BelVet-SAC

Belgian Veterinary Surveillance of Antibacterial Consumption

National consumption report

2013

Summary

This fifth BelVetSAC report, covers the results of the data collection on veterinary antibacterial consumption in Belgium in the year 2013. 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 2013. 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 2013, plus the number of dairy cattle present in Belgium times 500 kg of metabolic weight per head.

As the usage data are concerned, this report shows for the **second year in a row a decrease** in the **total consumption** of antibacterial compounds in veterinary medicine of **-6,6%** between 2012 and 2013. Due to the relative stable animal production (expressed in biomass -0,3%) the **decrease expressed in mg/kg biomass is -6,3%.** When using 2011 as a reference, a reduction of -12,7% (expressed in mg/kg biomass) was achieved between 2011 and 2013, distributed over a reduction of -13,3% in antibacterial pharmaceuticals and -10,2% in antibacterial premixes.

When looking more in detail to the different types of antibacterials used, it is observed that the penicillines (31,1%), sulphonamides (28,7%), and tetracyclines (24,1%) remain the three most used antibacterial classes. This year a substantial decrease in sulphonamide plus trimethoprim use and a limited decrease in penicillin and tetracycline use was observed. In contrast to last year, in 2013 the use 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 has substantially decreased. This is mainly due to the large reduction in use of flumequine. The use of the macrolides is reduced in 2013 by 3,8%.

Explaining the reasons for this second year in row of substantial reduction of antibacterial consumption in animals in Belgium, after many years of stabilization, remains difficult. However it is noticeable that since January 2012 AMCRA has become active in Belgium. During the first two year this organization has spent enormous efforts to sensitize all stakeholders involved in animal production concerning the importance of restricted antibacterial usage. On top of this it has issued guides on good management and antibacterial use as well as many advises that can, through several actions, lead to a reduced antibacterial consumption. It is believed that the observed reductions are the first results of these efforts which are continued and even intensified in 2014. Also in 2009 the ESVAC project to collect antibacterial usage data in all EU member states was started. Additionally EMA has provided guidelines for specific classes of antibacterials (fluoroquinolones, cefalosporines) which should result in a harmonization of the summary product characteristics (SPC) in which testing of the susceptibility of the strain in advance is

recommended. Also the preventive use of antibacterials is no longer acceptable according to these guidelines.

Although these results show a positive and hopeful evolution they should by no means be interpreted as a sign to relax the efforts on sensibilisation, guidance and regulation. On the contrary, when the achieved results are compared to the surrounding countries with a comparable animal production, it is clear that efforts should be further intensified.

Samenvatting

Dit vijfde BelVetSAC rapport omvat de resultaten van het gebruik van antibacteriële middelen bij dieren in België in 2013. 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 2013 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 tussen 2012 en 2013 met 6,6% gedaald (277850,3 kg in 2012; 259449,5kg in 2013). Dit is het tweede jaar oprij dat een duidelijke daling genoteerd wordt. De totale biomassa geproduceerd in 2013 in België is heel lichtjes gedaald t.o.v. 2012 (-0,3%) waardoor de daling in gebruik in absolute aantallen zich ook vertaald in een daling uitgedrukt in mg per kg geproduceerde biomassa van 6,3%. In de afgelopen twee jaar werd een totale reductie van 12,7% gerealiseerd (in mg per kg geproduceerde biomassa) en dit verdeeld over de farmaceuticals (13,3%) en de premixen (10,2%). Deze resultaten tonen een hoopvolle verderzetting van de dalende trend die in 2012 werd ingezet maar moeten tegelijk een motivatie zijn om de inspanningen nog verder aan te wakkeren om een verdere duurzame daling te realiseren

Wanneer meer in detail naar de verschillende types antibacteriëlemiddelen die worden gebruikt gekeken wordt merken we dat penicillines (31,1%), sulphonamides + TMP (28,7%) en tetracyclines (24,1%) de drie meest gebruikte antibacteriële klassen blijven. Dit jaar viel een substantiële reductie in het sulphonamide gebruik en een beperkte reductie in het penicilline en tetracycline gebruik op. In tegenstelling tot vorig jaar is ook het gebruik van de meest kritisch belangrijke antibacteriëlemiddelen de humane gezondheidszorg zoals de 3° en 4° generatie cefalosporines en de fluoroquinolonen voor het eerst ook aanzienlijk gezakt (-17,4 %). Ook het gebruik van de macroliden is lichtjes gedaald met 3,8%.

Duiden wat specifiek aan de basis ligt van een tweede daling op rij blijft moeilijk . Wel kan opgemerkt worden dat sedert 2009 het ESVAC project is gestart en in januari 2012 AMCRA van start is gegaan in België. In het eerste twee werkjaren van de vzw 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. Daarnaast heeft op Europees vlak EMA voor bepaalde klassen van antibacteriële stoffen (fluoroquinolones, cefalosporines) richtsnoeren uitgevaardigd die moeten leiden tot harmonisatie van de

samenvatting van de productkenmerken en bijsluiters waarin het “vooraf testen van de gevoeligheid van de oorzakelijke kiem” wordt aanbevolen. Ook het uitsluitend preventief gebruik van antibiotica is niet meer aanvaardbaar. Aanvullend heeft de vzw AMCRA ook gidsen voor goede management praktijken in de veehouderij en verantwoord antibioticumgebruik opgesteld alsook allerhande adviezen die op verschillende manieren naar een rationele reductie van het antibioticumgebruik kunnen leidden.

Alhoewel de resultaten een positieve trend vertonen, mogen ze op geen enkele manier geïnterpreteerd worden als een teken om de inspanningen van sensibilisatie, begeleiding en regelgeving te verminderen. Wel in tegendeel, wanneer de gerealiseerde dalingen worden vergeleken met de cijfers van de omliggende lidstaten met eenzelfde type veehouderij wordt duidelijk dat de inspanningen verder geïntensifieerd moeten worden.

Résumé

Ce cinquième rapport BelVetSAC reprend les résultats de l'utilisation d'antibactériens chez les animaux en Belgique en 2013. Les données comprennent tous les antibactériens qui ont été vendus à des pharmaciens ou vétérinaires en Belgique (= médicaments pharmaceutiques antibactériens), ainsi que les prémélanges antibactériens administrés via un aliment médicamenteux. Il s'agit donc de données concernant l'utilisation d'antibactériens, aussi bien chez les animaux d'élevage que chez les animaux de compagnie. Pour pouvoir proportionner l'utilisation au nombre d'animaux présents, cette consommation est divisée par la biomasse, à savoir la somme des kilogrammes de viande de porc, de volaille et de bœuf produite en Belgique au cours de l'année 2013, majorée du nombre de vaches laitières présentes multiplié par leur poids métabolique.

La consommation totale d'antibiotiques dans la médecine vétérinaire, exprimée en tonnes de substance active, a baissé de 6,6% % entre 2012 et 2013 (277 850,3 kg en 2012 ; 259449,5kg kg en 2013). C'est la deuxième année consécutive que l'on constate une nette diminution. La biomasse totale produite en Belgique 2013 a très légèrement baissé par rapport à 2012 (-0,3%). Cette baisse de la consommation exprimée en chiffres absolus se traduit également par une baisse de la consommation exprimée en mg de substance active par kg de biomasse produite, égale à 6,3% %. Au cours des deux dernières années, on a réalisé une réduction totale de 12,7% (en mg/kg de biomasse produite) répartie sur les produits pharmaceutiques (13,3%) et les prémélanges (10,2%). Ces résultats montrent une continuation prometteuse de la tendance à la baisse amorcée en 2012, mais doivent également constituer une motivation pour redoubler encore les efforts en faveur d'une diminution durable.

Lorsque l'on s'attarde sur les différents types d'antibiotiques utilisés, on remarque que les pénicillines (31,1%), les sulfonamides (28,7%) et les tétracyclines (24,1%) restent les trois classes d'antibactériens les plus utilisées. Cette année, tandis que l'on a remarqué une forte augmentation de l'utilisation de tétracyclines, on a observé une baisse substantielle de l'utilisation de sulfonamides et une légère baisse de l'utilisation de pénicillines. Contrairement à l'an dernier, l'utilisation des antibiotiques les plus « critiques » en médecine humaine, comme les céphalosporines de 3ème et 4ème génération et les fluoroquinolones, a également baissé considérablement pour la première fois (-17,4 %). L'utilisation des macrolides a fait l'objet d'une légère diminution de 3,8 %.

Il est difficile de définir exactement ce qui est à l'origine d'une deuxième diminution consécutive. Cependant, on peut remarquer que le projet ESVAC a été lancé en 2009 et qu'AMCRA a démarré en Belgique en janvier 2012. Au cours des deux premières années d'existence de l'a.s.b.l. AMCRA, une énergie folle a été consacrée pour sensibiliser toutes les parties concernées au besoin d'une réduction responsable de l'utilisation d'antibiotiques. En

outre, pour certaines classes d'antibactériens (fluoroquinolones, céphalosporines), l'EMA a publié à l'échelle européenne des lignes de conduite censées mener à une harmonisation du résumé des caractéristiques du produit et des notices dans lesquels il est conseillé de « tester au préalable la sensibilité du germe causal ». Aussi, l'utilisation exclusivement préventive d'antibiotiques n'est plus acceptable. A titre de mesure complémentaire, l'a.s.b.l. AMCRA a également rédigé des guides relatifs aux bonnes pratiques de gestion dans le secteur de l'élevage et à l'utilisation responsable des antibiotiques, ainsi que toutes sortes de conseils qui peuvent, d'une façon ou d'une autre, permettre une réduction rationnelle de l'utilisation des antibiotiques.

