BelVet-SAC

Belgian Veterinary Surveillance of Antibacterial Consumption

National consumption report

2014

Summary

This sixth BelVetSAC report, covers the results of the data collection on veterinary antibacterial consumption in Belgium in the year 2014. Data consist of all veterinary antibacterials sold to a veterinarian or pharmacist in Belgium and of antibacterial premixes incorporated in medicated feed intended to be used in Belgium for the year 2014. 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 2014, plus the number of dairy cattle present in Belgium times their metabolic weight per head.

After two years of reduced use, this report shows **a substantial increase** in the **total consumption** of antibacterial compounds in veterinary medicine of **+3,2%** during 2014 compared to 2013. Due to the increase in animal production (expressed in biomass +2,1%) the **increase expressed in mg/kg biomass is +1,1%.** When using 2011 as a reference, still a reduction of 11,8% is achieved, distributed over a reduction of 12,2% in antibacterial pharmaceuticals and 10,0% in antibacterial premixes. Between 2007 and 2014 a total decrease of 23,3% is seen. Since September 2013 the use of Zinc oxide in therapeutic doses in piglets for two weeks after weaning is allowed. In 2013 with the first 4 months of allowance, 8075 kg of active substance of Zinc Oxide was used in Belgium. In 2014 the use further **increased substantially to 81 964 kg,** this corresponds to an estimated treatment of 70% of the raised piglets.

When looking more in detail to the different types of antibacterials used, it is observed that the penicillines (82,6 tons; 30,8%) sulphonamides and trimethoprim (77,3 tons; 28,9%) and tetracyclines (61,9 tons; 23,1%) remain the three most used antibacterial classes. In 2014 the use of penicillins increased by 2,2%, also a remarkable increase in the use of macrolides (+33,2%) and aminosydes (+11,0%) is observed. The use of the cephalosporins has increased in comparison to 2013 with 4,1% as well as the use of quinolones (+5,3%). The use of polymixines (almost entirely colistin sulphate) has dropped substantially with 28,1%. This reduction is seen for the second year in a row which is likely due to start of the use of zinc oxide as an alternative for colistin use in the treatment of post weaning diarrhea in piglets. However, given the very widely application of ZnO, the reduction in use of colistin is lesser than initially expected.

The obtained results on antimicrobial consumption in animals in 2014 are in all aspects very disappointing. It was believed / hoped that the continuous efforts in terms of information and sensibilisation by many concerned parties would result in a continued reduction in antimicrobial consumption as observed in the previous two years. . During 2014 no obvious animal health problems or parameters are known that would imply more antibiotic treatment to maintain the same level of animal health or welfare as in the previous years. Therefore the increased use can only be attributed to a relaxed attitude of

all stakeholders involved towards responsible and restricted antimicrobial use, regardless of the efforts and advices produced by AMCRA and others.

In conclusion, this disappointing result in 2014 should be seen as a strong motivator both to increase the efforts through sensibilisation and information and besides that to explore more stringent measures to force all stakeholders involved towards a reduction in use

Samenvatting

Dit zesde BelVetSAC rapport omvat de resultaten van het gebruik van antibacteriële middelen bij dieren in België in 2014. De gegevens omvatten alle antibacteriële middelen die werden verkocht aan een apotheker of dierenarts in België (=antibacteriële farmaceutica) evenals de antibacteriële voormengsels die via gemedicineerd diervoeder worden toegediend. Het betreft dus data over het gebruik van antibacteriële 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 2014 aangevuld met het aantal aanwezige melkkoeien vermenigvuldigd met hun metabool gewicht.

De totale consumptie van antibacteriëlemiddelen in de diergeneeskunde, uitgedrukt in ton actieve substantie, is na twee jaar op rij van substantiële daling, in 2014 met **+3,2% gestegen**. De totale biomassa geproduceerd in 2014 in België is met 2,1% gestegen waardoor waardoor de **stijging in gebruik in gebruik uitgedrukt in mg per kg geproduceerde biomassa +1,1%** bedraagt. Als 2011 als referentiejaar wordt genomen kan er nog steeds een reductie van 11,8% (in mg per kg geproduceerde biomassa) worden genoteerd opgedeeld in een reductie van 12,2% voor de farmaceuticals en 10,0% voor de premixen.

Wanneer meer in detail naar de verschillende types antibacteriëlemiddelen die worden gebruikt gekeken wordt merken we dat penicillines (82,6 ton; 30,8%), sulphonamides + TMP (77,3 tons; 28,9%) en tetracyclines (61,9 tons; 23,1%) de drie meest gebruikte antibacteriële klassen blijven. Het gebruik van penicillines is in 2014 met 2,2% gestegen. Er is tevens een opmerkelijke stijging in het gebruik van macroliden (+33,2%) en aminosiden (+11,0%) vast te stellen. Ook het gebruik van cefalosporines is met 4,1% gestegen en het gebruik van fluoroquinolones met 5,3%. Het gebruik van polymixines (bijna uitsluitend colistine sulfaat) is substantieel gedaald (-28,1%). Deze daling wordt voor het tweede jaar op rij vastgesteld en is vermoedelijk gerelateerd aan het gebruik van zink oxide als alternatief voor colistine in de behandeling van speendiarree. Echter, gegeven de zeer brede inzet van ZnO, is de waargenomen reductie in colistine lager dan initieel verwacht.

Het is duidelijk dat de resultaten voor 2014 in alle opzichten als erg teleurstellend moeten gezien worden. Het was verwacht / gehoopt dat de aanhoudende inspanningen van informatie en sensibilisatie door alle betrokken partijen zouden resulteren in het doorzetten van de trend die in de twee voorgaande jaren was te zien. Bovendien zijn er in in 2014 geen bijzondere diergezondheidsproblemen geweest die een stijging van het antibioticumgebruik zouden kunnen verklaren / rechtvaardigen. De enige verklaring die dus kan gevonden worden is een verminderde aandacht voor een verantwoordelijk en restrictief antibioticumgebruik door alle betrokken partijen. Dit ondanks de aanhoudende sensibilisatie en advisering vanuit AMCRA en anderen.

In conclusie kan gesteld worden dat dit teleurstellend resultaat moet gezien worden als een duidelijke en sterke motivator om het de inspanningen met betrekking tot informatie en sensibilisatie verder op te drijven maar evenzeer om de mogelijkheid voor implementatie van meer strikte maatregelen te onderzoeken die alle betrokkenen dwingen tot een sterkere reductie in gebruik.

Résumé

Ce sixième rapport BelVetSAC comprend les résultats de l’utilisation d’antimicrobiens chez les animaux en Belgique en 2014. Les données reprennent tous les antimicrobiens qui ont été vendus à un pharmacien ou un vétérinaire en Belgique (= produits pharmaceutiques antimicrobiens) ainsi que les prémélanges antimicrobiens qui ont été administrés au moyen d’aliments médicamenteux pour animaux. Il s’agit donc de données relatives à l’utilisation de substances antimicrobiennes tant chez les animaux d’élevage que chez les animaux de compagnie. Pour pouvoir comparer l’utilisation par rapport au nombre d’animaux présents, on utilise comme dénominateur la biomasse. Elle est calculée comme la somme des kilogrammes de viande de porcs, volailles et bovins produits en Belgique en 2014 additionnée du nombre de vaches laitières présentes multiplié par leur poids métabolique.

La consommation totale de produits antimicrobiens en médecine vétérinaire, exprimée en tonnes de substance active, a **augmenté** de **+3,2%** en 2014 après deux années consécutives de diminution substantielle. La biomasse totale produite en 2014 en Belgique a augmenté de 2,1%. **L’augmentation de l’utilisation de produits antimicrobiens exprimée en mg par kg de biomasse produite** est ainsi de **+1,1%**. Si l’on prend 2011 comme année de référence, on peut encore noter une réduction de 11,8% (en mg par kg de biomasse produite), répartie comme suit : une réduction de 12,2% pour les produits pharmaceutiques et de 10,0% pour les prémélanges.

Lorsqu’on regarde en détail les différents types de produits antimicrobiens utilisés, on remarque que les pénicillines (82,6 tonnes ; 30,8%), les sulfonamides + TMP (77,3 tonnes ; 28,9%) et les tétracyclines (61,9 tonnes ; 23,1%) restent les trois classes d’antimicrobiens les plus utilisés. L’utilisation de pénicillines a augmenté de 2,2% en 2014. Il faut également noter une augmentation notable de l’utilisation de macrolides (+33,2%) et d’aminosides (+11,0%). L’utilisation de céphalosporines a également augmenté de 4,1% et l’utilisation de fluoroquinolones de 5,3%. L’utilisation de polymixines (presqu’exclusivement du sulfate de colistine) a substantiellement diminué (-28,1%). Cette diminution est constatée pour la deuxième année de suite et est probablement liée à l’utilisation d'oxyde de zinc comme alternative à la colistine dans le traitement de la diarrhée de sevrage. Toutefois, vu l’emploi très large du ZnO, la réduction de l’utilisation de la colistine est moins importante qu’initialement attendu.

Il est clair que les résultats pour 2014 doivent être considérés à tous points de vue comme très décevants. On espérait/s’attendait à ce que les efforts continus en matière d’information et de sensibilisation fournis par toutes les parties concernées se traduisent par la poursuite de la tendance observée au cours des deux années précédentes. En outre, aucun problème particulier de santé animale pouvant expliquer/justifier une augmentation

de la consommation d'antimicrobiens n'a eu lieu en 2014. La seule explication qui peut donc être trouvée est une diminution de l'attention accordée à l'utilisation responsable et restrictive d'antimicrobiens par toutes les parties concernées et ce malgré la sensibilisation et les conseils continus de la part de l'AMCRA et d'autres.

Pour conclure, on peut dire que ce résultat décevant doit être vu comme une source de motivation claire et forte pour stimuler davantage les efforts en matière d'information et de sensibilisation mais également pour examiner la possibilité d'implémentation de mesures plus strictes qui forcent tous les intéressés à réduire plus fortement l'utilisation d'antimicrobiens.

