# 4

# ANTIMICROBIAL CONSUMPTION IN ANIMALS

# 4. Antimicrobial consumption in animals

**Highlights:** In 2022, the **total consumption** of antimicrobials in animals amounted to 86.2 tonnes of active compound of products approved for animals. Additionally, 109.7 kg of active compound of products approved for humans were used for **companion animals** or unspecified category.

The **pig sector** consumed 82.8% of all prescribed veterinary antimicrobials, equal to 71.3 tonnes active compound. Calculated in treatment proportions, an estimated 2.7% (26.9 DAPD) of all pigs, on average, received antimicrobial treatment per day in 2022. In sows and piglets and in finishers, the treatment proportions remained at 1.5%, corresponding to 15.4 DAPD and 14.8 DAPD, respectively. The highest treatment proportion was observed in the treatment of weaners: 9.8%, corresponding to 98.1 DAPD. This was an increase compared to 2021 (91.2 DAPD) and could be a result of the ban of the use of prescribed zinc oxide use in pig production by June 2022 (Textbox 4.1). Most notably, there was an increase in neomycin, used to treat post-weaning diarrhoea.

Over time, the antimicrobial classes used in the treatment of pigs have changed notably. The critically important antimicrobials: 3rd and 4th generation cephalosporins, glycopeptides, polymyxins, and fluoroquinolones have been phased out. However, over the last decade, there has been an increase in the consumption of macrolides from 6.4 DAPD to 7.1 DAPD, aminoglycosides from 1.5 DAPD to 4.1 DAPD, and simple penicillins from 2.9 DAPD to 3.0 DAPD. During the same period, the consumption of tetracyclines has decreased from 10.1 DAPD in 2013 to 3.9 DAPD in 2022.

In 2022, antimicrobial consumption in **cattle** amounted to 8.2 tonnes. Approximately two thirds of the consumption were used to treat older cattle (>1 year). Over the past decade, the total antimicrobial consumption has decreased for older cattle (>1 year), from 2.9 DAPD to 2.0 DAPD. During the same period, a decrease in the total consumption from 8.2 DAPD to 6.7 DAPD was observed in young cattle. Also in cattle, the changes in usage of antimicrobial classes are noticeable i.e., there has been an increased consumption of macrolides, tetracyclines and simple penicillins (beta-lactamase sensitive penicillins) for treatment of younger cattle and increased consumption of simple penicillins (beta-lactamase sensitive penicillins) for intramammary treatment.

The antimicrobial consumption in **poultry** was 1,259.5 kg and has only increased by 53.6 kg from 2021 to 2022. In 2022 the consumption of macrolides increased by 214.1 kg active compound compared to 2021, which was likely caused by disease in several flocks in a single farm.

In 2022, cephalosporins were prescribed mainly for **pets and horses** (61.1 kg) or as intramammary treatment for **cattle** (45.6 kg). Furthermore, fluoroquinolones (14.2 kg) were prescribed almost exclusively for horses and pets.

## 4.1 Introduction

The DANMAP programme began monitoring the national consumption of antimicrobials in humans and animals in 1995. Since the early 1990s, there has been increased political and public focus on the consumption of antimicrobials in the Danish animal production. This has resulted in discontinued usage of antimicrobials for growth promotion combined with several other initiatives, including voluntary bans on the use of 3rd and 4th generation cephalosporins in the pig and cattle production, as well as regulatory legislation regarding therapeutic use.

Figure 4.1 presents the total consumption of antimicrobials in animals and humans since 1990 and 1997, respectively. Increases in, and intensification of, pig production has also had a significant impact on the overall consumption during this time.

The observed decrease in antimicrobial consumption after 1994 was foremost due to the discontinued usage of antimicrobials for growth promotion and most likely also the result of 1) limitation of veterinary practitioners' profit from sales of medicine; 2) implementation of Veterinary Advisory Service contracts (VASCs) with regular visits from the veterinarian to promote preventive veterinary strategies and optimize antimicrobial consumption; and 3) enforcement of the so-called "cascade rule" [Order (DK) 142/1993], limiting the prescription of (cheaper) extemporaneously produced medicines.

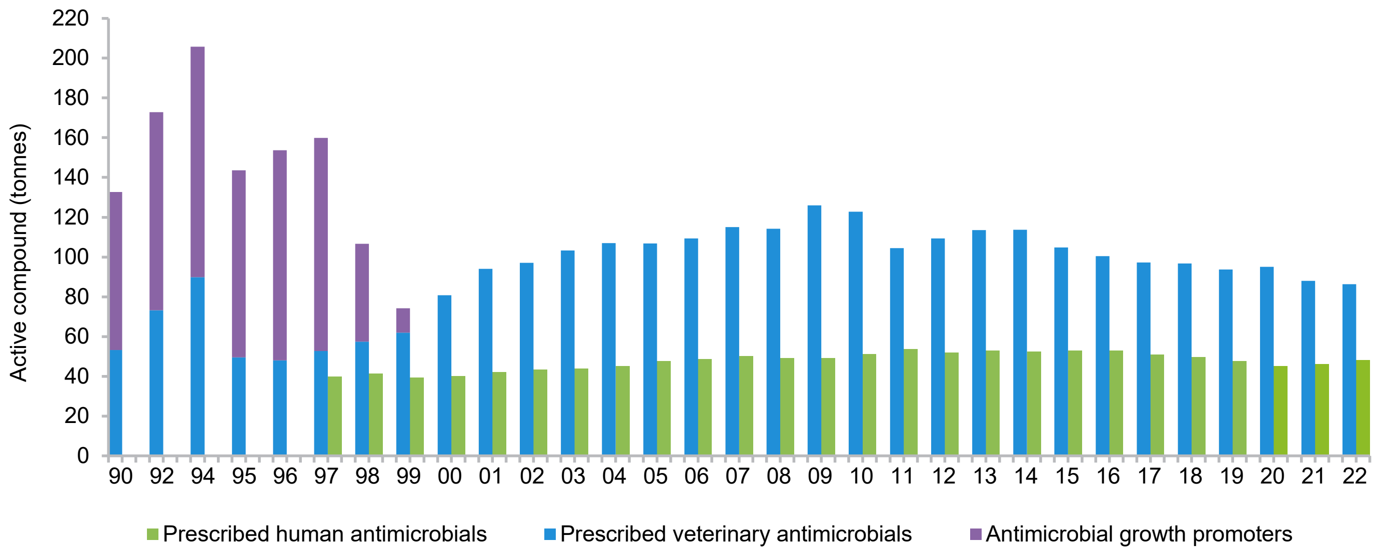
Other important interventions were the restriction on the use of fluoroquinolones in production animals through legislation implemented in 2002 and 2003, and the voluntary ban on the use of cephalosporins in the pig production in 2010, followed by a similar initiative in the dairy cattle production in 2014. Furthermore, the cattle production implemented a ban on use of 3rd and 4th generation cephalosporins for cattle from 2019.

The national action plan against antimicrobial resistance has had several goals throughout time. Initially, a 10% reduction of antimicrobial consumption in production animals by 2014 compared to the 2009 level was set as a national target. In 2015 the national action plan to reduce livestock-associated MRSA called for a 15% reduction in antimicrobial consumption in pigs from 2015 to 2018.

To achieve the action plan goals, the Yellow Card initiative was established in 2010, introducing surveillance at herd level and instating threshold values for antimicrobial consumption in individual herds to enable legal action on pig farmers with high antimicrobial consumption per pig [DANMAP 2010]. As a result, a distinct decrease in antimicrobial consumption was observed from 2010 to 2011.

Effects from other parts of the legislation may be less obvious but are also likely to have affected prescription patterns. As an example, the rules for group medication in pig herds were tightened in 2014 [Order (DK) 534 of 27/05/2014], calling for thorough laboratory diagnoses and frequent veterinary visits before and during prescription of antimicrobials for peroral treatment through water or feed of groups of pigs rather than injection treatment of individual pigs.

**Figure 4.1 Antimicrobial consumption for humans and all animal species, tonnes of active compound, Denmark** DANMAP 2022




Sources: Human therapeutics: The Danish Medicines Agency. Antimicrobials for animals: Data are based on reports from the pharmaceutical industry of total annual sales (until 2001), from the Federation of Danish pig producers and slaughterhouses (1994-1995), from the Danish Medicines Agency and Danish Plant Directorate (1996–2000), and since 2001 from VetStat. For DANMAP 2022, consumption data were extracted from the VetStat on 22 May 2023 and include all antimicrobials approved for use in animals for the period 2004-2022

In 2016, the Yellow Card initiative was revised, adding on multiplication factors to adjust the consumption of certain antimicrobials. Tetracyclines were multiplied by 1.2, and the factor was increased to 1.5 in 2017. Fluoroquinolones, cephalosporins and colistin (added in 2017) were given the highest multiplication factor of 10 [DANMAP 2017].

In 2017, the Ministry of Environment and Food in Denmark and the Ministry of Health in Denmark presented a new One Health strategy against antimicrobial resistance, setting the framework for reducing the development and occurrence of antimicrobial resistance (AMR).

At the same time, two national action plans to reduce AMR were introduced, setting specific targets to further reduce the antimicrobial consumption for both humans and animals in the coming years. As part of the political agreement on the veterinary strategy 2018-2021 (Veterinærforlig III), an Advisory Committee on Veterinary Medicines was established in 2018.

Also, to reduce the need for disposal of excess antimicrobials, veterinarians and pharmacies were permitted to split packages of veterinary medicine as from 2019 [Order (DK) 1655/2018]. This initiative may also enhance surveillance by reducing the difference between amounts of antimicrobials prescribed and amounts consumed.

Official treatment guidelines for pigs and cattle have been available since 1996. The guidelines provide specific recommendations for selection of the appropriate antimicrobial treatment of all common problems in the major production animal species. Since 2005, the Danish Veterinary and Food Administration (DVFA) has updated the guidelines in collaboration with stakeholders and university experts. The guidelines were updated in 2010, when new dynamic evidence-based treatment guidelines for pigs were launched [DANMAP 2010, www.foedevarestyrelsen.dk/], and a revised version was published in April 2018. In June 2022, the use of prescribed zinc oxide in pig production was banned in Denmark (Textbox 4.1).

In 2012, to promote prudent use of antimicrobials in dogs and cats the Danish Veterinary Association (DVA) published treatment guidelines developed by clinical specialists and experts from the Faculty of Health and Medical Sciences at the University of Copenhagen and the National Food Institute, Technical University of Denmark. Revised treatment guidelines for dogs and cats were published in 2018. Similarly, DVA published treatment guidelines for use of antimicrobials in horses in 2017.

Order 2019/6 on veterinary medicinal products has applied since 28 January 2022. There is a particular focus on reducing the risk of antimicrobial resistance [Order (DK) 6/2019] (Textbox 4.2).

**4.1.1 Data sources**

In Denmark, antimicrobials are available by prescription only, and data on antimicrobial consumption have been collected since 1990.

Since 2001, data on all medicines prescribed for consumption in animals, including vaccines, antimicrobial growth promoters, and coccidiostatica have been recorded in the national database VetStat. Since 2010, the VetStat database has been hosted and maintained by DVFA. In June 2021, DVFA launched an updated platform for VetStat. The 2022 data presented in this report were extracted from this new VetStat on 22 May 2023. The data were extracted, analysed, and interpreted for DANMAP by the National Food Institute, Technical University of Denmark.

**4.1.2 Methods**

Metrics of antimicrobial consumption are numerous, each with its own advantages and limitations. Therefore, the selection of metrics used for monitoring must depend on the monitoring objective and the information available.

The total amount of antimicrobial consumption is measured in kg active compound and is used in Section 4.2 for the purpose of an overall crude comparison of consumption in the veterinary and human sectors (Figure 4.1).

