Federal Ministry
of Food
and Agriculture

Report of the Federal Ministry of Food and Agriculture on the Evaluation of the Antibiotics Minimisation Concept introduced with the 16th Act to Amend the Medicinal Products Act (16th AMG Amendment)

Evaluation based on section 58g of the Medicinal Products Act

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LIST OF ABBREVIATIONS USED

AG TAM	Working Group on Veterinary Medicinal Products of LAV *(Arbeitsgruppe Tierarzneimittel der LAV)*
AMG	Medicinal Products Act (Arzneimittelgesetz)
BfR	Federal Institute for Risk Assessment *(Bundesinstitut für Risikobewertung)*
BMEL	Federal Ministry of Food and Agriculture *(Bundesministerium für Ernährung und Landwirtschaft)*
BVL	Federal Office of Consumer Protection and Food Safety *(Bundesamt für Verbraucherschutz und Lebensmittelsicherheit)*
DART	German Antibiotic Resistance Strategy
DIMDI	German Institute for Medical Documentation and Information *(Deutsches Institut für Medizinische Dokumentation und Information)*
DIMDI-AMV	Ordinance on the Database-supported Information System on Medicinal Products of the German Institute for Medical Documentation and Information (DIMDI Medicinal Products Ordinance) *(Verordnung über das datenbankgestützte Informationssystem über Arzneimittel des Deutschen Instituts für Medizinische Dokumentation und Information [DIMDI-Arzneimittelverordnung])*
EMA	European Medicines Agency
HITier	Central database on animal identification and registration *(Herkunftssicherungs- und Informationssystem für Tiere)* (Database of the *Länder*)
HYP	Half-yearly period, e.g. HYP 14/2 stands for the second half of 2014. The following half-yearly periods are abbreviated in the same way.
HPCIA	Highest Priority Critically Important Antimicrobials
kg	Kilogram
BW	Body weight
LA/OS	"Long-acting/one-shot" preparations that have a duration of action of more than 24 hours
LAV	*Länder* Working Group for Consumer Protection *(Länderarbeitsgemeinschaft Verbraucherschutz)*
Länder report	"Evaluation of the 16^{th} AMG Amendment – Contribution of the *Länder*", prepared by the Working Group on Veterinary Medicinal Products (AG TAM) of the *Länder* Working Group for Consumer Protection (LAV)
OIE	World Organisation for Animal Health
QS	Qualität und Sicherheit GmbH
t	Tonnes
TF	Half-yearly treatment frequency per farm
VVVO	Livestock Trade and Transport Ordinance
WHO	World Health Organisation

GLOSSARY

Supplied quantities	see Supplied quantities of antibiotics
Supplied quantities of antibiotics	Data collected in line with DIMDI-AMVon the supply of antibiotic substances by pharmaceutical companies and wholesalers to veterinarians (these data correspond approximately to the "sales figures for antibiotic agents" as defined by ESVAC – European Surveillance of Veterinary Antimicrobial Consumption)
Antibiotics database	Veterinary medicinal product (TAM) database of the *Länder* in the central database on animal identification and registration (HITier)
Antibiotics Minimisation Concept	Provisions of sections 58a to 58d Medicinal Products Act (AMG)
Used quantities of antimicrobials	Data collected pursuant to section 58b AMG on the use of antibiotics in the types of production (see below) covered by the 16th AMG Amendment
Days of treatment	Number of days on which the medicinal product was administered
Third (3rd) quartile	The 3rd quartile is the value in a data distribution above which 25% of the individual data lie. Therefore, 75% of the individual data lie below the 3rd quartile.
First (1st) quartile	The 1st quartile is the value in a data distribution below which 25% of the individual data lie. Therefore, 75% of the individual data lie above the 1st quartile.
Indicators	Median (indicator 1) and third quartile (indicator 2) of treatment frequencies per farm. Calculated by the Federal Office of Consumer Protection and Food Safety (BVL) in accordance with section 58c (4) AMG for every half-yearly period for each of the types of production recorded from all farm treatment frequencies determined individually during a half-yearly period, and published at the end of March and September respectively in the Federal Gazette *(Bundesanzeiger).*

Median (2nd quartile)	The median is the value which is right in the middle of the data distribution. Half of the individual data lie below the median, half lie above.
Parenteral	Route of administration of substances (e.g. medicinal products or artificial nutrition) by means of injection or infusion that bypasses the gastro-intestinal tract
Used quantities	see Used quantities of antibiotics
Days of drug action	Number of days on which the medicinal product exerted its action. This term is used in the antibiotics database instead of the term "days of treatment" pursuant to section 58b (1) sentence (1) (3) AMG. There, as in this report, the term "days of drug action" covers the number of days of treatment, supplemented, where applicable, in the case of LA/OS preparations by the number of days on which the medicinal product retains its therapeutic drug level. The number of these days is to be specified by the veterinarian and may coincide with the number of days of treatment depending on the duration of action of the medicinal product or cover a longer period than the number of days of treatment.
Zoonosis	Zoonoses are diseases or infections that can be transmitted between humans and animals directly or indirectly in a natural manner. Viruses, bacteria, fungi etc. are potential zoonotic pathogens.
Zoonosis monitoring	Zoonosis monitoring entails the collection, analysis and publication of representative data on the occurrence of zoonotic pathogens and the related antibiotic resistance in food, feed and live animals. Zoonosis monitoring has been undertaken in the *Länder* as part of official food and veterinary control since 2009.

Types of production	Animal species and animal categories that come under the16th AMG Amendment pursuant to section 58a as follows:
Fattening calves	Fattening calves from weaning up to the age of and including eight months
Fattening cattle	Fattening cattle over the age of eight months
Fattening piglet	Piglets from weaning up to and including 30 kg
Fattening pigs	Fattening pigs over 30 kg
Fattening turkeys	Fattening turkeys from the date of hatching
Fattening chickens	Fattening chickens from the date of hatching

Summary

Humans and animals are often infected by the same bacterial pathogens and treated with the same antimicrobials. Consequently, they mutually influence the development of antimicrobial resistance. Resistant bacteria have acquired the ability to protect themselves from the effects of one or more antibiotics by altering their genetic make-up, thereby circumventing the intended action. The more frequently bacterial pathogens come into contact with antibiotics, the more resistance is promoted by selection pressure. The use of antibiotics is, therefore, a major contributory factor to increasing resistance. A key to preventing antibiotic resistance, therefore, lies in the prudent, responsible and generally reduced use of antibiotics in both human and veterinary medicine. Antibiotics are used in both human and veterinary medicine to treat bacterial infectious diseases. In Germany, many of the active substance classes used in human medicine are also authorised for use in veterinary medicine, including active substance classes classified as "Highest Priority Critically Important Antimicrobials" (HPCIAs, known as "critical active substance classes"). They are, therefore, particularly important for public health. No active substance class has been authorised solely for veterinary medicine, but several active substance classes are reserved for human medicine.

To reduce the further development and spread of antimicrobial resistance, the Federal Government has developed and implemented the concept set out in the German Antimicrobial Resistance Strategy (DART) in 2008. This strategy was continued in 2015 with the revised and updated follow-up strategy DART 2020. One of the main measures in DART in the field of veterinary medicine was the establishment of a system for the nationwide minimisation of antibiotic use in animal keeping in the case of specific fattening animals (cattle, pigs, chickens, turkeys). With the 16th Act to Amend the Medicinal Products Act (16th AMG Amendment) which came into force on 1 April 2014, a system of this kind was established for the first time in Germany. The Antibiotics Minimisation Concept laid down in this system (sections 58a to 58d AMG) pursues three goals, namely

- **Goal 1:** To reduce the use of antibiotic veterinary medicinal products in the keeping of certain fattening animals,

- **Goal 2:** To promote prudent and responsible antibiotic use in the treatment of diseased animals in order to limit the risk of the emergence and spread of antibiotic resistance, and

- **Goal 3:** To facilitate effective task performance by competent authorities, particularly on livestock farms.

The measures contained in the Antibiotics Minimisation Concept of the 16th AMG Amendment encompass the obligation of the animal keepers concerned to provide information on their livestock farming and their use of antibiotics, as well as the obligation for the competent authorities to calculate the half-yearly treatment frequency per farm on the basis of this information and to forward it to the Federal Office of Consumer Protection and Food Safety (BVL) and the animal keeper. Based on all individual treatment frequencies per farm determined in a half-yearly period (HYP), BVL then calculates the median (indicator 1) and the third quartile (indicator 2) of the treatment frequency per farm for each half-yearly period for each of the six types of production (fattening piglets, fattening pigs, fattening calves, fattening cattle, fattening chickens and fattening turkeys) governed by the 16th AMG Amendment. It then publishes these nationwide indicators in the Federal Gazette at the end of March and September respectively. The comparison of the treatment frequencies for each individual farm with the nationwide indicators published by BVL constitutes the basis for further action. If a farm's treatment frequency lies in the upper half of the values (above indicator 1, i.e. above the median), the animal keeper must identify, in consultation with a veterinarian, the causes and examine steps that could be taken to reduce the use of antibiotics. If the farm's treatment frequency lies in the upper quarter of the values (above indicator 2, i.e. above the 3rd quartile), the animal keeper must, after consultation with a veterinarian, draw up a written plan of action to reduce the use of antibiotics and submit it to the competent authority. The *Länder* are responsible for enforcing the provisions of the 16th AMG Amendment.

According to section 58g AMG, the Federal Ministry of Food and Agriculture (BMEL) must evaluate the effectiveness of the steps taken in accordance with sections 58a to 58d AMG and report on them to the Bundestag five years after the 16th AMG Amendment has come into force. With this evaluation report, the BMEL has complied with its legal obligation. The evaluation report presents an overall analysis based on various sub-studies. They include evaluations of the recorded supplied and used quantities of antibiotics and treatment frequencies (criterion 1), the resistance situation of bacteria from the food chain and pathogens of the affected animal species (criterion 2), the contribution of the *Länder* (*Länder* report) to the findings and the experiences of the competent authorities (criterion 3) and a nationwide survey on the experiences of livestock keepers and veterinarians (criterion 4).

The last-mentioned survey points to increased awareness of the problem of antimicrobial use and resistance in the target groups. The respondents stated that the 16th AMG Amendment had contributed to this heightened awareness and prudent use of antibiotics. The majority of the animal keepers and veterinarians reported the high burden involved in the notification and documentation duties and advice. A majority of the veterinarians who took part in the survey felt that a further reduction in the use of antibiotics would not be possible without this having a negative impact on animal health.

The results and the conclusions of the evaluation attributed to the three goals set out in the legislation are presented below.

Goal 1: To reduce the use of antibiotics in the keeping of fattening animals

The desired reduction in the use of antibiotics stipulated in the 16th AMG Amendment was achieved in all six types of production. This is demonstrated by the results presented below on the development in the supplied quantities of antimicrobials, the used quantities of antimicrobials and the treatment frequencies per farm.

Between 2011 and 2017, there was a total reduction of 57% in the quantities of antibiotic substances supplied by pharmaceutical companies and wholesalers (supplied quantities of antimicrobials) to veterinarians. The decline amounted to 467 t or 27.4% in the period from 2011 to 2014 and was significantly higher in the period from 2014 to 2017, i.e. 505 t or 40.8%. What is particularly noticeable is the substantial decline in the quantity supplied from 2014 to 2015 by 433 t or 35%. This is very likely an effect of the 16th AMG Amendment that came into force in April 2014.

A survey of the nationwide used quantities of antimicrobials that were used for the six types of production has been carried out in Germany since the second half-yearly period of 2014 (HYP 14/2). The total used quantity of antimicrobial substances fell, from HYP 14/2 to HYP 17/2, by a total of 94 t (31.6%) from 298 t to 204 t. By far the largest reduction was achieved in pigs (fattening piglets: 46% reduction from 87.5 t to 47.2 t, fattening pigs: 43% reduction from 115.0 t to 65.2 t). In contrast, the used quantities for fattening calves, fattening chickens and fattening turkeys remained almost unchanged over the same period (-4% for fattening turkeys, -1% for fattening chickens and -4% for fattening calves). In the case of fattening cattle there was a large percentage reduction of 76%, but the quantities used for this type of production were very small, i.e. 1.7 t and 0.4 t respectively.

The comparison of the annual supplied quantities with the total annual used quantities shows the following development in the period from 2015 to 2017. Whereas the total used quantity fell by 71 t (14.9 %) from 475 t in 2015 to 404 t in 2017, the supplied quantity fell by 72 t (9.0 %) from 805 t to 733 t. This development suggests that the reduced antimicrobial use for the types of production recorded has contributed more to the reduction in the supplied quantities than the use of antimicrobials for those animal species or types of production that are not subject to the 16th AMG Amendment.

For all types of production and all farm size categories, there was a significant reduction in treatment frequencies per farm between HYP 14/2 and HYP 17/2, but this varied depending on the type of production.

In the case of **fattening piglets** and **fattening pigs**, the treatment frequencies per farm and the nationwide figures fell continuously from HYP 14/2 to HYP 17/2.

In the first three (**fattening chickens**) and five (**fattening turkeys**) half-yearly periods, an initial drop in the nationwide indicators and a decrease in treatment frequencies were likewise observed, followed by a renewed increase in the nationwide indicators, and, particularly in the case of fattening chickens, also in the median of treatment frequency.

In the case of **fattening calves**, the nationwide indicators and the treatment frequencies per farm fell by 50% in the first two half-yearly periods and then remained stagnant on that level. The data indicate that there may be a subgroup of farms keeping fattening calves that should be considered separately. In this context, the *Länder* report lists the specialised weanling rearing farms.

In the case of **fattening cattle**, the indicators and treatment frequencies were close to zero. In this type of production the use of antibiotics was rather sporadic and on a comparatively low scale.

An **impact of farm size** on the level of treatment frequency was clearly discernible for all types of production. The values for treatment frequency in large farms that were higher than in small and medium farms indicate that animals in all types of production were treated more frequently with antibiotics in large farms than in smaller ones.

Goal 2: To promote prudent antibiotic use in fattening animals in order to reduce the resistance risk

The reduced use of antibiotics resulting from the 16th AMG Amendment had positive effects on the development of the resistance situation. The analysed data on the subject of the “prudent use of antibiotics” show that the spectrum of active substance classes used for the six types of production remained constant over the period from HYP 14/2 to HYP 17/2, i.e. there was no increased use of the critical active substance classes.

In order to assess the achievement of the goal regarding the element “prudent use of antibiotics”, the developments in the supplied and used quantities of antibiotics and treatment frequencies were considered separately for each class of active substance. The main question here was whether the reduction in the use of antibiotics achieved with the Antibiotics Minimisation Concept set out in the 16th AMG Amendment could possibly have led to the undesirable consequence that, when selecting the antibiotics used, there had been shifts towards active substance classes requiring low doses that are, moreover, of special significance for human medicine (fluoroquinolones, 3rd and 4th generation cephalosporins, macrolides and polypeptide antibiotics).

The five critical active substance classes for fattening piglets, fattening pigs, fattening calves and fattening cattle each amounted to less than 10% of the used quantity determined for the respective type of production. In contrast, in the case of fattening chickens and fattening turkeys, the share of critical active substance classes was approximately 40% of the used quantity determined in each case.

A plausibility check of the data sets provided strong pointers that polypeptide antibiotics are used at much higher doses in fattening chickens than envisaged in the authorisation conditions.

The individual active substance classes contributed to the reduction in the used quantity of antibiotics by a total of 94 t from HYP 14/2 to HYP 17/2 on the following scale: the consumed quantity of penicillins fell by around 31.8 t, of tetracyclines by around 30.9 t, of sulfonamides by around 13.7 t, of macrolides by around 7.7 t, of polypeptide antibiotics by around 4.38 t, of folic acid antagonists by 2.82 t and of aminoglycosides by 1.44 t. The used quantity of fluoroquinolones fell by around 0.4 t from 2.1 t to 1.7 t. For fenicols the used quantity increased from 0.8 t to 0.9 t during this period. For 3rd generation cephalosporins a slight increase in the used quantity from 20 kg to 21 kg was recorded in the course of the seven half-yearly periods. For 4th generation cephalosporins the used quantity fell from 35 kg to 31 kg during the same period. In summary, the reduction achieved in the consumed quantities of antibiotics can mainly be attributed both to the reduced use of “non-critical” active substance classes that had been administered in large quantities (penicillins, tetracyclines and sulfonamides) and to the reduced use of the "critical" active substance classes of macrolides and polypeptide antibiotics. In the case of fluoroquinolones and 3rd and 4th generation cephalosporins it was observed that their share of the total used quantity was consistently very low. Changes in the used quantities for these active substance classes could not, therefore, have made hardly any contribution to the reduction in the total used quantity of antibiotics.

The share of used quantities of antibiotics , i.e. the quantities of antibiotics actually used in the six types of production listed in the 16th AMG Amendment, in the supplied quantities of antibiotics, which are used as a measure of the total quantities of antibiotics used in veterinary medicine in one year, varies depending on the class of active substance between 30% and 70%. One exception are the active substance classes of 3rd and 4th generation cephalosporins with a share of approximately only 2% and approximately 6% respectively. In the case of fattening chickens and fattening turkeys, these latter classes of active substances are not used at all due to the lack of authorisation. Given the very small share of the used quantities of these active substance classes in the respective supplied quantities, it is not possible that the 16th AMG Amendment could have led to a significant reduction in the supplied quantities of these active substance classes. A differentiated analysis of the development of used quantities by type of production showed that the overall reduction in the used quantities of antibiotics was essentially due to the reduction in the used volumes of penicillins, tetracyclines, macrolides and polypeptide antibiotics in fattening piglets and fattening pigs. The development of used quantities for the other types of production contributed less to the overall reduction. The used quantity of long acting/one shot (LA/OS) preparations remained steady at around 2 t. It, therefore, only accounts for <1% of the total used quantity. This leads to the conclusion that these preparations were not used to any major degree to reduce treatment frequency after the entry into force of the 16th AMG Amendment. Given their low rate of use, the influence of these preparations on the overall development of treatment frequencies and the question as to the practical significance of varying information on what are known as "days of drug action" of these preparations may have been overestimated in the previous expert discussion.

In order to assess the attainment of the goal regarding the element "reduction of resistance risk", data from the bacterial species were analysed, which had been tested for their resistance to antimicrobial substances both within the framework of the national zoonosis monitoring in various food chains[1] and on the basis of the national resistance monitoring in animal pathogens in the period from 2009 to 2017. For this purpose, recourse was made to data on *Escherichia (E. coli)*, a common intestinal bacterium from healthy animals (commensals), *E. coli*, an animal pathogen, *Campylobacter (C.) jejuni* und C. coli, zoonotic agents and *Pasteurella (P.) multocida*, pathogens of respiratory infections. Regarding the answer to the question whether a reduction in the resistance risk was discernible, it should in principle be borne in mind that an assessment of the causal effect of legislation on the development of the resistance situation in various bacterial species is only possible to a limited extent due to the large number of influencing factors in the complex process of resistance formation, since it can be assumed that it takes three to five years for the resistance situation in the entire population to change as a result of reduced antibiotic use. The period from HYP 14/2 to HYP 17/2 covered in this evaluation is probably too short to be able to detect already now any change in the resistance situation as a consequence of different antibiotic use triggered by the 16th AMG Amendment.

The evaluation of the resistance data showed that the reduced and prudent use of antibiotics had positive effects on the development of the resistance situation in the six types of production. Thus, in the period under observation (2009 to 2017) there was an overall downward trend in the resistance of intestinal pathogens (commensal *E. coli*) normally found in the gut from the various food chains fattening calf, fattening pig, fattening chicken and fattening turkey. All four food chains showed a significant increase in the share of isolates that are sensitive to all antibiotics. The share of commensal *E. coli* and *Campylobacter spp.* isolates resistant to at least one active substance in the food chains

1 The food chain covers all stages of production from primary production by the farmer over food production at the slaughterhouse to food offered for sale in retail outlets.

fattening chicken and fattening turkey fattening was high and thus corresponded to the comparatively high treatment frequencies for these types of production.

In the case of *E. coli* and *P. multocida* from clinical diseases and *Campylobacter spp.*, the development of resistance was only partially decreasing and, in some cases, even increasing. The reasons for this cannot be clearly determined from the available data. The characteristics of the individual bacterial species certainly also play a role here.

Goal 3: To facilitate effective task performance by competent authorities, particularly on livestock farms

The check routines carried out to verify the plausibility of the data in the antibiotics database showed that the information provided by the animal keepers was of a high standard. Together with the success achieved in the reduction of used quantities and treatment frequencies, this indicates that the 16th AMG Amendment, the instruments created by the legislature (the parameter “half-yearly treatment frequency per farm”, the nationwide indicators, the duties for animal keepers set out in the Antibiotics Minimisation Concept and the control powers introduced into the law with the 16th AMG Amendment), enable the authorities, in principle, to fulfil their enforcement tasks set out in the 16th AMG Amendment.

In the opinion of the authorities of the *Länder*, the enforcement of the provisions of the 16th AMG Amendment presupposes a significant burden. The considerable administrative effort required of the competent authorities involved in enforcing the 16th AMG Amendment continues even after the initial phase has been completed and the necessary organisations and structures have been put in place. The opinion that a high burden is necessary in order to comply with the regulations, was also shared by the animal keepers and veterinarians involved in the survey. The *Länder* and the target groups surveyed also pointed out that, in order to further reduce the use of antibiotics, conceptual changes in pharmaceutical legislation alone would probably not suffice. Other areas of legislation that have a significant impact on animal health should also be included in order to reduce the need for antibiotic treatment by means of a holistic improvement in animal health . This would help to counteract the spread of resistance.

The availability of reliable, quantifiable indicators and the associated raising of awareness amongst all the stakeholders as well as the ensured nationwide comparability of farms were seen as positive by the *Länder* and the target groups.

Further conclusions

The central assessment of the data in this evaluation provides the opportunity for the first time to make statements on the scale and the details of antibiotic use in types of production with a high production volume that are based on data collected by the authorities. Consequently, it is likewise possible to identify correlations between antibiotic use and other factors such as farm size. In future, these new findings could be supported and further developed by a legal basis that permits repeated central evaluations of the data collected on antibiotic use in animals.

1. Introduction

1.1. Initial situation

In 2008, the German Antimicrobial Resistance Strategy "DART" was adopted and continued, in 2015, with the revised and updated follow-up strategy DART 2020. One of the main measures envisaged in DART in the field of veterinary medicine is the establishment of a system for the nationwide minimisation of the use of antibiotics in animal husbandry for certain fattening animals (cattle, pigs, chicken and, turkeys). This measure was introduced in the 16th AGM Amendment which entered into force on 1 April 2014. The Antibiotics Minimisation Concept defined therein (sections 58a to 58d AMG) pursues the goal of the detailed recording and reduction of the use of antibiotics on fattening farms.

According to the 16th AMG Amendment pursuant to section 58g AMG, the Federal Ministry of Food and Agriculture (BMEL) must report on the effectiveness of the measures taken pursuant to sections 58a to 58d AMG to the German Bundestag five years after the entry into force of the 16th AMG Amendment.

BMEL commissioned SAFOSO AG to participate, in an advisory and supportive capacity, in the preparation of this evaluation report. This report is an overall analysis that is based on the following sub-studies:

- Evaluation of the annual quantities of antibiotics supplied according to DIMDI-AMV (cf. list of abbreviations)
- Evaluation of the data on the use of antibiotics and treatment frequency for the types of production covered by the 16th AMG Amendment as part of the Antibiotics Minimisation Concept
- Evaluation of the development of the resistance situation of bacteria from zoonosis monitoring along the food chain originating from the relevant types of production
- Evaluation of the development of the resistance situation of pathogenic bacteria originating from the relevant types of production
- Contribution of the *Länder* (*Länder* report) on the findings and experiences of the competent authorities regarding the implementation of the 16th AMG Amendment (prepared by the Working Group on Veterinary Medicinal Products of the *Länder* Working Group for Consumer Protection)
- Nationwide survey on the experiences of animal keepers and veterinarians with the provisions and measures of the 16th AMG Amendment

1.2. Background information

The health of humans and animals is closely interwoven in many infectious diseases. Humans and animals are often infected by the same bacterial pathogens and treated with the same antibiotics. Consequently, they have a mutual impact on the development of antibiotic resistance. Antibiotics are used in both human and veterinary medicine to treat bacterial infectious diseases. These are approved preparations with a single active substance for various medical indications and also combinations of different active substances for oral, parenteral (cf. glossary) and local treatment or for other types of administration. The World Health Organisation (WHO) and the World Organisation for Animal Health (OIE) each keep a list that ranks the significance of the different classes of active substances for human and veterinary medicine [1, 2]. **Figure 1** gives an overview of the active substance classes available in Germany. It shows that all active substance classes approved in veterinary medicine are also approved in human medicine, including the active substance classes described by WHO as "Highest Priority Critically Important Antimicrobials" (HPCIAs).

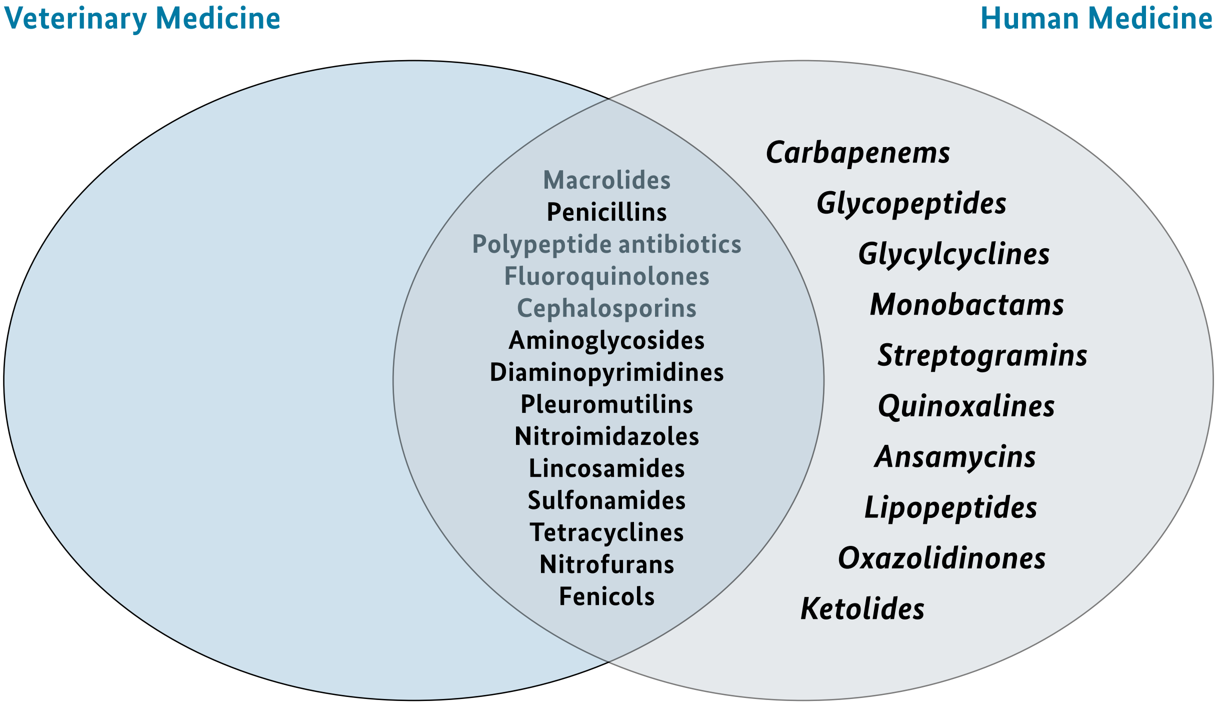


Fig. 1: Availability of 24 classes of active substances in human and veterinary medicine in Germany (coloured classes of active substances: Highest Priority Critically Important Antimicrobials according to the WHO classification)

Resistant pathogens have acquired the ability to protect themselves in different ways against the action of one or more antibiotics. The antibiotics are ineffective against these pathogens. Antimicrobial resistance results from a change in the bacterial genetic material, whereby resistance genes can also be transferred to other bacteria by different mechanisms. The more frequently bacterial pathogens come into contact with antibiotics, the greater the selection pressure, since only resistant germs survive. The use of antibiotics is, thus, a major contributory factor to increasing resistance. The problem is further exacerbated when antibiotics are used indiscriminately or inappropriately (misuse or overuse). Consequently, the key to limiting antibiotic resistance is the prudent, responsible and generally reduced professional use of antibiotics in both human and veterinary medicine. Against this backdrop, the use of antibiotics in animal husbandry should be minimised through improved management and hygiene measures to prevent infectious diseases. Furthermore, DART 2020 envisages the recording of supplied and used quantities of antibiotics and the ongoing monitoring of the resistance situation.

The Antibiotics Minimisation Concept introduced in the 16th AMG Amendment from 2014 is one of several measures aiming to curb antimicrobial resistance in the veterinary field. In 2000, guidelines for the prudent use of antibacterial veterinary drugs were developed for the first time by the Federal Veterinary Surgeons' Association (*Bundestierärztekammer*) (the Antibiotics Guidelines). Since 2006 there has been an EU-wide ban in harmonised feed legislation on antibiotic growth promotors. For many decades, all antibiotics administered to animals in Germany have, in principle, been available only on prescription. Other measures include the organisation of further training courses and the optimisation of the authorisation regulations for antibiotics for veterinary medicine (e.g. the formulation of instructions for special precautionary measures to be taken in conjunction with the granting of authorisations for veterinary medicinal products with active substances from the fluoroquinolones group). The systematic recording of the resistance situation in the field of veterinary medicine likewise dates back to the turn of the millennium. Since 2001, BVL has carried out representative resistance monitoring of animal pathogens and since 2009 BfR has been engaged in zoonosis monitoring along the food chain in cooperation with the authorities of the *Länder*. In 2004, a National Reference Laboratory for Antibiotic Resistance was also established at BfR.

