

Belgian Veterinary Surveillance of Antibacterial Consumption

National consumption report

2018

Publication : 19 June 2019

SUMMARY

This annual BelVet-SAC report is now published for the 10th time and describes the antibacterial use in animals in Belgium in 2018 and the evolution since 2011. For the first time this report combines sales data (collected at the level of the wholesalersdistributors and the compound feed producers) and usage data (collected at herd level). This allows to dig deeper into AMU at species and herd level in Belgium.

With -12,8% mg antimicrobial/kg biomass in comparison to 2017, 2018 marks the largest reduction in total sales of antimicrobials for animals in Belgium since 2011. This obviously continues the decreasing trend of the previous years, resulting in a cumulative reduction of -35,4% mg/kg since 2011. This reduction is evenly split over a reduction in pharmaceuticals (-13,2% mg/kg) and antibacterial premixes (-9,2% mg/kg). It is speculated that the large reduction observed in 2018 might partly be due to the effect of extra stock (of pharmaceuticals) taken during 2017 by wholesalers-distributors and veterinarians in anticipation of the increase in the antimicrobial tax for Marketing Authorisation Holders, which became effective on the 1st of April 2018. When comparing the results achieved in 2018 with the AMCRA 2020 reduction targets, the goal of reducing the overall AMU in animals with 50% by 2020 has not been achieved yet, however, the objective comes in range with still 14,6% to reduce over the next two years.

Considering the large reduction observed in total AMU in 2018, it is not surprising that also in the **pig sector a substantial reduction of -8,3% mg/kg between 2017 and 2018** is observed based upon the usage data. Translated to BD₁₀₀ this results in **decreases of the median BD₁₀₀ of -1,4% in fatteners (to 4,4 in 2018), -6% in weaners (16,6 in 2018), -18% in sucklers (1,8) and -3% in pigs for breeding (0,3)**. These are encouraging results for the pig sector, which has already put a lot of efforts in reducing their antibacterial use before 2018, starting with a private data-collection system (AB Register) already in 2014 and having also bore the entire weight of the antibacterial premix reduction. In this regard it is also promising to see that, even after largely achieving the goal of reducing the use of **antibacterial premixes** with 50% by 2017, a further step is taken, now already **resulting in a cumulative reduction of -69,8% mg/kg in comparison to 2011.** On top of these results, **the use of ZnO in therapeutic doses continues to decrease with another -21,3% mg/kg in 2018** and coincides with a further decrease of the **polymyxin use of -4,1% mg/kg** in 2018. Yet, challenges remain especially in the use in the weaners and the high using farms.

Even though broilers and veal calves account for a smaller part of the tonnes antibacterials used, the increase of respectively +13,8% mg/kg and +17,7% mg/kg for these sectors are quite disappointing results. The results for broilers might still appear rather modest, with a mg/kg result substantially below that of pigs and veal calves and a decrease of the median BD₁₀₀ with 2%, resulting in a broiler being treated for less than approx. 5% of its time on a majority of broiler farms. However, this must be interpreted with care as broilers are mostly treated at very young age which is reflected in high antimicrobial resistance levels. Together with the increase in use of fluoroquinolones in 2018, these should be alarming results for the poultry (broiler) sector, requiring urgent measures for reduction in the coming years.

Veal calves are known to be a difficult sector in terms of AMU. This is confirmed by the baseline level of AMU, which is highest in veal calves compared to all other animal categories (median use of almost 28% of the time in 2018). Yet the fact that there is still a large variation between farms shows the big potential for reducing the use at the sector level. As for broilers, **the veal calf sector is urged to take measures to reverse the increasing trend in the coming years.**

In regard to the different AMCRA colour classes, use of "yellow" (-12%) and "orange" (-14%) classes substantially reduced. Yet the use of the "red" products increased (+35%) after a very spectacular drop in 2016 and 2017. Although this proportional increase should be related to the currently low level of absolute use and did not put at risk the reduction target of -75% by 2020 (which was already achieved in 2017), it is an evolution that merits close surveillance. As noted above, this increase is entirely linked to the increased use in fluoroquinolones and more specifically the flumequine. From the first (usage) results available for 2019, it is anticipated that this will be a onetime event.

Conclusion

This report shows quite promising results again with the confirmation of the achievement of two out of the three quantitative goals (use of premixes and use of critically important antimicrobials) and a substantial further reduction of the overall consumption. 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. The pig sector is encouraged to sustain its efforts, while the broiler and veal calf sector are urged to increase their efforts.

SAMENVATTING

Dit 10^{de} BelVet-SAC rapport beschrijft de resultaten van het antibioticumgebruik bij dieren in België gedurende 2018 en de evolutie sinds 2011. Voor de eerste keer analyseert het rapport zowel verkoopdata (verzameld ter hoogte van de groothandelaars – verdelers en mengvoederfabrikanten) als gebruiksdata (verzameld op het niveau van de veehouderij). Deze combinatie laat toe om het gebruik meer in detail te bestuderen per sector (diersoort).