Since 2012, the metrics "defined animal daily dose" (DADD) and "proportion of population in treatment per day" (DAPD) have been added to monitor trends in antimicrobial consumption. These metrics are defined below, and for additional information on methodology, please see Chapter 10, Section 10.2.

The **Defined animal daily dose (DADD)** is the average maintenance dose per day for the main indication of a drug in the appropriate animal species. DADD is not defined at product level but for each antimicrobial, administration route, and animal species as mg active compound per kg live animal. DADDs were defined specifically for use in DANMAP based on current knowledge, and may vary from the prescribed daily dose, or the recommended dosage, in the summaries of product characteristics (SPC) or in the VetStat database.

The **Proportion of population in treatment per day (DAPD)** is used to describe trends in antimicrobial consumption in animals where possible. DAPD is equal to DADD per 1,000 animals per day, where "animals" are represented by their live biomass and adjusted for lifespan. The estimated live biomass is expressed as the number of standard animals with an estimated average weight on a given day. This may also be referred to as the "standard animals at risk". This metric allows for comparison of antimicrobial consumption between species regardless of large differences in body mass and lifespan.

DAPD, is a statistical measure that provides a rough estimate of the proportion of animals treated daily with a particular antimicrobial. For example, 10 DAPD means that an estimated 1.0% of the population, on average, receives a certain treatment on a given day this is repeating what is in Materials and Methods and does not belong in this chapter.

In DANMAP 2022, the treatment proportions DAPDs were calculated for pigs and cattle.

## 4.2 Total antimicrobial consumption in animals

Together with the introduction of the new VetStat database in 2021, the criteria for allocation antimicrobial consumption to the different animal species and age groups were revised i.e., consumption is allocated to the species and age group combinations from the categories defined in VetStat [Order (DK) 2542/2021]. This affected the calculated amounts per species while the overall trends of antimicrobial consumption remain the same.

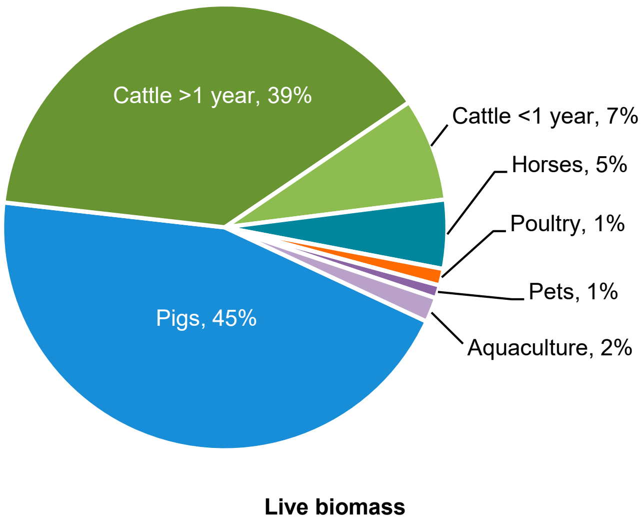
The total consumption of antimicrobials in all animals amounted to 86.2 tonnes active compound, representing a 2.1% (-1878.8 kg) decrease compared to 2021 (Figure 4.1). Like in previous years, the 2022 consumption in pigs, cattle and poultry comprised approximately 82.8%, 9.5%, and 1.5%, respectively, of the total antimicrobial consumption in animals (Figure 4.2).

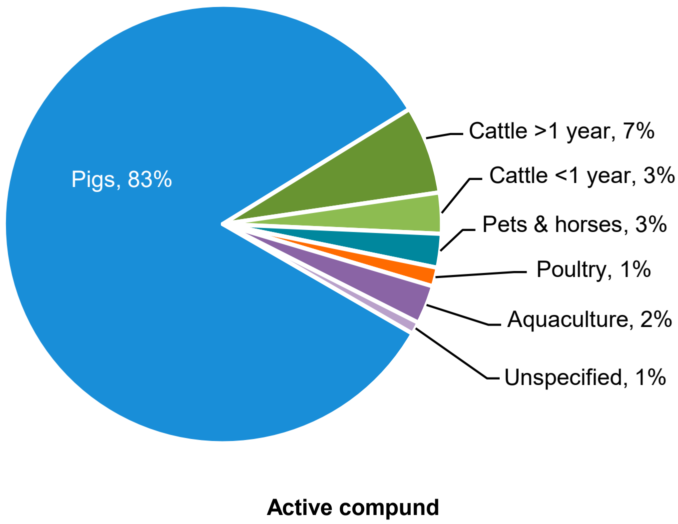
The pig production is the main driver of consumption of antimicrobials in animals in Denmark, due to the magnitude of the production. Cattle and pigs comprise almost equal proportions of the total live biomass. However, the vast proportion of cattle biomass consists of dairy cows, which have very low consumption of antimicrobials compared with growing animals such as slaughter pigs.

Historically, the overall consumption of kg active compound of antimicrobials was 58.1% lower in 2022 compared to 1994. A major part of this reduction can be explained by the discontinued consumption of growth promoters from 1994 to 1999.

Between 2000 (start of VetStat) and 2009, the amount of kg active compound of antimicrobials used in animals increased by 61.7% (Figure 4.1). During this period, the number of pigs produced also increased, as did the proportion of exported live pigs at approximately 30 kg. Since then, the proportion of these pigs has continued to increase, while there has been an overall gradual decrease in the consumption of antimicrobials in animals.

**Figure 4.2 Distribution of live biomass and antimicrobial consumption in main animal species, tonnes, Denmark** DANMAP 2022




The live biomass is estimated from census data (pigs, cattle, and companion animals) and production data (poultry, and aquaculture). The live biomass estimates for poultry (turkeys and broilers), aquaculture, horses and pets are based on 2012 data and may well be underestimated. The estimation procedures are described in Chapter 10, Section 10.2

**Table 4.1 Antimicrobial consumption by animal species and age group, kg active compound, Denmark** DANMAP 2022

| | Aminoglycosides | Amphenicols | Cephalosporins [a] | Fluoroquinolones | Lincosamides | Macrolides | Other antimicrobials [b] | Other quinolones | Penicillins, b-lactamase sensitive | Penicillins, others | Pleuromutilins | Sulfonamides and trimethoprim | Tetracyclines | 2021 | 2022 |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *Pigs* | 15159.0 | 578.8 | - | 0.1 | 2294.7 | 11586.1 | - | - | 11368.7 | 7862.3 | 7043.3 | 7043.3 | 10807.7 | 72344.8 | 71355.9 |
| Sows, piglets, gilts and boars | 2124.6 | 259.8 | - | 0.1 | 410.2 | 470.6 | - | - | 5892.5 | 2426.7 | 678.3 | 678.3 | 1113.7 | 19517.7 | 17083.0 |
| Weaners, =<30kg | 12958.3 | 297.9 | - | - | 1318.8 | 7780.7 | - | - | 1588.6 | 4797.1 | 2395.5 | 2395.5 | 7036.9 | 35571.6 | 39023.4 |
| Finishers and polts | 76.1 | 21.2 | - | - | 565.8 | 3334.8 | - | - | 3887.5 | 638.5 | 3969.5 | 3969.5 | 2657.1 | 17255.5 | 15249.5 |
| *Cattle* | 869.7 | 907.3 | 45.6 | - | 3.7 | 209.5 | 0.1 | - | 4300.6 | 544.2 | - | - | 950.8 | 9413.6 | 8177.9 |
| Intramammaries | 27.9 | - | 45.6 | - | 3.0 | - | 0.0 | - | 250.8 | 123.5 | - | - | - | 486.3 | 450.8 |
| Cows, bulls, heifers and steers >24 months | 205.0 | 11.6 | 0.0 | - | 0.5 | 61.8 | 0.1 | - | 3426.7 | 317.8 | - | - | 570.4 | 5522.7 | 4853.4 |
| Calves <12 months | 540.7 | 882.5 | - | - | 0.2 | 146.0 | 0.0 | - | 486.2 | 97.2 | - | - | 362.6 | 2834.2 | 2600.8 |
| Young cattle btw 12 and 24 months | 96.1 | 13.2 | - | - | - | 1.6 | 0.0 | - | 136.9 | 5.7 | - | - | 17.9 | 570.3 | 272.8 |
| *Poultry* | 49.0 | - | - | - | 15.0 | 382.7 | - | - | 217.1 | 129.3 | 19.0 | 19.0 | 437.2 | 1205.9 | 1259.5 |
| Poultry | - | - | - | - | - | - | - | - | - | - | - | - | - | 528.7 | - |
| Broilers | 27.3 | - | - | - | 11.6 | 291.0 | - | - | 4.9 | 42.5 | - | - | 267.7 | 344.9 | 652.7 |
| Layer hens | 0.7 | - | - | - | 0.3 | 49.0 | - | - | 96.5 | 21.7 | 18.8 | 18.8 | 16.5 | 66.6 | 204.6 |
| Turkeys | 5.9 | - | - | - | 3.0 | - | - | - | 111.2 | 57.6 | - | - | 117.5 | 243.1 | 295.2 |
| Other poultry | 15.1 | - | - | - | 0.1 | 42.8 | - | - | 4.6 | 7.5 | 0.3 | 0.3 | 35.5 | 22.6 | 107.0 |
| *Other production animals* | 0.5 | 143.9 | 0.0 | - | 0.0 | 0.2 | 0.0 | 366.5 | 0.9 | 1.2 | - | - | 5.3 | 1787.6 | 2460.0 |
| Aquaculture | - | 143.9 | - | - | 0.0 | - | 0.0 | 366.5 | - | - | - | - | 0.6 | 1771.2 | 2451.8 |
| Fur animals | - | - | - | - | - | - | - | - | - | - | - | - | - | 1.0 | 0.6 |
| Other | 0.5 | 0.1 | 0.0 | - | 0.0 | 0.2 | 0.0 | - | 0.9 | 1.2 | - | - | 4.7 | 15.5 | 7.6 |
| *Companion animals* | 2.9 | 0.4 | 61.1 | 12.5 | 66.8 | 0.2 | 76.2 | - | 14.0 | 469.2 | 0.1 | 0.1 | 41.5 | 2519.7 | 2143.3 |
| Horses | 0.3 | 0.0 | 0.0 | 0.0 | 0.0 | - | 0.2 | - | 4.5 | 0.2 | - | - | 7.3 | 113.1 | 148.5 |
| Pets | 1.7 | 0.0 | 22.3 | 3.9 | 16.5 | 0.2 | 24.3 | - | 9.4 | 79.5 | 0.1 | 0.1 | 22.3 | 484.8 | 345.7 |
| Unspecfied | 1.0 | 0.4 | 38.8 | 8.6 | 50.3 | - | 51.7 | - | 0.0 | 389.5 | - | - | 11.9 | 1921.8 | 1649.1 |
| *Unknown* [c] | 83.8 | 1.9 | 1.1 | 1.1 | 7.4 | 55.2 | 1.0 | 3.1 | 448.6 | 41.8 | 3.2 | 3.2 | 95.2 | 773.7 | 769.9 |
| Total | 16165.0 | 1632.3 | 107.8 | 13.7 | 2387.7 | 12233.9 | 77.2 | 369.5 | 16349.8 | 9047.9 | 7065.6 | 7065.6 | 12337.7 | 88045.3 | 86166.5 |
| *Products approved for human consumption* | | | | | | | | | | | | | | | |
| Horses | - | 0.0 | - | 0.0 | - | 0.6 | 0.3 | - | - | 0.0 | - | - | - | - | 0.9 |
| Pets | 0.0 | 0.0 | - | 0.1 | 0.0 | 0.9 | 3.0 | - | 1.6 | 2.3 | - | - | 1.7 | - | 10.3 |
| Unspecfied | - | 0.0 | - | 0.4 | - | 1.3 | 7.9 | - | 8.0 | 5.5 | - | - | 2.3 | - | 25.8 |
| Unknown [c] | 0.1 | 0.1 | 3.8 | - | - | 0.2 | 1.5 | - | 53.3 | 13.6 | - | - | - | - | 72.6 |
| Total | 16165.1 | 1632.5 | 111.7 | 14.2 | 2387.7 | 12236.8 | 89.9 | 369.5 | 16412.7 | 9069.3 | 7065.6 | 7065.6 | 12341.7 | | 86276.2 |

Data for 2022 were extracted from VetStat on 22 May 2023 for veterinary approved products, and on 17 August 2023 for human approved products
Combination products are split into active compounds
a) In 2022, 3rd and 4th generation cephalosporins were only used in pets (1.6 kg)
b) Including other antiinfectives, dermatologicals, ontological, opthamologicals, polymyxin, quinolones, and sulfonamides, plain
c) Including data with no information on animal species/age group, or mismatch between animal species and age group

As part of the EU project Alternatives to Veterinary Antimicrobials (AVANT) coordinated by the University of Copenhagen, Faecal microbiota transplantation (FMT) and other alternatives are being evaluated for whether they could be effective in the treatment of pigs with diarrhoea, and hence contribute to reducing antimicrobial consumption in pigs (Textbox 4.3).