Preface

Antibacterials are valuable tools in the preservation of animal health and animal welfare, and must be used responsibly as they may save lives and prevent animal suffering. However, The use of antibacterials invariably leads to selection of bacteria that are resistant against the substance used. Resistance can then spread in populations and the environment.
Antibacterial consumption in animals selects for antibacterial 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.

Today, antibacterial consumption and its link to antibacterial resistance in humans and animals is a worldwide point of concern. The World Health Organization has indicated the follow up of antibacterial resistance as one of the top priorities for the coming years. In 2013, the world economic forum has indicated the emergence of antibacterial resistance a global threat with the ability of destabilizing health systems, profound cost implications for economic systems and for the stability of social systems.

Given the importance in securing both public as animal health and since it is by far the leading driver for antibacterial resistance, it is crucial to measure the level of Antibacterial consumption and antibacterial resistance in animals. This is moreover also required at the European level where consumption data of antibacterials in veterinary medicine are collected by EMA (European Medicines Agency) in the framework of the ESVAC (European Surveillance of veterinary Antibacterial Consumption) project. Therefore the data collected and presented in this report also fit into the European commitments of Belgium. This sixth BelVetSAC report gives an overview of the consumption of antibacterials in veterinary medicine in Belgium in 2014 and describes evolutions in use since 2007.

Contents

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Materials and Methods

Data collection

1. Antibacterials antibacterials for veterinary use

a. Antibacterial pharmaceuticals

Sales data of all products in all pharmaceutical formulations registered on the Belgian market that contain antibacterials 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. Februari 2015 to upload the required data via a secured web-application (www.belvetsac.ugent.be). The required data consisted of all veterinary antibacterials sold in the year 2014 to a veterinarian or pharmacist in Belgium. In Belgium, Antibacterial products are only available on prescription or by delivery from the veterinarian. Belgian veterinarians can both use antibacterial 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 antibacterial containing veterinary medicinal products authorized and marketed on the Belgian market was provided, together with its market authorization holder and national code, formulation and package form. The wholesaler-distributor only needed to provide the number of packages sold for each product per year.

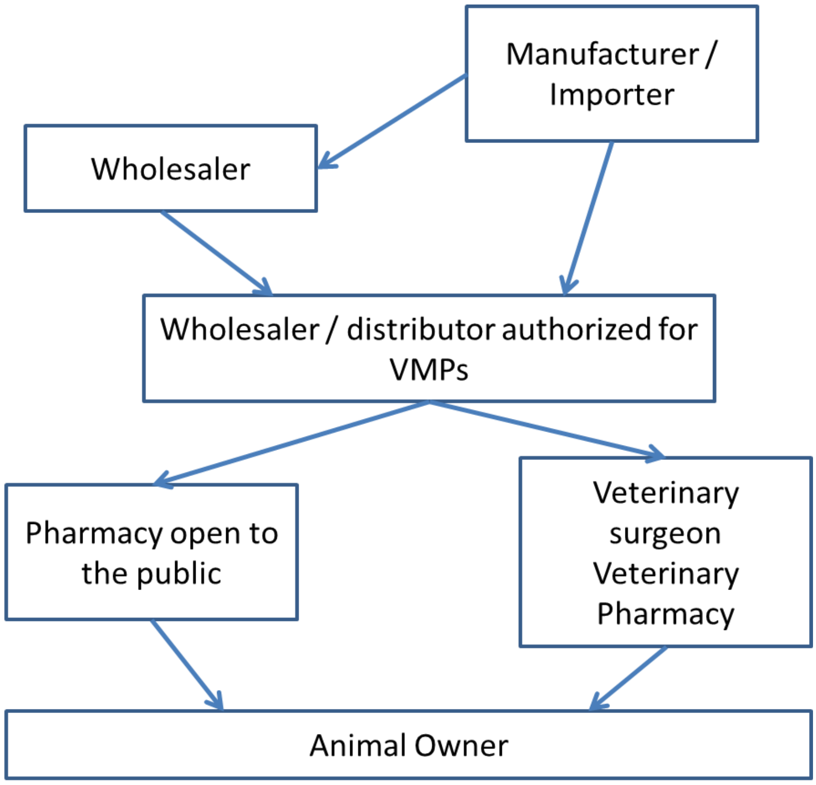


Figure 1. Distribution of Veterinary Medicinal products in Belgium.

b. Antibacterial premixes

As Antibacterial 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 collected. This was done by contacting all Belgian compound feed producers that are licensed to produce medicated feed http://www.favv-afsca.be/bo-documents/Inter_R0-1002_3_dierlijke_producten_erkende_bedrijven.PDF (n=57). They received a list of registered and marketed Antibacterial containing premixes. The feed mills were asked by letter dd. Februari 2014 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 on medicated feed delivered at Belgian farms 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 Antibacterial containing premixes for the year 2014. Antibacterial premixes can only be incorporated into medicated feed on prescription of a veterinarian.

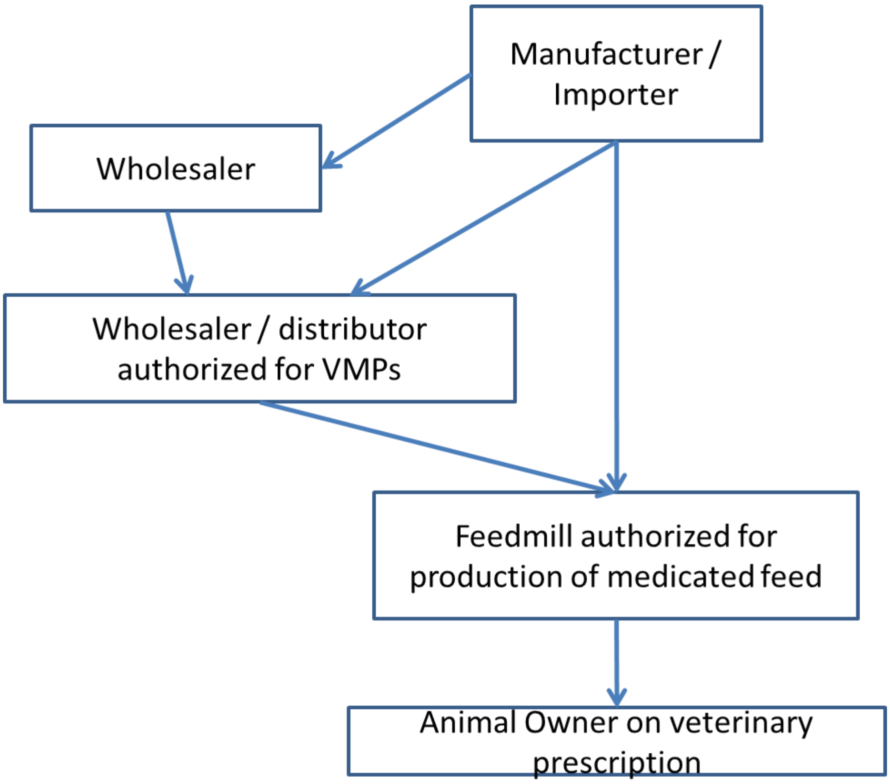


Figure 2. Distribution of Veterinary premixes in Belgium.

c. Antibacterial classes included

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

In the BelVetSAC data collection all antibacterials used for veterinary medicine are covered (Table 1). No antibacterials are excluded which is in contrast to the ESVAC reporting system where antibacterials for dermatological use and for use in sensory organs are excluded. This explains why data as presented in the report may partially divert from what is reported for Belgium in the ESVAC report.

Since the use of Zinc Oxide is authorized in Belgium since September 2013 data on Zinc Oxide were also collected and are presented separately.

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

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

2. Animal population

Animal population 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 population 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 in accordance with the ESVAC recommendations. This additional information consisted of:

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

As in the previous reports (BelVetSAC 2007-2009; BelVetSAC 2010; BelVetSAC 2011; BelVetSAC 2012, BelVetSAC 2013), 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 antibacterial 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 antibacterial 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 difficult. 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. In the future data collection at animal species level is intended and also at European level the ESVAC project is aiming at refining the data collection at species level.

For antibacterial premixes, already today we know for what animal species they are intended (only pigs, poultry and rabbits receive medicate feed) therefore we can further distinguish the use of antibacterial 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 compound 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. However, trends and evolutions in the different dataset can be compared. Only if large discrepancies were observed data validity was 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 were observed between the data provided in the subsequent years data validity was 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 antibacterial products sold in 2013 responded. All 57 compound feed producers, licensed for the production of medicated feed responded. Of these 5 indicated not to have produced any medicated feed and 52 delivered the data on antibacterial premixes incorporated in medicated feed to be used in Belgium. Based on the response rate data coverage is assumed to be 100%.

As in the previous year the internal data validation step showed to be of huge importance since important differences were found for two large wholesaler-distributor. Both were contacted but they confirmed that the provided information for 2014 was correct. Also for the producers of medicated feed 8 compound feed producers were identified with large differences in provided data in comparison to the previous year. Of these, 3 companies found out that they provided us with incorrect data and new, corrected, data files were foreseen.

In the cross-validation of the data with the databases with 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. As the cross-validation with Pharma.be is concerned, this is becoming increasingly more difficult and less valuable because only very crude data are provided by pharma.be (at the level of antimicrobial classes and not at the compound level as was done in the past). Moreover many of the observed substantial variations in antimicrobial consumption are origination from compounds that are both available as original product and as generic product. Data on the latter are largely lacking in the pharma.be database since these companies are often no member of pharma.be.

Number of antibacterial pharmaceuticals and premixes available on the Belgian market

Table 2 provides an overview of the number of antibacterial pharmaceuticals and the number of antibacterial premixes available on the Belgian market since 2009 according to the commented compendium of the Belgian Centre for Pharmacotherapeutic Information (www.bcfi-vet.be).

Table 2. Armatorium of antibacterial products on the Belgian market in between 2009 and 2014.

