antimicrobials were applied orally (86 per cent) and at group-level. Main therapy indications were metaphylactic/prophylactic measures (farrow-to-finish and fattening farms) or digestive tract diseases (breeding farms). The proportion of the 'highest priority critically important antimicrobials' was low (12 per cent). After determination of a threshold value, farms with a high antimicrobial use could be detected. Statistical tests showed that the veterinarian had an influence on the dosage, the therapy indication and the active substance. Orally administered antimicrobials were mostly underdosed, parenterally administered antimicrobials rather correctly or overdosed.

Introduction

The occurrence of antimicrobial resistance is an increasing phenomenon and represents a global problem both for human and animal health. One main risk factor for the development and the spread of resistant bacteria is an increased antimicrobial use (van den Bogaard and Stobberingh 2000). Evidence for an association between antimicrobial consumption in veterinary medicine and the occurrence of resistant bacteria in human beings is not fully investigated but exists (Tollefson and Miller 2000, Angulo and others 2004): As a consequence, the application of antibiotics in animal husbandry is strongly criticised. International organisations recommend monitoring programmes for the measurement of antimicrobial use in veterinary medicine in order to contribute to the containment strategies for antimicrobial resistance (WHO 1997, EMEA 1999, Nicholls and others 2001).

However, the collection of reliable drug application data in veterinary medicine is challenging. At that time, the only internationally standardised monitoring system consists of the collection of overall sales data in the context of the 'European Surveillance of Veterinary Antimicrobial Consumption' project (ESVAC) (EMA 2013). It enables the representation of antimicrobial use per country using the unit 'weight of active substance(s)' related to the animal bodyweight.

Unfortunately, sales data analyses are not helpful for their relation to resistance data for several reasons. First, the unit 'weight of active substance(s)' may lead to false interpretation when comparing results, as therapeutic potency differs from one antimicrobial substance to another one (Chauvin and others 2001, Nicholls and others 2001, Jensen and others 2004). Studies measuring the use of antibiotics can therefore be compared only when the units take into account differences in potency of antimicrobial substances (Chauvin and others 2001). Furthermore, sales data do not allow the quantification of antimicrobial consumption per animal species, as several drugs are accredited for more than one species. Yet, this is a prerequisite for the fixation of daily doses, which allow the expression of antimicrobial use as treatment frequency, taking into account differences in potency. In addition, sales data do not provide any information about the indications for antibacterial prescription.

For the development of antimicrobial reduction strategies, knowledge about in what animal species and for which diagnosis antimicrobial substances are prescribed is of particular importance. Data including this information could be provided by the end-user, such as the farmer. Unfortunately, sources of information from farmers are rarely officially accredited and are reputed to be inefficient or expensive unless well managed and thoroughly designed (Grave and others 2006). However, there are only few studies testing the feasibility and describing the quality of such application data (Menéndez González and others 2010, Merle and others 2012).

In Austria there are about 27,000 pig farms holding 2,900,000 pigs and producing around 530,000 tons of meat per year (Statistics

Veterinary Record (2014) doi: 10.1136/vr.102520

M. Trauffler, MVM,
J. Köfer, DVM,
Institute of Veterinary Public Health, University of Veterinary Medicine, Vienna, Veterinärplatz 1, Vienna 1210, Austria
A. Griesbacher, MSc,
K. Fuchs, PhD,
Division for Data, Statistics & Risk Assessment, Austrian Agency for Health and Food Safety, Zinsendorfgasse 27/1, Graz 8010, Austria

E-mail for correspondence: martine.trauffler@vetmeduni.ac.at

Provenance: not commissioned; externally peer reviewed

Accepted June 27, 2014

Austria 2014). Till now, little knowledge about how many antimicrobials are used in the Austrian pig sector exists.

In this study, drug application data, which were recorded directly by the farmer, were evaluated. The aims of the project were to (1) determine the plausibility of such application data and to (2) estimate the total amount of antimicrobial consumption in the study swine population using four different units of measurement.

Material and methods

Data collection

In Austria, when disease treatment requires a repeated or long-term medication, the dispensary of drugs from the veterinarian to the farmer is allowed and statutorily subject to the official documentation rules of the Animal Health Service Regulation 2009 (Anonymous 2009). Additional to this compulsory documentation, some meat production companies have implemented private quality-assurance systems, with extended supervision from the animal up to the food product. For the study at hand, data were collected in cooperation with a meat production company using such a private system for more than 10 years. The company in question contracts 76 pig farms and produces 10,750 tons of meat per year.

In the context of their system, farmers as well as veterinarians are obligated to record each drug application (farmers) or dispensary (veterinarians) via online platforms. As main source of data served the drug application records from farmers, who are required to enter the following information: (i) farm registration number, (ii) treatment date, (iii) drug name, (iv) drug authorisation number, (v) drug serial number, (vi) treatment duration (days), (vii) number of applications per day, (viii) therapy indication, (ix) swine age class (piglets (1.5–10 kg), weaner pigs (10–30 kg), fattened pigs <60 kg biomass, fattened pigs >60 kg biomass, sows, boars), (x) number of animals treated, (xi) type of treatment (group-level or individual), (xii) drug quantity per animal with unit and (xiii) total drug quantity with unit.

Drug dispensary records from veterinarians were additionally evaluated and served as a plausibility control for the farmers' records. They included the following information: (i) veterinarian's identity, (ii) farm's registration number, (iii) date of dispensary, (iv) drug name, (v) drug authorisation number, (vi) drug serial number, (vii) number of packs+pack art (package or flagon) and (viii) amount (pack size) with unit.

The platform of the farmers is equipped with drop-down lists for the information 'drug name' and 'unit of the drug quantity' in order to facilitate data entry. In addition, automatic plausibility checks are programmed into the software in order to reduce the occurrence of mistakes. For each drug application entry, it is verified whether the corresponding dispensary record of the veterinarian has been registered. In the case of non-accordance, farmers as well as veterinarians are automatically advertised by the system.

For this study, application and dispensary records from 75 conventional pig farms and their supervising veterinarians (19 in total) were analysed in the time period from January 2008 to December 2011. In that time period, 85,299 drug application records were registered. 49 of the farms were farrow-to-finish (FtF), 21 were fattening and five were breeding farms (farms only holding sows and selling piglets at an average weight of 30 kg biomass). In total, they kept around 77,300 pigs, representing about 3 per cent of the Austrian swine population. Mean herd size was 941 animals in FtF, 747 animals in fattening and 3100 animals in breeding farms.

