

# Changes in the use of antimicrobials and the effects on productivity of swine farms in Denmark

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**Objective**—To evaluate changes in antimicrobial consumption and productivity by Danish swine farms during 1992 to 2008.

**Sample Population**—All Danish swine farms for antimicrobial consumption data and a representative sample of Danish swine herds for productivity data.

**Procedures**—Antimicrobial consumption by Danish swine farms from 1992 to 2008 was determined and evaluated in light of policies to regulate antimicrobial consumption, changes in disease patterns, and productivity data. Trend analyses of productivity data were conducted before and after a ban on use of antimicrobial growth promoters (AGPs).

**Results**—Antimicrobial consumption peaked at 100 mg/kg of swine produced in 1992, decreased to 31 mg/kg in 1999, and increased to 49 mg/kg in 2008. Key factors for changes were regulations banning subtherapeutic use of antimicrobials and veterinary profits from the prescription and sale of antimicrobials in 1994 and termination of AGP use by January 2000. Pig production increased from 18.4 to 27.1 million pigs, and the mean number of pigs per sow per year raised for slaughter increased from 21 in 1992 to 25 in 2007. Average daily gain for weaning (< 35 kg) and finishing (> 35 kg) pigs was higher in 2008 than in 1992, but mortality rates for weaning and finishing pigs were similar in 1992 and 2008.

**Conclusions and Clinical Relevance**—From 1992 to 2008, antimicrobial consumption per kilogram of pig produced in Denmark decreased by > 50%. Furthermore, there was improvement in productivity, suggesting that long-term swine productivity was not negatively impacted by a ban on AGP use. (*Am J Vet Res* 2010;71:726–733)

Soon after their discovery, antimicrobials were used in veterinary medicine for the treatment of bacterial diseases and were also incorporated in animal feed as AGPs.<sup>1</sup> Since the 1950s, antimicrobials have become an integrated part of food animal production, with large quantities of antimicrobials used in food animal production systems globally.<sup>2</sup> However, because of concerns regarding antimicrobial-resistant bacteria being transmitted from food animals to humans, efforts have been launched throughout the world to promote the prudent use of antimicrobials in food animals.<sup>3,4</sup> The criteria that constitute prudent use of antimicrobials among differing production systems continue to be debated. In particular, the widespread subtherapeutic and routine in-feed use of antimicrobials for growth promotion has been a subject of controversy.

Swine are the main food animal species in Denmark. Approximately 90% of pork produced in Denmark is ex-

## ABBREVIATIONS

ADG	Average daily gain
AGP	Antimicrobial growth promoter
PMWS	Porcine multisystemic wasting syndrome
PRRS	Porcine reproductive and respiratory syndrome

ported, and Denmark is the largest exporter of pork in the world. The consumption of antimicrobial agents by food animals, including swine, has been monitored since 1990.<sup>5</sup> Many factors, including regulatory actions taken by the national authorities in Denmark and the European Union authorities, have influenced the amount and pattern of use of antimicrobials in animals during the past 2 decades. To our knowledge, the change in consumption over these 2 decades and the potential impact on swine productivity and health have not been evaluated.

The purpose of the study reported here was to assess the changes in consumption of antimicrobial agents by swine farms in Denmark from 1992 to 2008, evaluate the effects of factors (eg, regulatory actions, changes in productivity, or emergence of novel diseases) that might affect antimicrobial use, and determine the impact on health and productivity of swine in Denmark.

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## Materials and Methods

**Sample population**—Data for the total production of swine in Denmark were collected from an online database.<sup>a</sup> The consumption of antimicrobial agents by swine farms in Denmark is reported<sup>5</sup> annually. The National Committee for Pig Production operates a swine production records system. Approximately 10% of Danish swine producers voluntarily submit data to the records system on a monthly basis. The records system operates as an efficiency control program for benchmarking production characteristics of swine farms; it was assumed that the production trends determined over time by this program were representative for all swine producers. The sample size during 1992 to 2008 varied from 147 to 2,237 herds/y for herds comprising weaning pigs (< 35 kg) and 282 to 1,742 herds/y for herds comprising finishing pigs (> 35 kg). Results were reported as the mean value of data for 1 year based on records of a minimum of 170 continuous days during a period starting on August 15 and ending on November 14 of the following year.<sup>6-10</sup>

