BelVet-SAC

Belgian Veterinary Surveillance of Antibacterial Consumption

National consumption report

2017

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Summary

This ninth annual BELVET-SAC report describes the antibacterial use in animals in Belgium in 2017 and the evolution since 2011. As for 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.

For the 2017 BELVET-SAC results, it is very encouraging to see that the positive evolution noticed for the previous years, is observed again in 2017 with **a reduction of -7,4% mg active substance/kg biomass in comparison to 2016**. This is the **highest reduction observed in one year since 2011**. In absolute numbers this relates to a decrease in the use of antimicrobial compounds of –8,3% subdivided in a decrease of **-1.6% in pharmaceuticals and -46,3% in antibacterial premixes**. This is to be combined with a decrease of the biomass of -0,8% in 2017. When aggregating the effect of these subsequent efforts over the years, a **total reduction of -25,9%** (mg active substance / kg biomass) **in comparison with 2011** is already achieved**.** In 2017, for the second year in a row , the very substantial reduction in use of antibacterial premixes is remarkably. Moreover this reduction is achieved in combination with a very substantial reduction (-33,6%) in use of ZnO at therapeutic doses. This very substantial reduction in use of **antibacterial premixes has resulted in a cumulative decrease of -66,6% since 2011.** This means that the set **objective of -50% of use in antibacterial premixes by 2017 as defined in the AMCRA objectives (adopted by the Belgian government in 2016) has been largely achieved on time through continued autoregulation.**

When looking more in detail to the different classes of antibacterials used, penicillines (34,7%) stay the most important class of consumed antimicrobials, followed by tetracyclines (23,4%) and the sulphonamides (18,3%). For the majority of the antimicrobial classes, a decrease in use is observed again in 2017. This was most pronounced for the quinolones (-64,2%) and the cephalosporines of the 3° and 4° generation (-65,9%), but also very substantial for sulphonamides (-31,8%) and polymyxins (-13,3%). For the latter this is already the 4th year in a row that a substantial reduction is observed. **When comparing to 2012** (before authorization of ZnO) **the polymyxin use has dropped with 62,8%.**

As the use of the different AMCRA color classes is concerned, there is a substantial reduction in the use of the 'yellow' products (-26,3%) and a **very important reduction in use of the 'red' product (-64,6%)**. Only the 'orange' products increased with 2,9%. **In comparison to 2011, the cumulative reduction of red molecules is 84,4% whereas a reduction of 75% was aimed for by 2020 in the AMCRA objectives. Therefore it can be concluded that the second goal is also largely achieved, even 3 years before the set deadline. This result is a clear example of a successful co-regulation.**

As the overarching objective of 50% reduction in total use by 2020 is concerned, this is clearly not yet fully achieved. Up to 2017, a **cumulative reduction of -25,9% is achieved** since 2011. This is the result of a reduction of -16,4% in antibacterial pharmaceuticals and -66,6% in antibacterial premixes. Although this result is promising, it also means that we are **still 24,0 % away from this goal.** Which means that in the following years (2018-2020) a continued annual reduction of over 8% is required. This clearly will require efforts from all partners involved.

In this report, an attempt is made to provide an overview and evolution in use per species where possible. This remains however a very difficult exercise due to the fact that there are many products that are registered for multiple species. Nonetheless from the data it appears that the major reductions in use are achieved in pig and poultry production. This is not surprising given the very substantial reduction in use of medicated feed which is almost exclusively used in pigs.

For the first time, also the evolution in use of intramammary products is presented (mainly used in dairy cattle). These results show a very substantial reduction of -30,1% between 2013 and 2015, yet followed by two years of slight increase of use of IM products (+2,6% in 2016 and +2,6% in 2017). These changes are mainly the result of changes in the use of dry cow therapy whereas the use of applicators for the treatment of mastitis cases has remained relatively stable. This illustrates that the dairy sector also needs to take action in the responsible and reduced use of antimicrobials.

In 2017 a limited reduction in use of antibiotics in companion animals is observed vs 2016 both in total use (-3,5%) as in the use of the critical important antimicrobials (red molecules) of -7%.

It can be concluded that the 2017 report **shows very promising results again with the achievement of already two out of the three quantitative goals** (use of premixes and otherwise use of critically important antimicrobials). Also regarding overall antibiotic consumption, a substantial further reduction could be observed. These evolutions strengthen us in the believe that the third and overarching objective of a 50 % reduction in use remains feasible, yet substantial efforts from all stakeholders will be required.

Samenvatting

Dit negende BelVet-SAC verslag bevat de resultaten van de gegevensverzameling rond het gebruik van antibacteriële middelen bij dieren in België in het jaar 2017 en toont de evolutie sinds 2011. Net zoals in de voorgaande rapporten werd de data verzameld bij de groothandelaren-distributeurs van diergeneesmiddelen en de mengvoederfabrikanten die een vergunning hebben om gemedicineerde voeders te maken.

De BelVet-SAC resultaten voor 2017 zijn zeer bemoedigend in die zin dat de positieve evoluties die in de voorbijgaande jaren werden opgetekend ook dit jaar opnieuw werden vastgesteld met een reductie van **-7,4% mg actieve substantie/kg biomassa in vergelijking met 2016. Dit is de grootste reductie in 1 jaar opgetekend sedert 2011.** In kg actieve substantie komt deze reductie neer op een vermindering van -8,3% verdeeld over -1,6% in farmaceutica en -46,3 in premixen. Dit moet gecombineerd worden met een daling in de totale biomassa van -0,8%. **Cumulatief** komt dit neer op een reductie in het gebruik van antibacteriële middelen van **-25,9%** (mg actieve substantie/kg biomassa) sinds 2011. Voor het tweede jaar op rij is de heel forse daling in het gebruik van premixen zeer opmerkelijk. Bovendien is deze daling gerealiseerd in combinatie met een grote daling (-33,6%) in het therapeutisch gebruik van ZnO. Deze opeenvolgende dalingen in gebruik van antibacteriële premixen heeft reeds geresulteerd in een **cumulatieve reductie van -66,6% sinds 2011**. **Dit wil zeggen dat het vooropgestelde objectief van -50% reductie in gebruik van antibacteriële premixen tegen 2017**, zoals beschreven in de AMCRA doelstellingen en overgenomen door de Belgische overheid in 2016, **ruim werd behaald binnen de voorziene timing**. Dit is dan ook een **schoolvoorbeeld van een geslaagde autoregulatie**.

Wanneer het gebruik van de verschillende klassen van antibacteriële producten meer in detail wordt bekeken dan blijkt dat de penicillines (34,7%) de meest gebruikte klasse blijft, gevolgd door de tetracyclines (23,4%) en de sulphonamiden (18,3%). Voor de meerderheid van de klassen wordt opnieuw een vermindering in gebruik waargenomen in 2017. Deze reductie was het meest uitgesproken voor de quinolones (-64,2%) en de cephalosporines van de 3° en 4° generatie (-65,9%) maar evenzeer voorde sulphonamiden (-31,8%) en polymixines (-13,3%). Wat deze laatste klasse betreft is de waargenomen reductie reeds de 4° in een rij waardoor er **sedert 2012 (voor de toelating tot gebruik van ZnO) reeds een reductie van -62,8% in polymixine gebruik is waargenomen.**

Wat betreft de opdeling van de klassen van antibiotica in de verschillende AMCRA kleurcodes werd er dit jaar een substantiële reductie in het gebruik van de "gele" producten waargenomen (-26,3%) en een zeer belangrijke daling in het gebruik van de "rode" producten **(-64,6%)**. Enkel het gebruik van "oranje" producten steeg in beperkte mate met 2,9%. In vergelijking met 2011 is er een **cumulatieve reductie in het gebruik van "rode" moleculen met -84,4% gerealiseerd terwijl er een reductie van -75% tegen 2020 was vooropgesteld in de AMCRA doelstellingen. Bijgevolg kan er worden geconcludeerd dat ook deze tweede doelstelling ruimschots werd gehaald en dit 3 jaar voor de deadline.** Dit resultaat is een mooi voorbeeld van het effect van co-regulatie.

Wat de derde en omvattende doelstelling van -50% in het totale gebruik tegen 2020 betreft kan worden gesteld dat deze nog zeker niet gerealiseerd is. Wel is er **in vergelijking met 2011 reeds een cumulatieve reductie van -25,9% waar te nemen.** Dit is het resultaat van een reductie van -16,4% in het gebruik van farmaceutica en -66,6% in het gebruik van premixen. Ondanks het feit dat dit reeds een hoopgevend resultaat is wil het tevens zeggen dat er nog 24% reductie te realiseren is. Daarom zullen in de komende jaren (2018-2020) nog heel wat blijvende inspanningen moeten geleverd worden door alle betrokken partijen.

In dit rapport is er eveneens een poging gedaan om een evolutie in het gebruik per diersoort te schetsen voor zover mogelijk. Dit blijft evenwel een moeilijke oefening daar er heel wat antibiotica geregistreerd zijn voor gebruik bij meerdere diersoorten. Des als niet te min tonen de resultaten dat de grootste dalingen worden waargenomen bij producten die geregistreerd zijn voor gebruik bij varkens en varkens en pluimvee. Dit is niet verassend gezien de zeer belangrijke daling in het gebruik van premixen welke bijna uitsluitend bij varkens worden toegediend. Voor de eerste keer werd ook gekeken naar de evolutie in het gebruik van intramammaire producten bij melkvee. Deze resultaten tonen een substantiële daling in het gebruik tussen 2013 en 2015 van -30,1%. Deze heeft zich echter in de laatste twee jaar niet verder doorgezet gezien er dan telkens een beperkte stijging van +2,6% werd waargenomen. De evoluties over de jaren zijn voornamelijk een gevolg van wijzigingen in het gebruik van droogzetpreparaten daar waar het gebruik van uiertubes ter behandeling van mastitis gevallen relatief stabiel blijft. Dit resultaat toont duidelijk aan dat ook de melkveehouderij de nodige maatregelen moet nemen om het antibioticum gebruik verder te reduceren. Tenslotte werd in 2017 een beperkte daling in het gebruik van antibiotica bij hond en kat waargenomen zowel voor wat betreft het totaal gebruik (-3,5%) als voor wat betreft het gebruik van kritisch belangrijk antibiotica (rode moleculen) van -7%.

Op basis van deze resultaten kan worden geconcludeerd dat er in 2017 opnieuw belangrijke vooruitgang werd geboekt waarbij reeds twee van de drie doelstellingen werden behaald. Ook wat betreft het totaal gebruik werd de grootste reductie in één jaar gerealiseerd sedert 2011. Deze evoluties sterken ons in de overtuiging dat ook de derde en omvattende doelstelling van -50% tegen 2020 haalbaar blijft maar dit zal wel blijvende inspanningen vergen van alle betrokken partijen.

Résumé

Ce 9e rapport BelVet-SAC reprend les résultats de la collecte de données relatives à la consommation d'antibactériens chez les animaux en Belgique pour l'année 2017 et présente leur évolution depuis 2011. Tout comme dans les rapports précédents, les données ont été collectées chez les grossistes-répartiteurs de médicaments vétérinaires et les fabricants d'aliments composés qui ont une autorisation pour fabriquer des aliments médicamenteux.

Les résultats BelVet-SAC pour 2017 sont très encourageants en ce sens que les évolutions positives qui ont été notées au cours des années précédentes ont de nouveau été constatées cette année avec une réduction de **-7,4% de mg de substance active / kg de biomasse par rapport à 2016. C'est la plus importante réduction en 1 an depuis 2011.** En kg de substance active, cette réduction revient à une diminution de -8,3% répartie comme suit : -1,6% pour les produits pharmaceutiques et -46,3% pour les prémélanges. Cela doit être combiné avec une diminution de la biomasse totale de -0,8%. **De manière cumulée**, cela revient à une réduction de la consommation d'antibactériens de **-25,9%** (mg de substance active/kg de biomasse) depuis 2011. Pour la deuxième année consécutive, la très forte diminution de la consommation de prémélanges est très remarquable. De plus, cette diminution a été réalisée en combinaison avec une importante diminution (-33,6%) de l'utilisation thérapeutique d'oxyde de zinc (ZnO). Ces diminutions successives de la consommation de prémélanges antibactériens ont déjà entraîné une **réduction cumulée de -66,6% depuis 2011**. **Cela signifie que l'objectif fixé de réduire de -50% la consommation de prémélanges antibactériens d'ici 2017**, telle que décrit dans les objectifs d'AMCRA et repris par les autorités belges en 2016, **ont été largement atteints dans le timing prévu**. Il s'agit donc un **exemple type d'une autorégulation réussie**.

Lorsque l'on examine plus en détail la consommation des différentes classes d'antibactériens, il apparaît que les pénicillines (34,7%) restent la classe la plus utilisée, suivie des tétracyclines (23,4%) et des sulfamides (18,3%). Pour la majorité des classes, on observe de nouveau une diminution de la consommation en 2017. Cette réduction était la plus prononcée pour les quinolones (-64,2%) et les céphalosporines de 3e et 4e générations (-65,9%) mais également pour les sulfamides (-31,8%) et les polymixines (-13,3%). En ce qui concerne cette dernière classe, la réduction observée est déjà la 4e de suite, ce qui fait que **depuis 2012 (avant l'autorisation d'utilisation du ZnO), on observe déjà une réduction de -62,8% de la consommation de polymixine**.

En ce qui concerne la répartition des classes d'antibiotiques en différents codes couleur AMCRA, on a observé cette année une réduction substantielle de la consommation des produits « jaunes » (-26,3%) et une diminution très importante de l'utilisation des produits « rouges » **(-64,6%)**. Seule la consommation des produits « orange » a augmenté dans une mesure limitée de 2,9%. Par rapport à 2011, une **réduction cumulée de l'utilisation de molécules « rouges » de -84,4% a été réalisée tandis qu'une réduction de -75% d'ici 2020 était prévue dans les objectifs AMCRA. Par conséquent, on peut conclure que ce deuxième objectif a été largement atteint et ce 3 ans avant la date limite**. Ce résultat est un bel exemple de l'effet de corégulation.

En ce qui concerne le troisième et ambitieux objectif de -50% dans la consommation totale d'ici 2020, on peut affirmer que celui-ci n'a certainement pas encore été réalisé. **Par rapport à 2011, on peut toutefois déjà observer une réduction cumulée de -26,0%**. C'est le résultat d'une réduction de -16,4% de l'utilisation de produits pharmaceutiques et de -66,6% de l'utilisation de prémélanges. Bien que cela soit déjà un résultat prometteur, cela veut également dire qu'il reste encore une réduction de 24% à réaliser. C'est pourquoi dans les années à venir (2018-2020), de nombreux efforts soutenus devront être fournis par toutes les parties concernées.