Plausibility check of data

For further evaluations, only antimicrobial treatments for oral and parenteral application (counting 36,757 antimicrobial records) were considered and other medications (e.g. analgesics, vaccinations) were eliminated. Farmers' entries were completely reviewed and tested for implausibility or incorrect data. In the case of missing or questionable data, consultations were held with the quality-assurance representative of the given company. Drug-related entries (drug name, drug authorisation number, treatment duration) were verified for their accordance with the summary of the product characteristics (SPC, Austria Codex, www.pharmazie.com). The indicated number of animals treated was compared with the farm's production parameters. Errors were registered and corrected. Entries about the therapy indication, which must be entered freely without drop-down list, were revised and categorised as follows: cannibalism; chirurgical interventions; digestive tract diseases; general infections; gynaecological diseases; infections/inflammations; infections with involvement of several organ systems; injuries; 'implausible indications'; mastitis metritis agalactia; metaphylactic/prophylactic measures; orthopaedic diseases; other diseases and respiratory tract diseases.

As already described above, both platforms require the entering of the drug serial number. This serial number represents a unique label of each single drug package or flagon. It is registered by the veterinarian in connection with drug dispensary and also recorded by the farmer in connection with drug application. For the plausibility proof of the recorded drug amounts, the total amounts of dispensed and applied drugs were calculated for each single serial number and checked for mutual accordance (with a tolerance range of ±20 per cent of drug amount).

Antimicrobial consumption

Units of measurement

The easiest way to represent antimicrobial consumption is its expression in weight of active substance. Information about the composition of each preparation was obtained from the SPCs. The weight of active substance(s) used in each record was calculated: weight of active substance (mg)=drug amount (ml or g)×weight of active substance per unit (mg/ml or mg/g). For benzylpenicillin and colistin, which were given in international units (IU), the conversion factors were assigned based on the standards for the ESVAC project (benzylpenicillin: 1 IU=0.0006 mg; colistin: 1 IU=0.000049 mg) (EMA 2013).

In addition, three different daily doses were defined:

- The used daily dose per kg biomass (UDD_{kg}) was introduced by Timmerman and others (2006) and is defined as the administered dose per day per kg biomass of a drug. As it is based on real consumption data, it can differ between and within herds. In contrast to the definition of Timmerman and others (2006), where median values are calculated when different dosages for a drug are applied, the UDD_{kg} in this study was calculated separately for each data entry, according to the formula:

$$UDD_{kg}\,(mg/kg/day) = \frac{\text{weight of active substance (mg)}}{\text{number of treated animals} \times \text{average weight (kg)} \times \text{treatment duration (days)}}$$

- The animal daily dose per kg biomass (ADD_{kg}) is internationally defined as the maintenance dosage per day and per kg biomass of a drug for its main indication in one species (Jensen and others 2004). In this study, the average dosage per day and per kg biomass for the active substance(s) of each antibiotic product was defined according to the SPC. Subsequently, the median of all average dosages was calculated for each substance or substance combination and fixed as the ADD_{kg} (Fuchs and Obritzhauser 2010).
- The product-related daily dose for 1 kg biomass ($PrDD_{kg}$) was defined as 80 per cent of the maximal dosage per day and per kg biomass for the active substance(s) according to the SPC. This daily dose respects different dosage recommendations for each single product, even if the active substance is the same.

The treatment frequency was assessed by dividing the weight of active substance(s) by the UDD, the ADD or the PrDD, representing the 'number of UDDs' (nUDD), the 'number of ADDs' (nADD) or the 'number of PrDDs' (nPrDD), respectively.

The antimicrobial consumption was evaluated per year and the results were referred to the animal bodyweight (kg biomass produced). For this purpose, farmers were required to provide information about their annual production output. In FtF farms, the biomass of the sows (number of sows ×200 kg) was added to the production output. In breeding farms, the total biomass was calculated as the sum of the sows' biomass (number of sows ×200 kg) and the piglets' biomass (number of sows ×22 piglets per sow per year ×30 kg).

Quantification of antimicrobial consumption

The antimicrobial consumption was evaluated at three levels: in total, per farm-type and per farm. Means were calculated by dividing the total quantity of the yearly-consumed antimicrobials (in total, per farm-type or per farm) by the sum of the kg biomass produced (in total, per farm-type or per farm, respectively). As 14 per cent of antimicrobial records were eliminated in the course of the plausibility proof, the results were extrapolated to 100 per cent, because eliminating antimicrobial records that have taken place would have resulted in an underestimation. The first two levels were broken down to some variables such as the application form (oral or parenteral), the type of treatment (group-level or individual), the therapy indication and the active substance(s) according to the ATCvet classification system (The Anatomical Therapeutic Chemical classification system for veterinary medicinal products, www.whocc.no/atcvet). At farm-level, the between-farm variability was evaluated by calculating minimum, q_{25}, median, q_{75} and maximum values (descriptive statistics). In order to identify farms with a high antimicrobial use compared with the other farms within the same farm-type, a threshold value was fixed for the $nADD_{kg}$/kg/year according to the definition for outliers: Threshold value=q_{75}+(1.5×IQR) (Tukey 1977). Farms exceeding the threshold value were designated as 'outlier farms'. For graphic visualisation, a ratio was calculated by dividing the antimicrobial consumption per farm by the threshold value.

The correlation between the antimicrobial consumption and the farm size was evaluated with a bivariate Pearson correlation analysis. Furthermore, χ^2 tests for independence were performed in order to verify to what extent the veterinarian had an impact on the therapy indication and on the chosen active substance (ATCvet Code), and to verify if there were differences between the veterinarians concerning the frequency of supervising 'outlier farms' (Software: IBM SPSS Statistics V.20, 2011). For this purpose, the farm's veterinarian was allocated to each antimicrobial record and only the six most relevant veterinarians (supervising the most farms) were selected for the tests. Contingence coefficients (C) as well as P values (P) were calculated.

Accuracy of drug dosage

UDD_{kg}/ADD_{kg} ratios were calculated (Timmerman and others 2006) and a ratio between 0.75 and 1.25 was defined as the correct dosage. A lower ratio (<0.75) was considered as an underdosage, and a higher ratio (>1.25) as an overdosage. χ^2 Tests for independence were performed in order to verify the relation between the dosage accurateness and the active substance (ATCvet Code) (separately per application form) and between the dosage accurateness and the veterinarian (Software: IBM SPSS Statistics V.20, 2011). For this purpose, metric UDD_{kg}/ADD_{kg} ratios were encoded into ordinal data: underdosage, correct and overdosage. Again, only the six most relevant veterinarians were selected for the test. Contingence coefficients (C) as well as P values (P) were calculated.