Met een reductie van -12,8% mg antibiotica per kg biomassa in vergelijking met 2017, is 2018 het jaar met de grootste reductie in verkoop van antibiotica voor dieren in België sinds 2011. Met dit resultaat wordt de dalende trend van de voorgaande jaren duidelijk verder gezet wat resulteert in een cumulatieve reductie van -35,4% mg/kg sinds 2011. Deze daling is verdeeld over een daling van -13,2% mg/kg voor de farmaceuticals en -9,2% mg/kg voor de voormengsels. De schijnbaar sterke reductie in verkoop van farmaceuticals in 2018 is mogelijk een gevolg van het nemen van grotere stocks in 2017 in het vooruitzicht van de verhoging van de antibiotica taks voor de registratiehouders die op 1 April 2018 in voege is getreden. Als het resultaat wordt uitgezet tegenover de AMCRA-2020 doelstelling om het antibioticumgebruik met 50% te doen dalen tegen 2020, dan is het duidelijk dat deze doelstelling nog niet werd behaald maar wel binnen bereik komt met een reductie van 14,6% die in de komende twee jaar dient gerealiseerd te worden.

Gezien de sterke reductie in verkoop, is het niet verwonderlijk dat in de **varkenssector**, met het grootste aandeel in het totaal gebruik, een grote vermindering met **-8,3% mg/kg** wordt waargenomen tussen 2017 en 2018. Omgezet in BD₁₀₀ (aantal behandeldagen op 100 dagen) komt dit neer op een **reductie van de mediane BD₁₀₀ van -1,4% bij de vleesvarkens (tot 4,4 in 2018), -6% bij de gespeende biggen (16,6 in 2018), -18% bij de zuigende biggen (1,8 in 2018) en -3% bij de fokvarkens (0,3 in 2018)**. Dit zijn bemoedigende resultaten voor de varkenssector die de afgelopen jaren substantiële inspanningen heeft geleverd om het antibioticumgebruik te reduceren door o.m. het reeds in 2014 opzetten van een privé datacollectiesysteem (AB Register) en het dragen van het volledige gewicht van de reductie in gebruik van gemedicineerde voeders. Wat dit laatste betreft is het goed om zien dat zelfs na de zeer substantiële dalingen in het gebruik van **antimicrobiële premixen** in de voorgaande jaren, deze daling zich ook in 2018 verder zet wat finaal resulteert in een **cumulatieve reductie van -69,8% mg/kg** in **2018**) in parallel met een verdere reductie van het gebruik van **colistine van -4,1% mg/kg**. Dit neemt evenwel niet weg dat er ook in de varkenssector nog uitdagingen blijven, in het bijzonder voor wat betreft het gebruik bij gespeende biggen en voor bedrijven met een algemeen hoog gebruik.

Ondanks het feit dat braadkippen en vleeskalveren een kleiner aandeel hebben in het totaal gebruik van antibiotica bij dieren is de stijging in gebruik van respectievelijk +13,8% mg/kg en +17,7% mg/kg een teleurstellend resultaat. De stijging bij de braadkippen mag nog beperkt lijken gezien het gebruik in mg/kg nog substantieel lager is dan dit bij gespeende biggen en vleeskalveren en gezien de daling van de mediane BD₁₀₀ met 2% waardoor een braadkip op een meerderheid van bedrijven minder dan 5% van haar levensduur wordt behandeld. Echter, dit resultaat moet met de nodige voorzichtigheid worden geïnterpreteerd gezien de meeste behandelingen bij braadkippen plaatsvinden in de eerste levensweken en dit vroeg gebruik resulteert in een hoge selectie voor antibioticumresistentie. Dit gecombineerd met de stijging van het gebruik van fluoroquinolones in 2018 leidt tot een dringende oproep aan de braadkippensector om de nodige maatregelen te nemen om het antibioticumgebruik drastisch te reduceren in de komende jaren.

Dat het antibioticumgebruik in de vleeskalversector het hoogst is van alle sectoren (mediane BD₁₀₀ van 28 dagen) was sinds lang gekend. Echter de grote variatie die wordt waargenomen tussen de bedrijven toont aan dat er ook in deze sector nog een grote marge voor progressie is. Net zoals in de braadkippensector is er **ook in de vleeskalverensector dringend nood aan drastische maatregelen om het antibioticumgebruik te reduceren**.

Voor wat betreft de verschillende kleurcodes van de antibioticaklassen, is het gebruik van de producten met "gele" (-12%) en "oranje" (-14%) kleurcode aanzienlijk gedaald. Echter het gebruik van de **kritisch belangrijke "rode" producten is gestegen met 35%**. Alhoewel deze stijging moet bekeken worden in het licht van het huidige lage niveau in totaal gebruik en de stijging de reductie doelstelling van -75% die vorig jaar reeds was behaald niet in het gedrang brengt, is het toch een zorgelijke evolutie die een nauwgezette opvolging vereist. Zoals hoger reeds opgemerkt is deze stijging volledig te wijten aan een stijging van het fluoroquinolone gebruik (in het bijzonder flumequine) voornamelijk in de braadkippen sector en voor een veel geringer deel in de kalversector. Gebaseerd op de eerste resultaten van 2019 wordt verwacht dat dit een éénmalig fenomeen zal zijn.

