



Belgian Veterinary Surveillance of Antimicrobial Consumption

National consumption report

2011

Summary

This third BelVetSAC report, covers the results of the data collection surveillance of veterinary antimicrobial consumption in Belgium in the year 2011. Data consist of all veterinary antimicrobials sold to a veterinarian or pharmacist in Belgium and of antimicrobial premixes incorporated in medicated feed intended to be used in Belgium for the year 2011. It includes thus consumption data for farm animals as well as companion animals. The denominator for animal production was the biomass (in kg) calculated as the sum of the amount of beef, pork and poultry meat produced in 2011, plus the number of dairy cattle present in Belgium times 500 kg of metabolic weight per head.

The overall consumption of antimicrobials in veterinary medicine in total tons of active substance (antimicrobial pharmaceuticals + antimicrobial premixes) is almost equal to 2010 (decrease of 0,1%). This total number is the result of a decrease in the use of antimicrobial premixes of 3,9% and an increase in the use of antimicrobial pharmaceuticals of 0,9%. This result is a confirmation of the status quo seen since 2008 in the total consumption of antimicrobials in veterinary medicine. The reduction in the use of antimicrobial premixes is a positive trend. After 3 consecutive years of increase this is the first year that a mild reduction is observed. This probably indicates that the shift in use between pharmaceuticals and premixes which was observed in the previous years has likely stopped. When looking at the antimicrobial use in function of the biomass produced in Belgium in 2011 a small increase (0,9%) is observed. This is the first year since data are collected (2007) that an increase in antimicrobial consumption per kg biomass produced is seen. This increase is entirely due to the increased use of antimicrobial pharmaceuticals per kg biomass (+1,8%), whereas the antimicrobial premixes used per kg biomass produced reduced with 3,0%.

As in the previous years the 3 most applied antimicrobial classes are the penicillines (88 tons, 29.3%) followed by the sulphonamides and trimethoprim (85 tons, 28.4%) and the tetracyclines (72 tons, 24.2%). Yet both the use of sulphonamides and trimethoprim and tetracyclines was reduced in comparison to 2010 (-4.5% and -1.9% respectively) whereas the use of penicillins keeps on increasing (+9.7% in comparison to 2010) and therefore has become the most used group of antimicrobials in veterinary medicine in 2011. Unfortunately also the use of critically important antimicrobials according to the WHO such as cephalosporins, quinolones and macrolides increased with 8,8%; 2,8% and 16,3% respectively

In comparison to several other European countries with comparable animal production systems this indicates a high use of antimicrobials in veterinary medicine in Belgium. For many years the antimicrobial consumption per kg biomass in Belgium was lower than for The Netherlands whereas in 2011 a remarkably higher level than the Netherlands is observed since large reductions in used antimicrobials are realized in The Netherlands and not yet in Belgium.

These results reemphasize the need for vigorous actions directed to all stakeholders, towards a reduced use of antimicrobials. Since the first of January 2012 the Knowledge Center on Antimicrobial Consumption and Resistance in Animals in Belgium (AMCRA) has become fully operational and is currently working on numerous advises and actions, going from sensibilisation over the concept of improved and detailed data collection at the level of the veterinarian and the end user for food producing animals to proposals of guidelines for prudent and reduced antimicrobial use. All these measures and advises have to guide the whole veterinary sector towards a rational reduction of the antimicrobial use in animals. From 2013 onwards these advises could start to result in real changes which then should also become visible in the data recorded in BelVetSac.

Samenvatting

Dit derde BelVetSAC rapport omvat de resultaten van het gebruik van antimicrobiële middelen bij dieren in België in 2011. De gegevens omvatten alle antimicrobiële middelen die werden verkocht aan een apotheker of dierenarts in België (=antimicrobiële farmaceutica) evenals de antimicrobiële voormengsels die via gemedicineerd diervoeder worden toegediend. Het betreft dus data over het gebruik van antimicrobiële middelen bij zowel landbouwhuisdieren als gezelschapsdieren. Om het gebruik in verhouding tot het aantal aanwezige dieren te kunnen plaatsen wordt als noemer de biomassa berekend als de som van de geproduceerde kilogrammen varkens-, pluimvee- en rundveevlees in België in 2011 aangevuld met het aantal aanwezige melkkoeien vermenigvuldigd met hun metabool gewicht (500 kg/stuk).

De totale consumptie van antibiotica in de diergeneeskunde, uitgedrukt in ton actieve substantie, is zo goed als hetzelfde gebleven als in 2010 (daling van 0.1%). Dit totaal is het resultaat van een daling in gebruik van antimicrobiële premixen van 3.9% en een stijging van het gebruik van antimicrobiële farmaceutica van 0.9%. Dit resultaat is een bevestiging van de status quo die wordt gezien sinds 2008 in de totale antibioticum consumptie in de diergeneeskunde in België. Na drie jaar van gestage groei van het aandeel van antimicrobiële premixen in het totaal is er dit jaar voor het eerst een beperkte daling van het gebruik van deze vorm van geneesmiddeltoediening. Dit is een positieve evolutie. Het betekent waarschijnlijk ook dat de uitwisseling in gebruik tussen antimicrobiële farmaceutica en premixen, die in de voorgaande jaren werd opgemerkt, tot een einde is gekomen. Wanneer we het antibioticum gebruik uitzetten in functie van de hoeveelheid geproduceerde biomassa dan zien we voor het eerst sinds het begin van de dataverzameling (2007) een lichte stijging van het gebruik (+0.9%) in verhouding tot het voorgaande jaar. Deze stijging is volledig het gevolg van de stijging in gebruik van antimicrobiële farmaceutica per kg biomassa (+1,8%) terwijl het gebruik van antimicrobiële premixen per kg biomassa gedaald is met 3.0%.

Net zoals in de voorgaande jaren zijn de drie meest gebruikte klassen van antibiotica de penicillines (88 ton, 29.3%) gevolgd door de sulfonamiden en trimethoprim (85 ton, 28.4%) en de tetracyclines (72 ton, 24.2%). Zowel het gebruik van sulphonamiden en trimethoprim en tetracyclines is gedaald in vergelijking met 2010 (-4.5% en -1.9% respectievelijk) terwijl het gebruik van de penicillines blijft stijgen (+9.7% in vergelijking met 2010) waardoor deze klasse nu de meest gebruikte is geworden. Jammer genoeg is ook het gebruik van de door de WHO aangeduide klasse van antibiotica van kritisch belang voor de humane gezondheidszorg zoals de cefalosporines en de quinolonen en macroliden gestegen met respectievelijk 8.8%, 2.8% en 16.3%.

In vergelijking tot verschillende andere Europese landen met een vergelijkbare dierlijke productie betekent dit resultaat een hoog gebruik van antibiotica in de diergeneeskunde in België. Voor verschillende jaren was het gebruik van antibiotica uitgedrukt per kg biomassa in België lager dan in Nederland terwijl in 2011 het gebruik in België aanzienlijk hoger is dan in Nederland als gevolg van de drastische daling in het antibioticumgebruik in Nederland in 2011.

De resultaten herbevestigen de nood aan duidelijke acties naar alle betrokken sectoren om het gebruik van antimicrobiële middelen bij dieren verder te reduceren. Sinds de eerste januari 2012 werd het kenniscentrum **Antimicrobial Consumption and Resistance in Animals** in België (AMCRA) operationeel. Binnen het AMCRA wordt momenteel gewerkt aan verschillende adviezen en acties die gaan van sensibilisatie over een verbeterde dataverzameling op niveau van veehouder en dierenarts tot gidsen voor voorstellen voor voorzichtig en gereduceerd gebruik. Al deze maatregelen en adviezen hebben als doel de hele sector te begeleiden naar een rationele reductie van het antibioticumgebruik bij dieren. Vanaf 2013 zouden deze adviezen zich ook moeten vertalen in concrete veranderingen die eveneens tot uiting zullen komen in de gegevens die in BelVetSac worden geregistreerd.

Résumé

Ce troisième rapport BelVetSAC traite des résultats de la surveillance de la collecte de données en matière de consommation d'antimicrobiens vétérinaires en Belgique durant l'année 2011. Les données se composent de tous les antimicrobiens vétérinaires vendus en Belgique à un vétérinaire ou un pharmacien et des prémélanges antimicrobiens incorporés dans des aliments médicamenteux destinés à être utilisés en Belgique en 2011. Elles comprennent donc les données de consommation pour les animaux d'élevage ainsi que les animaux de compagnie. Le dénominateur pour la production animale était la biomasse (en kg) calculée comme somme de la quantité de viande bovine, de viande porcine et de volaille produite en 2011, ainsi que le nombre de vaches laitières présentes en Belgique multiplié par leur poids métabolique (500 kg/tête).

La consommation totale d'antimicrobiens en médecine vétérinaire en tonnage total de substances actives (antimicrobiens + prémélanges antimicrobiens) est presque égale à celle de 2010 (diminution de 0,1%). Ce nombre total est le résultat d'une diminution de l'utilisation de prémélanges antimicrobiens de 3,9% et d'une augmentation de la consommation d'antimicrobiens de 0,9%. Ce résultat est une confirmation du statu quo observé depuis 2008 dans la consommation totale d'antimicrobiens en médecine vétérinaire. La réduction observée dans la consommation de prémélanges antimicrobiens est une tendance positive. Après 3 années consécutives d'augmentation, c'est la première année pour laquelle on observe une légère réduction. Cela indique probablement que le glissement en matière de consommation, des médicaments aux prémélanges, qui a été observé durant les années précédentes, a probablement cessé. Lorsque l'on observe la consommation d'antimicrobiens en fonction de la biomasse produite en Belgique en 2011, on constate une légère augmentation (0,9%). C'est la première année depuis que les données sont collectées (2007) que l'on observe une augmentation de la consommation d'antimicrobiens par kg de biomasse produite. Cette augmentation est entièrement due à l'augmentation de la consommation de médicaments antimicrobiens par kg de biomasse (+1,8%), tandis que la consommation de prémélanges antimicrobiens per kg de biomasse produite a diminué de 3,0%.

