BelVet-SAC

Belgian Veterinary Surveillance of Antimicrobial Consumption

National consumption report

2012

Summary

This forth BelVetSAC report, covers the results of the data collection on veterinary antimicrobial consumption in Belgium in the year 2012. 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 2012. 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 2012, plus the number of dairy cattle present in Belgium times 500 kg of metabolic weight per head.

Between 2011 and 2012, there has been a substantial decrease of 7,1% in the total consumption of antimicrobials in veterinary medicine in Belgium (299036,6 kg in 2011; 277850,23 kg in 2012). In this period, the use of antimicrobial pharmaceuticals decreased with 7,9%, and the use of antimicrobial premixes decreased with 3,5%. When looking at the trend from 2007 onwards (start data collection) a decrease of 20,3% in total consumption is observed. A substantial part of this decrease is realized between 2007 and 2008. Between 2008 and 2011 a status quo around 300 tons was observed and in 2012 again a substantial decrease is seen. As the total biomass produced in 2012 in Belgium was almost totally equal to 2011 the same decreasing trends in usage in function of the production are observed with a decrease of 6,9% of the total mg consumed per kg biomass produced. This result is distinctly different from the previous years where a relative status quo of antimicrobial consumption was seen between 2008 and 2011.

It is hoped for that these results are the start of a trend to be continued in the years to come since the second ESVAC report clearly shows that the antimicrobial consumption in Belgium is high in comparison to most other European countries.

When looking more in detail to the evolution in the different types of antimicrobials used, it is observed that the sulphonamides and trimethoprim (31,1%), penicillines (29,7) and tetracyclines (22,7) remain the three most used antimicrobial classes. However, what is more worrisome is that the use of molecules of critical importance for human medicine such as the cephalosporines of the 3° and 4° generation and the fluoroquinolones is increasing for the second year in a row. Therefore there is urgently need for measures to restrict the use of these molecules. AMCRA has very recently advised to strongly restrict the use of these molecules for those situations where it can be shown that no other alternatives are available.

Relating this significant reduction in total antimicrobial consumption in comparison to 2011 and previous years to specific measures or actions is of course very difficult. However it is noticeable that since January 2012 AMCRA has become active in Belgium. During this first year this organization has spent enormous efforts to sensitize all stakeholders involved in animal production concerning the importance of restricted antimicrobial usage. It is believed

(hoped) that the observed reduction are the first results of these efforts which are continued and even intensified in 2013.

Although these results show a positive and hopeful evolution they should by no means be interpreted as a sign to relax the efforts concerning the sensitization, guidance and legislation to move the whole sector further towards a rational reduction of the antimicrobial usage. On the contrary, these results should be seen as a motivator for all stakeholders involved to continue and even increase the efforts for a rational reduction of antimicrobial usage.

Samenvatting

Dit vierde BelVetSAC rapport omvat de resultaten van het gebruik van antimicrobiële middelen bij dieren in België in 2012. 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 2012 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 tussen 2011 en 2012 met 7,1% gedaald (299036,6 kg in 2011; 277850,23 kg in 2012). Deze substantiële daling is het gevolg van een daling van het gebruik pharmaceuticals met 7.9% en een daling van het gebruik van antimicrobiële premixen van 3,5%. Wanneer we deze resultaten vergelijken met 2007 (begin van de datacollectie) wordt een daling van 20,3% in totale consumptie waargenomen. Een aanzienlijk deel van deze daling werd gerealiseerd tussen 2007 en 2008. Tussen 2008 en 2011 werd een relatief status quo waargenomen terwijl in 2012 opnieuw een aanzienlijke daling wordt opgemerkt.

De totale biomassa geproduceerd in 2012 in België is zo goed als hetzelfde als in 2011 waardoor de daling in gebruik in absolute aantallen zich ook vertaald in een daling uitgedrukt in mg per kg geproduceerde biomassa van 6,9%. Dit resultaat is duidelijk verschillend van de voorgaande jaren waar een relatief status quo werd opgemerkt. We hopen dat deze resultaten de start zijn van een trend die in de komende jaren wordt verdergezet aangezien uit de resultaten van het tweede ESVAC rapport duidelijk is gebleken dat het antibioticumgebruik bij dieren in België hoog is in vergelijking met de meeste andere Europese landen.

Wanneer meer in detail naar de verschillende types antibiotica die worden gebruikt gekeken wordt merken we dat sulfonamiden en trimethoprim (31,1%), penicillines (29,7) en tetracyclines (22,7) de drie meest gebruikte antimicrobiële klassen blijven. Jammer genoeg is ook het gebruik van de door de WHO aangeduide klasse van antibiotica van kritisch belang voor de humane gezondheidszorg zoals de 3° en 4° generatie cefalosporines en de fluoroquinolonen voor het tweede jaar op rij gestegen. Om deze ongewenste evolutie te keren zijn er dringend maatregelen nodig die het gebruik van deze producten aan banden leggen. Het kenniscentrum **A**nti**m**icrobial **C**onsumption and **R**esistance in **A**nimals in België (AMCRA) heeft heel recent een advies uitgebracht dat sterke restricties oplegt aan het

gebruik van deze producten en bepaald dat deze enkel zouden mogen ingezet worden indien kan aangetoond worden dat geen andere producten werkzaam zijn.

Het is moeilijk om de belangrijke daling in totale consumptie van antibacteriële middelen in 2012 ten opzichte van de voorgaande jaren met zekerheid aan een bepaalde oorzaak te koppelen. Wel kan opgemerkt worden dat sedert januari 2012 AMCRA van start is gegaan in België. In het eerste werkjaar van AMCRA is er heel wat energie gestopt in de sensibilisatie van alle betrokken partijen met betrekking tot de noodzaak van een verantwoorde reductie van het antibioticumgebruik. Wij denken (hopen) dat de huidige resultaten een eerste teken zijn van het effect van deze inspanningen en die verder gezet en zelf nog geïntensifieerd worden in 2013.

Alhoewel de resultaten een positieve en hoopvolle evolutie tonen, mogen ze op geen enkele manier geïnterpreteerd worden als een teken om de inspanningen van sensibilisatie, begeleiding en regelgeving te verminderen. Wel in tegendeel, deze resultaten moeten aanzien worden als een motivatie voor alle betrokken partijen om de inspanningen die moeten leiden tot een rationele reductie van het gebruik van het gebruik van antimicrobiële middelen nog verder te intensifiëren.

Résumé

Ce quatrième rapport BelVetSAC traite des résultats de la collecte de données en matière de consommation d'antimicrobiens vétérinaires en Belgique durant l'année 2012. Les données se composent de tous les antimicrobiens vétérinaires vendus à un vétérinaire ou un pharmacien en Belgique et des prémélanges antimicrobiens incorporés dans des aliments médicamenteux destinés à être utilisés en Belgique en 2012. Elles comportent donc les données de consommation tant pour les animaux d'élevage que pour les animaux de compagnie. Le dénominateur pour la production animale était la biomasse (en kg) calculée comme la somme de la quantité de viande bovine, de viande porcine et de volaille produite en 2012, ainsi que le nombre de vaches laitières présentes en Belgique multiplié par leur poids métabolique (500 kg/tête).

Entre 2011 et 2012, il y a eu une diminution substantielle de 7,1% de la consommation totale d'antimicrobiens en médecine vétérinaire en Belgique (299.036,6 kg en 2011 ; 277.850,23 kg en 2012). Durant cette période, l'utilisation de médicaments antimicrobiens a diminué de 7,9% et l'utilisation de prémélanges antimicrobiens de 3,5%. Lorsque l'on observe la tendance à partir de 2007 (début de la collecte de données), on observe une diminution de 20,3% de la consommation totale. Une partie substantielle de cette diminution a été réalisée entre 2007 et 2008. Entre 2008 et 2011, un statu quo d'environ 300 tonnes a été observé et, en 2012 encore, on observe une diminution substantielle. Vu que la biomasse totale produite en 2012 en Belgique était presque totalement égale à celle de 2011, les mêmes tendances de diminution de l'utilisation en fonction de la production sont observées avec une diminution, exprimée en mg par kg de biomasse produite, de 6,9%. Ce résultat est clairement différent des années précédents où un statu quo relatif de la consommation d'antimicrobiens a été observé entre 2008 et 2011.

Il est à espérer pour cette raison que ces résultats soient le début d'une tendance qui se poursuive dans les prochaines années étant donné que le deuxième rapport ESVAC montre clairement que la consommation d'antimicrobiens en Belgique est élevée par rapport à celle dans la plupart des autres pays européens.

Lorsque l'on observe plus en détail l'évolution des différents types d'antimicrobiens utilisés, on observe que les sulphonamides (31,1%), pénicillines (29,7) et tétracyclines (22,7) restent les trois classes d'antimicrobiens les plus utilisées. Ce qui est toutefois plus inquiétant est que l'utilisation de molécules d'importance critique pour la médecine humaine telles que les céphalosporines de la 3e et 4e génération et les fluoroquinolones est en augmentation pour la seconde année consécutive. C'est pourquoi il est urgent de prendre des mesures visant à restreindre l'utilisation de ces molécules. L'AMCRA a très récemment recommandé de

restreindre fortement l'utilisation de ces molécules pour les situations où l'on peut prouver qu'aucune autre alternative n'est disponible.