**Policies and regulations limiting the use of antimicrobials**—In Denmark, a veterinary prescription is required for the use of antimicrobials for disease control. In 1994, public discussions regarding the increased consumption of relatively inexpensive and extemporaneously prepared tetracycline antimicrobials on swine farms prompted the Danish authorities to pass regulations that limited veterinary profits from the prescription and sale of antimicrobials and banned the prophylactic use of antimicrobials in food animals. The new legislation comprised several components. Restrictions were imposed that prohibit the use of extemporaneously prepared drugs when medicinal products could be used for a specific therapeutic indication. Limitations were placed on a veterinarian's ability to prescribe antimicrobial drugs to a maximum of 5 days of treatment for a specifically diagnosed disease, unless herd health contracts between the veterinarian and farmer allowed prescription for up to 35 days of treatment for a diagnosed disease or a disease that was expected in the pigs on the basis of the veterinarian's knowledge of the herd. It was mandated that a veterinarian register the use and delivery of drugs to farmed animals and maintain records of this use (available for inspection by veterinary officials for 3 years). It allowed a pharmacy to divide large boxes that contain several packages into single packages of antimicrobials to sell smaller quantities of antimicrobials at the same price as did veterinarians. Finally, it prohibited pharmacies and the pharmaceutical industry from offering economic incentives to veterinarians or others for the purpose of increasing product sales.

In an attempt to guide the choice of antimicrobial agents, detailed treatment guidelines for veterinarians were developed, and they have been updated annually since 1996.<sup>11</sup> These guidelines have been developed in collaboration with the relevant government authority, practicing veterinarians, and experts employed by universities. The guidelines provide specific recommendations for the selection of the appropriate antimicrobials for the treatment of all common indications in major food animal species.

In 2002, a new regulation was adopted that limited a veterinarian's ability to prescribe fluoroquinolones to animals raised for food consumption. A veterinarian can prescribe a fluoroquinolone for use in food animals only if the need for use can be documented and it can be determined that other approved drugs are ineffective. Furthermore, it is mandatory for the veterinarian to notify the district veterinary officer of this prescription.

**Actions limiting the use of AGPs**—In Europe, the use of antimicrobials in low doses as feed additives for growth promotion is not regarded as disease control and, consequently, has not required veterinary oversight or a prescription. Contrary to the situation in the United States, all other uses, which include in-feed and in-water use of antimicrobials for metaphylaxis and prophylaxis, require a prescription from a licensed veterinarian.

Concerns were raised during the 1960s in some European countries that the use of antimicrobials in food animals could lead to infections with resistant organisms in humans<sup>12</sup>; this prompted a ban on the use of antimicrobials for growth promotion in food animals if these antimicrobials were also important for therapeutic use in humans. This action was enforced on individual antimicrobials and did not consider potential resistance problems from the use of other antimicrobials belonging to the same class of drug. Thus, a number of antimicrobial compounds belonging to classes of drugs also used for treatment of domestic animals and humans were used as AGPs. Subsequently, this oversight may have allowed for the selection of bacterial resistance to other therapeutic drugs.<sup>1,13</sup> In 1995, glycopeptide-resistant enterococci were detected in pig and poultry production systems.<sup>1,13</sup> This prompted the Danish government to ban the use of avoparcin as an AGP. Furthermore, results of research in Denmark and other countries resulted in a ban for all use of avoparcin in the European Union in 1996. The Danish government banned the use of virginiamycin as an AGP in food animals in 1998.<sup>1,11</sup> This was followed by an overall ban of virginiamycin, bacitracin, tylosin, and spiramycin by the European Union in 1998. In 2003, the European Union made the decision to phase out all use of AGPs by the beginning of 2006.<sup>14</sup> However, the Danish swine industry decided to stop all use of AGPs in finishing pigs by April 1998 and in all swine by January 2000.