Comme les années précédentes, les 3 classes d'antimicrobiens les plus consommés sont les pénicillines (88 tonnes, 29,3%), suivis des sulfonamides et du triméthoprim (85 tonnes, 28,4%) et des tétracyclines (72 tonnes, 24,2%). Cependant, tant la consommation de sulfonamides que de triméthoprim, ainsi que de tétracyclines a été réduite par rapport à 2010 (respectivement -4.5% et -1.9%) tandis que la consommation de pénicillines continue d'augmenter (+9.7% par rapport à 2010) et celles-ci sont donc devenues le groupe d'antimicrobiens les plus consommés en médecine vétérinaire en 2011. Malheureusement, la consommation d'antimicrobiens d'importance critique selon l'OMS, tels que les

céphalosporines, quinolones et macrolides a augmenté respectivement de 8,8%, 2,8% et de 16,3%.

Par rapport à plusieurs autres pays européens avec des systèmes comparables de production animale, cela indique une consommation élevée d'antimicrobiens en médecine vétérinaire en Belgique. Pendant de nombreuses années, la consommation d'antimicrobiens par kg de biomasse en Belgique était inférieure à celle des Pays-Bas, tandis qu'en 2011, un niveau remarquablement plus élevé que celui des Pays-Bas est observé vu que de grandes réductions dans la consommation d'antimicrobiens sont réalisées aux Pays-Bas et pas encore en Belgique.

Ces résultats rappellent clairement la nécessité d'actions vigoureuses orientées vers les stakeholders et visant à obtenir une diminution de la consommation d'antimicrobiens. Le 1er janvier 2012, le Centre de connaissance sur Antimicrobial Consumption and Resistance in Animals in Belgium (AMCRA) est devenu entièrement opérationnel et travaille actuellement à plusieurs avis et actions, allant de la sensibilisation au concept de collecte de données improvisée et détaillée au niveau du vétérinaire et de l'utilisateur final pour des animaux producteurs de denrées alimentaires à des propositions de lignes directrices pour une consommation prudente et réduite d'antimicrobiens. Toutes ces mesures et avis doivent guider l'ensemble du secteur vétérinaire vers une réduction rationnelle de la consommation d'antimicrobiens chez les animaux. À partir de 2013, ces avis pourraient commencer à se traduire en changements réels qui deviendraient alors également visibles dans les données enregistrées dans BelVetSac.

Preface

Antimicrobials are valuable tools in the preservation of animal health and animal welfare, and must be cherished as they may save lives and prevent animal suffering. Nevertheless, antimicrobial consumption and its link to antimicrobial resistance in humans and animals has become a worldwide point of concern. The World Health Organization has indicated the follow up of antimicrobial resistance as one of the top priorities for the coming years. In 2008, the European Council, through the Council Conclusions on Antimicrobial Resistance called upon the Member States to strengthen surveillance systems and improve data quality antimicrobial resistance and the use of antimicrobial agents within human as well as veterinary medicine. This is repeated in the Council conclusions of 22 June 2012 on the impact of antimicrobial resistance in the human health sector and in the veterinary sector- a “One Health”.

Antimicrobial consumption in animals selects for antimicrobial resistant bacteria in animals, leading to therapy failure in bacterial infections. Yet it might also jeopardize human health through transfer of resistant bacteria or their resistance genes from animals to humans via direct or indirect contact. The magnitude of this risk still needs to be quantified while increasing evidence of resistance transfer between ecosystems is found.

Given the risks both for animal and public health and since it is by far the leading driver for antimicrobial resistance, it is crucial to measure the level of antimicrobial consumption and antimicrobial resistance in animals. This is moreover also required at the European level where consumption data of antimicrobials in veterinary medicine are collected by EMA (European Medicines Agency) in the framework of the ESVAC (European Surveillance of veterinary Antimicrobial Consumption) project. Therefore the data collected and presented in this report also fit into the European commitments of Belgium. This third BelVetSAC report gives an overview of the consumption of antimicrobial in veterinary medicine in Belgium in 2011.

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Materials and Methods

Data collection

1. Antimicrobials for veterinary use

a. Antimicrobial pharmaceuticals

Sales data of all products in all pharmaceutical formulations registered on the Belgian market that contain antimicrobials were aggregated. These data were asked from the 25 wholesaler-distributors that are registered for supplying veterinarians and pharmacies in Belgium with veterinary medicines during the observation period. The distributors are obliged by law (article 12sexies, Law on medicines 25th March 1964; Articles 221 and 228 Royal Decree 14th December 2006 on medicines for human and veterinary use) to keep record of all sales and to deliver these records to the competent authority of the Belgian authority (Federal Agency for Medicines and Health Products) on demand. They were asked by letter dd. 27th July 2011 to upload the required data via a secured web-application (www.belvetsac.ugent.be). The required data consisted of all veterinary antimicrobials sold in the year 2011 to a veterinarian or pharmacist in Belgium. In Belgium, antimicrobial products are only available on prescription or by delivery from the veterinarian. Belgian veterinarians can both use antimicrobial products in their daily practice, or sell them to animal owners (fig. 1). Sales from one wholesaler-distributor to another were excluded from the input data to prevent double counting. A pre-filled list of antimicrobial containing specialties registered and marketed on the Belgian market was provided, together with its market authorization holder and national code (if available), formulation and package form. The wholesaler-distributor only needed to provide the number of packages sold for each product per year.

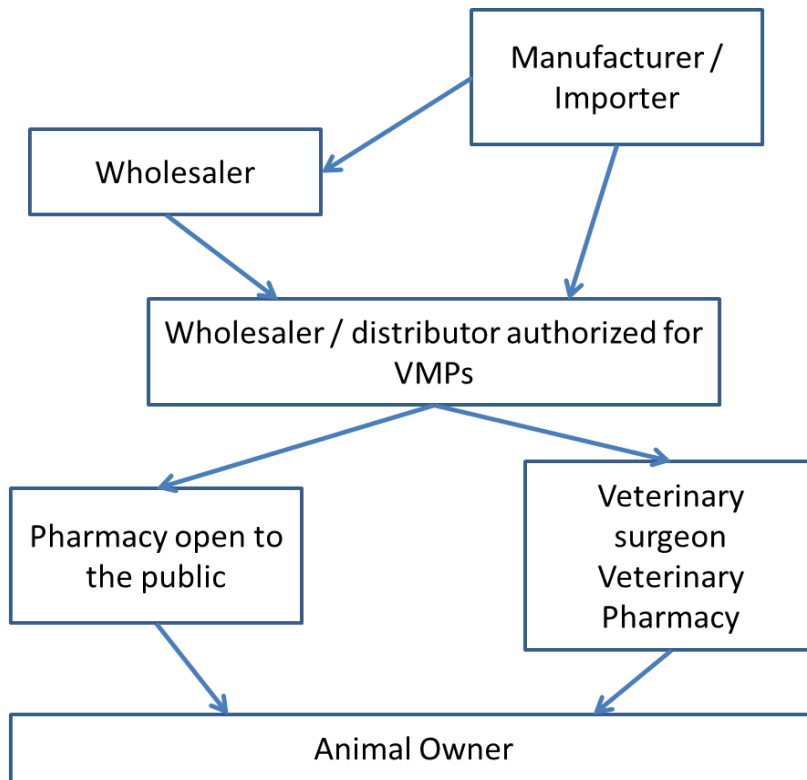


Figure 1. Distribution of Veterinary Medicinal products in Belgium.

b. Antimicrobial premixes

As antimicrobial premixes can be purchased by feed mills directly from the producers or wholesalers (not necessarily through wholesaler-distributors) (fig. 2) also data on medicated feed were to be collected. This was done by contacting all Belgian compound feed producers that are licensed to produce medicated feed (n=59). They received a list of registered and marketed antimicrobial containing premixes. The feed mills were asked by letter dd. 15th February 2012 to upload the required data, on legal basis of article 12sexies Law on medicines 25th March 1964; Article 221 and 228 Royal Decree 14th December 2006 on medicines for human and veterinary use. This data was also submitted via the secure web-application (www.belvetsac.ugent.be). Producers of medicated feed were asked to provide data on the use of antimicrobial containing premixes for the year 2011. Antimicrobial premixes can only be incorporated into medicated feed on prescription of a veterinarian.

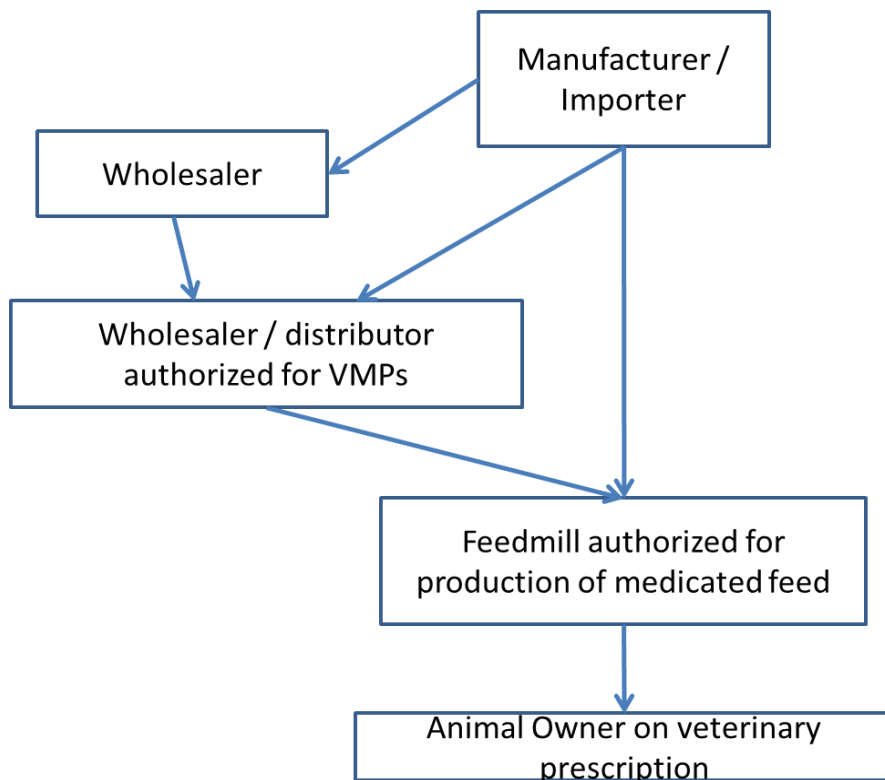


Figure 2. Distribution of Veterinary premises in Belgium.

c. Antimicrobial classes included

Table 1 provides an overview of the groups of antimicrobial agents covered in the BelVetSAC data-collection system, together with the corresponding ATCvet codes. The ATCvet codes included in each antimicrobial class are listed in appendix A.