Conclusie

Dit rapport toont opnieuw hoopgevende resultaten met de bevestiging van het behalen van twee van de drie kwantitatieve doelstellingen (gebruik van antimicrobiële premixen en kritisch belangrijke antibiotica). In het bijzonder voor wat betreft het totaal gebruik zijn er belangrijke dalingen gerealiseerd wat ons sterkt in het geloof dat het halen van de doelstelling van -50% tegen 2020 nog steeds realistisch is. Echter zullen er nog zeer belangrijke inspanningen moeten worden geleverd door alle betrokken partijen om dit doel effectief te realiseren. De varkenssector wordt aangemoedigd om verder te gaan op de ingeslagen weg daar waar de braadkippen- en kalversector wordt opgeroepen om dringend de inspanningen tot reductie van het antibioticumgebruik te intensifiëren.

RESUME

Ce 10^e rapport BelVet-SAC décrit les résultats de la consommation d'antibiotiques chez les animaux en Belgique en 2018 et son évolution depuis 2011. Pour la première fois, le rapport analyse à la fois les données des ventes (collectées au niveau des grossistes – distributeurs et fabricants d'aliments composés pour animaux) et les données d'utilisation (collectées au niveau de l'élevage). Cette combinaison permet d'étudier plus en détail la consommation par secteur (espèces animales).

Avec une réduction de **-12,8% mg d'antibiotiques par kg de biomasse** par rapport à 2017, 2018 est l'année qui connaît la plus forte baisse des ventes d'antibiotiques pour animaux en Belgique depuis 2011. Ce résultat s'inscrit clairement dans la tendance à la baisse des années précédentes et se traduit par une diminution cumulée de **-35,4% mg/kg depuis 2011**. Cellec i se subdivise en une diminution de **-13,2% mg/kg pour les produits pharmaceutiques** et de **-9,2 % mg/kg pour les prémélanges**. La forte baisse des ventes de produits pharmaceutiques est aussi une conséquence probable de l'augmentation des stocks en 2017 en prévision de l'augmentation de la taxe sur les antibiotiques pour les titulaires d'enregistrement, qui est entrée en vigueur le 1^{er} avril 2018. Si l'on compare ce résultat à l'objectif de l'AMCRA-2020 (réduction de l'utilisation des antibiotiques de 50% d'ici 2020), il est clair que cet objectif n'a pas encore été atteint mais peut l'être, étant donné qu'il ne faut plus réduire la consommation que de 14,6% dans les deux prochaines années.

Compte tenu du recul significatif des ventes, il n'est pas surprenant que dans le **secteur porcin**, qui représente la part la plus importante de la consommation totale, on constate une forte baisse de **-8,3% mg/kg** entre 2017 et 2018. Converti en BD₁₀₀ (nombre de jours de traitement sur 100 jours), cela correspond à une **réduction du BD**₁₀₀ **médian de -1,4% chez les porcs d'engraissement (4,4 en 2018)**, **-6% chez les porcelets sevrés (16,6 en 2018)**, **-18% chez les porcelets non sevrés (1,8 en 2018) et -3% chez les porcs reproducteurs (0,3 en 2018)**. Ces résultats sont stimulants pour le secteur porcin, qui a fourni ces dernières années des efforts considérables pour réduire l'utilisation des antibiotiques, notamment en mettant en place dès 2014 un système privé de collecte de données (Registre AB) et en ayant assumé seuls la réduction de l'utilisation des aliments médicamenteux. Sur ce dernier point, il est bon de noter que même après les diminutions très importantes de l'utilisation des prémélanges antimicrobiens au cours des dernières années, cette diminution se poursuit en 2018, ce qui se traduit finalement par une réduction cumulative de -69,8% mg/kg par rapport à 2011. De plus, l'utilisation de la **colistine du ZnO** continue de diminuer (**-21,3%** mg/kg en 2018) parallèlement à une nouvelle réduction de l'utilisation de la **colistine (-4,1% mg/kg)**. Toutefois, des défis subsistent également dans le secteur porcin, en particulier en ce qui concerne l'utilisation chez les porcelets sevrés ainsi que dans les élevages ayant un niveau élevé d'utilisation générale.

Bien que les poulets de chair et les veaux de boucherie aient une part plus faible dans l'utilisation totale d'antibiotiques chez les animaux, l'augmentation de l'utilisation de 13,8% mg/kg et 17,7% mg/kg, respectivement, est un résultat décevant. L'augmentation chez les poulets de chair peut sembler limitée car l'utilisation en mg/kg est encore considérablement plus faible que pour les porcelets sevrés ou les veaux de boucherie et parce qu'avec la diminution de 2% du BD₁₀₀ médian, le poulet de chair est traité dans la majorité des exploitations pendant moins de 5% de sa vie. Toutefois, ce résultat doit être interprété avec prudence puisque la majorité des traitements chez les poulets de chair ont lieu au cours des premières semaines de vie et que cette utilisation précoce entraîne une forte sélection pour la résistance aux antibiotiques. Cette situation, combinée à l'augmentation de l'utilisation des fluoroquinolones en 2018, conduit à lancer un appel urgent au secteur du poulet de chair pour qu'il prenne les mesures nécessaires afin de réduire considérablement l'utilisation des antibiotiques dans les années à venir.