Dans ce rapport, une tentative a également été faite de brosser un tableau de l'évolution de la consommation par espèce animale dans la mesure du possible. Cela reste toutefois un exercice difficile vu que de nombreux antibiotiques sont enregistrés pour une utilisation chez plusieurs espèces animales. Les résultats montrent néanmoins que les principales réductions sont observées pour des produits qui sont enregistrés pour une utilisation chez les porcs et la volaille. Ce n'est pas étonnant vu l'importante baisse de la consommation de prémélanges qui sont presqu'exclusivement administrés chez les porcs. Pour la première fois, nous avons également examiné l'évolution de la consommation de produits intrammaires chez le bétail laitier. Ces résultats montrent une diminution substantielle, de -30,1%, de la consommation entre 2013 et 2015. Celle-ci ne s'est toutefois pas poursuivie ces deux dernières années vu qu'une augmentation limitée de +2,6% a chaque fois été observée. Les évolutions au cours des années sont principalement une conséquence des modifications de la consommation de préparations utilisées au cours du tarissement là où l'utilisation de injecteur intramammaire pour traiter les cas de mastite reste relativement stable. Ce résultat montre clairement que le secteur de l'exploitation laitière doit prendre les mesures nécessaires pour réduire davantage la consommation d'antibiotiques. Enfin, en 2017, une réduction

limitée de la consommation d'antibiotiques chez les chiens et chats a été observée aussi bien en ce qui concerne la consommation totale (-3,5%) qu'en ce qui concerne la consommation d'antibiotiques d'importance critique (molécules rouges) de -7%.

À partir de ces résultats, nous pouvons conclure qu'en 2017, des progrès importants (deux des trois objectifs ont déjà été atteints) ont de nouveau été enregistrés. Egalement en ce qui concerne la consommation totale, la plus grande réduction en un an depuis 2011 a été réalisée. Ces évolutions renforcent notre conviction selon laquelle le troisième et ambitieux objectif de -50% reste réalisable d'ici 2020 mais celui-ci exigera toutefois des efforts constants de la part de toutes les parties concernées.

Preface

Antibacterials are valuable tools in the preservation of animal health and animal welfare, and must be used responsibly as they may save lives and prevent animal suffering. However, The use of antibacterials invariably leads to selection of bacteria that are resistant against the substance used. Resistance can then spread in populations and the environment.
Antibacterial consumption in animals selects for antibacterial resistant bacteria in animals, leading to therapy failure in bacterial infections. Yet it might also jeopardize human health through transfer of resistant bacteria or their resistance genes from animals to humans via direct or indirect contact.

Today, antibacterial consumption and its link to antibacterial resistance in humans and animals is a worldwide point of concern. The World Health Organization has indicated the follow up of antibacterial resistance as one of the top priorities for the coming years. In 2013, the world economic forum has indicated the emergence of antibacterial resistance a global threat with the ability of destabilizing health systems, profound cost implications for economic systems and for the stability of social systems. In May 2015 the World Health Assembly unanimously adopted the Global Action Plan[1] (GAP) on Antimicrobial Resistance developed by the World Health Organization (WHO) with the contribution of the Food and Agricultural Organization (FAO) and the World Organization for Animal Health (OIE), calling all Member States of the World Health Organization to put in place national action plans against AMR by mid-2017.

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 ninth BelVet-SAC report gives an overview of the consumption of antibacterials in veterinary medicine in Belgium in 2017 and describes evolutions in use since 2011.

[1] http://apps.who.int/gb/ebwha/pdf_files/WHA68/A68_ACONF1Rev1-en.pdf?ua=1

Contents

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Materials and Methods

Data collection

1. 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 23 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 2018 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 2017 to a veterinarian or pharmacist in Belgium**. In Belgium, Antibacterial products are only available on prescription or by delivery from the veterinarian. Belgian veterinarians can both use antibacterial products in their daily practice, or sell them to animal owners (fig. 1). Sales from one wholesaler-distributor to another were excluded from the input data to prevent double counting. A pre-filled list of antibacterial containing veterinary medicinal products authorized and marketed on the Belgian market was provided, together with its market authorization holder and national code, formulation and package form. The wholesaler-distributor only needed to provide the number of packages sold for each product per year.

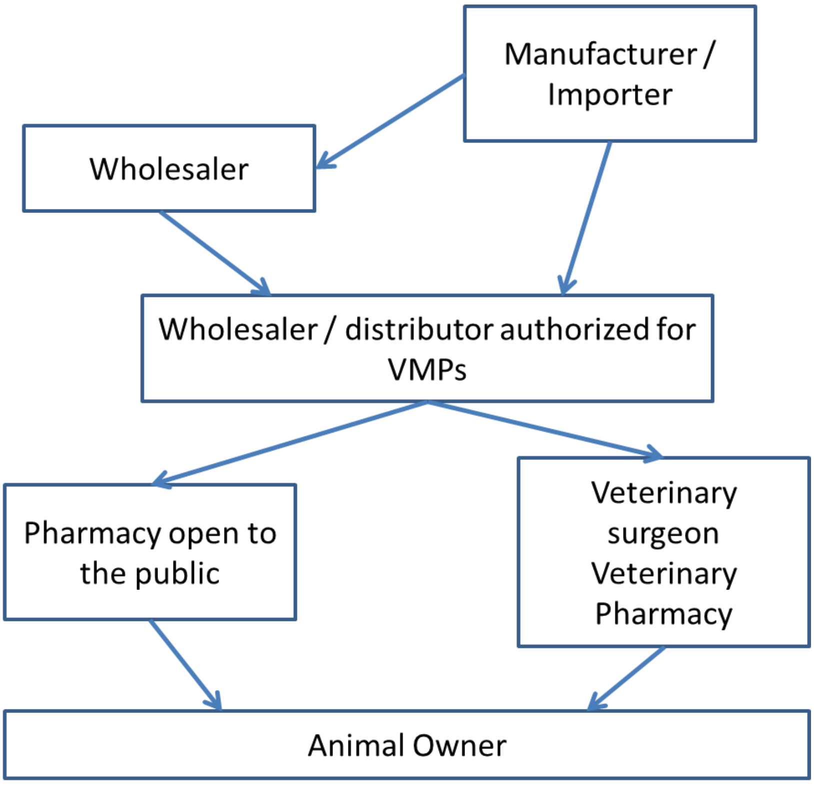


Figure 1. Distribution of Veterinary Medicinal products in Belgium.

b. Antibacterial premixes

As Antibacterial premixes can be purchased by feed mills directly from the producers or wholesalers (not necessarily through wholesaler-distributors) (fig. 2) also data on medicated feed were collected. This was done by contacting all Belgian compound feed producers that are licensed to produce medicated feed[2] (n=51). They received a list of registered and marketed Antibacterial containing premixes. The feed mills were asked by letter dd. January 2016 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 in 2017 was also submitted via the secure web-application[3]. Producers of medicated feed were asked to provide **data on the use of Antibacterial containing premixes as well as ZnO containing premixes for the year 2017**. Antibacterial and ZnO premixes can only be incorporated into medicated feed on prescription of a veterinarian.

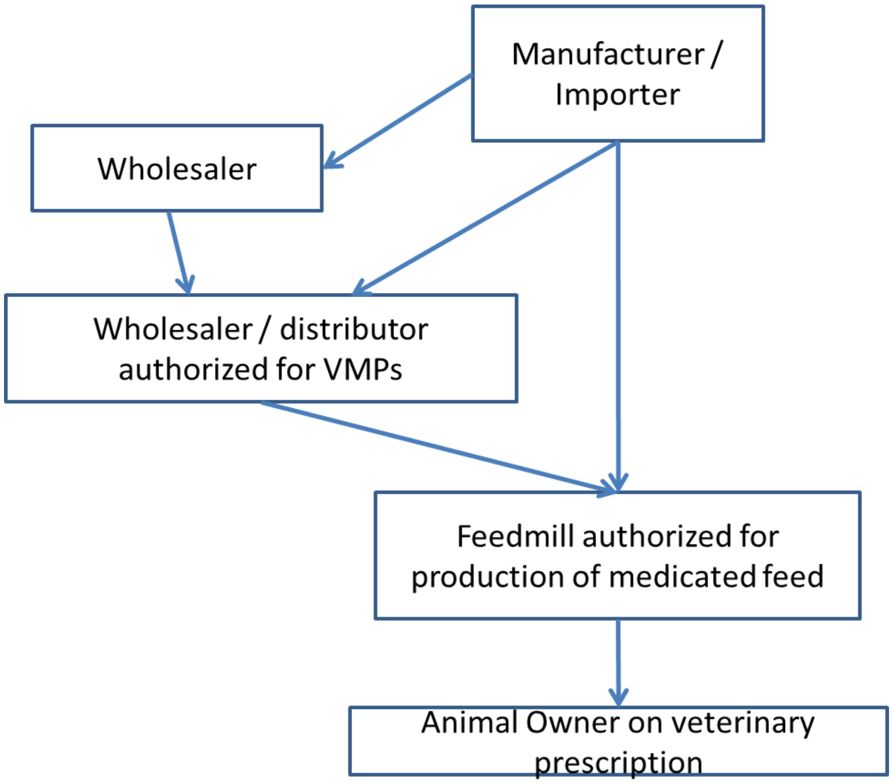


Figure 2. Distribution of Veterinary premixes in Belgium.

c. *Antibacterial classes included*

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

In the BelVet-SAC 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 consumption data as presented in this report may slightly differ from what is reported for Belgium in the ESVAC report.

As Zinc Oxide (ZnO) products (premixes) were authorized in Belgium since September 2013, sales data were collected and are presented separately.

[2] http://www.favv-afsca.be/bo-documents/Inter_R0-1002_3_dierlijke_producten_erkende_bedrijven.PDF
[3] www.BELVET-SAC.ugent.be

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

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

2. Animal population

Animal population data to calculate the produced biomass were derived from the Eurostat website[4].

From these animal population data, biomass (in kg) was calculated, according to Grave[5] et al., (2010), as the sum of the amount of meat of beef, pork, poultry and small ruminants 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 (BELVET-SAC 2007-2009; BELVET-SAC 2010; BELVET-SAC 2011; BELVET-SAC 2012, BELVET-SAC 2013, BELVET-SAC 2014, BELVET-SAC 2015, BELVET-SAC 2016)[6], 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 93% 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 and

[4] http://ec.europa.eu/eurostat/data/database
[5] Grave K, Torren-Edo J en Mackay D (2010). Comparison of the sales of veterinary antibacterial agents between 10 European countries. *Journal of Antibacterial Chemotherapy*, 65, 2037-2010
[6] http://www.belvetsac.ugent.be/

companion animals (dogs, cats, …) (estimated to be 7% 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.

Data validation

1. External data validation

To check for correctness and completeness the collected data on premixes were compared to data collected by the compound feed producing industry[7]. The datasets do not provide exactly the same information as the used data collection methodology is slightly different. However, trends and evolutions in the different datasets can be compared. If large discrepancies were observed data validity was further investigated and corrected, if needed.

To check for correctness of the reported pharmaceuticals data trends are compared with the data obtained from the market authorization holders (MAH) collected in the framework of the antibiotic tax as well as with the reported use data in Sanitel-Med.

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.

[7] www.bemefa.be

Results

Response rate and data validation

All of the 23 wholesaler-distributors, requested to deliver their sales data on veterinary antibacterial products sold in 2017, responded. All 51 compound feed producers, licensed for the production of medicated feed responded. Seven feed mills indicate not to have produced any medicated feed (any more) while 45 feed producers 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%.

Data providers get more and more accustomed to the system. In the last two years, the internal data validation step did not identify unexpected data entries. Therefore no data corrections were needed.

In the cross-validation of the data with the databases of BFA (Belgian Feed Association, formerly BEMEFA), comparable amounts and trends were found as presented in this report indicating again that the results presented for premixes are complete and also likely to be a realistic representation of the true use.

Number of antibacterial pharmaceuticals and premixes available on the Belgian market

Table 2 provides an overview of the number of antibacterial pharmaceuticals and antibacterial premixes available on the Belgian market since 2011 according to the commented compendium of the Belgian Centre for Pharmacotherapeutic Information[8].

Table 2. Armatorium of antibacterial products on the Belgian market in between 2009 and 2015.

	2011	2012	2013	2014	2015	2016	2017
Number of Antibacterial pharmaceuticals on the market	282	308	294	298	339	329	323
Number of Antibacterial premixes on the market	23	22	23	21	21	19	16
Total number of Antibacterial products on the market	305	330	317	319	360	348	339

The only new antibacterials registered on the market in the last 7 years are tildipirosin (2011), pradofloxacine (2011), fusidic acid (2014) and thiamfenicol (2015). The observed variation in available products is largely due to the marketing of new formulations or new generic products based on existing active substances.

[8] www.bcfi-vet.be

Animal biomass produced in Belgium

The produced biomass was calculated based on the Eurostat data for the years 2012-2017 as described above (Table 3).

Table 3. Animal Biomass produced in Belgium between 2012 and 2017

Animal biomass	2012	2013	2014	2015	2016	2017
Meat (ton)						
Pork	1 109 610	1 130 570	1 118 330	1 124 310	1 060 540	1 044 560
Beef	262 280	249 910	257 670	267 880	278 360	281 540
Poultry[a]	410 215	388 090	433 270	452 940	461 250	463 390
Sheep/goat[b]	2 163	2 410	2 560	2 720	3 020	3 230
Total biomass from meat production	**1 784 268**	**1 770 980**	**1 811 830**	**1 847 850**	**1 803 170**	**1 792 720**
Dairy cattle						
Dairy cattle (number)	503 500	515 990	519 090	528 780	529 780	519 160
Dairy cattle metabolic weight (ton)	251 750	257 995	259 545	264 390	264 890	259 580
Total biomass (ton)	**2 036 018**	**2 028 975**	**2 071 375**	**2 112 240**	**2 068 060**	**2 052 300**
Evolution since previous year	**-0.25%**	**-0.36%**	**+2.09%**	**+1.97%**	**-2.09%**	**-0.76%**

[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 BELVET-SAC reports.

[b] the biomass of sheep and goat was added to the total biomass for the first time in 2016. In all calculations and tables the new biomass (including sheep and goat) was adapted retrospectively to assure a correct evolution over time.

A **decrease in biomass production of 0,8%** is observed between 2016 and 2017.

Total consumption of Antibacterial drugs for veterinary use in Belgium

The total consumption of antibacterial products for veterinary use in Belgium is presented in Figure 3 in tons of active substance per year since the start of the data collection (2007). The total amount is subdivided into antibacterial pharmaceuticals and antibacterial compounds contained in antibacterial premixes incorporated into medicated feed intended to be used in Belgium.