1.3. Subject of the evaluation

The evaluation according to section 58g AMG focuses on the study of the effectiveness of the measures defined in sections 58a to 58d AMG, which the legislator introduced in order to quantify the scale and reduce the use of antibiotics in certain types of livestock. These measures include a number of duties for livestock keepers and the competent authorities, namely:

- Duties for livestock keepers to provide information on animal keeping (section 58a AMG),
- Duties for livestock keepers to provide information on the use of medicinal products (section 58b AMG),
- Duties for competent authorities to determine the half-yearly treatment frequency per farm,
- Duty of the Federal Office of Consumer Protection and Food Safety (BVL) to publish the indicators for the nationwide half-yearly treatment frequency for each type of production (section 58c AMG), and
- where applicable (when the indicator is exceeded) duties for livestock keepers to examine possible ways of reducing treatment with antibacterial substances, including the drawing up of written action plans for this (section 58d AMG).

The measures apply to farms that keep cattle, pigs, chickens and turkeys for fattening above a certain herd size.

BVL publishes the nationwide indicators on treatment frequency every six months in the Federal Gazette. The competent authorities of the *Länder* are responsible for monitoring and supervising the use of veterinary medicinal products, including compliance with the provisions of the 16th AMG Amendment. If the individual treatment frequency of a farm is higher than the BVL's published indicator 1 (i.e. above the median), the animal keeper must determine the causes in consultation with a veterinarian and look at what steps can be taken to reduce the use of antibiotics. If the treatment frequency per farm is higher than index 2 (i.e. above the 3rd quartile), the animal keeper must, after consultation with his veterinarian, draw up a written plan of action for antibiotic reduction and submit it to the competent authority.

1.4. Purpose of the evaluation

The purpose of the evaluation is to examine the extent to which the measures laid down in sections 58a to 58d AMG are effective in achieving the goals pursued by the 16th AMG Amendment. These are explained in the draft of the 16th Act to amend the Medicinal Products Act (Bundesrat printed document 555/12):

"The purpose of this Act is to take measures to reduce the use of antibiotics in animal keeping, and to promote and improve the prudent use and responsible handling of antibiotics in the treatment of diseased animals in order to limit the risk of the emergence and spread of antibiotic resistance and to enable the competent authorities to perform their tasks more effectively, particularly on livestock farms."

The above-mentioned goals can be formulated in more detail as follows:

Goal 1: To reduce the use of antibiotic veterinary medicinal products in the keeping of certain fattening animals,

Goal 2: To promote prudent and responsible antibiotic use in the treatment of diseased animals in order to limit the risk of the emergence and spread of antimicrobial resistance, and

Goal 3: To facilitate effective task performance by competent authorities, particularly on livestock farms.

The achievement of the goals was assessed using the following criteria, to which the sub-studies can also be attributed:

Criterion 1: The development over time of the scale and the spectrum of antibiotic use in the animal species and types of production covered by the 16th AMG Amendment.

Criterion 2: The development of antimicrobial resistance in bacteria originating from the animal species and types of production concerned.

Criterion 3: Findings and experiences of the competent authorities with regard to the performance of tasks in the enforcement of the provisions of sections 58a to 58d AMG.

Criterion 4: Experiences of livestock keepers and veterinarians with the provisions and measures of the 16th AMG Amendment.

2. Procedure, Methodology

2.1. Design of the evaluation

Based on a document analysis, the first step involved the preparation of an impact model of the measures introduced with the 16th AMG Amendment (**Figure 2**).

The "Output" level lists the results that were directly and immediately produced by the measures referred to in "Activities". The "Outcome" level details the effects of these results on the target group of the 16th AMG Amendment (i.e. livestock keepers and veterinarians). The "Impact" level describes the longer-term effects of the results on public health (e.g. the development of antibiotic resistance) and on agricultural production. The questions and indicators suitable for describing and verifying the progress and effectiveness of the measures taken pursuant to sections 58a to 58d AMG can thus be attributed to Output, Outcome and Impact. Annex 1 gives an overview of the questions and their attribution to the sub-studies.

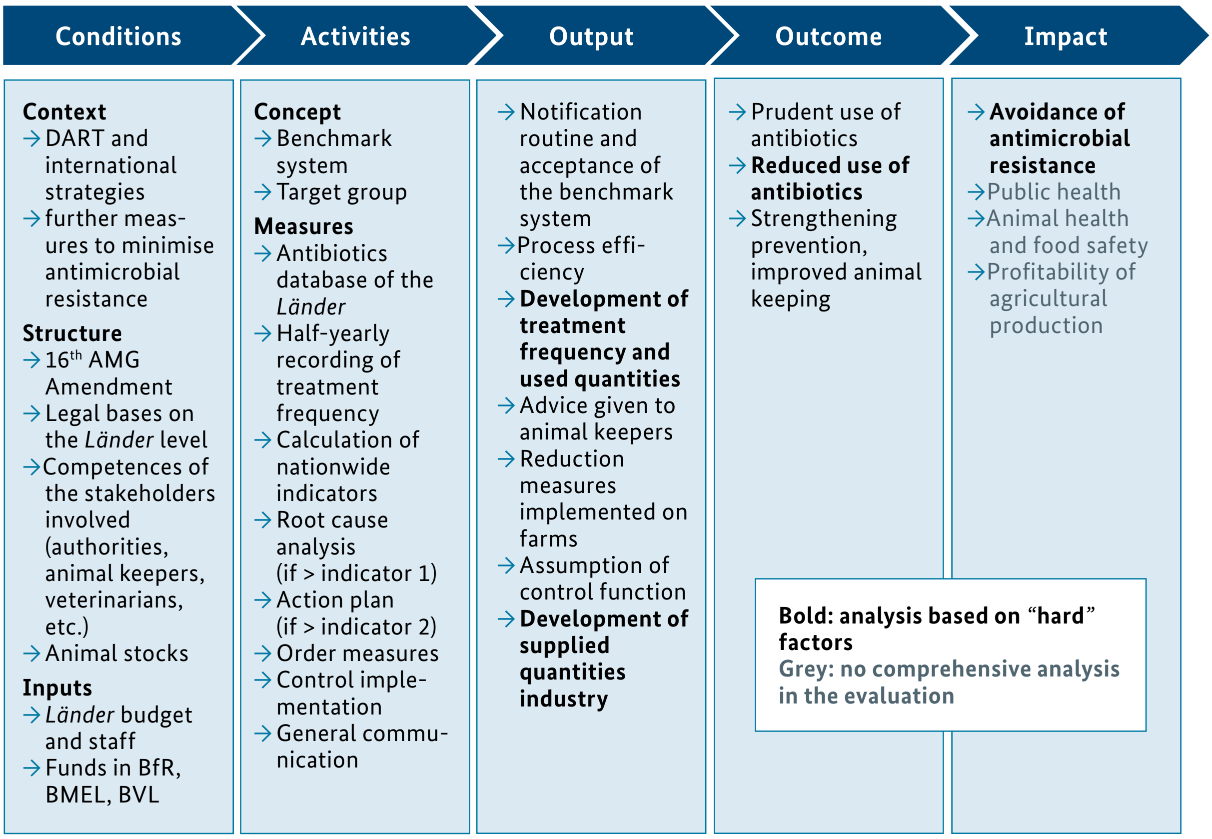


Fig. 2: Impact model for evaluation

This evaluation does not assess all aspects of the "Output", "Outcome" and "Impact" levels depicted in the impact model above, because in some cases no data are available (for instance on the impact of the measures on animal health) or because the study of certain impacts would exceed the evaluation remit defined in section 58g AMG, for example, examination of the possible impact on the profitability of certain agricultural production sectors.

The evaluation is based on the following main elements for which data are available to BMEL:

→ the evaluation of the annual supplied quantities of antibiotics according to DIMDI-AMV,

→ the evaluation of the official data of the *Länder* on antibiotic use and treatment frequency recorded in the antibiotics database within the framework of the Antibiotics Minimisation Concept,

→ the evaluation of the development of the resistance situation in bacteria from zoonosis monitoring,

→ the evaluation of the development of the resistance situation in pathogenic bacteria.

The assessment of the impact of the 16th AMG Amendment on aspects of enforcement is based on the *Länder* report on the findings and experiences of the competent authorities with regard to the enforcement of the 16th AMG Amendment, prepared by the Working Group on Veterinary Medicinal Products of the *Länder* Working Group for Consumer Protection. Furthermore, the results from a nationwide survey on the experiences of animal keepers and veterinarians with the provisions and measures of the 16th AMG Amendment will be included. The comments in the *Länder* report and the results from the nationwide survey are based on the experience and assessment of the *Länder* authorities, animal keepers and veterinarians with the 16th AMG Amendment.

2.2. Description of the sub-surveys

This evaluation is based on the sub-studies mentioned in the first chapter. The following sub-chapters describe the data sources and methods for all sub-surveys. A more detailed description can also be found in the individual sub-reports which are available in unabridged form in the annexes (in German).

It should be noted that the sub-studies are based on data from different time periods, from different animal populations or relate to different antibiotic substances. Due to the lack of linkage between the existing, different data sets, the comparability in particular of the development of treatment frequency with the quantities supplied and consumed, and with the development of resistance is limited (cf. **Annex 5**, Thematic area 3). In contrast, the availability of data on supplied quantities of antibiotics from 2011 onwards allows a comparison of developments before and after the introduction of the 16th AMG Amendment. This, in turn, permits the drawing of conclusions on the impact of the Antibiotics Minimisation Concept on this indicator.

2.2.1. Development of supplied quantities of antibiotics, used quantities of antibiotics and treatment frequency

Supplied quantities of antibiotics
Since 2011, pharmaceutical companies and wholesalers have been legally obliged to report the quantity of antibiotic substances supplied to veterinarians to the German Institute for Medical Documentation and Information (DIMDI)[2]. The reported supplied quantities thus represent the total quantity in tonnes of all supplied antibiotic substances. BVL is responsible for evaluating the recording of the supplied quantities of antibiotics. The evaluation took the data for the period from 2011 to 2017 into account.

2 Section 47 (1c) AMG and DIMDI Medicinal Products Ordinance (DIMDI-AMV)

Used quantities of antibiotics

The 16th AMG Amendment introduced the obligation for keepers of certain fattening animals (cattle, pigs, chickens and turkeys) to send their competent authority details of the animals kept and the use of veterinary medicinal products containing antibiotic ingredients.

This duty to report applies to the farms that keep animals of the following six types of production: "fattening calves" up to and including eight months, "fattening cattle" over the age of eight months, "fattening piglets" up to and including 30 kg, "fattening pigs" over 30 kg, "fattening chickens" and "fattening turkeys".

Following the entry into force of the 16th AMG Amendment on 1 April 2014, animal keepers with a duty of notification had to notify the keeping of these animals for the first time by 1 July 2014 (section 58a (3) AMG). Any changes to the information had to be notified within 14 working days (section 58a (4) sentence 1 AMG). Notifications on the use of medicinal products (§ 58b AMG) include the name of the veterinary medicinal product used, the number and type of animals treated, the number of days of treatment and the total quantity of antibiotics used ("medicinal products containing antibacterial substances"). The farms must also provide information on the total number of animals kept during the half-yearly period and on the number of animals entering and leaving the farm during the half-yearly period. Standardised notification is made in the veterinary medicinal products (TAM) database of the *Länder* in the central database on animal identification and registration (*HITier*) (antibiotics database of the *Länder*). For the calculation and evaluation of the development of the used quantities as well as the treatment frequency per farm for the purpose of evaluation, the anonymised data were made available to BMEL by the *Länder* on the basis of section 58f sentence 2 (2) AMG.

The data from the antibiotics database of the *Länder* therefore indicate the used quantities for the types of production covered by the 16th AMG Amendment (basic population of all farms subject to a reporting requirement). The usage figures for individual active substance classes for the six types of production of the 16th AMG Amendment, calculated on the basis of these data, are a subset of the quantities reported by pharmaceutical companies for certain active substances. The used quantities represent the share of antibiotic substance classes used in the six types of production of the 16th AMG amendment.

The evaluation of the used quantities from the pseudonymised data[3] for the purpose of assessment was carried out by BfR. The evaluation is based on the data from the second half-yearly period of 2014 (HYP 14/2) to the second half-yearly period of 2017 (HYP 17/2; in total seven half-yearly periods, 2.27 million reported antibiotic administrations from a total of 50,292 farms and 71,282 farm units).

In order to obtain valid results in the analysis, extensive plausibility routines were applied. Data on administrations were excluded from the evaluation if, for example, the specified used quantity was not considered plausible. For this purpose an average dosage of the active substance was assumed and the average weight of the animals at the time of administration of the antibiotic was estimated from the data in the database. If this estimated treatment weight was more than three times higher than the maximum weight of this animal species at slaughter, the data line was excluded. The administration of colistin was one exception to this rule. The dosage chosen for the plausibility check would have led to the exclusion of a large number of data sets. It was, therefore, assumed that the average dose of polypeptide antibiotics (DDDvet according to EMA) chosen for the plausibility check might not correspond to current practice. Therefore, administration data for colistin were excluded only when the estimated average treatment weight was twenty times higher than the maximum slaughter weight.

3 The amendment to the wording of section 58f sentence 2 AMG that was made in the Act on the Updating of the Provisions for Blood and Tissue Preparations Act and on the Amendment to Other Provisions (*Gesetz zur Fortschreibung der Vorschriften für Blut und Gewebezubereitungen und zur Änderung anderer Vorschriften*) that entered into force on 29 July 2017, made it possible to use the data collected in accordance with sections 58a to 58d AMG for the evaluation in accordance with section 58g. Before the data was transmitted to BMEL, the data was pseudonymised, thus preventing any conclusions being drawn about the identity of the farms.

Only those data lines that were complete and plausible with regard to important information were taken into account in the detailed analysis of the development of used quantities and treatment frequencies for each active substance class. A total of 6% of all administration lines were excluded from the detailed evaluation. If the exclusion criterion for colistin had not been adjusted, 96.4 t (54% of the used quantity) would have been excluded. The excluded data sets would have affected in particular the administrations to fattening chickens (90 % of the used quantity for fattening chickens).

Treatment frequency
The formula for the calculation procedure for determining the treatment frequency of a livestock farm and the procedure for determining the nationwide indicators are given in Chapter 3.1.1.

The evaluation of the development of treatment frequency for the purpose of the evaluation was carried out by BfR. This analysis is based on the same data set as the analysis of used quantities (see above). In addition to the nationwide development of the indicators, the pseudonymised data also permit statements on the development of the treatment frequency for each farm. To this end, the pseudonymised farm units were divided on a half-yearly basis into treatment frequency categories 1 to 3 (below indicator 1, between indicators 1 and 2 and above indicator 2).

In order to consider the impact of the number of animals kept on a farm on antibiotic usage and treatment frequency, a “farm size” variable was used on the basis of the “maximum number of animals kept in a half-yearly period” and the farm was assigned to a size class on the basis of the median of the values (maximum number of animals kept in a half-yearly period) for all half-yearly periods with corresponding information. For each of the six types of production, the farms were divided equally into three groups (small, medium and large; 33% of the farms with a known stock size). Some farms were not attributed to any group. These were (i) farms which had not reported any antibiotic use in any of the half-yearly periods and which were not, therefore, required to report stock data, (ii) farms with implausible livestock data and (iii) farms where the number of animals kept did not exceed the lower stock limits.

2.2.2. Development of antimicrobial resistance

In Germany, representative data on the occurrence of zoonotic agents and related antimicrobial resistance in food, feed and live animals are collected, evaluated and published as part of national zoonosis monitoring. Zoonoses are infectious diseases that are mutually transmissible between animals and humans. Zoonosis monitoring has been carried out by the *Länder* since 2009 as part of official food and veterinary monitoring. Zoonosis monitoring is based on the General Administrative Regulation on the recording, analysis and publication of data on the occurrence of zoonoses and zoonotic agents along the food chain (Allgemeine Verwaltungsvorschrift über die Erfassung, Auswertung und Veröffentlichung von Daten über das Auftreten von Zoonosen und Zoonoseerregern entlang der Lebensmittelkette – AVV Zoonosen Lebensmittelkette). Testing for resistance is carried out by BfR in compliance with the implementing decision 2013/652/EU[4], which defines the testing procedure, the active substances to be tested and the evaluation criteria for the majority of pathogens.

BVL continuously carries out representative studies on the resistance to pathogenic bacteria in food-producing animals and pets throughout Germany in order to make reliable statements about the current resistance situation and the development of resistance in animal pathogens. In 2001 BVL created a network of about 30 national laboratories that collect bacteria for testing according to a defined sampling plan and send them to BVL.

4 Commission Implementing Decision 2013/652/EU of 12 November on the monitoring and reporting of antimicrobial resistance in zoonotic and commensal bacteria (C (2013) 2145)

In order to analyse the development of antimicrobial resistance for the evaluation, data from the bacterial species were analysed which had been submitted both as part of zoonosis monitoring and on the basis of the national resistance monitoring of animal pathogens in the years 2009 to 2017 and which had been examined for their resistance to antimicrobial substances. Data on

→ *Escherichia (E.) coli*, a common intestinal bacterium in healthy animals (commensals),

→ *E. coli*, an animal pathogen,

→ *Campylobacter (C.) jejuni* and *C. coli, zoonotic* pathogens and

→ *Pasteurella (P.) multocida, pathogens* of respiratory disorders

were used for the evaluation.

The resistance data of commensal *E. coli* come from fattening pigs, fattening calves, fattening chickens and fattening turkeys on farms and from samples of the intestinal content of these animals at slaughter. Other animal pathogens were not included because they were derived from animal populations which are not covered by the provisions of sections 58a to 58d AMG or because there were no equivalents in zoonosis monitoring. Data on *Salmonella* were not included as the resistance situation of Salmonella differs greatly depending on the serovar (subspecies) and the results are therefore strongly influenced by the types that occur. Consequently, a time-based comparison would not be very robust given the limited number of isolates examined.

2.2.3. Information from the *Länder*

The *Länder* Working Group for Consumer Protection (LAV) has asked the Working Group on Veterinary Medicinal Products (AG TAM) to participate in the evaluation of the Antibiotics Minimisation Concept from the point of view of the *Länder*. The AG TAM set up a project group for this purpose. It is composed of representatives of the *Länder* of Baden-Württemberg, Bavaria, Brandenburg, Mecklenburg-Western Pomerania, Lower Saxony, North Rhine-Westphalia and Thuringia with the participation of representatives of the Federal Government. The *Länder* report focuses on the implementation and impact of the 16th AMG Amendment from the point of view of official control. The final version of the report was adopted by LAV on 19/20 November 2018 (**Annex 6**).

In addition to the *Länder* report, SAFOSO AG conducted guideline-backed telephone interviews with representatives of authorities from four *Länder* who had expressed an interest in taking part in a discussion.

2.2.4. Nationwide survey of animal keepers and veterinarians

SAFOSO AG conducted the nationwide online survey of the experiences of animal keepers and veterinarians with the provisions and the measures of the 16th AMG Amendment. Two separate electronic questionnaires were used to interview animal keepers and veterinarians. The two questionnaires were developed on the basis of the impact model and the overarching evaluation questions. In addition, a list of questions prepared by BMEL with comments from the *Länder* were taken into account. Furthermore, the results from two focus group discussions with veterinarians and animal keepers were included to consolidate the questionnaire. Access to the online survey could be controlled very securely as the participants first had to log into a restricted database (HITier or QS, cf. list of abbreviations). For this reason, the link was not published directly in any of the mailing lists. For data protection reasons, it was not possible to send the link directly via the authorities to the groups invited to participate either. Information and calls for participation were made via emailing lists and the websites of various trade associations and specialised journals. The survey was online from 20 July to 26 August 2018.

The survey responses received (728 from animal keepers and 212 from veterinarians) were cleaned once the survey had been completed. First, a total of 89 empty questionnaires (47 from animal keepers and 42 from veterinarians, if only the first 3 questions had been answered) were excluded from further evaluation. The remaining questionnaires were examined for completeness and conspicuous response patterns that could point to manipulation (e.g. recurring responses, short input time). On the basis of this plausibility check, 83 questionnaires from animal keepers were excluded from evaluation on the basis of unrealistic animal numbers, contradictory information on the animal species or type of production, or identical free text passages. The cleaned data set and the evaluations based on it can be regarded as robust and representative for the target group of livestock farms in Germany, even if the questionnaire was not exclusively accessible via the password-protected databases for some of the duration. There are no indications that the results have been falsified by unauthorised participants or have been deliberately manipulated.

After data cleaning, responses from 170 veterinarians and 598 animal keepers were evaluated. There were participants from all *Länder*, with veterinarians involved in practice in all *Länder* with the exception of the federal city states of Berlin and Hamburg, and the Saarland in the case of animal keepers. **Table 1** gives an overview of the answers by type of production. Animal keepers were asked to indicate all animal species kept and types of production (AT) subject to mandatory reporting and to indicate the most important one. Some of the questions only referred to the latter, whereby 552 animal keepers completed the questionnaire up to these questions. The veterinarians, on the other hand, were asked to indicate only the main animal species or type of production they attended to.

Table 1: Number of participants by animal species and type of production (AT)

Group		Fattening chicken	Fattening turkeys	Fattening piglets	Fattening pigs	Fattening calves	Fattening cattle
Vets	Primary AT attended to	7	7	51	46	48	11
Animal keepers	AT kept	60	27	95	211	211	232
Animal keepers	Most important AT	57	25	63	161	115	131

The results for the animal keepers revealed that the participating farms were composed as follows in terms of exceeding the indicators: 20% had never been higher than 1 and 20% had been higher than 1 but not higher than 2. A further 21% had been higher than indicator 2 once and 38% had already been higher than indictor 2 on several occasions. Furthermore, when comparing the assessments of animal keepers and veterinarians, it is important to note that the answers of the latter always refer to several farms, whereas the animal keepers could only provide information about their farm.

Further details of the survey can be found in **Annex 1**.

3. Results

3.1. State of play with the implementation of the Antibiotics Minimisation Concept

3.1.1. Description of the system in the Antibiotics Minimisation Concept in the 16th AMG Amendment

Since the introduction of the 16th AMG amendment, animal keepers who keep fattening animals of the animal species chickens, turkeys, cattle and pigs have a duty to submit the following notifications every 6 months:

- → Number of animals kept. This is used to calculate the average number of animals kept during the half-yearly period.
- → For each administration of an antibiotic: name of the medicinal product used; number and type of animals treated; number of days of treatment and, if applicable, so called "days of drug action".
- → Total quantity of the respective medicinal products used that contains antibacterial substances.
- → If no antibiotics were used, a "zero report" can be made voluntarily.

The types of production concerned are fattening calves from weaning up to and including eight months of age, fattening cattle from eight months of age, fattening piglets from weaning up to a body weight of 30 kg, fattening pigs with a body weight of more than 30 kg, fattening turkeys from the time of hatching and fattening chickens from the time of hatching.

The Implementing Ordinance for the Duty of Notification of Veterinary Medicinal Products (*Tierarzneimittel-Mitteilungendurchführungsverordnung*) sets out the provisions for the exemptions from the duties of notification of livestock keepers pursuant to sections 58a and 58b of the Medicinal Products Act (AMG) when no more than 20 cattle intended for fattening, 250 pigs intended for fattening, 1000 turkeys intended for fattening or 10,000 fattening chickens are kept on average on a farm during a half-yearly period. Smaller fattening farms, i.e. the ones that are below the stock lower limits given above are, therefore, exempt from the duties of notification set out in the 16th AMG Amendment. This helps to ease the administrative burden on animal keepers and authorities and does not impair the representativeness of the nationwide half-yearly treatment frequency, because only those fattening farms that contribute to a very minor degree to the use of antibiotics in commercial livestock farming are exempt from the duty of notification. Based on epidemiological-statistical examinations, it is clear that the representativeness of the determination of the indicators of the nationwide half-yearly treatment frequency is also guaranteed when the above-mentioned lower stock limits are applied to the respective type of production (see official statement of reasons, Bundesrat printed document 177/14).

The information is recorded in the antibiotics database of the *Länder* made available by the competent *Länder* authorities. This is part of the HITier database (animal identification and registration)[5]. The animal keeper's duty of notification can be delegated to third parties, e.g. a veterinarian or an organisation such as the private quality assurance company "QS" (*QS Qualität und Sicherheit GmbH*). From

5 www.hi-tier.de

the information collected on the administration of antibiotics and on animal stocks, the treatment frequency of the respective livestock farm is calculated according to a calculation method published in the announcement of the method for calculating the treatment frequency of a livestock farm by the competent authority on 21 February 2013[6].

For each individual farm and for each animal species and type of production, the competent authority separately determines the treatment frequency (TF) for all administrations during a half-yearly period using the formula below:

$$TF = \frac{\sum[(\text{Number treated animals})x(\text{Number treatment days})]}{\text{Average number of animals kept per half-yearly period}}$$

This is calculated directly in the antibiotics database, in which the above formula is stored for this purpose.

The half-yearly treatment frequency per farm is the measurable variable. It takes into account the average number of animals kept during the period, the number of active substances used during the respective administration period as well as, if applicable, the characteristic of proprietary medicinal products that are administered once and exert antibacterial action over a period of several days. They are known as long-acting or one-shot (LA/OS) preparations. For their calculation, the number of days of drug action is used in addition to the number of days of treatment. The treatment frequency per farm is the indicator used to describe the administration of antibiotics per farm. It enables the comparison of the use of antibiotics on farms that keep animals of the same type of production.

Pursuant to section 58c (4) AMG, BVL calculates the median (indicator 1) and the third quartile (indicator 2) of the treatment frequencies per farm from all the individual treatment frequencies determined per farm in one half-yearly period. It publishes these nationwide indicators in the Federal Gazette at the end of March and the end of September respectively. The comparison of the treatment frequency per farm with the nationwide indicators published by BVL is the basis for further action. If the half-yearly treatment frequency of a farm is higher than indicator 1, the farmer must, in consultation with a veterinarian, identify the causes which may have led to it exceeding the indicator and examine how the need for treatment with antibiotics can be reduced. If the half-yearly treatment frequency of a farmer is higher than indicator 2, the keeper must, in consultation with his/her veterinarian, draw up a written plan of action to reduce the use of antibiotics and forward it, unsolicited, to the competent authority. The competent authority then checks the plan and, if necessary, calls for improvements to the plan. The competent authority may require animal keepers to take concrete steps, e.g. vaccination, changes in husbandry, feed, stock density or hygiene. Fines may be imposed and, as a last resort, the temporary suspension of livestock keeping may be ordered.

The *Länder* authorities are responsible for enforcing the provisions of the 16th AMG Amendment. Whilst in some *Länder* a central office (e.g. a *Land* office) coordinates and carries out these tasks, in other *Länder* the lower *Land* authorities (districts, urban municipalities) are responsible. **Figure 3** gives a general overview of the stakeholders, processes and procedures. In most *Länder*, there are minor organisational variations in implementation.

6 Federal Gazette of 22 February 2013, BAnz. AT 22.02.2013

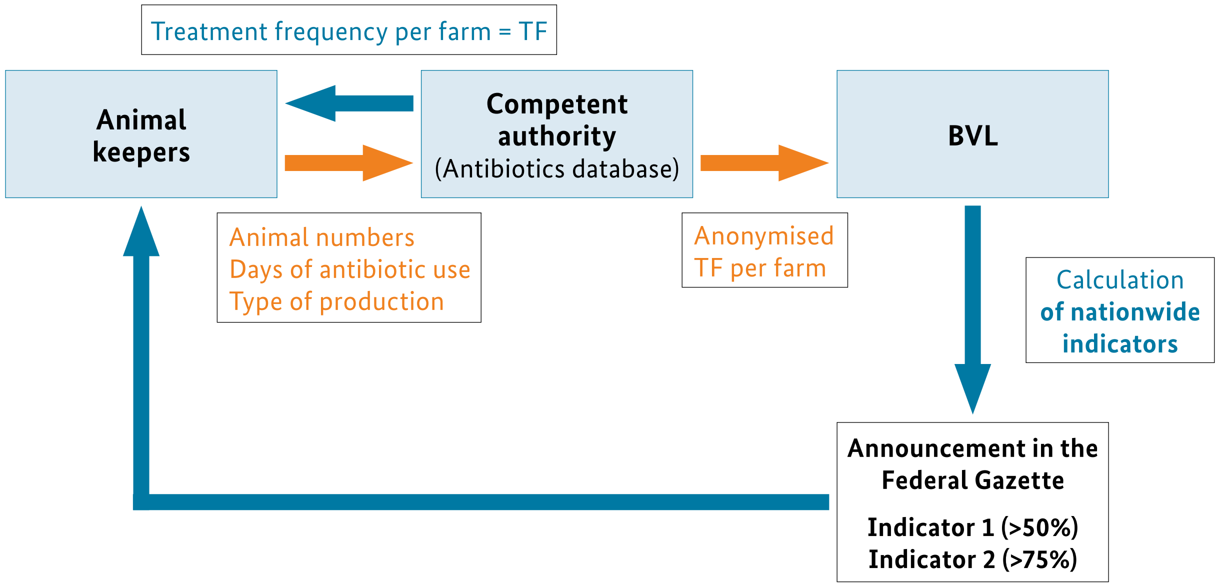


Fig. 3: Simplified depiction of the stakeholders and processes of the Antibiotics Minimisation Concept of the 16th AMG Amendment

3.1.2. Implementation status

The measures and provisions of the 16th AMG Amendment have been implemented since 1 April 2014, whereby in the period between the promulgation of the Act on 10 October 2013 and its entry into force on 1 April 2014 the preconditions for the application of the provisions were put in place and all the stakeholders involved established the necessary procedures. For example, the database for recording the necessary information was set up in HITier (see above), presented to the animal keepers and veterinarians responsible for entering the data, and all the farms and types of production with a duty of notification were registered. In addition, aids and instruments such as forms for drawing up action plans were developed and the procedures for monitoring the various requirements were established in the competent authorities. **Table 2** below gives an overview of the number of farms that submitted data to the relevant competent authority in HYP 17/2 on the basis of the duty of notification pursuant to section 58a AMG.