**Statistical analysis**—Trends in productivity data over time were analyzed via linear regression models by use of a statistical software package.<sup>b</sup> Data were analyzed by use of both mixed and generalized linear models. Outcome variables were the various productivity data (ie, ADG in weaning and finishing pigs, mortality rate of weaning pigs, percentage of dead and condemned finishing pigs, number of feed units [usable energy in 1 kg of barley {ie, 7.72 MJ}]/kg of gain in finishing pigs, number of pigs produced per sow per year, and total production of pigs). The explanatory variable was time (continuous variable). Additionally, time was coded as a categorical variable with the first category defined as the time period (1993 to 1998 for finishing pigs and 1993 to 1999 for weaning pigs) before the ban

Table 1—Mean number of feed units\* per kilogram of gain for weaning and finishing pigs raised in Danish swine production systems from 1996 to 2008.†

Type of pig	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
Weaning‡	—	—	—	—	—	—	—	1.97	2.06	2.07	2.04	2.02	1.97
Finishing§	2.94	2.91	2.9	2.89	2.89	2.89	2.88	2.86	2.87	2.88	2.87	2.89	2.83

\*Given as the useable energy in 1 kg of barley (ie, 7.72 MJ). †Productivity data for the Danish swine industry were collected beginning on August 15 and ending on November 14 of the following year and reported as the year in which the data collection period terminated. ‡Weaning refers to pigs that weighed < 35 kg. §Finishing refers to pigs that weighed > 35 kg. — = Not reported.

on AGP use and the second category defined as the time period after the ban on AGP use. An interaction between time and time before and after the ban on AGP use was included in the model to determine whether the trend in productivity data was significantly different before and after the ban on AGP use. Data for dead and condemned finishing pigs and the mortality rate of weaning pigs were transformed by use of the arc-cosine function. Then, 2 separate models were fitted to both outcome variables (1 model in which the outcome was not transformed for each variable and 1 model in which the outcome was transformed for each variable). The number of farms that provided productivity data varied from year to year; to adjust for this variation in the analyses, data from each year were weighted by the square root of the number of farms reporting productivity for that respective year. A value of  $P < 0.05$  was considered significant for all analyses.

## Results

**Evaluation of statistical methods**—Results from the data analysis did not differ significantly between the mixed and generalized linear models. Results of the analyses performed by use of transformed versus nontransformed outcome variables did not differ significantly. Therefore, only the results of the nontransformed outcome were reported. In addition, a dramatic change was observed in the mortality rate of weaning pigs after 2004. Therefore, trend analysis for the mortality rate of weaning pigs was only performed from 1992 until 2004.

### PRODUCTIVITY IN DANISH SWINE PRODUCTION

Data for the number of feed units per kilogram of gain in weaning pigs were unavailable from 1996 through 2002 (Table 1). The number of feed units per kilogram of gain in weaning pigs peaked in 2005; the value then remained relatively constant in 2006 and 2007, but decreased in 2008 to reach a value similar to that for 2005.

Total production of weaning pigs in Denmark was not affected by the ban on AGP use. Analysis of data obtained from a database<sup>a</sup> revealed that production of weaning pigs increased from 18.4 million pigs in 1992 to 27.1 million pigs in 2008, which was an increase of 47% (Figure 1). The number of pigs per sow per year steadily increased from approximately 21 to 25 during the 15-year study period. However, the increase was significantly higher after the ban on AGP use, compared with results for the period before the ban on AGP use (Table 2).