	2009[1]	2010	2011	2012	2013	2014
Number of Antibacterial pharmaceuticals on the market	283	292	282	308	294	**298**
Number of Antibacterial premixes on the market	20	21	23	22	23	**21**
Total number of Antibacterial products on the market	303	313	305	330	317	**319**

The only new antibacterials registered on the market in the last 5 years are gamithromycin (2009), tildipirosin (2011), pradofloxacine (2011) and fusidic acid (2014). The observed variation in available products is largely due to the marketing of new formulations or new generic products based on existing active substances.

Animal biomass produced in Belgium

The produced biomass was calculated based on the Eurostat data for the years 2008-2013 as described above (Table 3).

Table 3. Animal Biomass produced in Belgium between 2010 and 2014.

Animal biomass	2010	2011	2012	2013	2014
Meat (ton)					
Pork	1 123 769	1 108 255	1 109 610	1 130 570	1 118 330
Beef	263 142	272 286	262 280	249 910	257 670
Poultry[a]	404 343	402 753	410 215	388 090	433 270
Total biomass from meat production	**1 791 254**	**1 783 294**	**1 782 105**	**1 768 570**	**1 809 270**
Dairy cattle					
Dairy cattle (number)	517 700	510 600	503 500	515 990	519 090
Dairy cattle metabolic weight (ton)	258 850	255 300	251 750	257 995	259 545
Total biomass (ton)	**2 050 104**	**2 038 594**	**2 033 855**	**2 026 565**	**2 068 815**

[a] data on biomass of poultry production between 2008 and 2012 were retrospectively changed in the Eurostat database. The data presented in this report are in agreement with what is currently available in the Eurostat database and differ slightly from what was presented in previous BelVetSAC reports.

An **increase in biomass production of 2,1%** is observed between 2013 and 2014.

[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.

Total consumption of Antibacterial drugs for veterinary use in Belgium

The total consumption of antibacterial 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 antibacterial pharmaceuticals and the part of antibacterial compounds contained in antibacterial premixes incorporated into medicated feed intended to be used in Belgium.

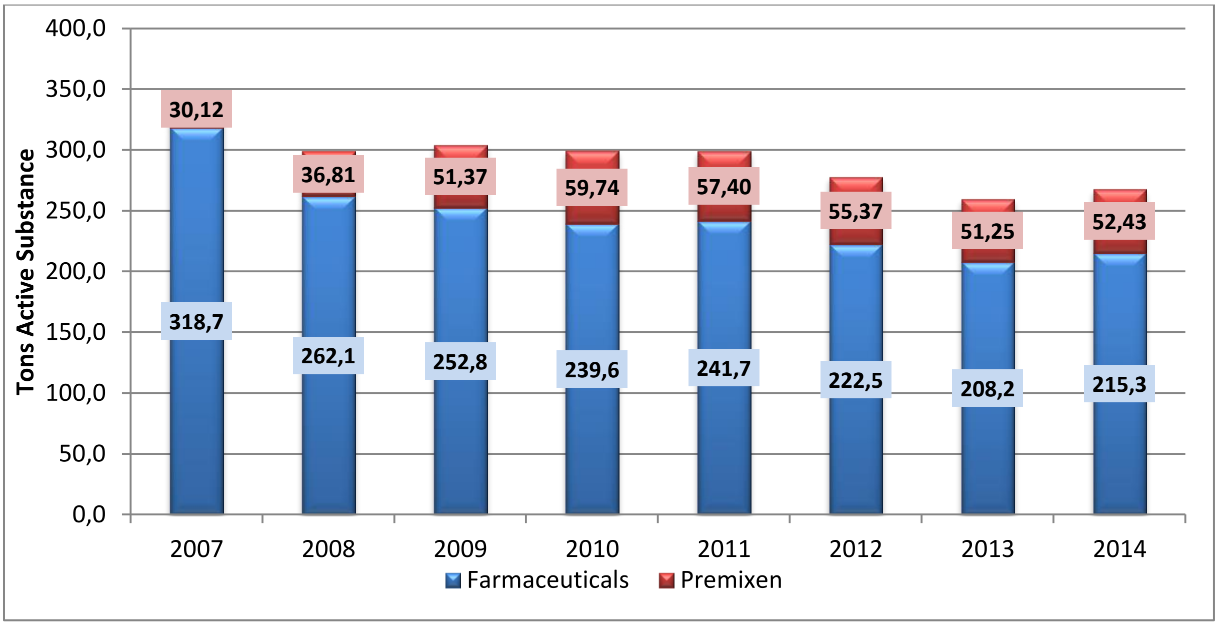


Figure 3. Total national consumption of antibacterial compounds for veterinary use in Belgium for the years 2007-2014 (tons active substance)

Between 2013 and 2014, there was an **increase of 3,2%** in the total consumption of antibacterials in veterinary medicine in Belgium (267 744,0 kg in 2014; 259 449,5kg kg in 2013). The use of antibacterial **pharmaceuticals increased with 3,4%** between 2013 and 2014, and the use of **antibacterial premixes increased with 2,3%.** When looking at the trend from 2007 onwards (start data collection) still a decrease of 23,2% in total consumption is observed, yet de decreasing trend of the last 2 years (2012 and 2013) has clearly come to a halt with even an increase of the antibacterial consumption in 2014.

Figures 4 and 5 show these data separately for the antibacterial pharmaceuticals and the antibacterial premixes.

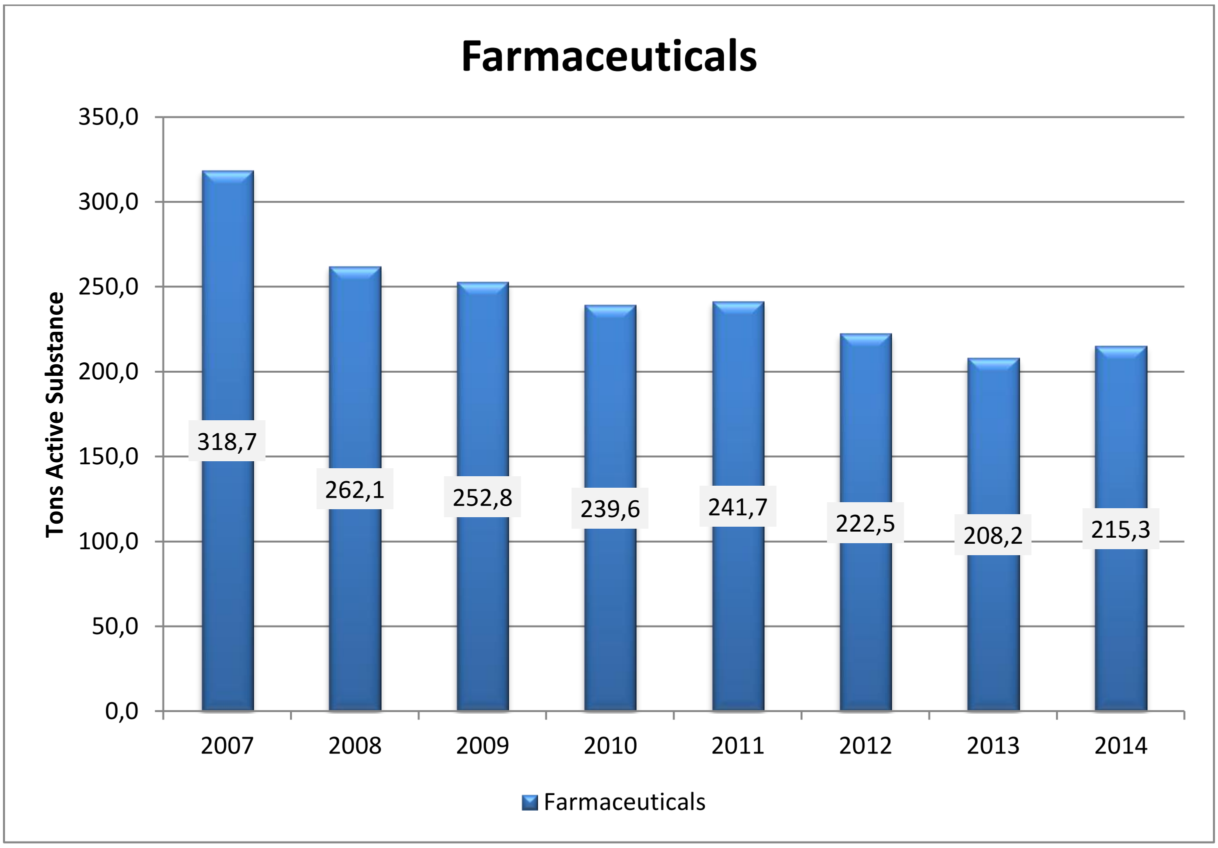


Figure 4. National consumption of antibacterial pharmaceuticals for veterinary use in Belgium for the years 2007-2014 (tons active substance)