Table 2: Number of farms that sent data in line with their duty of notification pursuant to section 58a AMG in the half-yearly period 17/2

	Fattening chickens	Fattening turkeys	Fattening piglets	Fattening pigs	Fattening calves	Fattening cattle	Total
Number of farms	2,156	1,070	7,192	19,081	11,425	18,800	59,724

The *Länder* report comments as follows on the status of notifications: *"The animal keepers basically comply with their duty of notification. Overall, the technical error rate of the notifications pursuant to sections 58a and 58b AMG has fallen since the introduction of the database and the reporting behaviour has steadily improved."*

3.1.3. Stakeholders' estimates of individual aspects of the system

In the case of the veterinarians participating in the survey and the information they provided on the accuracy of the treatment frequency, there were differences depending on the type of production:

- The majority (>50%) of veterinarians indicated that the TF usually reflected the actual use of antibiotics quite accurately for fattening chickens, fattening turkeys and fattening piglets.
- In the case of fattening pigs, there was no clear picture, as about one third of each group stated that the TF was "accurate", was "inaccurate due to irregular housing" or was "incomplete, as the use of antibiotics often took place in the upstream holding".
- In the case of fattening calves, the majority (>50%) of veterinarians rated the TF as "inaccurate due to irregular housing".
- In the case of fattening cattle, the TF was characterised as "incomplete", as the antibiotics were mainly used in the upstream holding.

In the case of the veterinarians, the survey revealed a two-way divide in opinions for all types of production on the subject of "lower limits for stock sizes" for the duty of notification. This question was not explicitly put to animal keepers, but was mentioned more frequently in the open final remarks (from 'must be increased' to 'must be abolished').

A further possible point of criticism is that there could be a shift of antibiotic treatments to areas that are not subject to the duty of notification specified in the 16th AMG Amendment. The *Länder* report contains explanations and examples of this: *"Since treatment with antibiotics on a fattening farm subject to a duty of notification has a negative effect on the farm's own treatment frequency against the backdrop of the current legal situation, there are frequent reports of treatment with antibiotics shifting to areas that are not subject to a duty of notification. For example, piglet production holdings that deliver piglets to the fattening farm immediately after weaning are not subject to a duty of notification pursuant to sections 58a and § 58b AMG. Suckling piglets kept in the above-mentioned piglet production holdings are treated there with antibiotics and this not recorded under the antibiotics minimisation strategy. It has been reported that fattening farms often only take animals from production holdings that have been treated with antibiotics irrespective of whether a disease has been diagnosed or not [...]. According to other reports, calves are quite often treated with antibiotics at collection centres or in livestock trading holdings and then transported pre-treated to fattening farms.*
Collection centres and livestock trading holdings are not deemed to be animal keepers as the animals are not kept there for even one day. They are not, therefore, subject to a duty of notification and the treatment of these calves is not recorded under the Antibiotics Minimisation Concept either."

3.2. Criterion 1: Development over time of the scale and the spectrum of antibiotic use

The following sections 3.2.1 to 3.2.5 contain comments on all types of production. At the end of Chapter 3, the most important results for each type of production are summarised separately in a data sheet.

3.2.1. Development of quantities of antibiotics supplied to veterinarians pursuant to the DIMDI Medicinal Products Ordinance

In 2017, a total of 733 t of antibiotics[7] were supplied to veterinarians based in Germany. Compared with the first recording in 2011, the reduction up to the recording in 2017 was around 973 t. This corresponds to a decrease of 57%. What is particularly noticeable is the substantial decline by 433 t or 35% in the supplied quantity between 2014 and 2015. The larger saving was made in the years 2014 to 2017. The quantities (t) from 2011 to 2017 are given in **Table 3** and **Figure 4**, the differences between the years 2011, 2014, 2015 and 2017 in **Table 4** and **Figure 5**. The supplied quantities of antibiotics do not permit any statement on the use of antibiotics in specific animal species and types of production as most veterinary medicinal products are authorised for several animal species. The main developments are described below.

Tetracyclines, penicillins, sulfonamides
These active substance classes are not ranked as critical (HPCIA) and, in terms of quantity, had the highest level [t] of supplied quantities. During the observation period 2011 to 2017, the supplied quantities of these active substances fell by at least half: for tetracyclines from 564 t to 188 t (-376 t or -66.7%), for penicillins from 528 t to 269 t (-259 t or -49%) and for sulfonamides from 185 t to 62 t (-123 t or 66.2%). When comparing the periods 2011 to 2014 and 2014 to 2017, it is noticeable that the supplied quantities of these active substance classes fell even more in the second period than in the first period (for tetracyclines -39.4% versus -45.1%; for penicillins -14.8% versus -40.2%; for sulfonamides -34.6% versus -48.4%), with a particularly large reduction between 2014 and 2015.

Macrolides, polypeptide antibiotics
Macrolides and polypeptide antibiotics belong to the critical (HPCIA) antimicrobial classes. The supplied quantities of polypeptide antibiotics were lower than those of the above-mentioned penicillins, tetracyclines and sulphonamides. Over the entire observation period, the supplied quantities of macrolides fell by around 118 t (68%) to 55 t, while the supplied quantities of polypeptide antibiotics fell by 53 t (-42.2%) to 74 t. If we compare the development in the periods 2011 to 2014 and 2014 to 2017, it can be seen that a lower proportion of the total reduction occurred in the first time period (for macrolides reduction by 64 t (-37.2%) and for polypeptide antibiotics by 21 t (-16.2%) and the larger percentage share in the reduction occurred in the second time period (for macrolides reduction by 54 t (-49.6%) and for polypeptide antibiotics 33 t (-31%). A particularly large reduction step was also observed from 2014 to 2015 for these two active substance classes.

7 Basic substance, no medicated premixes

Fluoroquinolones, 3rd/4th generation cephalosporins
The total volume of these active substance classes in t and their share in the total supplied quantities are comparatively low. However, they belong to the classes of antimicrobials ranked as critical (HP-CIA). During the observation period 2011 to 2017, the supplied quantities of these classes developed in different ways. In the case of fluoroquinolones, there was a 1.7 t (20.1%) increase in the supplied quantities from 8.2 t to 9.9 t. The same trend could also be observed for 3rd generation cephalosporins: 0.2 t increase from 2.1 t to 2.3 t (13.5%). However, in the case of 4th generation cephalosporins there was a decrease of 0.3 t from 1.4 t to 1.1 t (-25.6%). What these developments have in common is that the increases in supplied quantities mainly took place during the period from 2011 to 2014 or (for 4th generation cephalosporins) the reduction between 2011 and 2014 was less pronounced. During this period fluoroquinolones increased by 49.7% and subsequently decreased by 19.8% between 2014 and 2017. For cephalosporins the figures were +12.5% (3rd generation) and -1.8% (4th generation) in the earlier period and +0.9% (3rd generation) and -24.2% (4th generation) respectively in the later period. From 2014 to 2015, there was a reversal of the trend from an increase or stagnation to a decrease for all three active substances classes

Combination products
In the case of preparations containing several antibacterial substances, combination products, authorised for administration in animals in Germany, the supplied quantity of antibiotics of sulfonamides plus folic acid antagonists (trimethoprim) fell by around 60% between 2014 and 2017. The supplied quantity of sulfonamides decreased by 56.6 t (54.1%) from 95.6 t in 2014 to 39 t in 2017, and that of folic acid antagonists (trimethoprim) by 11 t (59%) from 19 t to 7.8 t. In the observation period from 2014 to 2017, there were hardly any changes in the supplied quantities of other two-fold active substance combinations.

Long-acting/one-shot (LA/OS) preparations
In 2011, the supplied quantities of antibacterial veterinary medicinal products with a duration of action of more than 24 hours ("long-acting, one-shot", LA/OS) amounted to 13.9 t, less than 1% of the total supplied quantities. For 2017, the supplied quantities of LA/OS of 19.4 t were calculated. This corresponds to a share of 3.7% of the total supplied quantities and, thus, to a three-fold increase in this share. In the period from 2011 to 2017, the supplied quantity of these veterinary medicinal products increased by 5.5 t or 39.7%. The biggest increases took place in the period from 2011 to 2014. In 2014, for example, the supplied quantities of LA/OS preparations amounted to 19.0 t. In the following two years, the supplied quantities fell to 16.8 t while in 2017 they rose again to around 19 t. As the supplied quantities of LA/OS preparations remained constant between 2015 and 2017, but the supplied quantities for all antibiotic active substances fell overall, the relative share of these preparations in the supplied quantities increased.

Form of administration
In 2017, preparations for oral administration accounted for the lion's share of supplied quantities of antibiotics (around 661.3 t or 90.2%). Approximately 57 t of the basic substance were used for parenteral administration. The number of preparations for parenteral administration increased by 1.8% between 2011 and 2017, while the number of preparations for oral administration decreased by 59.5%. Thus, the quantitative ratio between the two types of administration shifted in favour of parenteral administration. The ratio of oral to parenteral application was calculated to be approximately 11.7:1 in 2017. In 2016, this ratio was 12.5:1. The largest decrease in the supplied quantities of antibiotics for oral administration was recorded between 2014 and 2015 (2014: 1156 t, 2015: 739.0 t). The decrease was thus approximately 36%.

Table 3: Quantities [t] of antibacterial substances (supplied quantities of antibiotics) by active substance class supplied to veterinarians based in Germany, 2011 to 2017. Any deviations are due to rounding.

	2011	2012	2013	2014	2015	2016	2017
Tetracyclines	564	566	454	342	221	193	188
Penicillins	528	501	473	450	299	279	269
Macrolides	173	145	126	109	52.5	54.7	54.7
Sulfonamides	185	162	152	121	72.6	68.8	62.4
Polypeptide antibiotics	127	123	125	107	81.8	68.9	73.6
Aminoglycosides	47.1	40.5	39.4	37.8	24.7	26.1	29.3
Folic acid antagonists	39.9	26.2	24.3	19.1	10.3	9.8	7.8
Lincosamides	16.8	15.2	16.9	14.6	10.8	9.9	10.9
Fluoroquinolones	8.2	10.4	12.1	12.3	10.6	9.3	9.9
Pleuromutilins	14.1	18.4	15.5	13.0	11.2	9.9	13.4
Fenicols	6.1	5.7	5.2	5.3	5.0	5.1	5.6
1st gen. cephalosporins	2.0	2.1	2.1	2.1	1.9	2.0	2.0
3rd gen. cephalosporins	2.1	2.3	2.3	2.3	2.3	2.3	2.3
4th gen. cephalosporins	1.4	1.4	1.4	1.4	1.3	1.1	1.1
Other*	0.12	0.11	1.89	2.47	0.31	2.80	3.41
Total	**1,706**	**1,619**	**1,452**	**1,238**	**805**	**742**	**733**

* The group “Other” includes fusidic acid, ionophores, nitrofurans, nitroimidazoles.

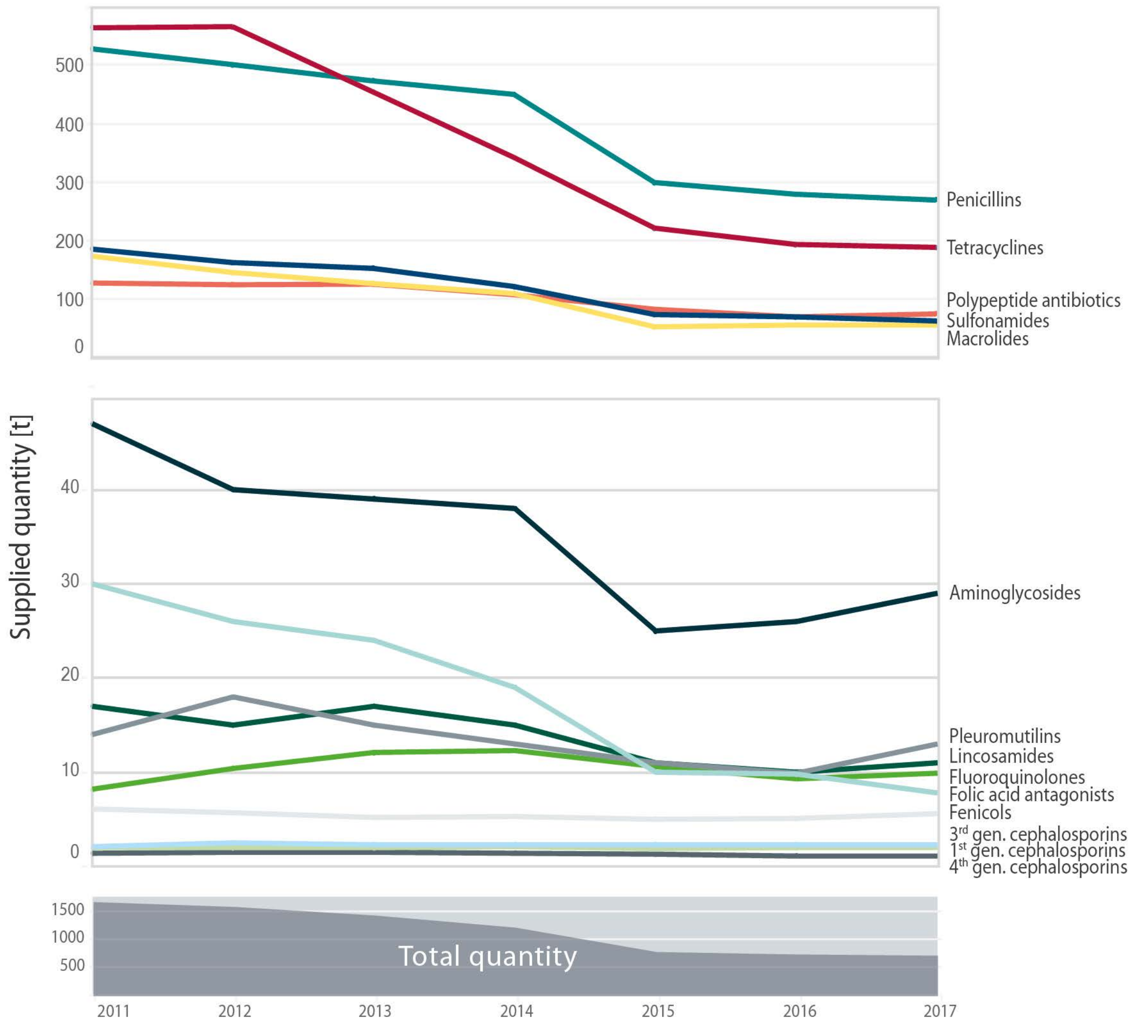


Fig 4: Change in quantity of antibacterial substances [t] supplied to veterinarians based in Germany by antibacterial substance class, 2011 to 2017.

Table 4: Differences [t and %] in the quantities of antibacterial substances (supplied quantities of antibiotics) supplied to veterinarians based in Germany by active substance class; 2011 to 2017, 2014 to 2015 and 2014 to 2017. Any deviations are due to rounding.

	Difference [t] 2011-2017	Difference [%] 2011-2017	Difference [t] 2011-2014	Difference [%] 2011-2014	Difference [t] 2014-2015	Difference [%] 2014-2015	Difference [t] 2014-2017	Difference [%] 2014-2017
Tetracyclines	-377	-66.7	-223	-39.4	-121	-35.5	-154	-45.1
Penicillins	-259	-49.0	-78	-14.8	-150	-33.4	-181	-40.2
Macrolides	-118	-68.4	-64.5	-37.2	-56.2	-51.7	-53.9	-49.6
Sulfonamides	-122	-66.2	-64	-34.6	-48.4	-40.0	-59	-48.4
Polypeptide antibiotics	-53.8	-42.2	-20.7	-16.2	-24.8	-23.3	-33.1	-31.0
Aminoglycosides	-17.8	-37.8	-9.4	-19.9	-13.1	-34.6	-8.5	-22.4
Folic acid antagonists	-22.1	-73.9	-10.7	-35.9	-8.9	-46.4	-11.3	-59.2
Lincosamides	-6.0	-35.4	-2.2	-13.1	-3.8	-26.3	-3.8	-25.7
Fluoroquinolones	+1.7	+20.1	+4.1	+49.7	-1.8	-14.5	-2.4	-19.8
Pleuromutilins	-0.7	-5.2	-1.1	-8.0	-1.8	-13.6	+0.4	+3.1
Fenicols	-0.5	-8.9	-0.8	-13.8	-0.2	-4.7	+0.3	+5.8
1st gen. cephalosporins	-0.06	-2.8	+0.04	+2.1	-0.13	-6.1	-0.10	-4.8
3rd gen. cephalosporins	+0.28	+13.5	+0.26	+12.5	-0.04	-1.5	+0.02	+0.9
4th gen. cephalosporins	-0.37	-25.6	-0.03	-1.8	-0.08	-5.4	-0.34	-24.2
Other*	+3.3	+2669	+2.4	+1911	-2.2	-87.3	+0.9	+37.7
Total	**-973**	**-57.0**	**-467**	**-27.4**	**-433**	**-35.0**	**-505**	**-40.8**

* The group "Other" includes fusidic acid, ionophores, nitrofurans, nitroimidazoles.

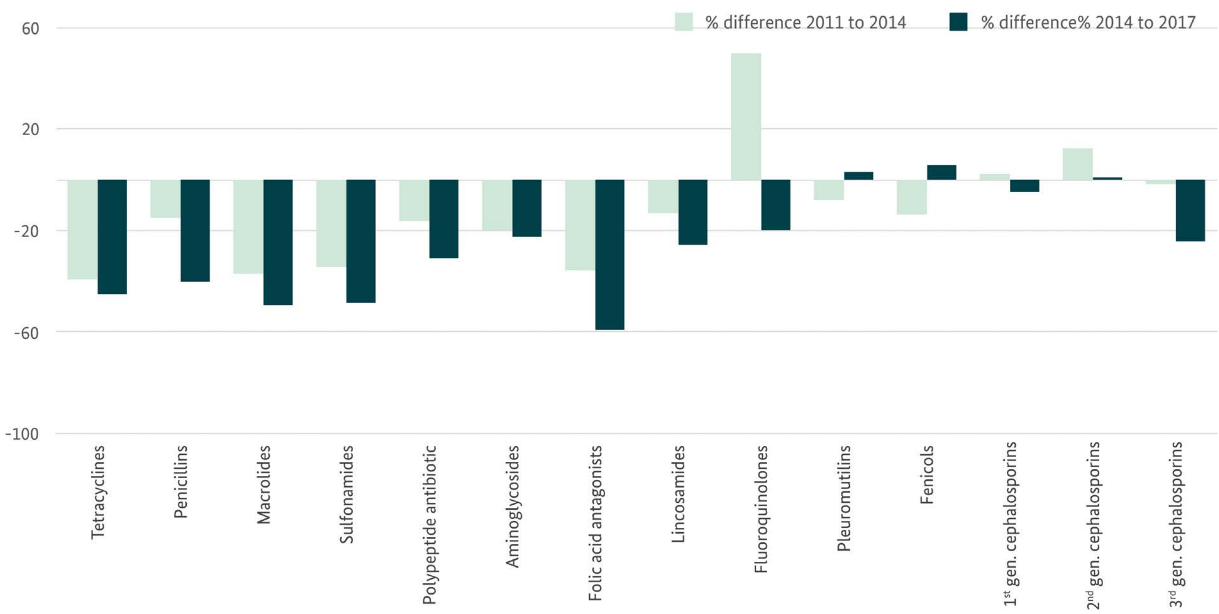


Fig 5: Presentation of the differences in the supplied quantities of antibiotics between 2011 and 2014 (light blue) and the years 2014 to 2017 (dark blue) in percent

3.2.2. Development of used quantities of antibiotics in farms with a duty of notification

Whereas the previous chapter presented the quantities of antibiotics supplied by pharmaceutical companies and wholesalers to veterinarians, this chapter explains the development of antibiotic usage. Section 58b of the German Medicinal Products Act (AMG) sets out the duty of animal keepers to notify the quantity of antibiotics actually used. These data thus provide the used quantities of antibiotics for the types of production listed in the 16th AMG Amendment. These used quantities are only a subset of the supplied quantity of antibiotics since the provisions of the 16th AMG Amendment cover only six types of production and farms above a certain size.

After a plausibility check, the total used quantity taken into account for all six types of production fell by 31.6% from 298 t in HYP 14/2 to 204 t in HYP 17/2. On the active substance class level, the used quantity fell by 26.7% (119.2 t, 87.4 t) for penicillins, by 38.5% (80.4 t, 49.4 t) for tetracyclines, by 58.3% (23.5 t, 9.8 t) for sulfonamides, by 21.7% (6.7 t, 5.2 t) for aminoglycosides and by 76.0% (3.7 t, 0.9 t) for folic acid antagonists. The reduction was significantly lower for macrolides at 28.9% (26.6 t, 18.9 t) and for polypeptide antibiotics at 16.0% (27.4 t, 23.0 t). The used quantity of fluoroquinolones decreased by 19.2% from 2.1 t to 1.7 t. While the usage of 4th generation cephalosporins fell by 11.1% (35 kg, 31 kg), the used quantity of 3rd generation cephalosporins was slightly higher in the first half-yearly periods, with an increase of 5% (20 kg, 21 kg) in HYP 17/2 that was slightly higher than the initial level of HYP 14/2. The total recorded used quantity of fenicols increased by 11.4% from 0.8 t to 0.9 t.

Table 5: Comparison of used quantities for all active substance classes between HYP 14/2 and HYP 17/2.

	Used quantity [t] in HYP 14/2	Used quantity [t] in HYP 17/2	Difference in used quantity [t] from HYP 14/2 to 17/2	Difference in used quantity [%] from HYP 14/2 to 17/2
Aminoglycosides	6.652	5.211	-1.441	-21.7
3rd gen. cephalospor.	0.020	0.021	+0.000	+0.7
4th gen. cephalospor.	0.035	0.031	-0.004	-11.1
Fenicols	0.813	0.905	+0.092	+11.4
Fluoroquinolones	2.135	1.726	-0.409	-19.2
Folic acid antagonists	3.715	0.893	-2.822	-76.0
Lincosamides	3.612	3.224	-0.388	-10.7
Macrolides	26.640	18.949	-7.692	-28.9
Penicillins	119.234	87.415	-31.819	-26.7
Pleuromutilins	3.906	3.273	-0.633	-16.2
Polypeptide antibiot.	27.427	23.045	-4.383	-16.0
Sulfonamides	23.459	9.782	-13.677	-58.3
Tetracyclines	80.373	49.447	-30.926	-38.5
Total	**298.022**	**203.921**	**-94.101**	**-31.6**

Figure 6 below shows very different changes in the quantities of active substances administered over time, broken down by class of active substance and type of production. It is clear that, despite an overall downward trend in some half-yearly periods, a rise, i.e. increased use compared to the previous half-yearly period, can also be observed.

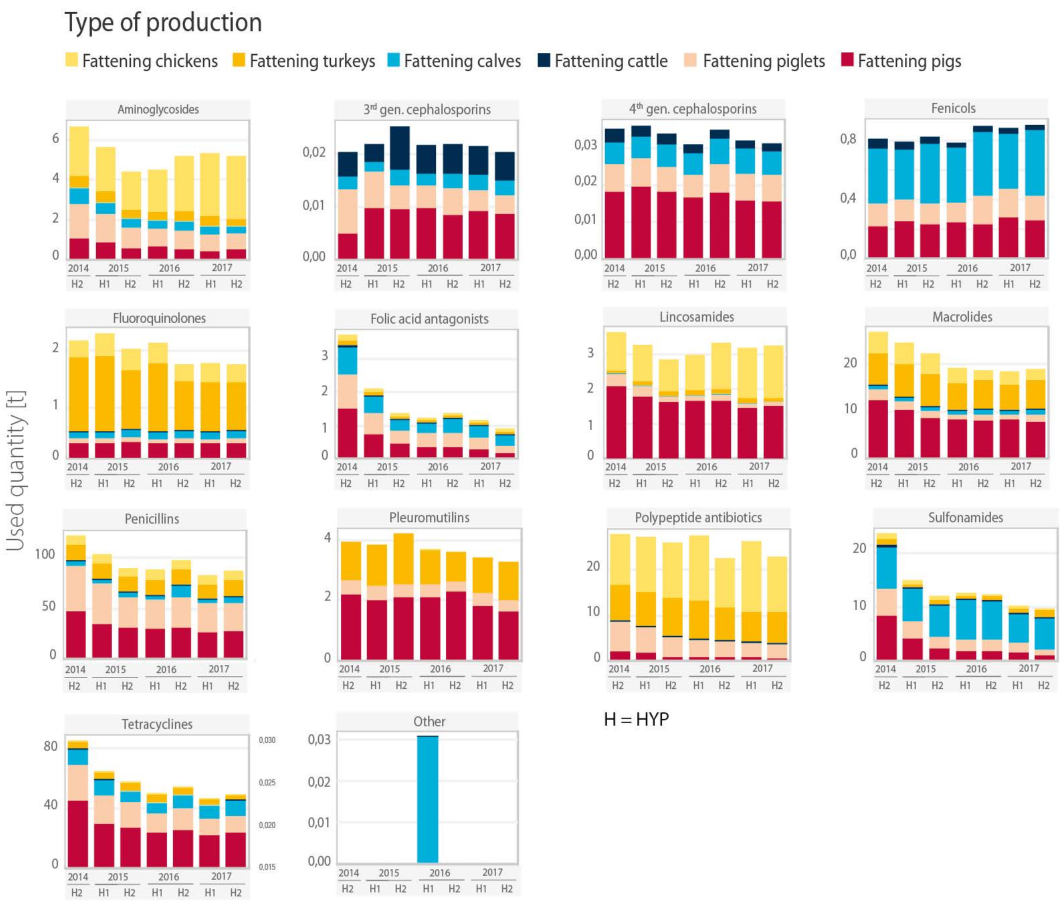


Fig 6: Development of used quantities of antibiotics [t] per active substance class. The scaling of the quantities differs between the active substance classes.

Development of used quantities of antibiotics for the individual types of production

Most of the total used quantity was used for fattening piglets and fattening pigs, followed by fattening turkeys, fattening chickens and fattening calves. Only small quantities were used for fattening cattle (see **Figure 7** below).

For all types of production, a reduction in the used quantity can be observed in HYP 17/2 compared to HYP 14/2, although the reduction varies considerably. **Table 6** below summarises the most important key data. The most significant reduction in the used quantity of antimicrobials was recorded for fattening piglets and fattening pigs. While 115.0 t of antimicrobials were used for fattening pigs in HYP 14/2, this had fallen by 43.3% to 65.2 t by HYP 17/2. For fattening piglets the used quantity fell by 46.1% from 87.5 t to 47.2 t. The reduction was significantly lower for fattening chickens, fattening turkeys and fattening calves. For fattening chickens the used quantity decreased by 0.9% from 29.7 t to 29.5 t, for fattening turkeys by 3.8% from 38.1 t to 36.7 t and for fattening calves by 3.9% from 26.0 t to 25.0 t. In the case of fattening cattle, an already very small used quantity fell by 76.4% from 1.3 t to 0.4 t.

Table 6: Comparison of total used quantities (t) for all types of production between HYP 14/2 and HYP 17/2.