Etablir un lien entre cette réduction significative de la consommation totale d'antimicrobiens par rapport à 2011 et aux années précédentes, et des mesures ou actions spécifiques est évidemment très difficile. On peut toutefois observer que, depuis janvier 2012, l'AMCRA est très active en Belgique. Durant cette première année, cette organisation a fait d'énormes efforts pour sensibiliser tous les stakeholders impliqués dans la production animale en ce qui concerne l'importance d'une utilisation restreinte des antimicrobiens. On pense (espère) que la réduction observée est le premier résultat de ces efforts qui se poursuivent et s'intensifient même en 2013.

Bien que ces résultats montrent une évolution positive et encourageante, ils ne doivent en aucun cas être interprétés comme un signe pour relâcher les efforts en matière de sensibilisation, d'information et de législation visant à pousser davantage l'ensemble du secteur vers une réduction rationnelle de l'utilisation d'antimicrobiens. Ces résultats doivent au contraire être vus comme un incitant pour tous les stakeholders impliqués dans la poursuite et l'augmentation de ces efforts pour arriver à une réduction rationnelle de l'utilisation d'antimicrobiens.

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. However, The use of antimicrobials invariably leads to selection of bacteria that are resistant against the substance used. Resistance can then spread in populations and the environment.
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.

Today, antimicrobial consumption and its link to antimicrobial resistance in humans and animals is 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 2012, the world economic forum has indicated the emergence of antimicrobial resistance a global threat with the ability of destabilizing health systems, profound cost implications for economic systems and for the stability of social systems.

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” perspective.
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 forth BelVetSAC report gives an overview of the consumption of antimicrobial in veterinary medicine in Belgium in 2012 and describes evolutions in use since 2007.

Contents

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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. January 2013 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 2012 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 veterinary medicinal products authorized 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.

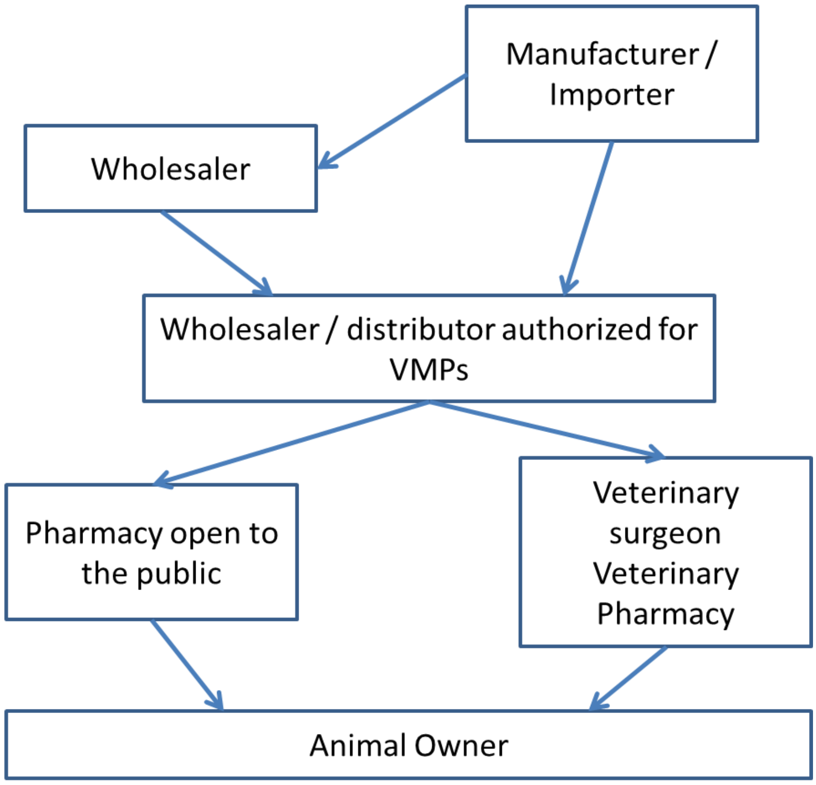


Figure 1. Distribution of Veterinary Medicinal products in Belgium.

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=57). They received a list of registered and marketed antimicrobial containing premixes. The feed mills were asked by letter dd. January 2013 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 antimicrobial containing premixes for the year 2012. Antimicrobial premixes can only be incorporated into medicated feed on prescription of a veterinarian.

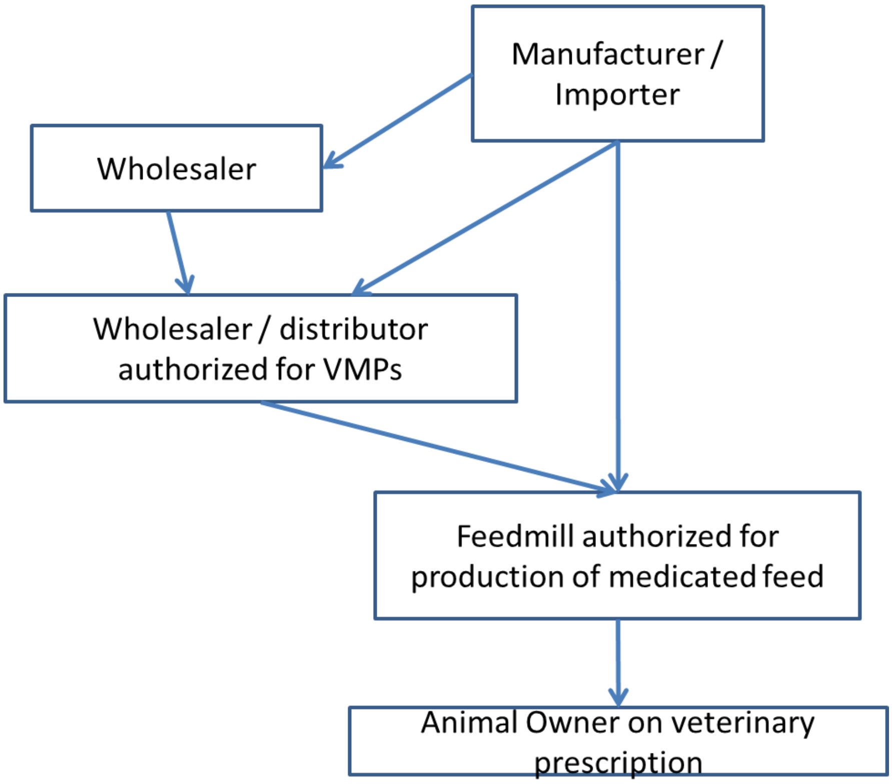


Figure 2. Distribution of Veterinary premixes in Belgium.

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 in accordance with the ESVAC recommendations. 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; BelVetSac 2011), 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. 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 antimicrobial 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 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. 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 are 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 antimicrobial products sold in 2012 responded. All 57 compound feed producers, licensed for the production of medicated feed responded. Of these 6 indicated not to have produced any medicated feed and 51 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%.

As in the previous year the internal data validation step showed to be of huge importance since one important difference was found in a large wholesaler-distributor (apparent reduction of sales around 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 since 2007 according to the commented compendium of the Belgian Centre for Pharmacotherapeutic Information 2007-2012respectively (www.bcfi-vet.be).

Table 2. Armatorium of antimicrobial products on the Belgian market in between 2007 and 2012.

	2007	2008	2009[1]	2010	2011	2012
Number of antimicrobial pharmaceuticals on the market	270	276	283	292	282	308
Number of antimicrobial premixes on the market	16	18	20	21	23	22
Total number of antimicrobial products on the market	286	294	303	313	305	330

With exception of gamithromycin (since 2009), no new active abtimicrobials were registered on the market in the reported years. Thus the observed increase in available products is

[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.

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 2008-2012 as described above (Table 3).

Table 3. Animal Biomass produced in Belgium between 2008 and 2012.

Animal biomass	2008	2009	2010	2011	2012
Meat (ton)					
Pork	1 056 169	1 082 036	1 123 769	1 108 255	1 109 610
Beef	267 274[a]	255 017	263 142	272 286	262 280
Poultry[b]	442 296[c]	442 296	404 343	402 753	410 215
Total biomass from meat production	**1 765 739**	**1 779 349**	**1 791 254**	**1 783 294**	**1 782 105**
Dairy cattle					
Dairy cattle (number)	517 800	517 700	517 700	510 600	503 500
Dairy cattle metabolic weight (ton)	258 900	258 850	258 850	255 300	251 750
Total biomass (ton)	**2 024 639**	**2 038 199**	**2 050 104**	**2 038 594**	**2 033 855**

[a] data on biomass of beef production in 2008 was 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.

[b] 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.

[c] data for 2008 are copied from the most adjacent year (2009) where figures were available.