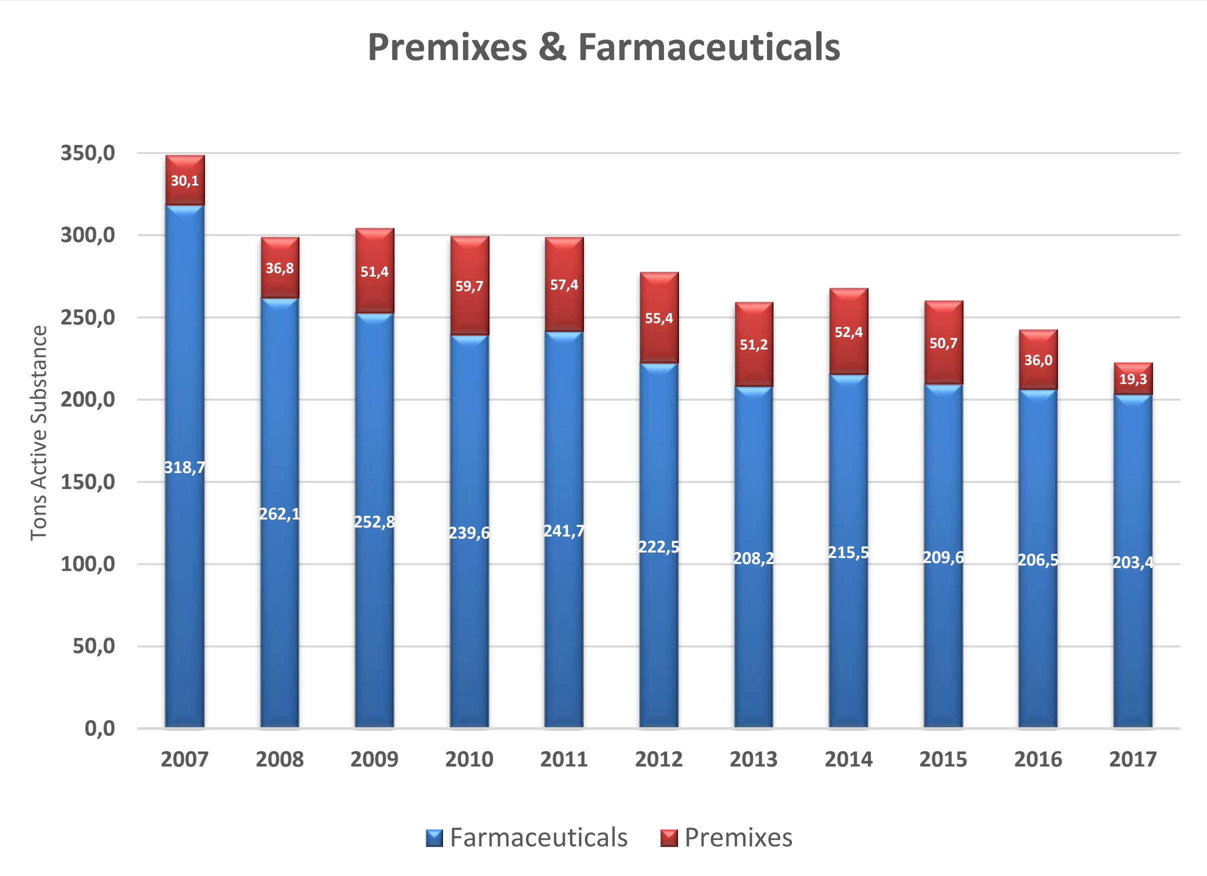


Figure 3. Total national consumption of antibacterial compounds for veterinary use in Belgium for the years 2007-2017 (tons active substance)

As 2011 has been selected as the reference year for all reduction initiatives (see further), further analysis shows the evolution from this year onwards.

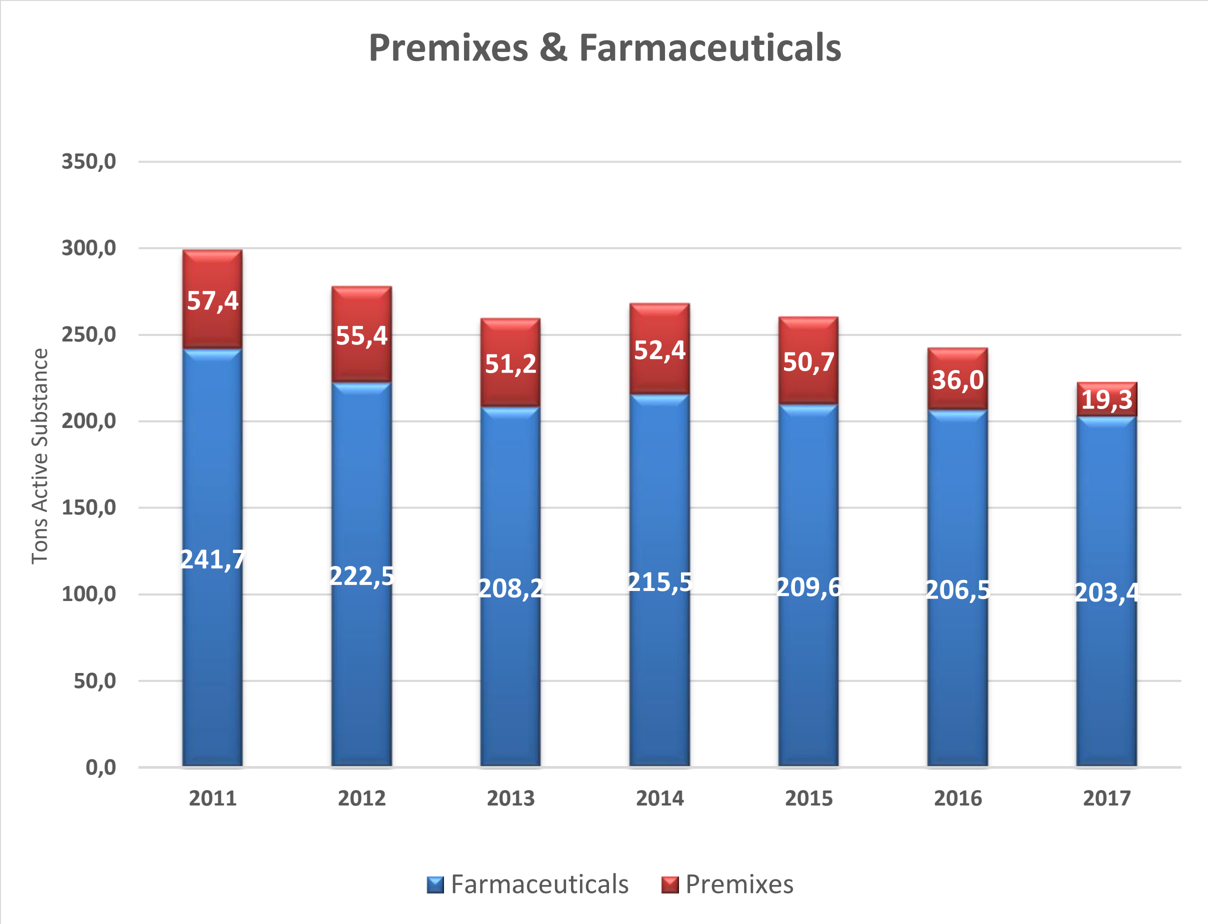


Figure 4. Total national consumption of antibacterial compounds for veterinary use in Belgium for the years 2011-2017 (tons active substance)

Between 2016 and 2017, there was a **decrease of -8,3%** in the total consumption of antibacterials in veterinary medicine in Belgium (222 465,2 kg in 2017; 242 490,4 kg in 2016). The use of antibacterial **pharmaceuticals decreased with -1,6%** between 2016 and 2017, and the use of **antibacterial premixes decreased with -46,3%.** After the slight increase in 2014, the decreasing trend which started again in 2015 clearly continued in 2016 and 2017. **Since 2011 (reference year for reduction initiative) a decrease of 25,6 % is realized in absolute volumes.**

Figures 5 and 6 show these data separately for the antibacterial pharmaceuticals and the antibacterial premixes.

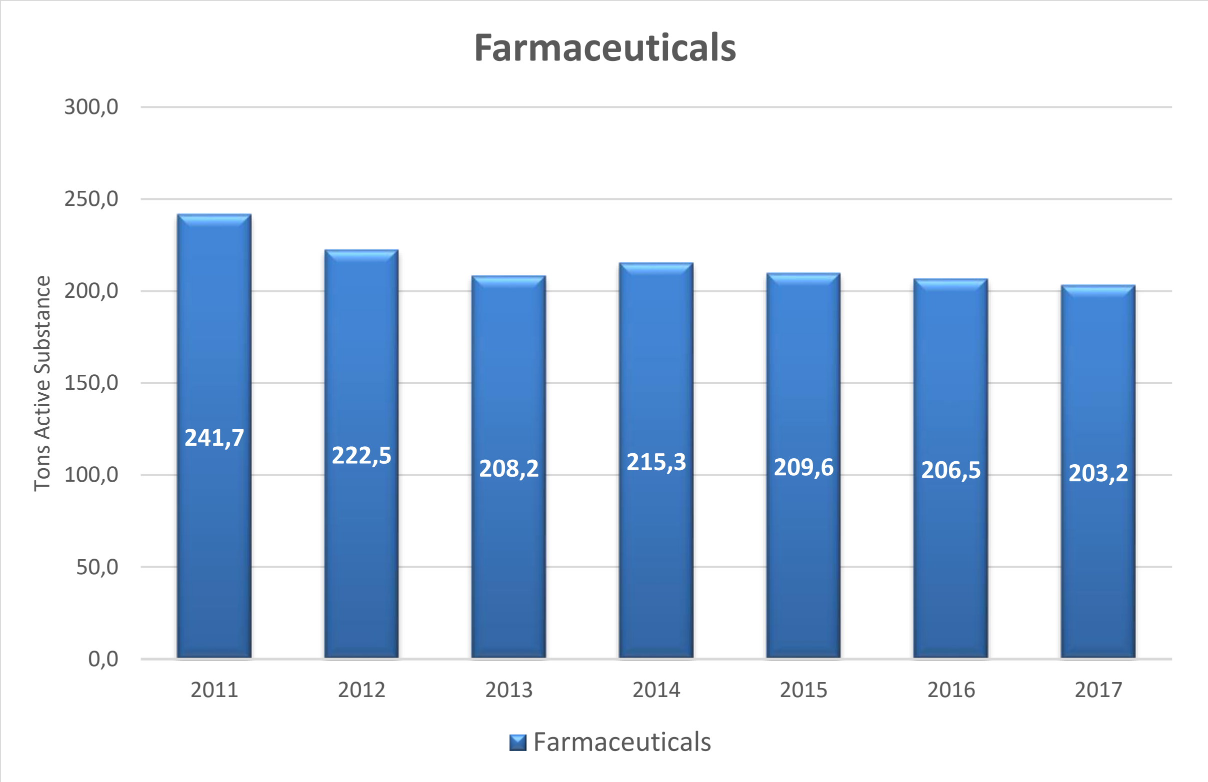


Figure 5. National consumption of antibacterial pharmaceuticals for veterinary use in Belgium for the years 2011-2017 (tons active substance)

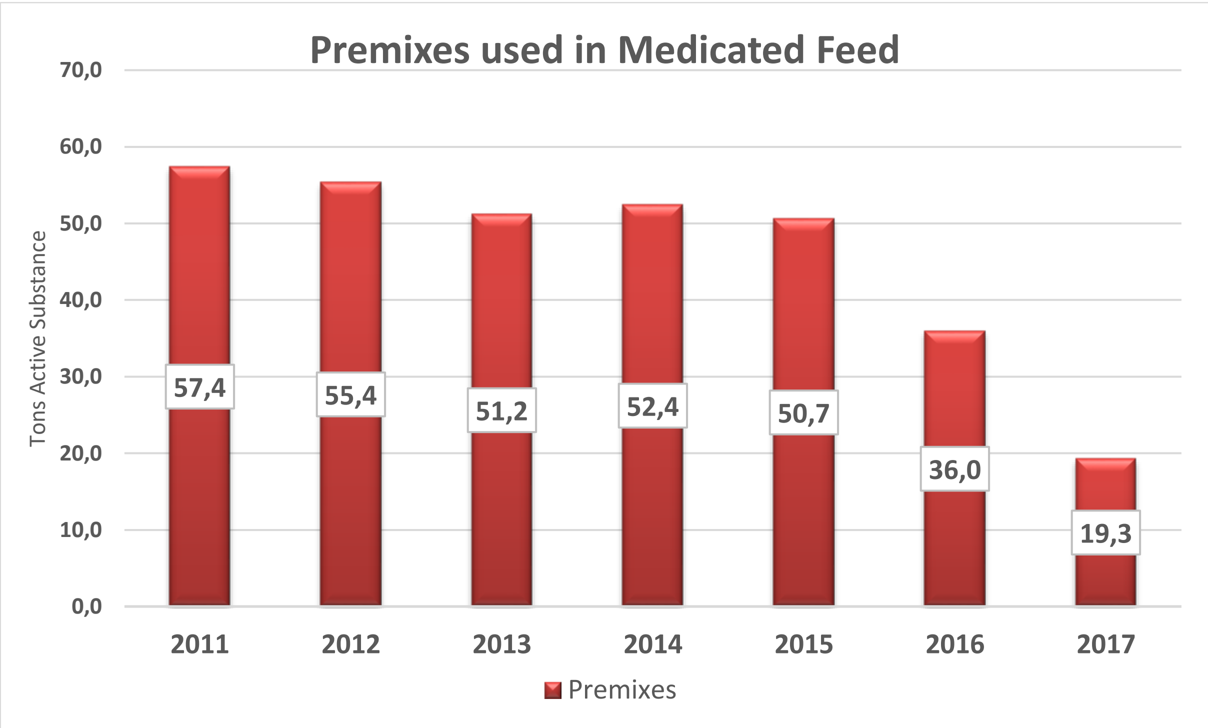


Figure 6. National consumption of antibacterial premixes in Belgium for the years 2011-2016 (tons active substance)

After an increase in use of antibacterial premixes between 2007 and 2010, the decreasing trend firstly observed in 2011 continued till 2013. In 2014 this decrease came to an end and a small increase was observed. Since 2015 the decrease resumed and accelerated in 2016 and 2017.

Since 2011 the data collection system allows to differentiate the animal species of destination for the antibacterial premixes. In 2016, 99,3% of the antibacterial premixes went to pig feed and only 0,7% was used in poultry or rabbit feed.

From September 2013, the use of Zinc oxide in therapeutic doses (corresponding to 2500 ppm of Zn) in piglets for two weeks after weaning is allowed. After an increased use between 2013 (use during only one quarter) and 2015 a first decrease was observed in 2016 where the total use of ZnO dropped to 74 388 kg (decrease with -14,7% in comparison to 2015). This decrease continued in 2017 with a drop in use of -33,6% as is presented in figure 7.