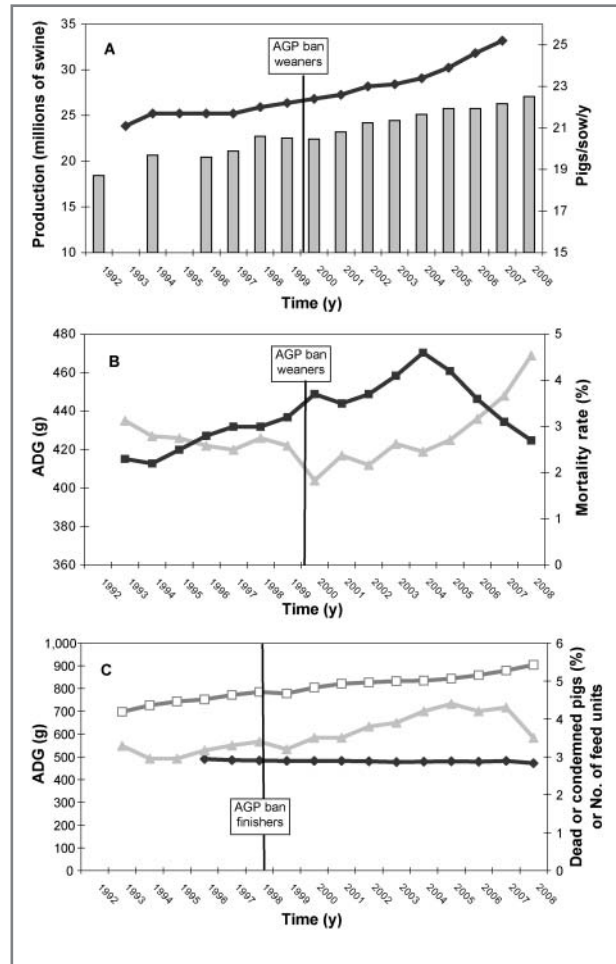


Figure 1—Data<sup>d</sup> of production characteristics for total production of pigs (millions of swine; gray bars) and mean number of pigs farrowed per sow per year (black diamonds; A), ADG (gray triangles) and mortality rate (black squares) in weaning pigs (B), and ADG (white squares), number of feed units (black diamonds) and the percentage of dead or condemned finishing pigs (gray triangles; C) raised in the Danish swine production system from August 15, 1991, through November 14, 2007. Data for total pig production were collected during the calendar year from January 1 through December 31; all other production values were collected from August 15 through November 14 of the following year and reported as the year in which the data collection period terminated. The ban on AGP use (vertical line) was instituted on April 1, 1998, and January 1, 2000, for finishing and weaning pigs, respectively. Weaning and finishing pigs weighed < 35 kg and > 35 kg, respectively.

As a result of the dramatic change observed in the mortality rate of weaning pigs after 2004, trend analysis of the mortality rate of weaning pigs was only performed from 1992 through 2004. A significant increase

Table 2—Results from statistical models constructed for reported variables of production data recorded from a database<sup>c</sup> for weaning (< 35 kg) and finishing (> 35 kg) pigs raised in the Danish swine production system from 1993 to 2008.

Variable	Effect	Estimate	SE	P
No. of pigs produced*	Intercept	18,327.00	266.89	—
	Year	511.84	29.61	< 0.001
No. of pigs born/sow†	Intercept	21.19	0.17	—
	Year	0.13	0.05	< 0.001
	After ban on AGP use	-1.97	0.47	0.002
	Prior to ban on AGP use	0	—	—
	Year after ban on AGP use*	0.24	0.06	0.003
Year prior to ban on AGP use*	0	—	—	
ADG of weaning pigs	Intercept	432.76	4.17	—
	Year	-1.87	1.00	0.009
	After ban on AGP use	-77.87	11.39	< 0.001
	Prior to ban on AGP use	0	—	—
	Year after ban on AGP use*	7.90	1.35	< 0.001
Year prior to ban on AGP use*	0	—	—	
Mortality rate of weaning pigs‡	Intercept	1.95	0.09	—
	Year	0.19	0.01	< 0.001
ADG of finishing pigs	Intercept	685.72	7.35	—
	Year	17.47	2.22	< 0.001
	After ban on AGP use	30.12	11.65	0.024
	Prior to ban on AGP use	0	—	—
	Year after ban on AGP use*	-6.80	2.37	0.014
Year prior to ban on AGP use*	0	—	—	
Mortality rate of finishing pigs§	Intercept	2.87	0.12	—
	Year	0.09	0.01	< 0.001
Feed unit/kg of gain in finishing pigs	Intercept	2.94	0.01	—
	Year	-0.01	0.00	< 0.001

\*Analyses included data from 1992. †Analyses included data from 1993 through 2007. ‡Analyses included data from 1993 through 2004 because of a reduction in mortality rate during 2004 through 2008 (ie, from 4.6% to 2.7%). §Analyses did not include data from 2008 because of a major reduction in mortality rate (ie, from 4.3% in 2007 to 3.5% in 2008).  
— = Not reported.

in mortality rate of weaning pigs was observed during the study period. However, this was not significantly different when compared with the mortality rate before and after the ban on AGP use.

Among finishing pigs, a significant decrease in feed unit per kilogram of gain was observed over time. Time (categorical variable) before and after the ban on AGP use did not have a significant effect, and there was no significant interaction between these 2 variables. However, as a result of an insufficient number of observations reported before the ban on AGP use, it was not possible to determine whether the apparent trend was significantly different.

The ADG of weaning pigs significantly decreased from 1992 until shortly after the ban on AGP use in January 2000; ADG significantly increased thereafter. Mortality rate of weaning pigs increased after 1994, peaked in 2004, and decreased from 2005 through 2008. The ADG for finishing pigs increased during the period from 1992 through 2008. Trend analysis indicated that this increase was significant over time. However, the increase in ADG was greater before the ban on AGP use than after the ban.