On sait depuis longtemps que l'utilisation d'antibiotiques dans le secteur des veaux de boucherie est la plus élevée de tous les secteurs (BD₁₀₀ médian de 28 jours). Toutefois, la forte variation observée entre les exploitations montre que dans ce secteur également, il existe encore une importante marge de progrès. Comme dans le secteur du poulet de chair, **des mesures drastiques visant à réduire l'utilisation d'antibiotiques sont également nécessaires de toute urgence dans le secteur des veaux de boucherie.**

En ce qui concerne l'utilisation des antibiotiques selon leur code couleur, l'utilisation des antibiotiques « jaunes » (-12%) et « oranges » (-14%) a considérablement diminué. Cependant, l'utilisation des **produits « rouges », d'importance critique, a augmenté de 35%**. Bien que cette augmentation doive être relativisée au vu du faible niveau de la consommation totale et ne compromette pas l'objectif de réduction de -75% déjà atteint l'an dernier, il s'agit d'une évolution préoccupante qui nécessite un suivi minutieux. Comme signalé plus haut, cette augmentation est entièrement due à une hausse de l'utilisation des fluoroquinolones (en particulier de la fluméquine), principalement dans le secteur des poulets de chair et, dans une moindre mesure, dans celui du veau de boucherie. On peut s'attendre à ce que ce résultat, basé sur les premières données de 2019, soit un phénomène ponctuel.

Conclusion

Ce rapport montre à nouveau des résultats prometteurs avec la confirmation que deux des trois objectifs quantitatifs (utilisation de prémélanges antimicrobiens et d'antibiotiques d'importance critique) sont atteints. Concernant l'utilisation globale en particulier, des diminutions significatives ont été obtenues, ce qui confirme notre conviction que l'objectif de -50% d'ici 2020 reste réaliste. Toutefois, toutes les parties concernées devront déployer des efforts très importants afin d'atteindre effectivement cet objectif. Le secteur porcin est encouragé à poursuivre dans cette voie, et ceux du poulet de chair et du veau de boucherie sont invités à intensifier d'urgence leurs efforts pour réduire l'usage d'antibiotiques.

PREFACE

Antibacterial products 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 antibacterial products 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 and vice versa 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 2015 the World Health Assembly unanimously adopted the Global Action Plan¹ (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 public as well 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 antibacterial products 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 tenth BelVet-SAC report gives an overview of the consumption of antibacterial products in veterinary medicine in Belgium in 2018 and describes evolutions in use since 2011.

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

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MATERIALS AND METHODS

ANTIMICROBIAL SALES DATA

Data collection

a) Antibacterials for veterinary use

i. 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 24 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, FAMHP) on demand. They were asked by letter dd. January 2019 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 2018 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.

ii. 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 feed² (n=48). They received a list of registered and marketed Antibacterial containing premixes. The feed mills were asked by letter dd. January 2019 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 2018 was also submitted via the secure web-application³. 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 2018**. Antibacterial and ZnO premixes can only be incorporated into medicated feed on prescription of a veterinarian.



Figure 2. Distribution of Veterinary premixes in Belgium.

iii. 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 <u>www.BELVET-SAC.ugent.be</u>

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

b) Animal population

Animal population data to calculate the produced biomass were derived from the Eurostat website⁴.

From these animal population data, biomass (in kg) was calculated, according to Grave⁵ 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, BELVET-SAC 2017)⁶, yearly consumption figures were put versus

⁴ <u>http://ec.europa.eu/eurostat/data/database</u>

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 <u>http://www.belvetsac.ugent.be/</u>

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 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

a) External data validation

To check for correctness and completeness the collected data on premixes were compared to data collected by the compound feed producing industry⁷. 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.

b) 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.bfa.be

ANTIMICROBIAL USE DATA

Data collection

a) Use of antibacterial products at farm level

Since 27 February 2017, veterinarians are legally obliged (RD of 02.07.2017 modifying RD of 21.07.2016) to register in the secured online data collection system Sanitel-Med all prescriptions, administrations and deliveries of antibacterial products (pharmaceuticals as well as premixes, incl. premixes containing ZnO as an antidiarrheal substance) on Belgian farms growing pigs, broilers, laying hens and veal calves. The system, developed and maintained by the FAMHP, is accessible as a web application or through automated data transfer using xml (webservices).

Registration is done by first creating a 'Medicinal Delivery Document' containing the identification of the veterinarian and the farm as well as the type, number and date of the reference document (Treatment and Delivery Document, prescription or 'register out' of the veterinarian). To this Medicinal Delivery Document, one or more 'notifications' are added, each representing a specific prescription, delivery or administration of an antibacterial product.

The following data need to be included in a notification:

The animal species and category for which the antibacterial product is intended.

The categories that can be selected are

- Pigs:
 - sows (PIGB);
 - gilts; fattening pigs (PIGF);
 - weaned piglets (PIGLW);
 - suckling piglets (PIGLU)
- Poultry:
 - broilers (BROIR);
 - laying hens (LAYIH)
- Veal:
 - Veal calve (VECLF)
- The name and quantity of the antibacterial product.

The product needs to be selected from a (regularly updated) medicinal product list containing all antibacterial product packages commercialized in Belgium, identified through a unique cti-ext key. As for the antimicrobial sales data, all groups of antibacterial agents listed in Table 1 are included. For pharmaceuticals, the number of packages needs to be registered, with the possibility of using decimals. For premixes, either the number of packages, the kg premix or the kg medicated feed in combination with the parts-per-million premix needs to be registered; using decimals is also possible.