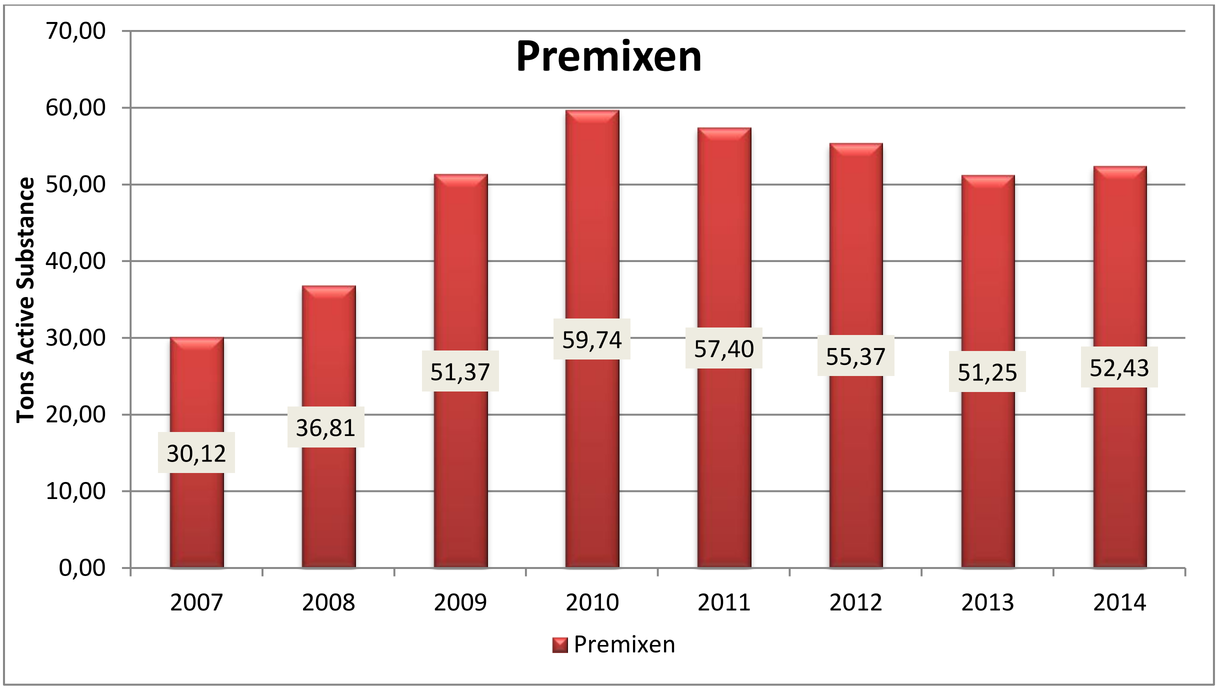


Figure 5. National consumption of antibacterial premixes in Belgium for the years 2007-2014 (tons active substance)

After an increase in use of Antibacterial premixes between 2007 and 2010, the decreasing trend firstly observed in 2011 continued to 2013. In 2014 this decrease came to an end and first small increase was observed again. Since 2011 the data collection system allows to differentiate the animal species of destination for the Antibacterial premixes. Over these years more than **99,6% of the antibacterial premixes go to pig feed**. In 2014 only 0,4% was used in poultry or rabbit feed.

Since September 2013 the use of Zinc oxide in therapeutic doses (corresponding to 2500 ppm of Zn) in piglets for two weeks after weaning is allowed (temporary authorization). In 2013, the first 4 months of allowance, 8075 kg of active substance of Zinc Oxide was used in Belgium. In 2014 the use further **increased substantially to 81 964 kg** as is presented in figure 6.

Given a treatment dose of 3kg of ZnO per ton of feed (corresponding tot 2500ppm Zn per kg) and an assumed consumption of 3-4 kg of feed in the first two weeks after weaning, it can be calculated that 81.964 kg ZnO corresponds to 27.321.333 kg of medicated feed. Calculating with 4 kg per piglet this accounts for an estimated 6.830.000 piglets treated (~ 70 % of all annually raised piglets).

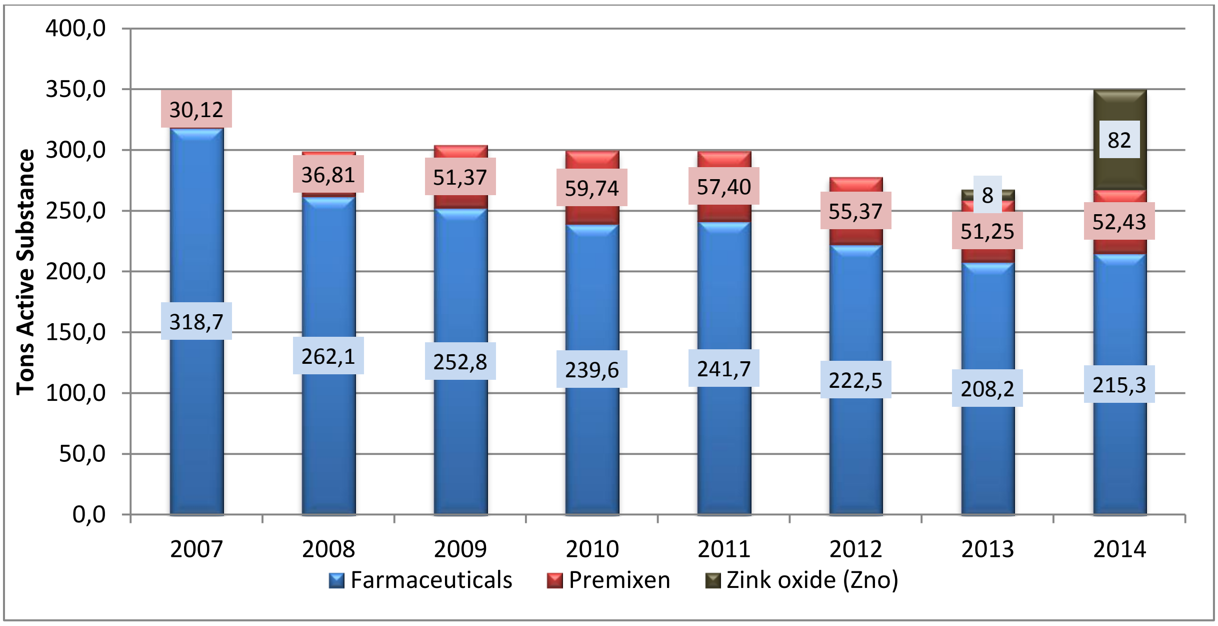


Figure 6. Total national consumption of antibacterial compounds for veterinary use in Belgium plus the use of ZnO for the years 2007-2014 (tons active substance)

Antibacterial use versus biomass

As described above, the total biomass production in 2014 in Belgium has increased with 2,1% in comparison to 2013. As a consequence the increasing trends in use observed in absolute values is slightly moderated in the relative numbers. For 2013, the mg of active substance used in comparison to the kg biomass produced was 128 mg/kg in 2014 this was 129,4 mg/kg. This is **an increase of 1,1% in comparison to 2013.**

Figure 7 presents these data, again subdivided into antibacterial pharmaceuticals and antibacterial premixes.

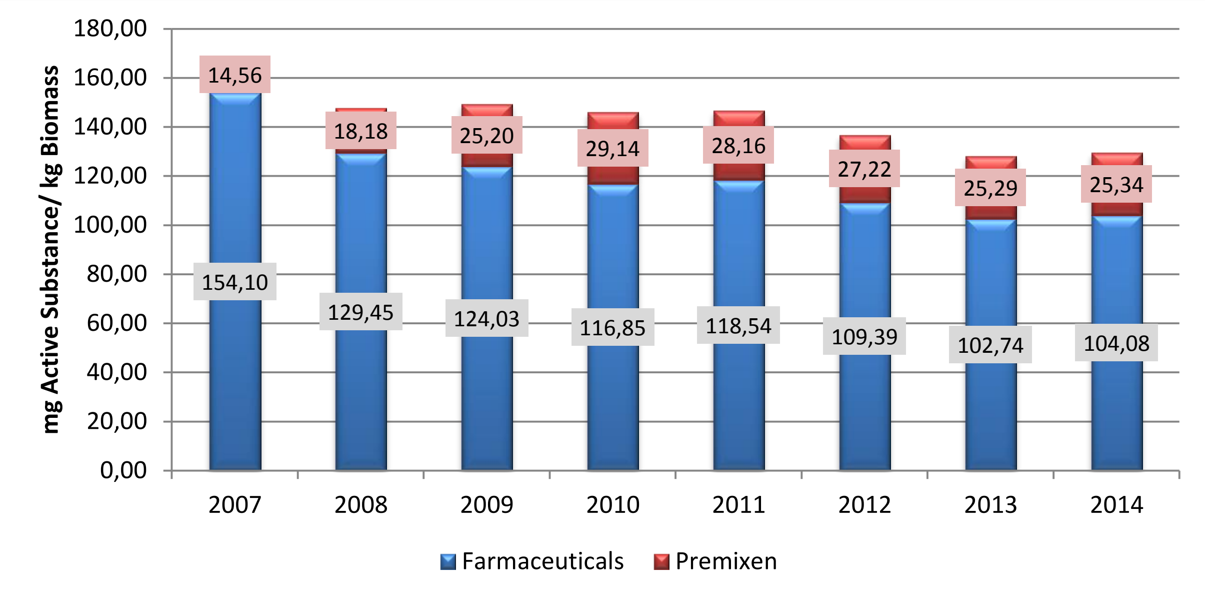


Figure 7. Total mg of active substance used per kg biomass produced in Belgium for 2007-2014.

After a substantial decrease in use per kg biomass produced in 2012 (-6,9%) and 2013 (-6.3%), the positive downward trend was fully stopped in 2014 and even **changed into an increase of 1,1% in 2014**.

When using 2011 as a reference (see AMCRA 2020 objectives), still a reduction of 11,8% is achieved, distributed over a reduction of 12,2% in antibacterial pharmaceuticals and 10,0% in antibacterial premixes. Between 2007 and 2014 a total decrease of 23,3% is seen.

Positioning of Belgium in comparison to the EU member states.

Since a number of years the European Medicines Agency (EMA) runs the European Surveillance of antibacterial Consumption (ESVAC) project that aims at collection Antibacterial usage data in all EU member states in a comparable manner allowing to evaluate trends and compare usage between countries. The data collected in Belgium and presented in the annual BelVetSAC reports are also collected in the framework of this EU wide ESVAC data collection effort.

In 2014, the fourth ESVAC report, presenting results on antibacterial usage in 26 EU /EEA countries in the year 2012 has become available (EMA, 2014). In this report the **antibacterial**

consumption in animals in these 26 countries in 2012 is presented in relation to the animal production in the country.

In figure 9 the results of the 26 countries included in the fourth ESVAC report are presented in mg active substance used and the animal production quantified by means of the Population Correction Unit (PCU) which is comparable to the biomass used in this BelVetSAC report but also includes small ruminants and horses and corrects more thoroughly for import and export.