The percentage of dead and condemned finishing pigs increased from 1992 through 1998; there was a decrease in this rate after the ban on AGP use in finishing swine in 1998. However, the percentage of dead and

condemned finishing pigs again increased from 3.2% in 1999 to 4.4% in 2005, which was followed by a reduction to 3.5% in 2008. The increase in the percentage of dead and condemned finishing pigs was significant over time. However, this trend did not differ significantly before and after the ban on AGP use.

#### CONSUMPTION OF ANTIMICROBIALS OVER TIME

Following the implementation of laws that restricted veterinary profits from antimicrobial sales in May 1995, analysis of data obtained from an aforementioned database<sup>5</sup> revealed that there was a reduction in the consumption of antimicrobials (especially tetracyclines) used for therapeutic indications (Table 3). The ban on AGP use of avoparcin (May 1995) and virginiamycin (January 1998) had no or only a marginal effect on the consumption of antimicrobials for therapeutic indications and on overall antimicrobial consumption (Figure 2). The phasing out of AGP use in finishing pigs did not result in immediate changes in antimicrobial consumption for therapeutic indications. In 1996, there was an outbreak of PRRS that involved > 1,100 Danish swine herds.<sup>15,c</sup> However, this event did not appear to influence the consumption of antimicrobial agents for therapeutic indications.

Following the termination of AGP use in all pigs by January 2000, there was an increase in antimicrobial



Table 3—Change in antimicrobial consumption\* for the Danish swine production system relative to pork production from 1992 to 2008.

Variable	1992	1994	1995	1996	1997	1998	1999	2000	2001	2002	2003	2004	2005	2006	2007	2008
Production (millions of kg of pigs produced)	1,442	1,604	1,582	1,592	1,639	1,770	1,781	1,748	1,836	1,892	1,898	1,967	1,988	1,957	2,046	1,985
<b>Therapeutic use</b>																
Tetracyclines	13.7	20.5	5.1	7.3	7.5	6.2	8.2	12.4	14.0	11.8	13.2	14.0	14.1	15.5	17.4	17.3
Macrolides, lincosamides, and pleuromutilins	1.1	6.3	5.3	4.2	3.5	3.5	4.3	7.9	8.8	9.2	8.5	11.6	11.0	10.5	11.0	12.8
Aminoglycosides	7.9	4.1	3.7	3.4	2.8	3.3	3.2	4.5	4.9	5.0	5.2	5.0	4.6	4.4	3.2	2.4
β-lactamase sensitive-type penicillins	4.5	3.5	3.3	2.7	4.1	4.8	5.0	5.2	5.4	5.9	6.7	7.6	8.0	8.2	8.2	8.3
Other penicillins and cephalosporins	2.8	1.7	1.8	2.3	2.3	2.3	2.3	2.6	3.1	3.6	4.2	5.1	4.7	4.3	4.2	4.0
Sulfonamide and trimethoprim	4.0	4.0	2.2	1.8	2.1	2.1	1.8	1.9	2.3	2.6	2.5	2.6	2.7	3.1	3.0	3.9
Other antimicrobials†	4.2	2.4	1.0	0.2	0.2	0.2	0.1	0.1	0.1	0.1	0.2	0.2	0.2	0.2	0.2	0.2
Total of therapeutic use‡	38.2	40.0	21.3	21.7	22.4	22.3	24.8	34.4	38.5	38.1	40.3	45.1	46.0	46.0	47.0	48.9
Estimated AGP use	62.2	58.6	51.2	59.1	58.8	26.6	6.5	0	0	0	0	0	0	0	0	0
Total antimicrobial use§	100.4	98.6	72.5	80.8	81.2	48.9	31.3	34.4	38.5	38.1	40.3	45.1	46.0	46.0	47.0	48.9

\*Antimicrobial consumption is defined as the number of milligrams of active compound consumed per kilogram of pig produced. †Other includes colistin, fluoroquinolones, metronidazole, and nitrofurantoin. ‡Results only include data for antimicrobials used for therapeutic indications in swine. Prior to 2001, consumption of antimicrobials for therapeutic indications in swine was estimated from the total consumption for pigs, assuming that 90% of the macrolide-lincosamide-pleuromutilin group, 77% of aminoglycosides, 90% of tetracyclines, 62% of β-lactamase sensitive-type penicillins, and 64% of the remaining penicillin and cephalosporin groups were used to treat swine (2001 and 2002 data<sup>4</sup>). §Combines the results of antimicrobials used for therapeutic indications and the estimated amount of antimicrobials used as an AGP.