Products used off-label need to be registered from the same list. Products used through cascade (products not registered in Belgium, products for human use or products prepared extemporaneously) need to be registered as 'Self-Defined Product' (SDP), requiring additional data fields to allow calculation of the delivered quantity of active substance (see below).

Veterinarians can register the data at any moment under the premise that all data from a given quarter need to be registered at the latest the 14th day of the following quarter. The farmer or responsible of the animals must check the correctness of the data from a given quarter at the latest the final day of the first month of the following quarter. This last day is called the 'Data-Lock-Point' (DLP), hence, there are four DLP in a year.

So-called 'third parties' (i.c. other Belgian data collection systems) can transfer the required data on behalf of a veterinarian and/or farmer. Nonetheless, the respective veterinarian and/or farmer remain responsible for the completeness, correctness and timeliness of the registrations.

Reprising Figure 1 explaining the origin of the antimicrobial sales data, the data from Sanitel-Med originate at the bottom of the chain, and concern data about the use of antibacterial products at the farm level (Figure 3). However, from the info provided above, it can be noted that not all Sanitel-Med data are 'use data' in a strict sense; indeed, a prescription or delivery is not 'proof' that the products have also been used in practice, especially not at the time of prescription or delivery. Nonetheless, it is deemed very likely that virtually all products prescribed or delivered are eventually used. It is furthermore assumed that by looking at the data over a period of one year, the lag between the moment of prescribing/delivering and using in practice will be averaged and play no relevant role in the calculation of the final result. Therefore, the Sanitel-Med data are referred to as 'use data' – in contrast to the BelVet-SAC data which are 'sales data'.



Figure 3. Origin of Sanitel-Med data concerning farm-level use of antibacterial pharmaceuticals.

A pseudonymized list with all notifications is accessible to AMCRA as a report, based on a query developed and maintained by the FAMHP, that can be pulled by AMCRA through a secured online business object tool provided by the Federal Agency for the Safety of the Food Chain (FAFSC). AMCRA extracts the report at least four times a year, i.e. after each DLP.

b) Number of animals present at the farms

The number of animals present at each farm is needed to calculate the animal mass 'at risk of treatment' at the farm (cfr. further in the text). The number is deduced from identification and registration data present in the SANITEL⁸ -database or, specifically for poultry farms, from SANITEL-data combined with data from the yearly 'Biosecurity-survey' organized by the FASFC.

⁸ http://www.afsca.be/dierlijkeproductie/dieren/sanitel/

i. Veal calf farms

The average number of calves present at each farm is calculated per month, taking into account the number of arrivals, births, departures and deaths on the farm notified in SANITEL. A query for calculating the average monthly occupation per farm is developed and maintained by the FAMHP. A pseudonymized report of the numbers per farm for each month is made available to AMCRA upon request.

ii. Poultry farms

The yearly FAFSC 'Biosecurity-survey' yields either a separate capacity for broilers and laying hens on a farm, a total capacity for broilers and laying hens on a farm, or a total capacity for either broilers or laying hens on a farm. Preference was given to these capacity numbers above SANITEL-data given the current incompleteness of data in the latter database. If for a given farm notifications were present in Sanitel-Med for a poultry category missing from the Biosecurity-survey but for which capacity data was available in SANITEL, the SANITEL-capacity was used.

The Biosecurity-survey data for the previous year are delivered in April as an Excel-sheet to AMCRA. The SANITEL-data are available as a pseudonymized report with the capacity numbers per poultry sanitary unit and production type. The report, based on a query developed and maintained by the FAMHP, can be pulled by AMCRA through a secured online business object tool provided by the Federal Agency for the Safety of the Food Chain (FAFSC). AMCRA extracts the report at least four times a year, at the start of each new trimester (beginning of January, April, July and October). The capacity for a given trimester is calculated as the average of the capacity at the start of the trimester and the capacity at the start of the following trimester.

iii. Pig farms

SANITEL-data include capacity data (updated whenever a change is made to the capacity, for example by building a new or changing an existing stable) as well as count data (the number of animals present needs to be registered in SANITEL by the herd veterinarian at least three times a year). The capacity is the preferred animal number in the calculations. If not available, count data are used. The number of suckling piglets is calculated from the number of sows using the formula $\# sucklers = \# sows \times \frac{27}{12}$. The number of gilts is added to the number of sows if these are present at the farm; if not, the gilts are counted as fattening pigs. No separate analysis is done for gilts.

A pseudonymized list with the capacity and count numbers per pig sanitary unit is accessible to AMCRA as a report, based on a query developed and maintained by the FAMHP, that can be pulled by AMCRA through a secured online business object tool maintained by the FAFSC. AMCRA extracts the report at least four times a year, at the start of each new trimester (beginning of January, April, July and October). The capacity for a given trimester is calculated as the average of the capacity at the start of the trimester and the capacity at the start of the following trimester..

c) Number of active farms

The number of active farms (i.e. having raised animals, hence, where antibacterial products *could* have been used), is needed to determine the reference population for benchmarking (cfr. further in the text). Being 'active' is encoded as a separate feature in SANITEL. Therefore, a pseudonymized list of active veal calf, poultry and pig farms is accessible to AMCRA as a report, based on a query developed and maintained by the FAMHP, that can be pulled by AMCRA through a secured online business object tool provided by the Federal Agency for the Safety of the Food Chain (FAFSC).