## 4.3 Antimicrobial consumption by animal species

### 4.3.1 Antimicrobial consumption in pigs

Most of the antimicrobials were consumed within the pig production in 2022. The total consumption in pigs was 71.3 tonnes of active compound, which was 988.9 kg less than in 2021 (Table 4.1).

The national MRSA action plan aimed to reduce the antimicrobial consumption in pigs by 15% in 2018 compared to 2014. This goal was reached in 2019, where the achieved reduction was 16%. A revised action plan with new targets were agreed upon in 2019 i.e., antimicrobial consumption in the pig production should decrease by 2% each year from 2019-2022 compared to the consumption level in 2018 (74.7 tonnes). To achieve this target, the antimicrobial consumption in 2022 should have been 70.3 tonnes of active compound, thus 1.1 tonnes of active compound lower than the observed for 2022.

The **treatment proportion** (DAPD) of the total population reflects the trends in selection pressure within the population. DAPD is much higher in weaners than in finishers and sows. The DAPDs in the pig population overall and by age group are presented in Figures 4.3 a. and 4.4. The distribution of parental and peroral administration for overall population and by age group are shown in Figures 4.3 b.- c.

Historically, DAPD increased from 2004 to 2009, followed by a clear decrease in 2010 and 2011 with introduction of the Yellow Card initiative. Since 2013, an overall slightly decreasing trend in treatment proportion has been observed (Figure 4.3 a).

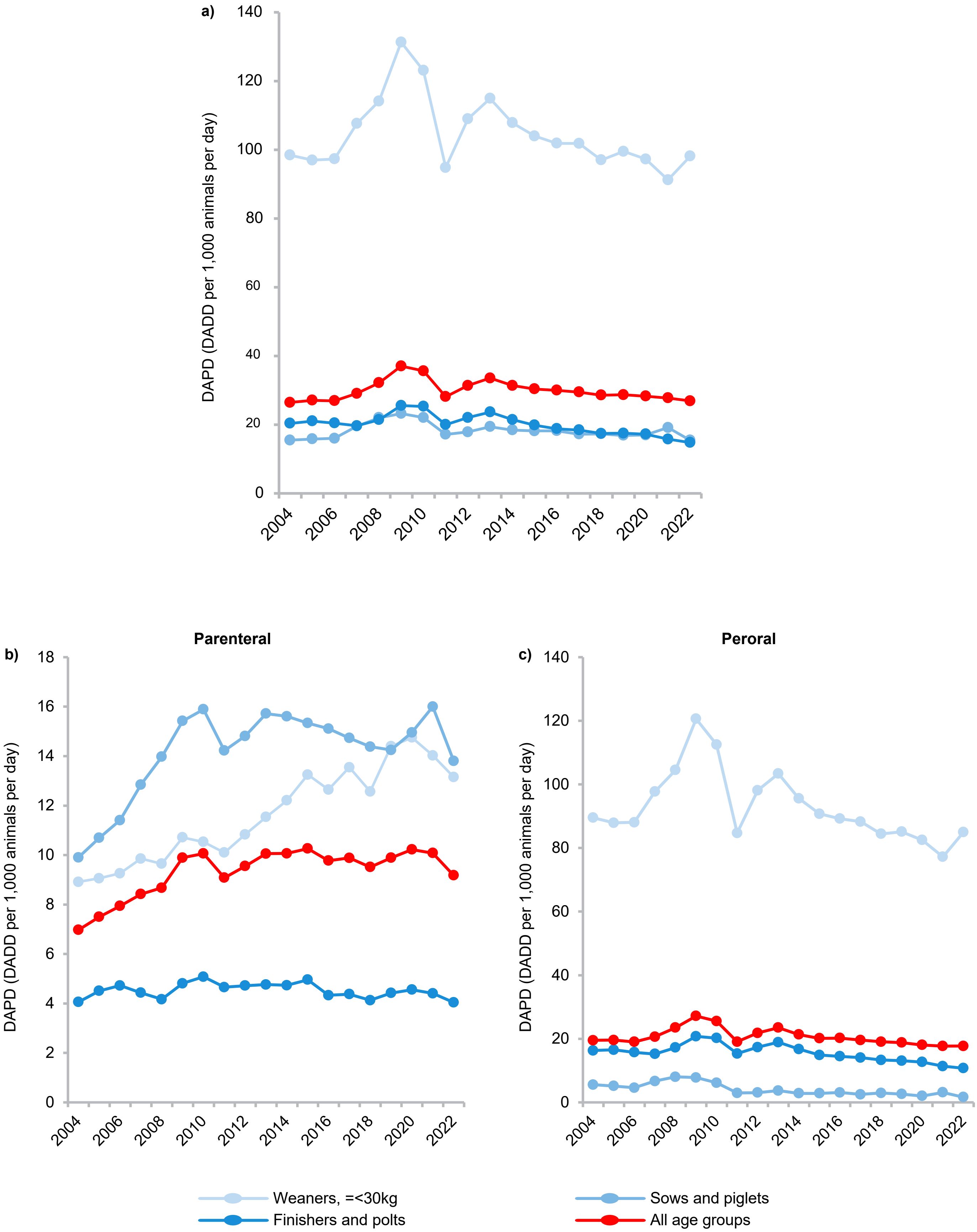
While there was a decrease in the antimicrobial consumption in pigs when inspecting crude consumption data (Table 4.1), the changes in the overall treatment proportion are more subtle and vary between age groups and antimicrobial classes. When comparing 2022 to 2021, DAPD decreased slightly in sows and finishers, but in weaners a considerable increase was observed (Figure 4.3 a.). Thus, on a given day in 2022, approximately 1.5% of sows, piglets and finishers, as well as 9.8% of weaners were treated with antimicrobials. The main prescription indication of antimicrobial consumption was for diarrhoea in weaners (Table 4.2).

Tetracyclines have been some of the most consumed antimicrobials in the Danish pig production, especially for oral treatment of gastrointestinal disease in weaners and finishers. The overall use of tetracyclines has decreased since 2013, and in both 2021 and 2022 the treatment proportion was at the lowest level registered in the last 18 years, with the most marked changes following the recent adjustments to the Yellow Card initiative (Figure 4.4).

The proportion of weaners treated with tetracycline on any given day has decreased from approximately 4.3% (42.9 DAPD) in 2013 to 1.7% (17.1 DAPD) in 2022. In contrast, the consumption of aminoglycosides, mainly neomycin, has increased by 67,6% from 15.4 DAPD in 2021 to 25.9 DAPD in 2022 and to some extent also lincosamides from 2.9 DAPD in 2021 to 3.9 DAPD in 2022 (Figure 4.4).

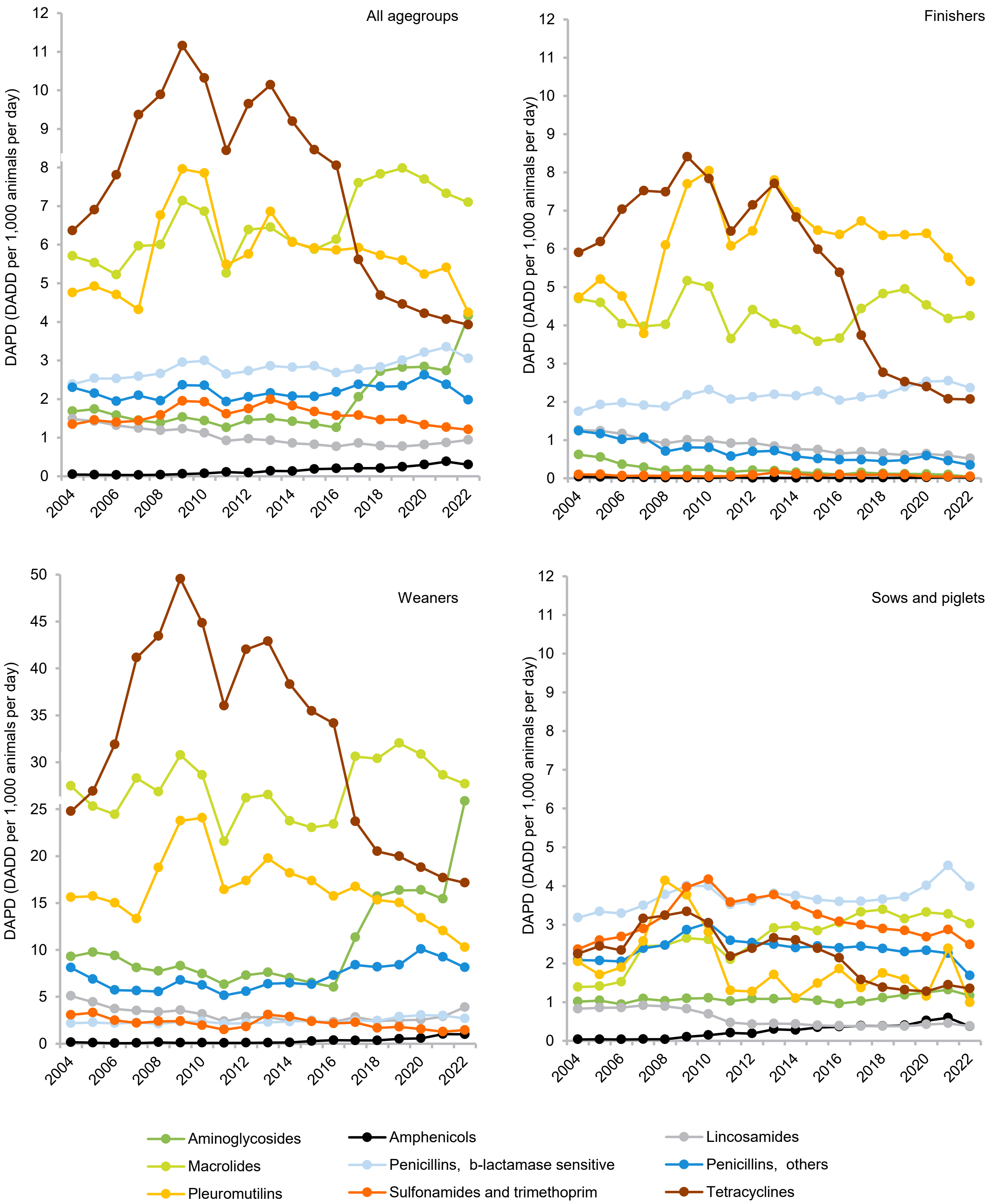
In 2022, no consumption of the critical important antimicrobials 3rd and 4th generation cephalosporins was registered in pigs (Table 4.1).