A decrease in biomass production of 0.2% is observed between 2011 and 2012. This almost status quo is the result of a small increase in pork and poultry production and a small decrease in beef production and number of dairy cattle present.

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.

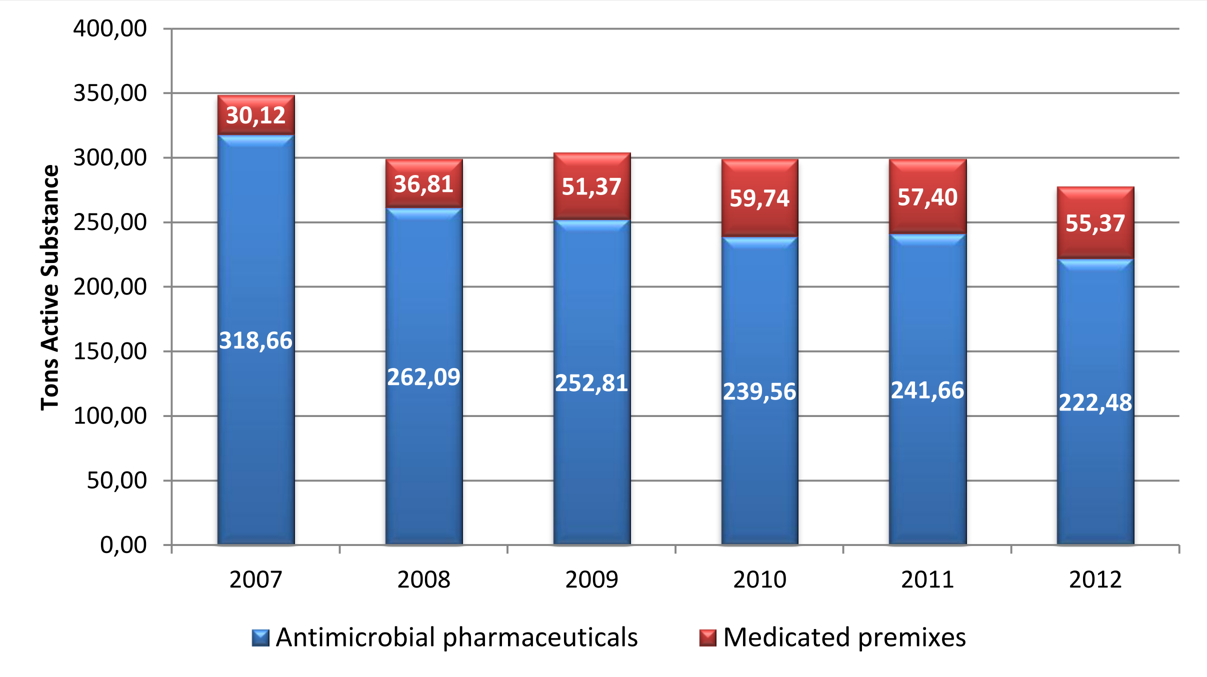


Figure 3. Total national consumption of antimicrobial compounds for veterinary use in Belgium for the years 2007-2012 (tons active substance)

Between 2011 and 2012, there was a substantial decrease of 7,2% in the total consumption of antimicrobials in veterinary medicine in Belgium (299036,6 kg in 2011; 277850,3 kg in 2012). The use of antimicrobial pharmaceuticals decreased with 7,9% between 2011 and 2012, and the use of antimicrobial premixes decreased with 3,5%. When looking at the trend from 2007 onwards (start data collection) a decrease of 20.3% in total consumption is observed. A substantial part of this decrease is realized between 2007 and 2008. Between 2008 and 2011 a status quo around 300 tons was observed and in 2012 again a substantial decrease is seen. Figures 4 and 5 show these data separately for the antimicrobial pharmaceuticals and the antimicrobial premixes.

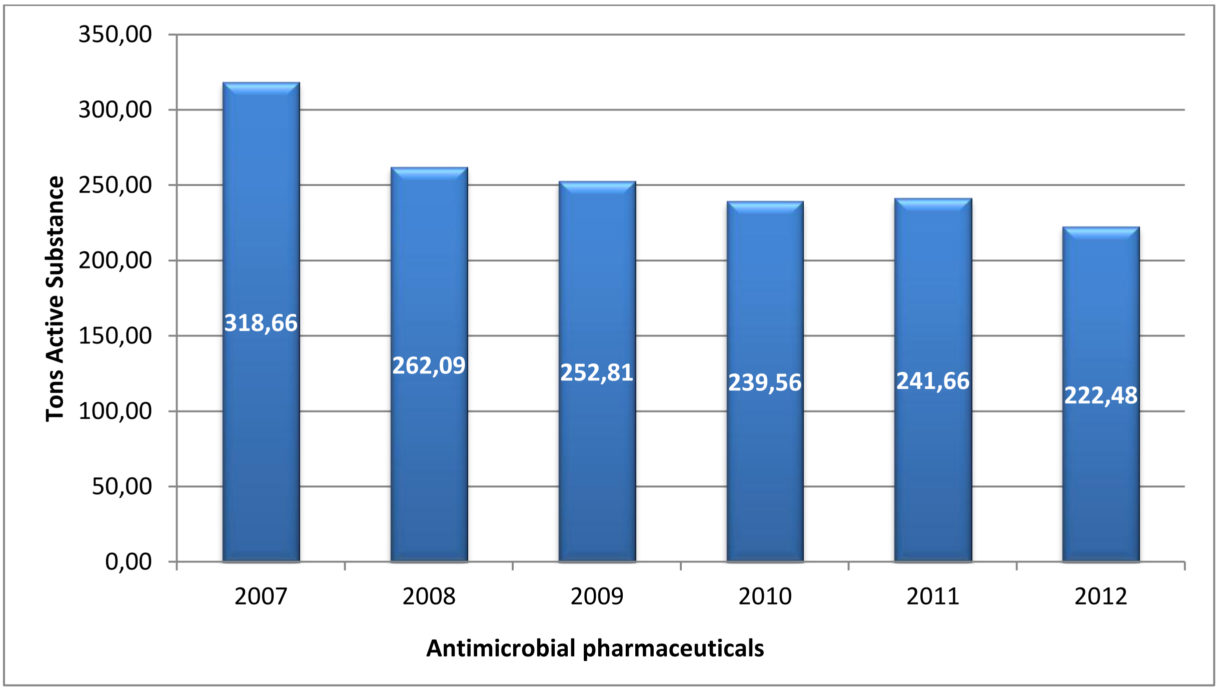


Figure 4. National consumption of antimicrobial pharmaceuticals for veterinary use in Belgium for the years 2007-2012 (tons active substance)

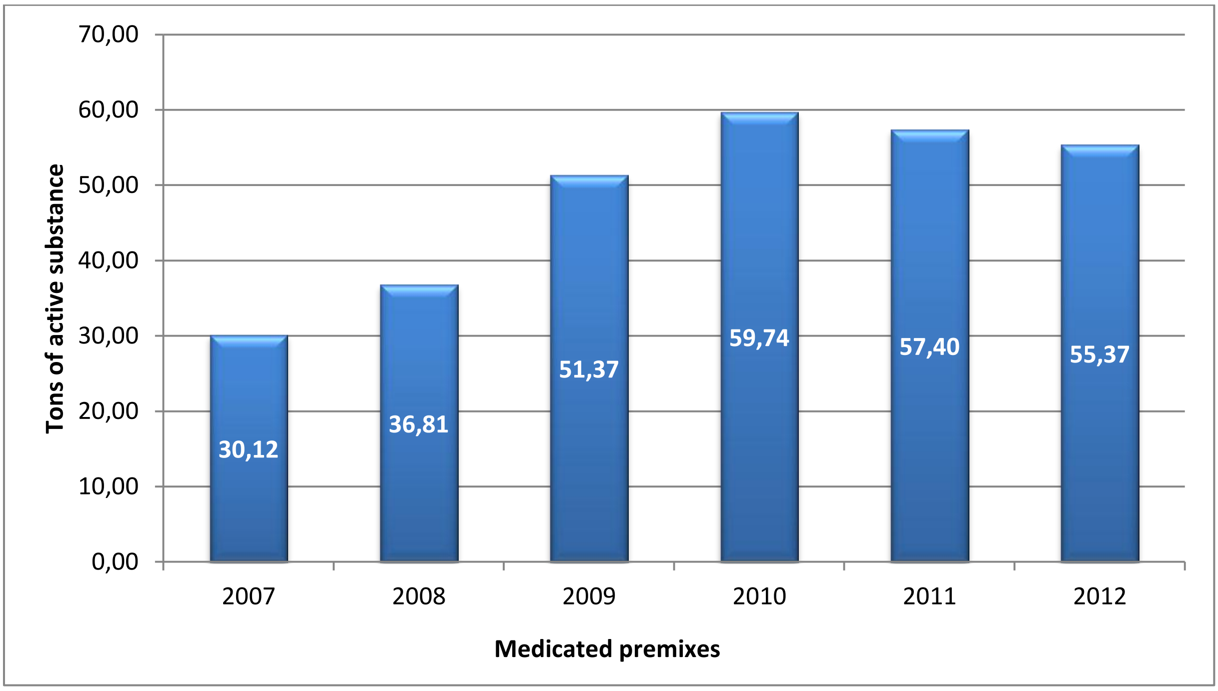


Figure 5. National consumption of antimicrobial premixes in Belgium for the years 2007 -2011 (tons active substance)

After an increase in use of antimicrobial premixes between 2007 and 2010, the slow decreasing trend firstly observed in 2011 is now confirmed. Since 2011 the data collection system allows to differentiate the animal species of destination for the antimicrobial premixes. In 2011 only 1,0% was used in poultry or rabbit feed whereas this has increased in 2012 to 3,2%. Still 96,8% is used in pig feed.