Data analysis

a) Numerator

i. Mg active substance used

This is calculated per Sanitel-Med notification, using the formula

active substance used (mg) = quantity antibacterial product \times strength

The quantity of antibacterial product is the number of packages times the number of units of antibacterial product per package. The strength is the number of units of active substance per unit of antibacterial product and is taken from the products' summary of product characteristics (SPC). If the active substance unit is given in international units, a transformation to mg is done using the conversion factors provided on the webpage of the AMCRA data analysis unit⁹. If the product contains more than one active substance, the calculation is done for each substance and the sum is made.

After calculating the total mg of active substance used per notification, the amounts can be aggregated by farm, by type of active substance, by animal category and by animal species. This numerator is used for the weight-based analysis of the antimicrobial use (see section c, p. 21).

ii. Number of DDDA_{bel} used

The DDDA_{bel} (the Defined Daily Dose Animal for Belgium) is the daily dose (in mg) per kg live bodyweight. This is calculated per notification using the formula

$\# DDDA_{bel} = mg active substance/DDDA_{bel}$

The DDDA_{bel}-values for all antibacterial products in the Sanitel-Med medicinal product list and for all self-defined products are defined and maintained by AMCRA in 'Antibacterial-dosing' lists made up per animal species¹⁰. The lists also contain the LA_{bel} (Long-acting factor defined for Belgium) of each product. This LA_{bel} factor corrects the longer duration of action of certain products in the calculation of the BD₁₀₀ (cfr. further in the text). For not-long-acting products, the LA_{bel} equals 1. The procedures for determining the DDD_{bel} and LA_{bel} values are also available on the AMCRA website¹⁰.

b) Denominator

i. Produced biomass per species

The biomass pork and poultry meat, as used in the sales data calculations, was used as denominator for pigs and poultry, respectively, at sector level. The biomass veal meat produced was obtained from the Eurostat website as the biomass 'Calve' slaughtered.

This denominator is used for both the weight-based analysis of the antimicrobial use.

ii. Mass animals at risk per animal category at farm level

Per animal category on each farm, the animal mass 'at risk of treatment' (in kg) is calculated using the formula

mass animals at risk (kg) = number of animals × estimated standard weight at treatment

⁹<u>https://www.amcra.be/swfiles/files/Principes%20voor%20bepalen%20van%20DDD-</u>

bel%20op%20productniveau(2)_109.pdf

¹⁰ <u>https://www.amcra.be/nl/analyse-antibioticagebruik/</u>

The following estimated standard weights at treatment were used (source: EMA 2013¹¹):

Suckling piglets	4 kg	Broilers	1 kg	Veal calves	80 kg
Weaned piglets	12 kg	Laying hens	2 kg		
Fattening pigs	50 kg				
Sows	220 kg				

This denominator is used for the dose-based analysis of the antimicrobial use.

c) Indicators for weight-based analysis of antimicrobial use

i. Mg used

To make a comparison between the yearly antimicrobial sales data, which include all animal species, and the antimicrobial usage data, in total and for each of the species (pigs, poultry, veal calves) separately, the total amount of active substance used in each species was calculated, from the sum of the mg used in all Sanitel-Med notifications for that species.

ii. Mg used versus produced biomass

Per animal species, the mg used was standardized by the produced biomass in ton. This allowed on the one hand to make a comparison with the total antimicrobial sales figure and on the other hand to compare usage among the three species as well as their evolution between 2017 and 2018.

d) Indicator for dose-based analysis of antimicrobial use

i. BD₁₀₀

To compare and follow-up the usage of antibacterial products in the different animal categories, the BD_{100} is used, which represents the % of time an animal is treated with antibacterials. This indicator is calculated with the general formula:

$$BD_{100} = \left[\binom{\#DDDA_{bel}}{kg \text{ animals at risk} \times days \text{ at risk}} \times LA_{bel} \right] \times 100$$

To obtain a result per combination of farm and animal category, the BD₁₀₀ is first calculated per Sanitel-Med notification and per month (i.e. with 30,42 days at risk and with the animals at risk determined for that month). Then, the sum of these BD₁₀₀ values over all notifications in one month is made, from which an average over the 12 months in the year is calculated, resulting in a final month-average BD₁₀₀ per animal category on a farm. The comparison between animal categories is then done based on the frequency distribution over all farm-animal category combinations that belong to the core reference population for benchmarking (cfr. below).

e) Extrapolation of 2017 data

For 2017 only 10 months data were available (27 February 2017 until 31 December 2017). To make the comparison between 2017 and 2018, these 10-months data were extrapolated to 12-months data by dividing with 10 and multiplying by 12.