**Figure 4.3 a Total antimicrobial consumption in the pig production, DAPD, Denmark. b. and c. Total antimicrobial consumption in the pig production at administration level, DAPD, Denmark** DANMAP 2022




"Sows and piglets" include treatment in boars, where boars constitute 4-5% of the estimated live biomass for the age group. DAPDs are calculated as the number of standard doses for one kg animal divided by the estimated live biomass in the age group of the total population (in tonnes)

**Figure 4.4 Antimicrobial consumption in the total pig production and in each age group at antimicrobial class level, DAPD, Denmark**
DANMAP 2022




DAPDs are calculated as the number of standard doses for one kg animal divided by the estimated live biomass in the age group or the total population (in tonnes)
The age group "sows and piglets" includes treatment in boars, where boars constitute 4-5% of the estimated live biomass for the age group

**Table 4.2 Prescription indications for parentally and perorally administration of antimicrobials at antimicrobial class level in pigs, DAPD, Denmark** DANMAP 2022

| | Sows, piglets, gilts and boars | | | | | | | Weaners, =<30kg | | | | | | | Finishers and polts | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Gastrointestinal disorders | Joints, limbs, hooves, central nervous system, skin | Metabolism, digestion, circulation | Reproduction, urogenital system | Respiratory disorders | Udder | Unknown | Gastrointestinal disorders | Joints, limbs, hooves, central nervous system, skin | Metabolism, digestion, circulation | Reproduction, urogenital system | Respiratory disorders | Udder | Unknown | Gastrointestinal disorders | Joints, limbs, hooves, central nervous system, skin | Metabolism, digestion, circulation | Reproduction, urogenital system | Respiratory disorders | Udder | Unknown |
| *Parenteral* | | | | | | | | | | | | | | | | | | | | | |
| **Total** | **1.03** | **6.32** | **0.07** | **2.10** | **2.60** | **1.68** | **0.00** | **4.73** | **5.66** | **0.02** | **0.00** | **2.73** | **-** | **0.00** | **0.87** | **2.89** | **0.00** | **0.01** | **0.26** | **0.00** | **0.00** |
| Aminoglycosides | 0.07 | 0.63 | 0.00 | 0.01 | 0.02 | 0.00 | - | 0.12 | 1.20 | 0.00 | 0.00 | 0.03 | - | - | 0.00 | 0.01 | - | 0.00 | 0.00 | - | 0.00 |
| Amphenicols | 0.10 | 0.12 | 0.01 | 0.02 | 0.12 | 0.01 | - | 0.12 | 0.07 | 0.00 | - | 0.22 | - | 0.00 | 0.00 | 0.00 | - | - | 0.01 | - | - |
| Fluoroquinolones | 0.00 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| Lincosamides | 0.03 | 0.29 | 0.00 | 0.00 | 0.02 | 0.00 | - | 0.06 | 0.05 | 0.00 | - | 0.01 | - | - | 0.00 | 0.50 | 0.00 | 0.00 | 0.01 | - | - |
| Macrolides | 0.14 | 0.32 | 0.00 | 0.05 | 2.30 | 0.15 | 0.00 | 0.53 | 0.10 | 0.00 | - | 2.13 | - | - | 0.22 | 0.01 | - | 0.00 | 0.03 | - | 0.00 |
| Penicillins, b-lactamase sensitive | 0.02 | 2.65 | 0.00 | 0.74 | 0.03 | 0.56 | 0.00 | 0.00 | 2.53 | 0.01 | 0.00 | 0.14 | - | 0.00 | 0.00 | 2.16 | 0.00 | 0.01 | 0.19 | 0.00 | 0.00 |
| Penicillins, others | 0.04 | 1.30 | 0.01 | 0.10 | 0.04 | 0.05 | 0.00 | 0.08 | 1.53 | 0.00 | 0.00 | 0.07 | - | - | 0.00 | 0.08 | - | 0.00 | 0.01 | - | - |
| Pleuromutilins | 0.01 | 0.11 | 0.04 | 0.01 | 0.03 | 0.00 | 0.00 | 0.11 | 0.01 | 0.00 | - | 0.03 | - | - | 0.12 | 0.06 | 0.00 | 0.00 | 0.01 | - | - |
| Sulfonamides and trimethoprim | 0.49 | 0.06 | 0.00 | 1.07 | 0.00 | 0.86 | - | 1.18 | 0.06 | 0.00 | 0.00 | 0.00 | - | - | 0.01 | 0.01 | - | - | 0.00 | - | - |
| Tetracyclines | 0.13 | 0.85 | 0.00 | 0.10 | 0.05 | 0.05 | 0.00 | 2.53 | 0.10 | - | - | 0.11 | - | - | 0.52 | 0.05 | 0.00 | 0.00 | 0.01 | - | 0.00 |
| *Peroral* | | | | | | | | | | | | | | | | | | | | | |
| **Total** | **0.58** | **0.17** | **0.01** | **0.04** | **0.84** | **0.00** | **-** | **65.82** | **5.00** | **0.06** | **0.00** | **14.07** | **0.00** | **0.01** | **9.68** | **0.44** | **0.00** | **0.00** | **0.60** | **-** | **0.00** |
| Aminoglycosides | 0.43 | 0.00 | - | 0.00 | - | 0.00 | - | 24.42 | 0.02 | 0.01 | - | 0.05 | 0.00 | 0.00 | 0.02 | - | - | - | - | - | - |
| Amphenicols | 0.00 | 0.00 | 0.00 | - | 0.00 | - | - | 0.05 | 0.10 | - | - | 0.42 | - | - | 0.00 | - | - | - | 0.01 | - | - |
| Fluoroquinolones | 0.00 | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - | - |
| Lincosamides | 0.03 | 0.00 | - | 0.00 | - | - | - | 3.73 | 0.03 | - | - | 0.00 | 0.00 | 0.00 | 0.01 | - | - | - | - | - | - |
| Macrolides | 0.01 | 0.00 | - | - | 0.04 | - | - | 19.72 | 0.23 | 0.01 | 0.00 | 4.98 | - | 0.00 | 3.90 | 0.02 | - | - | 0.06 | - | - |
| Penicillins, others | 0.05 | 0.05 | 0.00 | 0.01 | 0.03 | - | - | 1.07 | 3.66 | 0.04 | - | 1.67 | - | - | 0.02 | 0.12 | 0.00 | - | 0.12 | - | - |
| Pleuromutilins | 0.03 | 0.10 | 0.00 | 0.01 | 0.65 | - | - | 9.33 | 0.44 | 0.00 | - | 0.37 | - | - | 4.59 | 0.20 | 0.00 | - | 0.15 | - | 0.00 |
| Sulfonamides and trimethoprim | 0.00 | 0.00 | - | - | 0.00 | - | - | 0.07 | 0.10 | - | - | 0.05 | - | - | 0.02 | - | - | - | 0.00 | - | - |
| Tetracyclines | 0.02 | 0.01 | 0.00 | 0.02 | 0.11 | - | - | 7.45 | 0.42 | 0.01 | - | 6.52 | - | 0.01 | 1.12 | 0.09 | - | 0.00 | 0.26 | - | - |

Data for 2022 were extracted from VetStat on 22 May 2023
Combination products are split into active compounds

### 4.3.2 Antimicrobial consumption in cattle

Legislation-supported thresholds for antimicrobial consumption in cattle have been in place since 2011. In 2022, approximately 8.2 tonnes were recorded for use in cattle, of which approximately 450.8 kg of active compound were used for intramammary therapeutic or dry-cow treatment (Table 4.1).

About 33.6% of the antimicrobial consumption for systemic treatment was used for young cattle (<12 months), and the rest were used to treat adult cattle (>12 months) (Table 4.1). The production of veal, beef and milk has remained relatively stable over the past 5 years (Chapter 2, Table 2.3).

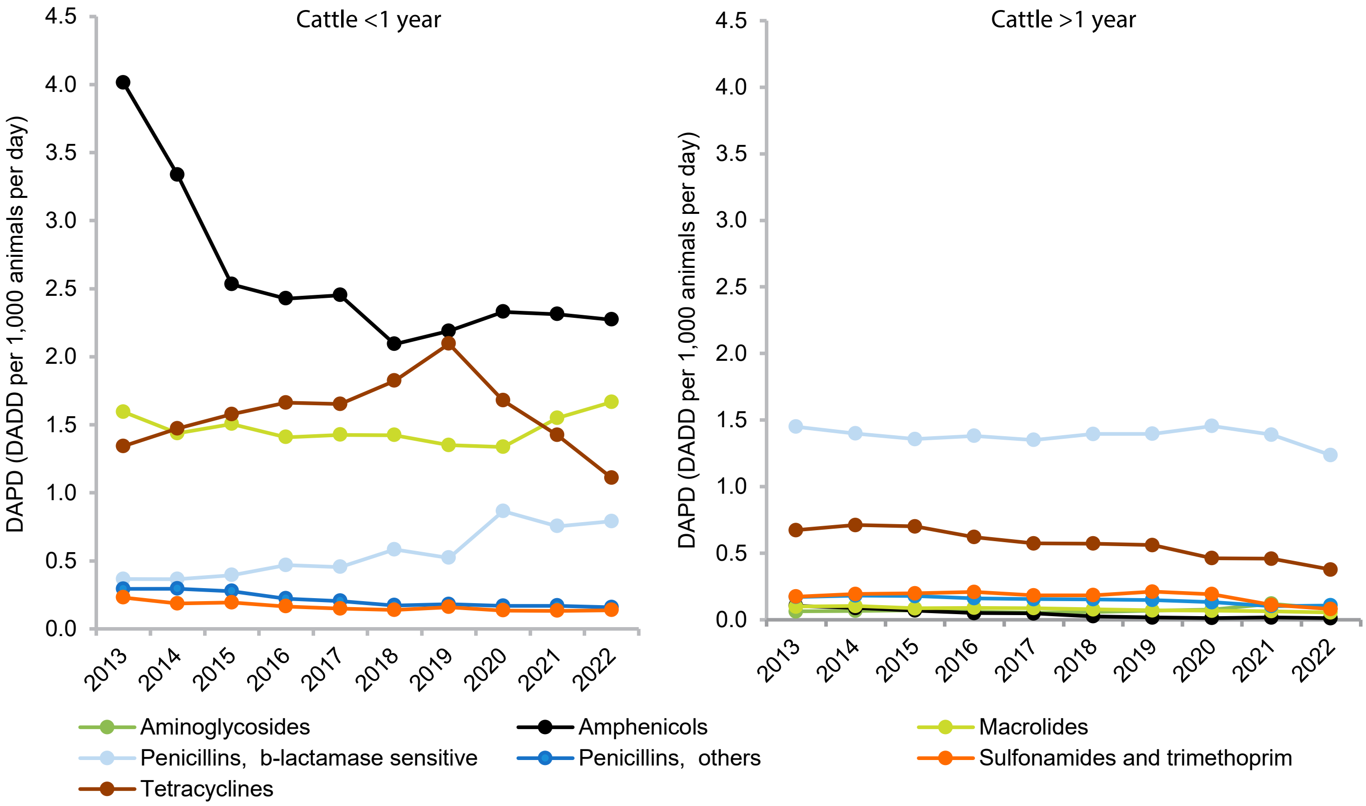
Measured in kg active compound, in adult cattle, the consumption was 15.2% lower in 2022 than in 2021. Moreover, there has been a gradual decrease in the overall use of antimicrobials for systemic treatment in adult cattle over the past decade. The consumption was 23.4% lower in 2022 compared to 2018 and 30.5% lower than in 2013.