Results

Plausibility check of data

Inaccurate information, usually due to simple typing errors or confusions in choosing preformulated answers, could be observed. In some entries, unrealistic treatment durations were seen (101 antimicrobial records; 0.3 per cent). Because of their small number, the adjustment of these durations to the maximal treatment duration according to the SPC seemed to be justified. Furthermore, the given age class was not always plausible, for example, mastitis in piglets (162 records; 0.5 per cent). In such cases, the indications were considered to be plausible and the age class was adjusted. Sometimes, the number of treated animals exceeded the farm´s production parameters (39 records; 0.1 per cent). As the farmers could enter the therapy indication freely, this information was very heterogeneous and colloquially described. For this reason, therapy indications were categorised according to the categories described above. In general, the plausibility check of data revealed inconsistencies, causing a time-consuming data processing.

Verifying the drug serial numbers of each drug package or flagon for accordance between the dispensed and applied drug amounts showed accordance for 57 per cent of the records. In 22 per cent of the records, the farmers applied less and in 10 per cent the farmers applied more than the veterinarian did dispense to them; 11 per cent of data were not evaluable because of missing serial numbers. For antimicrobial consumption analyses, data with more applications than dispensaries were eliminated together with some other implausible entries. Finally, for the quantification of the antimicrobial use, 86 per cent of the data (31,684 antimicrobial records) were evaluated.

Antimicrobial consumption

Quantification of antimicrobial consumption

Table 1 visualises the weight of active substance(s) annually consumed, the kg biomass annually produced, as well as the antimicrobial consumption from 2008 until 2011. In total, 33.9 mg/kg/year,

TABLE 1: Weight of active antimicrobial substance (kg) administered, biomass produced (kg) and antimicrobial consumption (units of measurement: mg/kg/year, $nUDD_{kg}$/kg/year*, $nADD_{kg}$/kg/year* and $nPrDD_{kg}$/kg/year*) in 75 conventional pig farms from 2008 to 2011

	Σ Weight of active substance (kg)	Σ Biomass produced (kg)	mg/kg/year	$nUDD_{kg}$/kg/year*	$nADD_{kg}$/kg/year*	$nPrDD_{kg}$/kg/year*
In total (n=75)						
2008	414	11,072,000	37.4	4.8	2.3	2.9
2009	419	11,611,000	36.1	5.3	2.0	2.7
2010	310	11,872,500	26.1	4.6	1.8	2.2
2011	484	13,465,000	35.9	4.8	1.8	2.3
Average	407	12,005,125	33.9	4.9	1.9	2.5
Farrow-to-finish farms (n=49)						
2008	198	7,358,000	27.0	2.6	1.5	1.8
2009	237	7,732,000	30.6	2.3	1.5	2.0
2010	173	7,919,000	21.9	2.2	1.3	1.6
2011	230	9,074,000	25.4	1.9	1.2	1.5
Average	210	8,021,000	26.2	2.2	1.4	1.7
Fattening farms (n=21)						
2008	158	2,670,000	59.3	9.3	3.7	4.5
2009	97	2,779,500	35.0	8.3	2.0	2.9
2010	64	2,791,500	22.8	5.3	1.5	2.1
2011	60	3,128,500	19.1	4.9	1.4	1.9
Average	97	2,842,500	34.1	6.9	2.2	2.8
Breeding farms (n=5)						
2008	57	1,044,000	54.5	9.3	3.9	5.9
2009	85	1,099,500	77.6	19.0	5.3	7.1
2010	73	1,162,500	63.0	19.7	5.4	6.3
2011	194	1,262,500	153.5	25.0	6.8	9.1
Average	102	1,142,125	87.2	18.2	5.4	7.1

*Treatment frequency: nUDD, number of used daily doses; nADD, number of animal daily doses; nPrDD, number of product-related daily doses

4.9 UDD_{kg}/kg/year, 1.9 ADD_{kg}/kg/year and 2.5 $PrDD_{kg}$/kg/year were consumed (average). Overall, 86 per cent of the total use ($nADD_{kg}$/kg/year) were administered via oral, and 14 per cent via parenteral application form. The antimicrobial use per farm-type is also illustrated in Table 1. FtF farms showed a stable and fattening farms a decreasing antimicrobial consumption from 2008 to 2011. In general, breeding farms consumed the most antibiotics. In FtF farms, 61 per cent of the total use were group-treatments, which is a low percentage compared to the fattening and the breeding pig farms (both 92 per cent).

Table 2 shows the proportion of the different antimicrobial substances on the total antimicrobial consumption per year in $nADD_{kg}$/kg/year. As can be seen from the table, lincosamides in combination with other antibacterials were the most used antimicrobial substance (20 per cent of total consumption), followed by amoxicillin, oxytetracycline and colistin. The proportion of the 'highest priority critically important antimicrobials' (WHO 2012), of which macrolides played a major role, was low (12 per cent of total consumption).

Differences were found concerning the distribution of the antimicrobial use to the therapy indication (Table 3). Metaphylactic/prophylactic measures constituted the major indication in FtF and fattening farms (29 and 46 per cent, respectively), followed by respiratory tract diseases (22 and 23 per cent, respectively) and digestive tract diseases (14 and 18 per cent, respectively). In breeding farms, digestive tract diseases played a dominant role (36 per cent), followed by infections with involvement of several organ systems (25 per cent). The active substances that were used for the treatment of metaphylactic/prophylactic measures and for respiratory tract diseases in FtF and fattening pig farms are illustrated in Table 4.

Median values of the antimicrobial use at farm-level ranged between 0.3 ADD_{kg}/kg/year (fattening farms, 2010) and 2.3 ADD_{kg}/kg/year (fattening farms, 2008) (Table 5). Fig 1 visually brings out the FtF farms with a higher antimicrobial consumption than the threshold value. Particularly in 2011, several FtF farms used higher amounts of antimicrobials.

The farm size had no significant impact on the antimicrobial consumption. χ^2 Tests for independence revealed that the veterinarian had a significant impact on the therapy indication (C=0.5; P<0.001) in FtF farms (in fattening farms the conditions for statistical tests were not fulfilled) and on the chosen active substance (ATCvet Code) (C=0.7; P<0.001). In addition, differences between the veterinarians concerning the frequency in supervising 'outlier farms' were exploratory detected but could not be verified by a statistical test because the prerequisites for the χ^2 test were not fulfilled.