	Quantity used [t] HYP 14/2	Quantity used [t] HYP 17/2	Difference Quantity used [t] HYP 14/2 to 17/2	Difference Quantity used [%] HYP 14/2 to 17/2
Fattening piglets	87.5	47.2	-40.3	-46.1
Fattening pigs	115.0	65.2	-49.8	-43.3
Fattening chickens	29.7	29.5	-0.3	-0.9
Fattening turkeys	38.1	36.7	-1.5	-3.8
Fattening calves	26.0	25.0	-1.0	-3.9
Fattening cattle	1.7	0.4	-1.3	-76.4
Total	**298.0**	**203.9**	**-94.1**	**-31.6**

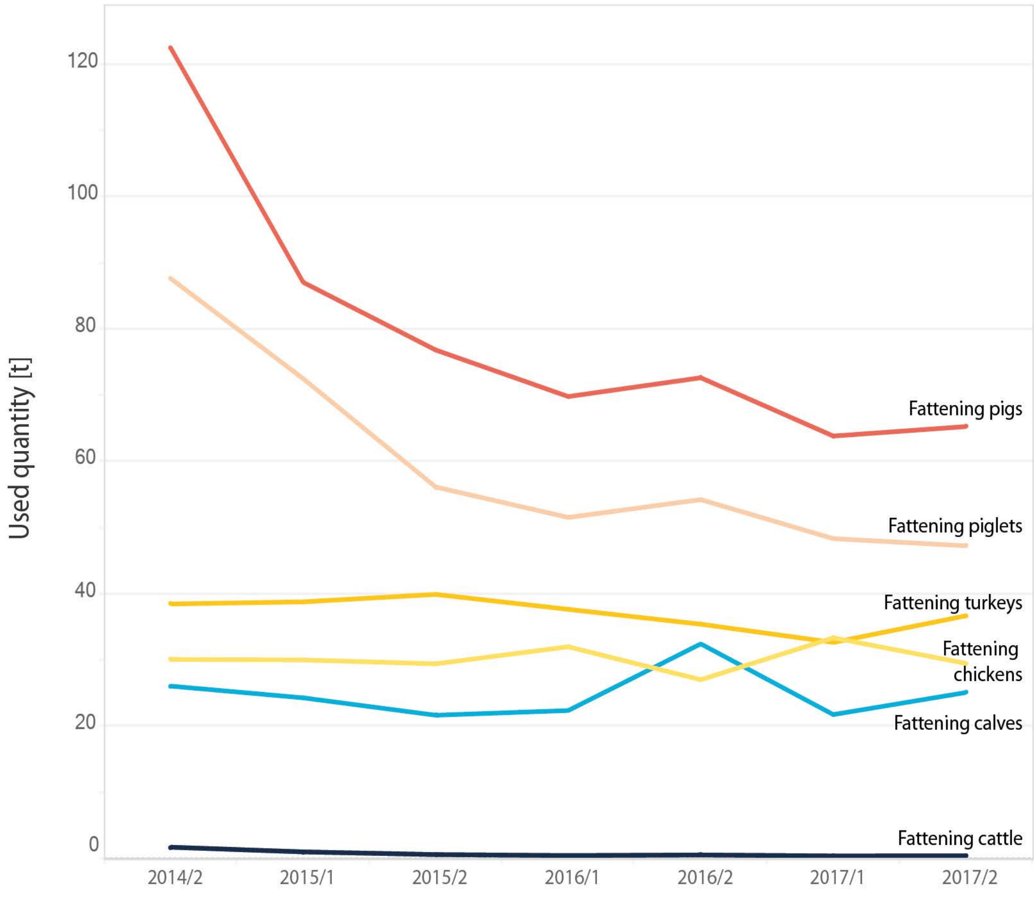


Fig 7: Trend in used quantities of antimicrobials [t] for the individual types of production

Use of active substance classes in the individual types of production

Depending on the type of production, different active substance classes account for the largest share of the used quantity. In line with the high overall quantities used for pigs (fattening piglets and fattening pigs), administration in pigs (fattening piglets and fattening pigs) accounts for the highest proportion of most active substance classes. In contrast, the largest share of aminoglycosides was used in fattening chickens.

Polypeptide antibiotics were most widely used in fattening chickens and fattening turkeys, while macrolides were used in roughly equal shares in poultry (fattening chickens and fattening turkeys) and in pigs (fattening piglets and fattening pigs) and only in small quantities in cattle (fattening calves and fattening cattle). 3rd and 4th generation cephalosporins have been used in cattle and pigs. They have not been authorised for use in fattening chickens or fattening turkeys. Fluoroquinolones were most commonly used in fattening turkeys. Fenicols were mainly used in fattening calves. Lincosamides were most commonly used in fattening pigs and fattening chickens. The data sheets give details of the development of the used quantities of different active substance classes for the individual types of production.

Combination products

For the types of production covered by the 16th AMG Amendment, five different classes of active substances were used in combination products. Sulfonamides accounted for the largest share, followed by aminoglycosides, folic acid antagonists, lincosamides and penicillins. While for sulfonamides and folic acid antagonists a clear decrease could be observed especially in the period HYP 14/2 to HYP 15/2, the use of aminoglycosides and lincosamides in combination products has increased slightly since HYP 16/1. Overall, penicillins were scarcely used at all in combination products. While aminoglycoside-lincosamide combinations were used in particular for fattening chickens, the combination sulfonamide-folic acid antagonist (trimethoprim) was mainly used for fattening piglets, fattening pigs and fattening calves.

Long-acting and one-shot preparations

Long-acting and one-shot preparations (LA/OS) are injection preparations and are, therefore, used in pigs and cattle, but not in poultry. A total of eight different active substance classes are used as LA/OS. Penicillins and fenicols accounted for the largest share of the consumed quantities of LA/OS, of which approximately 650-800 kg each were used in LA/OS preparations per half-yearly period. Tetracyclines accounted for a much smaller share. Aminoglycosides were used in small quantities. Macrolides and fluoroquinolones were used on a similar scale to tetracyclines. 3rd and 4th generation cephalosporins were used in very small quantities (<100 kg) as LA/OS preparations in the groups of production considered. The used quantity of LA/OS preparations fluctuated between 1.8 and 2.2 t in the period under observation. Together with the overall reduction in total used quantity, this led to an increase in the share of these preparations in total used quantity from 0.6% to 0.9%.

3.2.3. Comparison of the supplied quantities of antibiotics and the used quantities of antibiotics in farms with a duty of notification

Table 7 and **Figure 8** illustrate the share of the annual used quantities of antibiotics in the supplied quantities of antibiotics between 2015 and 2017 in the six types of production covered by the 16th AMG Amendment.

In 2015, the used quantity was 59.0% (474.7 t) of the total supplied quantity of 805.3 t. In 2016, this share fell to 57.5% (426.9 t of 742.3 t). A further reduction in this share was observed in 2017. The share of the used quantities accounted for 55.1% (404.1 t of 733.1 t). As a result, the used quantity of antibiotics in the types of production covered by the 16th AMG Amendment fell slightly more than the supplied quantity of antibiotics for all animal species and types of production.

The picture for the individual active substance classes varied considerably between 2015 and 2017. The used quantities of penicillins and tetracyclines, which made up the largest share of the total used quantity, accounted for 64% and 53% of the supplied quantity in the three years under observation. The share of used quantities for sulfonamides and aminoglycosides in the supplied quantity was significantly lower (34% and 38%, respectively). In contrast, the main share of macrolides and polypeptide antibiotics was used in the types of production covered by the AMG Amendment. The share of the used quantity in the supplied quantity was 76% of the 161.8 t of macrolides and 68% of the 224.3 t of polypeptide antibiotics. For fluoroquinolones, the used quantity amounted to 39% of the supplied quantity in the years 2015 to 2017. In contrast, only minor quantities of cephalosporins were used in the types of production covered by the 16th AMG Amendment. The share was approximately 2% for 3rd generation cephalosporins and 6% for 4th generation cephalosporins. The usage of 1st generation cephalosporins was not reported in the antibiotics database. About 59% of the supplied quantities of lincosamides, 64% of pleuromutilins and 32% of fenicols were used for the types of production covered by the 16th AMG Amendment.

The change in the shares of used quantities in the supplied quantities for the individual active substance classes is shown separately for the years 2015, 2016 and 2017 in **Figure 8**. For most active ingredient classes, the share of used quantities in the supplied quantities decreased over the three years, i.e. in the types of production covered by the AMG Amendment, the quantity fell more markedly than in the total supplied quantity. In contrast, the share of the used quantity of 4th generation cephalosporins increased from 5.3% in 2015 to 6.0% in 2017. This means that the used quantity (from 0.070 t to 0.064 t) decreased to a lesser extent than the supplied quantities (from 1.325 t to 1.062 t) during this period. The share of the used quantity of polypeptide antibiotics in the supplied quantity also increased slightly in 2017 compared with 2015 (from 65.0% to 66.9%). The used quantity fell to a lesser extent (from 53.2 t to 49.2 t) than the supplied quantity (from 81.8 t to 73.6 t).

Table 7: Comparison of the used quantities of antibiotics with the supplied quantities of antibiotics in the period 2015 to 2017. Supplied quantity (in tonnes) and share of used quantity as a % of supplied quantity for the individual active substance classes

Year	Active substance class	Supplied quantity [t]	Used quantity [t]	Share [%]
2015	Aminoglycosides	24.687	10.002	40.52
2016		26.140	9.691	37.07
2017		29.303	10.542	35.98
2015	1st generation cephalosporins	1.947	0	0
2016		1.962	0	0
2017		1.974	0	0
2015	3rd generation cephalosporins	2.280	0.047	2.07
2016		2.301	0.043	1.89
2017		2.335	0.042	1.80
2015	4th generation cephalosporins	1.325	0.070	5.30
2016		1.122	0.066	5.91
2017		1.062	0.064	5.98
2015	Fenicols	5.026	1.611	32.06
2016		5.121	1.682	32.85
2017		5.577	1.788	32.06
2015	Fluoroquinolones	10.555	4.258	40.35
2016		9.339	3.820	40.90
2017		9.905	3.465	34.99
2015	Folic acid antagonists	10.261	3.488	33.99
2016		9.768	2.620	26.82
2017		7.808	2.051	26.27
2015	Lincosamides	10.769	6.073	56.39
2016		9.877	6.264	63.42
2017		10.857	6.386	58.82
2015	Macrolides	52.463	46.986	89.56
2016		54.663	37.922	69.37
2017		54.723	37.506	68.54
2015	Penicillins	299.446	194.280	64.88
2016		278.969	179.735	64.43
2017		269.056	170.560	63.39
2015	Pleuromutilins	11.218	8.054	71.80
2016		9.944	7.377	74.19
2017		13.374	6.701	50.10
2015	Polypeptide antibiotics	81.842	53.211	65.02
2016		68.918	50.184	72.82
2017		73.576	49.231	66.91
2015	Other*	0.314	0	0
2016		2.795	0.031	1.10
2017		3.405	0	0
2015	Sulfonamides	72.619	26.984	37.16
2016		68.787	23.159	33.67
2017		62.399	19.882	31.86
2015	Tetracyclines	220.530	119.665	54.26
2016		192.550	104.296	54.17
2017		187.753	95.847	51.05

* The group “Other” includes fusidic acid, ionophores, nitrofurans, nitroimidazoles.

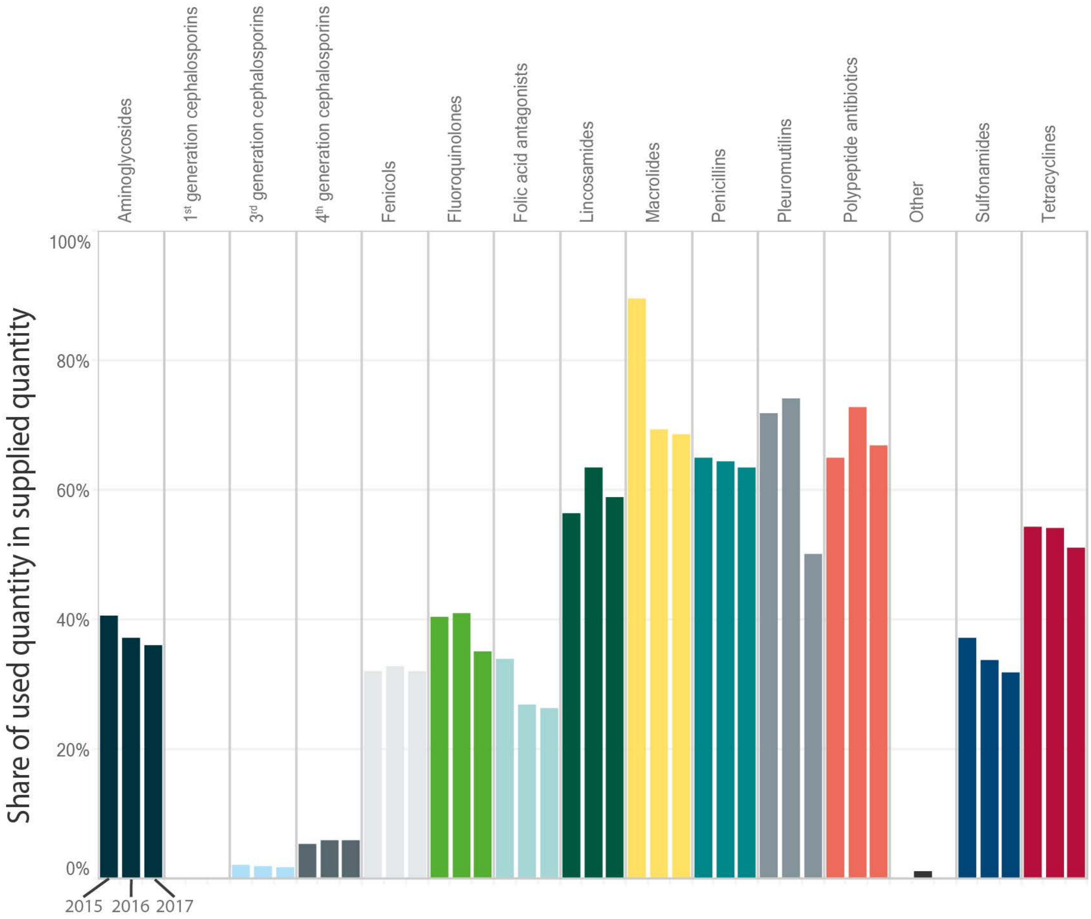


Fig 8: Graphic of the comparison of used quantities of antibiotics with the supplied quantities of antibiotics (see Table 7). Used quantities as % of the supplied quantity (set as 100%) for the individual active substance classes in the period 2015 to 2017. The group "Other" includes fusidic acid, ionophores, nitrofurans and nitroimidazoles.

3.2.4. Development of treatment frequency per farm

Development of the nationwide indicators

Figure 9 shows the development over time of the two nationwide indicators 1 and 2 from HYP 14/2 to HYP 17/2. For fattening pigs, fattening piglets and fattening turkeys, a statistically significant downward trend in the key figures for the treatment frequency per farm was observed over the entire period. This clear trend was not observed for fattening calves, fattening cattle and fattening chickens.

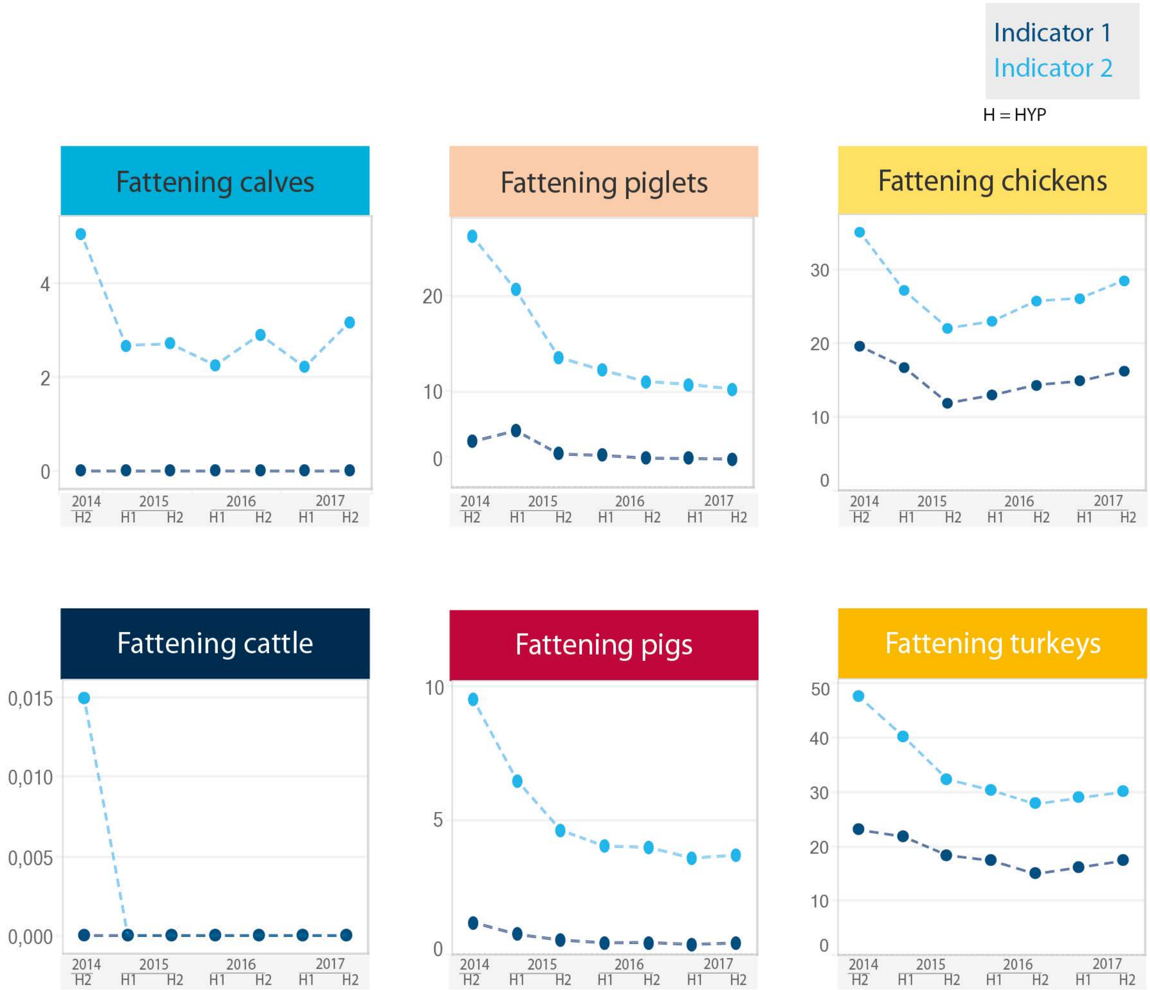


Fig 9: Development over time of the nationwide indicators published by BVL, in each case for indicator 1 (dark blue) and indicator 2 (light blue)

Farms that do not use antibiotics

The share of farms with a treatment frequency of "zero" for all seven half-yearly periods with a recorded treatment frequency differed depending on the type of production. It accounted for 11.9% of the 5,339 farms with fattening piglets, 11.3% of the 14,151 farms with fattening pigs, 6.3% of the 1,309 farms with fattening chickens, 4.9% of the 736 farms with fattening turkeys, 30.4% of the 6,092 farms with fattening calves and 52.1% of the 12,623 farms with fattening cattle.

Consideration of the ongoing development of treatment frequency per farm

Consideration of the ongoing development of treatment frequency, i.e. taking into account the values for individual farms in all seven half-yearly periods under observation, did not reveal a clear picture. The mean average treatment frequencies per farm over the last two half-yearly periods under observation (period HYP 17/1 and HYP 17/2) were lower for all types of production than for the first two half-yearly periods under observation (period HYP 14/2 and HYP 15/1). However, for all types of production the statistical analysis shows that, for the majority of the individual farms, no significant change in trend in treatment frequency per farm can be demonstrated across the individual half-yearly periods. A statistically significant reduction in treatment frequency per farm for fattening piglets was the most frequent occurrence. This trend was the least pronounced for farms with fattening chickens. Trends in the ongoing development of treatment frequencies per farm are given in **Figure 10**.

Consideration of the development of treatment frequency per farm by farm size

The general trend towards a significant reduction in treatment frequency per farm in HYP 17/1 and HYP 17/2 in comparison with the initial period HYP 14/2 and HYP 15/1 applies to all types of production and all farm size classes (see Chapter 2.2.1., sub-section "Treatment frequency"). **Figure 10** shows the distribution of the treatment frequency per farm in all seven half-yearly periods under observation for all six types of production, broken down into the three farm size classes. The median and the 3rd quartile of the treatment frequency per farm showed a similar course in all three farm size classes, albeit on different levels. On large farms the median and the 3rd quartile generally showed a higher value than in medium and small-sized farms.

Fig 10: Development of the treatment frequency per farm over the seven half-yearly periods by type of production and farm size. The bars extend from the 1st to the 3rd quartile, i.e. they include the middle 50% of the values.

Consideration of the development of treatment frequency per farm by class of treatment frequency

The analysis of the development of treatment frequency within the three treatment frequency classes (see Chapter 2.2.1., subsection "Treatment frequency") also gives a similar picture (**Figure 11**). In all three treatment frequency classes, similar trends can be seen in the development of the median of treatment frequencies. The significant downward trend of the median and 3rd quartile in fattening piglets and fattening pigs is particularly evident in treatment frequency class 3 (above indicator 2). However, it is also recognisable for the treatment frequency category 2 (between indicator 1 and indicator 2). The downward trend is likewise most evident in fattening turkeys in treatment frequency category 3. However, the reduction can also be seen to a lesser extent in treatment frequency category 2. In fattening chickens it becomes clear that the increase in treatment frequency observed from HYP 16/1 onwards mainly concerned treatment frequency categories 2 and 3. In fattening cattle there is no clear change in the treatment frequency in treatment frequency category 3.

Fig 11: Development of the treatment frequency per farm over seven half-yearly periods by type of production and treatment frequency class. The bars extend from the 1st to the 3rd quartiles. They, therefore, include the middle 50% of the values.

Continuity in the classification of farms by treatment frequency per farm and size of farm
If one considers the periods during which a continuous exceeding of indicator 2 was observed, it becomes clear that the phases during which indicator 2 was exceeded, were not always continuous or spanned longer periods. **Figure 12** gives the number of farms that were above indicator 2 in no half-yearly period, in one or in several consecutive half-yearly periods. The share of farms which were below indicator 2 in all seven half-yearly periods under observation (i.e. were not above indicator 2 in any half-yearly period) is highest for all types of production and varied between 35.8% (fattening chickens) and 52.2% (fattening cattle). The share of farms that were above indicator 2 over all seven half-yearly periods differs between the individual types of production. A total of 12.5% of farms with

fattening calves were above indicator 2 in all seven half-yearly periods. For the other types of production, this share was between 1.1% (fattening chickens) and 6.6% (fattening piglets). The number of half-yearly periods when indicator 2 was exceeded, also differed between the individual farm size classes. Small farms more frequently never exceeded indicator 2 in any half-yearly period. Medium and large farms, by contrast, were above indicator 2 more frequently in several half-yearly periods. For fattening cattle 34% of large farms were above indicator 2 in all seven half-yearly periods. For fattening piglets this share was 13.8% and for fattening turkeys 11.8% of the large farms. With increasing farm size, the share of farms in the treatment frequency category 3 also increased. These data are not shown here (see **Annex 2**).

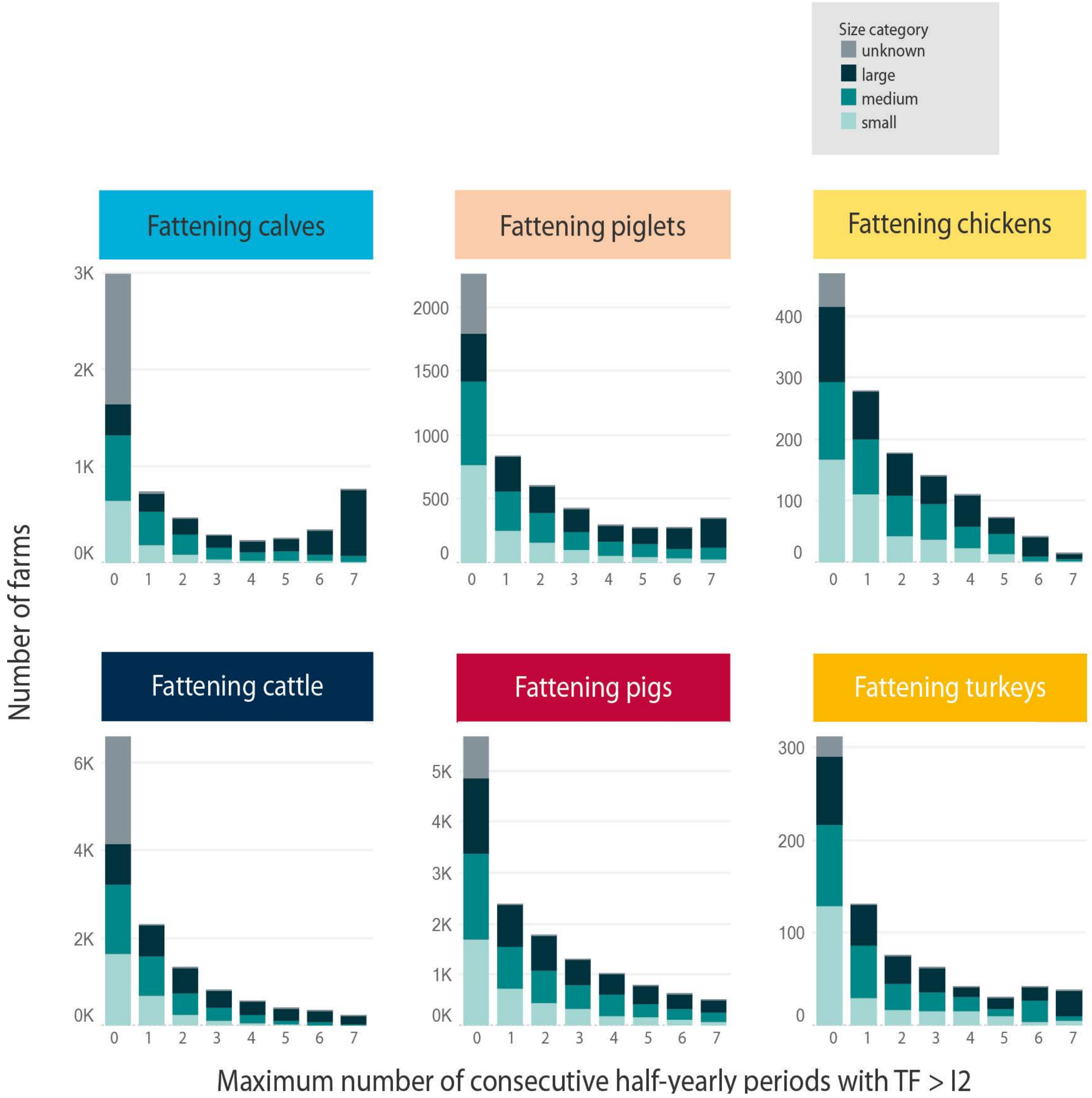


Fig 12: Number of farms and half-yearly periods in which indicator 2 was continuously exceeded. The exceeding of the indicator must have taken place in consecutive half-yearly periods.

Change in classification of farms in a different treatment frequency category

A change to a different treatment frequency category in the following half-yearly period took place to varying degrees depending on the individual types of production (see **Table 8** below). In the case of farms in treatment frequency category 1 (below indicator 1) and farms in treatment frequency category 3 (above indicator 2), classification in the same treatment frequency category was most frequently observed in the following half-yearly period (usually more than 50%). For farms in treatment frequency category 2 (between indicator 1 and indicator 2), this trend was less clear and a move to treatment frequency category 1 (below indicator 1) or to treatment frequency category 3 (above indicator 2) was observed. With increasing farm size, the share of farms in treatment frequency category 3 (above indicator 2) also rose.

Table 8: Probability of change in classification in the treatment frequency (TF) categories, taking into account all farms for which treatment frequencies are available for the entire period

	Probability of change			
Type of production	**from TF category**	**to TF category TF ≤ I1**	**I1 < TF ≤ I2**	**TF > I2**
Fattening calves	TF ≤ I1	89.1 %	7.0 %	3.9 %
Fattening calves	I1 < TF ≤ I2	24.3 %	56.1 %	19.6 %
Fattening calves	TF > I2	8.5 %	16.7 %	74.8 %
Fattening cattle	TF ≤ I1	92.2 %	0.0 %	7.8 %
Fattening cattle	I1 < TF ≤ I2	48.2 %	0.0 %	51.8 %
Fattening cattle	TF > I2	49.6 %	0.0 %	50.4 %
Fattening piglets	TF ≤ I1	77.8 %	16.9 %	5.3 %
Fattening piglets	I1 < TF ≤ I2	31.1 %	48.2 %	20.8 %
Fattening piglets	TF > I2	9.5 %	24.5 %	66.1 %
Fattening pigs	TF ≤ I1	75.0 %	16.4 %	8.7 %
Fattening pigs	I1 < TF ≤ I2	29.5 %	46.5 %	24.0 %
Fattening pigs	TF> I2	16.9 %	25.8 %	57.3 %
Fattening chickens	TF ≤ I1	72.9 %	18.1 %	9.0 %
Fattening chickens	I1 < TF ≤ I2	36.3 %	35.7 %	28.0 %
Fattening chickens	TF > I2	19.3 %	30.4 %	50.2 %
Fattening turkeys	TF≤ I1	72.6 %	19.0 %	8.4 %
Fattening turkeys	I1 < TF ≤ I2	38.4 %	39.5 %	22.1 %
Fattening turkeys	TF > I2	14.4 %	25.1 %	60.5 %

Comparison of the development of average treatment frequencies recorded for active substance classes

If one looks at the treatment frequency in the last two half-yearly periods compared to the first two half-yearly periods, a significant reduction can be observed for the average treatment frequency for most active substance classes (**Table 9**). In contrast, an increase in the treatment frequency for 3rd generation cephalosporins in fattening calves and for aminoglycosides and lincosamides in fattening chickens was observed. No significant change in the average treatment frequency was observed for fluoroquinolones in fattening chickens, fenicols in fattening piglets and fattening pigs, and for aminoglycosides and lincosamides in fattening turkeys.