However, measured as treatment proportions, the use in adult cattle has been between 2.3 and 3.2 DAPD from 2013 to 2021. In 2022, the treatment proportion was 2.0 DAPD, compared to 2.3 DAPD in 2021 and 2.9 DAPD in 2013.

The main indication for treatment in adult cattle was mastitis (udder), and simple penicillins (beta-lactamase sensitive) accounted for 47.5% of the antimicrobial consumption in this age group (Figures 4.5 and 4.6).

The antimicrobial consumption in calves and young cattle increased until 2012, followed by a slight decrease in the following years with approximately 8.2 DAPD used in 2013, 6.9 DAPD used in 2018 and 6.7 DAPD used in 2022. Measured in kg active compound, there has been an 8.2% reduction from 2021 to 2022. The main indication for systemic treatment in calves is respiratory disease followed by joint/limb and gastrointestinal infections (Table 4.3).

**Figure 4.5 Antimicrobial consumption in cattle production by age groups at antimicrobial class level, DAPD, Denmark** DANMAP 2022




DAPDs are calculated as the number of standard doses for one kg animal divided by the estimated live biomass in the age group or the total population (in tonnes)
Intramammary applications are not included (doses needed for calculating DAPD not available)
The DAPDs of amphenicols in cattle <1 year differ from previous reports, due to missing data in the old VetStat

**Table 4.3 Prescription indications for parentally and perorally administration of antimicrobials at antimicrobial class level in cattle, DAPD, Denmark**
DANMAP 2022

| | Cattle <1 year | | | | | | | Cattle >1 year | | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Gastrointestinal disorders | Joints, limbs, hooves, central nervous system, skin | Metabolism, digestion, circulation | Reproduction, urogenital | Respiratory disorders | Udder | Unknown | Gastrointestinal disorders | Joints, limbs, hooves, central nervous system, skin | Metabolism, digestion, circulation | Reproduction, urogenital | Respiratory disorders | Udder | Unknown |
| *Parenteral* | | | | | | | | | | | | | | |
| Total | 0.20 | 0.80 | 0.01 | 0.02 | 4.90 | 0.02 | 0.00 | 0.02 | 0.43 | 0.02 | 0.36 | 0.11 | 1.01 | 0.00 |
| Aminoglycosides | 0.00 | 0.10 | 0.00 | 0.00 | 0.05 | 0.00 | 0.00 | 0.00 | 0.04 | 0.00 | 0.01 | 0.00 | 0.02 | 0.00 |
| Amphenicols | 0.00 | 0.04 | 0.00 | 0.00 | 2.21 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.01 | 0.00 | - |
| Lincosamides | 0.00 | 0.00 | - | - | 0.00 | - | - | 0.00 | 0.00 | - | 0.00 | 0.00 | 0.00 | - |
| Macrolides | 0.02 | 0.11 | 0.00 | 0.00 | 1.42 | 0.00 | 0.00 | 0.00 | 0.03 | 0.00 | 0.00 | 0.02 | 0.01 | - |
| Penicillins, b-lactamase sensitive | 0.01 | 0.36 | 0.00 | 0.01 | 0.40 | 0.01 | 0.00 | 0.01 | 0.19 | 0.01 | 0.09 | 0.01 | 0.93 | 0.00 |
| Penicillins, others | 0.03 | 0.04 | 0.00 | 0.00 | 0.08 | 0.00 | 0.00 | 0.00 | 0.03 | 0.00 | 0.03 | 0.04 | 0.01 | 0.00 |
| Sulfonamides and trimethoprim | 0.12 | 0.00 | 0.00 | 0.00 | 0.01 | 0.00 | - | 0.01 | 0.01 | 0.00 | 0.04 | 0.00 | 0.02 | 0.00 |
| Tetracyclines | 0.01 | 0.15 | 0.00 | 0.00 | 0.73 | 0.00 | - | 0.00 | 0.12 | 0.01 | 0.19 | 0.03 | 0.02 | 0.00 |
| *Peroral* | | | | | | | | | | | | | | |
| Total | 0.43 | 0.02 | 0.00 | 0.00 | 0.31 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | - |
| Aminoglycosides | 0.42 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | 0.00 | - | 0.00 | 0.00 | 0.00 | 0.00 | - |
| Amphenicols | - | 0.02 | - | 0.00 | - | - | - | 0.00 | 0.00 | 0.00 | 0.00 | - | - | - |
| Macrolides | 0.00 | - | - | - | 0.11 | - | - | - | - | - | - | - | 0.00 | - |
| Penicillins, others | - | - | - | - | - | - | - | - | - | - | 0.00 | - | - | - |
| Tetracyclines | 0.01 | - | 0.00 | - | 0.20 | - | 0.00 | 0.00 | - | - | - | 0.00 | - | - |

Data for 2022 were extracted from VetStat on 22 May 2023
Combination products are split into active compounds

In calves and young cattle, treatment (DAPD) with amphenicols (florfenicol) has decreased steadily since 2020, although amphenicols are still the most frequently prescribed (33.8%), followed by macrolides and tetracyclines, 24.8% and 16.5%, respectively.

The use of fluoroquinolones in cattle has been close to zero for the last decade. Fluoroquinolones are only prescribed in food-producing animals as a last-line drug, based on microbiological analysis and susceptibility testing in an accredited laboratory. Use of fluoroquinolones in food-producing animals is also notifiable to the DVFA. No fluoroquinolones were registered for consumption in cattle in 2022.

In 2014, the cattle production began to phase out the use of 3rd and 4th generation cephalosporins used for systemic treatment, resulting in a significant drop in 2015. In 2019, the cattle production implemented a ban on use of 3rd and 4th generation cephalosporins in all cattle, and no use has been registered since 2020.

By the year of 2020 the board of Danish dairy and beef producers strategy for good udder health aimed at a 20% reduction in the use of antimicrobials for treatment of mastitis and other cattle diseases compared to 2012, as well as lowering of geometric mean bulk tank cell counts to 150,000.The dairy industry also aims to promote the use of simple penicillins (beta-lactamase sensitive penicillins) when dry-cow therapy or mastitis treatment is required.

The board of Danish dairy and beef producers renewed it's strategy for disease prevention in calves and cows, including good udder health for 2021-2023. The goals are, for the given time period, a 10% reduction in use of antimicrobials for treatment of cattle <1 year old and a reduction of 3% in cattle >1 year old on average annually. Moreover, they aim to reduce the proportion of milk producers with a cell count >200,000 from 60% to 30%.

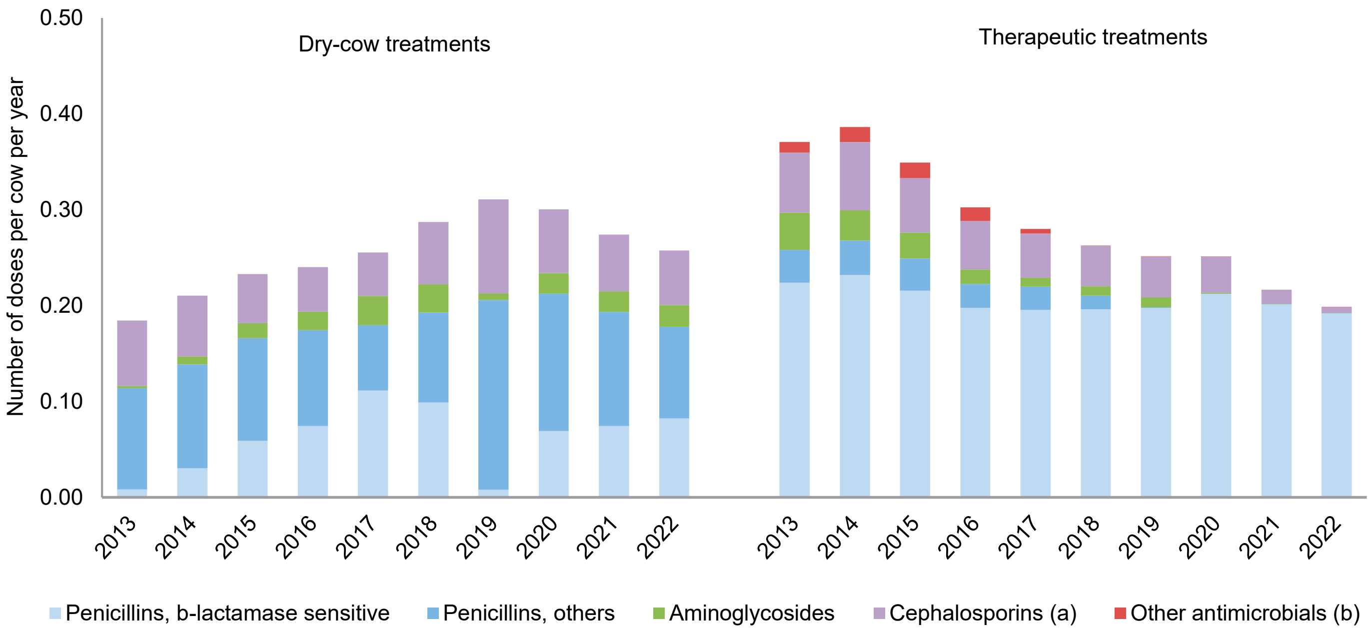
In 2022, the overall antimicrobial consumption in cattle was 25% lower than in 2013 and the bulk tank milk counts were at 185.400 in February 2022.

Most antimicrobials administered parenterally in cattle are used in dairy cows, primarily to treat mastitis (Table 4.3). The consumption of intramammary treatment, measured as doses per cow per year, is shown in Figure 4.6. The consumption of simple penicillins (beta-lactamase sensitive penicillins) has increased, whereas the consumption of 1st generation cephalosporins has decreased.

In 2019, there was a remarkable shift in the dry-cow treatments and the use of the beta-lactamase sensitive penicillins for this purpose almost ceased, while the use of the other penicillins, especially cloxacillin, increased. This shift was caused by a product shortage, where the only beta-lactamase sensitive penicillins for dry-cow treatment was unavailable for longer periods of 2019, and other penicillins especially products containing cloxacillin, had to be used instead [Personal communication; Michael Farre, Danish Agriculture and Food Council]. In 2020 and onwards, it again shifted to the use of only beta-lactamase sensitive penicillins (Figure 4.6).

For therapeutic treatments, beta-lactamase sensitive penicillins remained the most used antimicrobial class.

**Figure 4.6 Consumption of antimicrobials for intramammary application in cattle, treatments per cow per year, Denmark** DANMAP 2022




For intramammary treatment, the consumption has been estimated as the number of doses
Combination products are split into active compounds
a) 1st generation cephalosporins only
b) Includes lincomycin for dry-cow treatments. For therapeutic treatment, mainly sulfonamides-trimethoprim, but also lincomycin and bacitracin

### 4.3.3 Antimicrobial consumption in poultry

The poultry production comprises broiler production, egg layers, and turkey production. In addition, there is a small production of ducks, geese, and game birds. Conventional broiler farms have a very high level of biosecurity, and the antimicrobial consumption in broiler production is generally low compared with other species. Accordingly, disease outbreaks in just a few farms can markedly affect the national statistics on antimicrobial usage in the poultry sector (Table 4.4).

Previously, VetStat did not allow easy differentiation of antimicrobial use in different types of poultry production. However, this has been amended in the new VetStat. From June 2021 antimicrobial use has been reported in more detail, subsequently in a few years it will be possible to follow trends in antimicrobial usage in the different types of poultry production.