Accuracy of drug dosage

Table 6 illustrates the dosage accurateness for oral and parenteral antibiotic treatments. The UDD_{kg}/ADD_{kg} ratio revealed that oral applications were correctly dosed in 8 per cent and parenteral applications in 42 per cent of the entries. The oral application form was generally underdosed (75 per cent), whereas the parenteral application form was rather overdosed (41 per cent). χ^2 Tests revealed a relation between the dosage and the active substance in parenteral applications (C=0.5; P<0.001). In oral treatments, colistin, amoxicillin, tylosin, enrofloxacin and lincosamides in combination with other antibacterials were often underdosed (out of the most used antimicrobials). In parenteral treatments, primarily tylosin, danofloxacin and penicillins in combination with other antibacterials were generally overdosed (out of the most used antimicrobials) (Table 1). It was also noted that the veterinarian had a significant impact on the dosage accurateness (C=0.3; P<0.001). Overall, a wide distribution concerning the veterinarians' dosage choice was seen. Whereas some veterinarians mostly applied a correct dosage, some few veterinarians showed a high number of under- or overdosages.

Discussion

Collecting reliable data for the measurement of antimicrobial consumption in animal husbandry is a great challenge. Whereas overall sales data are relatively easy to gather, the collection of on-farm data is difficult and rarely standardised. In 2010, Fuchs and Obritzhauser successfully estimated antimicrobial use in Austrian cattle, pig and poultry production by evaluating veterinarians' dispensary records. Yet, the evaluation of dispensary records is subject to limitations, because

TABLE 2: Active substances used for antimicrobial treatment in 75 conventional pig farms

ATCvet Code	Active substance	$nADD_{kg}$/kg/year*					
		2008	2009	2010	2011	Average	Per cent
QA07AA01	Neomycin	0.0	0.0	0.0	0.0	0.0	0.0
QA07AA10	Colistin	0.3	0.3	0.4	0.3	0.3	16.2
QA07AA91	Gentamicin	0.0	0.0	0.0	0.0	0.0	0.0
QJ01AA02	Doxycycline	0.2	0.1	0.0	0.1	0.1	5.6
QJ01AA03	Chlortetracycline	0.0	0.0	0.0	0.0	0.0	0.8
QJ01AA06	Oxytetracycline	0.3	0.3	0.3	0.4	0.3	16.5
QJ01AA56	Oxytetracycline, combinations	0.0	0.0	0.0	0.1	0.0	1.7
QJ01BA90	Florfenicol	0.0	0.0	0.0	0.0	0.0	0.4
QJ01CA01	Ampicillin	0.0	0.0	0.0	0.0	0.0	0.1
QJ01CA04	Amoxicillin	0.3	0.5	0.3	0.4	0.4	19.1
QJ01CE09	Procaine benzylpenicillin	0.0	0.0	0.0	0.0	0.0	0.3
QJ01DD90	Ceftiofur	0.0	0.0	0.0	0.0	0.0	1.0
QJ01DE90	Cefquinome	0.0	0.0	0.0	0.0	0.0	1.2
QJ01EW03	Sulfadimidine and trimethoprim	0.0	0.0	0.0	0.0	0.0	0.0
QJ01EW10	Sulfadiazine and trimethoprim	0.1	0.0	0.0	0.0	0.0	2.2
QJ01EW11	Sulfamethoxazole and trimethoprim	0.0	0.0	0.0	0.0	0.0	0.8
QJ01EW13	Sulfadoxine and trimethoprim	0.0	0.0	0.0	0.0	0.0	0.1
QJ01FA90	Tylosin	0.2	0.1	0.1	0.1	0.1	6.4
QJ01FA91	Tilmicosin	0.0	0.0	0.0	0.0	0.0	0.1
QJ01FA94	Tulathromycin	0.0	0.0	0.0	0.0	0.0	0.9
QJ01GA90	Dihydrostreptomycin	0.0	0.0	0.0	0.0	0.0	0.0
QJ01GB03	Gentamicin	0.0	0.0	0.0	0.0	0.0	0.0
QJ01GB05	Neomycin	0.0	0.0	0.0	0.0	0.0	0.5
QJ01MA90	Enrofloxacin	0.0	0.0	0.0	0.0	0.0	0.3
QJ01MA92	Danofloxacin	0.0	0.0	0.0	0.0	0.0	1.4
QJ01MA93	Marbofloxacin	0.0	0.0	0.0	0.0	0.0	0.7
QJ01RA01	Penicillins, combinations with other antibacterials	0.0	0.0	0.0	0.0	0.0	1.6
QJ01RA94	Lincosamides, combinations with other antibacterials	0.6	0.3	0.5	0.2	0.4	20.4
QJ01XQ01	Tiamulin	0.0	0.0	0.0	0.0	0.0	1.0
QJ01XQ02	Valnemulin	0.0	0.0	0.0	0.0	0.0	0.0
Total		2.2	2.0	1.8	1.8	1.9	100.0

Represented as a percentage of total antimicrobial consumption (expressed in $nADD_{kg}$/kg/year*)
*Treatment frequency: nADD, number of animal daily doses

TABLE 3: Therapy indications for antimicrobial treatments in farrow-to-finish (FtF), fattening and breeding pig farms (expressed in $nADD_{kg}$/kg/year*)

	Antimicrobial consumption, average values (2008–2011)					
	FtF farms (n=49)		Fattening farms (n=21)		Breeding farms (n=5)	
Therapy indication	$nADD_{kg}$/kg/year*	Per cent	$nADD_{kg}$/kg/year*	Per cent	$nADD_{kg}$/kg/year*	Per cent
Cannibalism	0.0	0.5	0.0	1.4	0.1	1.1
Chirurgical interventions	0.0	0.0	0.0	0.0	0.0	0.0
Digestive tract diseases	0.2	13.6	0.4	18.2	1.9	35.9
General infections	0.1	6.8	0.0	0.1	0.1	1.9
Gynaecological diseases	0.0	1.7	0.0	0.0	0.4	7.9
Infections/Inflammations	0.1	4.6	0.0	0.0	0.0	0.5
Infections with involvement of several organ systems	0.2	11.7	0.1	7.2	1.3	25.2
Injuries	0.0	0.3	0.0	0.2	0.1	1.1
'Implausible indications'	0.1	4.0	0.0	0.0	0.2	3.4
Mastitis metritis agalactia	0.0	3.0	0.0	1.3	0.1	1.5
Metaphylactic/prophylactic measures	0.4	29.1	1.0	46.1	0.1	1.5
Orthopaedic diseases	0.0	2.1	0.0	1.8	0.2	3.0
Other diseases	0.0	0.8	0.0	0.6	0.0	0.8
Respiratory tract diseases	0.3	21.9	0.6	23.2	0.9	16.1
Total	1.4	100.0	2.2	100.0	5.4	100.0

*Treatment frequency: nADD, number of animal daily doses

dispensed antibiotics are not always applied, as demonstrated in this study.