¹¹ <u>https://www.ema.europa.eu/en/documents/scientific-guideline/revised-european-surveillance-veterinary-antimicrobial-consumption-esvac-reflection-paper-collecting_en.pdf</u>

Quality control for defining the core reference population for benchmarking

To adequately follow-up the usage within an animal category, the core reference population for benchmarking is defined as the group of animal category-farm combinations that are in consecutive years active during the whole year, have no errors in their Sanitel-Med notifications and fulfil the conditions with respect to minimum herd size and empty stables.

The 2018 reference population for benchmarking was defined as described below.

a) Active during the whole year

Only when a farm was encoded active during the whole year, the farm was eligible for inclusion in the benchmarking reference population. However, poultry farms encoded as 'active' yet not having any registration in Sanitel-Med and missing from the 2018 FAFSC Biosecurity-survey were considered inactive in 2018 and were excluded from the benchmarking reference population. Likewise, pig farms encoded as 'active' but not having any registration in Sanitel-Med and either having no recent count date (i.e. count date before 2018) or having a recent count date (i.e. count date in 2018) but with counts for all pig categories equalling zero, were considered inactive in 2018 and excluded from the benchmarking reference population. Finally, veal calf farms encoded as 'active' yet not having any registration in Sanitel-Med and having zero animals for each month in 2018 were considered inactive in 2018 and excluded from the benchmarking reference population.

b) Notification errors

Two types of errors are distinguished:

- i. Notifications that cannot be processed due to missing data on the number of animals present at the farm.
- ii. Notifications where the delivered quantity is considered erratic.

Farmers are made aware of these errors through 'error reports', providing them the opportunity to take the necessary steps to adjust the data. Farms that have notification errors that have not been adjusted or have not been confirmed as correct were excluded from the benchmarking reference population.

c) Empty stables

Leaving the stables empty for a short period after cleaning and disinfection is an appropriate practice for an adequate biosecurity management. However, if the stables are empty for several months, this will largely influence the result of the month-average BD₁₀₀ calculation. Therefore, pig farms with recent count data equalling zero at the start of two consecutive trimesters were excluded from the benchmarking reference population. Similarly, veal calf farms with at least one month without animals were excluded from the benchmarking reference population. For poultry farms, the SANITEL nor biosecurity-survey data allow to check for empty stables; no extra criteria for potential vacancy were thus applied for poultry farms.

d) Minimum herd size requirements

To avoid extreme BD₁₀₀ values caused by very low numbers of animals present at the farm for a certain category, a minimum herd size is defined, as shown below:

Weaned piglets	50 animals	Broilers	4900 animals	Veal calves	25 animals
Fattening pigs	100 animals	Laying hens	4900 animals		
Sows	10 animals				

Poultry and pig farms with animal numbers below the minimum for at least one quarter were excluded from the reference population for benchmarking. Veal calf farms with animal numbers below the minimum for at least one month were excluded from the reference population.

To compare the antimicrobial use in 2018 with that in 2017, the reference population for 2017 was defined similarly as described above for 2018. The core reference population 2017-2018 was then defined as the group of farms being part of both the 2017 and 2018 reference populations.

RESULTS

ANTIMICROBIAL SALES DATA

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. Six 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 three 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 Information¹².

	2011	2012	2013	2014	2015	2016	2017	2018
Number of Antibacterial pharmaceuticals on the market	282	308	294	298	339	329	323	325
Number of Antibacterial premixes on the market	23	22	23	21	21	19	16	18
Total number of Antibacterial products on the market	305	330	317	319	360	348	339	343

Table 2. Armatorium of antibacterial products on the Belgian market in between 2011 and 2018.

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.

¹² www.bcfi-vet.be

Animal biomass produced in Belgium

The produced biomass was calculated based on the Eurostat data for the years 2013-2018 as described above (Table 3).

Table 2. Animal biomass produced in Belgium between 2012 and 2018.

Animal biomass	2013	2014	2015	2016	2017	2018
Meat (ton)						
Pork	1 130 570	1 118 330	1 124 310	1 060 540	1 044 560	1 073 120
Beef	249 910	257 670	267 880	278 360	281 540	277 310
Poultry	388 090	433 270	452 940	461 250	463 390	469 590
Sheep/goat ^a	2 410	2 560	2 720	3 020	3 230	3 090
Total biomass from meat production	1 770 980	1 811 830	1 847 850	1 803 170	1 792 720	1 823 110
Dairy cattle						
Dairy cattle (number)	515 990	519 090	528 780	529 780	519 160	529 250
Dairy cattle metabolic weight (ton)	257 995	259 545	264 390	264 890	259 580	264 625
Total biomass (ton)	2 028 975	2 071 375	2 112 240	2 068 060	2 052 300	2 087 735
Evolution since previous year	-0.36%	+2.09%	+1.97%	-2.09%	-0.76%	+ 1.73%

^a 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.

An increase in biomass production of +1.73% is observed between 2017 and 2018.

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 2007-2018 (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 2011-2018 (tons active substance).

Between 2017 and 2018, there was a **decrease of -11,3%** in the total consumption of antibacterials in veterinary medicine in Belgium (197 511,5 kg in 2018; 222 722,8 kg in 2017). The use of antibacterial **pharmaceuticals decreased with -11,7%** between 2017 and 2018, and the use of **antibacterial premixes decreased with -7,6%**. This is the fourth year in a row of decreasing use and the largest relative reduction seen since the start of the measurements. **Since 2011 (reference year for reduction initiative) a decrease of 34.0% 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 2011-2018 (tons active substance).