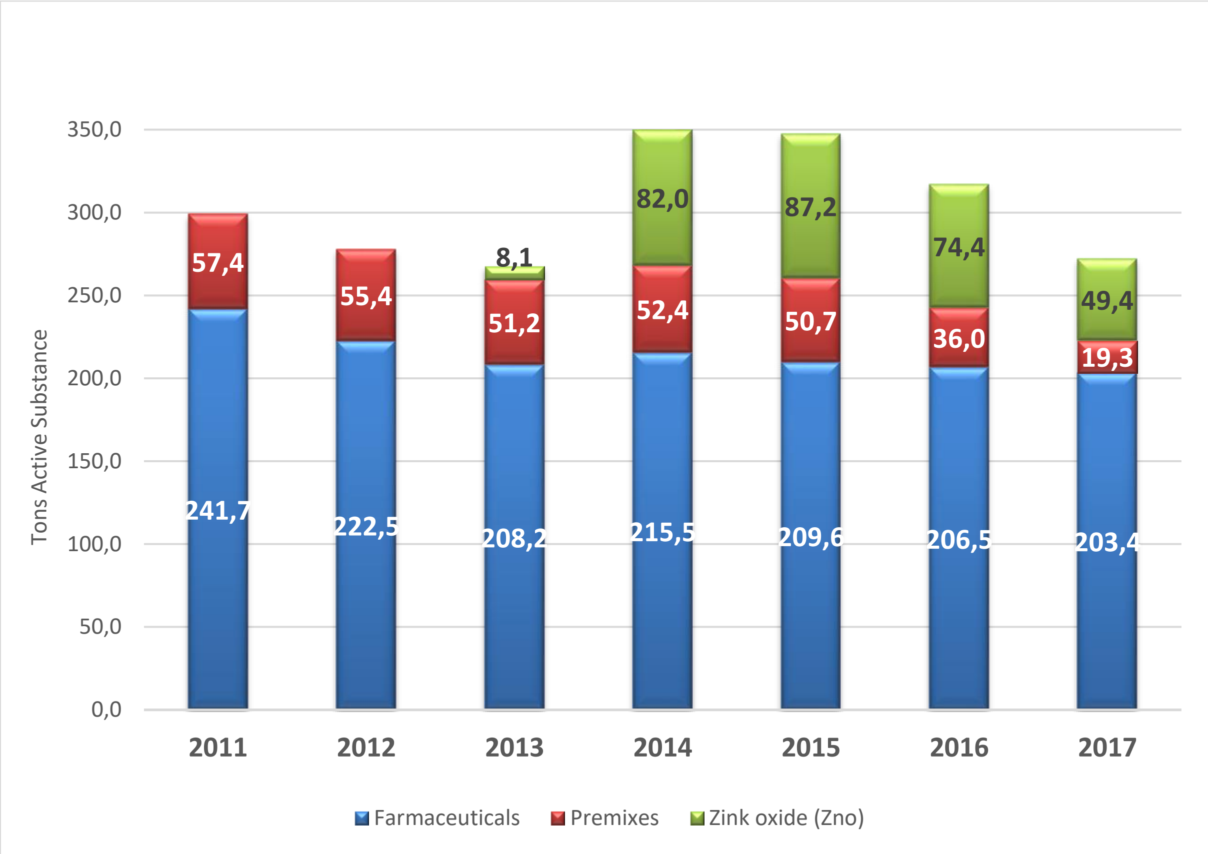


Figure 7. Total national consumption of antibacterial compounds for veterinary use in Belgium plus the use of ZnO for the years 2011-2017 (tons active substance)

Antibacterial use versus biomass

As described above, the total biomass production in 2017 in Belgium has decreased with 0,8% in comparison to 2016. As a consequence the decreasing trends in use observed in absolute values (kg) are somewhat moderated in the relative numbers (mg/kg). For 2016, the mg of active substance used in relation to a kg biomass produced was 117,3 mg/kg whereas in 2017 this is 108,5 mg/kg. This means **a decrease of -7,4% in comparison to 2016.** Split into the different pharmaceutical forms (premix vs other forms) , a moderated decrease of -0,9% is observed in the antibacterial pharmaceuticals and a huge decrease of -45,9% in the antibacterial premixes.

Figure 8 presents these data, again subdivided into antibacterial pharmaceuticals and antibacterial premixes.

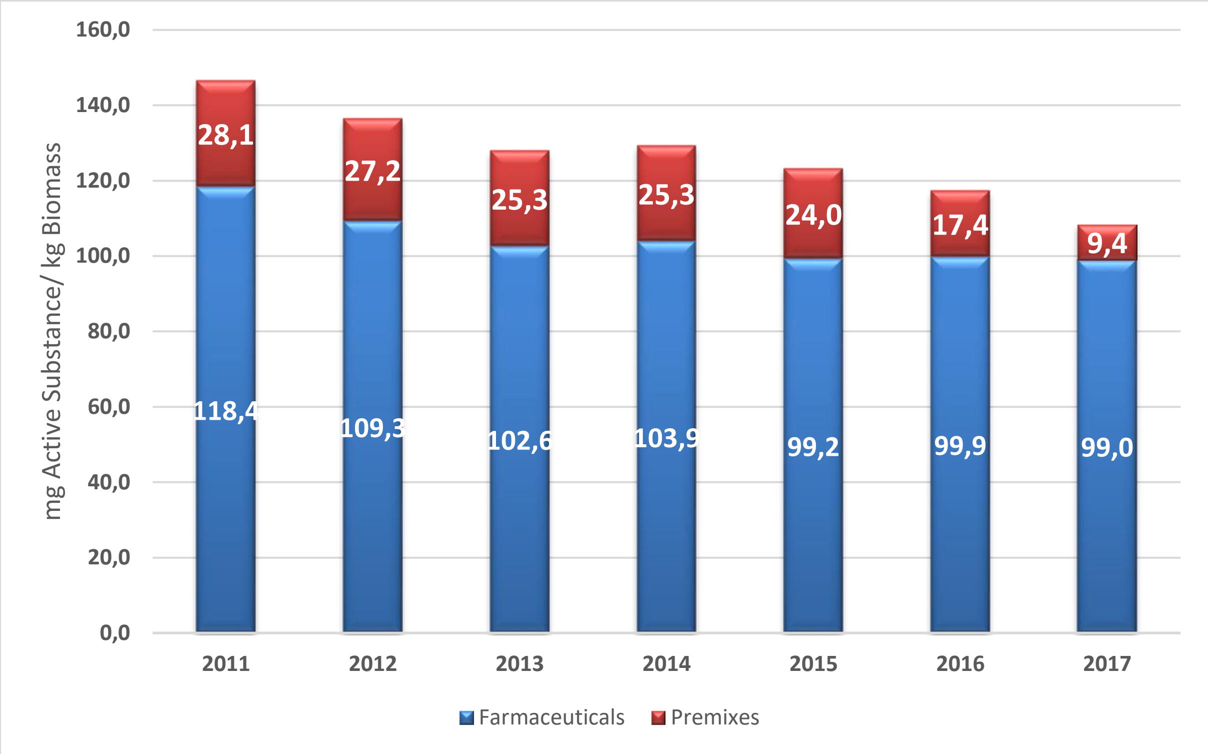


Figure 8. Total mg of active substance used per kg biomass produced in Belgium for 2011-2017.

In 2017 the decreasing trend (-7,4%) as seen in 2016 (-4,8%) and 2015 (-4,7%) continued after the limited increase (+1,1%) observed in 2014. When using 2011 as a reference (see AMCRA 2020 objectives), a cumulative reduction of -25,9% is achieved, distributed in a reduction of -16,4% in antibacterial pharmaceuticals and -66,6% in antibacterial premixes (Fig. 9).

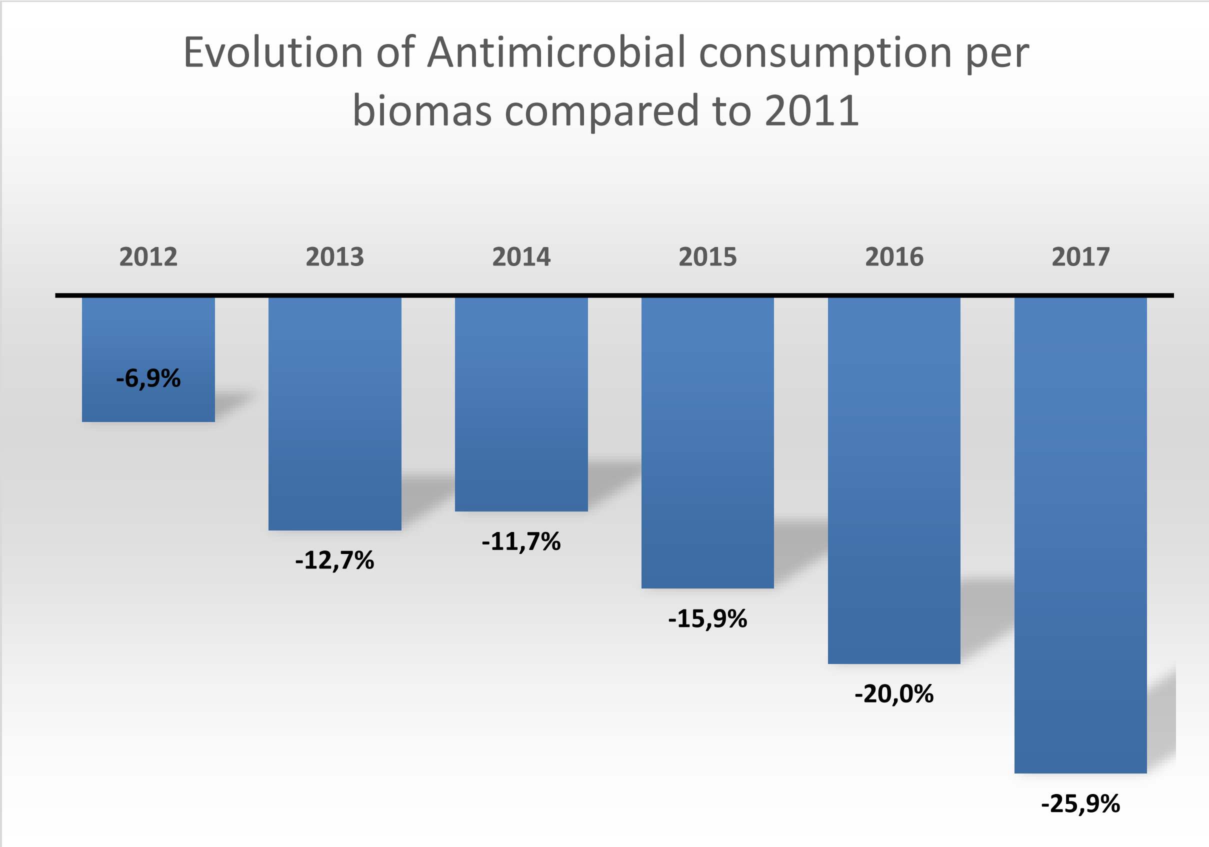


Figure 9. Evolution of antimicrobial consumption per kg biomass produced in Belgium with 2011 as reference year.

Positioning of Belgium in comparison to the EU member states.

Since 2009 the European Medicines Agency (EMA) runs the European Surveillance of antibacterial Consumption (ESVAC) project that aims at collection of Antibacterial sales data in all EU member states in a comparable manner allowing to evaluate trends and compare usage within and between countries. The data collected in Belgium and presented in the annual BELVET-SAC reports are also collected in the framework of this EU wide ESVAC data collection effort.

In 2017, the seventh ESVAC report, presenting results on antibacterial usage in 30 EU /EEA countries in the year 2015 was released[9]. In this report the **antibacterial consumption in animals in 2015 is presented in relation to the animal production in the country.**

In figure 10 the results of the 30 countries included in the seventh 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 BELVET-SAC report but also includes species as horses and rabbits and corrects more thoroughly for import and export.

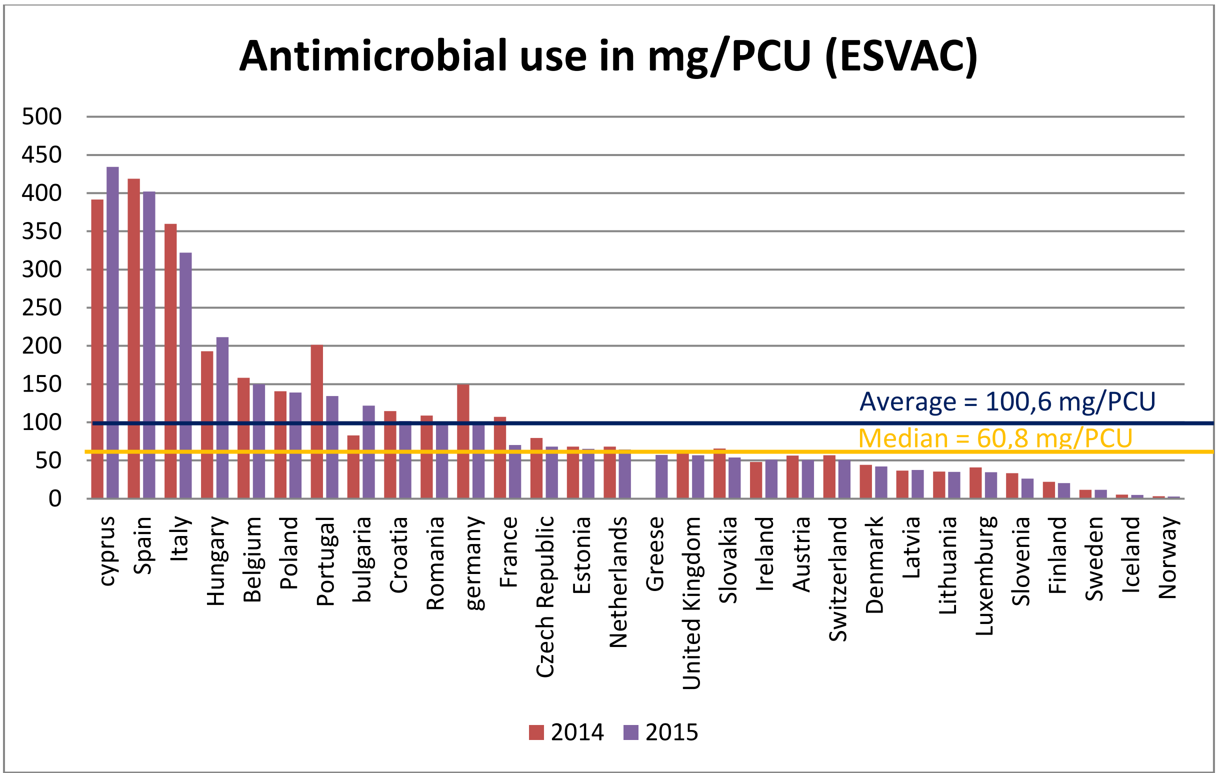


Figure 10. Sales for food-producing species, including horses, in mg/PCU, of the various veterinary antibacterial classes, by country between 2014-2015 (source: 6°, 7° ESVAC report on Sales of veterinary Antibacterial agents).

When looking at figure 10, it can be observed that Belgium sits at the fifth position in terms of Antibacterial usage expressed in mg/PCU in 2015. To be noticed these data do not yet include the substantial decrease in use in Belgium achieved in 2016 and 2017 but obviously, also other countries do take initiates to further reduce antibiotic use.

Compared to neighboring countries (France, Luxemburg, Germany, United Kingdom, The Netherlands (Figure 11)) with a relatively comparable structure of livestock farming, the use in Belgium remains high and very substantial further reductions

[9] http://www.ema.europa.eu/docs/en_GB/document_library/Report/2017/10/WC500236750.pdf

are required to achieve the same levels. Obviously, when comparing countries one has to take into account the composition of the animal population (eg. relative proportion of ruminants versus monogastric species).