Bien que les résultats montrent une tendance positive, ils ne peuvent en aucune façon être interprétés comme un signe indiquant que les efforts de sensibilisation, d'accompagnement et de réglementation peuvent être réduits. Au contraire, lorsque l'on compare les diminutions réalisées avec les chiffres des Etats membres voisins ayant le même type d'élevage, il est clair que les efforts doivent être davantage intensifiés.

Preface

Antibacterials are valuable tools in the preservation of animal health and animal welfare, and must be responsibly used 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. The magnitude of this risk still needs to be quantified while increasing evidence of resistance transfer between ecosystems is found.

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 fifth BelVetSAC report gives an overview of the consumption of antibacterials in veterinary medicine in Belgium in 2013 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 2014 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 2013 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 (if available), formulation and package form. The wholesaler-distributor only needed to provide the number of packages sold for each product per year.

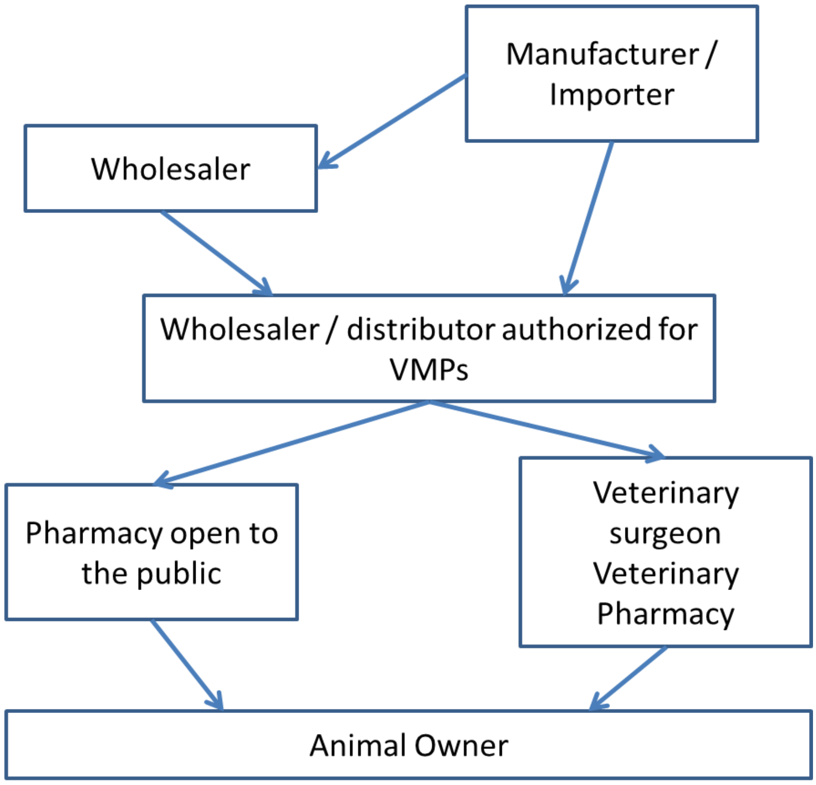

Figure 1. Distribution of Veterinary Medicinal products in Belgium.

b. 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 (n=60). They received a list of registered and marketed Antibacterial containing premixes. The feed mills were asked by letter dd. Februari 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 Antibacterial containing premixes for the year 2013. Antibacterial premixes can only be incorporated into medicated feed on prescription of a veterinarian.

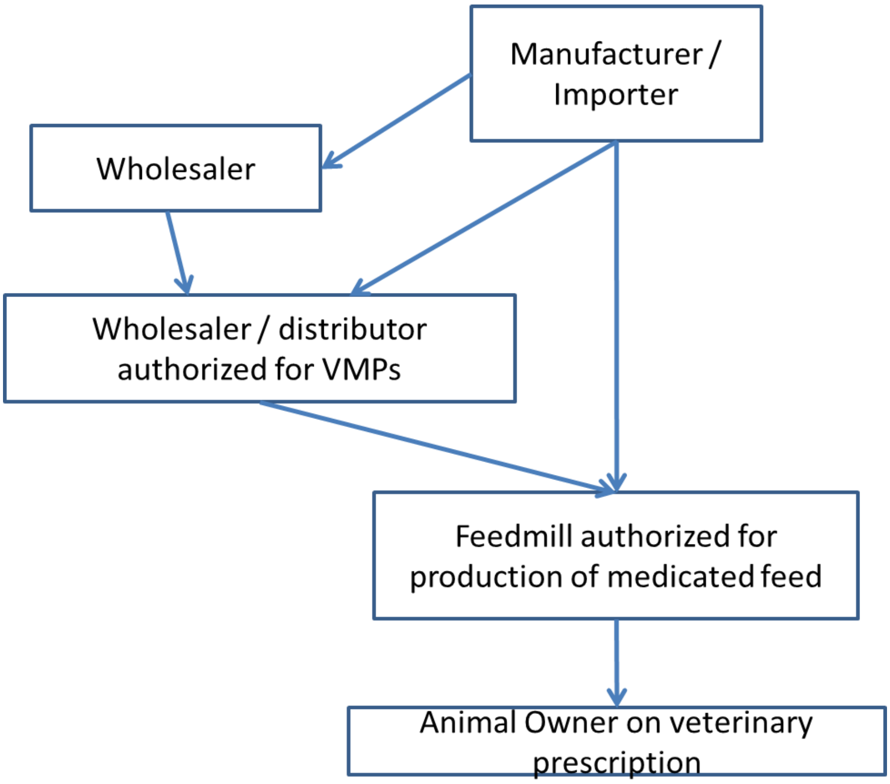

Figure 2. Distribution of Veterinary premixes in Belgium.

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 are always marginally higher than 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 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 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), 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.

Recently a overview study of Filippitzi et al., 2014 has attempted to extrapolate the results of several in depth studies on Antibacterial use in pigs, poultry and veal calves in Belgium towards the whole population in order to make a rough estimate of the proportion of use in the different species. The results of this study are given in the results section.

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 60 compound feed producers, licensed for the production of medicated feed responded. Of these 8 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 one important difference was found in a large wholesaler-distributor (apparent reduction of sales around 80%). 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 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 2007 according to the commented compendium of the Belgian Centre for Pharmacotherapeutic Information 2007-2012respectively (www.bcfi-vet.be).

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

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

The only new antibacterials registered on the market in the last 5 years are gamithromycin (2009), tildipirosin (2011) and pradofloxacine (2011). The observed variation in available

[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.

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 2008 and 2013.

Animal biomass	2009	2010	2011	2012	2013
Meat (ton)					
Pork	1 082 036	1 123 769	1 108 255	1 109 610	1 130 570
Beef	255 017	263 142	272 286	262 280	249 910
Poultry[a]	442 296	404 343	402 753	410 215	388 090
Total biomass from meat production	**1 779 349**	**1 791 254**	**1 783 294**	**1 782 105**	**1 768 570**
Dairy cattle					
Dairy cattle (number)	517 700	517 700	510 600	503 500	515 990
Dairy cattle metabolic weight (ton)	258 850	258 850	255 300	251 750	257 995
Total biomass (ton)	**2 038 199**	**2 050 104**	**2 038 594**	**2 033 855**	**2 026 565**

[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.

A decrease in biomass production of 0,3% is observed between 2012 and 2013.

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.

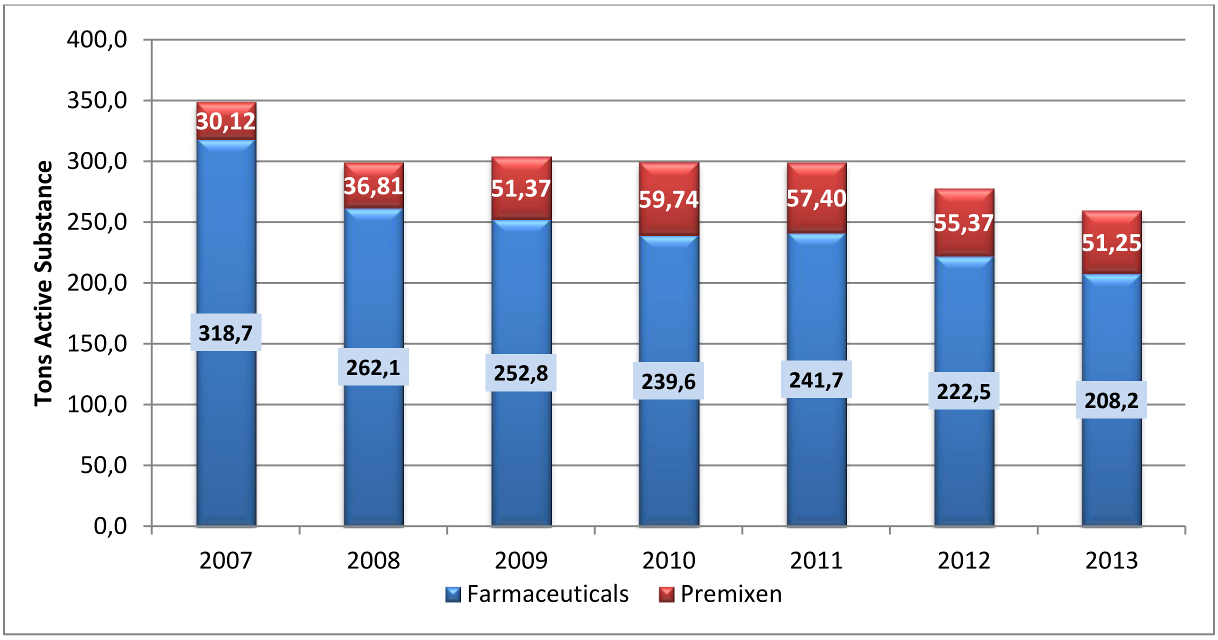

Figure 3. Total national consumption of antibacterial compounds for veterinary use in Belgium for the years 2007-2013 (tons active substance)