Antimicrobial use versus biomass

As described before the total biomass production in Belgium has remained relatively stable in comparison to 2011. As a consequence the decreasing trends in use observed in absolute values are very comparable to what is observed when the use is plotted against the amount of biomass produced. For 2012, the mg of active substance used in comparison to the kg biomass produced was 136,6 mg/kg. This is a decrease of 6,9% in comparison to 2011. Figure 6 presents these data, again subdivided into antimicrobial pharmaceuticals and antimicrobial premixes.

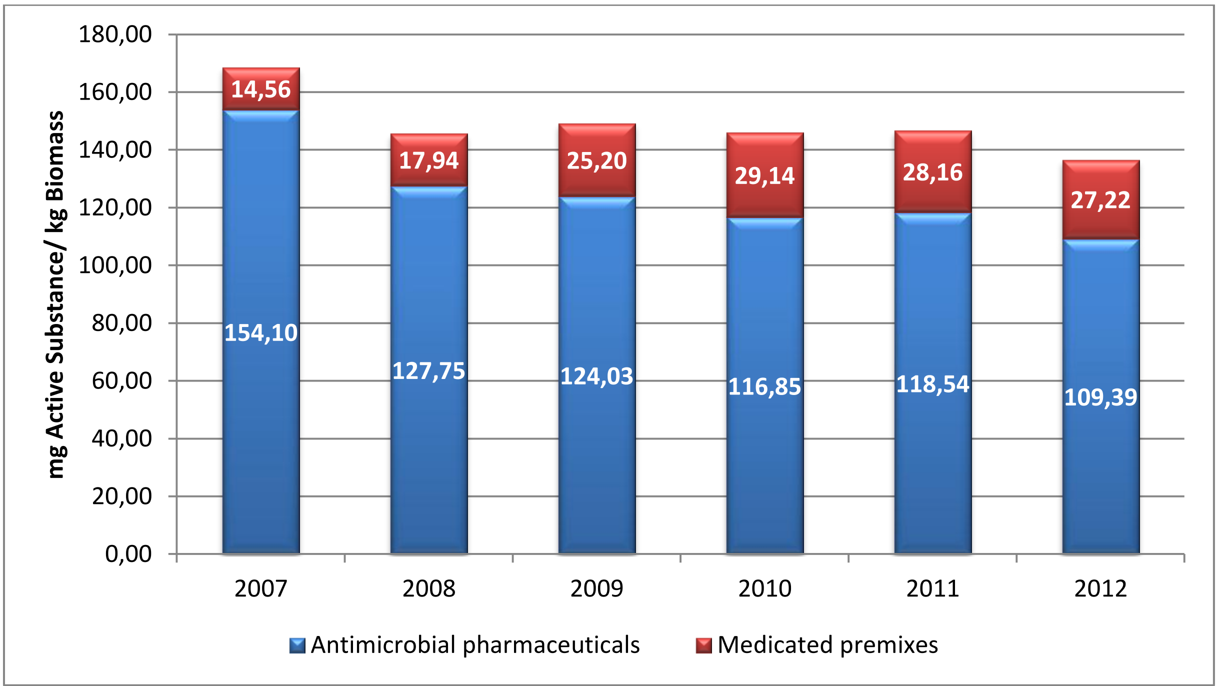


Figure 6. Total mg of active substance used per kg biomass produced in Belgium for 2007-2012. Note that the absolute values of mg/kg differ slightly from number presented in previous BelVetSac reports due to retrospective change in the production numbers reported in Eurostat (see table 3).

After a small increase in use per kg biomass produced in 2011, this year a substantial decrease is observed. Between 2007 and 2012 a total decrease of 19,0% is seen.

Looking only at antimicrobial pharmaceuticals in function of the biomass produced, a decrease of 7,7% is observed between 2011 and 2012, whereas for the medicated premixes a decrease of 3,3% is seen.

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

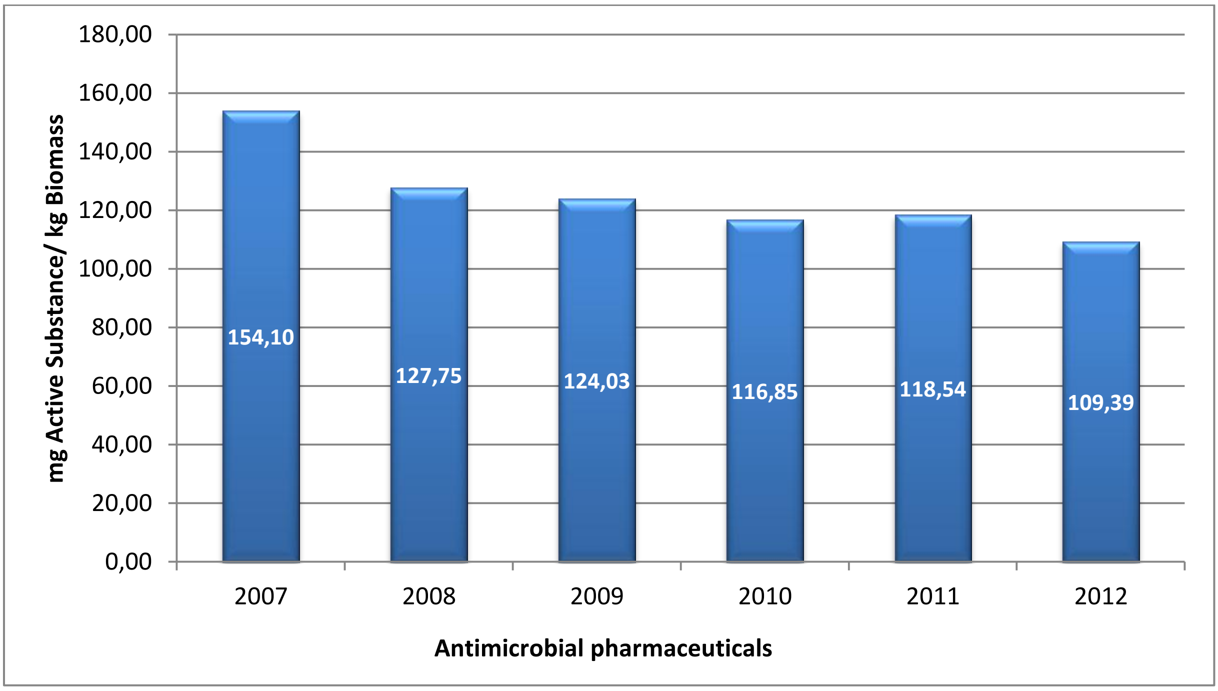


Figure 7. Mg active substance of antimicrobial pharmaceuticals used per kg biomass in Belgium for 2007-2012.