In the BelVetSac data collection all antimicrobials used for veterinary medicine are covered (Table 1). No antimicrobials are excluded which is in contrast to the ESVAC reporting system where antimicrobials for dermatological use and for use in sensory organs are excluded. This explains why data as presented in the report are always marginally higher than what is reported for Belgium in the ESVAC report.

Table 1. groups of antimicrobial agents covered in the data collection and corresponding ATCvet codes.

Groups of antimicrobial agents	ATCvet codes
Antimicrobial agents for intestinal use	QA07AA; QA07AB
Antimicrobial agents for dermatological use	QD06A; QD06BA
Antimicrobial agents for intrauterine use	QG51AA; QG51AC; QG51AE; QG51AX QG51BA; QG51BC; QG51BE
Antimicrobial agents for systemic use	QJ01
Antimicrobial agents for intramammary use	QJ51
Antimicrobial agents for use in sensory organs	QS01AA; QS01AB QS02AA QS03AA
Antimicrobial agents for use as antiparasitic	QP51AG

2. Animal production

Animal production data to calculate the produced biomass were derived from the Eurostat website

(http://epp.eurostat.ec.europa.eu/portal/page/portal/agriculture/data/main_tables).

From these animal production data, biomass (in kg) was calculated, according to Grave et al., (2010), as the sum of the amount of beef, pork and poultry meat produced that year in Belgium plus the number of dairy cattle present in Belgium times 500 kg of metabolic weight per head.

Data analysis

The total number of packages sold per product for all wholesalers was linked to a for that purpose developed database that contained all additional product information. This additional information consisted of:

- the different active antimicrobial substances the product contains per ml for liquids or mg for solids
- the weight per substance
- the number of units in one package
- for active substances expressed in International Units: the conversion factor to mg
- calculated from the above: the total amount of active substance (per active substance) in one package
- the ATC vet code for each (combination of) active substance(s) required for the ESVAC (European Surveillance of Veterinary Antimicrobial Consumption) reporting

Through this extra information, the number of packages sold can be converted to the amount of active substance used.

All sales data on antimicrobial feed premixes included in the data from wholesaler-distributors were excluded from the above data-source to prevent double counting. Data concerning antimicrobial premixes from medicated feed producers were added to the data on pharmaceuticals from wholesaler-distributors to account for total coverage of veterinary antimicrobial consumption in Belgium.

As in the previous reports (BelVetSac 2007-2009; BelVetSac 2010), yearly consumption figures were put versus biomass as a yearly adjusted denominator according to the methodology described by Grave et al. (2010). The animal species included were based upon the vast majority of the biomass present (estimated to be 92% of the total biomass present in Belgium). It should however be made clear that the calculation of the biomass does not contain other animal species such as horses, rabbits, small ruminants and companion animals (dogs, cats, ...) (estimated to be 8% of the biomass present in Belgium), whereas the collected data on antimicrobial use also covers the use in these species. The biomass also includes animals slaughtered in Belgium but raised in other countries and it excludes animals raised in Belgium but slaughtered abroad.

The fact that many antimicrobial products are registered for use in different animal species and that there are currently no data available on the proportions of products used in the different species makes extrapolation up to animal species level unachievable at this moment. The Market Authorization Holders of the products do provide estimated proportions to be included in the product related pharmacovigilance periodic safety update reports, yet these estimates are not always at hand, and are often based on limited data. For these reasons it was not feasible to use these data for this report.

For antimicrobial premixes however we do know for what animal species they are intended (only pigs and poultry receive medicate feed) therefore we can further distinguish the use of antimicrobial premixes.

Data validation

1. External data validation

To check for correctness and completeness the collected data were also compared to data collected by sector organizations. For the pharmaceutical industry data were provided by Pharma.be (www.pharma.be) and for the feed producing industry data were provided by BEMEFA (www.bemefa.be). In none of both datasets data were totally equal since slightly different data collection systems are used and not all producers or wholesalers are member of the respective sector organizations. Trends and evolutions in the different dataset were compared and only if large discrepancies were observed data entry mistakes were further investigated and corrected, if needed.

2. Internal data validation

For each of the data entries of the wholesaler-distributor or compound feed producers results were compared with the data entries of the previous years by the same companies. If large, unexpected, discrepancies are observed between the data provided in the subsequent years data entry mistakes were further investigated and corrected, if needed.

Results

Response rate and data validation

All the 25 wholesaler-distributors, requested to deliver their sales data on veterinary antimicrobial products sold in 2011 responded. All 59 compound feed producers, licensed for the production of medicated feed responded. Of these 7 indicated not to have produced any medicated feed and 52 delivered the data on antimicrobial premixes incorporated in medicated feed to be used in Belgium. Based on the response rate data coverage is assumed to be 100%.

In the internal data validation step one important difference was found in a large wholesaler-distributor (apparent reduction of sales > >50%). After further investigation it turned out that incorrect data were provided and this was corrected in a new data delivery.

In the cross-validation of the data with the databases of pharma.be and BEMEFA comparable amounts and trends were found as presented in this report again indicating that the results presented are likely to be a good representation of reality.

Number of antimicrobial pharmaceuticals and premixes available on the Belgian market

Table 2 provides an overview of the number of antimicrobial pharmaceuticals and the number of antimicrobial premixes available on the Belgian market for the years 2007-2011 according to the commented compendium of the Belgian Centre for Pharmacotherapeutic Information 2007, 2008, 2009, 2010 and 2011 respectively (www.bcfi-vet.be).

Table 2. Armatorium of antimicrobial products on the Belgian market in between 2007 and 2011.

	2007	2008	2009 ¹	2010	2011
Number of antimicrobial pharmaceuticals on the market	270	276	283	292	282
Number of antimicrobial premixes on the market	16	18	20	21	23
Total number of antimicrobial products on the market	286	294	303	313	305

With exception of gamithromycin (since 2009), no new active substances were registered on the market in the reported years. Thus the observed increase in available products is largely due to the marketing of new formulations or new generic products based on existing active substances.

¹ Data on the number of antimicrobial pharmaceuticals and premixes on the market in 2007-2009 differ slightly from these reported in the first BelVetSac report (2007-2009). The data in the previous report were incomplete, but had no impact on the quantification of the amount of antimicrobials used.

Animal biomass produced in Belgium

The produced biomass was calculated based on the Eurostat data for the years 2007-2011 as described above (Table 3)

Table 3. Animal Biomass produced in Belgium between 2007 and 2011.

Animal biomass	2007	2008	2009	2010	2011
Meat (ton)					
Pork	1 063 277	1 056 169	1 082 036	1 123 769	1 108 255
Beef	272 863	216 547	255 017	263 142	272 286
Poultry	469 304 ^a	469 304 ^a	469 304	505 882	495 795
Total biomass from meat production	1 805 444	1 742 020	1 806 357	1 892 793	1 876 336
Dairy cattle					
Dairy cattle (number)	524 900	517 700	517 700	517 700	510 600
Dairy cattle metabolic weight (ton)	262 450	258 850	258 850	258 850	255 300
Total biomass (ton)	2 067 894	2 000 870	2 065 207	2 151 643	2 131 636

^a numbers are copied from the most adjacent year where figures were available.

A decrease in biomass production of 1% is observed between 2010 and 2011. This slight decrease is mainly due to a decrease in pork and poultry production and a lower number of dairy cattle present whereas the beef production increased slightly.

Total consumption of antimicrobial drugs for veterinary use in Belgium

The total consumption of antimicrobial drugs for veterinary use in Belgium is presented in Figure 3 in tons of active substance per given year. The total amount is subdivided into the part of antimicrobial pharmaceuticals and the part of antimicrobial compounds contained in antimicrobial premixes incorporated into medicated feed intended to be used in Belgium.

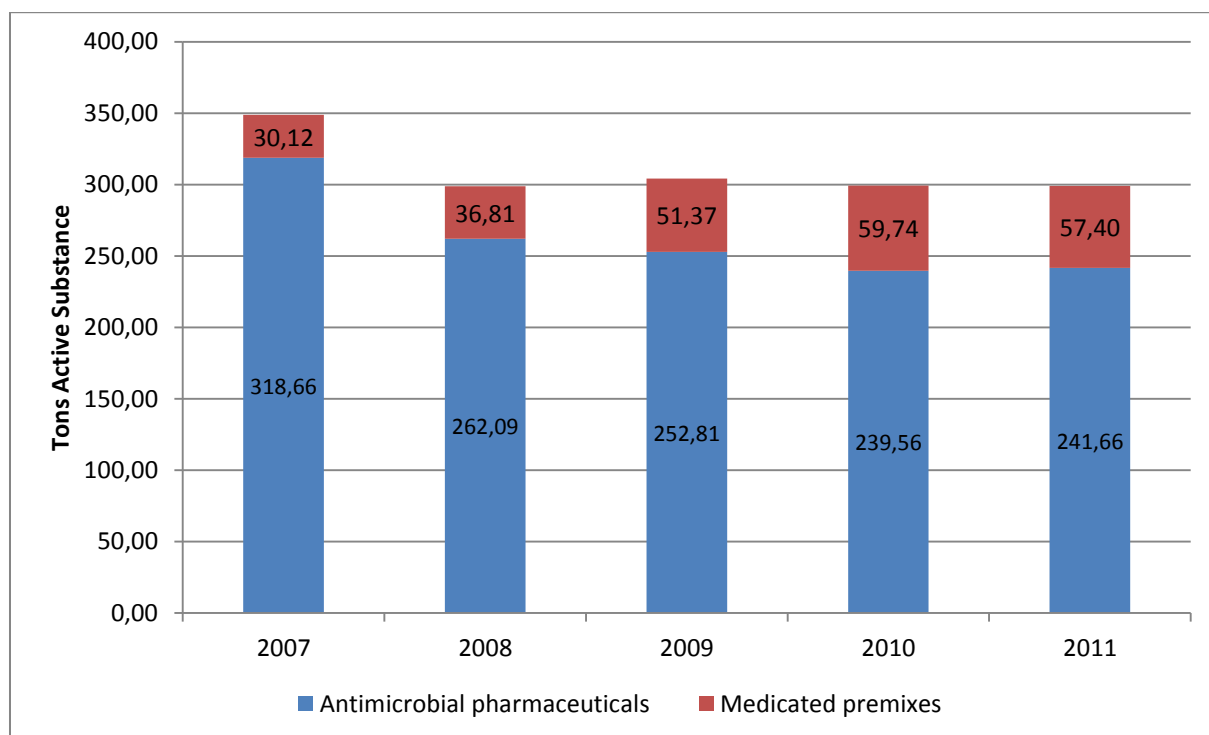


Figure 3. Total national consumption of antimicrobial compounds for veterinary use in Belgium for the years 2007-2011 (tons active substance)

Between 2010 and 2011, there is a very small decrease of 0,1% in the total consumption of antimicrobials in veterinary medicine in Belgium (299285,1 kg in 2010; 299036,6 kg in 2011). The use of antimicrobial pharmaceuticals increased with 0,9% between 2010 and 2011, whereas the use of antimicrobial premixes decreased with 3,9%. When looking at the trend from 2007 onwards (start data collection) a decrease of 14.3% in total consumption is observed. Yet this decrease is largely realized between 2007 and 2008. Since 2008 the total consumption has stabilized and no significant reduction is seen anymore. Figures 4 and 5 show these data separately for the antimicrobial pharmaceuticals and the antimicrobial premixes.