Between 2012 and 2013, there was a **decrease of 6,6%** in the total consumption of antibacterials in veterinary medicine in Belgium (277850,3 kg in 2012; 259449,5kg kg in 2013). The use of antibacterial pharmaceuticals decreased with 6,4% between 2012 and 2013, and the use of antibacterial premixes decreased with 7,4%. When looking at the trend from 2007 onwards (start data collection) a decrease of 25,6% in total consumption is observed.

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

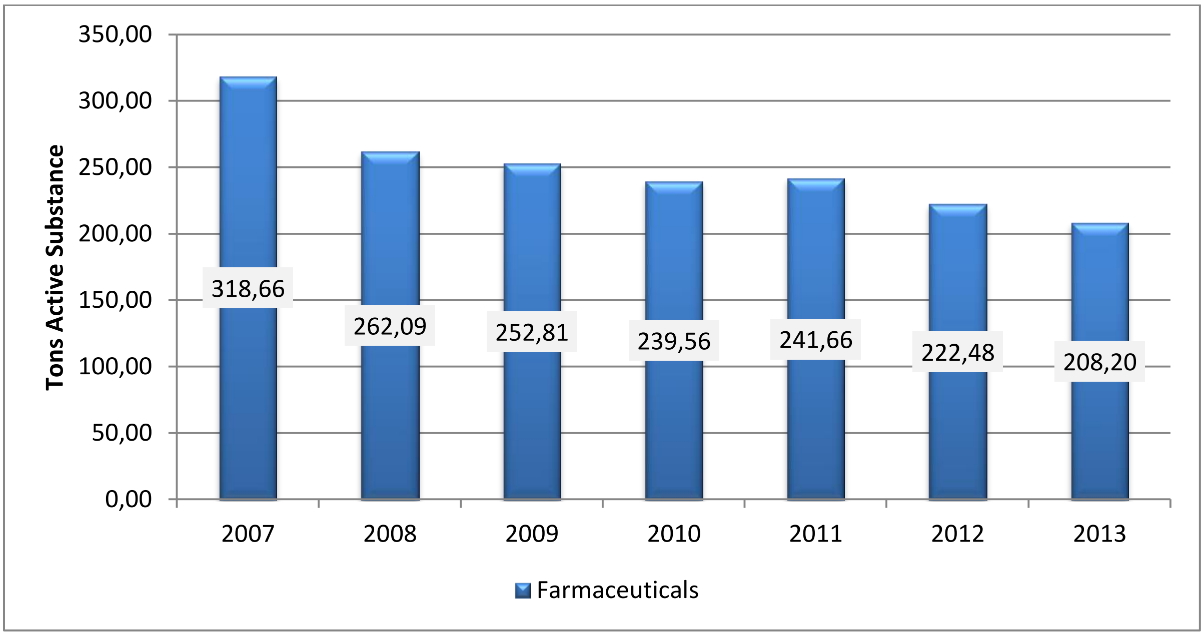

Figure 4. National consumption of antibacterial pharmaceuticals for veterinary use in Belgium for the years 2007-2013 (tons active substance)

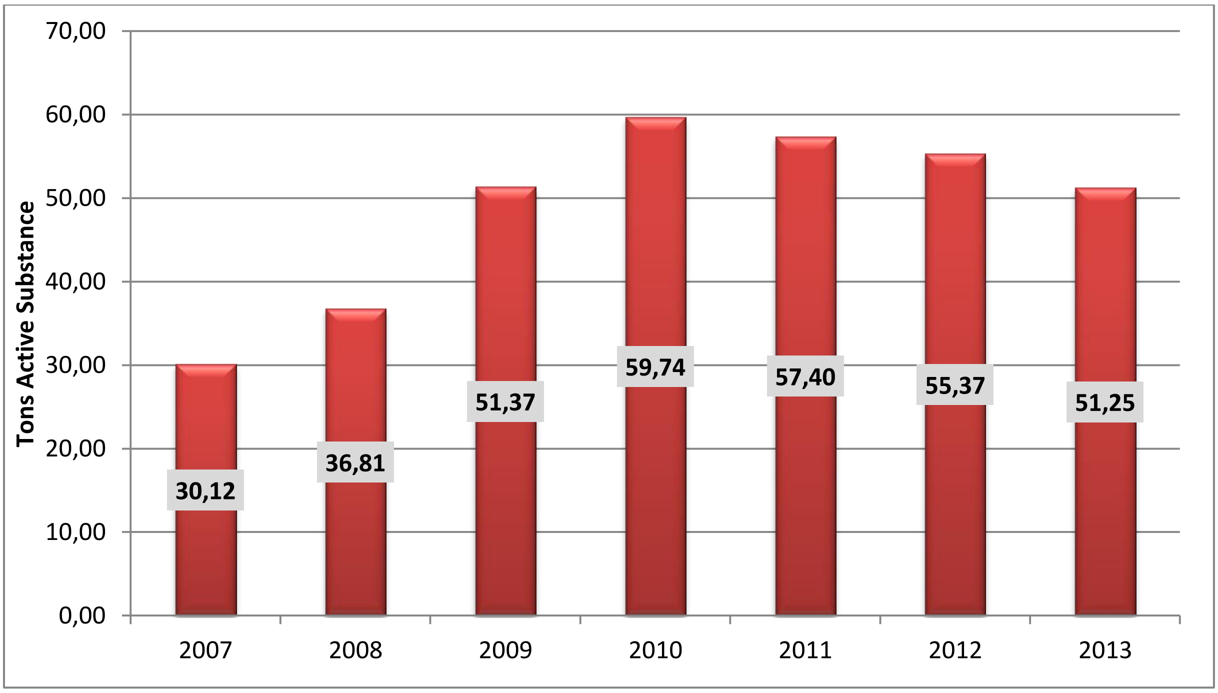

Figure 5. National consumption of antibacterial premixes in Belgium for the years 2007 -2013 (tons active substance)

After an increase in use of Antibacterial premixes between 2007 and 2010, the decreasing trend firstly observed in 2011 further continues. Since 2011 the data collection system allows to differentiate the animal species of destination for the Antibacterial premixes. Over these years more than 99,% of the antibacterial premixes go to pig feed. In 2013 only 0,7% was used in poultry feed and 0,05% in rabbit feed.

Since September 2013 the use of Zinc oxide in therapeutic doses (2500 ppm) in piglets for two weeks after weaning is allowed. In the field it is seen that this product is now used very often. In the first 4 months of allowance 8075 kg of active substance of Zinc Oxide were used in Belgium.

Antibacterial use versus biomass

As described above, the total biomass production in 2013 in Belgium has been slightly reduced (-0,3%) in comparison to 2012. As a consequence the decreasing trends in use observed in absolute is largely comparable to the decrease observed in relative numbers. For 2012, the mg of active substance used in comparison to the kg biomass produced was 136,6 mg/kg in 2013 this was 128.0. This is **a decrease of 6,3% in comparison to 2012.**

Figure 6 presents these data, again subdivided into antibacterial pharmaceuticals and antibacterial premixes.