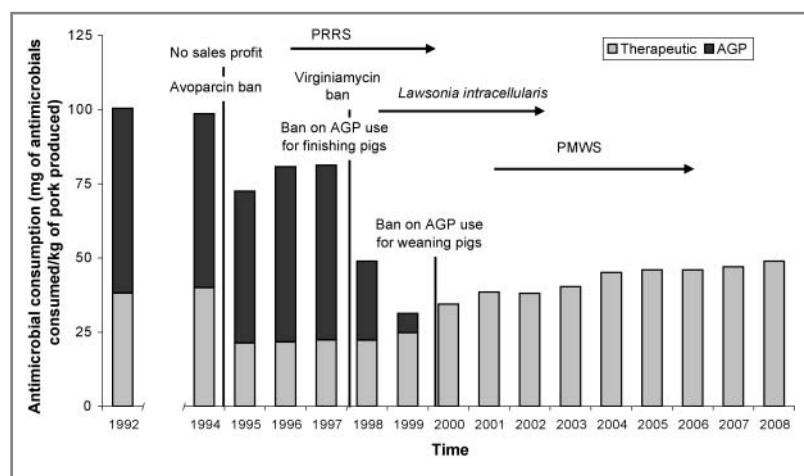


Figure 2—Consumption of antimicrobials for use as AGPs (black bars) or for therapeutic administration (gray bars) from 1992 to 2007 by the Danish swine production system. Notice the ban on use of avoparcin and on veterinary profits from the prescription and sale of antimicrobials, the ban on AGP use in finishing pigs and on use of virginiamycin in all pigs that was instituted in 1998, and the ban on AGP use in weaning pigs that was instituted in January 2000. Outbreaks of PRRS (1996 to 2000), disease attributable to *Lawsonia intracellularis* (1998 to 2002), and PMWS (2001 to 2006) are indicated (arrows). Weaning and finishing pigs weighed < 35 kg and > 35 kg, respectively.

consumption for therapeutic indications in 2000 and 2001. This increase may have been caused by a concurrent outbreak of disease caused by *Lawsonia intracellularis* in weaning pigs.<sup>16</sup> In 2001, PMWS was first diagnosed in a Danish herd; this disease affected 626 herds by December 2005.<sup>17</sup> Since 2002, the consumption of antimicrobials has continued to increase with minor fluctuations; this increase in antimicrobial consumption was mainly the result of the increased use of tetracycline and macrolide antimicrobials. The main AGP used in pigs before the ban on AGP use was tylosin, which was also the main macrolide antimicrobial

used for therapeutic indications. The total consumption of macrolides used as an AGP and for therapeutic indications decreased from 62,959 kg in 1997 to 11,446 kg in 2008; this corresponded to a decrease of 82% for antimicrobial consumption per pig produced.

## Discussion

The study reported here was an observational study of the relationship between data reported on productivity characteristics of the Danish swine production system and consumption of antimicrobial agents from 1992 to 2008. The reduction in antimicrobial consumption from 1994 to 1995 can be explained by the limitation of sales incentives paid to veterinarians imposed by Danish authorities. The ban on use of avoparcin and virginiamycin (1995 and 1998, respectively) and the prohibition of all AGP use in finishing pigs (after April 1998) appeared to have only a limited effect, if any, on the amount of other

antimicrobials used for therapeutic indications; this is in agreement with the findings of a herd-level study.<sup>18</sup>

In 1996, an attenuated vaccine against PRRS was used in > 1,100 Danish swine herds to vaccinate 3- to 18-week-old pigs.<sup>15,c</sup> Unfortunately, this strain reverted to virulence and further advanced the spread of PRRS in Denmark.<sup>15,c</sup> However, this did not seem to influence the consumption of antimicrobials for therapeutic indications. The complete cessation of all AGP use by January 2000 coincided with an increase in the consumption of antimicrobials for therapeutic indications. The ban on AGP use in weaning pigs appears to be the most

likely explanation, although the concurrent outbreak of disease attributable to *Lawsonia intercellularis* in Danish swine herds<sup>16</sup> may have contributed to this as well.