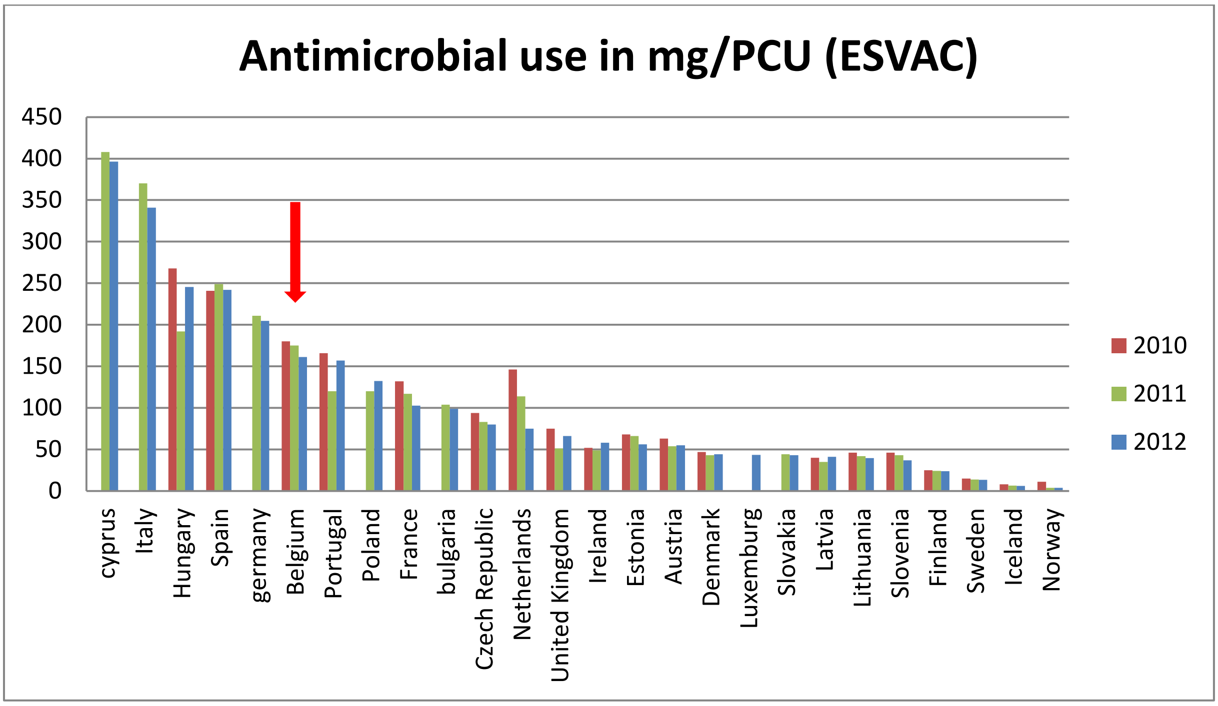


Figure 8. Sales for food-producing species, including horses, in mg/PCU, of the various veterinary Antibacterial classes, by country between 2010-2012 (source: 2°, 3°, 4° ESVAC report on Sales of veterinary Antibacterial agents).

When looking at figure 9 it can be observed that Belgium remains at the sixth highest level of Antibacterial usage expressed in mg/PCU in 2012. This indicates that many EU countries are using substantially less antibacterials in relation to the magnitude of their animal production. The reduction in antibacterial consumption observed in 2013 may improve this situation, yet in 2014 there will certainly be no improvement whereas many other countries throughout the EU take measures and organize campaigns to reduce Antibacterial usage and therefore will likely improve their situation. As a consequence, with the results of 2014 Belgium may even go up in the ranking of highest consumers of antimicrobials per kg biomass produced.

Antibacterial use per class of Antibacterial compounds

1. Total consumption (Antibacterial pharmaceuticals and premixes)

In Figure 9 the total consumption of antibacterials per class (ATC level 3 or 4) is presented.

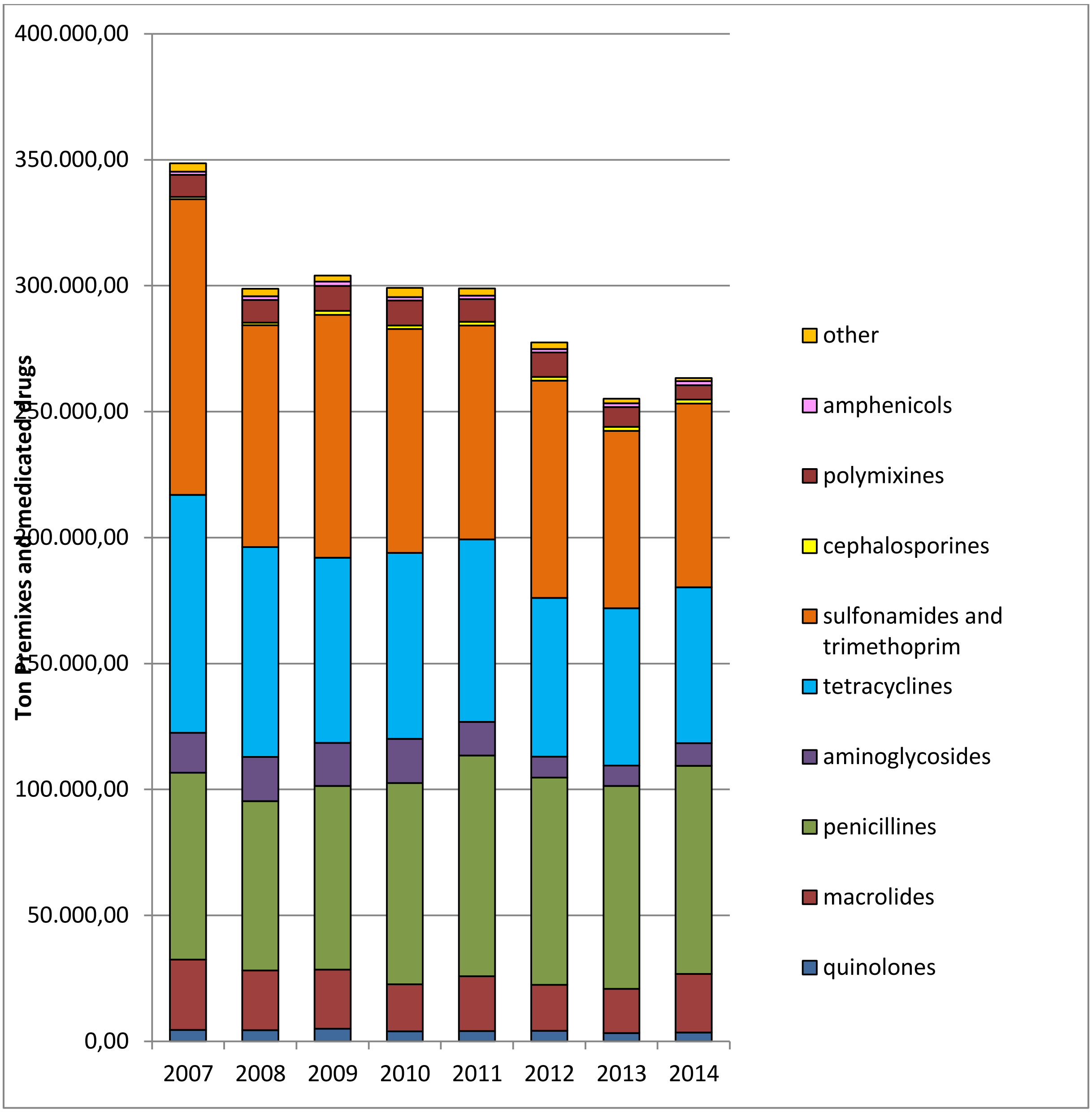


Figure 9. Total Antibacterial use per class of antibacterials.

In 2014, the most used group of antibacterials were the penicillines (82,6 tons; 30,8%) followed by the sulphonamides and trimethoprim (77,3 tons; 28,9%) and the tetracyclines (61,9 tons; 23,1%). 2014 is the second year in a row where the penicillines have become the most used compound. In table 5 the evolution of the used products per antimicrobial class in the last 4 years is presented.

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

	Totaal				Evolution		
Class	2011	2012	2013	2014	'11 » '12	'12 » '13	'13 » '14
penicillins	87.863,3	82.467,8	80.816,9	82.561,7	-6,1%	-2,0%	2,2%
sulphonam & trimethoprim	84.902,8	86.273,5	74.556,9	77.346,2	1,6%	-13,6%	3,7%
tetracyclines	72.454,1	63.006,2	62.411,1	61.901,1	-13,0%	-0,9%	-0,8%
macrolides	21.843,0	18.191,8	17.503,9	23.319,2	-16,7%	-3,8%	33,2%
polymixins	9.102,7	9.635,8	7.875,5	5.659,1	5,9%	-18,3%	-28,1%
aminosydes	13.166,9	8.313,9	8.089,6	8.982,6	-36,9%	-2,7%	11,0%
quinolones	4.088,5	4.216,9	3.315,1	3.491,7	3,1%	-21,4%	5,3%
other	2.771,0	2.578,1	1.827,0	1.263,2	-7,0%	-29,1%	-30,9%
cephalosporins	1.489,7	1.529,8	1.540,4	1.603,6	2,7%	0,7%	4,1%
fenicols	1.354,4	1.435,5	1.513,3	1.616,1	6,0%	5,4%	6,8%
Totaal (kg)	**299.037**	**277.649**	**259.450**	**267.744**	**-7,15%**	**-6,55%**	**+ 3.2 %**

In 2014 the use of penicillins increased by 2,2% (table 5), also a remarkable increase in the use of macrolides (+33,2%) and aminosydes (+11,0%) is observed. The increased use of macrolides is almost solely due to an increase in the use of tylosine (see table 6). The increased use in aminosydes is mainly due to an increase in use of linco-spectine. The use of the cephalosporins has increased in comparison to 2013 with 4,1% as well as the use of quinolones (+5,3%). The use of polymixines (almost entirely colistin sulphate) has dropped substantially with 28,1%. This reduction is seen for the second year in a row which is likely due to start of the use of zinc oxide as an alternative for colistin use in the treatment of post weaning diarrhea in piglets. However, given the very widely application of ZnO (~70% of population; see above) the reduction in use of colistin is lesser than initially expected. Moreover these data suggest that in some cases zinc oxide and colistin are used simultaneously although this is not allowed according to the SPC's of the ZnO premixes.