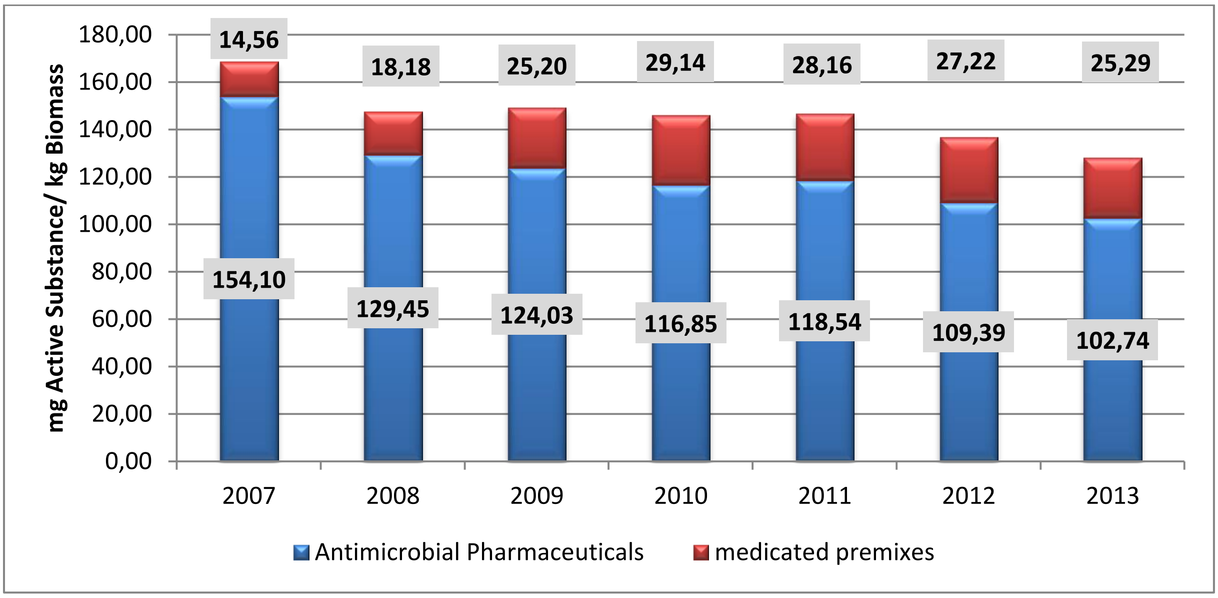

Figure 6. Total mg of active substance used per kg biomass produced in Belgium for 2007-2013. Note that the absolute values of mg/kg differ slightly from number presented in previous BelVetSAC reports due to retrospective change in the production numbers reported in Eurostat (see table 3).

After a substantial decrease in use per kg biomass produced in 2012 (-6,9%), the positive downward trend is continued in 2013, however the decrease is a little less.

When using 2011 as a reference (see AMCRA 2020 objectives), a reduction of 12,7% was achieved, distributed over a reduction of 13,3% in antibacterial pharmaceuticals and 10,2% in antibacterial premixes. Between 2007 and 2013 a total decrease of 24,1% is seen.

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

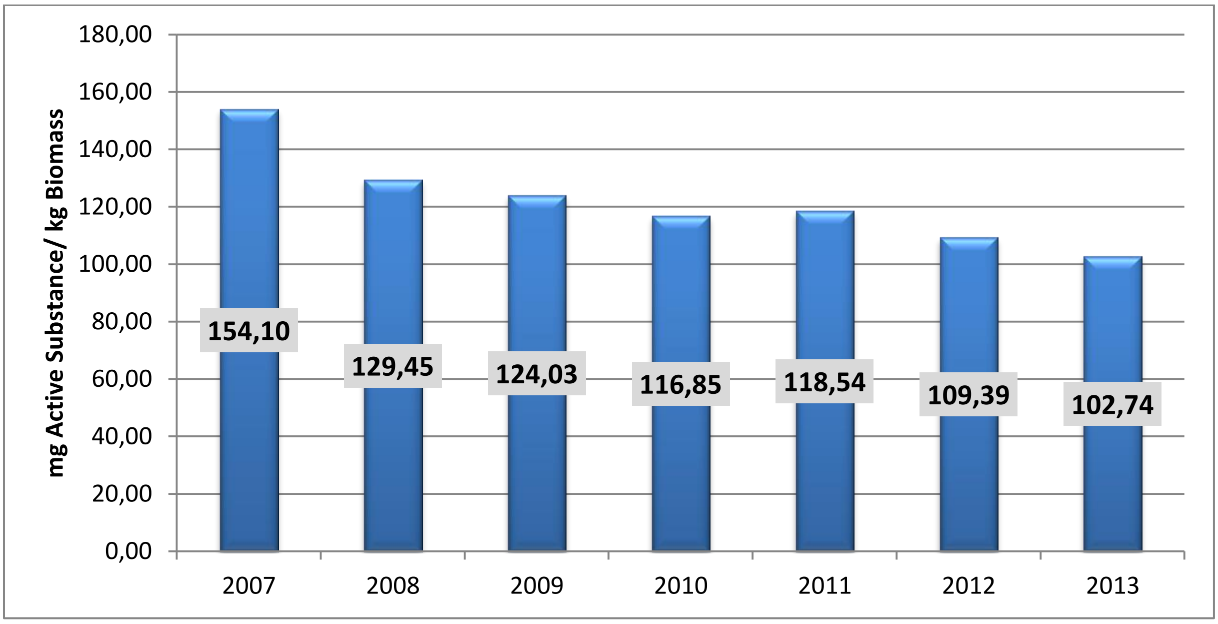

Figure 7. Mg active substance of antibacterial pharmaceuticals used per kg biomass in Belgium for 2007-2013.

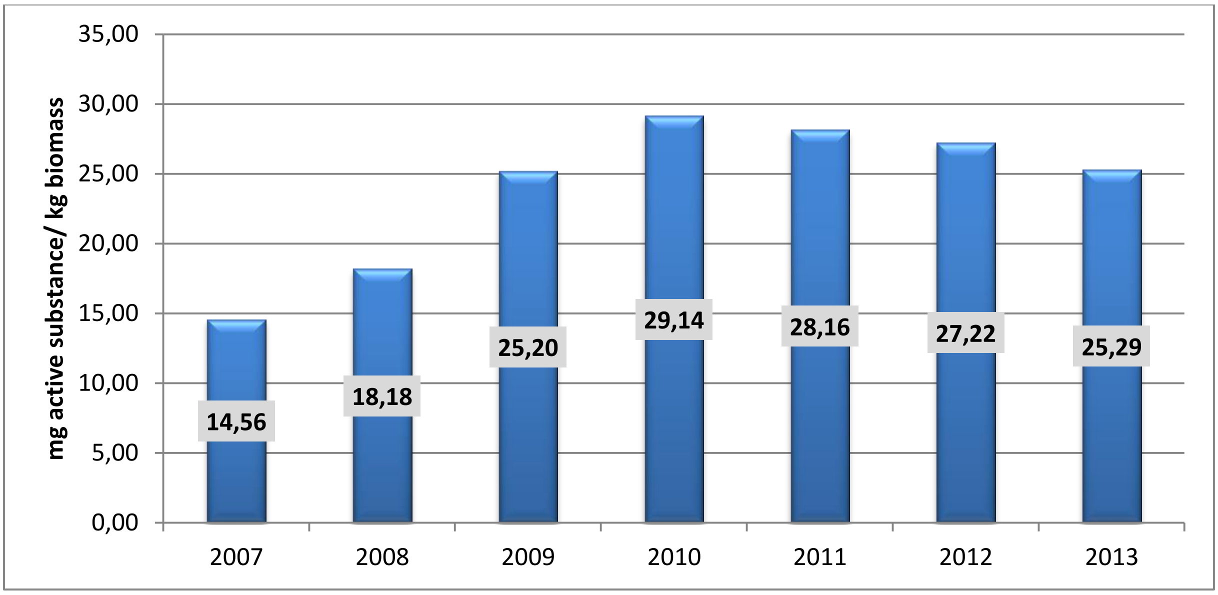

Figure 8. Mg active substance of antibacterial premixes used per kg biomass in Belgium for the years 2007 -2013.

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 October 2013, the third ESVAC report, presenting results on antibacterial usage in 25 EU /EEA countries in the year 2011 has become available (EMA, 2013). In this report the antibacterial consumption in animals in these 25 countries in 2011 is presented in relation to the animal production in the country.

In figure 9 the results of the 25 countries included in the third 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.

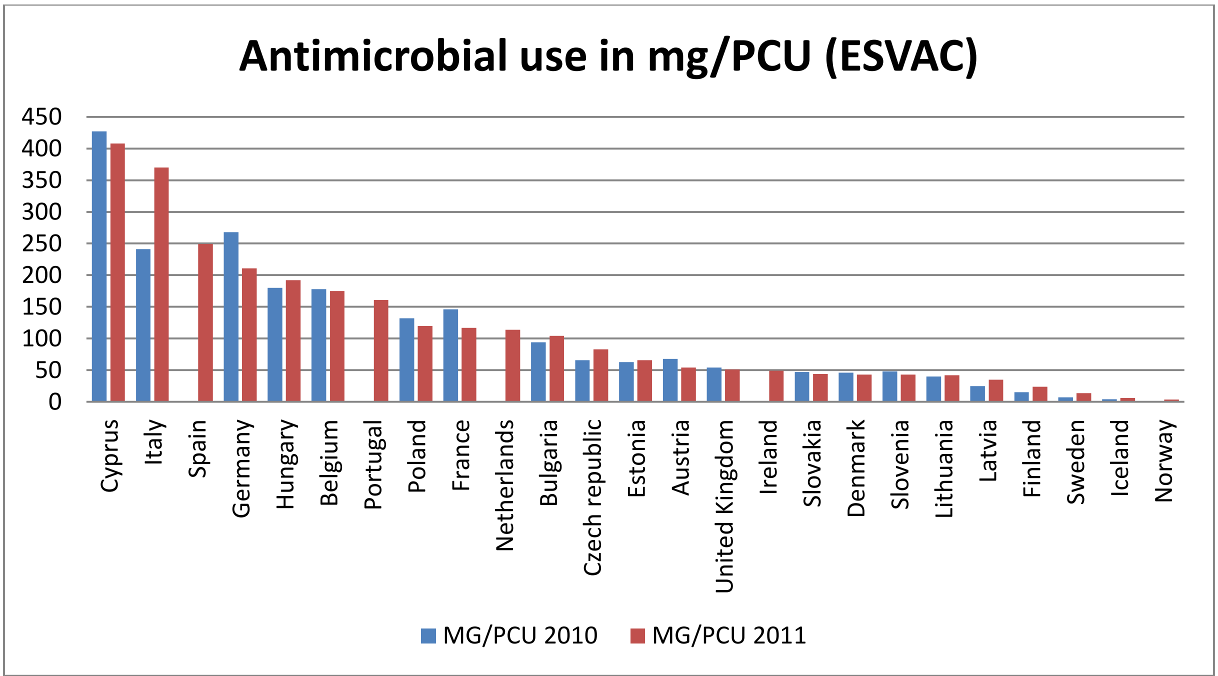

Figure 9. Sales for food-producing species, including horses, in mg/PCU, of the various veterinary Antibacterial classes, by country, for 2011 (source: third ESVAC report, Sales of veterinary Antibacterial agents in 25 EU/EEA countries in 2011 p 28).