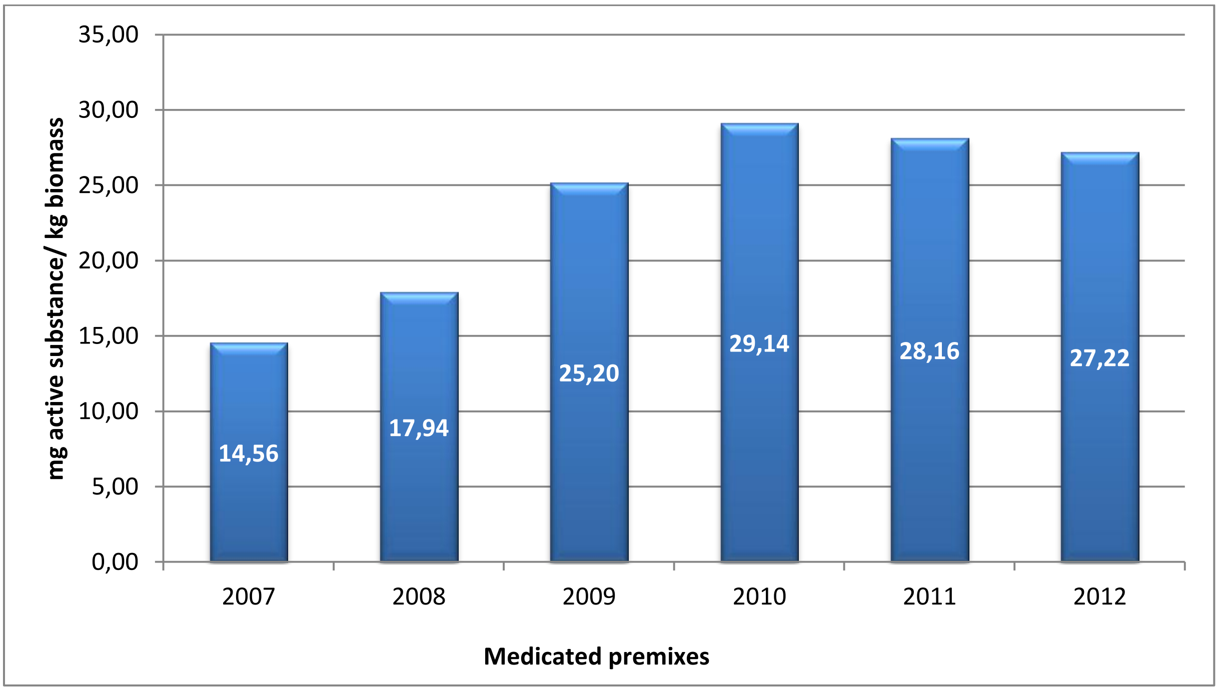


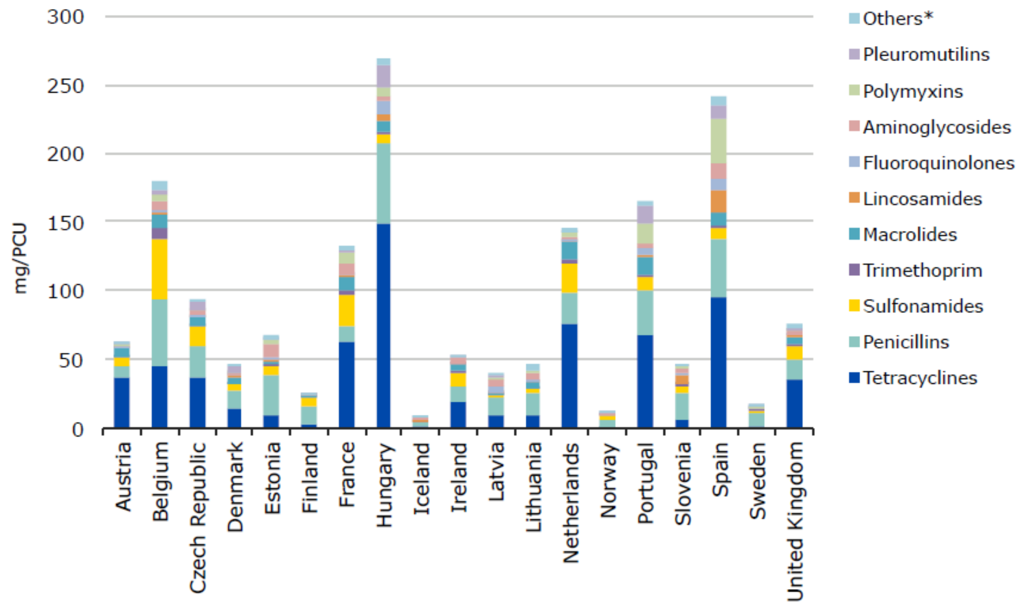
Figure 8. Mg active substance of antimicrobial premixes used per kg biomass in Belgium for the years 2007 -2012

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 antimicrobial Consumption (ESVAC) project that aims at collection antimicrobial usage data in all EU member states in a comparable manner allowing to evaluate trends en 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 October 2012, the second ESVAC report, presenting results on antimicrobial usage in 19 EU /EEA countries has become available (http://www.ema.europa.eu/docs/en_GB/document_library/Report/2012/10/WC500133532.pdf). In this report the antimicrobial consumption in animals in these 19 countries in 2010 is presented in relation to the animal production in the country.

In figure 9 the results of the 19 countries included in the second ESVAC report are presented in mg active substance used (subdivided into the different antimicrobial classes) 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.



[1] Differences between countries can partly be explained by differences in animal demographics, in the selection of antimicrobial agents and in dosage regimes, among other factors. * Amphenicols, cephalosporins, other quinolones and other antibacterials (classified as such in the ATCvet system).

Figure 9. Sales for food-producing species, including horses, in mg/PCU, of the various veterinary antimicrobial classes, by country, for 2010 (source: Second ESVAC report, Sales of veterinary antimicrobial agents in 19 EU/EEA countries in 2010 p 23).

When looking at figure 9 it can be observed that Belgium had the third highest level of antimicrobial usage expressed in mg/PCU in 2010. This is obviously not a very good result and indicates that many EU countries are using substantially less antimicrobials in relation to the magnitude of their animal production. The reduction in antimicrobial consumption observed in 2012 may improve this situation but on the other hand it is know that in many countries throughout the EU measures and campaigns to reduce antimicrobial usage are started or implemented suggesting that also other countries will likely reduce the usage. It needs to noted that not all EU countries are including in this report since some member states did not provide the necessary data. Important animal production countries such as Italy, Poland, Germany, Greece are missing in the comparison. In the coming years it is expected that more EU MS will provide this data. Belgium strongly supports the ESVAC initiative and supports that all EU countries provide the necessary data.

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 → 2012), 32,1% of the compounds used were sulphonamides and trimethoprim, 26,5% penicillines, 26,3% tetracyclines and 7,6% macrolides.

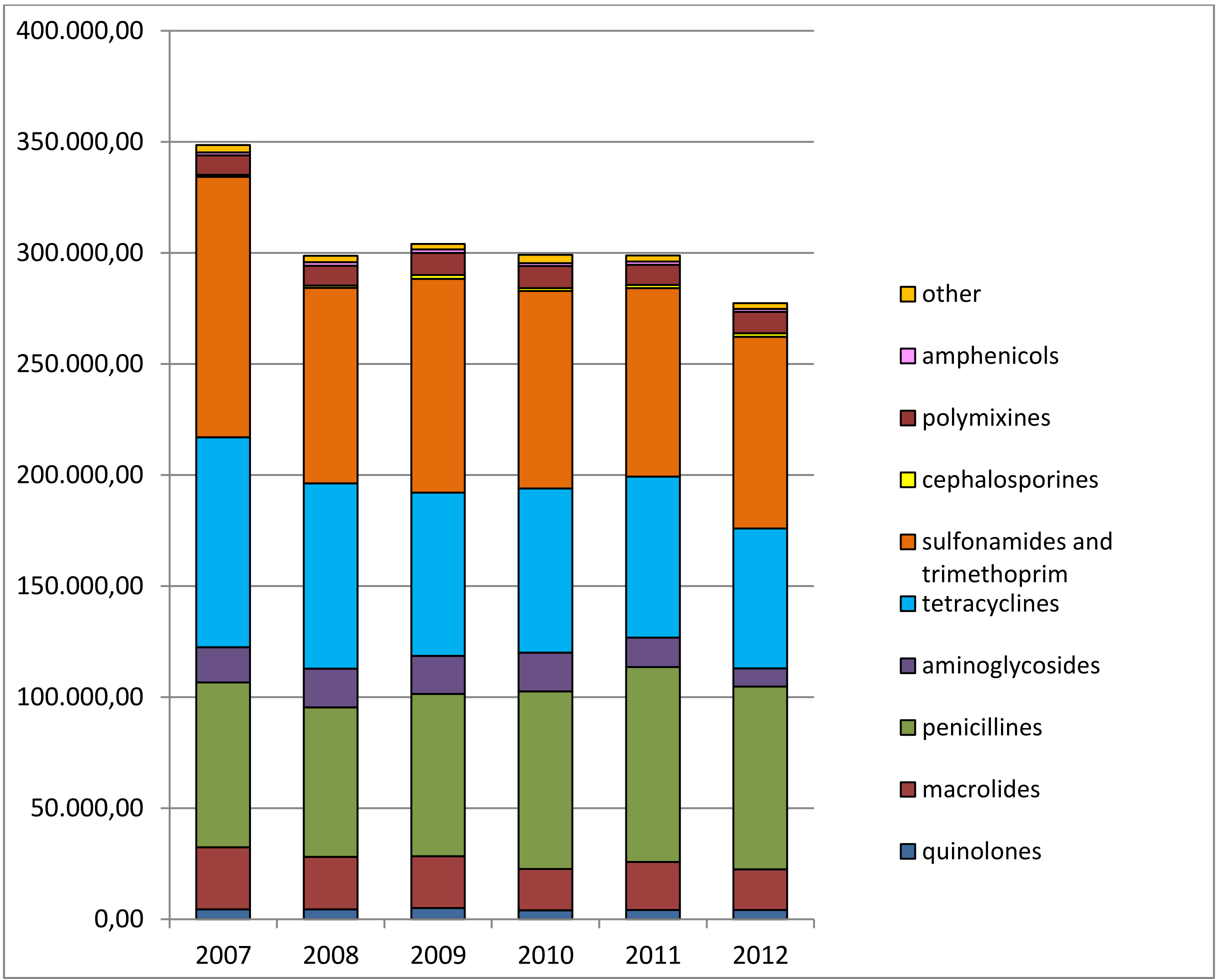


Figure 10. Total antimicrobial use per class of antimicrobials.