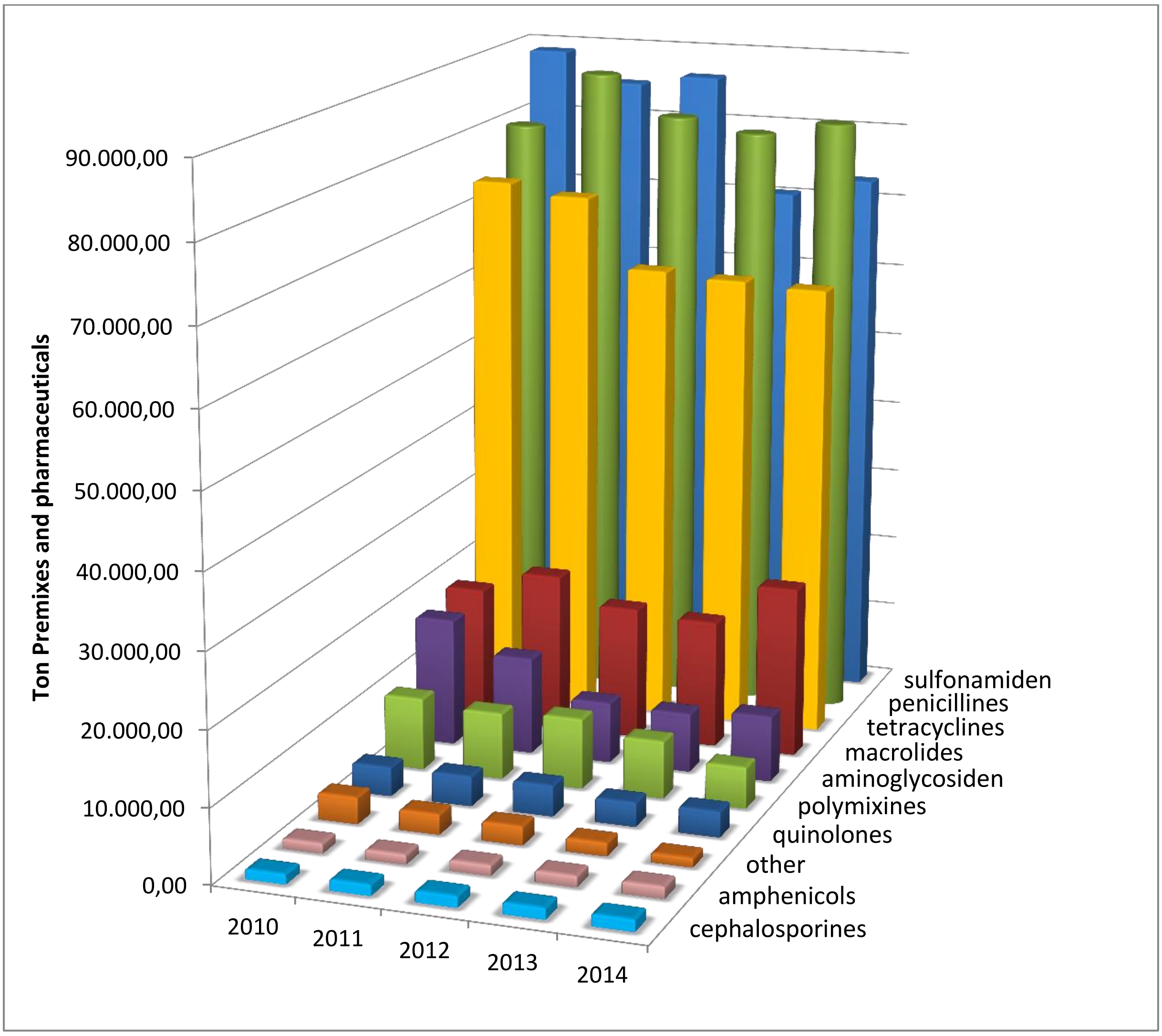


Figure 10: Evolution in the antibacterial consumption (kg) per antibacterial class. (Sulphonamides include also trimethoprim)

In 2013 AMCRA (center of expertise on Antimicrobial Consumption and Resistance in Animals (www.amcra.be)) has produced it first guides on responsible antibacterial consumption (AMCRA, 2013). In these guides the different antibacterial classes available in veterinary medicine are given a color to differentiate them in terms of importance for human and animal health. The ranking of importance is based on the WHO list on antibacterial used in veterinary medicine with importance for human health (http://apps.who.int/iris/bitstream/10665/77376/1/9789241504485_eng.pdf) and the lists produces by the world animal health organization (OIE) concerning the importance of antibacterials for veterinary health (http://web.oie.int/downld/Antibacterials/OIE_list_Antibacterials.pdf). When producing the lists priority was given to human health.

The group of yellow products contains the antibacterial classes with the lowest importance for human medicine in terms of resistance selection and transfer and therefore no additional restrictions, on top of the legal requirements, are suggested for the use of these compounds. The yellow group contains the majority of the penicillins, the sulphonamides (and diaminopyrimidines), the cephalosporins of the first generation and the phenicols.

The group of orange products are of higher importance for human medicine and should therefore be used restrictively and only after good diagnostics allowing to target the therapy. The orange group contains the highest amount of different molecules including all available macrolides, the polymixins, the aminoglycosides, the tetracyclines and the aminopenicillins.

The red group of products are the products of the highest importance for human medicine and therefore their use should be avoided in veterinary medicine as much as possible. AMCRA advises to use these molecules only under very strict regulations. This group contains the cephalosporins of the 3° and 4° generation and the fluoroquinolones.

In figure 11 the evolution of use of the different color groups of antibacterials over the last 4 years is presented. From this figure it can be seen that the orange groups is the most widely used group whereas the red molecules are only limitedly used when expressed in kg active substance. Yet the red molecules are generally more modern molecules with a high potency and therefore a low molecular weight in relation to their treatment potential. In 2014 an increase in use in all three groups is observed. Obviously the increase in use in the red molecules is the most worrisome.

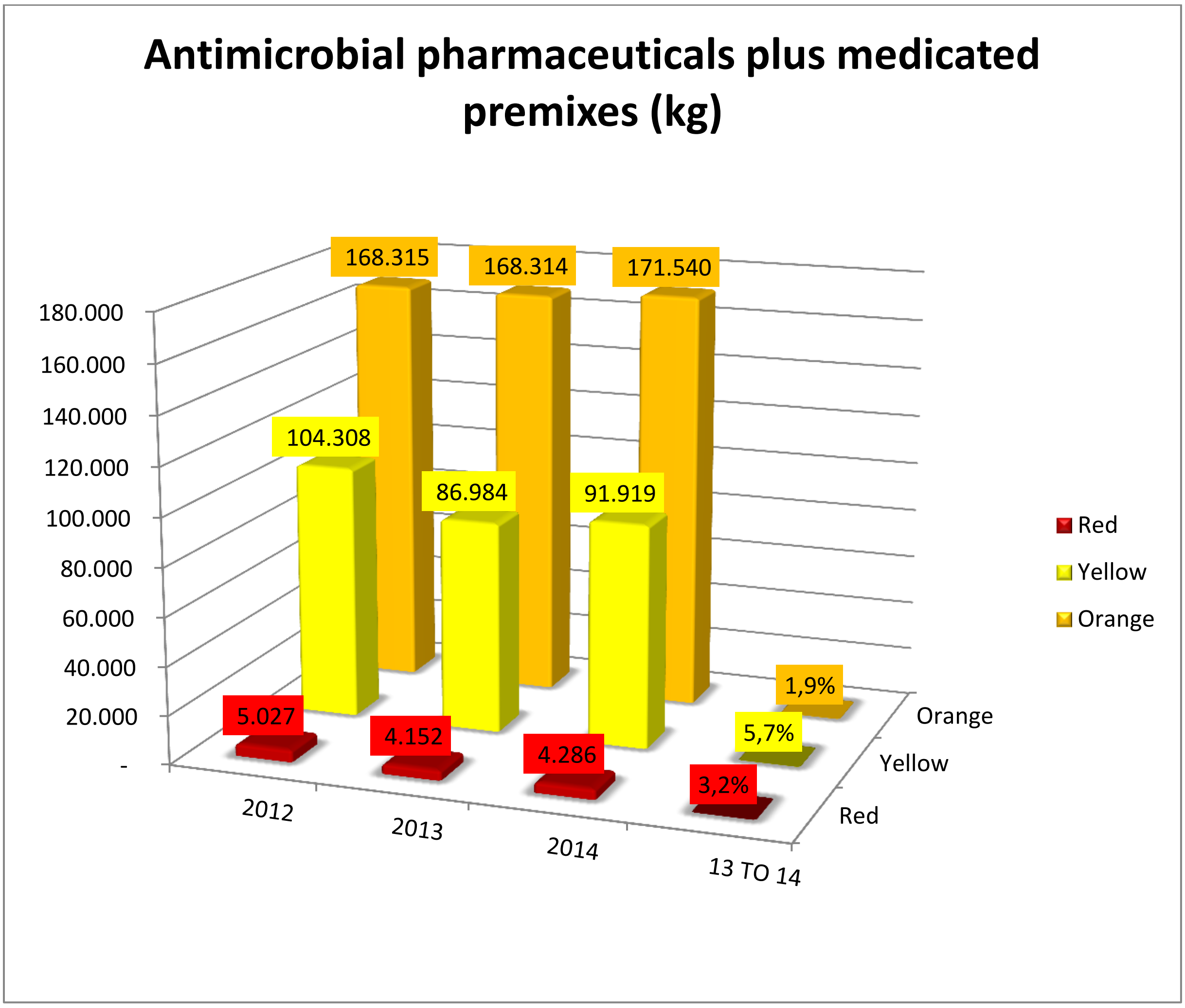


Figure 11: Evolution in the antibacterial consumption (kg) per antibacterial color group between 2012 and 2014.