The next step to head for antimicrobial consumption analyses is the involvement of the end-user in data collection form, which was previously described in several studies (Chauvin and others 2002, Timmerman and others 2006, Stevens and others 2007, Jordan and others 2009, Menéndez González and others 2010, Moreno 2012). The plausibility control of the data showed that the collection of drug application data by the farmer is feasible, but associated with some limitations. Inaccurate information in farmers' records was frequently observed, but attention must be drawn to the fact that veterinarians' records were not completely plausible either. Analogous findings have also been described in another study (Menéndez González and others 2010). One can conclude from this that training courses and educational advertising both for farmers and veterinarians would be beneficial for the implementation of such a system.

The comparison between dispensed and applied drug amounts for the drug serial numbers revealed accordance in only 57 per cent of records. This might be due to the fact that the farmers could choose the following units from a drop-down list: ml, mg, g, kg, pieces or injectors. As a consequence, confusions in quantity units were foreseen. In response to the results of this study, the software of the given company will be extended with advanced automatic plausibility checks in the future. This upgrade includes:

TABLE 4: Active substances used for metaphylactic/prophylactic measures and respiratory tract diseases in farrow-to-finish (FtF) and fattening pig farms

		Percentage of total antimicrobial consumption in $nADD_{kg}$/kg/year*			
		Metaphylactic/prophylactic measures		Respiratory tract diseases	
ATCvet		FtF farms (n=49)	Fattening farms (n=21)	FtF farms (n=49)	Fattening farms (n=21)
Alimentary tract and metabolism					
QA07AA10	Colistin	34.4	0.0	0.0	0.0
QA07AA91	Gentamicin	0.1	0.0	0.0	0.0
Anti-infectives for systemic use					
QJ01AA02	Doxycycline	2.0	11.5	18.2	4.3
QJ01AA03	Chlortetracycline	0.0	0.0	0.3	0.0
QJ01AA06	Oxytetracycline	23.9	3.5	47.3	21.6
QJ01AA56	Oxytetracycline, combinations	0.0	0.7	0.0	0.9
QJ01BA90	Florfenicol	0.0	0.0	2.7	2.2
QJ01CA01	Ampicillin	0.0	0.0	0.0	0.0
QJ01CA04	Amoxicillin	7.2	0.4	5.9	47.6
QJ01CE09	Procaine benzylpenicillin	0.0	0.0	0.2	0.0
QJ01DD90	Ceftiofur	1.3	1.7	0.2	0.0
QJ01DE90	Cefquinome	0.0	0.0	1.2	1.8
QJ01EW10	Sulfadiazine and trimethoprim	0.0	0.0	1.1	8.1
QJ01EW11	Sulfamethoxazole and trimethoprim	3.3	0.0	0.0	0.2
QJ01FA90	Tylosin	1.3	3.1	2.0	2.4
QJ01FA91	Tilmicosin	0.0	0.0	0.9	0.0
QJ01FA94	Tulathromycin	1.2	0.0	4.3	0.0
QJ01GB05	Neomycin	3.2	0.0	0.0	0.0
QJ01MA90	Enrofloxacin	0.0	0.0	0.3	0.0
QJ01MA92	Danofloxacin	0.9	0.0	0.9	1.0
QJ01MA93	Marbofloxacin	0.1	0.0	0.8	0.4
QJ01RA01	Penicillins, combinations with other antibacterials	0.6	0.0	0.2	0.0
QJ01RA94	Lincosamides, combinations with other antibacterials	18.8	79.1	13.6	8.7
QJ01XQ01	Tiamulin	1.5	0.0	0.0	0.8
Total		100.0	100.0	100.0	100.0

Represented as a percentage of total antimicrobial consumption (expressed in $nADD_{kg}$/kg/year*)
*Treatment frequency: nADD, number of animal daily doses

TABLE 5: Descriptive statistics for the antimicrobial consumption at farm-level (expressed in $nADD_{kg}$/kg/year*)

	nADD$_{kg}$/kg/year*							
	N							
	Valid	Missing	Average	Min	q_{25}	Median	q_{75}	Max
Farrow-to-finish farms (n=49)								
2008	48	1	1.5	0.0	0.3	1.0	2.7	4.7
2009	48	1	1.5	0.0	0.3	0.9	2.3	5.8
2010	48	1	1.4	0.0	0.3	0.7	2.4	5.8
2011	49	0	1.2	0.0	0.3	0.6	1.7	4.7
Fattening farms (n=21)								
2008	19	2	3.5	0.0	0.8	2.3	6.5	12.8
2009	19	2	2.0	0.0	0.1	1.2	3.8	5.8
2010	19	2	1.6	0.0	0.0	0.3	2.4	9.3
2011	21	0	1.3	0.0	0.2	0.7	1.6	5.8
Breeding farms (n=5)								
2008	5	0	3.6	0.0	0.5	0.7	8.3	9.3
2009	5	0	3.5	0.0	0.6	0.9	7.7	14.0
2010	5	0	3.5	0.0	0.4	0.6	8.1	14.0
2011	5	0	5.0	0.0	0.8	2.2	10.5	15.1

*Treatment frequency: nADD, number of animal daily doses

automatic comparison between the entered drug amount and the recommended dosage according to the SPC; automatic comparison between the entered therapy indication and the indications given in the SPC; as well as a restriction of the available drug amount units (ml or g).

Expressing antimicrobial consumption in number of daily doses takes into account differences in potency of antimicrobial substances (Chauvin and others 2001). Whereas the defined daily dose in human medicine has been developed, an analogous daily dose for veterinary medicine has not been defined yet. The ADD_{kg} has been introduced by Jensen and others (2004) as the maintenance dose per day per kg biomass for a drug for its main indication in one species. The results of this study can be converted into the Belgian 'Treatment Incidence', which indicates how many animals per 1000 receive a daily dose of an antibiotic, by multiplying the daily doses per year with the factor 2.74 (Ghent University 2014). Thus, one can conclude that 1.9 ADD_{kg}/kg/year (average, 75 farms) is coequal to the treatment of 0.5 per cent of the study swine population per day. This is a relatively low consumption compared with other Austrian studies (Obritzhauser and others 2011). However, the treatment frequency expressed in nUDD showed an antimicrobial consumption of 4.9 UDD_{kg}/kg/year, which means that 1.3 per cent of the study swine population has been under antimicrobial treatment on a certain day. The UDD has been defined by Timmerman and others (2006) as the administered dose per day per kg biomass of a drug. It is based on real consumption and is independent of farmer's non-compliance; it may therefore describe the actual consumption more accurately than daily doses based on theoretical dosage recommendations.