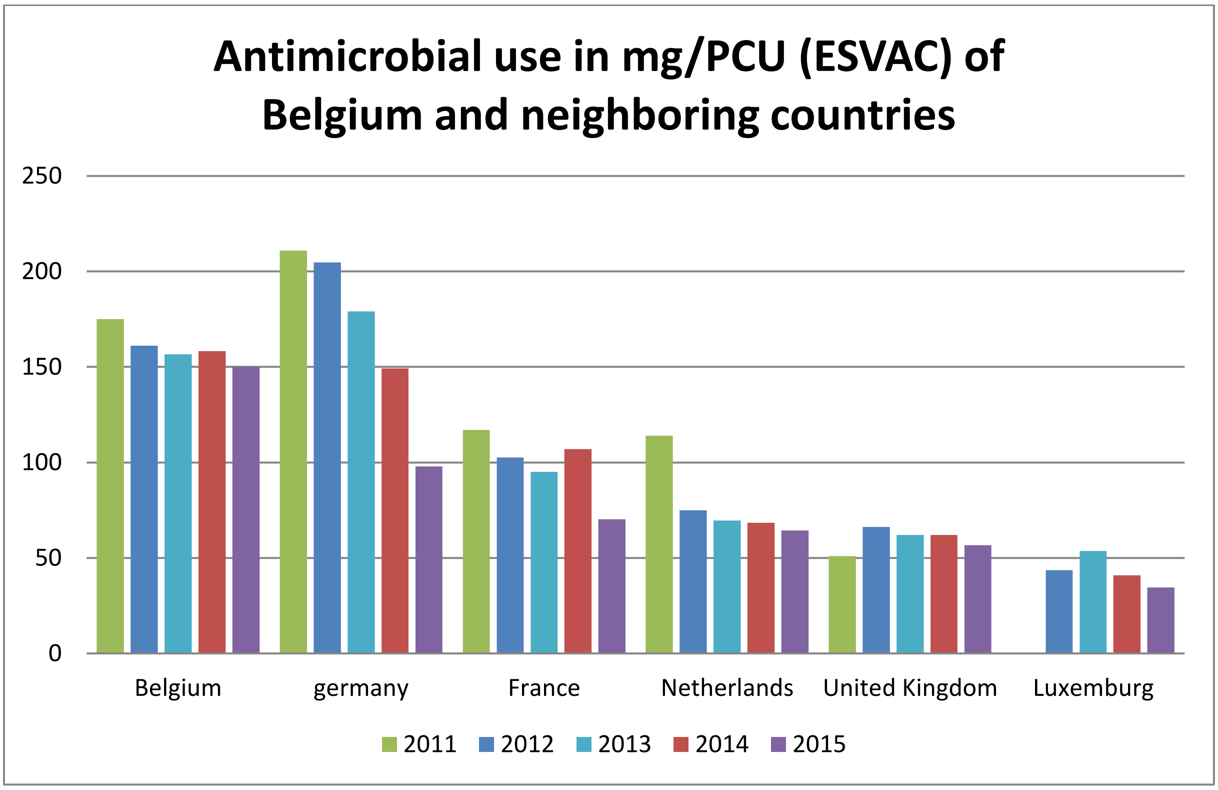
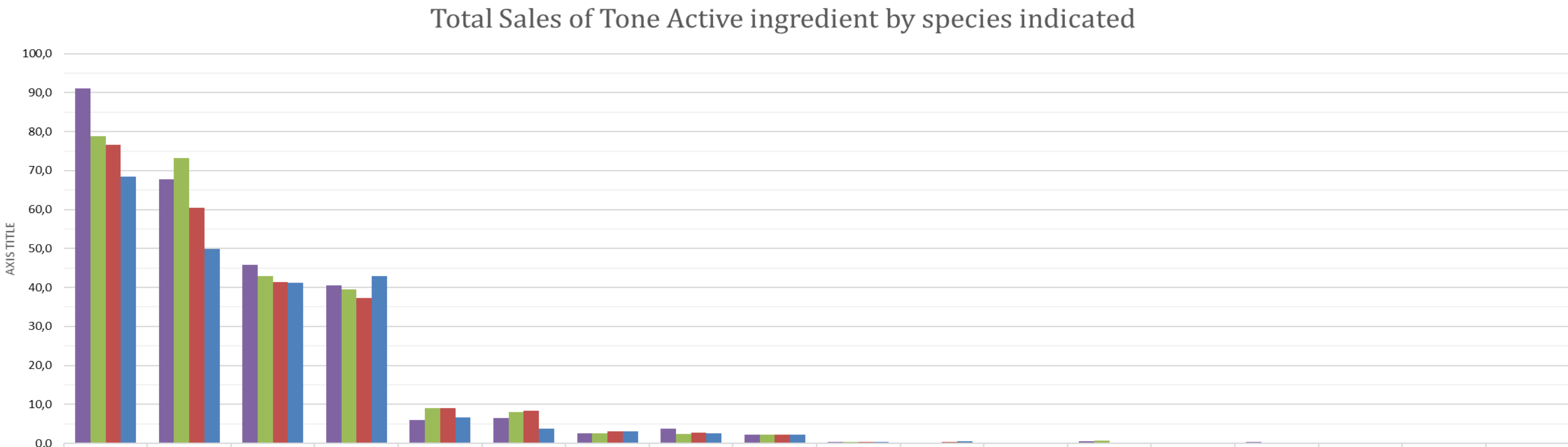


Figure 11. Overall sales of antimicrobials for food-producing species in mg/PCU between 2011-2015 (source: 4°-7° ESVAC report on Sales of veterinary Antibacterial agents) for Belgium and neighboring countries.

Species specific antibacterial use

As mentioned before, a majority of the antibacterial products available on the Belgian market is registered for multiple species. In figure 12 an overview is given of total sales and proportion of total sales according to the authorized target species.

In 2017 antibacterials that are registered solely for pigs are most used (30,8%) followed by antibacterials registered for both pigs and poultry (22,4%). The third most used antibacterial pharmaceuticals are the ones registered for cattle, pigs and poultry (18,5%). The largest decrease in use over the last 4 years is observed in the first two categories (pigs; pigs & poultry).



	Pig Only	Pig & Poultry	Bovine Pig & poultry	Bovine & Pig	Poultry Only	Bovine Pig & Sheep	Bovine Only	Bovine & Pig & Sheep +	Companion Animal	Bovine Pig & Companion Animal	Bovine Pig & Horse	Pig & Sheep	Bovine & Poultry	Bovine & Companion Animal	Other	Bovine Pig Horse & Companion Animal	Horse	Bovine & Sheep
2014	91,2	67,7	45,8	40,5	6,0	6,5	2,6	3,7	2,2	0,3	0,2	0,1	0,6	0,1	0,4	0,1	0,0	0,1
2015	78,8	73,2	42,8	39,4	9,1	8,1	2,6	2,3	2,2	0,3	0,2	0,2	0,6	0,1	0,2	0,1	0,1	0,1
2016	76,6	60,4	41,5	37,4	9,0	8,3	3,0	2,7	2,2	0,4	0,3	0,2	0,2	0,2	0,1	0,1	0,1	0,1
2017	68,5	49,8	41,2	42,8	6,6	3,8	3,1	2,5	2,1	0,4	0,4	0,2	0,1	0,2	0,1	0,1	0,1	0,1

AXIS TITLE

Figure 12. Antibacterial use of pharmaceuticals per authorized species, evolution between 2014 and 2017.

Intramammary products in dairy cattle

Other types of antimicrobial products that can be allocated to mainly one animal species are the intramammary products used for prevention (DC = dry cow therapy) and otherwise for treatment of udder infections (LC= lactating cows).

A. <u>total use of intramamary products</u>

In figure 13 an overview is given of the use of intramammary products for treatment of udder infections in the last five years separated into the classes of active substance and related to the biomass of dairy cows present in that year (table 3).

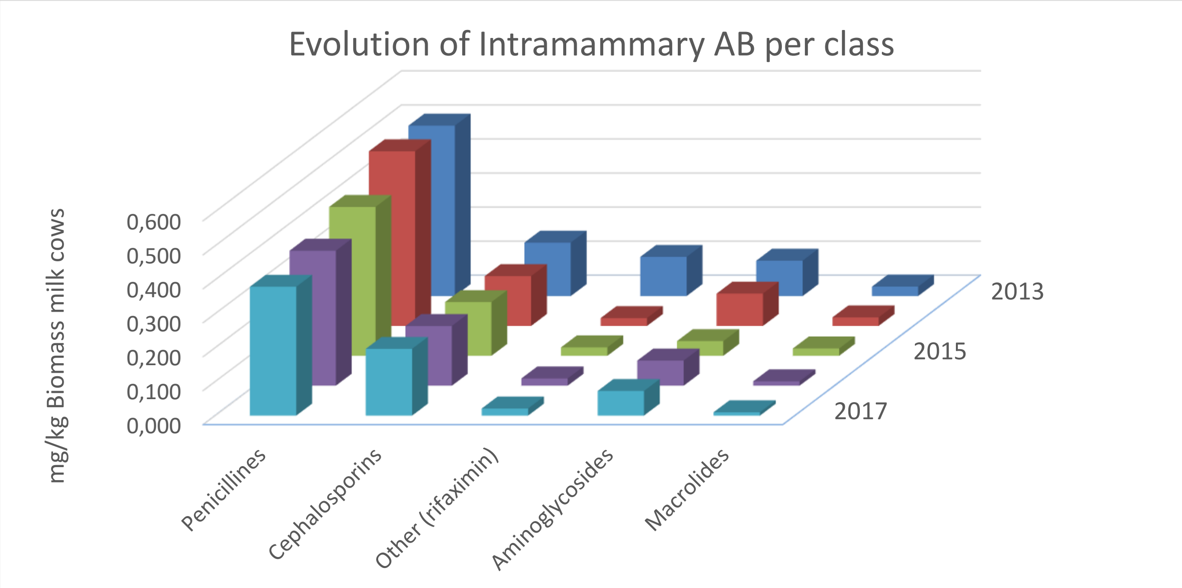


Figure 13. Evolution in use of antimicrobials for intramammary treatment between 2013 and 2017.

In figure 14 the evolution in use over the last five years of intramammary products is presented.

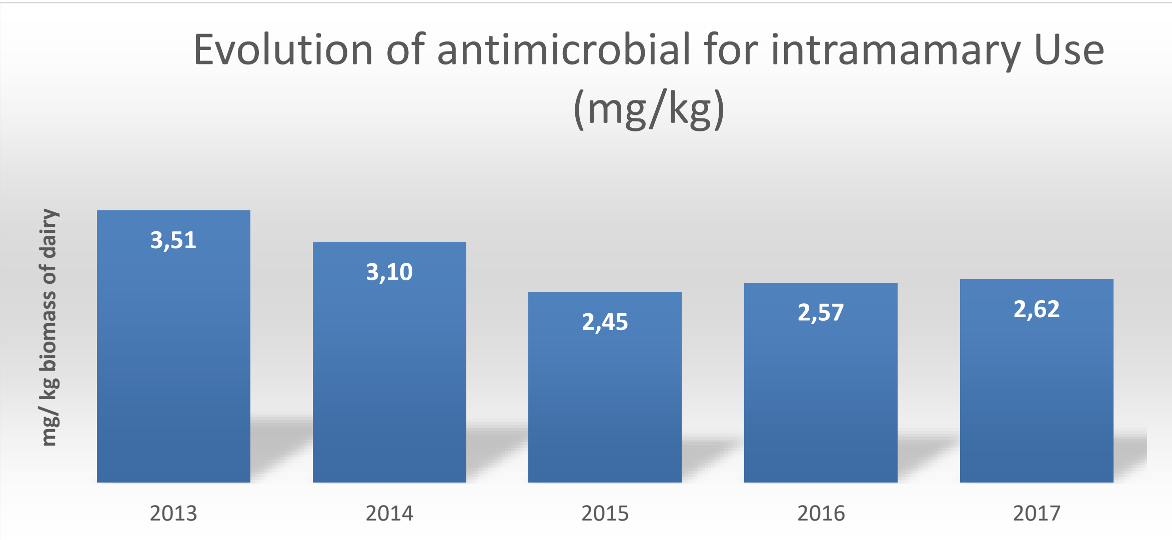


Figure 14. Evolution in use of antimicrobials for intramammary treatment expressed per kg biomass of dairy cattle between 2013 and 2017.

From the results of figure 14 it can be seen that the use if IM preparations was substantially reduced between 2013 and 2015 (-30,1%), however since 2015 it has slightly increased again (+6,8%).

B. Number of DC and LC injector per dairy cow.

These results can also be presented as the number of injectors used per cow per year.

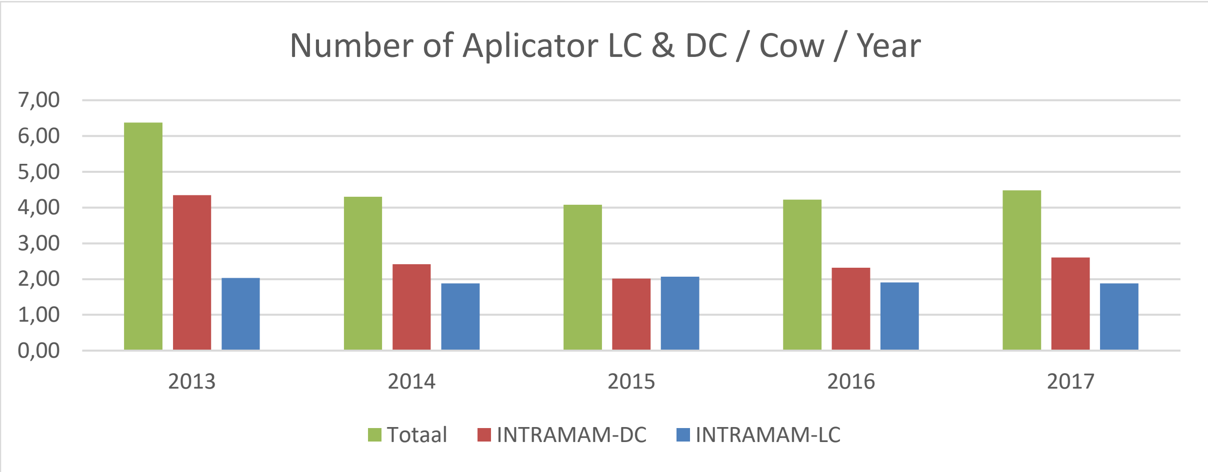


Figure 15. Evolution in use of number of intramammary preparations used per cow present over the last 5 years.

Also from the number of applicators used per cow per year a substantial reduction in use of intramammary applicators was observed between 2013 and 2015 which is mainly due to a reduction of the use of DC applicators. Since 2015 there is again a limited increase in the use of DC applicators which indicates that there is no indication of a further implementation of selective dry cow therapy. The number of applicators used for the treatment of mastitis cases remains relatively stable over the years.

Antibacterial pharmaceuticals in dogs and cats

In 2017, 2137 kg of active substance was used in dogs and cats, corresponding to a -3,5% reduction in comparison to 2016 (2212 kg active compound). The evolution since 2014 is shown below.