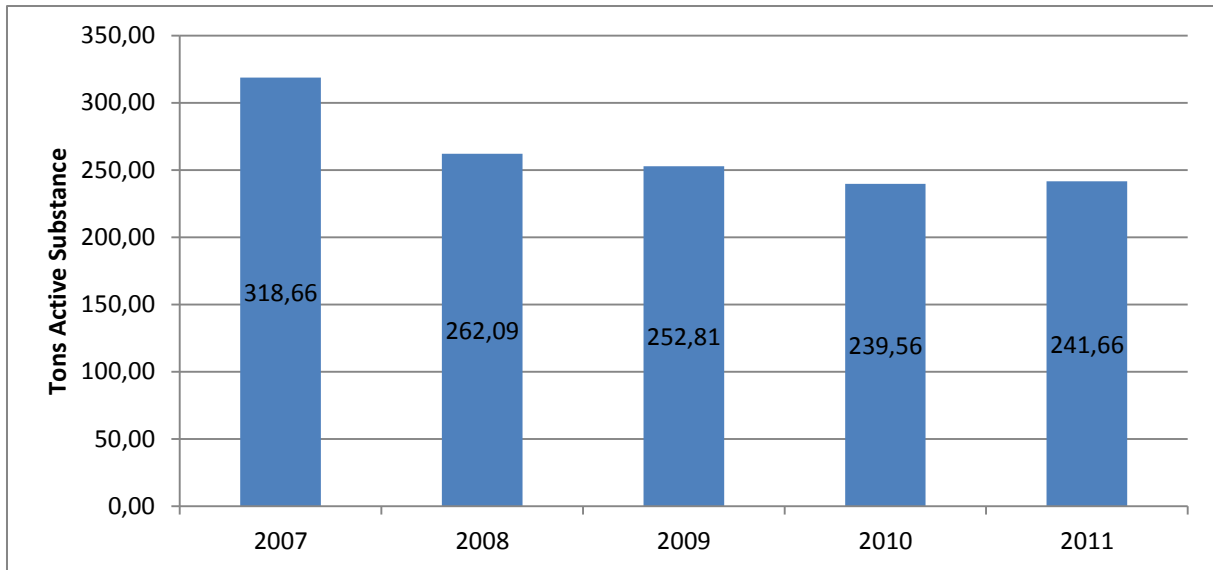


Figure 4. National consumption of antimicrobial pharmaceuticals for veterinary use in Belgium for the years 2007-2011 (tons active substance)

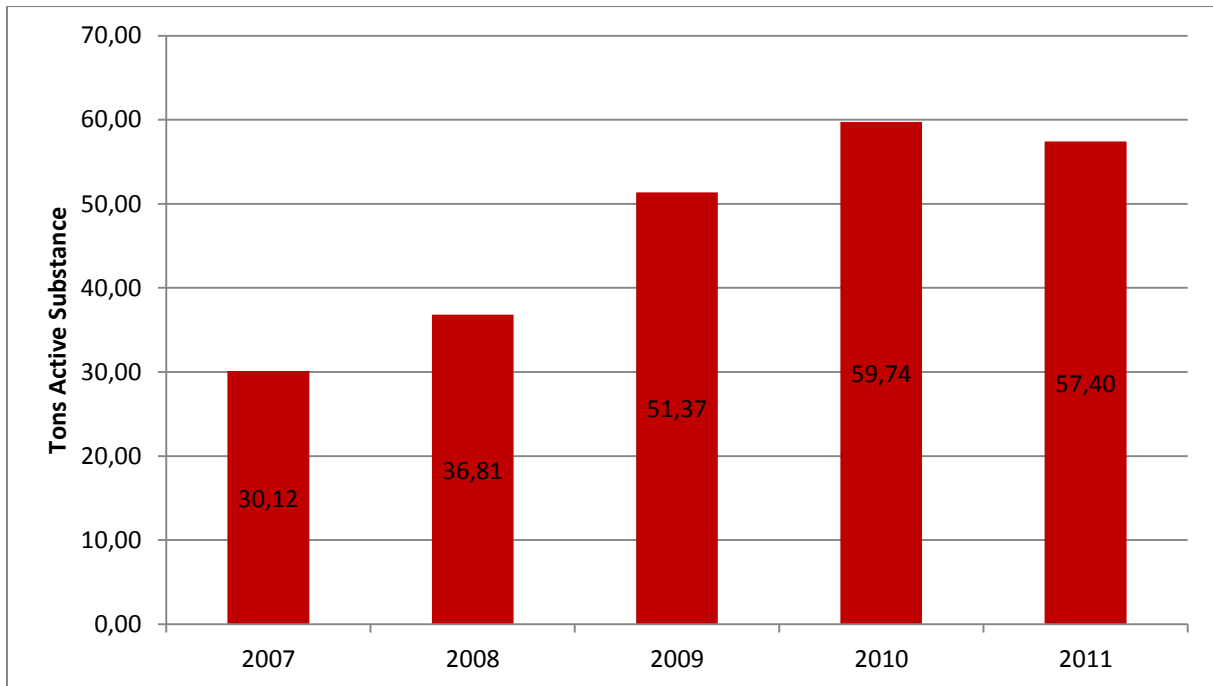


Figure 5. National consumption of antimicrobial premixes in Belgium for the years 2007 -2011 (tons active substance)

Since 2011 the data collection system allows to differentiate the animal species of destination for the antimicrobial premixes. The results show that 98.97% of the antimicrobial premixes are used in pig feed whereas only 1.03% is used in poultry or rabbit feed.

Antimicrobial use versus biomass

The amount of antimicrobial compounds used in animals in Belgium was plotted against the amount of biomass produced. For 2011, this number was 140,3 mg/kg. This is an increase of 0,9% in comparison to 2010. This increase is in contrast to the small decrease (-0,1%) in absolute volume of consumed antimicrobials due to the decrease of the produced biomass (-1%). Figure 6 presents these data, again subdivided into antimicrobial pharmaceuticals and antimicrobial premixes.

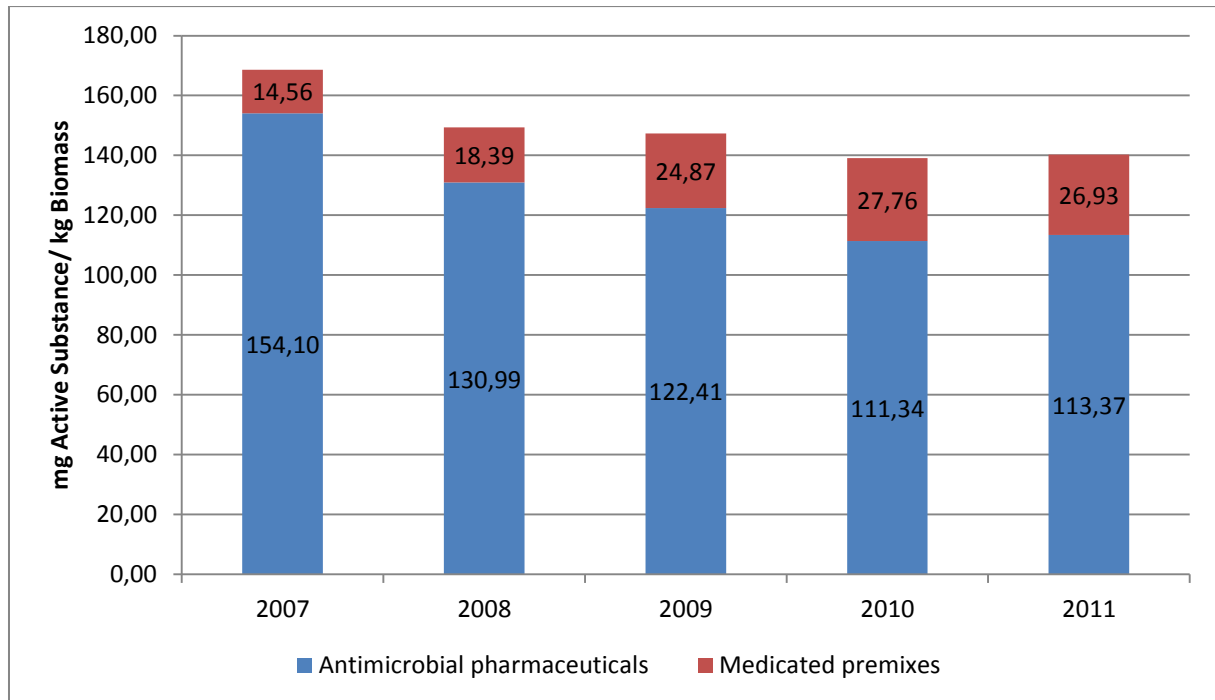


Figure 6. Total mg of active substance used per kg biomass produced in Belgium for 2007-2011.

2011 is the first year since the start of the data collection (2007) that a (small) increase in amount of antimicrobials consumed per kg biomass is observed. As a result, the positive decreasing trend of the 4 previous years has stopped. Between 2007 and 2011 there is still a total decrease of 16,8%.