In 2022, the total antimicrobial usage has increased by 53.6 kg active compound compared to 2021 (Table 4.4). While the consumption of penicillins, tetracyclines and others, has decreased by 104.7 and 186.3 kg active compound respectively, the macrolide consumption has increased by 214.1 kg active compound. The increase is very likely caused by disease in several flocks in a single farm [personal communication, Susanne Kabel, Danish Agriculture and Food Council]. For the past decade, cephalosporins have not been used in the poultry production, and the use of fluoroquinolones stopped in 2021. Colistin has not been used since 2016.

**Table 4.4 Consumption of antimicrobials in poultry, kg active compound, Denmark** DANMAP 2022

| | Aminoglycosides | Amphenicols | Fluoroquinolones | Lincosamides | Macrolides | Other antibacterials (a) | Penicillins, b-lactamase sensitive | Penicillins, others | Pleuromutilins | Sulfonamides and trimethoprim | Tetracyclines | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| 2013 | 36.0 | 9.0 | 0.0 | 17.7 | 293.0 | 1.4 | 171.9 | 220.1 | 4.1 | 61.6 | 488.5 | 1303.3 |
| 2014 | 21.4 | 8.5 | 0.1 | 10.5 | 399.5 | 2.3 | 133.3 | 373.8 | 0.4 | 82.6 | 604.0 | 1636.4 |
| 2015 | 258.5 | 4.4 | 1.0 | 129.1 | 133.3 | 9.5 | 204.4 | 566.0 | 0.5 | 446.0 | 816.6 | 2569.2 |
| 2016 | 60.2 | 4.8 | 0.0 | 23.8 | 175.6 | 8.0 | 264.6 | 257.6 | 0.4 | 111.0 | 764.6 | 1670.6 |
| 2017 | 64.9 | 5.1 | 0.0 | 31.7 | 244.9 | 1.0 | 355.6 | 334.8 | 0.5 | 84.6 | 487.5 | 1610.4 |
| 2018 | 50.6 | - | 0.0 | 25.3 | 195.0 | - | 357.8 | 242.6 | 0.8 | 36.6 | 521.1 | 1429.7 |
| 2019 | 54.8 | 0.2 | 0.0 | 27.4 | 274.8 | - | 368.4 | 234.3 | 0.6 | 64.2 | 694.3 | 1719.1 |
| 2020 | 58.2 | - | 0.0 | 29.0 | 156.9 | - | 334.1 | 237.3 | 0.2 | 54.6 | 1587.9 | 2458.3 |
| 2021 | 53.9 | - | - | 25.2 | 168.6 | - | 112.5 | 188.9 | 0.4 | 33.0 | 623.5 | 1205.9 |
| 2022 | 49.0 | - | - | 15.0 | 382.7 | - | 217.1 | 129.3 | 19.0 | 10.2 | 437.2 | 1259.5 |

Data for 2022 were extracted from VetStat on 22 May 2023
VetStat does not differentiate between consumption in the different sectors of poultry production
Combination drugs are divided into active compounds
a) Other antibacterials also include other quinolones and polymyxins

### 4.3.4 Antimicrobial consumption in aquaculture, and companion animals

**Aquaculture**

Antimicrobial consumption in aquaculture is mainly driven by the summer air temperatures and hours of summer sunlight because bacterial diseases are more likely to occur when water temperatures are high [Villumsen and Bojesen, 2022. Microbiol Spectr. 10(5):e0175222]. Although the aquaculture production continues to focus on developing improved vaccination strategies to reduce the risk of bacterial diseases that may require treatment with antimicrobials, the antimicrobial consumption varies significantly from year to year. In 2022 the antimicrobial consumption increased by 5% compared to the average consumption in the previous five years. The increase was solely due to increased usage of combination products of sulfonamides and trimethoprim (Table 4.5).

In 2022, mainly three antimicrobial classes were used to treat bacterial infections in aquaculture: 79.2% of sulfonamides and trimethoprim, 14.9% of other quinolones (oxolinic acid), and 5.9% of amphenicols (florfenicol) (Table 4.5).

**Table 4.5 Consumption of antimicrobials in aquaculture, kg active compound, Denmark** DANMAP 2022

| | Amphenicols | Other antibacterials(a) | Other quinolones | Penicillins, others | Sulfonamides and trimethoprim | Tetracyclines | Total |
|---|---|---|---|---|---|---|---|
| 2013 | 180.5 | 0.2 | 961.1 | 10.1 | 2278.6 | 1.8 | 3432.3 |
| 2014 | 297.1 | - | 1706.3 | 9.8 | 3132.1 | - | 5145.2 |
| 2015 | 311.1 | - | 1019.5 | 5.2 | 1655.0 | 0.7 | 2991.5 |
| 2016 | 313.9 | 0.0 | 900.1 | 13.6 | 1085.9 | 0.4 | 2313.9 |
| 2017 | 350.3 | 0.1 | 652.3 | 35.1 | 679.3 | 0.1 | 1717.2 |
| 2018 | 323.5 | 0.0 | 949.3 | 51.6 | 2292.6 | 0.5 | 3617.5 |
| 2019 | 292.6 | - | 456.5 | 43.9 | 1720.9 | 22.0 | 2535.9 |
| 2020 | 341.2 | 0.0 | 574.9 | 27.1 | 1030.2 | 1.0 | 1974.3 |
| 2021 | 295.4 | 0.2 | 392.3 | 19.5 | 1088.9 | 0.8 | 1797.2 |
| 2022 | 143.9 | 0.0 | 366.5 | - | 1940.8 | 0.6 | 2451.8 |

Data for 2022 were extracted from VetStat on 22 May 2023
Combination products are split into active compounds
a) Other antibacterials also includes lincosamides

**Companion animals - horses and pets**

The information available on antimicrobial consumption in companion animals is not as accurate as for production animals, since VetStat allows registration of antimicrobials for companion animals without defining animal species. Table 4.6 shows the antimicrobial consumption registered for companion animals in three categories: horses, pets, and "unspecified". In addition, the Table 4.6 includes the category "unknown", which are products where the animal species was not registered.

The total amount of antimicrobials estimated for consumption in companion animals in 2022 was 2180.4 kg (Table 4.6, Figure 4.7). Since human approved antimicrobial products were not included in DANMAP 2021 a comparison to the previous year will be inaccurate. In total, 109.7 kg active compound of products approved for humans was used for companion animals in 2022 (Table 4.7).

As in previous years, a substantial amount of sulfonamide/trimethoprim registered as used for pets is oral paste, a product normally used for horses. Thus, a substantial amount of sulfonamide/trimethoprim included in Table 4.6 is likely to have been used for horses (165.5 kg in 2022 and 270.8 kg in 2021).

A large proportion of antimicrobials for dogs and cats are prescribed for the treatment of chronic or recurrent disease, mainly dermatitis. Due to the close contact between owners and their pets, repeated use of critically important antimicrobials may pose a risk to the owners, and the use of these antimicrobials is therefore monitored carefully. Since the treatment guidelines by DVA were published in 2012 (revised in 2018), the use of cephalosporins has been reduced from 272.7 kg in 2012 to 61.1 kg of active compound in 2022 (Table 4.6 and 4.7).

In 2022, the consumption of fluoroquinolones in companion animals, mainly dogs and cats, was 14.2 kg active compound and represented the majority (91.6%) of fluoroquinolones used in all animals (Table 4.1, 4.6 and 4.7). Similarly, the pets accounted for 55.7% (61.1 kg) of all the cephalosporins consumed in animals (Table 4.1, 4.6 and 4.7). In 2022, the consumption of 3rd generation cephalosporins were registered in the unspecified category, 1.6 kg active compound in total. 4th generation cephalosporins were not used in 2022.

**Table 4.6 Estimated consumption of antimicrobials for horses, pets and unspecified animals, kg active compound, Denmark**