When looking at figure 9 it can be observed that Belgium had the sixth highest level of Antibacterial usage expressed in mg/PCU in 2011. 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 2012 and 2013 may improve this situation but on the other hand it is know that in many countries throughout the EU measures and campaigns to reduce Antibacterial usage are started or implemented suggesting that also other countries will likely reduce the usage.

Antibacterial use per animal species

As mentioned before, the BelVetSAC datacollection system does not allow for clear allocation of the use towards the different animal species. However lately some exercises have been conducted to try to differentiate the total use a little more.

First, the dataset allows to select all antibacterials sold as tablets. Since these tablets are almost solely used for companion animals, the sales figures presented are thought to be a good estimate for sales of tablets of veterinary Antibacterial agents for companion animals.

In 2013 the total amount of active substance of antibacterials sold as tablets is 1858 kg which accounts for 0,9% of the Antibacterial pharmaceuticals used in 2013 and 0,7% of total amount of antibacterials (pharmaceuticals and premixes) used in 2013. Yet one needs to be careful in interpreting this result since besides tablets also other pharmaceutical formulations such as injectable or topical used products (often registered for multiple species) can be administered. Moreover, antibacterial products marketed for human use are also used in companion animals, in application of the 'cascade' (Articles 10 and 11 of Directive 2001/82/EC of the European Parliament and of the Council). Consequently, the data do not give a complete picture of the sales patterns of antibacterial agents in companion animals.

In a recent study op Filippitzi et al. (2014) an attempt was made to extrapolate the results of three specific studies, describing the use of antibacterials in detail in pigs (Callens et al., 2012), white veal calves (Pardon et al., 2012) and poultry (Persoons et al., 2012) in Belgium to the annual national level of antibacterial consumption by the respective animal sectors. The objective of this extrapolation attempt was to provide estimates on antibacterial consumption for the actual species at national level and was made according to the methodology proposed in the ESVAC scientific guidelines paper on collection of reliable and standardized data on consumption of antibacterial agents by animal species (Anonymous, 2013), which could be summarized as follows:

Amount of antibacterials administered nationally, per species =

= amount of antibacterials used in the studied population × (whole national population) / (studied population)

The results of the extrapolation were compare to the results of the total use in Belgium I,n 2009 as presented in first BelVetSAC report. The year 2009 was selected as reference since the studies report on data that were collected in 2009 and 2010.

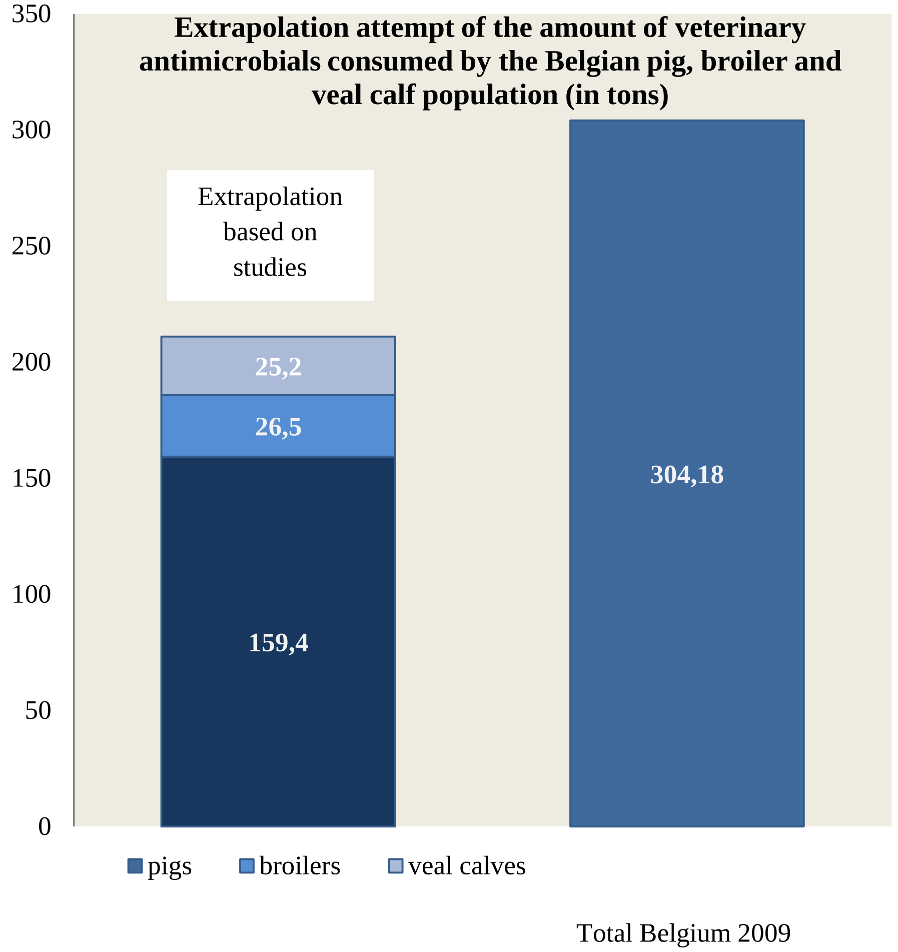

Figure 10. Left column: estimated amount of antibacterials used per year in Belgian pigs, broilers and veal calves at national level, after extrapolating farm-level data from selected studies; right column: total amount of antibacterial pharmaceuticals and medicated premixes used in Belgium in 2009. (Filippitzi et al., 2014).

Obviously, it can be expected that there is a large uncertainty margin around the results of the extrapolations and therefore these results should be interpreted carefully. Moreover several important animal species such as dairy and meat producing cattle, as well as small ruminants, horses,… are not included. None the less some general conclusion can be drawn. The first conclusion is that the vast majority of antibacterials used in Belgium are administered to pigs. This also suggest that that is the sector where the most effect can be obtained from measures for antibacterial reduction. The second conclusion is that, although the veal production sector is not that large in Belgium, there is a substantial amount of antibacterials going to this sector.

Antibacterial use per class of Antibacterial compounds

1. Total consumption (Antibacterial pharmaceuticals and premixes)

In Figure 11 the total consumption of antibacterials per class (ATC level 3 or 4) is presented.