The scale of the reduction was very varied too, depending on the individual types of production and active substance classes. The average treatment frequency for penicillins in fattening piglets and fattening turkeys was reduced by more than two days of treatment, but was reduced only slightly for fattening calves and fattening cattle. The frequency of use of tetracyclines was most markedly reduced in fattening piglets, but a reduction of about one day of treatment was also observed in fattening calves and fattening pigs. A similar picture emerged for sulfonamides and folic acid antagonists, where a reduction of about one day of treatment could also be observed in fattening chickens and fattening turkeys. The reduction in the treatment frequency was not so clear for macrolides. The most significant reduction, by almost one day of treatment, was observed for fattening piglets for this active substance class. Polypeptide antibiotics were used significantly less frequently, especially in fattening piglets, for which the average treatment frequency decreased by four treatment days. In fattening calves, fattening pigs and fattening turkeys the treatment frequency was reduced by approximately one day, in fattening chickens the reduction was the lowest. Fluoroquinolones were used significantly less frequently only in fattening turkeys, the average treatment frequency decreased by more than one day of treatment. The frequency of use of 3rd and 4th generation cephalosporins decreased only very moderately. In fattening calves the treatment frequency with 3rd generation cephalosporins increased slightly.

Table 9: Result of the comparison of the average treatment frequencies determined for each active substance class for the different types of production in HYP 14/2 and HYP 15/1 as well as in HYP 17/1 and HYP 17/2.

Active substance class	Fattening calves	Fattening cattle	Fattening piglets	Fattening pigs	Fattening chickens	Fattening turkeys
Aminoglycosides	-0.11	-0.03	-0.54	-0.06	0.61	-0.51
3rd gen. cephalosporins	0.03	-0.01	-0.33	0.00		
4th gen. cephalosporins	-0.02	-0.02	-0.03	-0.01		
Fenicols	-0.03	-0.04	-0.02	-0.01		
Fluoroquinolones	-0.06	-0.02	-0.07	-0.02	0.02	-1.13
Folic acid antagonists	-1.03	-0.13	-1.71	-1.21	-1.23	-1.42
Lincosamides	-0.03	-0.04	-0.45	-0.04	0.61	0.73
Macrolides	-0.11	-0.06	-0.93	-0.27	-0.80	-0.55
Penicillins	-0.13	-0.03	-2.69	-0.51	-0.87	-2.27
Pleuromutilins			-0.35	-0.31		-0.44
Polypeptide antibiotics	-1.22	-0.39	-4.15	-1.31	-0.23	-0.96
Sulfonamides	-1.17	-0.19	-1.73	-1.22	-1.24	-0.68
Tetracyclines	-0.97	-0.11	-1.86	-0.99	-0.53	-0.76

This table presents the change in treatment frequency (median) in farms with at least one antibiotic administration. A significant downward trend in treatment frequency is highlighted in green, a significant upward value in red. Values without any significant change are highlighted in grey, white cells indicate that no administration was reported. The numerical values indicate the difference between the average treatment frequencies in the two periods under observation.

3.2.5. Development in the number of indicated days of drug action

Since only the term “days of drug action” is used in the antibiotics database of the *Länder* for practical reasons and not the term “days of treatment” pursuant to section 58b (1) sentence 1 (3) AMG, the term “days of drug action” used below encompasses the number of days of treatment, and in the case of LA/OS preparations in addition the number of days on which the medicinal product retains its therapeutic drug level.

The number of days of drug action reported for the individual active substance classes varies considerably. In general, there is a tendency to report a shorter duration of action for combination products than for the corresponding monoproducts. For 3rd generation cephalosporins and fluoroquinolones a duration of drug action of one day was frequently reported for fattening calves and fattening cattle, whereas three days were most frequently reported for fattening piglets and fattening pigs. In the case of fattening chickens and fattening turkeys, the reporting on the duration of action was less heterogeneous than for the other types of production.

Over the seven half-yearly periods under observation, changes in the reporting on the duration of drug action could also be observed. Whereas folic acid antagonists, penicillins, pleuromutilins, polypeptides and 3rd generation cephalosporins showed a decrease in the median of the reported days of drug action, macrolides showed an increase in this median. In addition, it can be seen that the scattering of the reported days of drug action decreased for some active substance classes. This applies to aminoglycosides, folic acid antagonists, lincosamides and macrolides. A similar trend is indicated for fluoroquinolones and sulfonamides in the last half-yearly period under observation.

In the case of the use of LA/OS preparations, a standardisation to seven active days was recognizable for 3rd generation cephalosporins and macrolides; for other active substance classes this trend is less clear. At the end of the period under observation, the median of days of drug action for fluoroquinolones was 3 days, and for 4th generation cephalosporins and tetracyclines it was 4 days. For aminoglycosides, fenicols and penicillins, no change in the reporting on the days of drug action was observed and it fluctuated between 2 and 4 days in the half-yearly periods.

3.3. Criterion 2: Development of antimicrobial resistance in the bacteria of the relevant types of production

3.3.1. Commensal *E. coli*

Overall, the resistance of *E. coli* normally occurring in the gut (commensal) in the various relevant types of production in the period under observation from 2009 to 2017 showed a downward trend (**Table 10**). There are differences between both the food chains considered and the different active substance classes. The food chain encompasses all stages of production, from primary production on the farm, through food production in the slaughterhouse, to food offered for sale in the retail trade. In all four food chains (fattening calf, fattening pig, fattening chicken and fattening turkey) there was a significant increase in the share of isolates that were sensitive to all antimicrobials tested and a significant decrease in isolates that were resistant to more than three active substances.

Development of resistance rates in commensal *E. coli* during the period from 2009 to 2017, differentiated by individual active substances

The picture is more heterogeneous in the case of the individual active substances. Whereas resistance to tetracycline and sulfonamides was on a downward trend in all food chains, this was not uniform for ampicillin (penicillin), trimethoprim (folic acid antagonist) and gentamicin (aminoglycoside). For colistin (polypeptide antibiotic) and cefotaxime (3rd generation cephalosporin), a decrease in the share of resistant isolates was observed in two food chains only, namely colistin in turkeys and cefotaxime in fattening chickens. These two also had the highest initial resistance values. Compared to ciprofloxacin (fluoroquinolone), resistance in fattening calves showed a fall in frequency whereas resistance rates increased in turkeys.
A comparison of the individual years with the most recent data collected (2016 for fattening chickens and fattening turkeys and 2017 for fattening pigs and fattening calves) likewise reveals a mainly downward trend in resistance rates whereby the difference to the initial phase (2009 to 2013) is more often significant compared to the years 2014 to 2015. The differences can partly be explained by the fact that the number of isolates is limited which means that numerical differences are not statistically significant. But it can also indicate a flattening effect of the measures. In comparison to 2014, the resistance situation in 2016 for fattening chickens and fattening turkeys showed significant reductions only for multi-resistant isolates. In the case of fattening pigs, only the share of isolates sensitive

to all substances increased. For fattening calves, a comparison of the data for the last available year did not show any improvement in the resistance situation. The share of isolates sensitive to all active substances mentioned was stable or increased in all food chains. Nevertheless, the share of commensal *E. coli* isolates in fattening chickens and fattening turkeys resistant to at least one active substance was still very high in 2016 (70-80%). In the case of fattening pigs, the share was around 50%. In fattening calves, the share of resistant isolates decreased from >80% in 2009 to around 50% in 2017.

From the public health angle, priority is given to resistance to active substances classified as critical (HPCIA) by the WHO, i.e. 3rd and 4th generation cephalosporins, fluoroquinolones, macrolides and polypeptide antibiotics. The latter are mainly represented by the active substance colistin. The share of isolates resistant to colistin (polypeptide antibiotic) decreased in fattening turkeys only. In fattening turkeys, however, resistance to ciprofloxacin (fluoroquinolone), which is also a substance of critical importance, increased significantly. Here, significantly higher resistance rates are observed in the isolates of fattening chickens and fattening turkeys than in those of fattening calves and fattening pigs.

Table 10: Trend in resistance rates for commensal *E. coli* isolates from samples taken from stocks and gut content at the slaughterhouse to the antibiotics included in the analysis from 2009 to 2017

All active substances	**Fattening chickens**	**Fattening turkeys**	**Fattening pigs**	**Fattening calves**
Share sensitive to all active substances	grey	green	green	green
Share sensitive to all active substances incl. colistin	green	green	green	green
Share multi-resistant (>3 active substances)	green	green	green	green
Share multi-resistant (>3 active substances) incl. colistin	green	green	green	green
Active substance classes (tested active substance)				
Fluoroquinolones (ciprofloxacin)	grey	red	grey	green
Polypeptide antibiotics (colistin)	grey	green	grey	grey
3rd generation cephalosporins (cefotaxime)	green	grey	grey	grey
Penicillins (ampicillin)	grey	green	green	green
Tetracyclines (tetracycline)	green	green	green	green
Sulfonamides (sulfamethoxazole)	green	green	green	green
Folic acid antagonists (trimethoprim)	grey	green	green	green
Aminoglycosides (gentamicin)	green	green	grey	green

Green symbolises a positive development (increase in the share of sensitive isolates or decrease in the share of resistant isolates). A significant increase in the resistance rate is shown in red. If there has been no significant change during the period, this is shown in grey. No data were available for colistin for 2009, therefore the overall evaluation is given with (2010 to 2017) and without colistin (2009 to 2017).

3.3.2. *Campylobacter spp.*

Overall, less clear trends were observed in the resistance of *Campylobacter spp.* from the four food chains considered. Moreover, in terms of isolates from meat, sufficient samples were available for evaluation only from fattening chickens and fattening turkeys. In fattening pigs and fattening calves, *Campylobacter* are very rarely found on carcasses and meat which means that only isolates from gut content or faeces were available. Furthermore, almost without exception, *C. coli* are detected in fattening pigs which means that no isolates of *C. jejuni* could be evaluated either.
It was consistently shown that *C. coli* isolates were more resistant than *C. jejuni* isolates. The trends over time highlighted clear differences between the active substances. Whereas there was an increase in the resistance to ciprofloxacin and nalidixic acid of *C. jejuni* from fattening chickens and fattening turkeys, of *C. coli* from fattening pigs and of *C. jejuni* from fattening calves, resistance to tetracycline and erythromycin decreased in the *C. coli* of fattening turkeys. The resistance of *C. jejuni* from fattening turkeys and fattening chickens to streptomycin fell. No other significant trends were observed.

Table 11: Trend in resistance rates of Campylobacter isolates to antimicrobials included in the analysis from 2009 to 2017

	Fattening chickens		Fattening turkeys		Fattening pigs	Fattening calves	
All active substances	*C. coli*	*C. jejuni*	*C. coli*	*C. jejuni*	*C. coli*	*C. coli*	*C. jejuni*
Share of sensitive isolates	grey	grey	grey	grey	grey	grey	grey
Active substance classes (tested active substance)							
Fluoroquinolones (ciprofloxacin)	grey	red	grey	red	red	grey	grey
Quinolones (nalidixic acid)	grey	red	grey	red	red	grey	red
Macrolides (erythromycin)	grey	grey	green	grey	grey	grey	grey
Tetracyclines (tetracycline)	grey	red	green	grey	grey	grey	grey
Aminoglycosides (streptomycin)	grey	green	grey	green	grey	grey	grey
Aminoglycosides (gentamicin)	grey	grey	grey	grey	grey	grey	grey

Green symbolises a positive development (increase in the share of sensitive isolates or decrease in the share of resistant isolates). A significant increase in the resistance rate is shown in red. If there has been no significant change during the period, this is shown in grey.

When the analysis was performed without taking isolates from food from retail outlets into account, a significant decrease in the resistance of *C. coli* to erythromycin was observed in fattening chickens. However, the changes in the resistance of *C. jejuni* to streptomycin and tetracycline were no longer significant. The exclusion of food isolates likewise leads to changes in the food chain of fattening turkeys. Here, the decrease in resistance to tetracycline and erythromycin was significant in both species considered. The increase in resistance of *C. jejuni* to ciprofloxacin was no longer significant.

If one compares the situation for the individual years with the last year for which data were available[8], the upward trend in resistance in the three food chains considered (no data available here for fattening pigs) is confirmed for ciprofloxacin, especially for *C. jejuni*. Lower resistance rates to tetracycline were also found in fattening chickens in the two years prior to 2016. For fattening turkeys an increase in the resistance rates of *C. jejuni* to ciprofloxacin can be observed. At the same time, *C. coli* from fattening turkeys showed a decrease in resistance rates to tetracycline and erythromycin.

3.3.3. Bacterial isolates from clinically diseased animals (*E. coli and P. multocida*)

The resistance situation in isolates from diseased animals showed a partially different trend from the isolates of commensal bacteria. It should be noted that the resistance rates at the beginning of the period under observation varied depending on the bacterial species. Whereas the initial resistance level was generally high for *E. coli* isolates, it was rather low for *P. multocida* isolates. For the latter it is, therefore, generally more difficult to determine statistically significant reductions.

Overall, the resistance of clinical *E. coli* isolates from various animal species presented a stable to slightly downward trend. In this context 'stable' means that no significant differences to the study year 2017 could be found. Moreover, no significant increase in fully sensitive isolates could be demonstrated. For enrofloxacin (fluoroquinolone) in fattening chickens, a significant decrease in the resistance rate was, however, shown for the years 2009, 2011 and 2015. Sporadic positive effects were also observed with the active substances cefotaxime (3rd generation cephalosporin), ampicillin (penicillin) and tetracycline. The isolates of fattening piglets showed the highest decrease in resistance rates.

In *P. multocida* isolates, on the other hand, a significant increase in resistance rates was observed compared to the macrolides tilmicosin and tulathromycin. There was no change in the resistance rates to the active substances gentamicin (aminoglycoside) and cefotaxime (3rd generation cephalosporin).

Annex 4 contains more detailed information.

8 for fattening chickens and fattening turkeys 2016, for fattening calves 2015

3.4. Criterion 3: Findings and experiences of the competent authorities and criterion 4: Experiences of animal keepers and veterinarians

3.4.1. Observations on reduced consumption

A growing awareness amongst animal keepers and veterinarians when using antibiotics in recent years is confirmed in the *Länder* report. It states: "*The quantities of antibiotics supplied in accordance with the DIMDI Medicine Products Ordinance have been reduced by more than half since the discussion about the introduction of an Antibiotics Minimisation Concept in 2011. This is also reflected in the data of the state antibiotics database for the calculation of treatment frequency per farm. [...] The use of antibiotics in livestock farming has been significantly reduced.*"

86% of the veterinarians participating in the survey were also of the opinion that the use of antibiotics had clearly fallen (44%) or had shown a tendency to decrease (42%) since 2014. The opinion that the use of antibiotics had declined tended to be shared by animal keepers. However, the reduction was assessed more cautiously: to a larger degree (39%) unchanged use was observed and to a lesser degree (20%) a clear decrease; a tendency to decrease was observed by 37%. A small share of respondents (2%) stated that use had increased. The results can be explained by the animal species kept by the participants and their, in some cases, elevated use of antibiotics (see Chapter 2.2.4. on the survey methodology).

The veterinarians interviewed reported a shift in their prescribing behaviour towards using fewer combination products (especially for the types of production fattening turkeys, fattening piglets, fattening pigs and fattening cattle, around 50% less for each of them) and around one third reported making greater use of old/conventional antibiotic active substance classes for fattening piglets, fattening pigs and fattening calves. Also 29% of animal keepers reported the use of other active substances (not further specified) in the change in treatment practice on their farm.

3.4.2. Observations on greater awareness of antibiotic use

The *Länder* report states: "*Many animal keepers have developed an awareness of the problem and wish to optimise their stock themselves. In addition to the fundamental raising of awareness about the use of antibiotics, there now also seems to be an economic incentive to avoid infectious diseases as far as possible*".

Almost 90%[9] of the veterinarians surveyed found that there was increased awareness of this subject amongst animal keepers and also 80% among veterinarians. More than 60% agreed that the legislation had helped to reduce the use of antibiotics. An impact along the lines of more informed use and increased recourse to other animal health measures (70% respectively) was likewise observed. Just under 60% of animal keepers stated that the 16th AMG Amendment had contributed to more informed use of antibiotics and increased recourse to animal health measures such as vaccination.

9 "agree wholeheartedly", "agree", "tend to agree" on a six-level answer scale from full agreement to complete rejection of the respective statement

3.4.3. Observations on patterns of use and days of drug action

According to the target groups interviewed, the use of antibiotics has generally changed as follows:

→ Increased treatment of individual animals was cited by both veterinarians and animal keepers of the relevant types of production (fattening piglets, fattening pigs, fattening calves) as the most frequent change.

→ The following changes were also frequently mentioned by veterinarians: delayed prescription (40%) and shorter treatment duration (32%).

The *Länder* report states: *"As a result, the value [of days of drug action] is to be determined by the veterinarians. It can have a major impact on the level of treatment frequency and may be the decisive factor when it comes to whether an animal keeper is a "frequent consumer" of antibiotics on the farm or not. During controls it was, therefore, observed that the one-shot administration of an identical antibiotic to an animal species was recorded in the database as one day of drug action but also as 7 days of drug action. Both veterinarians and animal keepers quickly identified this "varied practice", but it cannot be controled or penalised by the authority"*.

Over 90% of veterinarians stated that they "always" (64%) or "mostly" (28%) adhere to the recommended days of drug action. However, 5% also stated that they "never" adhered to it. The animal keepers who had not delegated responsibility for this notification, stated that they always (76%) or mostly (11%) complied with the days of drug action recommendation in their notifications. More than 70% of the veterinarians interviewed agreed that their work was made more difficult by the fact that the days of drug action had not been laid down in a binding manner. A binding definition of days of drug action was requested by all the target groups interviewed.

3.4.4. Observations on vaccinations and other health measures

The *Länder* report states: "*On the positive side, there has been an increase in preventive measures to avoid infections (e.g. vaccinations) and a shift from oral group treatments to parenteral treatment of individual animals since the 16th AMG Amendment. On-site inspections and the review of action plans revealed that many farms have intensified their diagnostics, carried out treatments and hygiene measures (e.g. strict introduction into/removal from procedures, cleaning and disinfection of drinking water systems) more consistently and optimised their management (e.g. by improving the stable climate and feeding with a higher crude fibre content and acidification as well as extending suckling periods). [...] Overall it can be said that animal keepers can influence many things on the farm in order to improve animal health and keep it on a high level. Most animal keepers made use of these opportunities and they must continue to do so to ensure good animal health.*"

Animal keepers and veterinarians stated the following in this context: Both survey groups mentioned that they make the most frequent use of preventive measures (vaccines) as increasingly administered veterinary medicinal products, followed by alternative ways of alleviating the symptoms of an infection (e.g. anti-inflammatory drugs, homeopathic or herbal active substances). Prebiotics and probiotics, essential oils, cortisone, vitamins and other feed additives were also used. However, 33% of veterinarians stated that they would not use other veterinary medicinal products instead of antibiotics.

With regard to other measures taken both as part of an action plan and as a general investment in the improvement of animal health, the veterinarians in the survey most frequently cited the following (median, estimated percentage of clients who use this measure): increased vaccination 25%, improved hygiene 20% and improved feed/feed supplements 15%. According to animal keepers, the following measures were the most frequently taken: increased vaccination (37%), improved husbandry/climate/conversion (39%), improved hygiene (38%), and improved feed/feed additives (34%). In some cases, these statements were of course the same as for the question about alternative treatment methods/veterinary medicinal products.

3.4.5. Observations on the variable “treatment frequency”

The *Länder* believe it makes sense to keep the half-yearly rhythm for the half-yearly recording of antibiotic use, as stipulated in the 16th AMG Amendment. This is explained in the *Länder* report: *“For the time being, the Länder are of the opinion that it makes sense to maintain the half-yearly recording of antibiotic use. In this way, seasonal fluctuations for instance and, by extension, climate-related causes with regard to the use of antibiotics on a farm can be proven.”*

However, the *Länder* authorities take a critical view of the periods set for implementing the measures: *“Based on experience with the evaluation period, the following periods seem to be too long, as they force animal keepers to refer to events in the distant past when drawing up an action plan. Some measures were already taken before the action plan was drawn up and the plan is drawn up retrospectively.”*

Animal keepers and veterinarians found that the treatment frequency can only be used to a limited degree for animal health advice and management decisions. This is mainly due to late communication which leads to the late drawing up of action plans. Whereas the indicator calculation is either too frequent (veterinarians 27%, animal keepers 30%) or as frequent as is appropriate (veterinarians 23%, animal keepers 56%), for only 22% (veterinarians) and 28% (animal keepers) is it communicated early enough for them to be able to use it as a basis for advice or management decisions. The animal keepers interviewed used the data compiled for the communication of antibiotic use rarely (31%) or not at all (54%) for other internal purposes. Among the veterinarians surveyed, 45% also stated that they used other data only for advice, and only <10% therefore attributed a relevant benefit for animal health advice to indicator 2.

3.4.6. Observations on the impact on animal health and animal welfare

The *Länder* report states in this context: *“What is unacceptable is the failure to treat diseased animals, which is highly problematic in terms of animal welfare. This was reported in individual cases: it seems that the animal keeper informed the attending veterinarians that no further treatment should be given because this could possibly lead to an exceeding of the indicator. There are also reports that there was an increase in slaughter findings at slaughterhouses indicating inadequate treatment of animals. No valid data on this have been available up to now in the Länder as the Antibiotics Minimisation Concept does not include any procedure for comparing the frequency of antibiotic use on a farm with statistical parameters to describe animal health.”*

In the survey of animal keepers and veterinarians, both groups were asked about their impressions of the change in animal health since the 16th AMG Amendment came into force. The veterinarians had noticed an increase in fatalities, diseased animals and slaughter findings. All the changes mentioned in the questionnaire were detected less frequently by the animal keepers. For both the statements on the increase and decrease in the phenomena mentioned, about two-thirds of the respondents answered “I never observed this” or “I rarely observed this”.

A majority of veterinarians agreed to consider more frequently whether an animal should still be treated or culled (58%)[10]. This statement was also made by a majority of animal keepers (63%). Only just over 20% of veterinarians agreed that the 16th AMG Amendment promoted animal health and that a further reduction in the use of antibiotics was possible without this having a negative impact on animal health.

10 “agree wholeheartedly”, “agree”, “tend to agree” on a total six-level answer scale from full agreement to complete rejection of the respective statement

Both the survey of animal keepers and veterinarians and the *Länder* report discussed the possible link between the (reduced) use of antibiotics and animal welfare aspects. A majority (80%) of both veterinarians and animal keepers stated that since the 16th AMG Amendment had come into force, they felt they were being tugged to and fro between their duty to both protect animals and reduce antibiotic use.

Both in the *Länder* report and as a result of talks with participants from the focus group discussions, information from a slaughterhouse veterinarian and representatives of the competent authorities in the *Länder*, the topic was addressed of establishing an overarching animal health index by creating a central animal health database that draws together medicinal product, animal welfare and animal health legislation.

3.4.7. Observations on the action plans

The main measures taken in the action plans and the characteristics of the accompanying advice have already been described in the section "Observations by animal keepers and veterinarians regarding vaccinations and other health measures". This section focuses on the preparation, implementation and monitoring of the measures by the competent authorities, i.e. on the process and not on the content of the measures.

Based on their experiences, the *Länder* note: *"The scale and the quality of the action plans very much depend on the responsible veterinarian in charge and can vary considerably. In some cases, the action plans are individually tailored to the respective farm in cooperation with the veterinarian attending the stock. In other cases, however, they are prepared solely by veterinarians or with little involvement of animal keepers. Some veterinarians use a simple system of text modules to draw up action plans; these action plans are less farm specific and are basically the same from one half-yearly period to the next. All in all, the quality of the action plans has steadily increased since the AMG Amendment came into force in the opinion of the Länder."*

According to the information provided in the survey, animal keepers, aside from a few exceptions (3%), involved their veterinarian in drawing up the action plan (pursuant to the provision in section 58d (2) first sentence AMG). The veterinarian, therefore, has a central role to play and is an extremely influential factor in terms of the plan's quality and chances of success.

There were difficulties in agreeing on and implementing the action plan. From the *Länder* report: *"On-site controls have shown that most animal keepers are willing to implement measures according to the plan. [...] Difficulties in the implementation of the action plan were observed, inter alia, on farms whose structural conditions and management were good, but where antibiotic treatment was necessary because of the organisational disease-promoting structure (e.g. calf fattening [many origins with different health status], piglets from different producers)."*

In the survey, only 20% of veterinarians agreed with the following statement "Reaching agreement on the action plan is simple and efficient", 65% disagreed with the statement "The notification/transmission of the action plan is simple and efficient" and only 30% were of the opinion that "The assessment of the plan by the competent authority is competent and timely" or "The required information makes sense"[11]. According to veterinarians, the measures planned so far could be fully (6%), mostly (34%) or slightly (38%) implemented on their clients' farms. Implementation was viewed more positively by the animal keepers than by the veterinarians: The measures taken could be fully (26%), largely (42%) or only partially (17%) implemented. For 15% they were scarcely implemented or not implemented at all.

11 "tend not to agree", "do not agree", "do not agree at all" on a total six-level answer scale from full agreement to complete rejection of the respective statement

The *Länder* report comments as follows on the reduction potential: *"A reduction in antibiotic use is not possible to an unlimited degree. Given the major reduction in the nationwide indicators, a properly treated, unique disease incident can already lead to an exceeding of indicator 2. The preparation of an action plan only makes sense if there is potential for improvement on the farms. If this is not the case, an action plan constitutes an unnecessary bureaucratic burden for animal keepers, consulting veterinarians and the monitoring authorities."*

In the survey, 43% of respondents attributed a later improvement in the treatment frequency per farm to the measures taken, but 53% were unable to reduce it. Approximately 90% of veterinarians agreed with the statements "For some clients all possible measures have been exhausted" and "For some clients the implementation of the measures is not economically feasible".

3.4.8. Observations on the administrative burden and benefits

Overall, the enforcement of the provisions of the 16th AMG Amendment on antibiotic reduction is associated with a considerable burden for the authorities, in their opinions, as was explained in the telephone interviews by representatives of the *Länder* authorities. In all *Länder*, more staff had to be deployed in the appropriate places, but this was accompanied, at least temporarily, by increased individual workloads of the employees of the responsible authorities. According to the authorities interviewed and the *Länder* report, animal keepers continue to require considerable assistance and advice in meeting the notification requirements, one reason being the complex data entry in the database. Plausibility checks of the data and the clarification of non-notified zero declarations are also time-consuming for the enforcement authorities (differentiation between farms that have not actually used antibiotics (they are not obliged to submit a "zero notification") and those that have inadmissibly failed to make a notification). There is also an administrative burden regarding the monitoring of the timely submission and review of action plans. The major effort it takes to identify non-notifiers (farms who, given their orientation and stock size, would have a duty of notification but fail to comply with it) has decreased over time since the introduction of the 16th AMG Amendment as most of the existing farms with a duty of notification have been reported and registered as such.

Despite the existing enforcement burden, the *Länder* report comes to the conclusion: *"In summary, it can be stated that the Antibiotics Minimisation Concept has, from the point of view of the Länder, become well established in principle among the stakeholders and has been successfully implemented by them".*
It is also generally acknowledged that the 16th AMG Amendment has made a contribution to the reduced use of antibiotics and to the prudent use of other animal health measures in animal husbandry. The quantification and comparison possibilities created for the use of antibiotics are generally seen as positive by the enforcement authorities for farms, veterinarians and authorities. For example, authorities can plan controls more from the risk angle than before, and animal keepers can work with their veterinarians to react when their use of antibiotics is comparatively high. This helps to increase efficiency.

The *Länder* report notes with regard to the notification burden: *"The animal keepers needed extensive support and assistance to comply with the notification requirements. This was provided by authorities throughout Germany in countless telephone consultations up to lengthy explanations on how to use the database. (...) Despite the above-mentioned efforts, the quality of the notifications is still unsatisfactory for the monitoring authorities: incorrect data entries and error reports in the antibiotic database still occur. The rather high error rate stems firstly from the complex nature of data entry and secondly from notifications in which – either deliberately or negligently – for instance incorrect animal numbers or too few days of treatment/drug action are indicated. The authorities have to carry out time-consuming plausibility checks in order to detect, among other things, notification errors and violations. The highest error rate was recorded for notifications of medicinal product use by third parties with simultaneous notification of animal numbers by the animal keeper."*

According to the participants in the survey, most notifications of antibiotic use are undertaken by veterinarians on behalf of their clients: 95%[12] of farms have delegated the notifications to veterinarians. 57% of the veterinarians used QS exclusively or predominantly for the notifications. 7% used either QS or HITier in equal proportions and 36% used HITier exclusively or predominantly. The interviewed veterinarians estimated the time required for notification to be 8% (median, scattering of 0% – 50%) of their veterinary working hours. Around two thirds of the veterinarians interviewed (68%) rated the time taken to be long (37%), very long (8%) or far too long (24%). 60% of animal keepers stated that they had delegated the notification of antibiotic use to their veterinarian. The estimated time needed by the animal keepers who themselves prepared the antibiotic notifications was 60 minutes per notification period (half-year) (median, scattering 3 to 1,500 minutes). 30% of respondents stated that they had received support from the authorities on one or more occasions for their notifications.