In 2012, the most used group of antimicrobials were the sulphonamides and trimethoprim (86 tons, 31,1%) followed by the penicillines (82 tons, 29,7%) and the tetracyclines (63 tons, 26,3%). Both the use of penicillins and tetracyclines was reduced in comparison to 2011 (-6,1% and -13% respectively) whereas the use of sulphonamides and trimethoprim was increased (+1,6% in comparison to 2011) and therefore has become again the most used group of antimicrobials in veterinary medicine in 2012. Unfortunately also the use of critically important antimicrobials according to the WHO such as cephalosporins and quinolones increased further in 2012. This increase is limited in absolute values of active substance since these molecules have a low molecular weight, however they are of high importance in terms of resistance selection both for animals as well as humans and therefore this increase is unwanted. In table 5 and figure 11 an overview of the evolution of the use of the different classes of antimicrobials between 2010, 2011 and 2012 is given.

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

Class of antibiotics	2010	2011	2012	'10 » '11	'11 » '12
penicillins	80.082,5	87.863,3	82.467,8	9,7%	-6,1%
Sulphonamides and trimethoprim	88.939,1	84.902,8	86.273,5	-4,5%	1,6%
tetracyclines	73.838,2	72.454,1	63.006,2	-1,9%	-13,0%
macrolides	18.787,1	21.843,0	18.191,8	16,3%	-16,7%
polymyxins	9.879,5	9.102,7	9.635,8	-7,9%	5,9%
aminosydes	17.382,2	13.166,9	8.313,9	-24,3%	-36,9%
quinolones	3.978,1	4.088,5	4.216,9	2,8%	3,1%
Other	3.646,7	2.771,0	2.578,1	-24,0%	-7,0%
cephalosporins	1.368,9	1.489,7	1.529,8	8,8%	2,7%
fenicols	1.382,7	1.354,4	1.435,5	-2,0%	6,0%
Totaal (kg)	**299.285,1**	**299.036,6**	**277.649,2**	**-0,08%**	**-7,15%**

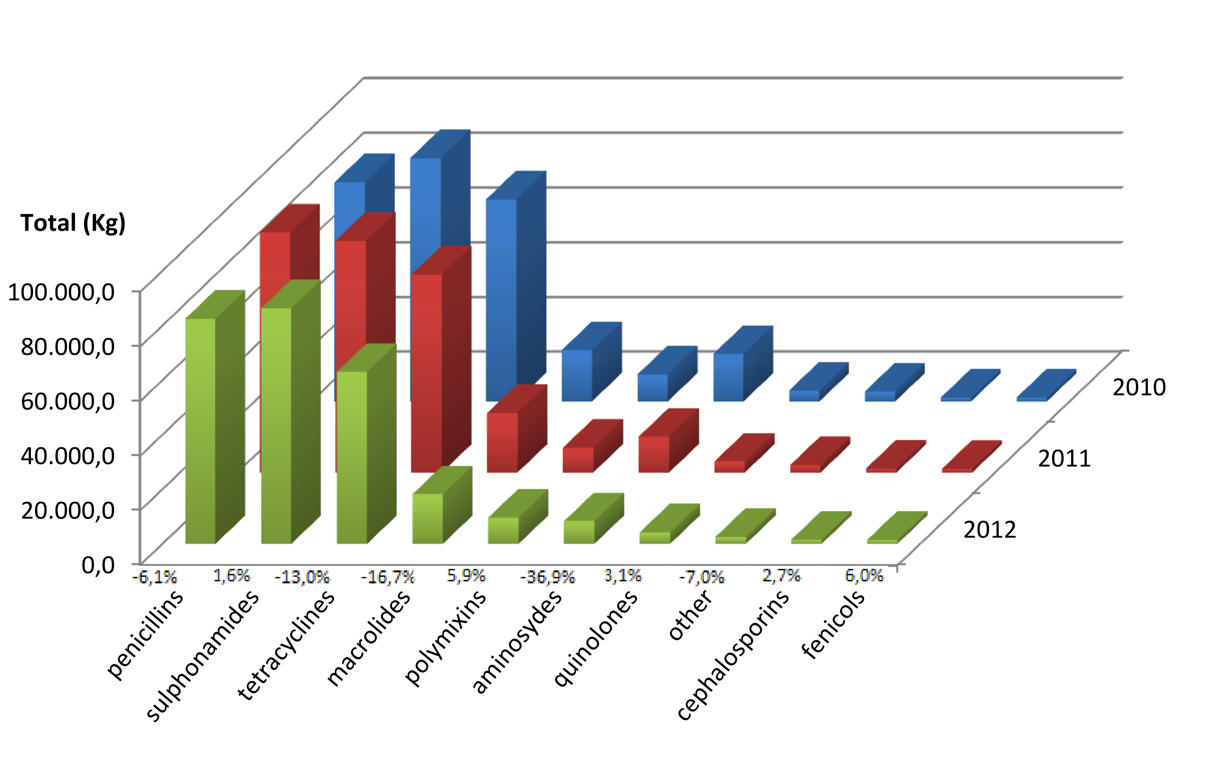


Figure 11: Evolution in the antimicrobial consumption (kg) per antimicrobial class. (Sulphonamides include also trimethoprim)

In the first semester of 2013 AMCRA (center of expertise on Antimicrobial Consumption and Resistance in Animals (www.amcra.be)) has produced it first guides on responsible antimicrobial consumption (AMCRA, 2013). In these guides the different antimicrobial 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 antimicrobial 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 antimicrobials for veterinary health (http://web.oie.int/downld/Antimicrobials/OIE_list_antimicrobials.pdf). When producing the lists priority was given to human health.

The group of yellow products contains the antimicrobial classes with the lowest importance for human and veterinary 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 penicillines, the sulphonamides, the cephalosporines of the first generation and the fenicols.

The group of orange products are of higher importance for human and veterinary 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 polimixines, the aminoglycosides, the tetracyclines and some penicillines.

The red group of products are the products of the highest importance for human and veterinary 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 cephalosporines of the 3° and 4° generation and the fluoroquinolones.

In figure 12 the evolution of use of the different color groups of antimicrobials 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 used limitedly 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. The largest decrease in use in the last year is seen in the orange group. Whereas a slight increase in use is observed in the yellow and red group. Especially this increase in use of red molecules is highly unwanted.

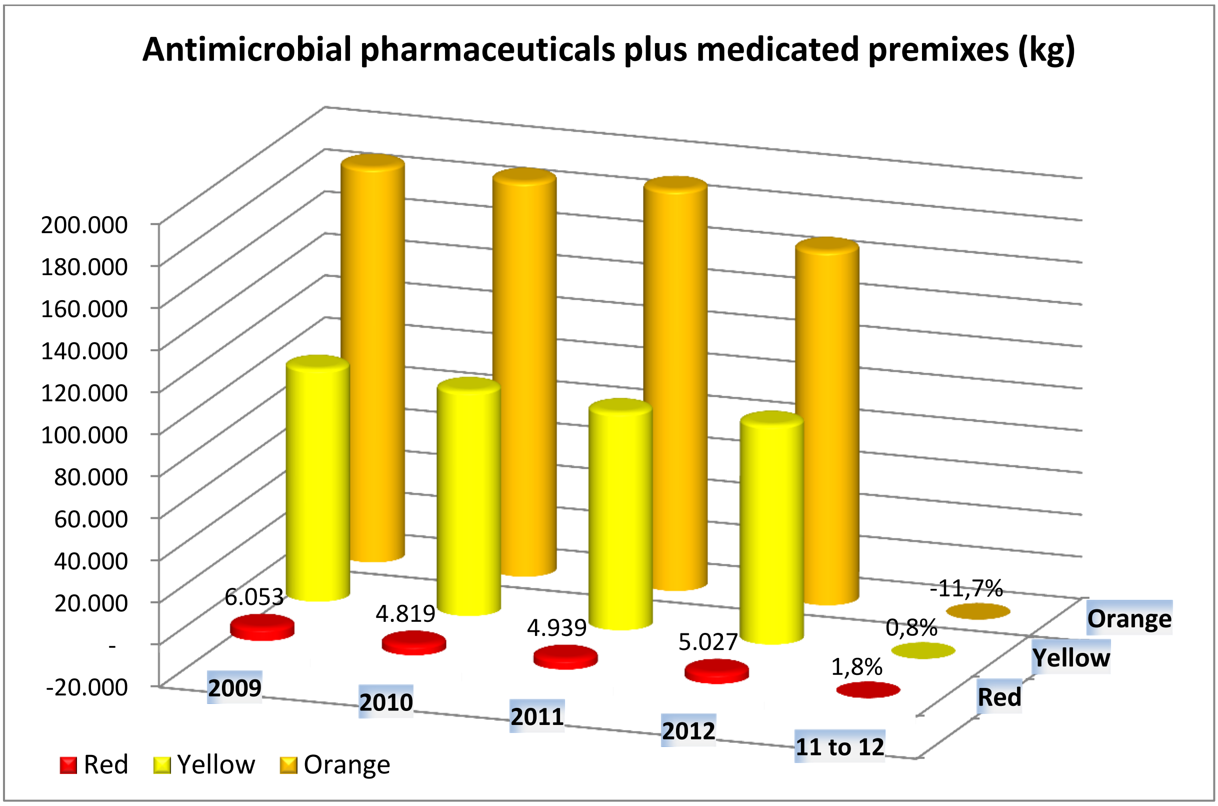


Figure 12: Evolution in the antimicrobial consumption (kg) per antimicrobial color group between 2009 and 2012.