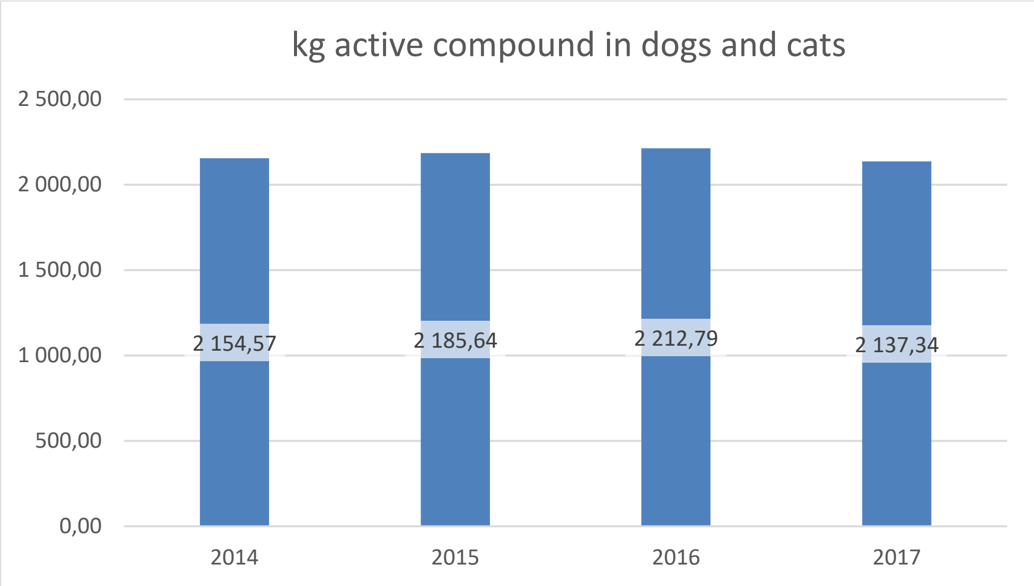
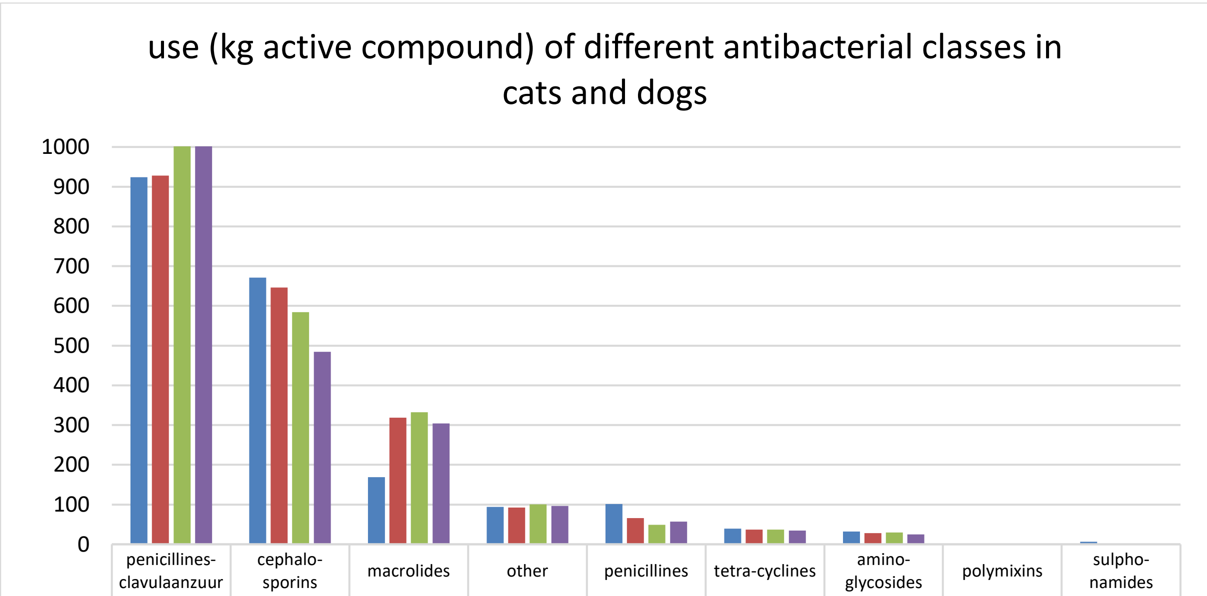


Figure 16. Evolution of antibacterial pharmaceuticals only registered for dogs and cats between 2014 and 2017

Penicillines & Clavulanic acid (1074,3 kg) are the most used antibacterial compound in dogs and cats, followed by cephalosporines (484,6 kg) and macrolides (304,0 kg).



	penicillines-clavulaanzuur	cephalo-sporins	macrolides	other	penicillines	tetra-cyclines	amino-glycosides	polymixins	sulpho-namides
2014	924,21	671,52	169,31	94,04	101,02	39,18	32,39	0,96	6,12
2015	927,97	646,13	318,97	92,49	66,16	37,22	28,26	0,89	0,00
2016	1011,93	584,54	332,71	100,47	49,43	37,32	30,01	0,83	0,00
2017	1074,26	484,65	304,01	96,69	56,76	34,47	24,73	0,75	0,00

Figure 17. Use of different antibacterial classes in products only registered for dogs and cats

Antibacterial use per class of Antibacterial compounds

1. Total consumption (Antibacterial pharmaceuticals and premixes)

In Figure 18 and table 4 the total consumption of antibacterials per class (ATC level 3 or 4 is presented).

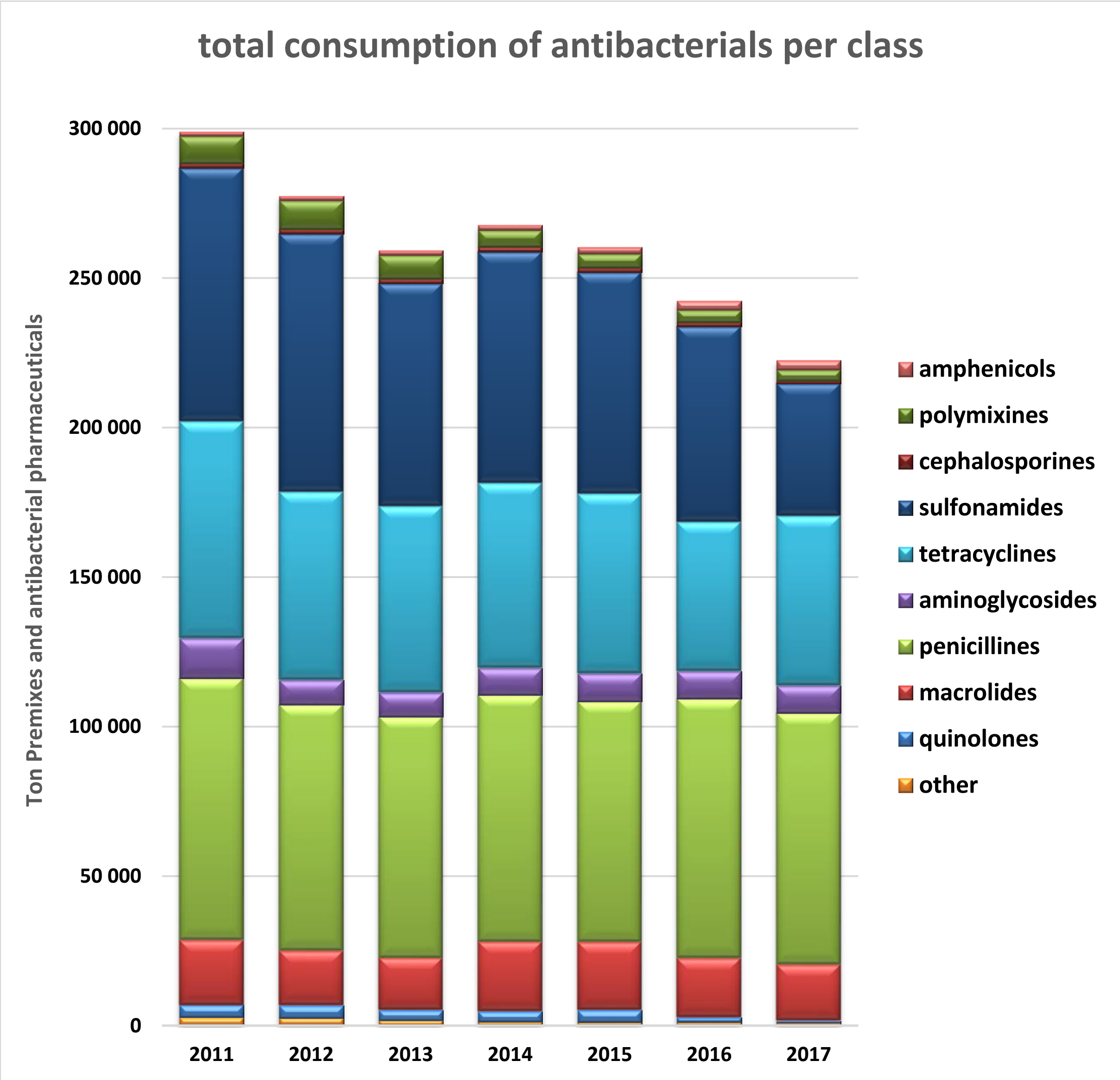


Figure 18. Total Antibacterial use per class of antibacterials from 2011 to 2017.

In 2017, the most used group of antibacterials remained the penicillines (84,6 tons; 34,7%). The tetracyclines (56,8 tons; 23,4%) have become the second most used group followed by the sulphonamides and trimethoprim (44,3 tons; 18,3%). 2017 is the fifth year in row where penicillines are the most used compound. In table 4 the evolution of the used products per antimicrobial class in mg/kg biomass in the last 5 years is presented.

Table 4. The evolution of use (mg/kg biomass) per antimicrobial class since 2011.

	Totaal							evolution						
Class AB Mg/kg Biomass	2011	2012	2013	2014	2015	2016	2017	'11 » '12	'12 » '13	'13 » '14	'14 » '15	'15 » '16	'16 » '17	2017%
penicillins	43,10	40,55	39,88	39,91	38,09	42,03	40,96	-5,9%	-1,6%	0,1%	-4,6%	10,3%	-2,6%	37,78
tetracyclines	35,54	30,98	30,80	29,92	28,49	24,16	27,66	-12,8%	-0,6%	-2,8%	-4,8%	-15,2%	14,4%	25,51
sulphonam & trimethoprim	41,65	42,42	36,79	37,39	35,08	31,64	21,56	1,9%	-13,3%	1,6%	-6,2%	-9,8%	-31,8%	19,89
macrolides	10,71	8,94	8,64	11,27	10,80	9,57	9,18	-16,5%	-3,4%	30,5%	-4,2%	-11,4%	-4,0%	8,47
aminosydes	6,46	4,09	3,99	4,34	4,47	4,48	4,49	-36,7%	-2,3%	8,8%	3,1%	0,2%	0,3%	4,15
polymixins	4,47	4,74	3,89	2,74	2,25	2,03	1,76	6,1%	-18,0%	-29,6%	-17,6%	-9,9%	-13,3%	1,62
fenicols	0,66	0,71	0,75	0,78	0,99	1,46	1,50	6,2%	5,8%	4,6%	26,5%	47,3%	3,0%	1,38
other	1,36	1,27	0,90	0,61	0,57	0,55	0,50	-6,7%	-28,9%	-32,3%	-6,1%	-3,8%	-9,4%	0,46
cephalosporins 1G	0,31	0,35	0,35	0,39	0,37	0,44	0,41	12,9%	-1,9%	12,7%	-4,4%	16,3%	-6,7%	0,37
quinolones	2,01	2,07	1,64	1,69	1,92	0,82	0,29	3,4%	-21,1%	3,2%	13,7%	-57,5%	-64,2%	0,27
cephalosporins 3&4G	0,42	0,40	0,41	0,38	0,35	0,25	0,09	-4,5%	3,7%	-7,0%	-9,5%	-28,3%	-65,9%	0,08
Total mg/kg Biomas	**146,69**	**136,51**	**128,02**	**129,42**	**123,39**	**117,43**	**108,40**	**-6,94%**	**-6,22%**	**1,09%**	**-4,66%**	**-4,83%**	**-7,69%**	**100**

In 2017 the use of penicillins, the most used compound, decreased with 2,6% while the use of tetracyclines incrased substantially with more than 14%. The sulphonamides and trimethoprim on the other hand, decreased with more than 31%. The large increase in use of phenicols in 2016 (+47,3%) continued in 2017 with an additional smaller increase.

The quinolones showed for the second year in a row a very substantial decrease (-64,2%). This decrease is driven by a decrease of flumequine (-71%), enrofloxacine (-57%) and marbofloxacine (-68%) (table 5). Also for cephalosporines of the 3° and 4° generation a very large reduction was observed in 2017 of -65,9%. This is mainly due to the substantial decrease in use of ceftiofur and to a lesser extend the use of cefquinome.

The decreased use of polymyxines (almost entirely colistin sulphate) is observed for the fifth year in a row with a decrease of -13,5% in 2017. This is a positive trend given the simultaneousl decrease in use of zinc oxide as an alternative for colistin use in the treatment of post weaning diarrhea in piglets meaning alternative treatments without use of antibiotics or ZnO may have been used more frequently. When comparing to 2012 (before authorization of ZnO products), polymyxine use has dropped with 62,8%.

AMCRA (center of expertise on Antimicrobial Consumption and Resistance in Animals)[10] published its first guidelines on responsible antibacterial consumption in 2013 and made them available online since 2016. In these guidelines, 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 with importance for human health[11] and the lists produced by the World Animal Health Organization (OIE) indicating the importance of antibacterials for veterinary health[12]. When producing these 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 polymyxins, 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 19 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 group is the most widely used group whereas the red molecules are only limitedly used when expressed in mg active substance per kg biomass. Yet the red molecules are generally more modern molecules with a high potency and therefore a low molecular weight in relation to their treatment potential. In 2017 a decrease in all groups is seen, with for the second year in a row a huge decrease in the red group (-64,6%). **In comparison to 2011 (reference year) the reduction of red molecules is 84,4% whereas a reduction of 75% was aimed for by 2020.**

[10] www.amcra.be
[11] http://apps.who.int/iris/bitstream/10665/77376/1/9789241504485_eng.pdf
[12] http://web.oie.int/downld/Antibacterials/OIE_list_Antibacterials.pdf

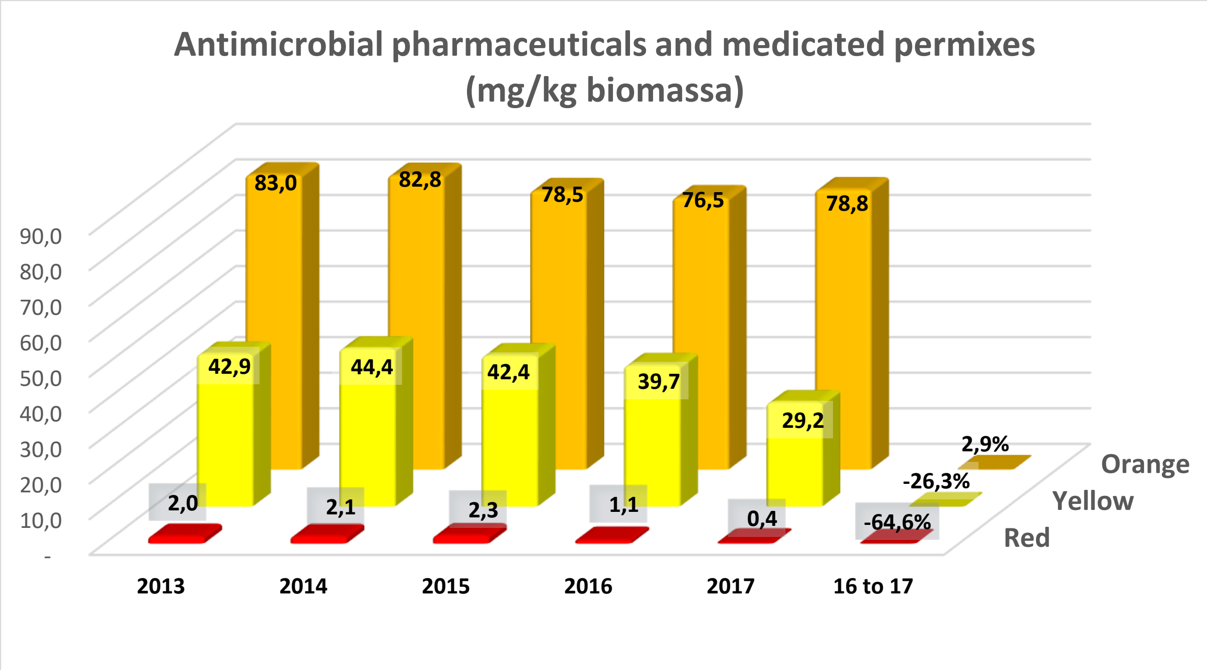


Figure 19: Evolution in the antibacterial consumption (mg/kg) per antibacterial color group between 2013 and 2017.