Looking only at antimicrobial pharmaceuticals in function of the biomass produced, an increase of 1,8% is observed between 2010 and 2011, whereas for the medicated premixes a decrease of 3,0% is seen. This is the first reduction of used medicated premixes observed after a gradual increase in the last 4 years.

Figures 7 and 8 show these data separately for the antimicrobial pharmaceuticals and the antimicrobial premixes .

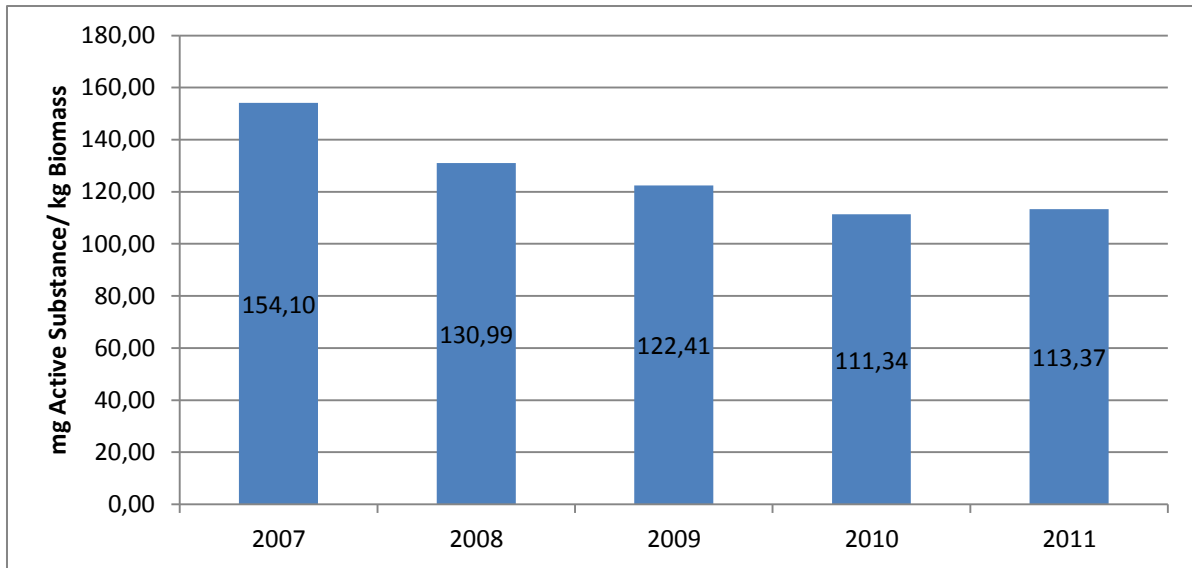


Figure 7. Mg active substance of antimicrobial pharmaceuticals used per kg biomass in Belgium for 2007-2011.

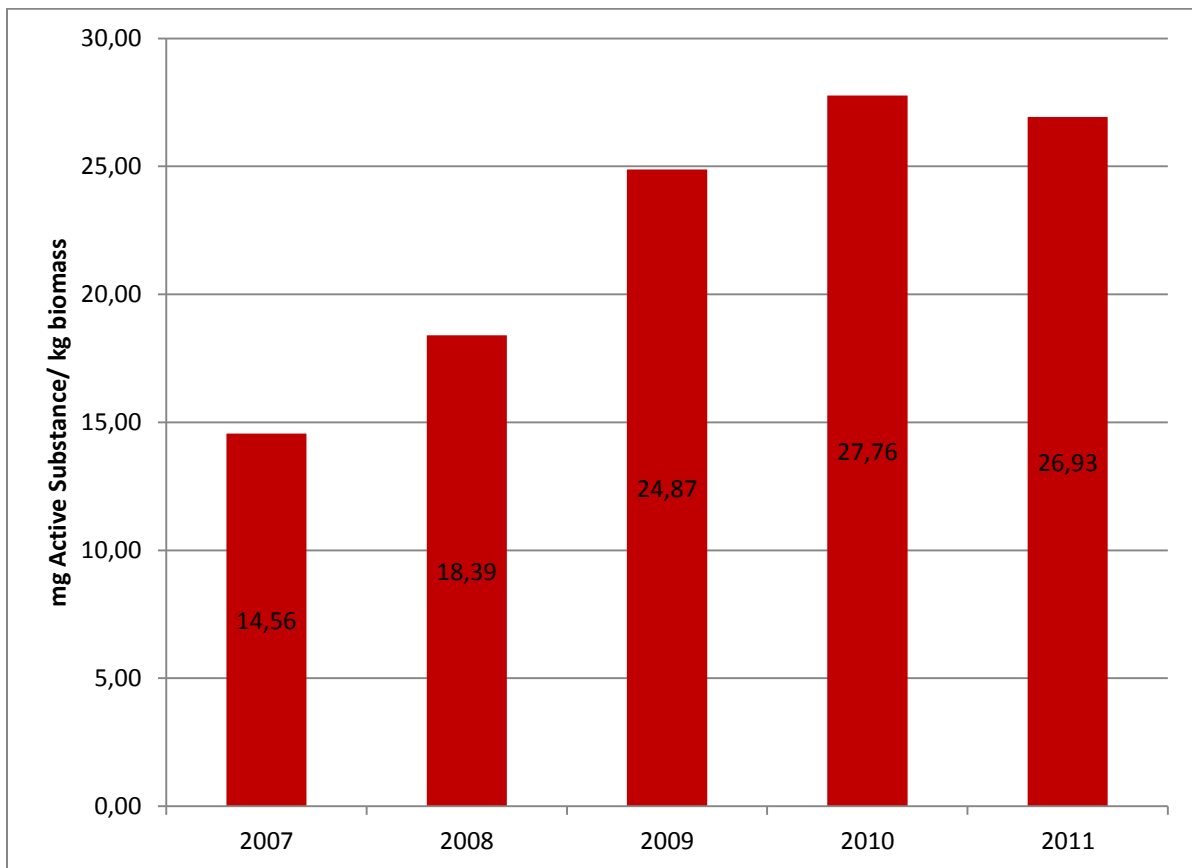


Figure 8. Mg active substance of antimicrobial premixes used per kg biomass in Belgium for the years 2007 -2011

Comparison of Belgium with The Netherlands for the last 5 years.

The results of Belgium, expressed in mg active compound per kg biomass were compared with The Netherlands, a country with a relatively comparable animal production structure, for the years 2007 - 2011.

Data from The Netherlands from 2007 - 2011 were obtained from the MARAN 2009, 2010 and 2012 report (www.lei.wur.nl), as well as the amount of biomass produced according to Eurostat database (epp.eurostat.ec.europa.eu), from which the amount used per kg biomass produced was calculated in the same way as done for Belgium.

Table 4. Mg active substance used per kg biomass produced in The Netherlands in the years 2007 – 2010.

Year	Antimicrobial consumption (kg) ¹	Biomass produced (tons) ²	mg active compound/ kg biomass
2007	590 000	3 141 488	188
2008	529 000	3 228 214	164
2009	495 000	3 239 767	153
2010	433 000	3 234 538	134
2011	338 000	3 337 971	101

¹ MARAN report 2009, 2010 and 2012

² Eurostat (epp.eurostat.ec.europa.eu)

In Figure 9 the results of the Netherlands are compared to the results of Belgium for 2007-2011

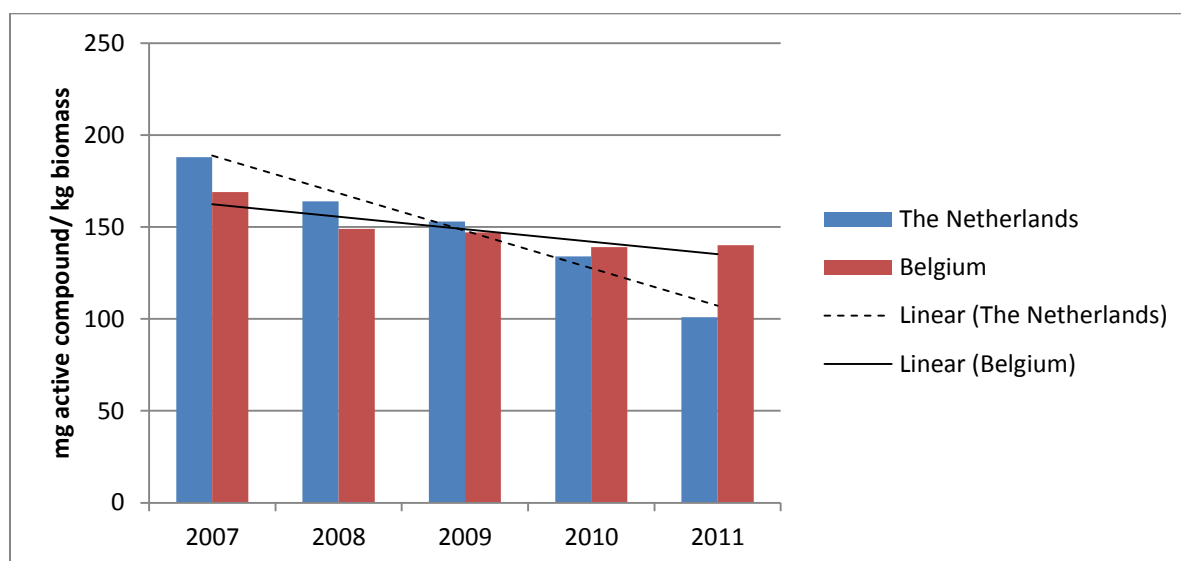


Figure 9. Comparison of mg active substance used per kg biomass produced between Belgium and The Netherlands for the years 2007 – 2011 (including trendlines).

In 2007, Belgium used 10.1% less antimicrobial active substance per kg biomass than The Netherlands. Yet due to the remarkable decrease of antimicrobial consumption in The Netherlands especially in 2010 and 2011 and the much slower decrease in Belgium, the consumption per kg biomass in 2011 was almost 39% higher in Belgium in comparison to The Netherlands.

A much more elaborated comparison of many different European countries is expected to become available from the ESVAC project by the end of 2012.

Antimicrobial use per class of antimicrobial compounds

1. Total consumption (antimicrobial pharmaceuticals and premixes)

In Figure 10 the total consumption of antimicrobials per class (ATC level 3 or 4) is presented. On average (2007 → 2011), 30,7% of the compounds used were sulphonamides and trimethoprim, 25,6% tetracyclines, 24,6% penicillines and 7,4% macrolides.