One reason for the discrepancy between nADD and nUDD is underdosage. Other possible reasons could be an overestimation of the fixed ADDs, the application of different dosage regimen or the use for other therapy indications (Chauvin and others 2001). In Austria, dosage recommendations according to the SPC are widely divergent for one active substance, essentially complicating the fixation of ADDs. For this reason, the PrDD, which takes into account these differences in dosage recommendations, has been defined as a potential alternative to the ADD. Between the nPrDD and the nUDD, minor discrepancy was detected, which approves these considerations. Finally, it is important to state that the daily doses described in this and in other studies (Timmerman and others 2006, Menéndez González and others 2010, Obritzhauser and others 2011, Callens and others 2012) are developed at national level. As a consequence, a comparison of antimicrobial consumption between countries is not possible with these indicators.

The evaluation of the dosage accuracy revealed a high number of inappropriate dosages with an underdosage for orally and a correct/overdosage for parenterally applied antimicrobials. Similar results have been illustrated in other studies (Timmerman and others 2006, Regula and others 2009, Callens and others 2012). Misuse of antimicrobial substances in animal husbandry is assumed to be one main risk factor for the development and spread of resistant bacteria (Wise and others 1998, Aarestrup 2005). Catry and others (2003) pointed

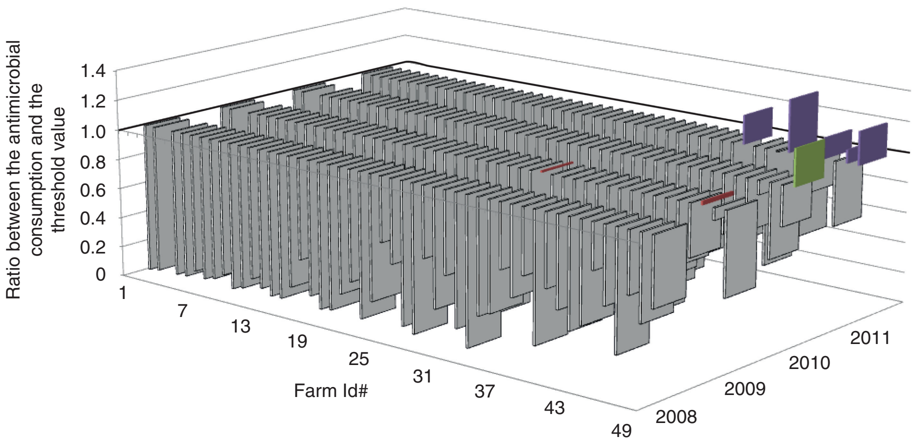

FIG 1: Exceeding of the threshold value (threshold value=q_{75}+(1.5×IQR) (Tukey 1977)) for the antimicrobial consumption (in number of animal daily doses per kg biomass per year - $nADD_{kg}$/kg/year) in 49 farrow-to-finish farms from 2008 until 2011. Ratios were calculated by dividing the antimicrobial consumption per farm by the threshold value. Consequently, a ratio of 1 represents an antimicrobial consumption equal to the threshold value. In the figure, farms with a higher consumption than the threshold value ('outlier farms') are coloured. Farms are sorted by their total consumption in four years

TABLE 6: Accurateness of drug dosage for oral and parenteral antimicrobial treatments in 75 conventional pig farms: UDD_{kg}/ADD_{kg}*,† ratios (ratio<0.75: underdosage; ratio>1.25: overdosage)

		Records (n=31,684)							
		Oral treatments				Parenteral treatments			
ATCvet	Active substance(s)	Underdosage (%)	Correct dosage (%)	Overdosage (%)	Total (n)	Underdosage (%)	Correct dosage (%)	Overdosage (%)	Total (n)
Alimentary tract and metabolism									
QA07AA01	Neomycin	100	0	0	16				
QA07AA10	Colistin	63	9	28	1024				
QA07AA91	Gentamicin	75	13	13	18				
Anti-infectives for systemic use									
QJ01AA02	Doxycycline	71	11	18	253				
QJ01AA03	Chlortetracycline	97	3	0	44				
QJ01AA06	Oxytetracycline	45	17	38	293	33	37	29	1508
QJ01AA56	Oxytetracycline, combinations	61	39	0	64				
QJ01BA90	Florfenicol	100	0	0	17	23	49	29	944
QJ01CA01	Ampicillin	71	14	14	17	33	20	47	60
QJ01CA04	Amoxicillin	81	4	15	819	19	48	33	6021
QJ01CE09	Procaine benzylpenicillin					17	20	63	694
QJ01DD90	Ceftiofur					19	59	22	1868
QJ01DE90	Cefquinome					8	60	32	5088
QJ01EW03	Sulfadimidine and trimethoprim					1	54	45	139
QJ01EW10	Sulfadiazine and trimethoprim	50	22	28	28	1	54	45	676
QJ01EW11	Sulfamethoxazole and trimethoprim	54	3	43	47	30	28	42	367
QJ01EW13	Sulfadoxine and trimethoprim					2	98	1	779
QJ01FA90	Tylosin	97	2	1	772	7	4	89	1025
QJ01FA91	Tilmicosin	60	20	20	18				
QJ01FA94	Tulathromycin					39	14	47	932
QJ01GA90	Dihydrostreptomycin					0	8	92	12
QJ01GB03	Gentamicin					98	1	1	93
QJ01GB05	Neomycin	12	85	2	61				
QJ01MA90	Enrofloxacin	100	0	0	319	9	66	24	1329
QJ01MA92	Danofloxacin					3	11	86	1679
QJ01MA93	Marbofloxacin					36	24	41	1239
QJ01RA01	Penicillins, combinations with other antibacterials					13	13	74	2453
QJ01RA94	Lincosamides, combinations with other antibacterials	67	12	22	506	35	42	23	343
QJ01XQ01	Tiamulin	49	11	40	45	59	40	2	63
QJ01XQ02	Valnemulin	100	0	0	11				
Total		75	8	17	4372	17	42	41	27,312

*UDD_{kg}: Used daily dose per kg biomass
†ADD_{kg}: Animal daily dose per kg biomass

out that the underdosage of antimicrobials might positively influence the occurrence of antimicrobial resistance. As approximately 86 per cent of antimicrobials were applied orally in this study, one can conclude that the main part of the therapies was given in an underdosed quantity. Reasons for under- or overdosages in prescribing antibiotics may be manifold and are thought to be a misestimating of the animal bodyweight (Timmerman and others 2006, Menéndez González and others 2010), economic motives on the farmer´s side or an intended overdosage for practical reasons. When interpreting these results, we must however consider that the UDD is strongly influenced by the treatment duration, the number of treated animals, the animal age class and the average weight of the animals. Implausibility concerning these four factors, especially differences between the average weight of the animals and the real bodyweight, might distort the results.