A similar graph with products exclusively registered for dogs and cats (Fig. 20) shows a more moderate reduction in use of the red molecules (-7%) and an increase in use of the orange molecules of +2% is observed. As the biomass of dogs and cats in Belgium is unknown it is difficult to relate this data to any change in biomass of these species.

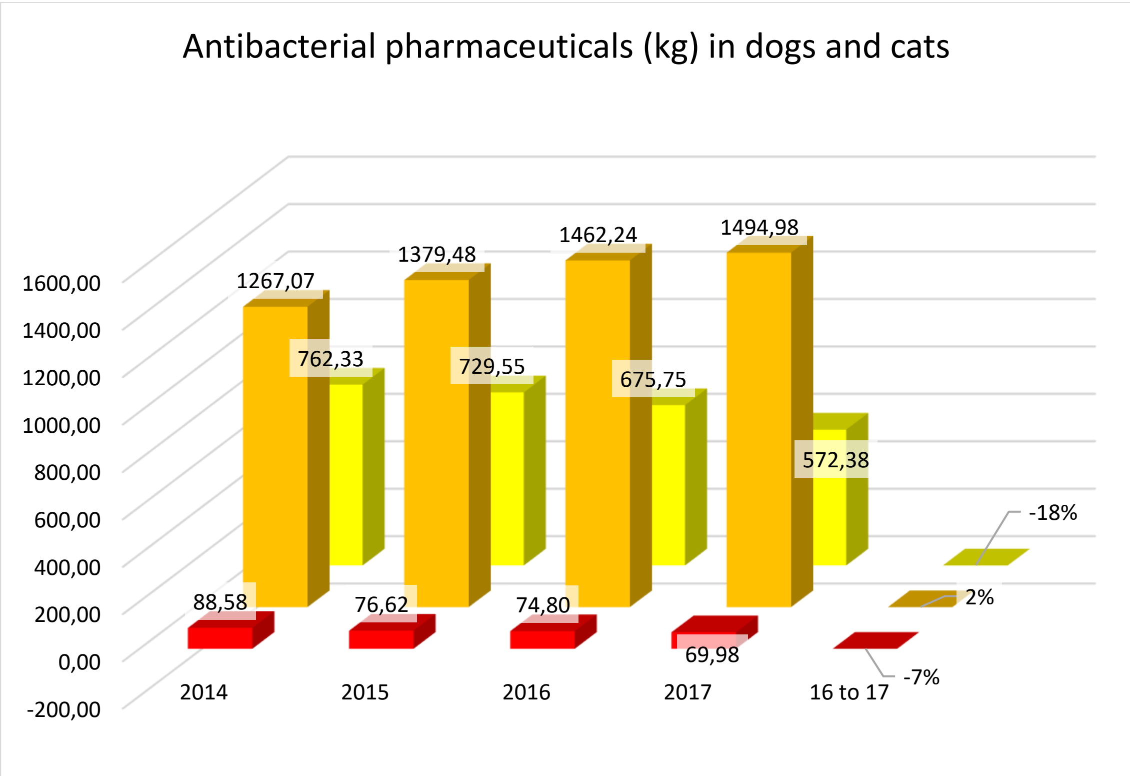


Figure 20: Evolution in the antibacterial consumption (kg active compound) per antibacterial color group for compounds exclusively registered for use in dogs and cats between 2014 and 2017.

2. Antibacterial pharmaceuticals

In Figure 21 the consumption of antibacterials per class (ATC level 3 or 4) is presented for the pharmaceuticals.

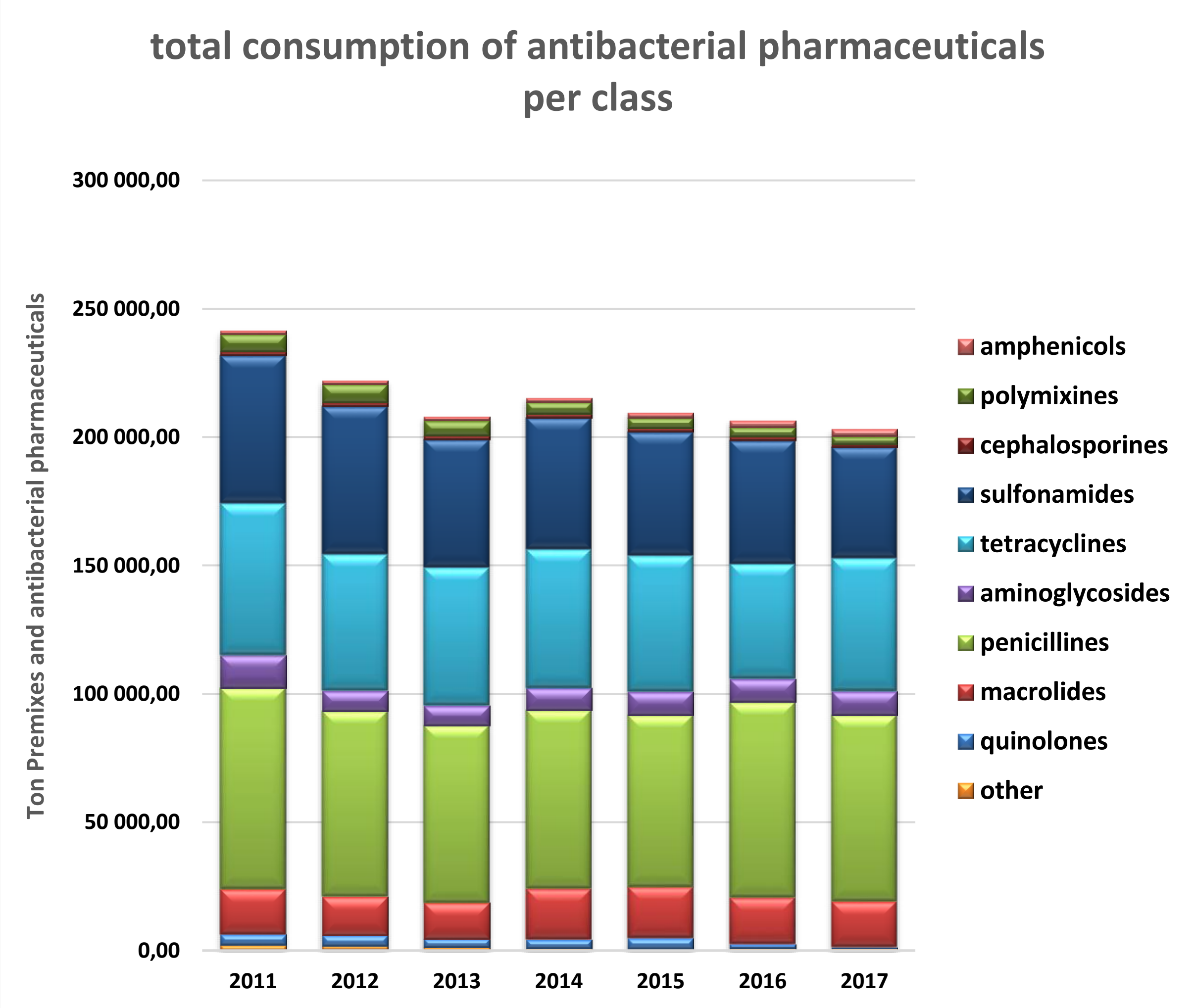


Figure 21. Use of antibacterial pharmaceuticals per class of antibacterials between 2011 and 2017.

3. Antibacterial premixes

In Figure 22 the consumption of antibacterials per class (ATC level 3 or 4) is presented for the antibacterial premixes.

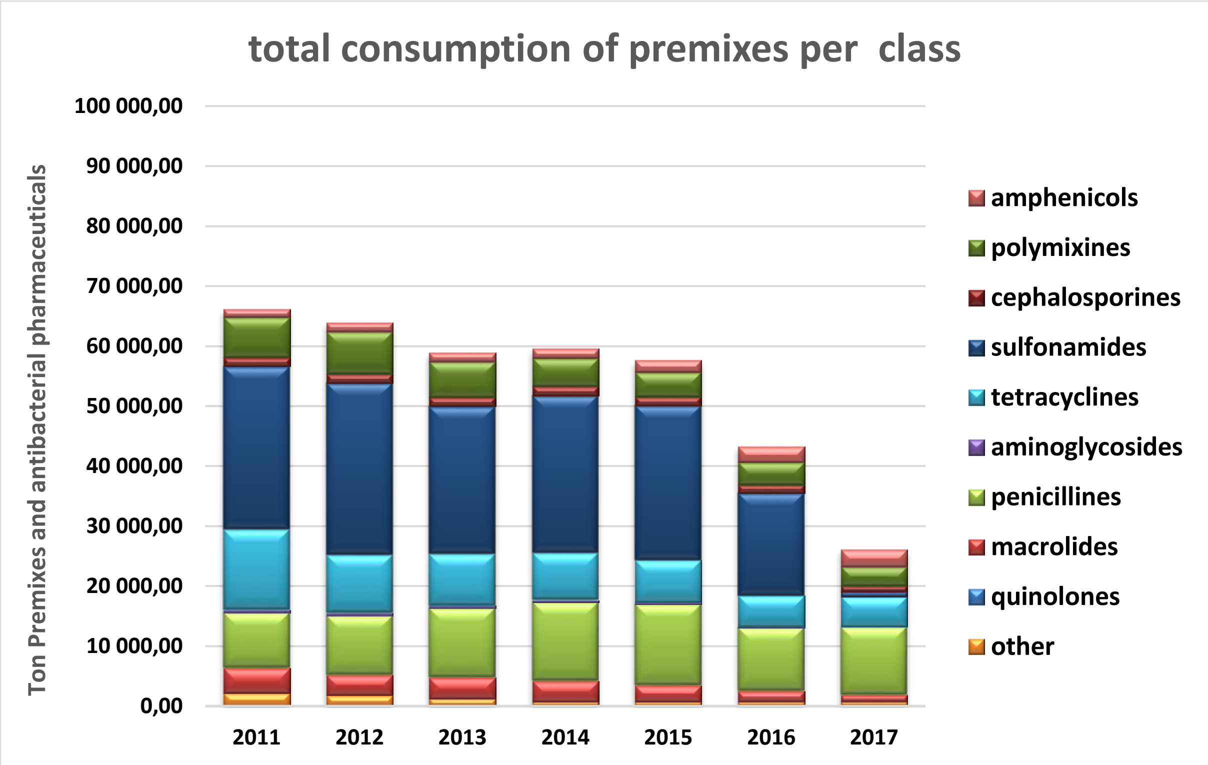


Figure 22. Use of antibacterial premixes per class of antibacterials between 2011 and 2017.

Antibacterial use per active substance

Table 5 gives the amounts used per individual active substance, grouped per class of antibacterials.

Table 5: Antibacterial use per active substance

		total Kg					Antimicrobial pharmaceuticals (kg)					Medicated premixes (kg)				
Class	Antimicrobial compound	2013	2014	2015	2016	2017	**2013**	**2014**	**2015**	**2016**	**2017**	**2013**	**2014**	**2015**	**2016**	**2017**
cephalosporins 1G	cefalexine	674,9	767,7	740,4	837,3	763,0	674,9	767,7	740,4	837,3	763,0					
cephalosporins 1G	cefalonium	13,8	12,3	12,8	12,2	10,2	13,8	12,3	12,8	12,2	10,2					
cephalosporins 1G	cefapirine	5,2	12,8	20,7	31,7	44,3	5,2	12,8	20,7	31,7	44,3					
cephalosporins 1G	cefazoline	10,0	16,7	15,6	17,7	16,0	10,0	16,7	15,6	17,7	16,0					
fenicols	chlooramfenicol	0,0	-	-	-	-	0,0	-	-	-	-					
fenicols	florfenicol	513,3	1 616,1	2 084,5	3 006,5	3 077,5	1 512,7	1 580,3	1 984,1	632,3	2 816,2	0,6	35,8	100,5	374,1	261,3
other	metronidazol	92,4	94,0	92,5	100,5	96,7	92,4	94,0	92,5	100,5	96,7					
other	tiamuline	1 547,5	1 047,6	1 032,3	994,2	879,0	1 028,2	615,7	548,3	640,4	624,6	519,3	431,8	484,0	353,8	254,4
other	valnemuline	38,7	59,3	11,2	-	0,3	-	-	-	-	-	38,7	59,3	11,2	-	0,3
other	zink bacitracine	33,0	39,2	48,6	23,3	28,9	33,0	39,2	48,6	23,3	28,9					
penicillines	benethamine penicilline	10,5	8,1	10,2	22,1	33,7	10,5	8,1	10,2	22,1	33,7					
penicillines	cloxacilline	379,9	393,4	337,7	286,9	260,0	379,9	393,4	337,7	286,9	260,0					
penicillines	fenoxymethylpenicilline	294,2	378,3	537,0	796,4	864,2	294,2	378,3	537,0	796,4	864,2					
penicillines	nafcilline	12,0	7,1	7,2	6,3	6,0	12,0	7,1	7,2	6,3	6,0					
penicillines	penethamaat	293,9	6,8	146,1	184,8	235,2	293,9	6,8	146,1	184,8	235,2					
penicillines	procaïne benzylpenicilline	7 507,7	10 113,0	10 508,4	10 359,3	9 426,0	7 507,7	10 113,0	10 508,4	10 359,3	9 426,0					
sulphonamides	sulfachloorpyridazine natrium	724,8	847,0	1 098,2	1 094,5	1 176,4	724,8	847,0	1 098,2	1 094,5	1 176,4					
sulphonamides	sulfadiazine	60 689,0	62 414,9	59 403,3	51 631,2	33 703,6	40 196,5	40 610,9	37 954,0	37 350,2	32 971,4	20 492,5	21 804,0	21 449,3	14 281,0	732,3
sulphonamides	sulfadimidine natrium	1,8	0,0	-	-	-	1,8	0,0	-	-	-					
sulphonamides	Sulfadoxine	458,9	511,7	587,9	922,8	1 174,1	458,9	511,7	587,9	922,8	1 174,1					