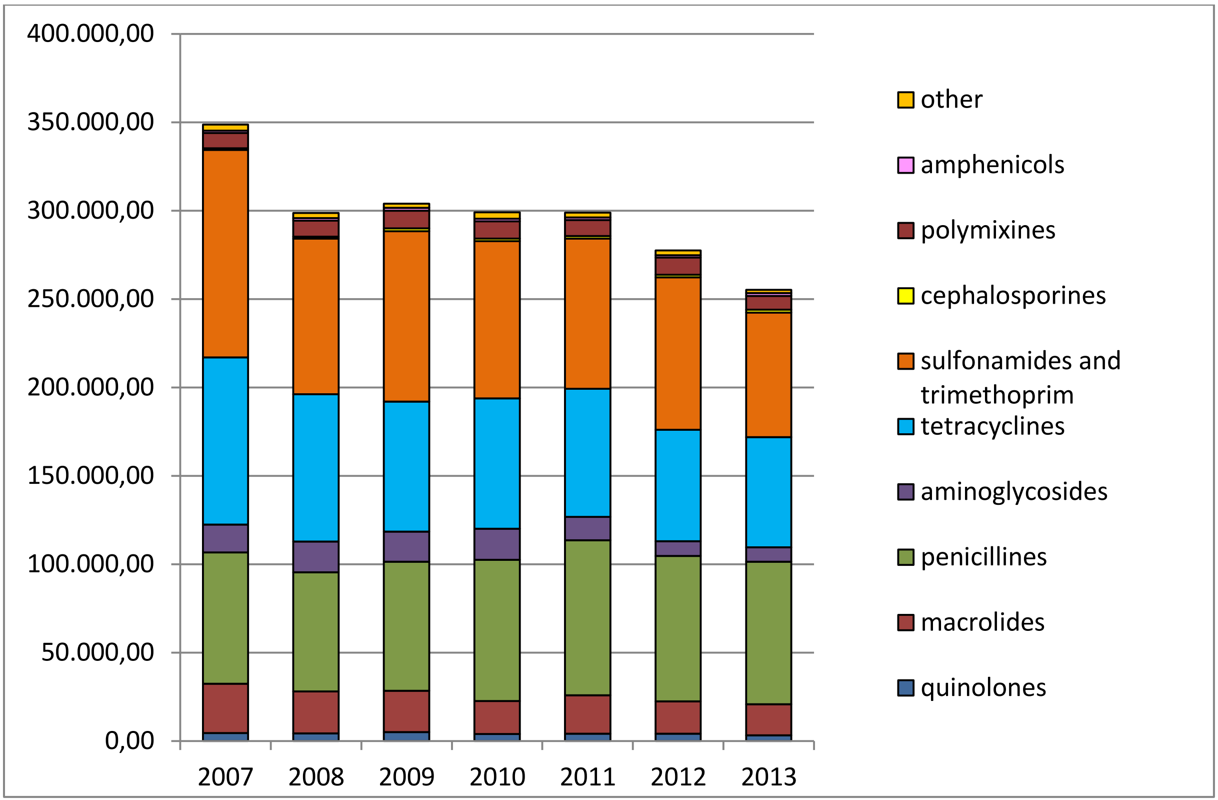

Figure 11. Total Antibacterial use per class of antibacterials.

In 2013, the most used group of antibacterials were the penicillines (81 tons, 31,1%) followed by the sulphonamides and trimethoprim (70,4 tons, 27,2%) and the tetracyclines (63 tons, 24,1%). In previous years sulphonamides and trimethoprim have always been the most used compound, 2013 is the first year where the penicillines are on number one. This is due to a substantial decrease in use of sulphonamides and trimethoprim (-13,6%) and only a limited reduction in use of the penicillines (-2,0%). The use of tetracyclines only reduced slightly (-0.9%) (Table 5). The use of the cephalosporins has remained almost stable in comparison to 2012 whereas the use of the quinolones is reduced remarkably (-21,4%) which is almost entirely due to a reduction of flumequine use. The use of polymixines (almost entirely colistine sulphate) has dropped substantially with 18.3% (1760 kg active substance) which is likely due to start of the use of zinc oxide as an alternative for colistine use in the treatment of post weaning diarrhea in piglets.

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

	Totaal				evolution		
Class	2010	2011	2012	2013	'10 » '11	'11 » '12	'12 » '13
penicillins	80.082,5	87.863,3	82.467,8	80.816,9	9,7%	-6,1%	-2,0%
sulphonamides and trimethoprim	88.939,1	84.902,8	86.273,5	74.556,9	-4,5%	1,6%	-13,6%
tetracyclines	73.838,2	72.454,1	63.006,2	62.411,1	-1,9%	-13,0%	-0,9%
macrolides	18.787,1	21.843,0	18.191,8	17.503,9	16,3%	-16,7%	-3,8%
polymixins	9.879,5	9.102,7	9.635,8	7.875,5	-7,9%	5,9%	-18,3%
aminosydes	17.382,2	13.166,9	8.313,9	8.089,6	-24,3%	-36,9%	-2,7%
quinolones	3.978,1	4.088,5	4.216,9	3.315,1	2,8%	3,1%	-21,4%
other	3.646,7	2.771,0	2.578,1	1.827,0	-24,0%	-7,0%	-29,1%
cephalosporins	1.368,9	1.489,7	1.529,8	1.540,4	8,8%	2,7%	0,7%
fenicols	1.382,7	1.354,4	1.435,5	1.513,3	-2,0%	6,0%	5,4%
Totaal (kg)	**299.285**	**299.037**	**277.649**	**259.450**	**-0,08%**	**-7,15%**	**-6,55%**

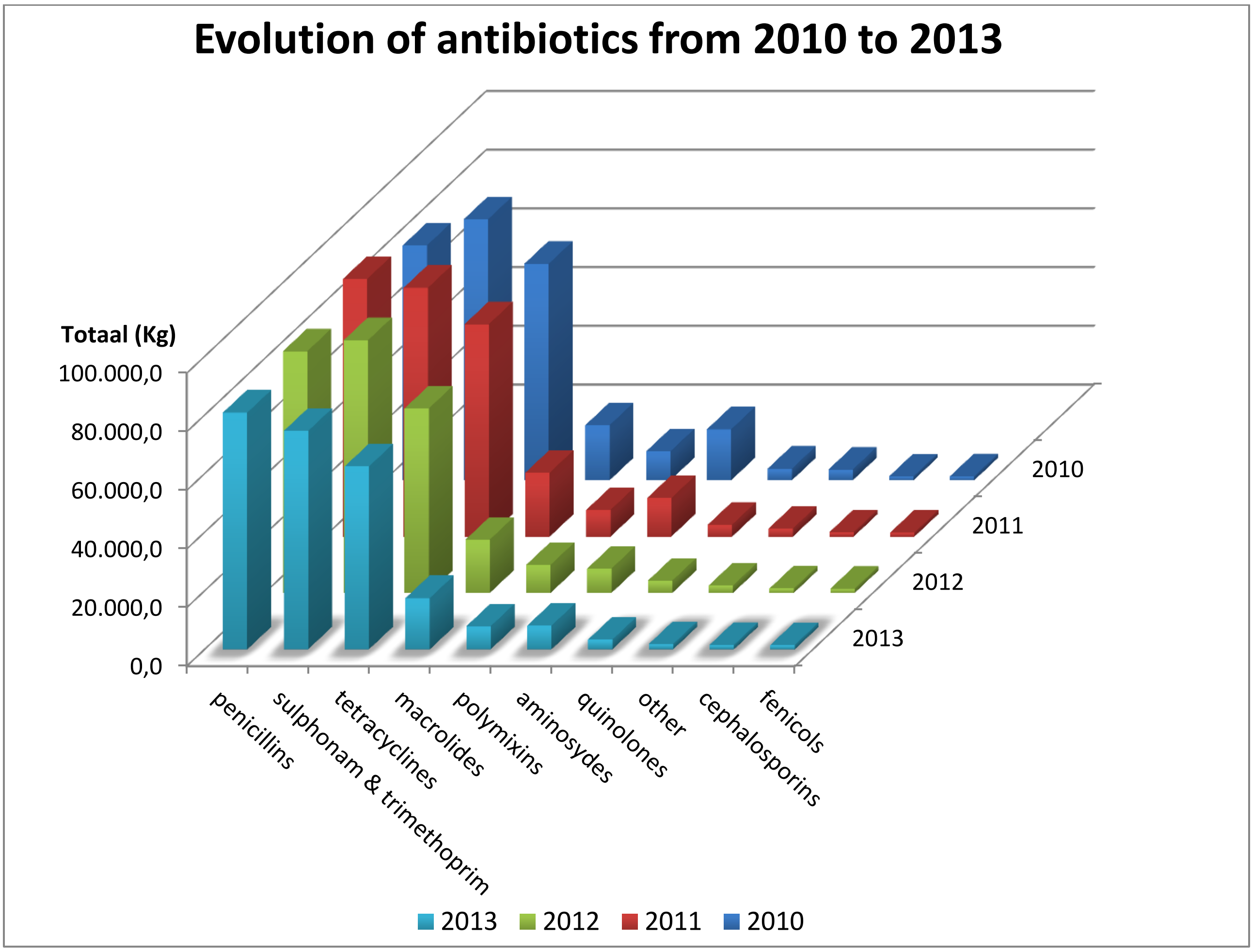

Figure 12: Evolution in the antibacterial consumption (kg) per antibacterial class. (Sulphonamides include also trimethoprim)

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 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 13 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. The largest decrease in use in absolute values the last year is seen in the yellow group. Whereas a slight increase in use is observed in the orange group. In the red group a remarkable decrease is observed which is entirely explained by a very substantial decrease in use of flumequine (-44%).