The mean over the study population per farm-type showed a high consumption for breeding farms; although, between-farm variability illustrated that breeding farms did generally not consume more antibiotics than FtF or fattening farms (median values). Responsible for the high consumption in means was one single breeding farm, consuming twice (2009) until almost fourfold (2011) the threshold value. The discrepancy between the mean and the evaluation at farm-level highlights the necessity for drug consumption analyses at farm-level, because farms using significantly higher amounts of antibiotics may strongly influence the results.

For evaluations, metaphylactic and prophylactic measures were consolidated in one category. They represented the main indication for antimicrobial therapy in FtF and fattening pig farms (29 and 46 per cent, respectively), which is an outcome also found in another study (Callens and others 2012). This proportion might even be higher, because an overlap of other therapy indications cannot be completely excluded. In Austria, the preventive treatment with antimicrobial substances is only allowed for metaphylactic reasons. Nevertheless, in the study at hand, metaphylactic measures only played a minor role, whereas prophylactic measures were much more often indicated. Apparently, high productivity pressure still leads the farmers to consult prophylactic antimicrobial treatment in order to reduce animal mortality.

The definition of a threshold value brought out the farms with a higher consumption than other farms within the same farm-type. In this study, the definition for outliers was fixed as threshold value, which is an arbitrary determination. In other countries, different thresholds are described (Alban and others 2013, Anonymous 2014). A significant correlation between the antimicrobial consumption and the farm size could not be detected. However, it is conspicuous that the breeding farm mentioned above not only showed the highest consumption but also kept the most animals. In contrast to this outcome, other researchers reported a higher antimicrobial consumption in association with smaller pig herds (Hybschmann and others 2011, Vieira and others 2011).

The usage of antimicrobials varied considerably between the farms, which has also been found out in other investigations (Timmerman and others 2006, Pol and Ruegg 2007, van der Fels-Klerx and others 2011, Moreno 2014). Reasons for high between-farm variations are supposed to be herd-specific diseases, differences in herd management systems or veterinarian prescription habits (Hybschmann and others 2011). In FtF farms, 61 per cent of the total consumption were administered at group-level, which is a low proportion compared to the other two farm-types. This is in line with their low share of orally applied antibiotics (80 v 93 per cent in fattening and 93 per cent in breeding farms) and their minor discrepancy between nUDD and nADD. One can conclude from this outcome that less treatment at group-level may result in a higher amount of parenterally applied antibiotics and consequently lead to a higher level of correct dosages.

The results of this study clearly underline the need for on-farm data for the measurement of antimicrobial use in veterinary medicine. However, further measures are necessary in order to improve data quality. It is important to note that the results of this study are not representative for the whole country because a sampling frame of 75 pig farms (representing about 3 per cent of the Austrian swine population) is too small. The non-finite evaluation possibilities that can be performed by means of those informative data must be emphasised. Well established and technically mature quality-assurance systems should be officially accredited in future. In particular, the labelling of each single drug package or flagon with a serial number was identified as a useful tool to check the plausibility of recorded drug amounts. For the interpretation of antimicrobial consumption, the unit of measurement is crucial. UDDs, ADDs and PrDDs could be used complementarily, representing real or standardised consumption, respectively.

Acknowledgements

A particular thank you goes to the company providing the data, and to their farmers and their veterinarians for participating in the study.

Funding This research was funded by the K-project PVM (Preventive Veterinary Medicine; project number 825339) handled by the Austrian FFG (The Austrian Research Promotion Agency) and by Vet-Austria, a cooperation among the Austrian Federal Ministry of Health, the Austrian Agency for Health and Food Safety and the University of Veterinary Medicine Vienna.

References

AARESTRUP, F. M. (2005) Veterinary drug usage and antimicrobial resistance in bacteria of animal origin. *Basic & Clinical Pharmacology & Toxicology* **96**, 271–281

ALBAN, L., DAHL, J., ANDREASEN, M., PETERSEN, J. V. & SANDBERG, M. (2013) Possible impact of the "yellow card" antimicrobial scheme on meat inspection lesions in Danish finisher pigs. *Preventive Veterinary Medicine* **108**, 334–341

ANGULO, F. J., NARGUND, V. N. & CHILLER, T. C. (2004) Evidence of an association between use of anti-microbial agents in food animals and anti-microbial resistance among bacteria isolated from humans and the human health consequences of such resistance. *Journal of Veterinary Medicine B* **51**, 374–379

ANONYMOUS (2009) Verordnung des Bundesministers für Gesundheit über die Anerkennung und den Betrieb von Tiergesundheitsdiensten (Tiergesundheitsdienst-Verordnung 2009 - TGD-VO 2009), Bundesgesetzblatt II Nr. 434/2009, Austria. www.ris.bka.gv.at

ANONYMOUS (2014) Gesetz über den Verkehr mit Arzneimitteln (Arzneimittelgesetz – AMG). "Arzneimittelgesetz in der Fassung der Bekanntmachung vom 12. Dezember 2005 (BGBl. I S. 3394), das durch Artikel 2a des Gesetzes vom 27. März 2014 (BGBl. I S. 261) geändert worden ist"

CALLENS, B., PERSOONS, D., MAES, D., LAANEN, M., POSTMA, M., BOYEN, F., HAESEBROUCK, F., BUTAYE, P., CATRY, B. & DEWULF, J. (2012) Prophylactic and metaphylactic antimicrobial use in Belgian fattening pig herds. *Preventive Veterinary Medicine* **106**, 53–62

CATRY, B., LAEVENS, H., DEVRIESE, L. A., OPSOMER, G. & DE KRUIF, A. (2003) Antimicrobial resistance in livestock. *Journal of Veterinary Pharmacology and Therapeutics* **26**, 81–93

CHAUVIN, C., BELOEIL, P. A., ORAND, J. P., SANDERS, P. & MADEC, F. (2002) A survey of group-level antibiotic prescriptions in pig production in France. *Preventive Veterinary Medicine* **55**, 109–120

CHAUVIN, C., MADEC, F., GUILLEMOT, D. & SANDERS, P. (2001) The crucial question of standardisation when measuring drug consumption. *Veterinary Research* **32**, 533–543

EMA (2013) European Surveillance of Veterinary Antimicrobial Consumption. "Sales of veterinary antimicrobial agents in 25 EU/EEA countries in 2011" (EMA/236501/2013)