All stakeholders interviewed pointed out that some data entries had to be made twice or at different locations and that the veterinary fields requiring notifications (veterinary medicinal products, animal health, animal welfare) were not currently interlinked. For example, the number of animals kept (stock notification) had to be notified, once in accordance with animal health law/Livestock Trade and Transport Ordinance (*Viehverkehrs-Verordnung* – VVVO) and once in accordance with veterinary medicinal product law (section 58a AMG). If the data notified pursuant to the VVVO are to be entered in the veterinary medicinal products database, a one-off authorisation is required. Furthermore, the animal keeper must provide written confirmation in each notification period that there has been no deviation from the veterinary treatment instructions if the recording of antibiotic use has been delegated to the veterinarian. This administrative burden was deemed by all the groups interviewed to be time-consuming and unnecessary.

The *Länder* report notes regarding the question of the benefit: *"The majority of animal keepers do not doubt the purpose and the legality of the 16th AMG Amendment. Overall, there is growing awareness of the issue of 'antibiotic consumption by type and quantity' amongst veterinarians and animal keepers."*

Due to the above-described burden for different stakeholders resulting from the individual measures and provisions or their implementation, the relationship between burden and benefit is also viewed critically by some of the stakeholders. The survey participants were unanimous in their view that the benefits would be felt in terms of raising awareness and contributing to a reduction in use. More than 60% of veterinarians agreed that the legislation had made a contribution to reducing antibiotic use. The expediency of the legislation was also approved by 40% of animal keepers. However, less than 20% of veterinarians and 26% of animal keepers felt that there was an acceptable relationship between burden and benefit. Only just over 20% of the veterinarians in each case agreed that the 16th AMG Amendment promoted animal health and that a further reduction in the use of antibiotics was possible[13].

3.5. Data sheets

The data sheets on the following pages give a separate overview of the figures and developments for each type of production.

12 Clients of the participating veterinarians who have delegated their duty of notification to their veterinarian, estimations as %

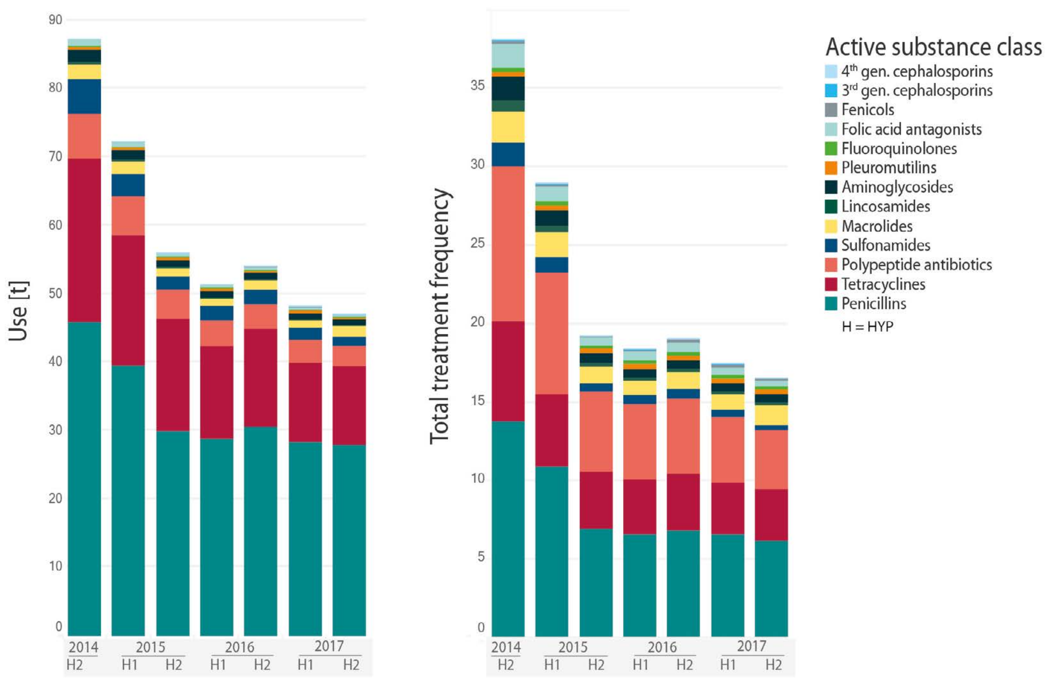
13 "agree wholeheartedly", "agree", "rather agree" on a total six-step answer scale from full agreement to full rejection of the respective statement

Data Sheet

Fattening piglets

Consumed quantities

For fattening piglets, the used quantity fell from around 87 t in HYP 14/2 by 40 t (46%) to 47 t in HYP 17/2. Penicillins and tetracyclines were used most frequently. For these two active substance classes, which account for more than 75% of the total used quantity for this type of production, a major reduction in the used quantity over time can be observed, from 46 t to 28 t for penicillins and from 24 t to 12 t for tetracyclines (see diagram). In relation to the total used quantity in the respective half-yearly period, the share of penicillin use increased from 52.6% in HYP 14/2 to 59.2% in HYP 17/2. The share of sulfonamides in the total used quantity fell from around 6% in HYP 14/2 to around 3% in HYP 17/2. The used quantity of macrolides fell from 2.2 t to 1.7 t. Its share in total used quantity, however, increased from 2.6% to 3.5%. 3rd and 4th generation cephalosporins together accounted for less than 0.02% of the total used quantity for this type of production. Fluoroquinolones stagnated at a used quantity of 0.08 t, increasing their share of used quantity from 0.1% to 0.2%. The consu used med quantities of polypeptide antibiotics have fallen steadily since HYP 14/2. The used quantity of long-acting/one-shot preparations for this type of production fell from 0.4 t to 0.3 t.



Developments in the type of production fattening piglets over 7 HYPs
Left: Development of used quantity for each active substance class
Right: Development of total treatment frequencies for each active substance class

Treatment frequency

There has been a statistically significant decrease in treatment frequency for fattening piglets since 2014 and it was the most pronounced in the comparison of the types of production. This decline was observed on small, medium and large farms whereby the treatment frequency remained on a higher level in large farms than in medium and small farms. Treatment frequency for each active substance class: in fattening piglets the use of penicillins and polypeptide antibiotics is predominant, followed by tetracyclines. A downward trend can be observed for these three active substance classes. Penicillins were used on at least 50% of the farms. At least 25% of the farms used polypeptide antibiotics or tetracyclines in each half-yearly period or they used fluoroquinolones or macrolides in individual half-yearly periods. For sulphonamides and folic acid antagonists a clear drop in treatment frequencies is discernible.

Resistance

Commensal *E. coli*

There are no specific results from the food chain for fattening piglets, as they are only included in the category "fattening pigs" before they reach slaughter and the food chain.

***E. coli*, clinical isolates**

The results for the *E. coli* isolates from piglets are presented on behalf of the animal species "pig" since their resistance behaviour does not differ from that of the production stages young pigs or fattening pigs. In the case of *E. coli* isolates from piglets, an increase in fully sensitive isolates was shown. The number of isolates that were fully sensitive has increased almost steadily since study year 2010 to a rate of 21% in 2017. At the same time, the rate of isolates that were resistant to more than three substances decreased in a similarly steady manner (about 21% in 2017). The increase in fully sensitive isolates was statistically significant for the study years 2009 to 2012. Since study year 2015, the change in resistance rates has not been statistically significant for any of the active substances tested.

All active substances	2009	2010	2011	2012	2015	2016
Share sensitive to all active substances	green	green	green	green	grey	grey
Share multi-resistant (>3 active substances)	grey	grey	green	green	grey	grey
Active substance classes (tested active substances)						
Fluoroquinolones (ciprofloxacin)			grey	grey	grey	grey
Fluoroquinolones (enrofloxacin)	grey	grey	grey	grey	grey	grey
Polypeptide antibiotics (colistin)	grey	grey	green	green	grey	grey
3rd gen. cephalosporins	grey	grey	grey	grey	grey	grey
Penicillins (ampicillin)	grey	grey	green	pale green	grey	grey
Tetracyclines (tetracycline)	green	green	green	green	grey	grey
Sulfonamides+folic acid antagonists	green	pale green	green	green	grey	grey
Aminoglycosides (gentamicin)	grey	grey	grey	grey	grey	grey

Comparison of the resistance rates *E. coli* clinical isolates with the antibiotics included in the analysis for the years 2009 to 2017.
2017 was chosen as the reference year. Green symbolises a positive development (significant increase in the share of sensitive isolates or decrease in the share of resistant isolates). Grey areas indicate no difference between the respective year and the reference year. Pale green indicates changes at a lower significance level of p<0.1.

Fattening piglets in the survey

According to veterinarians

- → the prescribing of combination products for fattening piglets has decreased (51%)
- → veterinarians do not immediately prescribe antibiotics for fattening piglets (49%)
- → individual animal treatments have increased (47%)
- → more vaccines (65%) and more anti-inflammatory drugs (57%) are used

According to animal keepers

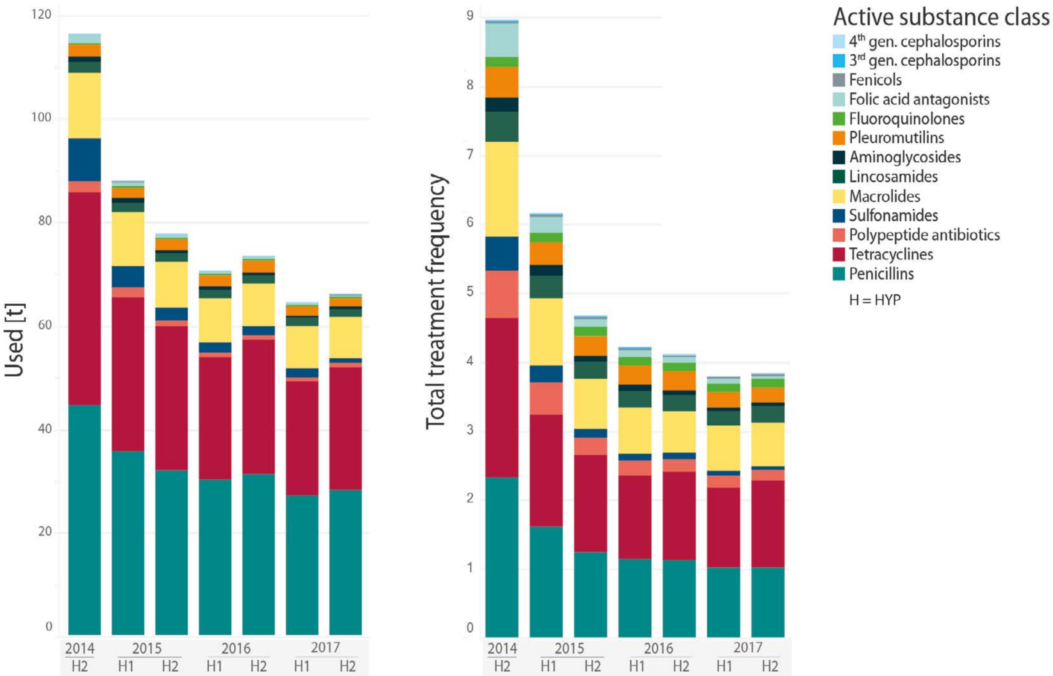
- → the use of antibiotics has changed in such a way that more individual animals are treated (55%) and other active substances are used (33%).
- → thought is given more frequently in the case of fattening piglets as to whether an animal should be treated antibioticly or better culled ("completely correct" 21%; "correct" 32%; "quite correct" 16%)
- → the most frequently taken measure was "improved feeding, feed additives" (69%), followed by "increased vaccination" (51%).

Data Sheet

Fattening pigs

Consumed quantities

A total of approximately 115 t of antibiotics were used for fattening pigs in HYP 14/2. This quantity had fallen by 50 t (43%) to approximately 65 t by HYP 17/2. This reduction in the quantity in t constitutes the biggest drop in used quantity of all the types of production considered. Penicillins and tetracyclines, which accounted for 74% (44.1 t and 40.5 t respectively) of the total used quantity for this type of production in HYP 14/2, made up 76% (27.8 t and 23.4 t respectively) of the used quantity in HYP 17/2. The share of sulfonamides in the total used quantity fell from approximately 7% (8.3 t) in HYP 14/2 to approximately 1.5% (1.0 t) in HYP 17/2. Therefore, the used quantities for these three active substance classes all decreased. The used quantities of macrolides and polypeptide antibiotics likewise fell significantly by 37% and 66%, respectively, from 12.4 t to 7.8 t (macrolides) and from 2.2 t to 0.7 t (polypeptide antimicrobials). The used quantities of fluoroquinolones and 3rd and 4th generation cephalosporins were low and scarcely changed at all. The total used quantity of long-acting/one-shot preparations rose from 0.7 t to 0.8 t.



Developments in the type of production fattening pigs over 7 HYPs
Left: Development of use for each active substance class
Right: Development of total treatment frequencies for each active substance class

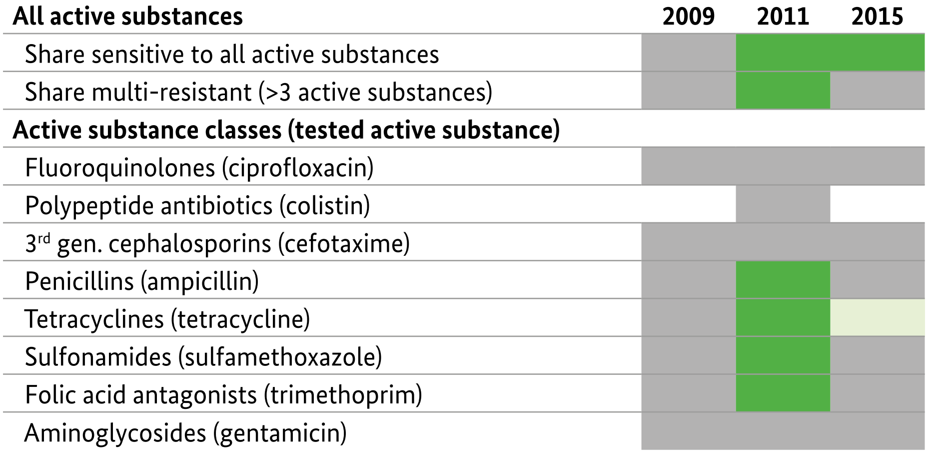
Treatment frequency

The treatment frequency for fattening pigs has fallen significantly since 2014. This decline was observed on small, medium and large farms. The treatment frequency remained on a higher level in large farms than in medium and small ones. **Treatment frequencies for each active substance class:** penicillins were used on at least 50% of the farms and tetracyclines or fluoroquinolones on at least 25% in each half-yearly period. For macrolides this was only the case for HYPs 14/2 to 16/1, after which the share was further reduced. For the two dominant active substance classes tetracyclines and penicillins, there was a downward trend in treatment frequency (3rd quartile from 1.7 to 0.3 for penicillins, from 2.1 to 0.1 for tetracyclines). There was scarcely any recourse to sulfonamides and folic acid antagonists (trimethoprim) (the active substance was used on less than 25% of farms; from HYP 15/2 even in less than 5% of farms). The treatment frequency also decreased for macrolides, polypeptide antibiotics, 3rd and 4th generation cephalosporins and fluoroquinolones. The reduction in the treatment frequency was only minor for cephalosporins. In any case, 3rd generation cephalosporins were hardly used at all. If one compares the trends in used quantities and treatment frequencies, a downward trend can be observed in each case.

Resistance

Commensal *E. coli*

For fattening pigs the share of isolates that were resistant to at least one or more than 3 substances was lower in 2017 than in 2011 and 2015. Between 2015 and 2017 there was an increase in the share of isolates sensitive to all tested substances.



Comparison of the resistance rates from isolates of commensal *E. coli* isolates from fattening pigs in 2009, 2011 and 2015 with those from 2017. Green symbolises a statistically significant positive development (increase in the share of sensitive isolates or decrease in the share of resistant isolates) in isolates from 2017. Grey areas indicate no difference between the respective year and the reference year. Pale green indicates changes at a lower significance level of $p<0.1$.

***E. coli*, clinical isolates**

The data on clinical isolates are presented in the data sheet "Fattening piglets" for the animal species "pig" as their resistance behaviour does not differ from that of the production stages young pig or fattening pig. In the case of *E. coli* isolates from fattening piglets, a significant increase in fully sensitive isolates was detected in the study years 2009 to 2012. This was accompanied by a steady decline in the number of multiple-resistant isolates.

Fattening pigs in the survey

According to veterinarians

- the prescribing of combination products for fattening pigs has decreased (48%)
- there is more individual animal treatment (54%)
- more vaccines (61%) and more anti-inflammatory drugs (50%) are used

According to animal keepers

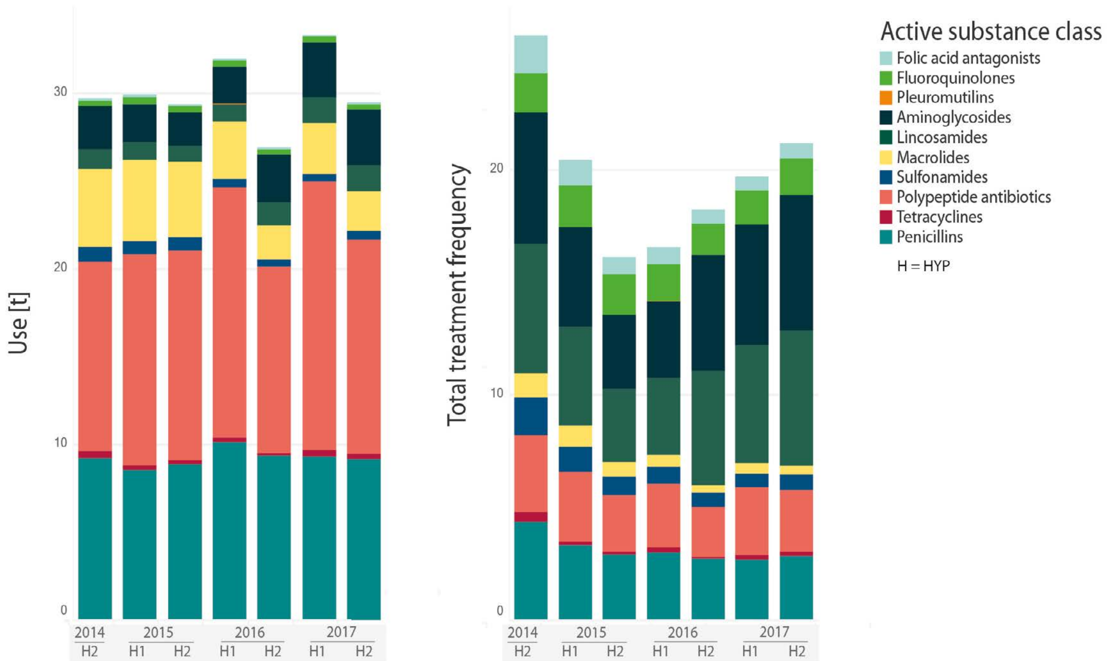
- the use of antibiotics has "clearly decreased" (30%) decreased or at least "tended to decrease" (35%). The treatment of individual animals has increased markedly (55%).
- thought is given more frequently as to whether an animal should be treated with an antibiotic or better culled ("completely correct" 23%; "correct" 31%; "quite correct" 14%)
- one measure that was taken more frequently than for all other types of production was the change in the origin of the animals (35%)

Data Sheet

Fattening chickens

Consumed quantities

The total used quantity for fattening chickens was between 29 t and 33 t over the observed half-yearly periods. Polypeptide antibiotics accounted for the largest individual share of the total used quantity, both in terms of the type of production fattening chickens and of the total used quantity of polypeptide antibiotics for all types of production. This share was 36.2% (10.8 t) for fattening chickens in HYP 14/2 and it rose to 41.3% (12.2 t) in HYP 17/2. Penicillins were also frequently used for this type of production. At 9.2 t in HYP 14/2, they accounted for 31.1%. In HYP 17/2 it likewise amounted to 9.2 t with a share of 31.1%. The share of aminoglycosides in the total used quantity was also highest for fattening chickens out of all types of production. In HYP 14/2 they accounted for a share of 8.2% (2.4 t) and in HYP 17/2 for a share of 10.7% (3.1 t) in the total used quantity for this type of production. Tetracyclines and sulfonamides were only used in limited quantities in fattening chickens. The used quantity of macrolides, another important active substance class for fattening chickens, was halved from 4.4 t in HYP 14/2 to 2.2 t in HYP 17/2, as was their share in the total used quantity (from 14.9% to 7.6%). The share of fluoroquinolones in the respective half-yearly period remained relatively constant at approximately 0.35 t. This corresponds to a share of between 12% in the total used quantity. Aminoglycoside-lincosamide combinations were used in particular for fattening chickens. The use of aminoglycosides and lincosamides increased by around 30%.



Developments in the type of production broilersfor 7 half-yearly periods
Left: Development of used quantity for each active substance class
Rights: Development of total treatment frequency for each active substance class

Treatment frequency

There has been a statistically significant decrease in treatment frequency since 2014. This decline was observed on small, medium and large farms whereby the treatment frequency remained higher on large farms than on medium and small ones. However, the reduction in treatment frequency was lowest among fattening chickens out of all types of production and has risen steadily again since HYP 15/2. **Treatment frequency for each active substance:** in fattening chickens the use of aminoglycosides, penicillins, lincosamides and polypeptide antibiotics was dominant. For penicillins, a downward trend can be observed in all farm size classes. In addition, at least 25% of the farms used penicillins, aminoglycosides, lincosamides or polypeptide antibiotics in all half-yearly periods. Fluoroquinolones were used by at least 5% of the farms in all half-yearly periods. There is no clear trend for the development of the treatment frequency for fluoroquinolones.

Resistance

Commensal *E. coli*

Overall there is an upward trend for the share of sensitive isolates in fattening chickens. However, no significant reduction in resistance rates could be observed for fluoroquinolones and polypeptide antibiotics (colistin).

All active substances	**2009**	**2010**	**2011**	**2013**	**2014**
Share sensitive to all active substances					
Share sensitive to all active substances incl. colistin					
Share multi-resistant (>3 active substances)					
Share multi-resistant (>3 active substances) incl. colistin					
Active substance classes (tested active substances)					
Fluoroquinolones (ciprofloxacin)					
Polypeptide antibiotics (colistin)					
3rd gen. cephalosporins (cefotaxime)					
Penicillins (ampicillin)					
Tetracyclines (tetracycline)					
Sulfonamides (sulfamethoxazole)					
Folic acid antagonists (trimethoprim)					
Aminoglycosides (gentamicin)					

Comparison of the resistance rates of commensal *E. coli* isolates from broilers in 2009-2014 with those from 2016. Green symbolises a statistically significant positive development (increase in the share of sensitive isolates or decrease in the share of resistant isolates) in 2016 compared to the year shown. Grey areas indicate no difference between the respective year and the reference year. Pale green indicates changes at a lower significance level of p<0.1. No data were available for colistin for 2009 and 2010, therefore the overall evaluation is presented with (2011-2016) and without colistin (2009-2016).

***E. coli*, clinical isolates**

Overall there were scarcely any significant changes in the resistance rates of *E. coli* from fattening chickens[1]. The fluoroquinolone enrofloxacin was an exception. Here, a significant decrease in the resistance rate in 2017 compared to the years 2009, 2011 and 2015 was observed. Overall, the share of isolates with less than 3 resistances was predominant (60% – 92%).

All active substances	**2009**	**2010**	**2011**	**2012**	**2013**	**2014**	**2015**	**2016**
Share sensitive to all active substances								
Share multi-resistant (>3 active substances)								
Active substance classes (tested active substances)								
Fluoroquinolones (ciprofloxacin)								
Fluoroquinolones (enrofloxacin)								
Polypeptide antibiotics (colistin)	Cannot be evaluated							
3rd gen. cephalosporins (cefotaxime)								
Penicillins (ampicillin)								
Tetracyclines (tetracycline)								
Sulfonamides+folic acid antagonists (Sulfamethoxazole+trimethoprim)								
Aminoglycosides (gentamicin)								

Comparison of the resistance rates of *E. coli*, clinical isolates with the antimicrobials included in the analysis in the years 2009 to 2017.
2017 was chosen as the reference year. The colouring is the same as in the diagram for commensal *E. coli*.

Fattening chickens in the survey

According to veterinarians

- the treatment frequency generally reflects the use of antibiotics in fattening chickens quite accurately (57%), more than for other types of production
- veterinarians do not immediately prescribe antibiotics for fattening chickens (57%)

According to animal keepers

- the use of antibiotics in fattening chickens has changed particularly markedly: “clearly decreased” (21%) or “tended to decrease” (46%), followed by improvements in feed and hygiene (42% respectively).

1 Due note is to be taken of the low isolate numbers for this animal species, as this means their significance is limited.

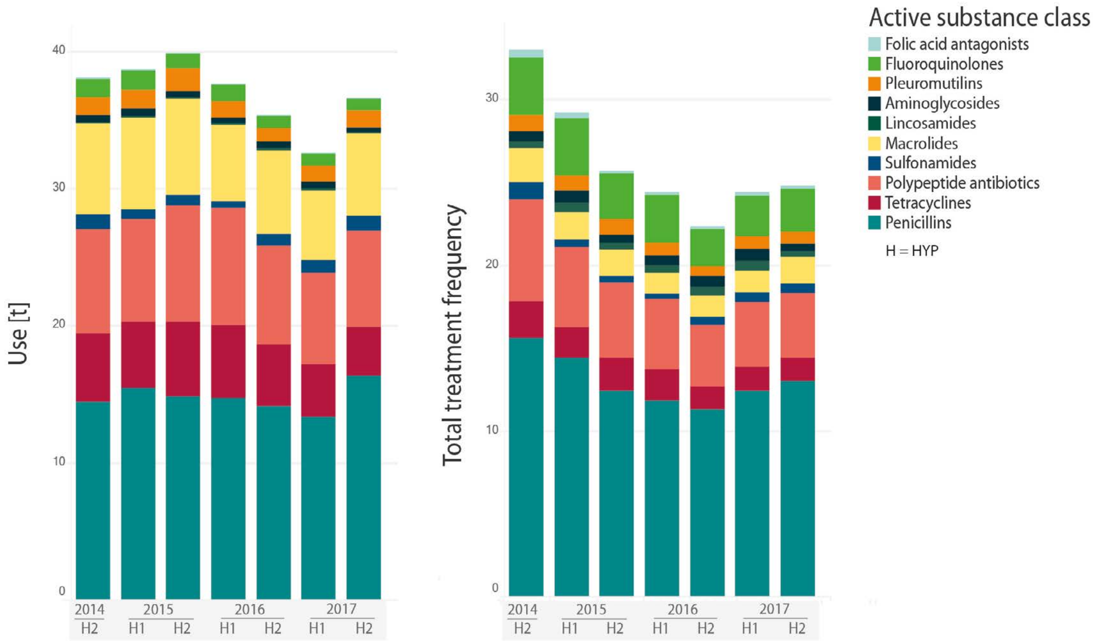
Data Sheet

Fattening turkeys

Consumed quantities

The total used quantity for fattening turkeys remained relatively stable between 33 t and 40 t during the period under observation. In HYP 14/2 penicillins accounted for the largest share, 38% (14.5 t), in total used quantity for this type of production. This share became even larger, 44.7% (16 t), up to HYP 17/2. The used quantities of tetracyclines fell from 5.0 t (13%) to 3.5 t (10%) over the period under observation. Other important active substance classes were macrolides with 6.0 t and polypeptide antibiotics with 7.0 t used quantity in HYP 17/2.

No uniform trend can be observed for these active substance classes; their share of the total used quantity remained relatively steady at around 17% (macrolides) and 19-23% (polypeptide antibiotics). Turkeys accounted for the largest share (around 50%) of the used quantity of fluoroquinolones in all types of production. Within the type of production fattening turkeys, it fell however from 3.4% (HYP 14/2) to 2.4% (HYP 17/2).