From 2001 to 2002, there was a minor reduction in antimicrobial consumption. In 2001, PMWS was first diagnosed in a Danish herd; since that time, the number of herds with PMWS has increased substantially, especially during 2003 to 2005.<sup>17</sup> By December 2005, PMWS had been diagnosed in 626 herds by personnel at the diagnostic laboratory at the National Veterinary Institute. The occurrence of PMWS can cause a significant increase in antimicrobial use at the farm level, with use being greater in sows than in weaning pigs.<sup>19</sup> Thus, PMWS may explain a portion of the increasing antimicrobial consumption in weaning pigs and sows from 2002 to 2004 and the increase in antimicrobial consumption in weaning pigs from 2004 to 2005; this is supported by the geographic distribution of PMWS and increasing antimicrobial use during these years, both of which were localized almost entirely in Jutland and Funen, Denmark.<sup>5</sup>

The continued increase in antimicrobial consumption during 2006 to 2008 is more difficult to explain. It is highly unlikely that this increase can be related to the ban on AGP use that was enacted almost 10 years earlier. Increased antimicrobial consumption was not associated with an increase in the mortality rate of weaning pigs, which has decreased since 2004. One explanation could be the large reduction (50%) in the purchase price of some of the commonly used antimicrobials (eg, tetracycline, tiamulin, and tylosin), which has made it much cheaper to use antimicrobials rather than other disease control measures such as vaccination and infection control practices. These aspects must be investigated.

It is important to recognize that the different classes of antimicrobials are not of equal importance for human and food animal health.<sup>20</sup> Thus, an overall reduction in antimicrobial consumption could be associated with a negative impact on the health of humans or food animals if the consumption was changed toward more critically important drugs. Therefore, it is also important to notice that the main increase in therapeutic antimicrobials has been in macrolides and tetracyclines and not in more potent drugs such as third-generation cephalosporins and fluoroquinolones. Before 2001, third- and fourth-generation cephalosporins and fluoroquinolones were not separately registered, but instead they were summed together with other  $\beta$ -lactam antimicrobials (ie,  $\beta$ -lactam and other penicillins) and other antimicrobials (ie, colistin, metronidazole, and nitrofurantoin), respectively. However, the use of third- and fourth-generation cephalosporin antimicrobials has gradually increased from approximately 0.04% of total antimicrobial consumption for swine in 2001 to 0.13% in 2008. Fluoroquinolone consumption has decreased from 0.13% for swine in 2001 to almost nothing (total registered use, 5 g) in 2008.

Few estimates exist on antimicrobial consumption for food animal production in other countries. In 1999, before the ban on AGP use, the European Medicines Agency estimated the consumption for AGP use and therapeutic indications for 1996 and compared this val-

ue with food animal production in 15 European countries during 1997.<sup>21</sup> Mean consumption was 98 mg of antimicrobials/kg of meat and poultry produced (range, 24 to 184 mg/kg). In the United States, there are different estimates of antimicrobial consumption. One estimate<sup>22</sup> was 12,630,000 kg for consumption in all animal species (including companion animals) in 2007, whereas another estimate was 11,158,000 kg for nontherapeutic use in cattle, pigs, and poultry in 1999.<sup>23</sup> However, the certainty of these estimates<sup>22,23</sup> is unknown. Total meat production in the United States was 37,258,500,000 kg in 1999 and 41,809,400,000 kg in 2007.<sup>4</sup> Thus, both of these estimates imply that the consumption of antimicrobials in the United States is approximately 300 mg/kg of meat produced. This is considerably higher than the mean European Union value and higher than the mean value for any other country in Europe.