2. Antibacterial pharmaceuticals

In Figure 12 the consumption of antibacterials per class (ATC level 3 or 4) is presented for the pharmaceuticals.

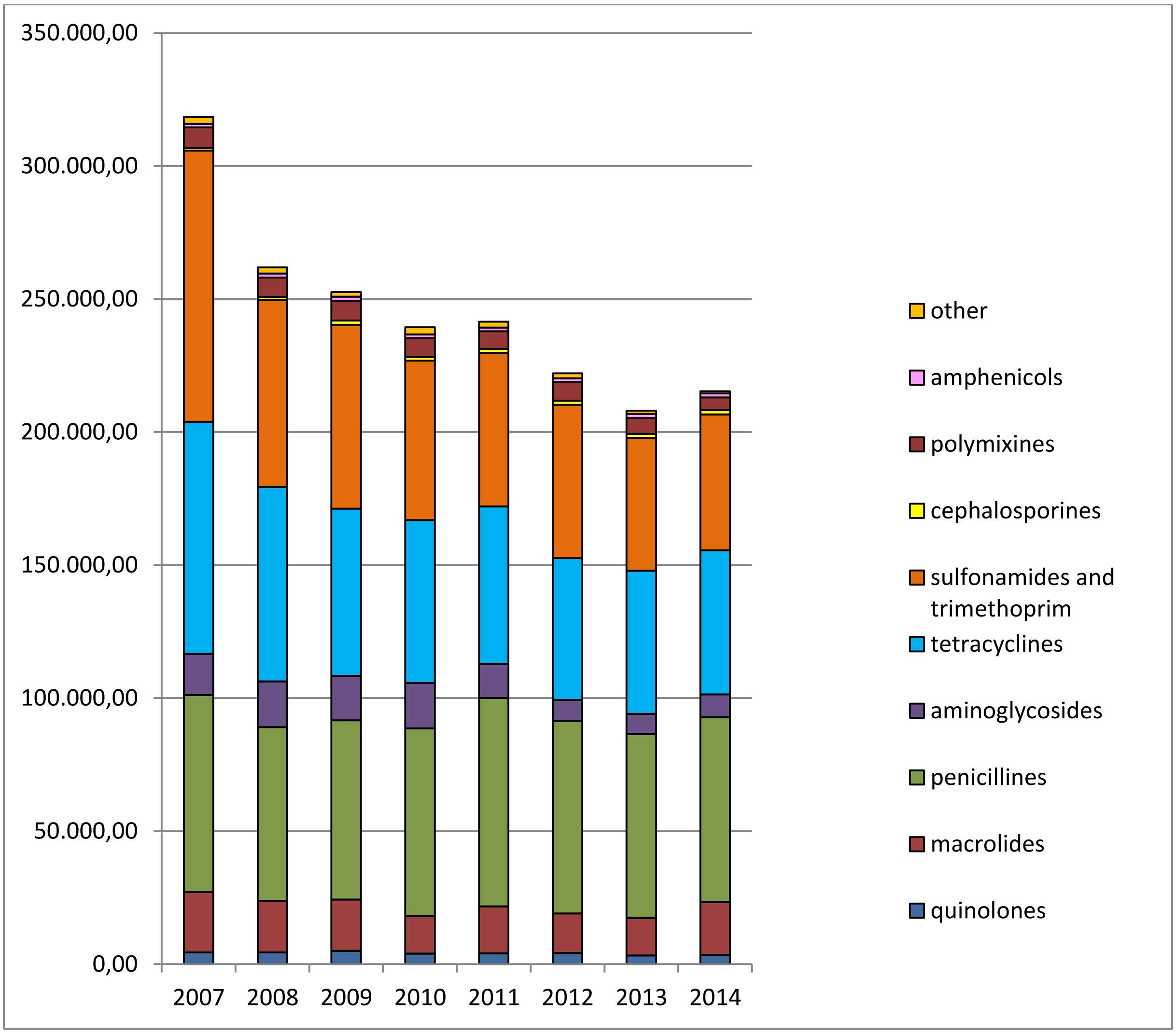
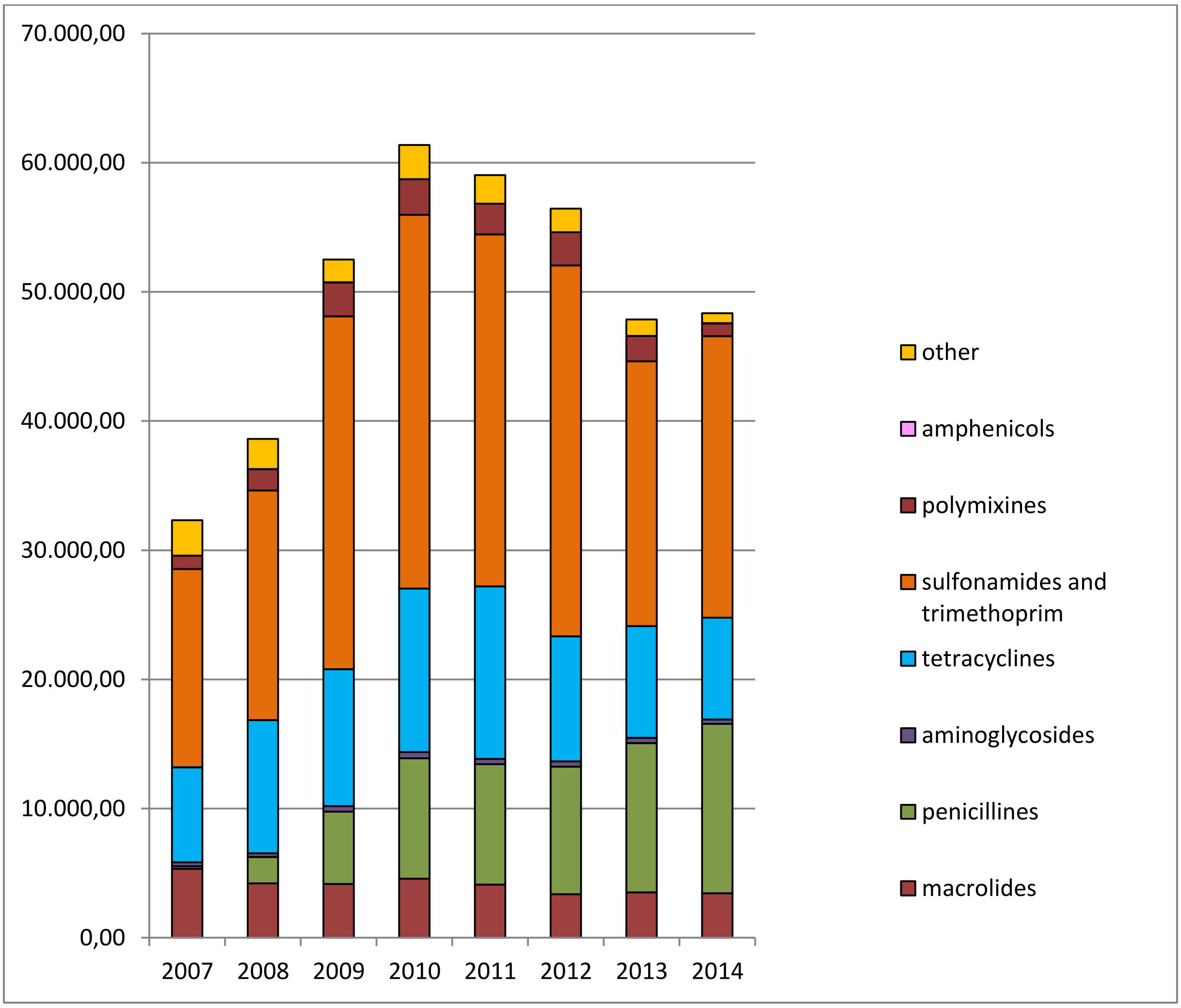


Figure 12. Use of antibacterial pharmaceuticals per class of antibacterials between 2007 and 2014.

3. Antibacterial premixes

In Figure 13 the consumption of antibacterials per class (ATC level 3 or 4) is presented for the Antibacterial premixes.

Figure 13. Use of antibacterial premixes per class of antibacterials between 2007 and 2014.