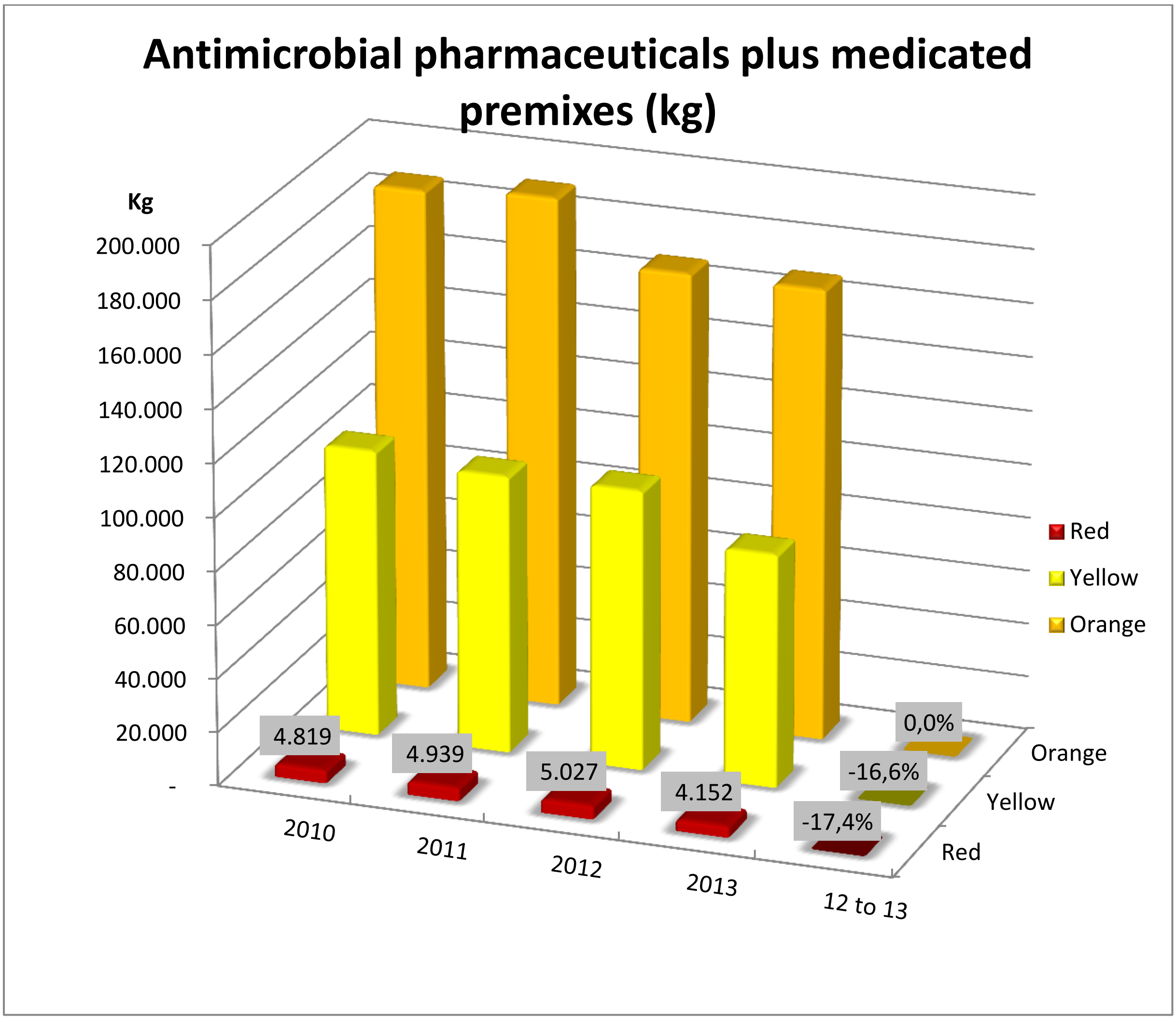

Figure 13: Evolution in the antibacterial consumption (kg) per antibacterial color group between 2010 and 2013.

2. Antibacterial pharmaceuticals

In Figure 14 the consumption of antibacterials per class (ATC level 3 or 4) is presented for the pharmaceuticals.

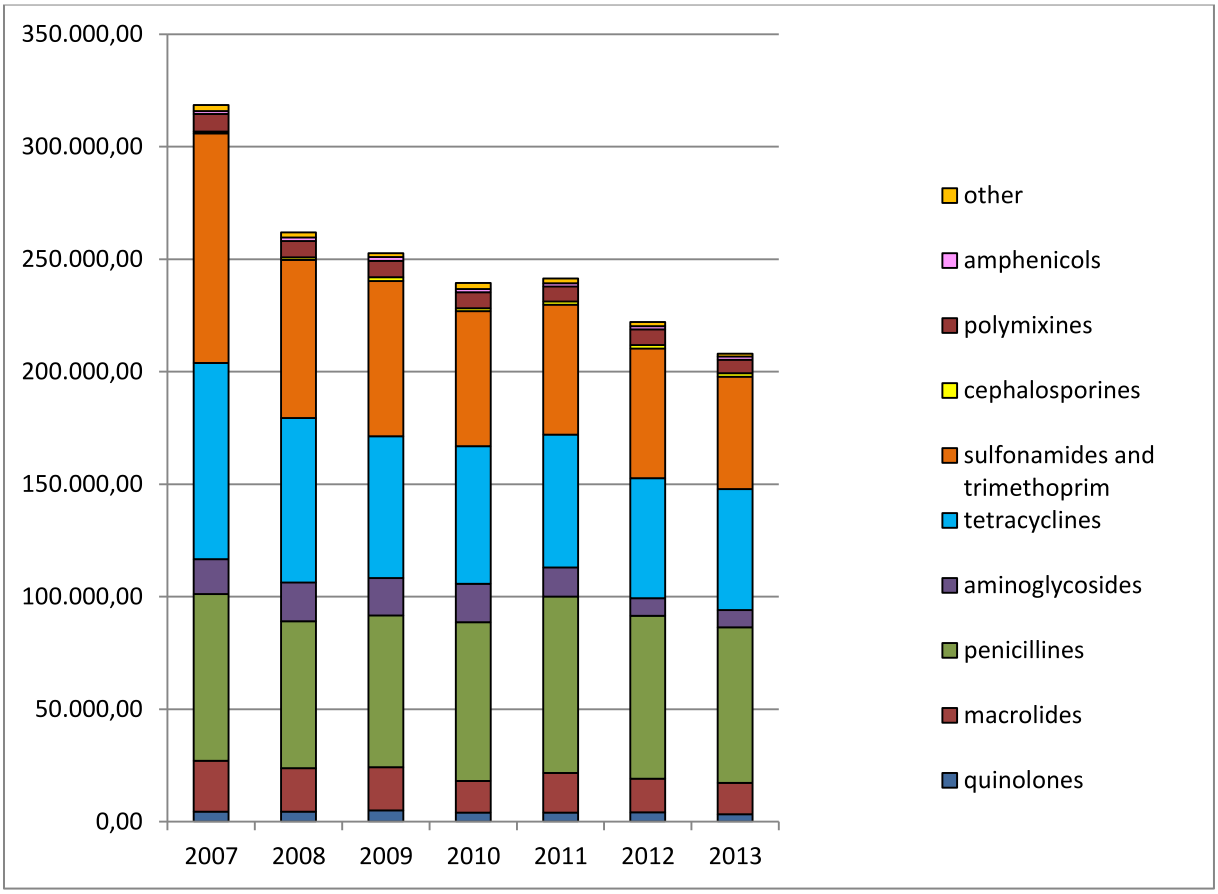

Figure 14. Use of antibacterial pharmaceuticals per class of antibacterials between 2007 and 2013.

3. Antibacterial premixes

In Figure 15 the consumption of antibacterials per class (ATC level 3 or 4) is presented for the Antibacterial premixes.

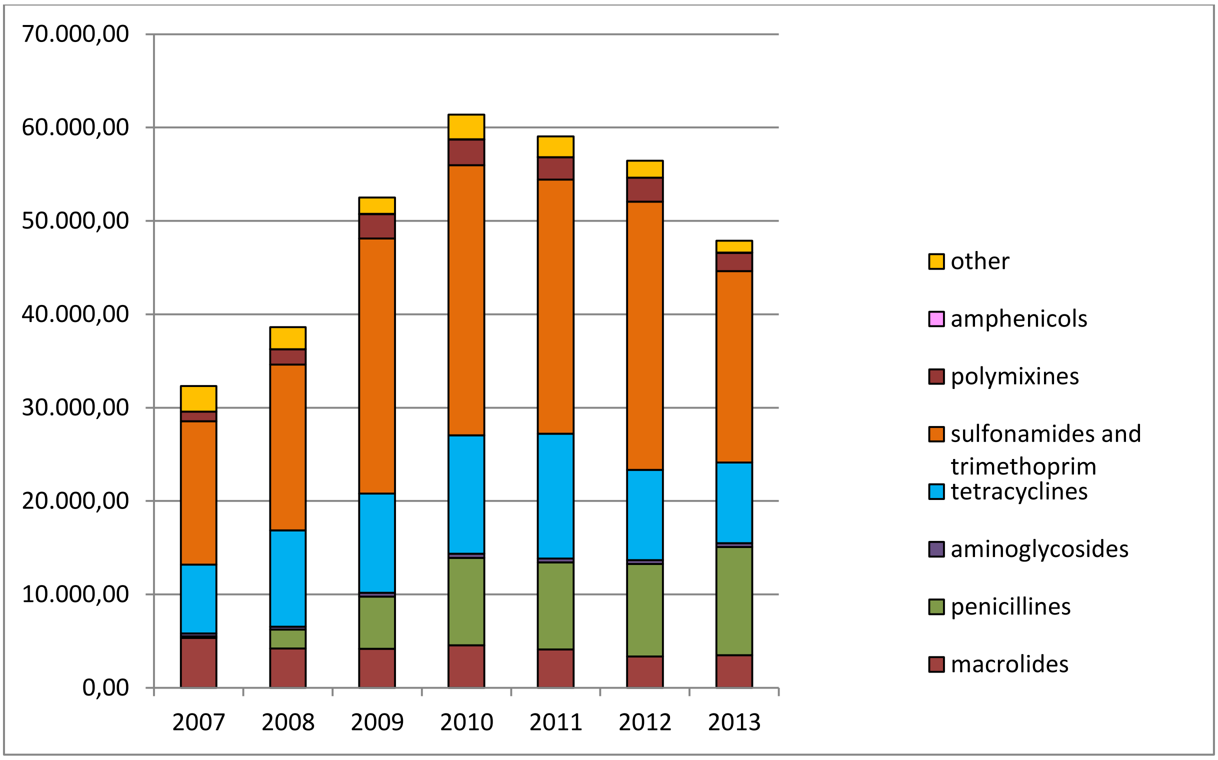

Figure 15. Use of antibacterial premixes per class of antibacterials between 2007 and 2013.