Developments in type of production fattening turkeys over 7 half-yearly periods
Left: Development of used quantity for each active substance class
Right: Development of total treatment frequency for each active substance class

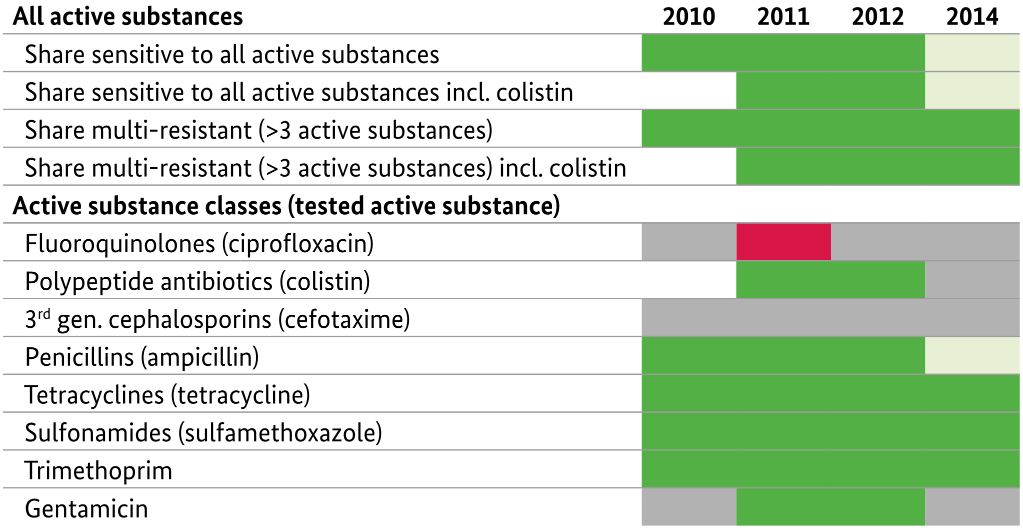
Treatment frequency

There has been a statistically significant decrease in treatment frequency for fattening turkeys since 2014. This decline was observed on small, medium and large farms, with the treatment frequency remaining on a higher lever on large farms than on medium and small ones. **Treatment frequency for each active substance class:** The use of penicillins, polypeptide antibiotics, macrolides, tetracyclines and fluoroquinolones is predominant in turkeys. The highest treatment frequencies for each active substance were recorded for penicillins. In the case of fattening turkeys, penicillins were used in at least 50% of farms in all half-yearly periods. In addition, at least 25% of the farms used fluoroquinolones or polypeptide antibiotics in all half-yearly periods and macrolides or tetracyclines in most of the half-yearly periods.

Resistance

Commensal *E. coli*

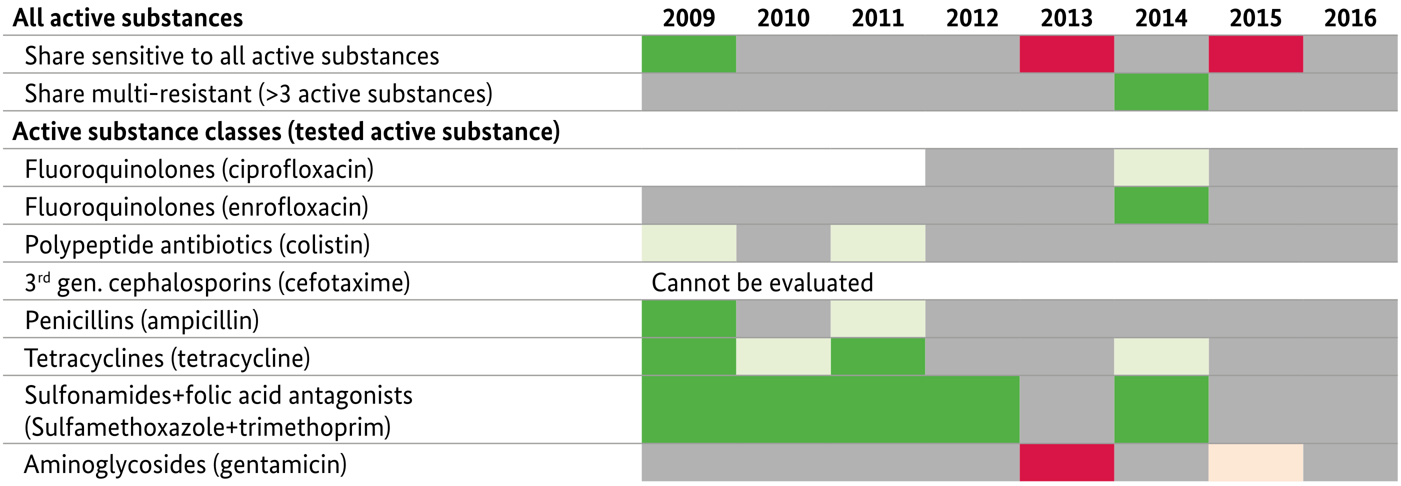
Overall, less resistance was observed in 2016 than in the previous years. Exceptions to this downward trend are the resistance of *E. coli* isolates from the turkey meat food chain to the fluoroquinolone ciprofloxacin, which was higher in 2016 than in 2011 and the unchanged low resistance to cephalosporins.



Comparison of the resistance rates of commensal *E. coli* isolates from turkeys in 2010 – 2014 with those from 2016. Green symbolises a statistically significant positive development (increase in the share of sensitive isolates or decrease in the share of resistant isolates) in isolates from 2016. A significant increase in the resistance rate is shown in red. Grey areas indicate no difference between the respective year and the reference year. Pale green indicates changes at a lower significance level of $p<0.1$. No data were available for colistin for 2010. Therefore, the overall evaluation is presented with (2011-2016) and without colistin (2010-2016).

E. coli, clinical isolates

E. coli isolates from fattening turkeys showed a significant decrease in resistance rates in 2017 compared to previous years for older active substances such as tetracycline and trimethoprim/sulfamethoxazole. For enrofloxacin, a significant change could only be seen compared to 2014. For some active substances (e.g. gentamicin), however, there was a decrease in the number of fully sensitive isolates compared to 2013. The share of fully sensitive isolates rose to 57% by study year 2015 but fell again to 37% by study year 2017. At the same time, the share of isolates that were resistant to more than 3 substances stabilised at around 10%.



Comparison of the resistance rates of *E. coli*, clinical isolates, with the antimicrobials included in the analysis in the years 2009 to 2017. 2017 was chosen as the reference year. The colouring is the same as in the diagram for commensal *E. coli*.

Fattening turkeys in the survey

According to veterinarians

- the treatment frequency usually reflects antibiotic use in fattening turkeys quite accurately (57%), more than in the other types of production
- more vaccines (71%) have been used since the adoption of the 16th AMG Amendment

According to animal keepers

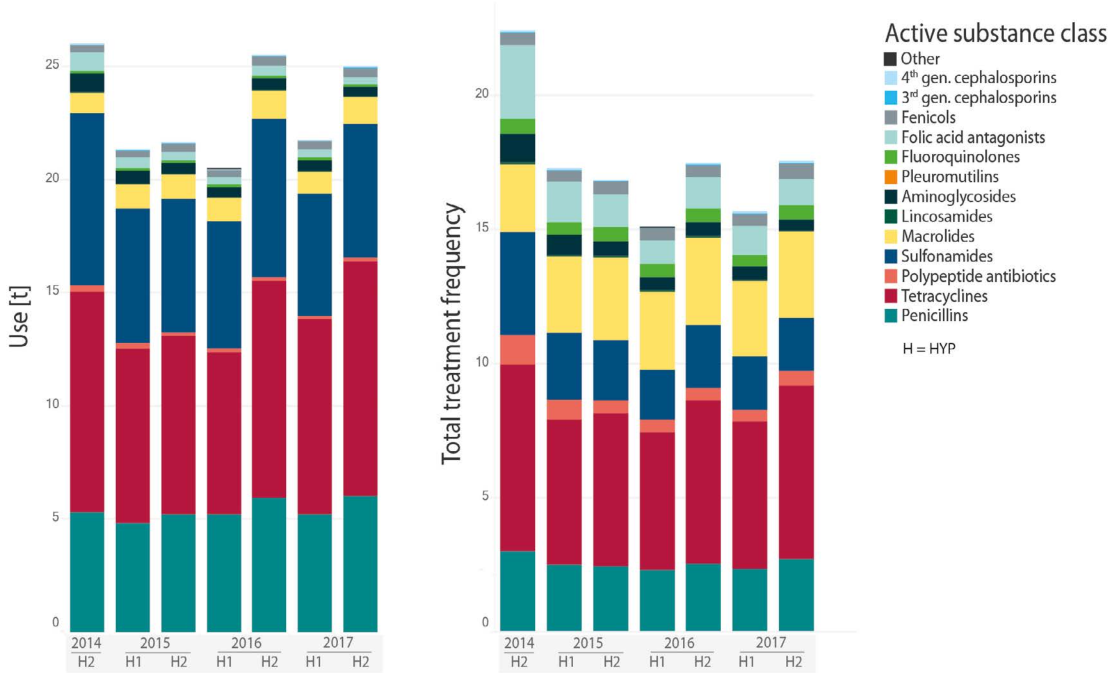
- the use of antibiotics in fattening turkeys has changed particularly markedly: “clearly decreased” (32%) or “tended to decrease” (52%)

Data Sheet

Fattening calves

Consumed quantities

For the type of production fattening calves the total used quantity over the half-yearly periods under observation was relatively constant between 21 t and 26 t. Tetracycline was the most used, followed by sulphonamides and penicillins. Out of these active substance classes, a trend for a quantitative reduction was only recognisable for sulfonamides from 7.6 t in HYP 14/2 to 5.9 t in HYP 17/2. In terms of the total used quantity for fattening calves in the respective half-yearly period, the share of tetracyclines and penicillins rose from HYP 14/2 to HYP 17/2 from 37% (9.7 t) to 41% (10.4 t) and from 20% (5 t) to 24% (6 t) respectively. In the case of the macrolides and Fluoroquinolones, the used quantities increased from HYP 14/2 to HYP 17/2 (for macrolides: from 0.9 t to 1.2 t; for fluoroquinolones: from 0.12 t to 0.13 t) whereas for polypeptide antibiotics there was a clear decrease in used quantities from 0.30 t to 0.16 t. Together, 3rd and 4th generation cephalosporins accounted in a constant manner for less than 0.05% of the total used quantity. For fattening calves the used quantity of long-acting/one-shot preparations increased over the period under observation from 0.6 t to 0.7 t.



Developments in the type of production fattening calves over 7 half-yearly periods
Left: Development of the used quantity for each active substance class
Right: Development of total treatment frequency for each active substance class

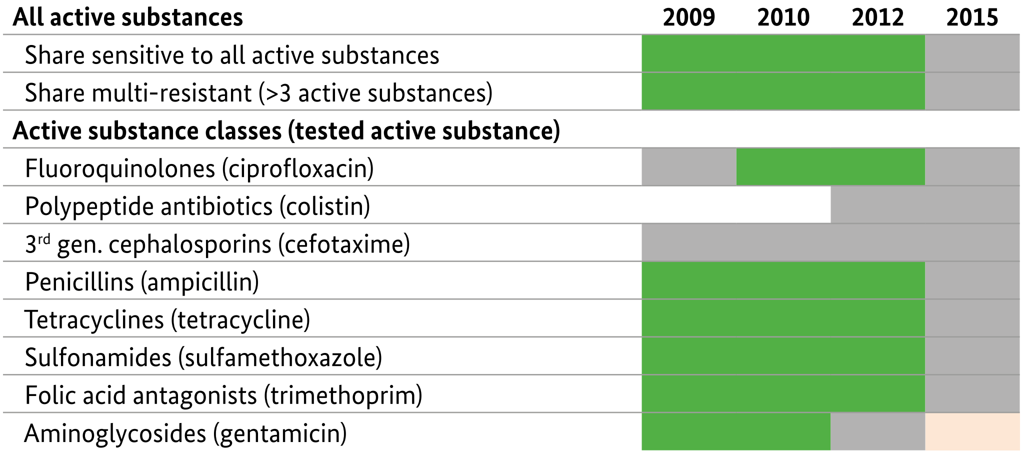
Treatment frequency

There has been a statistically significant decrease in treatment frequency for fattening calves since 2014. This decline was observed on small, medium and large farms, with the treatment frequency remaining on a higher lever on large farms than on medium and small ones. **Treatment frequency for each active substance class:** In fattening calves the use of tetracyclines is predominant, followed by sulfonamides and penicillins. For sulfonamides and folic acid antagonists, a clear decrease in treatment frequency can be observed. The trend was not uniform for tetracyclines. Polypeptide antibiotics also recorded a marked decrease but this only applies to a small number of farms with frequent administration. For this type of production none of the active substance groups was used in at least 50% of the farms, which means that the median for each active substance group was always zero. At least 25% of the farms have used fenicols, fluoroquinolones, macrolides, penicillins or tetracyclines in at least one half-yearly period.

Resistance

Commensal *E. coli* [1]

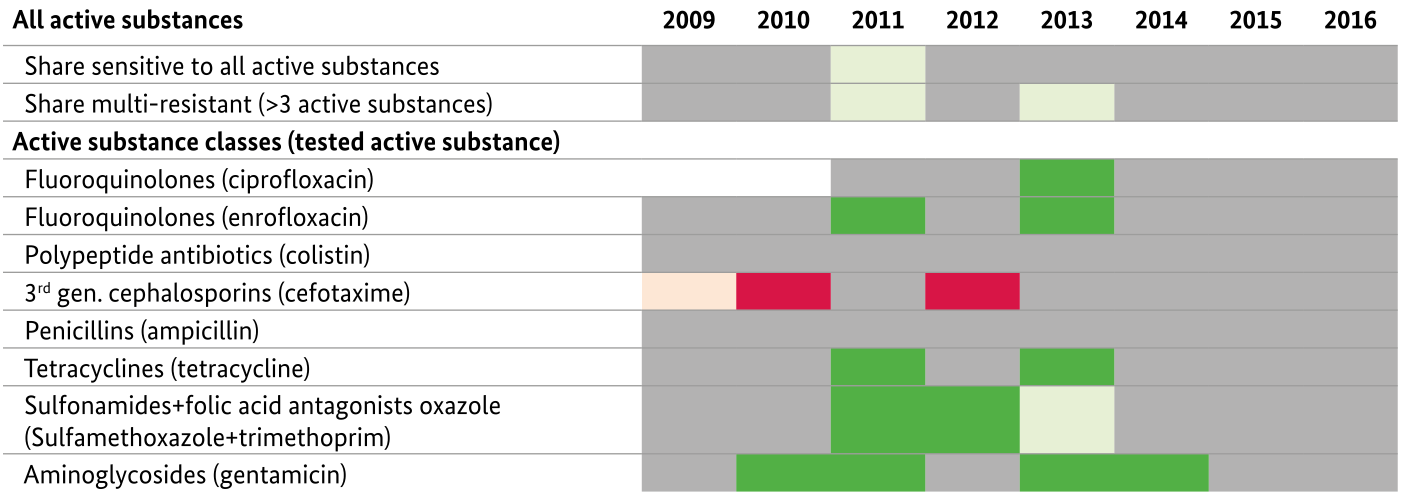
Samples of fattening calves and young cattle showed more marked differences between 2009-2012 and 2017 than between 2015 and 2017. A trend towards lower numbers of multi-resistant isolates was also observed for isolates in this group.



Comparison of the resistance rates of commensal *E. coli* isolates from calves/young cattle with the antimicrobials included in the analysis in 2009, 2010, 2012 and 2015 with those from 2017. Green symbolises a statistically significant positive development (increase in the share of sensitive isolates and a decrease in the share of resistant isolates) in isolates from 2017. A significant increase in the resistance rate is shown in red. Grey areas indicate no difference between the respective year and the reference year. Pale green or pale red indicates changes at a significance level of p<0.1.

E. coli, clinical isolates [2]

Clinical *E. coli* isolates from fattening calves showed a significant increase in resistance to the active substance cefotaxim in 2017 compared to 2010 and 2012. Compared to enrofloxacin, trimethoprim/sulfamethoxazole, tetracycline and gentamicin there were significant decreases in resistance rates. From 2015 onwards, no significant changes could be observed any longer.



Comparison of the resistance rates of pathogenic *E. coli* with the antibiotics included in the analysis in the years 2009 to 2017.
2017 was chosen as the reference year. The same colouring is used here as in the chart for commensal *E. coli*.

Fattening calves in the survey

According to veterinarians

- the calculated treatment frequency does not reflect antibiotic use very accurately because stabling is done irregularly (56%)

According to livestock keepers

- the way antibiotics are used in fattening calves has changed. Different active substances are used and there are more treatments of individual animals (30% respectively)
- the most frequently used measure for fattening calves was “improvement of husbandry/climate/rebuild” (56%), followed by improvements in feed and hygiene (42% each)

1 Data on resistance in fattening calves and young cattle up to one year are collected in accordance with the Commission Implementing Decision 2013/652/EU. These considered populations. Hence they partly concern the group of cattle up to 8 months and partly the group of cattle over 8 months.

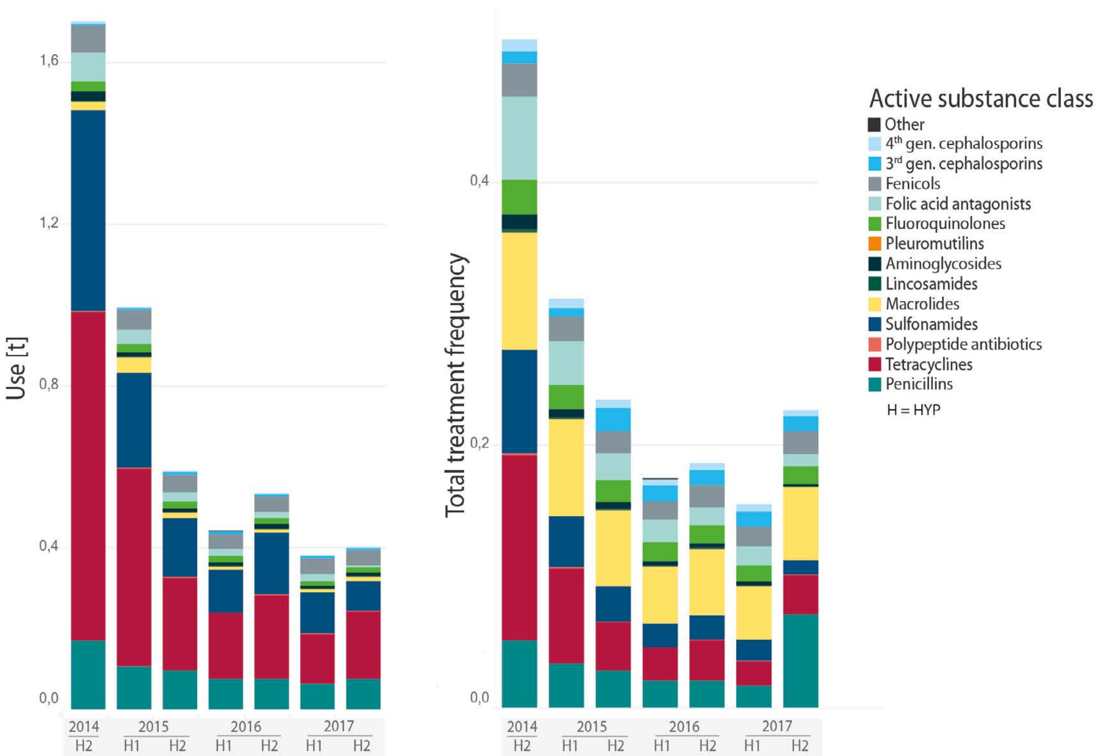
2 Isolates from calves have been included in the evaluation from study year 2009. Isolates from young cattle (up to 8 months) have been recorded since study year 2012 and have been included in the calculations since then.

Data Sheet

Fattening cattle

Consumed quantities

A comparison of total used quantity in the six types of production revealed the lowest level of antibiotics (less than 1 t per half-yearly period) was used in fattening cattle except for HYP 14/2. Tetracyclines made up the largest share, 33%-49%, of the total used quantities in the individual half-yearly periods. The quantity of tetracyclines fell from 0.8 t in HYP 14/2 to 0.2 t in HYP 17/2. Other active substance groups with high shares of used quantities were sulfonamides, followed by penicillins. Their used quantities also fell from 0.5 t to 0.1 t and from 0.2 t to 0.08 t between HYP 14/2 and HYP 17/2. The used quantities of 4th generation cephalosporins, fluoroquinolones and macrolides likewise fell during this period. In the case of 3rd generation cephalosporins, however, no such decline was observed. The share of fluoroquinolones, macrolides and cephalosporins in the total used quantity for fattening cattle increased. The use of long-acting/one-shot preparations for fattening cattle accounted for 0.1 t respectively and did not change between HYP 14/2 and HYP 17/2.



Developments in the type of production fattening cattle over 7 half-yearly periods
Left: Development of the used quantity for each active substance class
Right: Development of total treatment frequency for each active substance class

Treatment frequency

There has been a statistically significant decrease in the treatment frequency in fattening cattle since 2014. This decline was observed on small, medium and large farms, with the treatment frequency remaining on a higher level on large farms than on small and medium ones. Overall, the treatment frequencies were on a low level. For fattening cattle the share of farms that do not use antibiotics was 52.1% and was, therefore, the highest among the types of production considered. **Treatment frequencies for each active substance class:** For fattening cattle, only penicillins were used in at least 5% of the farms in each half-yearly period. In addition, in individual half-yearly periods, at least 5% of the farms were exposed to fenicols, fluoroquinolones or macrolides.

Resistance

Commensal *E. coli* / *E. coli*, clinical isolates:
Resistance data are collected for cattle in the group of fattening calves and young cattle up to the age of 1 year pursuant to the Commission Implementing Decision 2013/652/EU. In contrast to fattening calves, fattening cattle are not slaughtered between the ages of 8 to 12 months, but only at the age of 18 to 24 months (or older). Studies show that there are considerable differences in the use of antibiotics between fattening cattle and fattening calves in the same age groups[1]. Therefore, no data on commensal *E. coli* are presented here for this type of production. No specific resistance data for the clinical *E. coli* isolates for this type of production are available either.

Fattening cattle in the survey

According to veterinarians
- the treatment frequency does not fully reflect the use of antibiotics as administration is undertaken in the upstream holding (63%)
- the prescription of combination products for fattening cattle has decreased (55%) and delayed prescription often takes place (46%)
- more anti-inflammatory drugs are used (55%)

According to animal keepers
- the use of antibiotics has "clearly fallen" for 8% and "tended to fall" for 28% of the respondents for fattening cattle, for 62% it has remained unchanged
- in most cases (68%), no other veterinary medicinal products are used instead of antibiotics
- many fattening cattle keepers feel unsure about possible consequences of exceeding the indicators ("fully correct" 44%; "correct" 25%; "quite correct" 8%)

1 Niedersächsisches Ministerium für Ernährung, Landwirtschaft, Verbraucherschutz und Landesentwicklung / Niedersächsisches Landesamt für Verbraucherschutz und Lebensmittelsicherheit (2011): Bericht über den Antibiotikaeinsatz in der landwirtschaftlichen Nutztierhaltung in Niedersachsen (Ministry of Rural Affair, Food, Agriculture, Consumer Protection and Rural Development of the Land of Lower Saxony/ *Land* Office for Consumer Protection and Food Safety 2011 Report on Antibiotic Use in Livestock Farming in Lower Saxony.)

4. Evaluation of Goal Attainment

The evaluation of the effectiveness of the measures pursuant to sections 58a to 58d of the 16th AMG Amendment focuses on the assessment of the development of the use of antibiotics (Goal 1) and the prudent use of antibiotics (Goal 2) for the six types of production governed by the 16th AMG Amendment, and on an analysis of the development of the bacterial resistance situation (Goal 2). Only a general estimation can be undertaken of the question regarding the extent to which Goal 3 has been attained, i.e. whether the instruments introduced by the 16th AMG Amendment also enable the authorities to undertake efficient enforcement.

4.1. Goal 1: To reduce the use of antibiotics in the keeping of fattening animals

The developments in the supplied and used quantities of antibiotics and in treatment frequency outlined in the results for criterion 1 are presented and discussed below.

4.1.1. Development of the supplied quantities of antibiotics pursuant to the DIMDI-Medicinal Products Ordinance and of the used quantities in accordance with the antibiotics database of the *Länder*

As the supplied quantities of antibiotics have been recorded since 2011, it is possible to compare the development of this parameter before and after the introduction of the Antibiotics Minimisation Concept (2014). The decrease in supplied quantities amounted to 467 t or 27.4% in the period from 2011 to 2014 and this decline, 505 t or 40.8%, was far more pronounced in the period from 2014 to 2017. What is particularly noticeable is the major drop of 433 t or 35% in the supplied quantity between 2014 and 2015. This is very probably an effect of the 16th AMG Amendment which came into force in April 2014 and introduced the statutory provisions for an Antibiotics Minimisation Concept. However, it is not possible to prove this connection as the supplied quantities cannot be attributed to the different types of production and it was not possible to record the used quantities for the whole of 2014 because only the data on the used quantities in the second half of 2014 were available for this evaluation. No robust estimation can, therefore, be made as to whether the sharp reduction of 35% in the supplied quantity from 2014 to 2015 is mainly due to a parallel reduction in the used quantities during this period.

The survey of the nationwide quantities of antibiotic active substance classes used for the six types of production described in this evaluation report was carried out for the first time in Germany as a result of a change in the legal situation regarding the use of the data recorded during the implementation of the 16th AMG Amendment. The amendment to section 58f AMG was undertaken in July 2017 in the Act on Updating the Provisions for Blood and Tissue Preparations and Amending Other Provisions (*Gesetz zur Fortschreibung der Vorschriften für Blut- und Gewebezubereitungen und zur Änderung anderer Vorschriften* – BlGewVFG). The explicit aim of this amendment was to make the data collected in conjunction with the Antibiotics Minimisation Concept available for the purposes of this evaluation.

The new legal situation meant it was possible, within the framework of this evaluation, to undertake for the first time and on a one-off basis the central anonymised evaluation of the data collected nationwide by the authorities for each type of production on antibiotic use, including the used quantities for each active substance class. As no corresponding data were available for Germany for the period before the entry into force of the 16th AMG Amendment, it was not possible to compare the development of the used quantities with those from the period prior to the introduction of the

Antibiotics Minimisation Concept. The plausibility check of the data carried out before further analysis confirms the high quality of the data. 6% of the data were excluded.

The total used quantity of antibiotic active substances fell by a total of 94 t (31.6%) from 298 t to 204 t from HYP 14/2 to HYP 17/2. This reduction was not continuous because the total quantity increased by up to 2% in both HYP 16/2 and HYP 17/1.

A comparison of the annual supplied quantities with the development of the total annual used quantity reveals the following development in the period 2015 to 2017. Whereas the total used quantity fell by 71 t (14.9%) from 475 t in 2015 to 404 t in 2017, the supplied quantity decreased by 72 t (9.0%) from 805 t to 733 t. Thus, the decrease in the total used quantity in tonnes corresponded almost exactly to the reduction in supplied quantities over the same three-year period. This suggests that the reduction in antibiotic use in the types of production covered by the 16th AMG Amendment contributed more to the reduction in the supplied quantity than the use of antibiotics in those animal species and types of production not governed by the 16th AMG Amendment.

A differentiated examination of the used quantities determined for the various types of production demonstrates the scale of the reduction in antibiotic use for the individual types of production listed in the 16th AMG Amendment:

→ Between HYP 14/2 and HYP 17/2 by far the largest reduction in the used quantity was recorded for **fattening pigs and fattening piglets**. The used quantity for fattening piglets fell by 46% from 87.5 t to 47.2 t and that of fattening pigs by 43% from 115.0 t to 65.2 t.

→ In contrast, the used quantities for **fattening calves, fattening chickens and fattening turkeys** were almost unchanged over the same period (fattening turkeys -4%, fattening chickens -1%, fattening calves -4%). In the case of fattening cattle there was a large percentage reduction of 76%, but the quantities used were very low – 1.7 t in HYP 14/2 and 0.4 t in HYP 17/2 respectively.

4.1.2. Development of nationwide indicators and treatment frequencies

The development of the nationwide indicators published every six months by BVL in the Federal Gazette and the treatment frequencies per farm over time determined in the course of this evaluation also revealed differences between the different types of production.

A parallel development of treatment frequencies and used quantities can only be observed for fattening cattle, fattening piglets and fattening pigs; for the other types of production (fattening calves, fattening chickens, fattening turkeys) a decrease in treatment frequency was not associated with a parallel decrease in used quantities.

Fattening piglets and fattening pigs: Both the reduction in the nationwide indicators and the reduction in treatment frequency per farm were continuous. The reduction in treatment frequencies over the half-yearly periods was particularly evident in the case of fattening piglets and fattening pigs for those farms that were in treatment frequency categories 2 and 3 (i.e. above indicators 1 and 2). The development in treatment frequency and the used quantities therefore met, for these two types of production, the expectation that the Antibiotics Minimisation Concept introduced by the 16th AMG Amendment would permanently lower antibiotic use.

Fattening chickens and fattening turkeys: In the first three (fattening chickens) and five (fattening turkeys) half-yearly periods, farms with fattening chickens and fattening turkeys also recorded an initial decline in the nationwide indicators and a decrease in treatment frequency. However, in the later recording periods, a renewed increase in the nationwide indicators and, in particular, in the median of the treatment frequency for fattening chickens, was observed. The observed development of the treatment frequency for farms with fattening chickens and fattening turkeys did not, therefore, meet the expectation that the Antibiotics Minimisation Concept would result in a lasting and continuing gradual fall in the nationwide indicators and treatment frequency per farm over time.

There may only be relatively minor differences with regard to the practice of using antibiotic veterinary medicinal products to treat fattening turkeys and in particular fattening chickens on livestock farms. This assumption is based on the following results that highlight the particularities of farms with fattening chickens:

- In the case of farms with fattening chickens which were above indicator 2 for several half-yearly periods, this was not linked to the size of farm and thus differed fundamentally from the distribution for the other types of production in which large farms in particular were above indicator 2 for very long periods.
- The development over time of the mean treatment frequency was comparable in all three treatment frequency categories for farms with fattening chickens.
- Compared to farms with other types of production, farms with fattening chickens are considerably more likely to switch back to a better treatment frequency category after exceeding indicator 2.