DANMAP 2022

| | Aminoglycosides | Amphenicols | Cephalosporins | Fluoroquinolones | Lincosamides | Macrolides | Other antibacterials [a] | Penicillins, b-lactamase sensitive | Penicillins, others | Sulfonamides and trimethoprim | Tetracyclines | Total |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| *Horses* | | | | | | | | | | | | |
| 2013 | 1.4 | 1.8 | 0.2 | 0.0 | - | - | 0.0 | 8.2 | 0.1 | 86.8 | 5.4 | 104.0 |
| 2014 | 1.4 | 0.3 | 0.4 | 0.0 | - | 0.1 | 0.0 | 9.3 | 0.2 | 98.0 | 6.7 | 116.5 |
| 2015 | 2.8 | 0.4 | 0.4 | 0.0 | 0.0 | 0.1 | 0.0 | 6.9 | 0.1 | 114.4 | 4.8 | 129.7 |
| 2016 | 0.8 | 0.4 | 0.1 | 0.0 | - | - | 0.0 | 5.1 | 0.0 | 108.0 | 5.2 | 119.7 |
| 2017 | 0.9 | 0.3 | 0.1 | 0.0 | - | - | 0.0 | 5.3 | 0.1 | 106.4 | 3.0 | 116.1 |
| 2018 | 0.7 | 0.0 | 0.2 | . | - | 0.1 | 0.0 | 5.7 | 0.0 | 100.6 | 3.8 | 111.1 |
| 2019 | 0.9 | - | 0.1 | 0.0 | - | 0.0 | 0.0 | 4.9 | 0.0 | 94.2 | 3.8 | 104.0 |
| 2020 | 0.5 | - | 0.0 | 0.0 | - | - | 0.0 | 4.2 | 0.0 | 111.5 | 3.5 | 119.7 |
| 2021 | 0.2 | - | 0.0 | 0.0 | 0.0 | 0.0 | 0.1 | 5.2 | 0.1 | 105.5 | 2.0 | 113.1 |
| 2022 | 0.3 | 0.0 | 0.0 | 0.0 | 0.0 | - | 0.2 | 4.5 | 0.2 | 136.0 | 7.3 | 148.5 |
| *Pets* | | | | | | | | | | | | |
| 2013 | 3.6 | 0.3 | 75.1 | 4.8 | 16.6 | 3.2 | 7.3 | 7.9 | 114.0 | 252.3 | 19.4 | 504.6 |
| 2014 | 5.6 | 0.6 | 81.3 | 5.0 | 19.0 | 5.0 | 7.0 | 12.1 | 122.3 | 261.0 | 13.3 | 532.3 |
| 2015 | 4.8 | 3.6 | 61.8 | 5.6 | 21.8 | 3.3 | 8.6 | 13.2 | 123.4 | 226.2 | 20.4 | 492.7 |
| 2016 | 3.4 | 3.4 | 55.3 | 5.4 | 21.8 | 2.3 | 7.6 | 9.8 | 131.2 | 269.1 | 21.5 | 530.7 |
| 2017 | 3.8 | 0.7 | 41.7 | 5.2 | 18.4 | 1.7 | 8.4 | 9.2 | 125.8 | 272.4 | 19.3 | 506.6 |
| 2018 | 3.9 | 0.3 | 35.9 | 4.9 | 17.5 | 1.7 | 14.8 | 10.0 | 113.7 | 253.2 | 21.1 | 477.1 |
| 2019 | 3.7 | 0.3 | 32.3 | 4.5 | 17.2 | 7.4 | 15.6 | 10.4 | 108.4 | 236.8 | 14.8 | 451.4 |
| 2020 | 4.3 | 0.6 | 30.7 | 5.1 | 19.1 | 3.8 | 18.1 | 12.9 | 103.4 | 262.3 | 17.7 | 478.0 |
| 2021 | 3.2 | 0.7 | 28.0 | 4.7 | 19.2 | 2.2 | 20.9 | 11.4 | 100.1 | 270.8 | 23.7 | 484.8 |
| 2022 | 1.7 | 0.0 | 22.3 | 3.9 | 16.5 | 0.2 | 24.5 | 9.4 | 79.5 | 165.5 | 22.3 | 345.7 |
| *Unspecfied* | | | | | | | | | | | | |
| 2013 | 18.4 | 0.0 | 155.4 | 8.6 | 47.0 | 0.1 | 26.2 | 1.0 | 416.3 | 843.6 | 17.4 | 1534.0 |
| 2014 | 18.3 | 0.0 | 131.8 | 8.2 | 50.0 | - | 26.7 | 2.3 | 419.6 | 967.6 | 20.2 | 1644.7 |
| 2015 | 14.4 | 0.3 | 95.6 | 8.6 | 45.7 | 0.0 | 25.1 | 1.4 | 413.7 | 944.8 | 15.9 | 1565.6 |
| 2016 | 14.9 | 0.4 | 81.6 | 9.6 | 47.6 | 0.3 | 26.3 | 2.2 | 456.1 | 1014.5 | 16.2 | 1669.7 |
| 2017 | 15.1 | 0.2 | 69.1 | 9.2 | 48.5 | 0.0 | 28.2 | 1.8 | 458.6 | 1071.1 | 14.6 | 1716.4 |
| 2018 | 13.8 | 1.3 | 61.4 | 9.7 | 44.2 | - | 34.8 | 1.7 | 443.2 | 1135.5 | 12.9 | 1758.6 |
| 2019 | 14.3 | 0.2 | 60.6 | 9.9 | 46.9 | 0.1 | 36.8 | 1.6 | 435.4 | 1139.2 | 15.5 | 1760.6 |
| 2020 | 10.0 | 0.4 | 56.9 | 10.7 | 49.8 | - | 40.0 | 2.7 | 440.9 | 1221.3 | 15.6 | 1848.4 |
| 2021 | 10.7 | 0.4 | 49.4 | 10.1 | 54.6 | - | 47.3 | 0.8 | 451.6 | 1282.5 | 14.4 | 1921.8 |
| 2022 | 1.0 | 0.4 | 38.8 | 8.6 | 50.3 | - | 51.7 | 0.0 | 389.5 | 1096.9 | 11.9 | 1649.1 |
| *Unknown* | | | | | | | | | | | | |
| 2013 | 187.0 | -57.7 | 8.3 | 3.2 | 13.6 | 41.9 | 44.9 | 551.3 | 199.4 | 292.3 | 174.6 | 1458.9 |
| 2014 | 176.8 | -95.0 | 5.9 | 1.5 | 7.9 | 44.8 | 66.9 | 511.4 | 187.9 | 322.9 | 164.9 | 1395.8 |
| 2015 | 219.2 | 129.9 | 5.5 | 1.9 | 23.1 | 50.0 | 22.0 | 529.2 | 162.7 | 340.5 | 168.4 | 1652.3 |
| 2016 | 175.9 | 202.2 | 2.7 | 1.7 | 6.4 | 19.5 | 14.0 | 506.2 | 211.9 | 274.4 | 124.5 | 1539.4 |
| 2017 | 237.1 | 117.2 | 3.6 | 0.9 | 9.0 | 52.7 | 9.2 | 573.6 | 122.8 | 279.1 | 156.0 | 1561.4 |
| 2018 | 266.9 | -44.2 | 3.6 | 1.3 | 9.0 | 20.8 | 5.9 | 564.1 | 149.3 | 176.1 | 105.3 | 1258.1 |
| 2019 | 336.2 | -11.4 | -8.3 | 1.4 | 9.8 | 33.1 | 5.0 | 537.8 | 140.2 | 109.3 | 147.8 | 1300.9 |
| 2020 | 296.1 | 1.9 | 1.5 | 1.5 | 11.2 | 17.3 | 12.5 | 539.0 | 151.3 | 16.4 | 141.1 | 1189.7 |
| 2021 | 117.2 | -4.7 | 0.9 | 1.7 | 8.1 | 4.8 | 6.8 | 371.6 | 111.4 | 20.8 | 135.0 | 773.7 |
| 2022 | 83.8 | 1.9 | 1.1 | 1.1 | 7.4 | 55.2 | 4.2 | 448.6 | 41.8 | 26.6 | 95.2 | 766.8 |

Data for 2022 were extracted from VetStat 22 May 2023
Combination products are split into active compounds
The estimates include all veterinary approved antimicrobials, for use in horses, pets, as well as products without a specified animal species (unknown)
a) Other antibacterials also include other otologicals, pleuromutilins, polymyxins and sulfonamides, plain

**Table 4.7 Estimated consumption in 2022 of veterinary and human approved antimicrobials for horses, pets and unspecified animals, kg active compound, Denmark** DANMAP 2022

| | Veterinary-approved | Human-approved | Total |
|---|---|---|---|
| *Horses* | | | |
| Aminoglycosides | 0.3 | - | 0.3 |
| Amphenicols | 0.0 | 0.0 | 0.0 |
| Cephalosporins | 0.0 | - | 0.0 |
| Fluoroquinolones | 0.0 | 0.0 | 0.0 |
| Lincosamides | 0.0 | - | 0.0 |
| Macrolides | - | 0.6 | 0.6 |
| Other antibacterials[a)] | 0.2 | 0.3 | 0.4 |
| Penicillins, b-lactamase sensitive | 4.5 | - | 4.5 |
| Penicillins, others | 0.2 | 0.0 | 0.3 |
| Sulfonamides and trimethoprim | 136.0 | - | 136.0 |
| Tetracyclines | 7.3 | - | 7.3 |
| *Pets* | | | |
| Aminoglycosides | 1.7 | 0.0 | 1.7 |
| Amphenicols | 0.0 | 0.0 | 0.0 |
| Cephalosporins | 22.3 | - | 22.3 |
| Fluoroquinolones | 3.9 | 0.1 | 4.0 |
| Lincosamides | 16.5 | 0.0 | 16.5 |
| Macrolides | 0.2 | 0.9 | 1.1 |
| Other antibacterials[a)] | 24.5 | 3.0 | 27.5 |
| Penicillins, b-lactamase sensitive | 9.4 | 1.6 | 11.0 |
| Penicillins, others | 79.5 | 2.3 | 81.8 |
| Sulfonamides and trimethoprim | 165.5 | 0.7 | 166.2 |
| Tetracyclines | 22.3 | 1.7 | 24.0 |
| *Unspecified* | | | |
| Aminoglycosides | 1.0 | - | 1.0 |
| Amphenicols | 0.4 | 0.0 | 0.4 |
| Cephalosporins | 38.8 | - | 38.8 |
| Fluoroquinolones | 8.6 | 0.4 | 9.0 |
| Lincosamides | 50.3 | - | 50.3 |
| Macrolides | - | 1.3 | 1.3 |
| Other antibacterials[a)] | 51.7 | 7.9 | 59.6 |
| Penicillins, b-lactamase sensitive | - | 8.0 | 8.0 |
| Penicillins, others | 389.5 | 5.5 | 395.0 |
| Sulfonamides and trimethoprim | 1096.9 | 0.5 | 1097.3 |
| Tetracyclines | 11.9 | 2.3 | 14.2 |
| *Unknown* | | | |
| Aminoglycosides | 83.7 | 0.1 | 83.8 |
| Amphenicols | 1.6 | 0.1 | 1.8 |
| Cephalosporins | 1.1 | 3.8 | 4.9 |
| Fluoroquinolones | 0.1 | - | 0.1 |
| Lincosamides | 7.4 | - | 7.4 |
| Macrolides | 55.2 | 0.2 | 55.3 |
| Other antibacterials[a)] | 3.9 | 1.5 | 5.4 |
| Penicillins, b-lactamase sensitive | 446.9 | 53.3 | 500.2 |
| Penicillins, others | 40.5 | 13.6 | 54.1 |
| Sulfonamides and trimethoprim | 26.9 | - | 26.9 |
| Tetracyclines | 94.5 | - | 94.5 |
| Total | 2906.2 | 109.7 | 3015.8 |

Data for 2022 were extracted from VetStat on 22 May 2023 for veterinary approved products, and on 17 August 2023 for human approved products
Combination products are split into active compounds
The estimates include all veterinary and human approved antimicrobials, for use in horses, pets, as well as products typically used for companion animals, but without a specified animal species (unspecified)
a) Other antibacterials include other antibacterials, other otologicals, pleuromutilins, polymyxins and sulfonamides (plain)

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## Textbox 4.1

# No more high dose zinc oxide in veterinary medicinal products

Following a review of the safety and effectiveness of veterinary medicinal products containing zinc oxide to be administered orally to food-producing species, in the spring of 2017, the European Medicines Agency (EMA) concluded that the benefits of zinc oxide for the prevention of diarrhoea in pigs did not outweigh the risks for the environment. Based on the review and recommendations from EMA, the European Commission issued a decision on the 26th of June, 2017, to withdraw all existing marketing authorisations. Member States could defer the withdrawal of the marketing authorisations for up to five years from that date.

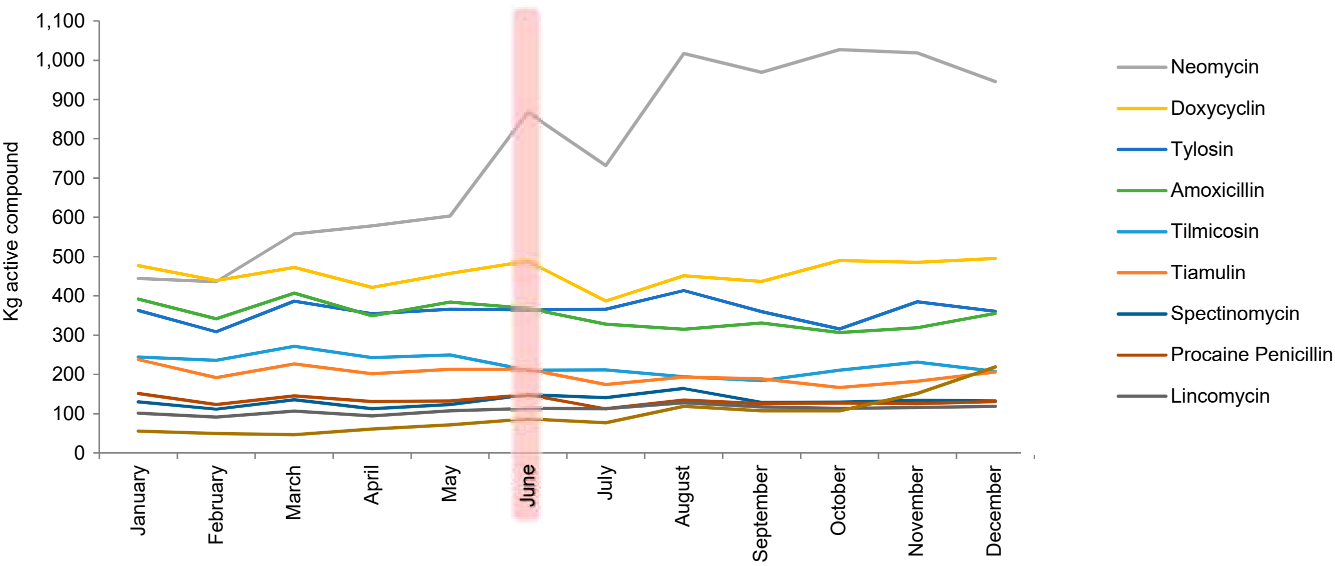
The Danish Medicines Agency implemented this decision on the 26th of June 2022. Thus, it has not been possible to use veterinary medicinal products (VMPs) containing zinc oxide for food-producing animals since then. It is still possible to add zinc oxide to the feed as a feed additive. However, this is at much lower doses than that found in the VMPs.