2. Antimicrobial pharmaceuticals

In Figure 13 the consumption of antimicrobials per class (ATC level 3 or 4) is presented for the pharmaceuticals.

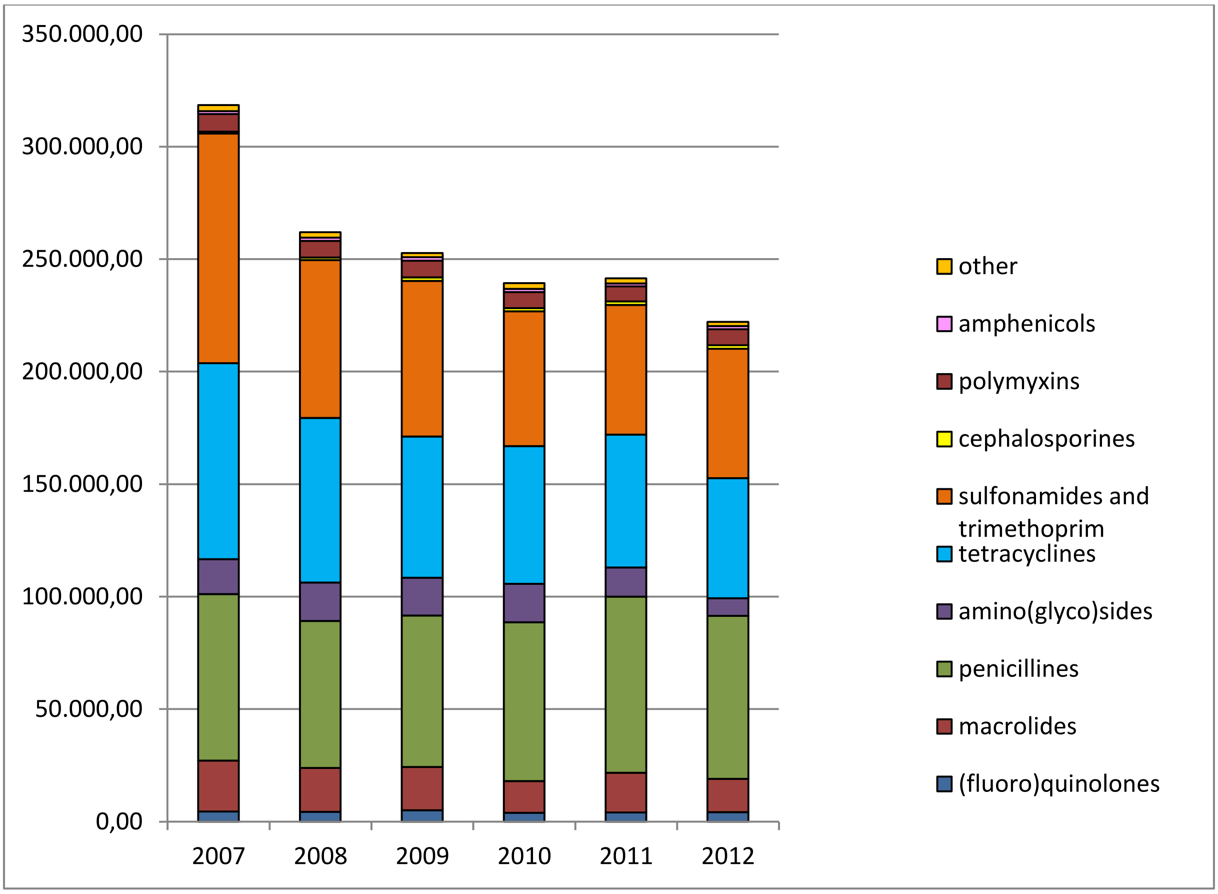


Figure 13. Use of antimicrobial pharmaceuticals per class of antimicrobials between 2007 and 2012.

3. Antimicrobial premixes

In Figure 14 the consumption of antimicrobials per class (ATC level 3 or 4) is presented for the antimicrobial premixes.

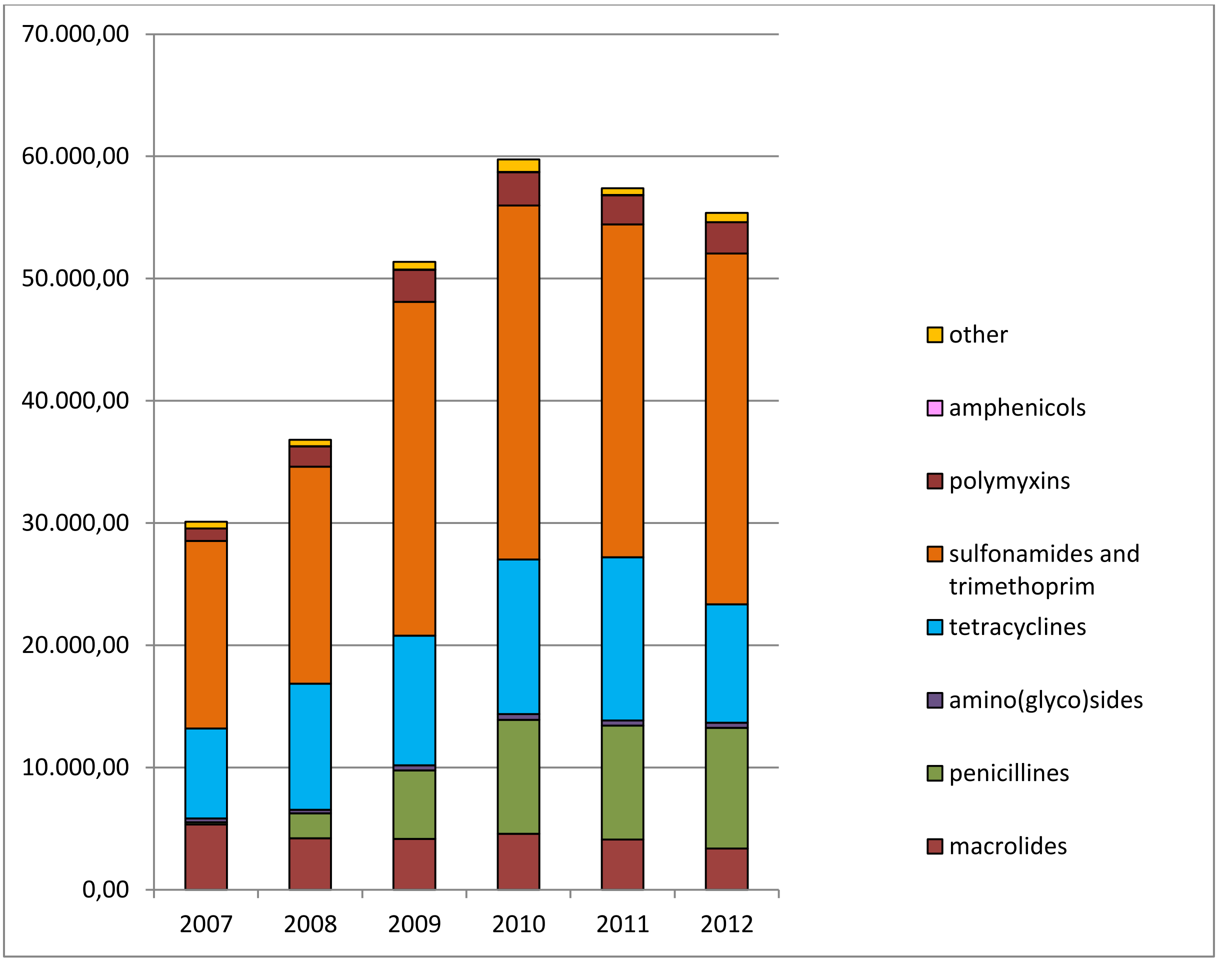


Figure 14. Use of antimicrobial premixes per class of antimicrobials between 2007 and 2012.