It is possible that the Antibiotics Minimisation Concept may not have developed its full effect in the production of fattening poultry because the production methods in the fattening poultry sector are relatively homogeneous. This seemingly leads to a relatively similar practice in antibiotic use on the majority of farms. Further data collection and evaluation would be necessary to explore this issue in more depth.

Fattening calves and fattening cattle: In the case of fattening calves, the nationwide indicators and the treatment frequency per farm were halved in the first two half-yearly periods and then stagnated at the level reached. In fattening cattle, the indicators and treatment frequencies were close to zero. For both types of production, after an initial decline, no change in the treatment frequency was observed on those farms that were above indicator 2 in the treatment frequency category.

Particularities of **fattening calves**: In the case of fattening calves, the share of farms that were above indicator 2 over all seven half-yearly periods was higher than in the other production groups and mainly comprised large farms. More extensive studies are needed to clarify whether there is a special “subgroup” of farms with a high treatment frequency (coinciding with large farm size) for this type of production. This is because findings on this issue cannot be extracted from the data available for this evaluation. Already shortly after the 16th AMG Amendment came into force, experts were discussing whether the type of production “fattening calves up to the age of eight months” defined in the 16th AMG Amendment was sufficiently differentiated. The available results indicate that an effective benchmarking along the lines of the Antibiotics Minimisation Concept introduced by the 16th AMG Amendment for this type of production is indeed hampered by the fact that, the legally regulated definition of the type of production “fattening calves”, results in farms being grouped together that differ greatly in terms of age, origin, keeping, management and antibiotic treatment of their animals.

Particularities of **fattening cattle**: Antibiotic treatments in fattening cattle were rare. Since less than a quarter of the farms had administered treatments in one half-yearly period, the nationwide indicator 2 has consistently had a value of zero since HYP 15/1. A fall below the nationwide indicator 2 was thus only possible for farms that had not carried out antibiotic treatment in a half-yearly period. It was not, therefore, possible to achieve the reduction in treatment frequency targeted by the Antibiotics Minimisation Concept of the 16th AMG Amendment in farms with this type of production using the fixed indicator 2 as an instrument.

Impact of farm size: For all types of production and farms in all size classes, there was a significant reduction in treatment frequency per farm between HYP 14/2 and HYP 17/2 although, as already mentioned, there was a renewed increase in recent recording periods for fattening chickens and fattening turkeys. However, an impact of farm size on the level of treatment frequency is clearly discernible. The higher values for treatment frequency determined for large farms compared to small and medium farms indicate that animals in all types of production on large farms were treated more frequently with antibiotics than animals on smaller farms. Large farms were above indicator 2 over a longer continuous period than medium and small farms. This effect was particularly pronounced on farms with fattening calves.Consequently, farm size and type of production proved to be important influencing factors on the development of treatment frequency.

4.2. Goal 2: To promote prudent antibiotic use in fattening animals to reduce the resistance risk

In order to assess the extent to which Goal 2 was attained, the developments of supplied and used quantities of antibiotics and treatment frequencies for the individual active substances are explained and discussed below. The components that are part of the prudent use of antibiotics in veterinary medicine in Germany are described in the “Guidelines for the Prudent Use of Veterinary Antimicrobial Drugs” of the German Federal Veterinary Surgeons’ Association (*Bundestierärztekammer*). Many of these components cannot be used in this evaluation as indicators for assessing the effects of the 16th AMG Amendment on the prudent use of antibiotics, because the necessary information on the individual cases of disease was not recorded in the context of the Antibiotics Minimisation Concept, e.g. the diagnosis made or the indication for antibiotic treatment.

According to the above-mentioned guidelines, the principle applies that in particular the active substance classes, fluoroquinolones and 3rd and 4th generation cephalosporins, which are of special importance for human medicine, should not be the first-line treatment. This principle is also set out in the relevant documents of the European Medicines Agency (EMA), the World Organisation for Animal Health (OIE) and the World Health Organisation (WHO), which have extended this provision to the active substance classes macrolides and polypeptide antibiotics. The principles of prudent use of antibiotics apply, of course, to all classes of active substances.

The approach adopted by the legislator in the Antibiotics Minimisation Concept involves measuring the reduction in antibiotic use on the basis of the indicator “treatment frequency” without taking into account the quantity and class of the active substance administered. It aims to bring about a quantitative reduction in the use of antibiotic medicinal products in the six types of production. The official justification states: *“The measured value “treatment frequency” should now be established as an indicator of the frequency of use of antibiotics as part of a binding Antibiotics Minimisation Concept, which is set out in more detail in the provisions of sections 58a and 58b”* (Printed document 555/12, p. 24). This means that a reduction in the total number of treatments, i.e. a reduction in the frequency of treatments on farms, should lead to a reduction in the total quantities of antibiotics used, without this resulting in a parallel shift in the choice of active substances towards those that are to be administered at low doses.

On the other hand, it is not a declared goal of the Antibiotics Minimisation Concept introduced by sections 58a to 58d of the 16th AMG Amendment, in addition to reducing the total quantity of antibiotic active substances, to also reduce the use of certain antibiotic active substances or classes of active substances, e.g. the active substances which are critically important for human medicine. In the parliamentary legislative procedure for the 16th AMG Amendment in 2012, the Bundesrat and the Federal Government discussed, amongst other things, the additional introduction of an “active substance-specific factor” in the calculation of a farm’s half-yearly treatment frequency. The idea of adding an "active substance-specific factor" to the calculation formula for treatment frequency was linked to the intention of weighting the classes of active substances used according to their importance for human medicine in order to prevent critically important active substance classes being used more frequently. In the end the legislator decided against this to avoid the new Antibiotics Minimisation Concept becoming overly complex. Nevertheless, the wording of Goal 2 in the 16th AMG Amendment ("To support the prudent and responsible use of antibiotics") expresses the following: It was an important concern of the legislator to ensure that the antibiotics minimisation strategy introduced by the 16th AMG Amendment did not lead to the undesirable consequence of a departure from the individual principles of prudent antibiotic use in favour of a pure quantity reduction. Therefore, the developments in the used quantities of individual active substance classes are examined below and also discussed from the point of view of whether there has been a shift in the spectrum towards the five active substance classes of critical importance for human medicine.

For the component "active substance used" in the prudent administration of antibiotics, data on the type of production were collected for the first time within the framework of the Antibiotics Minimisation Concept. With the aid of these data, the use of the five classes of active substances (fluoroquinolones, 3rd and 4th generation cephalosporins, macrolides and polypeptide antibiotics) in particular was examined in detail on the level of the individual types of production for this evaluation. A detailed analysis was undertaken of the developments of their supplied quantities and, more particularly, of their used quantities, the treatment frequencies for each active substance class and the change in treatment frequency over the course of time. Consequently, it is possible for the first time to evaluate the spectrum of active substances used for the individual types of production and to examine whether and, if so, how the 16th AMG Amendment has affected the choice of active substance for the individual types of production.

4.2.1. Plausibility of used quantities of antibiotics

The chosen procedure for the plausibility check permits the analysis of patterns of use. For polypeptide antibiotics, the plausibility check has provided strong pointers that they are used at far higher doses, particularly in fattening chickens, than the doses specified in the authorisation conditions. This should be seen as an opportunity to critically examine the reasons. The results of the plausibility check of the used quantities based on the information on the type of production treated, the number of animals treated and the duration of action also illustrate the importance of a correct specification of DDDvet values by EMA when, in accordance with the EMA's proposal, the frequency of therapies is to be determined on the basis of used quantities.

4.2.2. Relationship between supplied and used quantities

The share of used quantities of antibiotics, i.e. the quantities of antibiotics actually used in the six types of production covered by the 16th AMG Amendment, in the supplied quantities of antibiotics serves as a benchmark of the total quantities of antibiotics used in veterinary medicine in one year. It varies depending on the class of active substance between 30% and 70%. The active substance classes of 3rd and 4th generation cephalosporins, with shares of only around 2% and 6% respectively, are an exception. In the case of fattening chickens and fattening turkeys, these classes of active substances are not used at all due to the lack of authorisation. Given the very small share of the used quantities of these active substance classes in the respective supplied quantities, it is not possible for the 16th AMG Amendment to secure a significant reduction in the supplied quantities of these active substance classes.

4.2.3. Development of used quantities of antibiotics

The reduction in the used quantities of antibiotics is the result of both the reduced use of the "non-critical" active substances which are administered in large quantities, e.g. penicillins and tetracyclines, and the reduced use of certain critical active substance classes. Whereas macrolides and polypeptide antibiotics have played a significant role in reducing the total used quantity, fluoroquinolones and 3rd and 4th generation cephalosporins have hardly contributed to the reduction.

An examination based on the individual types of production shows that the overall reduction is mainly due to the reduction in the used quantities of individual active substance classes for fattening piglets and fattening pigs. In contrast, the development for fattening chickens, fattening turkeys, fattening calves and fattening cattle did little to reduce usage.

4.2.4. Consideration of used quantities and treatment frequencies by active substance class in the individual types of production

Fattening piglets and fattening pigs: The largest share of the total used quantities of penicillins and tetracyclines was used for fattening piglets and pigs. The average treatment frequency for penicillins and tetracyclines in fattening piglets was reduced by around two days of treatment. In fattening pigs, a reduction of between half a day and one whole day was observed. With regard to the spectrum of active substances used in pigs, the critical five classes of active substances only accounted for approximately 10%. Significant reductions in treatment frequency were achieved for these active substance classes in the case of macrolides and polypeptide antibiotics. In fattening piglets, the treatment frequency for macrolides was reduced by one day of treatment, for polypeptide antibiotics by as much as four days of treatment. For fattening pigs, the treatment frequency for polypeptide antibiotics was reduced by one day of treatment. The share of the five critical classes of active substances in the total used quantity for pigs has not changed significantly over the half-yearly periods, i.e. the reduction in treatment frequency was achieved by lowering the use of all classes of active substances.

Fattening chickens and fattening turkeys: In both fattening chickens and fattening turkeys it is noticeable that in the first half-yearly periods the used quantities remained the same, although treatment frequencies decreased. As was the case for fattening calves, the available data do not permit any reliable statements about the reasons for this divergent development. However, based on the following observations, it can be assumed that changes in the dosage of polypeptide antibiotics in veterinary practice may have played a role in the treatment of these types of production. In fattening chickens, the median of days of drug action for polypeptide antibiotics was usually three days, in fattening turkeys always four days. However, the scattering of the indicated days of drug action reveals a tendency to indicate a lower number of days of drug action. For individual half-yearly periods, a value for the median or the 3rd quartile with one less day of drug action can be observed for fattening chickens and fattening turkeys, i.e. in at least 25% of the farms using polypeptide antibiotics, fewer days of drug action were reported in these half-yearly periods than in other half-yearly periods. This development in the indicated days of drug action and the initially unchanged used quantities of polypeptide antibiotics, coupled with decreasing treatment frequencies for each specific active substance, would seem to indicate that the dose was increased.

Spectrum of active substances in fattening chickens: Fattening chickens account for the largest individual share of used quantities of polypeptide antibiotics. The used quantity of polypeptide antibiotics was still on the rise between HYP 14/2 and HYP 17/2, whereas the treatment frequency fell. With regard to the selection of active substances, about half of the used quantity can be attributed to the critical classes of active substances. Around 40% of the total used quantity is accounted for by polypeptide antibiotics alone in this type of production. The development of used quantities and treatment frequencies differentiated by class of active substance shows that the increase in the nationwide indicators observed for fattening chickens over the last four half-yearly periods can be attributed to increased treatment with a combination of aminoglycosides and lincosamides.

Spectrum of active substances in fattening turkeys: About half of the total used quantity of fluoroquinolones was used in fattening turkeys. They also accounted for the second largest single share of the cons used umed quantities of polypeptide antibiotics. With regard to the selection of active substances, it should be noted that around 40% of the used quantity is allocated to the critical classes of active substances. Over the course of time, there has been no change in the selection of active substances either in the used quantities or in the treatment frequencies, i.e. the use of the critical classes of active substances has not been further intensified in order to reduce the treatment frequency. With penicillins, it is noticeable that the treatment frequency for this specific active substance has been reduced by two treatment days without a corresponding reduction in used quantities. A similar phenomenon was observed with fluoroquinolones with a reduction of one day of treatment. As noted elsewhere, based on the available data it can only be presumed that a shorter treatment duration with higher doses is the reason for this observation.

Fattening cattle: Due to the low treatment frequencies and the small quantities used, it can be assumed in the case of fattening cattle that individual animal treatment was generally undertaken for this type of production. In terms of the active substances used, tetracyclines, penicillins and sulfonamides account for the largest share of the used quantity; the five critical active substance classes make up less than 10%.

Fattening calves: In the case of fattening calves, too, tetracyclines, penicillins and sulfonamides account for the largest share of the used quantity. Here, also, the five critical active substance classes make up less than 10%. Although the decrease in the used quantity and treatment frequency for polypeptide antibiotics is positive, an increase has been documented for the used quantities of fluoroquinolones, macrolides and 3rd and 4th generation cephalosporins. In contrast, the treatment frequencies for these active substance classes have remained the same or have fallen. It is not possible to ascertain what led to this, in individual cases, on the basis of the available data. The development of used quantities and treatment frequencies for fattening calves, in combination with the observations made under Goal 1 for this type of production, suggest that the Antibiotics Minimisation Concept was not able to bring about any change in antibiotic use on some of the farms.

Form of administration long-acting/one-shot preparations: The used quantity of LA/OS preparations in fattening calves, fattening cattle, fattening piglets and fattening pigs (these injectable drugs are not used in fattening chickens or fattening turkeys) remained almost unchanged at approximately 2 t (< 1% of the total used quantity), i.e. there was no shift to these preparations in order to reduce treatment frequency. Since the 16th AMG Amendment came into force, the topic of “days of drug action” has been repeatedly discussed in the context of enforcement, but also between the Federal Government and the Länder. This evaluation has shown that the practical importance of the possible variations for reporting “days of drug action” for LA/OS preparations, which had been deemed to be an important influencing factor on the development of nationwide treatment frequencies per farm, may have been overestimated due to the overall low rate of use of these products.

4.2.5. Impact on the resistance situation

Whether or not a bacterium is sensitive or resistant to an antibiotic depends on a number of factors. An important influencing factor is the use of antibiotics and the associated selection. The following evaluation took into account the fact that the results were based on data from different periods of time and different animal populations. As a result, it is only possible to link the development of treatment frequency and antibiotic quantities to a limited degree to the development of resistance. In addition, it must be assumed that it will take three to five years for the resistance situation in the entire population to change as a consequence of changes in antibiotic use. Against this backdrop, the period of time envisaged for this evaluation is rather short.

Overall, there was a downward trend in the resistance of intestinal pathogens (commensal E. coli), which normally occur in the gut, from the various food chains fattening calves, fattening pigs, fattening chickens and fattening turkeys in the period considered (2009 to 2017). In all four food chains there was a significant increase in the share of isolates sensitive to all antibiotics and a significant decrease in isolates resistant to more than three substances. Resistance to tetracyclines, sulfonamides and folic acid antagonists also declined in all food chains. This shows that the approach chosen, namely the reduction of antibiotic use, does lead overall to the desired goal.

However, there are also differences in the development of resistance between the food chains considered and the different active substance classes. The increase in the share of E. coli resistant to fluoroquinolones in fattening turkeys and *Campylobacter spp.* in several food chains is noticeable. It cannot be explained by the development in the used quantity or treatment frequency with fluoroquinolones after the introduction of the Antibiotics Minimisation Concept. Whether the increase in the supplied quantities of fluoroquinolones between 2011 and 2014 had an impact of this kind cannot be elucidated with the available data.

The share of commensal *E. coli* and *Campylobacter spp.* isolates resistant to at least one active substance in the food chains fattening chickens and fattening turkeys is high and thus corresponds to the comparatively high treatment frequencies for these types of production.In the case of *E. coli* and *Pasteurella multocida* from clinical diseases and Campylobacter spp., the development of resistance only declined in sub-areas, and in some cases it even increased. Why the different use of antibiotics did not have a similar positive effect on the resistance situation of isolates from clinical diseases as it did on commensal *E. coli* cannot be clarified on the basis of the available data.

The inconsistent development of the resistance situation in *Campylobacter spp.* and the bacterial species isolated from clinical diseases demonstrates impressively that the development of resistance is a complex process. It depends not only on the type of production and the class of active substance, but also on the bacterial species.

The inconsistent development of the resistance situation among the different bacterial species likewise shows that it is important not to limit the evaluation of the resistance situation to just one bacterial species but to include both bacterial colonisation of healthy animals and bacterial isolates from diseased animals.

4.3. Goal 3: To facilitate effective task performance by competent authorities, particularly on livestock farms

The legislator has introduced various instruments to enable the competent authorities to effectively perform their tasks pertaining to the enforcement of sections 58a to 58d AMG. These are the parameters “half-yearly treatment frequency per farm” and “nationwide indicators“, the duties of animal keepers to provide information on their livestock keeping, and on their use of medicinal products on the farms, and to submit a written action plan to the competent authority if they are above indicator 2. Furthermore, these instruments likewise include the new powers to issue orders pursuant to sections 58d (3) and (4) AMG, which were introduced for the first time in the 16th AMG Amendment and which the competent authority is empowered to use.

The test routines carried out to check the plausibility of the data in the antibiotics database showed that the information provided by the animal keepers was highly plausible. The good quality of the data reported to the antibiotics database shows that the activities undertaken by the *Länder* to ensure correct notifications by animal keepers have been effective. The successful reduction of used quantities and treatment frequencies described above also suggests that the instruments available to the competent authorities basically enable them to fulfil their tasks.

This opinion was also shared by the target groups interviewed for the purpose of this evaluation. The survey rated as positive the availability of reliable, quantifiable indicators, the associated raising of awareness amongst all the stakeholders and the resulting nationwide comparability of farms across Germany. The respondents considered the measurability of the progressive reduction in use to be motivating, even though implementation and enforcement constituted a major burden.

In the context of this evaluation BMEL cannot conclusively determine whether the available instruments are also suitable for ensuring the effectiveness of official enforcement formulated in Goal 3. The information required for this is not available to BMEL because of the sharing of responsibilities between the Federal Government and the *Länder*. Therefore, from the position of BMEL, only an approximate evaluation of this is possible.

First of all, it should be pointed out that, particularly in the initial phase, the application of the provisions of the 16th AMG Amendment at the *Länder* and district levels led to a major investment and communication burden which is mentioned in the *Länder* contribution to the evaluation of the 16th AMG Amendment. As a result of numerous consultations amongst the competent authorities of the *Länder* and with the federal authorities, especially in the first year after the entry into force of the 16th AMG Amendment, it was generally possible to make good progress in the application of the new provisions and the use of the envisaged instruments. However, the fact is that this situation is still ongoing and the administrative burden for the competent authorities involved in the enforcement of the 16th AMG Amendment is considerable, even after the completion of the initial phase and the putting in place of the necessary organisations and structures. This is outlined in the information available to BMEL, which stems from consultations with representatives of the higher *Länder* authorities on individual issues relating to the enforcement of the 16th AMG Amendment, and also from the presentation in the *Länder* contribution to the evaluation. The administrative burden for the enforcement authorities arises – in a nutshell – from the need to verify that animal keepers comply with the duties imposed on them and that the information they provide is correct, complete and plausible, and from the need to advise animal keepers on the fulfilment of their duties where necessary. In the course of the survey, the animal keepers confirmed the ongoing need for advice in conjunction with the fulfilment of their duties even though the competent authorities appear to be adopting a risk-based and pragmatic approach in the opinion of the respondents.

Both the *Länder* authorities (see *Länder* Report, page 16) and the animal keepers and veterinarians interviewed in the context of this evaluation have, therefore, been putting together proposals and information on possible changes to individual components of the Antibiotics Minimisation Concept since 2014 with a view to increasing the effectiveness of the administrative processes.

In addition, the *Länder* pointed out that conceptual changes in medicinal product law would not be sufficient to secure a further reduction of antibiotic use and that other areas of legislation that have a significant impact on animal health, should also be included in order to counter the spread of resistance by means of a holistic improvement in animal health. In their view, the upstream production areas (e.g. piglet producers, livestock traders) should also be included in order to exert an influence on animal health and, by extension, on the use of antibiotics.

These considerations reflect the desire of the authorities and animal keepers involved to reduce the burden, to increase efficiency and to pursue a comprehensive approach to improving animal health. They are not the subject of this report but should be addressed in future discussions on the possible need for legislative action.

4.4. Conclusions

4.4.1. Fundamental goal attainment

The reduction in the use of antibiotics, Goal 1 of the 16th AMG Amendment, was achieved in all six types of production. The Antibiotics Minimisation Concept introduced by the 16th AMG Amendment has thus proven itself to be fundamentally effective in reducing antibiotic use. This view is also shared by the *Länder*.

The one-off, particularly strong reduction in the supplied quantity in the year in which the Antibiotics Minimisation Concept was introduced (2014), was followed by a further drop in the supplied and used quantities of antibiotics and in treatment frequencies in the period up to and including 2017. The types of production covered by the 16th AMG amendment contributed to a greater degree to the reduction in the supplied quantity of antibiotics than the other animal species and types of production that are not governed by the Antibiotics Minimisation Concept of the 16th AMG amendment. However, the reduction successes for the different types of production are very different.

The prudent use of antibiotics mentioned in Goal 2 could also be proven, as far as this was possible on the systematic basis of the 16th AMG amendment for this context. The reduction in antibiotic use resulting from the Antibiotics Minimisation Concept introduced by the 16th AMG Amendment was not associated with any problematic shifts in the spectrum of active substance classes towards the increased use of what are known as "critical active substance classes" (fluoroquinolones, 3rd /4th generation cephalosporins, macrolides, polypeptide antibiotics) that are to be administered at low doses. The evaluation determined that the spectrum of active substance classes remained constant for the six types of production over the seven half-yearly periods observed.

The data on the resistance situation indicate that the reduced and prudent use of antibiotics has positive effects on the development of the resistance situation for the six types of production. This conclusion is subject to the reservation that risk management measures to improve a nationwide resistance situation are not generally associated with recognisable short-term effects but normally only manifest recognisable effects (e.g. change in the resistance rate of a specific pathogen in a food chain) after three years at the earliest.

In the overall evaluation, the observation can be made that, based on the findings on the prudent use of antibiotics and the development of the resistance situation in Goal 2, the desired improvements linked to this goal could be achieved, too. The parameter "treatment frequency per farm" is a suitable indicator for the benchmarking in the 16th AMG Amendment.

4.4.2. Differentiated consideration by type of production

The strongest effects with regard to reducing the used quantities and the treatment frequency per farm were recorded for farms **with fattening piglets and fattening pigs**. The reduction in the total used quantities of all types of production by 94 t is essentially due to the reduction in the use of pencillins and tetracyclines by 64 t for fattening piglets and fattening pigs. For these types of production, there was also a correlation between decreasing treatment frequencies per farm and the fall in used quantities over all seven half-yearly periods. With regard to the spectrum of active substances, critical classes of active substances are only used to a limited extent for these types of production.

For farms with **fattening chickens or fattening turkeys**, decreasing treatment frequencies in the first three respectively five observations periods contrasted with no decrease in used quantities. The observed development of the treatment frequency for farms with fattening chickens and fattening turkeys did not, therefore, meet the expectation linked to the Antibiotics Minimisation Concept. The reasons for this cannot be determined from the available data and require further elucidation. The available data indicate that the treatment of fattening turkeys and fattening chickens may have been carried out at higher doses coupled with shorter treatment duration. In addition, it may be that the structure and management of farms in this sector are largely homogeneous and only differ marginally from each other when it comes to antibiotic use, too.

With regard to the spectrum of active substances for these two types of production, it can be observed that approximately half of the quantity of active substances used can be attributed to the critical active substance classes. It can be assumed that polypeptide antibiotics are administered at considerably higher doses than envisaged in the authorisation conditions, particularly in the case of fattening chickens. Whether this practice violates the principles of prudent antibiotic use cannot be determined on the basis of the available data.

The high resistance rates of isolates from the food chains fattening chickens and fattening turkeys correspond to the high treatment frequencies identified for these types of production. In contrast, the increase in the share of E. coli resistant to fluoroquinolones in fattening turkeys cannot be explained by the development of the used quantity of fluoroquinolones or the treatment frequency with fluoroquinolones. It is not possible to clarify, on the basis of the available data, whether the observed increase in the supplied quantities of fluoroquinolones between 2011 and 2014 led to this rise.

The Antibiotics Minimisation Concept introduced by the 16th AMG Amendment did not significantly reduce antibiotic use on farms with **fattening calves or fattening cattle**. There are various reasons for this. The type of production **fattening calves**, which includes “fattening calves up to eight months”, is probably too heterogeneous to allow it to correspond to the existing specialisation and diversity in calf husbandry. In this context, the *Länder* report mentions the specialised weanling breeding farms, and the evaluated data also indicate that there could be a sub-group of farms with fattening calves that should be considered separately. In the opinion of the *Länder*, the age of calves on weaning, which may vary considerable depending on the production method, could furthermore play a role as it is only from that time onwards that fattening calves are governed by the provisions of the Antibiotics Minimisation Concept. In the case of the type of production **fattening cattle**, antibiotic administrations were rather sporadic and on a comparatively small scale. Consequently, the minimisation strategy introduced by of the 16th AMG Amendment was not able to trigger pronounced and systematic reduction effects here.

Apart from the above-mentioned pointers, no other factors can be derived from the data available for this evaluation that could explain the differences between the types of production. Further analyses of possible causes presuppose the collection of supplementary data and the admissibility of their use for nationwide evaluations.

With regard to the instrument of nationwide indicators, the clearly distinguishable developments in the evolution of nationwide indicators for the various types of production confirmed that the approach adopted by the legislator in the 16th AMG Amendment, which involved calculating nationwide indicators separately for each type of production, is a good approach.

4.4.3. Further findings

The unique opportunity to centrally evaluate the anonymised data reported as part of the evaluation of the Antibiotics Minimisation Concept, has generated several new findings, particularly regarding the major differences between the individual types of production in terms of the development of the total used quantities, the used quantities for each active substance and the treatment frequencies. For the first time, it is now possible for Germany to make statements on the scale and details of antibiotic use in types of production with a high production volume based on data collected by the authorities. In this context, it may also be possible to identify correlations between the use of antibiotics and other factors, e.g. farm size or the classification of a farm in a treatment frequency category. For all types of production, the average treatment frequency per farm and the share of farms in treatment frequency category 3 (above indicator 2) also increased with the size of the farms.

Furthermore, the data indicate that the reduction in the number of days of treatment also observed by the *Länder* is at least partly accompanied by an increase in the dose administered. However, whether this is in line with or contrary to the principles of prudent use of antibiotics cannot be assessed on the basis of the available data.

The practical significance of the possible variations in the indication of what are known as “days of drug action” in LA/OS preparation rates, which up to now had been seen as a significant influencing factor on the development of the nationwide treatment frequencies per farm, has possibly been overestimated so far due to the overall low rate of use of these products.

On the basis of their findings on the ground, the *Länder* have come to the conclusion that in order to achieve a holistic improvement in animal health, which should be the basis for a further reduction in antibiotic use, other legal areas should also be included in any deliberations on conceptual changes.

A further development of the new findings presupposes that the legislator will create a legal situation which will, in future, permit the repeated central evaluation of the data collected on the administration of antibiotics to animals.

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List of annexes

1. Fragestellungen zum Wirkungsmodell, Befragung Tierhalter und Tierärzte (Questions about the impact model, survey of animal keepers and veterinarians)

2. Bericht der Arbeitsgruppe Antibiotikaresistenz von BfR und BVL (AG ABR) zu Themenkomplex 1: Entwicklung der Antibiotikaabgabe- und -verbrauchsmengen sowie der Therapiehäufigkeit (Report of the Working Group Antimicrobial Resistance of BfR and BVL) (AG ABR) on thematic area 1: Development of supplied and used quantities of antibiotics and treatment frequency)

3. Bericht der AG ABR zu Themenkomplex 2: Entwicklung der Antibiotikaresistenz bei Tieren; Teil 1: Kommensale *E. coli* und *Campylobacter spp.* (Report of AG ABR on thematic area 2: Development of antibiotic resistance in animals, Part 1: Commensal *E. coli* and *Campylobacter spp.*)

4. Bericht der AG ABR zu Themenkomplex 2: Entwicklung der Antibiotikaresistenz bei Tieren; Teil 2: Klinische Isolate *E. coli* und *Pasteurella multocida* (Report of the AG ABR on thematic area 2: Development of antibiotic resistance in animals, Part 2: Clinical isolates *E. coli* and *Pasteurella multocida*)

5. Bericht der AG ABR zu Themenkomplex 3: Beziehung zwischen der Entwicklung der Abgabemengen, der Verbrauchsmengen und der Therapiehäufigkeit und der Resistenzentwicklung in den betrachteten Lebensmittelketten (Report of AG ABR on thematic area 3: Relationship between the development of supplied quantities, used quantities and treatment frequency and resistance development in the food chains considered)

6. Bericht zur Erfahrung der *Länder* der AG TAM (Report on the experience of the *Länder* of AG TAM)

The above-listed annexes (in German) can be downloaded from the BMEL homepage via the following link **www.bmel.de/Evaluierung16-AMG-Novelle**.

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