EMEA (1999) Antibiotic Resistance in the European Union Associated with Therapeutic Use of Veterinary Medicines. Report and Qualitative Risk Assessment by the Committee for Veterinary Medicinal Products. London, July 14, 1999 (EMEA/CVMP/342/99-corr-Final)

FUCHS, K. & OBRITZHAUSER, W. (2010) Modelling the consumption of antimicrobials in Austrian cattle, pigs and poultry production. AGES, Final report. (Methodenvergleich zur Erfassung von Antibiotikamengenströmen im Veterinärbereich in Österreich. Forschungsendbericht der AGES), in German

GHENT UNIVERSITY (2014) ABcheck: Check, improve and reduce! www.abcheck.ugent.be/v2/about/met/. Accessed 2014

GRAVE, K., JENSEN, V. F., MCEWEN, S. & KRUSE, H. (2006) Monitoring of antimicrobial drug usage in animals: methods and applications. In *Antimicrobial Resistance in Bacteria of Animal Origin*. Ed. F. M. Aarestrup. *ASM Press*. pp 375–395

HYBSCHMANN, G. K., ERSBØLL, A. K., VIGRE, H., BAADSGAARD, N. P. & HOUE, H. (2011) Herd-level risk factors for antimicrobial demanding gastrointestinal diseases in Danish herds with finisher pigs: a register-based study. *Preventive Veterinary Medicine* **98**, 190–197

JENSEN, V. F., JACOBSEN, E. & BAGER, F. (2004) Veterinary antimicrobial-usage statistics based on standardized measures of dosage. *Preventive Veterinary Medicine* **64**, 201–215

JORDAN, D., CHIN, J. J.-C., FAHY, V. A., BARTON, M. D., SMITH, M. G. & TROTT, D. J. (2009) Antimicrobial use in the Australian pig industry: results of a national survey. *Australian Veterinary Journal* **87**, 222–229

MENÉNDEZ GONZÁLEZ, S., STEINER, A., GASSNER, B. & REGULA, G. (2010) Antimicrobial use in Swiss dairy farms: quantification and evaluation of data quality. *Preventive Veterinary Medicine* **95**, 50–63

MERLE, R., HAJEK, P., KÄSBOHRER, A., HEGGER-GRAVENHORST, C., MOLLENHAUER, Y., ROBANUS, M., UNGEMACH, F.-R. & KREIENBROCK, L. (2012) Monitoring of antibiotic consumption in livestock: a German feasibility study. *Preventive Veterinary Medicine* **104**, 34–43

MORENO, M. A. (2012) Survey of quantitative antimicrobial consumption in two different pig finishing systems. *The Veterinary Record* **171**, 325

MORENO, M. A. (2014) Survey of quantitative antimicrobial consumption per production stage in farrow-to-finish pig farms in Spain. *The Veterinary Record Open* **1**, 1–10

NICHOLLS, T., ACAR, J., ANTHONY, F., FRANKLIN, A., GUPTA, R., TAMURA, Y., Thompson, S., Threlfall, E. J., Vose, D., van Vuuren, M., White, D. G., Wegener, H. C., Costarrica, M. L.; OFFICE INTERNATIONAL DES EPIZOOTIES AD HOC GROUP (2001) Antimicrobial resistance: monitoring the quantities of antimicrobials used in animal husbandry. *Revue scientifique et technique (International Office of Epizootics)* **20**, 841–847

OBRITZHAUSER, W., FUCHS, K., KOPACKA, I. & KÖFER, J. (2011) Estimating the consumption of antibiotics in Austrian cattle, pig an poultry production. Proceedings of the XVth ISAH Congress. Vol. **1**. Eds J. KÖFER & H. SCHOBESBERGER. Vienna, Austria, July 3 to 7, 2011. pp 585–587

POL, M. & RUEGG, P. L. (2007) Treatment practices and quantification of antimicrobial drug usage in conventional and organic dairy farms in Wisconsin. *Journal of Dairy Science* **90**, 249–261

REGULA, G., TORRIANI, K., GASSNER, B., STUCKI, F. & MÜNTENER, C. R. (2009) Prescription patterns of antimicrobials in veterinary practices in Switzerland. *The Journal of Antimicrobial Chemotherapy* **63**, 805–811

STATISTICS AUSTRIA (2014) Livestock Survey. Data from 2012 and 2013. www.statistik.at

STEVENS, K. B., GILBERT, J., STRACHAN, W. D., ROBERTSON, J., JOHNSTON, A. M. & PFEIFFER, D. U. (2007) Characteristics of commercial pig farms in Great Britain and their use of antimicrobials. *The Veterinary Record* **161**, 45–52

TIMMERMAN, T., DEWULF, J., CATRY, B., FEYEN, B., OPSOMER, G., DE KRUIF, A. & MAES, D. (2006) Quantification and evaluation of antimicrobial drug use in group treatments for fattening pigs in Belgium. *Preventive Veterinary Medicine* **74**, 251–263

TOLLEFSON, L. & MILLER, M. A. (2000) Antibiotic use in food animals: controlling the human health impact. *Journal of AOAC International* **83**, 245–254

TUKEY, J. W. (1977) Exploratory Data Analysis. Addison-Wesley

VAN DEN BOGAARD, A. E. & STOBBERINGH, E. E. (2000) Epidemiology of resistance to antibiotics. Links between animals and humans. *International Journal of Antimicrobial Agents* **14**, 327–335

VAN DER FELS-KLERX, H. J., PUISTER-JANSEN, L. F., VAN ASSELT, E. D. & BURGERS, S. L. G. E. (2011) Farm factors associated with the use of antibiotics in pig production. *Journal of Animal Science* **89**, 1922–1929

VIEIRA, A. R., PIRES, S. M., HOUE, H. & EMBORG, H.-D. (2011) Trends in slaughter pig production and antimicrobial consumption in Danish slaughter pig herds, 2002–2008. *Epidemiology and Infection* **139**, 1601–1609

WHO (1997) The Medical Impact of Antimicrobial Use in Food Animals. Report of a WHO Meeting, Berlin, Germany, October 13 to 17 1997, (WHO/EMC/ZOO/97.4)

WHO (2012) Critically Important Antimicrobials for Human Medicine. 3rd edn. 2011. ISBN 978 92 4 150448 5

WISE, R., HART, T., CARS, O., STREULENS, M., HELMUTH, R., HUOVINEN, P. & SPRENGER, M. (1998) Antimicrobial resistance : is a major threat to public health. *British Medical Journal* **317**, 609–610