Antibacterial use per active substance

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

Table 6: Antibacterial use per active substance

		Total (kg)				Antimicrobial pharmaceuticals (kg)_GV				Medicated premixes (kg)_MD			
Class	Antimicrobial compound	2011	2012	2013	2014	2011	2012	2013	2014	2011	2012	2013	2014
Amino(glyco)sides	dihydrostreptomycine	4.236	0	13	9	4.236	0	13	9				
	gentamicine	132	127	127	127	132	127	127	127				
	kanamycine	15	23	18	18	15	23	18	18				
	neomycine	1.209	1.267	1.037	766	1.209	1.267	1.037	766				
	paromomycine	2.909	2.619	2.534	2.691	2.909	2.619	2.534	2.691				
	spectinomycine	4.473	4.076	4.198	5.225	4.139	3.766	3.883	4.960	334	311	314	265
	framycetinesulfaat		2	5	7		2	5	7				
	apramycine	192	198	159	142	96	96	60	55	96	103	98	87
Cephalosporins 1G	cefalexine	605	699	675	768	605	699	675	768				
	cefalonium	22	10	14	12	22	10	14	12				
	cefapirine	10	10	5	13	10	10	5	13				
	cefazoline	2	1	10	17	2	1	10	17				
Cephalosporins 3G	cefoperazon	6	4	6	5	6	4	6	5				
	cefovecin	10	10	9	9	10	10	9	9				
	ceftiofur	651	594	624	598	651	594	624	598				
Cephalosporins 4G	cefquinome	183	202	197	181	183	202	197	181				

Fenicols	chlooramfenicol	2	0	0	0	2	0	0	0				
	florfenicol	1.352	1.435	1.513	1.616	1.333	1.435	1.513	1.580	19	0	1	36
fluoroquinolones	danofloxacine	72	69	67	69	72	69	67	69				
	difloxacine	12	9	8	1	12	9	8	1				
	enrofloxacine	1.061	1.088	1.361	1.411	1.061	1.088	1.361	1.411				
	flumequine	2.675	2.734	1.535	1.565	2.675	2.734	1.535	1.565				
	ibafloxacine	1	1	1	0	1	1	1	0				
	marbofloxacine	267	308	335	438	267	308	335	438				
	orbifloxacine	1	2	3	3	1	2	3	3				
	pradofloxacine		6	6	5		6	6	5				
Macrolides	clindamycine	138	137	144	148	138	137	144	148				
	erythromycine	0	0	0	1	0	0	0	1				
	gamithromycine	26	18	20	20	26	18	20	20				
	lincomycine	5.654	5.218	4.425	4.803	5.055	4.516	3.962	4.538	599	702	463	265
	pirlimycine	0	0	0	0	0	0	0	0				
	spiramycine	111	22	24	76	111	22	24	76				
	tildipirosine		20	34	40		20	34	40				
	tilmicosine	4.489	2.917	4.118	4.380	2.614	1.446	2.361	2.467	1.875	1.471	1.757	1.913
	tulathromycine	57	70	109	101	57	70	109	101				

	tylosine	11.367	9.763	8.456	13.475	9.733	8.573	7.173	12.201	1.634	1.190	1.283	1.274
	tylvalosin		25	172	276		25	172	276				
Other	metronidazol	49	88	92	94	49	88	92	94				
	rifaximin	17	20	115	23	17	20	115	23				
	tiamuline	2.518	2.374	1.547	1.048	2.106	1.692	1.028	616	412	681	519	432
	valnemuline	153	69	39	59	0	0	0	0	153	69	39	59
	zink bacitracine	33	27	33	39	33	27	33	39				
penicillines	amoxicilline	72.827	68.667	71.897	71.420	63.510	58.782	60.332	58.320	9.317	9.885	11.565	13.101
	amoxicilline-clav	954	189	181	215	954	189	181	215				
	ampicilline	251	291	240	235	251	291	240	235				
	benethamine penicilline			10	8			10	8				
	cloxacilline	513	416	380	393	513	416	380	393				
	fenoxymethylpenicilline	249	385	294	378	249	385	294	378				
	nafcilline	0	0	12	7	0	0	12	7				
	penethamaat	290	314	294	7	290	314	294	7				
	procaïne benzylpenicilline	12.779	12.205	7.508	10.113	12.779	12.205	7.508	10.113				
polymixins	colistinesulfaat	9.102	9.635	7.875	5.658	6.724	7.064	5.896	4.694	2.378	2.571	1.979	964
	polymyxine B sulfaat	1	1	0	1	1	1	0	1				
sulphonamides	sulfachloorpyridazine	886	555	725	847	886	555	725	847				

	natrium												
	sulfadiazine	68.913	70.439	60.689	62.415	46.227	46.519	40.196	40.611	22.687	23.920	20.493	21.804
	sulfadimethoxine natrium	0	0	0	0	0	0	0	0				
	sulfadimidine natrium	423	178	2	0	423	178	2	0				
	sulfadoxine	386	520	459	512	386	520	459	512				
	sulfamethoxazol	84	107	101	661	84	107	101	661				
	sulfanilamide	0	11	11	0	0	11	11	0				
	trimethoprim	14.211	14.462	12.570	12.912	9.674	9.678	8.472	8.551	4.537	4.784	4.099	4.361
Tetracyclines	chloortetracycline	3.088	1.364	750	633	781	578	371	511	2.306	786	379	122
	doxycycline	53.865	45.904	49.962	50.665	45.227	38.137	42.168	43.264	8.639	7.767	7.793	7.401
	oxytetracycline	15.501	15.738	11.700	10.603	13.089	14.609	11.231	10.259	2.412	1.129	469	344

Discussion

In the context of the increasing (awareness about) antibacterial resistance development, comparable data and evolutions on antibacterial consumption are of utmost importance. This annual BelVetSAC report is now published for the sixth time and describes the antibacterial use in animals in Belgium in 2014 and the evolution since 2007.

As in the previous reports data were collected at the level of the wholesaler-distributors for the antibacterial pharmaceuticals and at the level of the compound feed producers for the antibacterial 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. 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. This external and internal data validation has once again proven to be indispensable since several data errors were found in the provided data which could be corrected. In the second ESVAC report it is stated that at least 3 years of successive data collection are needed to gain experience and improve the data collection system to be able to provide accurate data. We only can confirm this experience.

Although the collected data are valuable and show essential overall antibacterial consumption trends, it is important to realize that the data are also very crude and some sources of bias may be present. First of all it would be useful to have data where antibacterial consumption can be attributed to the different animal species. This would allow to monitor and refine trends per species. Equally it would be better to have data on the number of treatments that can be attributed to an animal during its live span (or any set period of time) rather than the amount of kg of a given compound consumed since the number of treatments is much more relevant in relation to the development of antibacterial resistance than the total amount of antibacterials consumed. In 2014 collection of data on antibacterial consumption at herd level started in the pig sector (Belpork data collection system started from January 2014). First reports of this initiative were provided to the individual farmers in December 2014. Also the governmental (Federal Agency for the Safety of the Food Chain and the Federal Agency for Medicines and Health Products) data collection system which is currently under development aims at collecting this type of detailed information.

Another possible source of bias is the fact that we cannot be absolutely sure that all products sold in Belgium by the wholesaler-distributors are also used in Belgium. Veterinarians living near the country borders may also use medicines bought in Belgium to treat animals abroad.

The beneficial evolution seen during 2012 and 2013 (with a respective reduction of -6,9% and -6,3% in mg substance/kg biomass) could not be sustained in 2014. On the contrary, in 2014 an **increase in total consumption of +3,2% expressed in absolute volumes and +1,1% expressed in mg/kg biomass** produced was observed. This is a very disappointing evolution since it was believed / hoped that the continuous efforts in terms of information and sensibilisation by many concerned parties would result in a continued reduction of the use of antimicrobials in veterinary medicine. When compared to 2011 (used as reference year for the start of the sensibilisation campaigns) a reduction of -11,8% (mg substance per kg biomass) can be observed despite the increased level of use during 2014.

When looking more in detail to the different types of antibacterials used, it is observed that for the second year in a row the penicillines (30,8%) form the largest group of consumed antimicrobials, followed by the sulphonamides (28,9%), and tetracyclines (23,1%). In 2014 an increase in use of almost all antimicrobial classes was observed with the highest increase for macrolides and aminosydes. The increase in use of macrolides is almost entirely due to a very substantial increased use of tylosine. The increase for the aminoglycoside class concerns particularly spectinomycine. The only three classes in which a reduction was observed in 2014 are tetracyclines (-0,8%) polymixines (-28,1%) and others (-30,9%). The substantial reduction in use of polymixines (almost entirely due to the reduction in use of colistin) is observed for a second year in a row (level of 2014 is 41,3% lower in comparison to 2012). This is likely the result of the allowance of use of ZnO in piglets for the treatment of post weaning diarrhea. One could deduct however from the amount of ZnO used in 2014 that over 70 % of all produced piglets were treated (based on the estimated consumption of 4 kg medicated feed per piglet containing 3000 ppm ZnO during 2 weeks post weaning) while the respective reduction of colistin is clearly less substantial, over all since 2012: - 42 % (premixes : - 62 % ; other forms: - 33 %, also administration to calves). It may implicate that both substances are administered at the same time which is clearly in contradiction with the guidelines and aims of the temporal allowance of the use of ZnO.

The reduction in use of the category "others" is due to the reduction in use of tiamuline. This might partially explain the increase in use of the macrolides since tylosine and tiamuline are frequently used for the same indications and may be therefore exchangeable. Unfortunately, in 2014 also a substantial increased use (+3,2%) of molecules of critical importance for human medicine (grouped in the category of the "red" antibacterials such as the cephalosporines of the 3° and 4° generation and the fluoroquinolones) was observed. The increase during 2014 concerns mainly FQ, there is only an increase otherwise in use of the 1st generation Cephalosporins.

It is not always obvious to find clear explanations for the observed trends in antimicrobial consumption. After two rather successful years of reduction in use (2012, 2013) it was believed / hoped that the efforts in information and sensibilisation made by AMCRA and others were having an impact to be translated into a trend towards reduced use.

Unfortunately this trend was not confirmed and in 2014 even an increase in antibacterial consumption could is observed. This is of course a disappointing evolution because during 2014 no obvious animal health problems or parameters are known that would imply more antibiotic treatment to maintain the same level of animal health or welfare as in the previous years. Therefore the increased use can only be attributed to a relaxed attitude by all stakeholders involved towards responsible and restricted antimicrobial use.

These results may be an indication of the limits of what can be achieved through information and sensibilisation alone. However there was also within AMCRA the engagement of stakeholders to reach certain targets by 2017 (reduction of 50 % of premix use) or by 2020 (50 % reduction of all antibiotics). So also the mechanism of auto regulation is under pressure. It could be questioned if a durable reduction in antibiotic use would require besides effective sensibilisation campaigns also increasingly more strict regulation.

Conclusion

This report shows, after two consecutive years of substantial reduction, a slight increase in total antibacterial consumption in animals in Belgium in 2014. This disappointing result should be seen as a strong motivator both to increase the efforts through sensibilisation and information and besides that to explore more stringent measures to force all stakeholders involved towards a reduction in use.

Acknowledgements

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

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Appendix

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

Class of Antibacterials	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