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	2010	2011	2012	2013	2010	2011	2012	2013	2010	2011	2012	2013
Amino(glyco)sides	apramycine	228	192	198	159	118	96	96	60	110	96	103	98
	dihydrostreptomycine	8.653	4.236	0	13	8.653	4.236	0	13				
	gentamicine	141	132	127	127	141	132	127	127				
	kanamycine	13	15	23	18	13	15	23	18				
	neomycine	1.071	1.209	1.267	1.037	1.071	1.209	1.267	1.037				
	paromomycine	2.826	2.909	2.619	2.534	2.826	2.909	2.619	2.534				
	spectinomycine	4.450	4.473	4.076	4.198	4.093	4.139	3.766	3.883	357	334	311	314
	framycetinesulfaat			2	5			2	5				
Cephalosporins 1G	cefalexine	502	605	699	675	502	605	699	675				
	cefalonium	12	22	10	14	12	22	10	14				
	cefapirine	11	10	10	5	11	10	10	5				
	cefazoline	2	2	1	10	2	2	1	10				
Cephalosporins 3G	cefoperazon	7	6	4	6	7	6	4	6				
	cefovecin	9	10	10	9	9	10	10	9				
	cefquinome	147	183	202	197	147	183	202	197				
Cephalosporins 4G	ceftiofur	679	651	594	624	679	651	594	624				
Fenicols	chlooramfenicol	2	2	0	0	2	2	0	0				

	florfenicol	1.381	1.352	1.435	1.513	1.360	1.333	1.435	1.513	21	19	-	1
Macrolides	clindamycine	141	138	137	144	141	138	137	144				
	erythromycine	-	-	0	-	-	-	0	-				
	gamithromycine	32	26	18	20	32	26	18	20				
	lincomycine	4.838	5.654	5.218	4.425	4.340	5.055	4.516	3.962	498	599	702	463
	pirlimycine	0	0	0	0	0	0	0	0				
	spiramycine	313	111	22	24	313	111	22	24				
	tilmicosine	5.534	4.489	2.917	4.118	3.216	2.614	1.446	2.361	2.318	1.875	1.471	1.757
	tulathromycine	57	57	70	109	57	57	70	109				
	tylosine	7.871	11.367	9.763	8.456	6.122	9.733	8.573	7.173	1.749	1.634	1.190	1.283
	tildipirosine			20	34			20	34				
	tylvalosin			25	172			25	172				
Other	metronidazol	68	49	88	92	68	49	88	92				
	rifaximin	14	17	20	115	14	17	20	115				
	tiamuline	3.316	2.518	2.374	1.547	2.524	2.106	1.692	1.028	792	412	681	519
	valnemuline	212	153	69	39	-	-	-	-	212	153	69	39
	zink bacitracine	37	33	27	33	37	33	27	33				
penicillines	amoxicilline	66.497	72.827	68.667	71.897	57.164	63.510	58.782	60.332	9.333	9.317	9.885	11.565
	amoxicilline-clav	953	954	189	181	953	954	189	181				
	ampicilline												

		326	251	291	240	326	251	291	240				
	cloxacilline	543	513	416	380	543	513	416	380				
	fenoxymethylpenicilline	99	249	385	294	99	249	385	294				
	nafcilline	2	0	0	12	2	0	0	12				
	benethamine penicilline				10,5				10				
	penethamaat	274	290	314	294	274	290	314	294				
	procaïne benzylpenicilline	11.389	12.779	12.205	7.508	11.389	12.779	12.205	7.508				
polymixins	colistinesulfaat	9.878	9.102	9.635	7.875	7.134	6.724	7.064	5.896	2.744	2.378	2.571	1.979
	polymyxine B sulfaat	1	1	1	0	1	1	1	0				
fluoroquinolones	danofloxacine	78	72	69	67	78	72	69	67				
	difloxacine	23	12	9	8	23	12	9	8				
	enrofloxacine	946	1.061	1.088	1.361	946	1.061	1.088	1.361				
	flumequine	2.683	2.675	2.734	1.535	2.683	2.675	2.734	1.535				
	ibafloxacine	1	1	1	1	1	1	1	1				
	marbofloxacine	247	267	308	335	247	267	308	335				
	orbifloxacine	0	1	2	3	0	1	2	3				
	pradofloxacine			6	6			6	6				
sulphonamides	sulfachloorpyridazine natrium	2.438	886	555	725	2.438	886	555	725				
	sulfadiazine	70.314	68.913	70.439	60.689	46.197	46.227	46.519	40.196	24.117	22.687	23.920	20.493
	sulfadimethoxine natrium	478	-	-	-	478	-	-	-				

	sulfadimidine natrium	466	423	178	2	466	423	178	2				
	sulfadoxine	283	386	520	459	283	386	520	459				
	sulfamethoxazol	83	84	107	101	83	84	107	101				
	sulfanilamide	-	-	11	11	-	-	11	11				
	trimethoprim	14.877	14.211	14.462	12.570	10.054	9.674	9.678	8.472	4.823	4.537	4.784	4.099
tetracyclines	chloortetracycline	2.288	3.088	1.364	750	884	781	578	371	1.404	2.306	786	379
	doxycycline	57.216	53.865	45.904	49.962	47.827	45.227	38.137	42.168	9.389	8.639	7.767	7.793
	oxytetracycline	14.334	15.501	15.738	11.700	12.465	13.089	14.609	11.231	1.869	2.412	1.129	469

Discussion

In the context of the increasing awareness of antibacterial resistance development, comparable data and evolutions on antibacterial consumption are of utmost importance. This annual BelVetSAC report is now produced for the fifth time and describes the antibacterial use in animals in Belgium in 2013 and the evolutions 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 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 antibacterial 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 antibacterial resistance than the total amount of antibacterials consumed. Recently started initiatives on the collection of data on antibacterial consumption at herd level in the pig sector (Belpork data collection system started January 2014) will provide in the near future the above described type of detailed information on a large part of the pig sector. 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 in development, aims at collecting this type of detailed information.

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

As the usage data are concerned, this report shows for the **second year in a row a decrease** in the **total consumption** of antibacterial compounds in veterinary medicine of **-6,6%** between 2012 and 2013. Due to the relative stable animal production (expressed in biomass -0,3%) the **decrease expressed in mg/kg biomass is -6,3%.**

When using 2011 as a reference, a reduction of 12,7% (expressed in mg/kg biomass) was achieved between 2011 and 2013, distributed over a reduction of 13,3% in antibacterial pharmaceuticals and 10,2% in antibacterial premixes.

When looking more in detail to the different types of antibacterials used, it is observed that the penicillines (31,1%), sulphonamides (28,7%), and tetracyclines (24,1%) remain the three most used antibacterial classes. This year a substantial decrease in sulphonamide use and a limited decrease in penicillin and tetracycline use was observed. In contrast to last year, in 2013 the use 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 has substantially decreased. This is mainly due to the large reduction in use of flumequine. The use of the macrolides is reduced in 2013 by 3,8%.

Explaining the reasons for this second year in row of substantial reduction of antibacterial consumption in animals in Belgium, after many years of stabilization, remains difficult. However it is noticeable that since January 2012 AMCRA has become active in Belgium. During the first two year this organization has spent enormous efforts to sensitize all stakeholders involved in animal production concerning the importance of restricted antibacterial usage. On top of this it has issued guides on good management and responsible antibacterial use as well as many advises that can, through several actions, lead to a reduced antibacterial consumption. It is believed that the observed reductions are the first results of these efforts which are continued and even intensified in 2014. Also in 2009 the ESVAC project to collect antibacterial usage data in all EU member states was started. Additionally EMA has provided guidelines for specific classes of antibacterials (fluoroquinolones, cefalosporines) which should result in a harmonization of the summary product characteristics (SPC) in which testing of the susceptibility of the strain in advance is recommended. Also the preventive use of antibacterials is no longer acceptable according to these guidelines.

Although these results show a positive and hopeful evolution they should by no means be interpreted as a sign to relax the efforts on sensitization, guidance and regulation. On the contrary, when the achieved results are compared to the surrounding countries with a comparable animal production, it is clear that efforts should be further intensified.

Conclusion

This report shows, for the second year in a row a reduction in total antibacterial consumption in animals in Belgium both in absolute values as in comparison to the total biomass produced. This result should be seen as a starter of a trend that needs to be sustained for many years as well as a motivator for all stakeholders involved to continue and even increase the efforts for a rational reduction of antibacterial usage. The comparison to the proposed goals indicates that, to achieve all goals set, some efforts will even need to be increased.

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