The number of swine in the Danish swine industry has continued to increase from < 20 million swine/y to > 27 million swine/y during the past 15 years. The number of swine produced per sow per year has also steadily increased, which indicates both the efficacy of the Danish swine industry as well as the production pressure that is put on the pigs. Because mortality rate and ADG of weaning pigs are objective criteria that can be measured over time and also are highly reproducible, these factors were used as key indicators for productivity and health of weaning pigs. The mortality rate of weaning pigs increased from 1995 to 2004 but decreased markedly during the subsequent 3 years. It was expected that the ban on AGP use (January 2000) for weaning pigs and the rapidly increasing prevalence of PMWS during 2001 to 2005 would influence the increase in mortality rate of weaning pigs for these years. However, no effect of the ban on AGP use on the mortality rate of weaning pigs was detected. Mortality rates have improved considerably during recent years, and the total number of pigs raised for slaughter per sow per year has increased continuously during this entire time period (1993 to 2007). Similarly, ADG in weaning pigs was not negatively affected when assessing this variable over the entire study period. In fact, ADG decreased from 1992 to approximately the time of the ban on AGP use, which was followed by an increase thereafter. Thus, the potential negative effects of the ban on AGP use on both mortality rate and ADG of weaning pigs seem to be negligible, or there may even have been a benefit, especially when looking at the long-term effects. Similarly for finishing pigs, no effect on mortality rate was observed and ADG continued to increase. However, the increase was slightly but significantly less after the ban on AGP use, compared with the results before the ban on AGP use. Whether this difference in the ADG increase is because ADG was approaching a plateau or because of the ban on AGP use needs to be further evaluated. These findings support conclusions reached in a study<sup>18</sup> conducted at the herd level. The ban on AGP use did not cause any important or lasting effects on productivity, although an increase in diarrhea among weaning pigs was observed during the first year of the ban on AGP use and caused an increase in consumption of antimicrobials for therapeutic indications in weaning pigs.<sup>18</sup>

In addition to the ban on AGP use and the emergence and spread of new pathogens, a number of other factors might directly or indirectly have influenced the consumption of antimicrobials used for therapeutic indications in swine in Denmark. Recommendations for the inclusion of protein in the feed have changed over time, as have the production systems, trade between farmers, and price on antimicrobials and feed; all of these factors might influence antimicrobial use and are difficult to account for in a controlled manner. This also illustrates the complexity of factors that influence the use of antimicrobials in any type of farm animal production system.

It should be mentioned that the aggregate results described in the study reported here suggest minimal detriment to the industry as a whole. However, such an analysis may not reveal all negative and positive impacts of the imposed legislation on antimicrobial use. The data reported here were mean values for the entire Danish swine industry, for all production systems, and among a random subset of monitored herds. Therefore, the negative and positive impacts for individual pigs and farms may have been obscured.

Data regarding the effects of a ban on AGP use are also available from other countries. Switzerland imposed a ban on AGP use for swine farms in 1999, but they found no effect on the use of antimicrobials for therapeutic indications.<sup>24</sup> In Finland, antimicrobials used for the treatment of diarrhea in weaning pigs did not increase significantly after a ban on AGP use in 1999.<sup>25</sup> In Norway, a significant reduction in the consumption of antimicrobials for therapeutic indications followed a ban on AGP use.<sup>26</sup> However, in Sweden, a ban on AGP use in 1986 was followed by an increase in the consumption of antimicrobials for therapeutic indications, with antimicrobial consumption returning to the same level as before the ban on AGP use after almost 10 years.<sup>26</sup> To our knowledge, data on the effects of a ban on AGP use on productivity in the pig industry of other countries are not available. However, in both Denmark<sup>27</sup> and the United States,<sup>28</sup> the effect of a ban on AGP use in poultry is negligible or even nonexistent. Unfortunately, few studies have been conducted following the ban on AGP use in all 27 European Union member states in 2000.

Detailed treatment guidelines for veterinarians in Denmark have been developed and updated annually since 1996. The extent to which veterinarians adhere to these guidelines or the effect they have on the total consumption of antimicrobials or the patterns of antimicrobial consumption has not been assessed. Analysis of results from the study reported here suggests, with 1 exception, that the effect appears to be relatively minor; this may have resulted in a reduction in antimicrobial consumption of macrolides with a concurrent increase in the use of tetracyclines for treatment during 2005 to 2008.

Globally, there is limited experience with various interventions and their effect on antimicrobial consumption for food animal production.<sup>29</sup> On the basis of our experience in Denmark, regulatory actions and financial incentives can be effective in changing the consumption of antimicrobials, whereas the effects of other actions have not been definitively proven.

From 1992 to 2008, a reduction (> 50%) in antimicrobial consumption per kilogram of pig produced was observed in Denmark. This change was associated with the implementation of policies to discontinue the use of antimicrobials as AGPs. During the same period, overall swine productivity improved markedly, which suggests that the change in antimicrobial consumption has not had a negative impact on long-term swine productivity.

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