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

		Total (kg)				Antimicrobial pharmaceuticals (kg)_GV				Medicated premixes (kg)_MD			
Class	Antimicrobial compound	2009	2010	2011	2012	2009	2010	2011	2012	2009	2010	2011	2012
Amino(glyco)sides	Apramycine	254	228	192	198	164	118	96	96	90	110	96	103
	Dihydrostreptomycine	7.783	8.653	4.236	0	7.783	8.653	4.236	0				
	Gentamicine	163	141	132	127	163	141	132	127				
	Kanamycine	11	13	15	23	11	13	15	23				
	Neomycine	1.299	1.071	1.209	1.267	1.299	1.071	1.209	1.267				
	Paromomycine	1.424	2.826	2.909	2.619	1.424	2.826	2.909	2.619				
	Spectinomycine	6.050	4.450	4.473	4.076	5.717	4.093	4.139	3.766	333	357	334	311
	Framycetinesulfaat				2				2				
Cephalosporins 1G	Cefalexine	604	502	605	699	604	502	605	699				
	Cefalonium	18	12	22	10	18	12	22	10				
	Cefapirine	14	11	10	10	14	11	10	10				
	Cefazoline	0	2	2	1	0	2	2	1				
Cephalosporins 3G	Cefoperazon	6	7	6	4	6	7	6	4				
	Cefovecin	8	9	10	10	8	9	10	10				
	Cefquinome	151	147	183	202	151	147	183	202				
Cephalosporins 4G	Ceftiofur	866	679	651	594	866	679	651	594				
Fenicols	Chlooramfenicol	2	2	2	0	2	2	2	0				
	Florfenicol	1.666	1.381	1.352	1.435	1.649	1.360	1.333	1.435	17	21	19	-
Macrolides	Clindamycine	137	141	138	137	137	141	138	137				

	Erythromycine	54	-	-	0	54	-	-	0				
	Gamithromycine	26	32	26	18	26	32	26	18				
	Lincomycine	6.084	4.838	5.654	5.218	5.529	4.340	5.055	4.516	555	498	599	702
	Pirlimycine	0	0	0	0	0	0	0	0				
	Spiramycine	732	313	111	22	732	313	111	22				
	Tilmicosine	4.874	5.534	4.489	2.917	2.616	3.216	2.614	1.446	2.258	2.318	1.875	1.471
	Tulathromycine	66	57	57	70	66	57	57	70				
	Tylosine	11.554	7.871	11.367	9.763	10.200	6.122	9.733	8.573	1.354	1.749	1.634	1.190
	Tildipirosine				20				20				
	Tylvalosin				25				25				
Other	Metronidazol	72	68	49	88	72	68	49	88				
	Rifaximin	10	14	17	20	10	14	17	20				
	Tiamuline	2.041	3.316	2.518	2.374	1.648	2.524	2.106	1.692	393	792	412	681
	Valnemuline	234	212	153	69	-	-	-	-	234	212	153	69
	Zink bacitracine	31	37	33	27	31	37	33	27				
Penicillines	Amoxicilline	62.385	66.497	72.827	68.667	56.785	57.164	63.510	58.782	5.599	9.333	9.317	9.885
	Amoxicilline-clav	768	953	954	189	768	953	954	189				
	Ampicilline	484	326	251	291	484	326	251	291				
	Cloxacilline	514	543	513	416	514	543	513	416				
	Fenoxymethylpenicilline	157	99	249	385	157	99	249	385				
	Nafcilline	33	2	0	0	33	2	0	0				
	Penethamaat	283	274	290	314	283	274	290	314				

	Procaïne benzylpenicilline	8.527	11.389	12.779	12.205	8.527	11.389	12.779	12.205				
Polymyxins	Colistinesulfaat	9.906	9.878	9.102	9.635	7.280	7.134	6.724	7.064	2.627	2.744	2.378	2.571
	Polymyxine B sulfaat	1	1	1	1	1	1	1	1				
(Fluoro)quinolones	Danofloxacine	81	78	72	69	81	78	72	69				
	Difloxacine	27	23	12	9	27	23	12	9				
	Enrofloxacine	1.046	946	1.061	1.088	1.046	946	1.061	1.088				
	Flumequine	3.633	2.683	2.675	2.734	3.633	2.683	2.675	2.734				
	Ibafloxacine	4	1	1	1	4	1	1	1				
	Marbofloxacine	231	247	267	308	231	247	267	308				
	Orbifloxacine	0	0	1	2	0	0	1	2				
	Pradofloxacine				6				6				
Sulphonamides	Sulfachloorpyridazine natrium	1.701	2.438	886	555	1.701	2.438	886	555				
	Sulfadiazine	71.502	70.314	68.913	70.439	48.741	46.197	46.227	46.519	22.761	24.117	22.687	23.920
	Sulfadimethoxine natrium	460	478	-	-	460	478	-	-				
	Sulfadimidine natrium	747	466	423	178	747	466	423	178				
	Sulfadoxine	230	283	386	520	230	283	386	520				
	Sulfamethoxazol	130	83	84	107	130	83	84	107				
	Sulfanilamide	6.598	-	-	11	6.598	-	-	11				
	Trimethoprim	14.995	14.877	14.211	14.462	10.443	10.054	9.674	9.678	4.552	4.823	4.537	4.784
Tetracyclines	Chloortetracycline	2.211	2.288	3.088	1.364	826	884	781	578	1.385	1.404	2.306	786
	Doxycycline	54.719	57.216	53.865	45.904	46.313	47.827	45.227	38.137	8.406	9.389	8.639	7.767
	Oxytetracycline	16.567	14.334	15.501	15.738	15.760	12.465	13.089	14.609	807	1.869	2.412	1.129

Discussion

In the context of the increasing awareness of antimicrobial resistance development, comparable data and evolutions on antimicrobial consumption are of utmost importance. This forth BelVetSac report describes the antimicrobial use in animals in Belgium in 2012 and describes the evolutions in use since 2007.

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. This external and internal data validation has once again proven to be indispensable since a major data error was 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 be able to provide accurate data. We can confirm this experience.

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 (and vice versa).

In September 2012 the working group on data collection of the AMCRA (knowledge center on **a**nti**m**icrobial **c**onsumption and **r**esistance in **a**nimals in Belgium) has drafted an advise on the development of a data collection system at herd level which meets with the above mentioned requirements and largely excludes the possible sources of bias. Currently the Federal Agency for the Safety of the Food Chain and the Federal Agency for Medicines and Health Products are studying if and how to implement such a system.

As the usage data are concerned, this report shows a substantial decrease in consumption of antimicrobial compounds in veterinary medicine of 7,2% between 2011 and 2012. Since the total biomass produced in 2012 is almost equal to the production in 2011, a very comparable decrease of 6,9% is observed in mg consumed per kg biomass produced. This decrease is seen both in the consumption of antimicrobial pharmaceuticals (-8,0%) as well as premixes (-3,5%). This result is distinctly different from the previous years where a relative status quo of antimicrobial consumption was seen between 2008 and 2011. In 2012, a substantial reduction in use is observed and this is a positive result as it is known that the use of antimicrobials is the principal driver of resistance development and the best way to stop this evolution is a reduction in antimicrobial consumption. It is hoped for that this is a trend that can be confirmed in the years to come since the comparison with other EU countries (second ESVAC report) clearly shows that the antimicrobial consumption in Belgium is high in comparison to most other EEA countries.

When looking more in detail to the evolution in the different types of antimicrobials used, it is observed that the sulphonamides (31,1%), penicillines (29,7) and tetracyclines (22,7) remain the three most used antimicrobial classes with an important decrease in use of the tetracylines (-13%) and an increase in use of the sulphonamides (+1,6%). However, what is more worrisome is that also the use of molecules of critical importance for human medicine (grouped in the category of the “red” antimicrobials) such as the cephalosporines of the 3° and 4° generation and the fluoroquinolones is increasing for the second year in a row. These molecules have the potential to select for different types of resistance that are of high importance both for veterinary and human medicine. Therefore there is an urgent need for measures to restrict the use of these molecules. AMCRA has very recently issued guides on responsible antimicrobial use and part of the advice given in these guides is to strongly restrict the use of the “red” molecules for those situations where it can be shown that no other alternatives are available.

Relating this significant reduction in total antimicrobial consumption in comparison to 2011 and previous years to specific measures or actions is of course very difficult. However it is noticeable that since January 2012 AMCRA has become active in Belgium. During this first year this organization has spent enormous efforts to sensitize all stakeholders involved in animal production concerning the importance of restricted antimicrobial usage. It is believed (hoped) that the observed reduction are the first results of these efforts which are continued and even intensified in 2013.

Although these results show a positive and hopeful evolution they should by no means be interpreted as a sign to relax the efforts concerning the sensitization, guidance and legislation to move the whole sector further towards a rational reduction of the antimicrobial usage.

Conclusion

This report shows a substantial reduction in total antimicrobial consumption in animals in Belgium in comparison to 2011 both in absolute values as in comparison to the total biomass produced. This should only be seen as a starter of trend that needs to be sustained for many years. The increase in use of critically important antimicrobials is of high concern and warrants action. These results should be seen as a motivator for all stakeholders involved to continue and even increase the efforts for a rational reduction of antimicrobial usage.

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.

We would like to thank Gudrun Sommereyns from the Belgian Centre for Pharmacotherapeutic Information for the provided information and Steven Bruneel of the faculty of Veterinary Medicine, Ghent University for his excellent technical assistance and web development.

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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