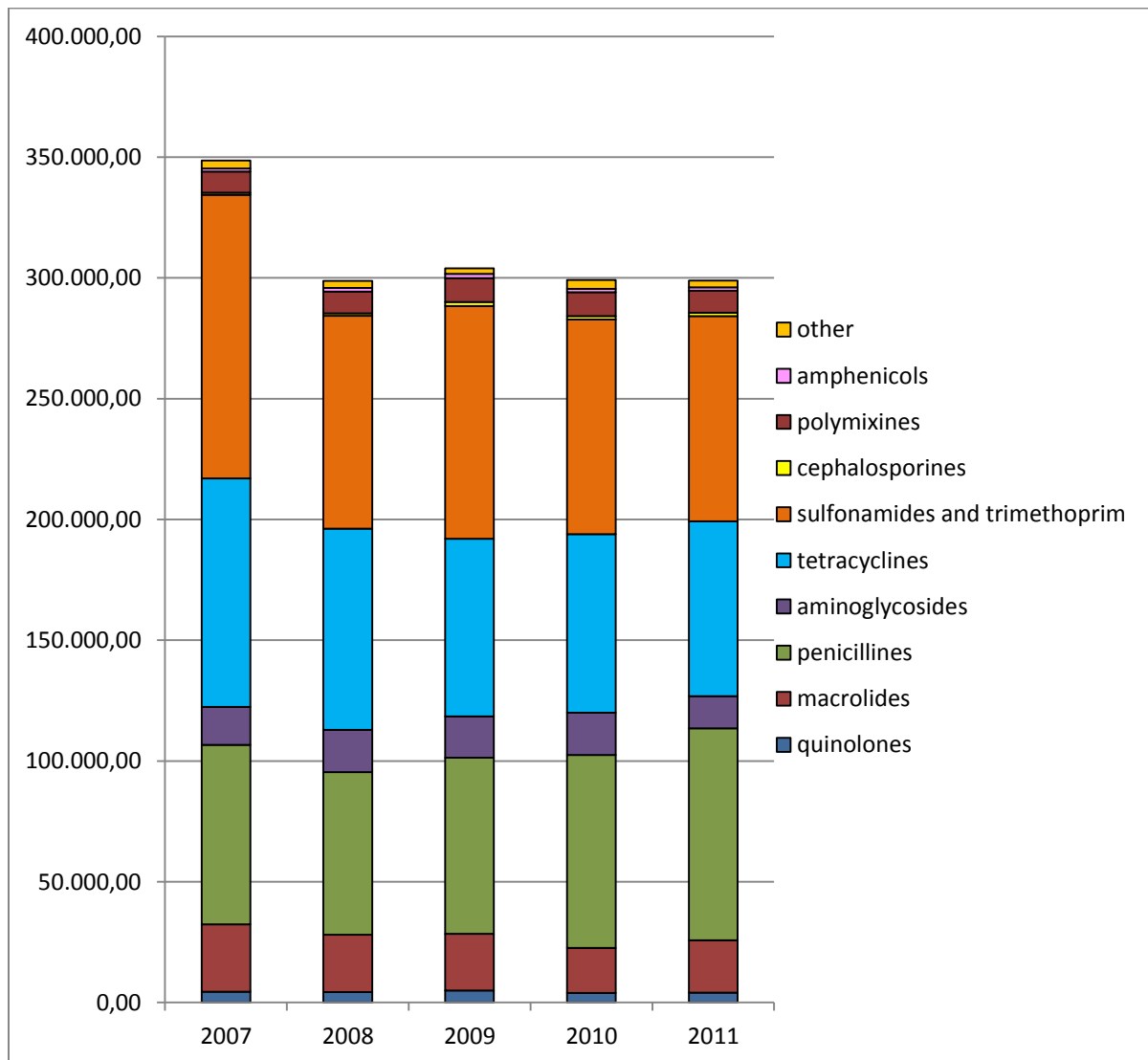


Figure 10. Total antimicrobial use per class of antimicrobials.

In 2011, the most used group of antimicrobials were the penicillins (88 tons, 29.3%) followed by the sulphonamides and trimethoprim (85 tons, 28.4%) and the tetracyclines (72 tons, 24.2%). Yet both the use of sulphonamides and trimethoprim and tetracyclines was reduced in comparison to 2010 (-4.5% and -1.9% respectively) whereas the use of penicillins keeps on increasing (+9.7% in comparison to 2010) and therefore has become the most used group of antimicrobials in veterinary medicine in 2011. In table 5 an overview of the evolution of the use of the different classes of antimicrobials between 2010 and 2011 is given. Unfortunately also the use of critically important antimicrobials according to the WHO such as cephalosporins, quinolones and macrolides increased in 2011.

Table 5: Evolution in the antimicrobial consumption (kg) per antimicrobial class.

Class	2010	2011	evolution
aminoglycosides	17.382,2	13.166,9	-24,3%
cephalosporins	1.368,9	1.489,7	8,8%
fenicols	1.382,7	1.354,4	-2,0%
macrolides	18.787,1	21.843,0	16,3%
other	3.646,7	2.771,0	-24,0%
penicillins	80.082,5	87.863,3	9,7%
polymixins	9.879,5	9.102,7	-7,9%
quinolones	3.978,1	4.088,5	2,8%
sulphonamides	88.939,1	84.902,8	-4,5%
tetracyclines	73.838,2	72.454,1	-1,9%
Totaal (kg)	299.285,1	299.036,6	-0,1%

2. Antimicrobial pharmaceuticals

In Figure 11 the consumption of antimicrobials per class (ATC level 3 or 4) is presented for the pharmaceuticals.

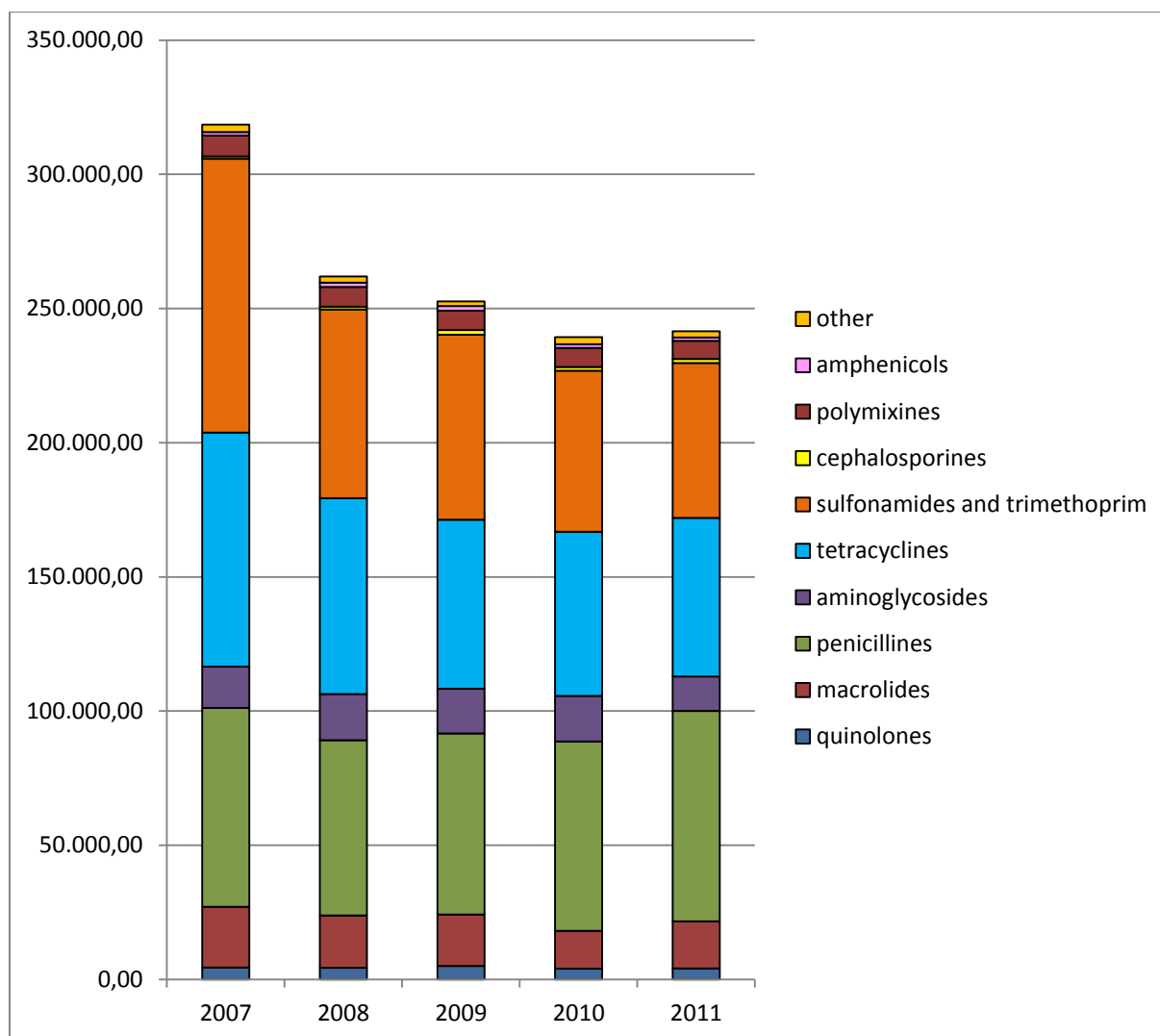


Figure 11. Use of antimicrobial pharmaceuticals per class of antimicrobials between 2007 and 2011.

3. Antimicrobial premixes

In Figure 12 the consumption of antimicrobials per class (ATC level 3 or 4) is presented for the antimicrobial premixes.