sulphonamides	sulfamethoxazol	101,3	660,9	557,6	785,4	810,8	101,3	660,9	557,6	785,4	810,8					
sulphonamides	sulfanilamide	11,0	-	-	-	-	11,0	-	-	-	-					
sulphonamides	trimethoprim	12 570,1	12 911,8	12 351,8	10 906,3	7 390,8	8 471,6	8 551,0	8 061,9	8 050,1	7 244,4	4 098,5	4 360,8	4 289,9	2 856,2	146,5
amino(glyco)sides	Apramycine	158,5	141,6	97,9	79,5	49,5	60,1	54,6	37,0	26,3	12,5	98,4	87,0	60,9	53,2	37,0
amino(glyco)sides	dihydrostreptomycine	12,6	9,0	7,2	6,3	131,7	12,6	9,0	7,2	6,3	131,7					
amino(glyco)sides	framycetinesulfaat	5,3	6,5	6,3	11,3	16,3	5,3	6,5	6,3	11,3	16,3					
amino(glyco)sides	gentamicine	127,3	126,5	129,2	136,1	141,7	127,3	126,5	129,2	136,1	141,7					
amino(glyco)sides	Kanamycine	18,0	17,6	23,7	22,7	25,3	18,0	17,6	23,7	22,7	25,3					
amino(glyco)sides	Neomycine	1 036,7	765,9	336,0	683,8	672,9	1 036,7	765,9	336,0	683,8	672,9					
amino(glyco)sides	paromomycine	2 533,6	2 690,6	2 368,1	1 878,4	1 807,1	2 533,6	2 690,6	2 368,1	1 878,4	1 807,1					
amino(glyco)sides	spectinomycine	4 197,7	5 224,8	6 471,5	6 437,2	6 380,4	3 883,4	4 959,9	6 217,7	6 320,8	6 360,6	314,2	264,9	253,7	116,4	19,8
macrolides	clindamycine	144,3	148,1	144,1	142,7	121,2	144,3	148,1	144,1	142,7	121,2					
Macrolides	erythromycine	-	0,6	0,9	-	-	-	0,6	0,9	-	-					
Macrolides	gamithromycine	20,4	20,2	20,3	32,9	29,8	20,4	20,2	20,3	32,9	29,8					
Macrolides	lincomycine	4 425,1	4 803,0	5 631,8	4 582,0	4 990,6	3 962,1	4 538,0	5 378,0	4 465,6	4 970,8	463,0	265,0	253,7	116,4	19,8
Macrolides	pirlimycine	0,4	0,4	0,4	0,2	-	0,4	0,4	0,4	0,2	-					
Macrolides	spiramycine	23,8	75,5	248,0	195,4	183,7	23,8	75,5	248,0	195,4	183,7					
Macrolides	tildipirosine	34,0	39,6	44,5	48,9	48,5	34,0	39,6	44,5	48,9	48,5					
Macrolides	tilmicosine	4 118,1	4 380,1	4 159,7	3 785,5	3 160,2	2 361,3	2 467,2	2 540,3	2 637,1	2 344,6	1 756,9	1 912,9	1 619,4	1 148,4	815,6
Macrolides	tulathromycine	109,5	100,7	111,1	133,1	142,2	109,5	100,7	111,1	133,1	142,2					
Macrolides	tylosine	8 456,0	13 475,3	12 041,0	10 581,1	9 839,8	7 173,4	12 201,5	11 151,5	10 149,1	9 600,2	1 282,6	1 273,9	889,5	432,0	239,5
Macrolides	tylvalosin	172,4	275,7	377,9	259,8	330,2	172,4	275,7	377,9	259,8	330,2					
other	rifaximin	115,3	23,1	24,8	21,4	20,7	115,3	23,1	24,8	21,4	20,7					

penicillines	amoxicilline	71 897,2	71 420,3	68 574,8	74 840,9	72 929,0	60 332,5	58 319,6	55 025,1	64 267,8	61 549,1	11 564,7	13 100,7	13 549,7	10 573,1	11 380,0
penicillines	amoxicilline-clav	181,3	215,1	222,2	244,3	257,6	181,3	215,1	222,2	244,3	257,6					
penicillines	ampicilline	240,3	234,7	233,3	297,8	302,8	240,3	234,7	233,3	297,8	302,8					
polymyxins	colistinesulfaat	7 875,4	5 658,1	4 755,6	4 195,0	3 613,9	5 896,1	4 693,9	4 060,3	3 719,4	3 156,1	1 979,3	964,3	695,3	475,6	457,8
polymyxins	polymyxine B sulfaat	0,1	1,0	0,9	0,8	0,8	0,1	1,0	0,9	0,8	0,8					
tetracyclines	chloortetracycline	749,5	633,1	588,2	717,2	664,9	370,8	510,8	526,1	680,1	664,9	378,7	122,3	62,1	37,1	-
tetracyclines	doxycycline	49 961,7	50 664,6	49 134,3	38 130,4	46 540,0	42 168,4	43 263,6	42 364,9	33 120,0	41 705,1	7 793,3	7 401,0	6 769,4	5 010,4	4 834,9
tetracyclines	oxytetracycline	11 699,9	10 603,4	10 369,3	11 052,0	9 552,0	11 231,0	10 259,4	10 199,8	10 926,9	9 448,0	468,9	344,0	169,5	125,1	104,0
(fluoro)quinolones	danofloxacine	67,3	69,1	60,0	42,5	12,0	67,3	69,1	60,0	42,5	12,0					
(fluoro)quinolones	difloxacine	7,6	0,7	-	-	-	7,6	0,7	-	-	-					
(fluoro)quinolones	enrofloxacine	1 361,0	1 411,2	1 280,7	719,3	306,5	1 361,0	1 411,2	1 280,7	719,3	306,5					
(fluoro)quinolones	flumequine	1 534,5	1 564,5	2 197,5	610,6	176,0	1 534,5	1 564,5	2 197,5	610,6	176,0					
(fluoro)quinolones	ibafloxacine	1,0	-0,0	-	-	-	1,0	-0,0	-	-	-					
(fluoro)quinolones	marbofloxacine	335,1	438,2	504,0	306,6	99,0	335,1	438,2	504,0	306,6	99,0					
(fluoro)quinolones	orbifloxacine	2,8	3,4	3,1	3,0	2,7	2,8	3,4	3,1	3,0	2,7					
(fluoro)quinolones	pradofloxacine	5,7	4,7	3,4	2,9	2,5	5,7	4,7	3,4	2,9	2,5					
cephalosporins 3G	cefoperazon	6,1	5,5	6,5	5,9	5,0	6,1	5,5	6,5	5,9	5,0					
cephalosporins 3G	cefovecin	8,6	9,3	9,1	9,3	9,0	8,6	9,3	9,1	9,3	9,0					
cephalosporins 3G	cefquinome	197,2	180,7	179,9	132,6	89,2	197,2	180,7	179,9	132,6	89,2					
cephalosporins 4G	ceftiofur	624,5	598,4	537,1	366,6	71,4	624,5	598,4	537,1	366,6	71,4					

Discussion

In the context of the increasing (awareness on) antibacterial resistance development, comparable data and evolutions of antibacterial consumption (AMU) are of utmost importance. This annual BELVET-SAC report is now published for the ninth time and describes the antibacterial use in animals in Belgium in 2017 and the evolution since 2011.

As in 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 submitted in previous years and data collected by sector organizations.

Although this report also makes attempts to allocate AMU to specific species, this remains a crude estimate. From 2018 onwards, BelVet-Sac data can be complemented by species specific data collected from pigs, poultry and veal calves through SANITEL-MED. Although this information cannot replace the totality of antimicrobial sales in BE collected by the BELVET-SAC project, Sanitel-Med will provide more in depth insight per species and allow more targeted objectives and / or interventions.

Another point of attention is the fact that we cannot be absolutely sure that all products sold in Belgium by the wholesaler-distributors are also used in Belgium. Veterinarians living near the country borders may also use medicines bought in Belgium to treat animals abroad and vice versa, i.e. veterinarians from neighboring countries using products in Belgium that are not included in the BelVet-Sac. Again this effect will be eliminated once data are collected at herd level in the SANITEL-MED system.

Also the dependency on the biomass factor may influence the result. This means that changes regarding the net import or export of slaughter animals (increasing or decreasing biomass in BE) will have an influence on the outcome.

For the 2017 BELVET-SAC results, it is very encouraging to see that the positive evolution seen in 2012, 2013, 2015 and 2016 (with a respective reduction of -6,9%; -6,3%; -4,7%; -4,8% in mg substance/kg biomass) which was temporarily disrupted in 2014 (increase of +1,1% mg/kg biomass), was observed again in 2017 with **a reduction of -7,4% in mg active substance/kg biomass in comparison with 2016**. This is the **highest reduction observed in one year since 2011** which is used as the reference year. In absolute numbers this correlates to a decrease in AMU of –8,3% subdivided in a decrease of **-1.6% in pharmaceuticals and -46,3% in antibacterial premixes**. This is to be combined with a decrease of the biomass of -0,8% in 2017. When aggregating the effect of these subsequent efforts over the years, a **total reduction of -25,9%** (mg active substance / kg biomass) **in comparison with 2011** is already achieved**.**

In 2017, for the second year in a row, a very substantial reduction in use of antibacterial premixes is remarkably. This is the result of continuous efforts by compound feed producers having introduced a number of additional **auto-regulating** measures to reduce the use of antibacterial premixes combined with the withdrawal of some premixes from the market by one pharmaceutical company.

An important reduction is also achieved (-33,6%) in use of ZnO in therapeutic doses. This is leading the pathway towards a ban on use of ZnO in therapeutic doses in the future. In this context, it is important to notice the decreased use in parallel of the polymyxine class (almost entirely colistin sulphate) with a decrease of -13,5% in 2017 vs previous year. The simultaneous decrease – as zinc oxide is the alternative for mainly colistin use in the treatment of post weaning diarrhea in piglets – means that probably alternative treatments without use of colistin or ZnO are used more frequently.

This very substantial reduction in use of antibacterial premixes has resulted in a cumulative decrease of -66,6% since 2011. This means that the set objective of -50% of use in antibacterial premixes by 2017 as defined in the AMCRA objectives (adopted by the Belgian government in 2016) has been largely achieved on time.

When looking more in detail to the use of different classes of antibacterials, it is observed - as in previous years – that penicillines (34,7%) form the largest group of consumed antimicrobials, followed by tetracyclines (23,4%) and the sulphonamides (18,3%). While the top 3 remains stable, there is a shift between sulphonamides and tetracyclines for the second place. This is likely the result of the temporarily unavailability of sulphonamides in 2017 due to a manufacturing issue of the active substance. For the majority of the antimicrobial classes, a decrease in AMU was observed for 2017, most pronounced for the quinolones (-64,2%) and the cephalosporines of the 3° and 4° generation (-65,9%), but also very substantial for sulphonamides (-31,8%) and polymyxins (-13,3%). For the latter this is already the 4th year in a row that a substantial reduction is observed. **When comparing to 2012** (before authorization of ZnO) **the polymyxin use has dropped with 62,8%.** This year a remarkable increase (+14,4%) in use of tetracyclines is observed. This is likely linked to the unavailability of sulphonamides and the consequential shift to tetracyclines as alternative.

When looking at the use according to the different color classes a substantial reduction in use in the yellow products (-26,3%) and a very important reduction in use of the red product (-64,6%) is observed. Only in the orange products an increase of 2,9% is found. Especially the continued **very substantial reduction in use of molecules of critical importance for human medicine** (grouped in the category of the "red" antibacterials such as the cephalosporines of the 3th and 4th generation and the fluoroquinolones) is very positive. In 2016 already a reduction in use of -53,1% was observed and this year this is continued with a reduction **of –64,6%.** This is definitely the result of the implementation of the new legislation (RD of 21 July 2016) which introduced very strict limitations to the use of these "red molecules" in food producing animals from August 2016 onwards which was preceded by a number of autoregulation measures in guidelines of different quality labels in pig production.

In comparison to 2011 (reference year) the cumulative reduction of red molecules is 84,4% whereas a reduction of 75% was aimed for by 2020 in the AMCRA objectives (adopted by the Belgian government in 2016). Therefore can be concluded that this second goal is already largely achieved, even 3 years before the set deadline. This result is a clear example of a successful co-regulation.

The third and overarching objective of 50% reduction in total use by 2020 is clearly not yet achieved. Up to 2017, a **cumulative reduction of -25,9% is achieved** since 2011 (reference year for the AMCRA 2020 goals); i.e. a reduction of -16,4% in antibacterial pharmaceuticals and -66,6% in antibacterial premixes. Although this result is promising, we are **still 24,0 % away from achieving this goal**, meaning in the following years (2018-2020) a continued annual reduction of more than 8% is required. This will require efforts from all stakeholders involving the ongoing guidance (autoregulation) by the sector labels of livestock farming (a.o. installing Health Plans) and otherwise the identification of high users & prescribers (farmers & vets) who need to be actively approached to achieve substantial reductions. SANITEL-MED data analysis will be of upmost value for this.

Moreover, when comparing the Belgian results regarding AMU to the results of other European countries and especially our neighboring countries, it is clear there is still a substantial gap to be bridged relatively quickly not only to reduce the emergence and spread of resistance (genes) but considering also the increasing economic importance related to AMR and AMU status (where low AMU sometimes is used as a parameter of durability of livestock farming).

With this report, again an attempt is made to provide an overview on AMU in particular (groups of) species depending on the target species for which products are authorised. From these data it appears that the major reductions in use are achieved in pig and poultry production. This is not surprising given the very substantial reduction in use of medicated premixes which are almost exclusively used in pigs.

For the first time the evolution in use of intramammary products is presented. These results show a very substantial reduction of -30,1% between 2013 and 2015, yet followed by two years of slight increase of use of IM products (+2,6% in 2016 and +2,6% in 2017). This illustrates that the dairy sector also needs to take action in the responsible and reduced use of antimicrobials. In contrast to 2016, a limited reduction in AMU in companion animals is observed in 2017, both in total use (-3,5%) as in the use of the critically important antimicrobials (red molecules) (-7%).

Conclusion

This report again shows quite promising results with the achievement already of two out of the three quantitative goals (use of premixes and use of critically important antimicrobials). Also for the overall consumption, a substantial further reduction was observed. These evolutions strengthen us in the believe that also the third and overarching objective of a 50% reduction in use remains feasible, yet substantial efforts will be required from all stakeholders to obtain this goal.

Acknowledgements

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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