Zinc oxide as a VMP has primarily been used to control post-weaning diarrhoea in pigs. In the years leading up to the removal of VMPs containing zinc oxide, the Danish pig industry worked hard to find suitable alternatives in the post-weaning period. Despite these efforts, it has not been possible to find a solution that can replace the zinc oxide completely and at the same price. However, much good knowledge has been gained and many possible strategies to control post-weaning diarrhoea have been developed.

Despite this, there has been an increase in the antibiotic use for pigs in the post-weaning period since June 2022. Most notably, there has been an increase in the use of Neomycin (Figure 1) which is used to treat post-weaning diarrhoea in pigs. It should however be noted, that one dose of Neomycin contains more mg active compound than alternative treatment options and the rise in kg active compound will therefore seem larger. However, there is still a considerable increase in treatments for pigs in the post-weaning period.

The Danish Veterinary and Food Administration continues to follow the antibiotic use closely to see whether this rise in consumption is just a temporary trend or if new initiatives to reduce the antibiotic consumption in pigs are needed. The Danish Agriculture and Food Council and the Danish Veterinary and Food Administration are working together to find solutions for the farmers who find it difficult to get through the post-weaning period without VMPs containing zinc oxide.

**Figure 1 The development in tthe use of the ten most used antibiotics in weaned pigs (age group 56), 2022** DANMAP 2022




Changes in the 10 most commonly used active compounds for pigs in age group 56 (weaned pigs up to 30 kg). Medicinal zinc oxide was phased out in June 2022

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## Textbox 4.2

# New EU legislation on veterinary medicinal products

Order 2019/6 on veterinary medicinal products has applied since 28 January 2022. The Order aims to reduce the administrative burden, enhance the internal market and increase the availability of veterinary medicinal products, while guaranteeing the highest level of public and animal health and environmental protection. There is a particular focus on reducing the risk of antimicrobial resistance (AMR).

In Denmark, the responsibility for the legislation on veterinary medicinal products (VMPs) is shared between the Danish Veterinary and Food Administration (DVFA) and the Danish Medicines Agency (DMA).

The DVFA is responsible for the regulatory framework on the use of VMPs.

The DMA is responsible for the regulatory framework for the placing on the market, manufacturing, import, export, supply, distribution and pharmacovigilance.

**Provisions on the prescription and use of VMPs**
The provisions on the prescription and use of VMPs appear from Articles 105 - 118. Provisions of particular relevance for the use of antimicrobials are:

- Article 105(6) which states that the quantity of the medicinal products prescribed shall be limited to the amount required for the treatment or therapy concerned. As regards antimicrobial medicinal products for metaphylaxis or prophylaxis, they shall be prescribed only for a limited duration to cover the period of risk.

- Article 106(1) according to which VMPs must be used in accordance with the marketing authorisations. This means that the instructions given in the marketing authorisation (SPC), including the dose and duration of treatment, must be followed.

- Article 107 provides restrictions on the use of antimicrobial medicinal products.
  Antimicrobials must not be used routinely nor be used to compensate for e.g. poor hygiene.

  Restrictions are set for prophylaxis and metaphylaxis:
  - Prophylaxis only allowed in exceptional cases and only for an individual animal or a restricted number of animals when the risk of infection is very high.
  - Antibiotics for prophylaxis allowed to an individual animal only when the risk of infection is very high.
  - Antimicrobials for metaphylaxis only allowed when the risk of spread of an infection is high and no appropriate alternatives are available.

Antimicrobials listed in Order 2022/1255 are reserved for treatment of certain infections in humans. For many years, Denmark has had a fairly detailed legislation on the use of VMPs. This legislation has been continued with minor adjustments to ensure compliance with the Regulation.

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## Textbox 4.3

# Faecal microbiota transplantation for prevention of diarrhoea in pigs

**Background**

Faecal microbiota transplantation (FMT) is a medical procedure in which faecal material from a healthy donor is transplanted into the gastrointestinal tract of a recipient to restore a healthy microbial balance in the gut. The procedure is used in human medicine to treat certain gastrointestinal disorders associated with an imbalance of the gut microbiota, particularly recurrent *Clostridioides difficile* infection [1]. In veterinary medicine, transplants of faeces or ruminal fluid have been used in horses and cows to restore the gastrointestinal microbiome after antibiotic treatment. In pigs there is experimental evidence that transplants of intact faeces or faecal filtrates can be used to colonize the gut immediately after birth [2-3]. As part of the EU project AVANT (https://avant-project.eu/), which is coordinated by the University of Copenhagen, FMT and other alternatives to antibiotics are being evaluated as a tool to reduce antimicrobial use in animals. AVANT focuses on diarrhoea in pigs because this is the animal species that accounts for most antimicrobials use in animals (see chapter 4, Figure 4.2) and diarrhoea is the main indication for antimicrobial use in pigs [4]. Alternatives to antimicrobials are an attractive solution to reduce antimicrobial use in the management of this disease as well as to address the lack of effective therapies following the zinc ban, the restrictions in the use of colistin and the rise in neomycin resistance in the causative pathogen, enterotoxigenic Escherichia coli (see Text Box 9.2). In another project led by the University of Copenhagen (financed by the Independent Research Foundation Denmark and SEGES-Innovation), we established an experimental paradigm for faecal transplants in neonatal pigs and then applied this for an experiment under faming conditions. Here, we report the methodology and the most significant data from this experiment. Samples from this experiment are now subject to further analysis in AVANT to understand the microbial changes occurring in the gut microbiota of treated animals.

**Methods**

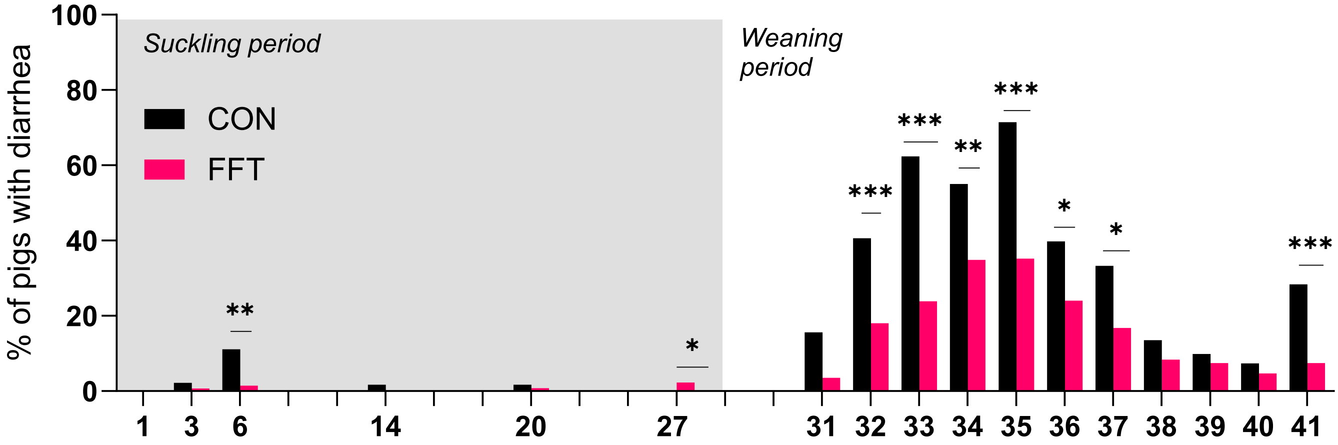
After thorough screening to exclude the presence of common pathogens, faeces from a healthy sow were diluted in a sterile buffer, centrifugated and filtrated using 0.45 µm membrane filters. The resulting filtrate was administered orally to 150 newborn piglets (FFT, 15 pigs from each of 10 litters) on the same farm as the donor sows to minimize the risk of pathogen transmission between farms. An equal number of piglets were treated with sterile buffer as the control group. On day 28, just before weaning, two piglets from each litter (40 piglets in total) were euthanized to collect intestinal tissue and content. The remaining piglets were weaned in a separate facility and transitioned to solid feed until the end of the study (41 days). A faecal scoring system was used to identify diarrhoeic piglets and the daily occurrence of diarrhoea and death were recorded in each group throughout the study.

**Results and discussion**

A significant lower occurrence of diarrhoea (Figure 1) and death (Figure 2) was observed in the weaning period compared to the control group. It should however be noted that considerable proportions of piglets in the treatment group suffered from diarrhoea and were euthanized or died during the post-weaning period (4% in the FFT group versus 16% in the control group), suggesting that although promising, FFT was unable to completely prevent post-weaning diarrhoea. Noteworthy, the experimental farm was selected based on its history of recurring post-weaning diarrhoea, and whether effects would be reproducible in other farms remains unknown at this stage. As it stands now, this intervention could help reduce the need for antimicrobials, but is unlikely to eliminate the use of antimicrobials to treat this disease when implemented in intensive pig farms. Further research is needed to optimize dosage, mode of administration, and donor selection, as well as to determine the individual effects of various components of filtrated transplants, including small bacteria, bacteriophages, and metabolites. During the latter part of the project, the AVANT consortium will evaluate how the use of antimicrobials in pig production would be reduced by the implementation of this and other alternatives to antimicrobials on a European scale.

**Figure 1 Daily occurrence (%) of piglets displaying symptoms of diarrhoea in the treatment (FFT) and control (CON) groups**

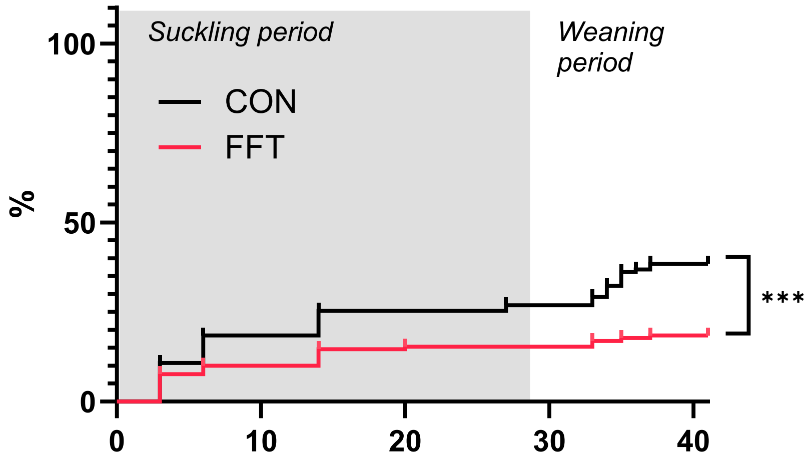
DANMAP 2022




Significant differences between groups are indicate as *p <0.05; **, p <0.01; ***, p <0.001

**Figure 2 Mortality rate (%) in the treatment (FFT) and control (CON) groups**

DANMAP 2022




Significant differences between groups are indicate as *p <0.05; **, p <0.01; ***, p <0.001

continued ... Textbox 4.3

Based on these results, the FMT protocol described in this study was selected by the AVANT consortium as one of the two interventions to be tested by a large clinical trial in Denmark, France and the Netherlands. However, the French and Danish national competent authorities denied the trial permission with reference to Regulation EC 767/2009, which prohibits to feed production animals with any material of faecal origin. Furthermore, this intervention cannot be considered a veterinary medicinal product as its content cannot be standardized and the active substance(s) are not characterised. A possible solution to this regulatory hurdle requires adaptation of feed legislation or new legislation to accommodate the development and commercialization of on-farm interventions that do not fall into the category of feed additives or veterinary medicines, while ensuring safety standards and efficacy. Accordingly, the AVANT consortium engaged with the European Commission and other stakeholders to initiate a legislative pathway to facilitate future clinical trials and commercialization of FMT approaches to prevent disease and reduce the use of antimicrobials in livestock.

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