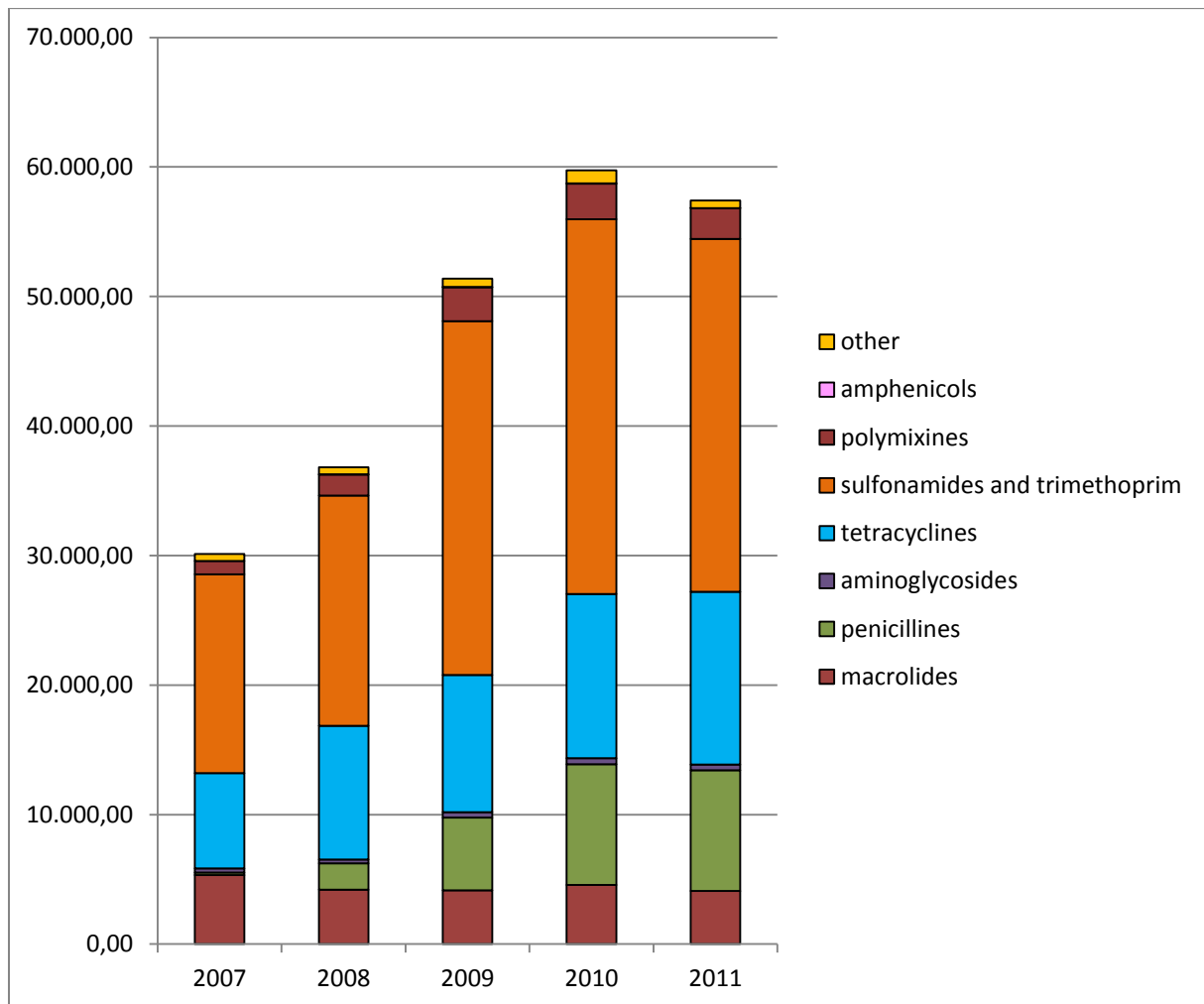


Figure 12. Use of antimicrobial premixes per class of antimicrobials between 2007 and 2011.

The slight decrease in use of antimicrobial premixes is largely due to a significant decrease in the use of sulphonamides and trimethoprim and a small decrease in use polymixines and macrolides, whereas a small increase in the use of tetracyclines is observed.

Antimicrobial use per active substance

Table 6 gives the amounts used per individual active substance, grouped per class of antimicrobials.

Table 6: Antimicrobial use per active substance

Class	Antimicrobial compound	Total (kg)					Antimicrobial pharmaceuticals (kg)					Medicated premixes (kg)				
		2007	2008	2009	2010	2011	2007	2008	2009	2010	2011	2007	2008	2009	2010	2011
aminoglycosides	apramycine	377,7	295,1	253,9	228,0	191,8	304,6	209,1	164,3	118,0	95,8	73,1	86,0	89,6	110,0	96,0
	dihydrostreptomycine	7.222,0	7.810,9	7.783,1	8.653,4	4.236,5	7.222,0	7.810,9	7.783,1	8.653,4	4.236,5					
	gentamicine	110,6	135,8	163,1	140,8	132,3	110,6	135,8	163,1	140,8	132,3					
	kanamycine	0,1	2,3	10,9	13,2	15,3	0,1	2,3	10,9	13,2	15,3					
	neomycine	1.430,9	1.377,2	1.299,5	1.071,1	1.209,1	1.430,9	1.377,2	1.299,5	1.071,1	1.209,1					
	paromomycine	1.526,8	1.647,3	1.423,5	2.825,8	2.909,3	1.526,8	1.647,3	1.423,5	2.825,8	2.909,3					
	spectinomycine	4.980,6	6.062,1	6.050,3	4.449,8	4.472,8	4.740,3	5.865,0	5.717,0	4.092,5	4.138,9	240,4	197,1	333,4	357,3	333,9
cephalosporins	cefalexine	171,7	238,7	604,4	502,2	605,2	171,7	238,7	604,4	502,2	605,2					
	cefalonium	8,6	17,7	17,7	12,5	22,4	8,6	17,7	17,7	12,5	22,4					
	cefapirine	14,3	14,6	13,8	11,0	10,4	14,3	14,6	13,8	11,0	10,4					
	cefazoline	0,4	0,8	0,4	2,2	1,5	0,4	0,8	0,4	2,2	1,5					
	cefoperazon	4,5	7,6	6,4	6,5	5,8	4,5	7,6	6,4	6,5	5,8					
	cefovecin	5,3	6,8	8,1	8,9	9,6	5,3	6,8	8,1	8,9	9,6					
	cefquinome	132,9	144,4	151,2	146,7	183,4	132,9	144,4	151,2	146,7	183,4					
	ceftiofur	571,7	655,7	865,6	678,9	651,3	571,7	655,7	865,6	678,9	651,3					
fenicols	chlooramfenicol	2,1	2,2	2,4	1,6	2,2	2,1	2,2	2,4	1,6	2,2					
	florfenicol	1.303,1	1.560,4	1.666,0	1.381,1	1.352,3	1.303,1	1.534,5	1.649,4	1.359,9	1.333,3	-	26,0	16,6	21,2	18,9
macrolides	clindamycine															

		146,2	154,4	136,9	141,0	138,1	146,2	154,4	136,9	141,0	138,1					
	erythromycine	49,9	50,0	53,9	-	-	49,9	50,0	53,9	-	-					
	gamithromycine	-	-	25,8	32,3	25,9	-	-	25,8	32,3	25,9					
	lincomycine	6.109,2	6.011,1	6.084,4	4.838,0	5.654,1	5.411,6	5.581,3	5.529,5	4.339,7	5.055,0	697,6	429,8	554,9	498,3	599,1
	pirlimycine	0,5	0,5	0,4	0,5	0,4	0,5	0,5	0,4	0,5	0,4					
	spiramycine	602,8	712,4	732,3	313,4	111,3	602,8	712,4	732,3	313,4	111,3					
	tilmicosine	6.147,9	4.968,2	4.873,7	5.534,2	4.488,7	3.209,0	2.438,9	2.615,8	3.216,3	2.614,0	2.938,9	2.529,3	2.257,8	2.317,9	1.874,7
	tulathromycine	51,1	53,4	66,0	56,8	57,5	51,1	53,4	66,0	56,8	57,5					
	tylosine	14.990,6	11.869,7	11.553,7	7.870,9	11.367,0	13.292,6	10.620,8	10.199,8	6.122,4	9.732,6	1.698,0	1.248,9	1.354,0	1.748,6	1.634,4
other	metronidazol	68,3	70,2	71,8	67,6	49,4	68,3	70,2	71,8	67,6	49,4					
	rifaximin	5,5	7,8	10,5	14,4	17,4	5,5	7,8	10,5	14,4	17,4					
	tiamuline	2.684,8	2.396,3	2.041,1	3.316,0	2.518,3	2.571,3	2.218,1	1.648,5	2.524,4	2.106,0	113,5	178,1	392,6	791,6	412,3
	valnemuline	432,8	352,9	233,6	212,3	152,8	-	-	-	-	-	432,8	352,9	233,6	212,3	152,8
	zink bacitracine	99,0	43,4	31,3	36,6	33,1	99,0	43,4	31,3	36,6	33,1					
penicillins	amoxicilline	64.345,2	56.577,5	62.384,6	66.496,7	72.827,2	64.150,3	54.538,6	56.785,1	57.164,0	63.510,0	194,8	2.038,8	5.599,5	9.332,7	9.317,2
	amoxicilline-clav	694,6	766,4	768,3	952,9	954,1	694,6	766,4	768,3	952,9	954,1					
	ampicilline	444,3	438,8	483,8	326,3	251,4	444,3	438,8	483,8	326,3	251,4					
	cloxacilline	433,9	463,4	514,5	542,8	512,6	433,9	463,4	514,5	542,8	512,6					
	fenoxymethylpenicilline	68,3	212,2	157,3	99,1	248,8	68,3	212,2	157,3	99,1	248,8					
	nafcilline	23,3	23,4	33,3	1,9	0,2	23,3	23,4	33,3	1,9	0,2					
	penethamaat	329,5	336,0	282,8	273,9	290,2	329,5	336,0	282,8	273,9	290,2					
	procaïne benzylpenicilline	8.022,8	8.646,0	8.526,9	11.389,0	12.778,8	8.022,8	8.646,0	8.526,9	11.389,0	12.778,8					

polymixins	colistinesulfaat	8.787,8	8.947,7	9.906,3	9.878,5	9.101,7	7.764,7	7.320,5	7.279,8	7.134,3	6.723,6	1.023,1	1.627,2	2.626,5	2.744,2	2.378,1
	polymyxine B sulfaat	0,7	1,2	1,1	1,0	1,0	0,7	1,2	1,1	1,0	1,0					
quinolones	danofloxacin	101,8	83,7	81,4	77,8	71,6	101,8	83,7	81,4	77,8	71,6					
	difloxacin	39,4	26,9	27,3	23,4	12,2	39,4	26,9	27,3	23,4	12,2					
	enrofloxacin	908,4	986,6	1.046,0	945,6	1.060,6	908,4	986,6	1.046,0	945,6	1.060,6					
	flumequine	3.239,0	3.070,5	3.633,0	2.682,9	2.674,8	3.239,0	3.070,5	3.633,0	2.682,9	2.674,8					
	ibafloxacin	3,2	4,0	3,6	1,1	1,0	3,2	4,0	3,6	1,1	1,0					
	marbofloxacin	196,4	231,9	230,5	247,3	267,4	196,4	231,9	230,5	247,3	267,4					
	orbifloxacin	0,7	0,6	0,1	0,0	0,8	0,7	0,6	0,1	0,0	0,8					
	sulfachloorpyridazine natrium	1.802,7	1.717,2	1.700,7	2.437,8	885,9	1.802,7	1.717,2	1.700,7	2.437,8	885,9					
Sulphonamides and trimethoprim	sulfadiazine	80.721,5	67.606,5	71.502,3	70.313,7	68.913,3	67.928,5	52.797,4	48.741,0	46.197,1	46.226,6	12.792,9	14.809,2	22.761,4	24.116,6	22.686,7
	sulfadimethoxine natrium	411,6	407,5	460,2	478,2	-	411,6	407,5	460,2	478,2	-					
	sulfadimidine natrium	1.161,6	829,5	747,4	465,9	423,4	1.161,6	829,5	747,4	465,9	423,4					
	sulfadoxine	254,3	251,5	229,9	283,3	385,6	254,3	251,5	229,9	283,3	385,6					
	sulfamethoxazol	79,0	105,7	129,6	83,4	83,8	79,0	105,7	129,6	83,4	83,8					
	sulfanilamide	16.070,3	2.940,1	6.598,0	-	-	16.070,3	2.940,1	6.598,0	-	-					
	trimethoprim	16.838,2	14.196,1	14.995,2	14.876,9	14.210,9	14.279,6	11.234,3	10.442,9	10.053,5	9.673,5	2.558,6	2.961,8	4.552,3	4.823,3	4.537,3
	tetracyclines	chloortetracycline	940,6	1.053,6	2.210,6	2.288,4	3.087,6	940,6	884,4	825,7	884,3	781,3	-	169,3	1.384,9	1.404,1
doxycycline		64.705,7	55.769,3	54.719,0	57.216,0	53.865,5	64.694,7	50.749,9	46.312,6	47.826,6	45.226,9	11,1	5.019,4	8.406,4	9.389,4	8.638,6
oxytetracycline		28.895,8	26.537,7	16.567,1	14.333,9	15.500,9	21.554,0	21.405,3	15.760,4	12.465,1	13.088,6	7.341,8	5.132,4	806,7	1.868,7	2.412,3

*Maccrolides inclusive lincosamides

Discussion

In the context of the increasing awareness of antimicrobial resistance development, comparable data and evolutions on antimicrobial consumption are of utmost importance. This third BelVetSac report describes the antimicrobial use in animals in Belgium in 2011. It is the follow up of the first and second BelVetSac report with the first complete data on the antimicrobial use of animals in Belgium between 2007 and 2010.

As in the previous reports data were collected at the level of the wholesaler-distributors for the antimicrobial pharmaceuticals and at the level of the compound feed producers for the antimicrobial premixes. This level both warrants the most complete data and is the closest possible level to the end-user that is practically achievable at this moment. Wholesaler-distributors were asked to provide only data on sales to veterinarians or pharmacists, no sales to other wholesaler-distributors, by which double counting could be avoided. Feed premixes do not necessarily follow the chain through wholesaler-distributors, but compound feed producers can purchase the premixes directly at the level of the producers or pharmaceutical wholesaler. To cover both, data were collected at the level of the compound feed producers. To improve data quality and correctness all data were validated against the data provided in the previous years and data collected by the sector organizations.

Although the collected data are valuable and show essential overall consumption trends, it is important to realize that the data are also very crude and some sources of bias in the data may be present. First of all it would be useful to have data where antimicrobial consumption can be attributed to the different animal species. This would allow to monitor trends per species. Equally it would be better to have data on the amount of treatments attributed to an animal during its live span rather than the amount of kg of a given compound consumed since the number of treatments (=Treatment incidence) is much more relevant in relation to the development of antimicrobial resistance than the total amount of antimicrobials consumed. In reference to this recently 3 scientific publications became available that discuss the antimicrobial consumption, expressed in treatment incidence, in pigs, poultry and veal production in Belgium (Callens et al., 2012, Persoons et al., 2012, Pardon et al., 2012). Although these studies are based on a sample of individual herds and therefore do not give a complete overview of the antimicrobial consumption, as is done in this BelVetSac report, they do describe the antimicrobial consumption in much more detail and clearly illustrate the huge variability observed between herds and production types.

Another possible source of bias is that in the current system we cannot be absolutely sure that all products sold in Belgium by the wholesaler-distributors were also used in Belgium. The possibility exists that veterinarians living near the country borders also use medicines bought in Belgium to treat animals abroad. Given the large pressure (e.g. awareness campaigns, legislative measures,...) on reduced antimicrobial use in the neighboring

countries (e.g. The Netherlands) it could be speculated that this phenomenon may become increasingly important. On the other hand antimicrobial medicated feed produced in a neighboring country may also be consumed in Belgium.

Only very recently the working group on data collection of the AMCRA (knowledge center on antimicrobial consumption and resistance in animals in Belgium) has drafted an advise on the development of a data collection system which meets with the above mentioned requirements and excludes the possible sources of bias. The feasibility of introducing such a system will be submitted to the competent authorities soon.

This report shows a decrease of 0,1% in the total consumption of antimicrobials in veterinary medicine between 2010 and 2011. When relating this progress to the evolution in the total biomass produced in 2011 there is even an increase of 0,9%. More precisely, the use of antimicrobial pharmaceuticals has increased with 0,9% (1,8% relative to the biomass) whereas the use of antimicrobial premixes has decreased with 3,9% (3,0% relative to the biomass). Although a total increase of 0,1% is marginal and essentially suggesting a status quo in comparison to the previous year, this result is very unsatisfactory. In relation to the biomass produced annually a slow but steady reduction of antimicrobials consumed per kg biomass produced was observed between 2007 and 2010. This favorable trend was not continued in 2011 and for the first time an increase is found. Since several years now there is an increasing awareness on antimicrobial resistance and it is recognized that the use of antimicrobials is the predominant driver of resistance development. Based on this a decrease of the total amount of antimicrobials consumed (and per kg biomass produced) is to be aimed at, as is done in many of the European countries (e.g. Denmark, The Netherlands, France). Therefore the relative status quo observed in Belgium since almost 4 years is not in line with aimed reduction. This is very obvious when comparing the results of Belgium to The Netherlands.

Since the publication of the first BelVetSac report Belgium has also become fully engaged in the European coordinated ESVAC data collection system. In the next EMA-ESVAC report which will likely become available before the end of 2012 also Belgian data will be included together with many other European countries. Then it will become clear where Belgium is situated in relation to the other EU member states.

The only positive evolution observed in 2011 is the decrease in use of medicated premixes, after four years of consecutive increase. Antimicrobial premixes are used almost exclusively in pig production (>98%) and therefore this decrease is also almost entirely a result of a decreased use in pig production. Whether the increase in use of pharmaceuticals has also occurred predominantly in pig production cannot be determined based upon the available data since the method of data collection does not allow to differentiate between animal species. However, a sort of trade off in pig production between pharmaceuticals and antimicrobial premixes is likely and therefore the observed opposite evolutions of

pharmaceuticals and premixes are probably only a shift from the use of antimicrobial premixes to pharmaceuticals.

These results reemphasize the need of actions directed to all stakeholders, towards a reduced use of antimicrobials. For this purpose the recently established AMCRA is currently preparing recommendations and guidelines to guide the whole sector towards a rational reduction of the antimicrobial use. The results of these actions will however only become apparent in 2012 at the earliest since the AMCRA only became fully operational from the first of January 2012.

Conclusion

This report shows a status quo in absolute numbers of the use of antimicrobials in animals in Belgium in comparison to 2010 and even a small increase when expressed in relation to the total biomass produced. Given the risks related to antimicrobial use in animals, a significant decrease rather than a small increase should be aimed at. Therefore the 2011 results are unsatisfactory and increased action and awareness is needed to regain the positive trend of reduction in antimicrobial use.

Acknowledgements

Belgian wholesaler-distributors and compound feed producers are much obliged for their cooperation and for providing the data on the consumption of antimicrobials in animals in Belgium.

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Appendix

Appendix A. ATCvet codes included in the different classes of antimicrobials

Class of antimicrobials	ATCvet codes included
aminoglycosides	QJ01FF01
	QJ01GB03; QJ01GB90
	QS01AA11
	QD06AX04
	QS02AA14; QS02AA57
	QG51AA04
	QA07AA06
	QJ51RG01
	QJ51CE59
	QJ01XX04
other	QJ01XX10
	QJ01XQ01; QJ01XQ02
	QJ51XX01
	QJ01RA04
cephalosporins	QJ01DB01
	QJ01DD90; QJ01DD91
	QJ51DB01; QJ51DB04; QJ51DB90
	QJ01DE90
	QJ51DE90
	QG51AX02
	QJ51DD12
	QJ51RD01
amphenicols	QJ01BA90
	QS01AA01
macrolides	QJ01FA02; QJ01FA90; QJ01FA92; QJ01FA91; QJ01FA94; QJ01FA95
	QJ01FF02; QJ01FF52
	QJ51RF03

	QJ51FF90
penicillins	QJ01CA01; QJ01CA04; QJ01CA51
	QJ51RC26
	QJ01CR02
	QJ51CF02
	QJ01CE02; QJ01CE09; QJ01CE30; QJ01CE90
	QJ51CA51
polymixins	QJ01XB01
	QA07AA10
	QS02AA11
pyrimidins	QJ01EW10; QJ01EW13
	QJ01EA01
quinolones	QJ01MA90; QJ01MA92; QJ01MA93; QJ01MA94; QJ01MA95; QJ01MA96
	QJ01MB07
sulfonamides and trimethoprim	QJ01EW09; QJ01EW11; QJ01EW12
	QJ01EQ03
tetracyclines	QJ01AA02; QJ01AA03; QJ01AA06
	QD06AA02; QD06AA03