Figure 6. National consumption of antibacterial premixes in Belgium for the years 2011-2018 (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. Despite the very sharp decrease in 2016 and 2017 an additional further reduction is observed in 2018.

Since 2011 the data collection system allows to differentiate the animal species of destination for the antibacterial premixes. In 2018, 99,7% of the antibacterial premixes went to pig feed and only 0,3% was used in poultry or rabbit feed.

From September 2013, the use of Zinc oxide (ZnO) 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 and continued in 2017 and 2018. In comparison to 2017 the use of ZnO reduced with -21,3% 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 2011-2018 (tons active substance).

Antibacterial use versus biomass

As described above, the total biomass production in 2018 in Belgium has increased with 1,7% in comparison to 2017. As a consequence the decreasing trends in use observed in absolute values (kg) is further enhanced by the fact that this reduced volume of antimicrobials is used in an increased population. For 2017, the mg of active substance used in relation to a kg biomass produced was 108,5 mg/kg whereas in 2018 this is 94,6 mg/kg. This means **a decrease of -12,8% in comparison to 2017.** Split into the different pharmaceutical forms (premix vs other forms), a substantial decrease of -13,2% is observed in the antibacterial pharmaceuticals and -9,2% 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 2011-2018.

The decrease of -12,8% in 2018 is the largest decrease seen in total consumption since the start of the reduction process in 2012. The reduction seen in 2018 is the fourth year in a row with a reduction in the total. Since the start of the reduction program, in six out of the seven years a reduction was obtained. When using 2011 as a reference (see AMCRA 2020 objectives), a cumulative reduction of -35,4% is achieved, distributed in a reduction of -27,3% in antibacterial pharmaceuticals and -69,6% 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 the 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 2018, the eighth ESVAC report, presenting results on antibacterial usage in 30 EU /EEA countries in the year 2016 was released¹³. In this report the **antibacterial consumption in animals in 2016 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 2015-2016 (source: 8th ESVAC report on Sales of veterinary Antibacterial agents).

When looking at figure 10, it can be observed that Belgium resides at the seventh position in terms of antibacterial usage expressed in mg/PCU in 2016. In 2015 this was still the fifth position. Noteworthy, these data do not yet include the substantial decrease in use in Belgium achieved in 2017 and 2018 but obviously, also other countries do take initiatives to further reduce antibiotic use.

¹³ <u>https://www.ema.europa.eu/en/documents/report/sales-veterinary-antimicrobial-agents-30-european-</u> countries-2016-trends-2010-2016-eighth-esvac_en.pdf

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



Figure 11. Overall sales of antimicrobials in mg/PCU between 2012-2016 (source: 5th-8th ESVAC report on Sales of veterinary Antibacterial agents) for Belgium and neighbouring 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 2018, antibacterials that are registered solely for pigs are most used (30,5%) followed by antibacterials registered for both pigs and poultry (21,4%). The third most used antibacterial pharmaceuticals are the ones registered for cattle, pigs and poultry (18,2%). The largest decrease in use over the last 4 years is observed in the first two categories (pigs; pigs & poultry).



Figure 12. Use of antibacterial pharmaceuticals and premixes per authorized species, evolution between 2014 and 2018.

Intramammary products in dairy cattle

Other types of antibacterial 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) Total use of intramammary products

In figure 13 an overview is given of the use of intramammary products for treatment of udder infections in the last four 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 2015 and 2018.

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



Figure 14. Evolution in use of antibacterial products for intramammary treatment expressed per kg biomass of dairy cattle between 2013 and 2018.

From the results of figure 14 it can be seen that the use of IM preparations was substantially reduced between 2013 and 2015 (-30%), however since 2015 it has steadily increased again (+16%).

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 6 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 a steady but limited increase in the use of DC applicators which indicates that there is no indication of a further implementation of selective dry cow therapy or an indication of more (latent) udder infections at drying off. The number of applicators used for the treatment of mastitis cases remains relatively stable over the years, however also here a substantial increase is seen in 2018.

Antibacterial pharmaceuticals in dogs and cats

In 2017, 2137 kg of active substance was used in dogs and cats. In 2018 this was 2393 kg, corresponding to an increase of +12,0% in comparison to 2017. The evolution since 2014 is shown below. In the last 5 years (with the exception of 2017) a constant increase in use of antimicrobials that are only registered for dogs and cats is observed. It is noteworthy to mention that we do not have an accurate estimate of the evolution in the total dog and cat population (denominator). Therefore the observed evolution cannot be placed in contrast to the possible evolution of the population size.









Penicillin/clavulanic acid (1041,0 kg) is the most used antibacterial compound in dogs and cats, followed by cephalosporines of the 1° and 2° generation (618,7kg) and macrolides (299,2 kg). In the cephalosporines of the 1° and 2° generation a substantial increase is observed in 2018 due to an increased use in cefalexine, a narrow spectrum cephalosporine. The increased use in "others" is due to an increase in use of metronidazole, administered in combination with spiramycine.

Antibacterial use per class of antibacterial compound

a) 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 2018.

In 2018, the most used group of antibacterials remained the penicillins (74,5 tons; 35,7%). The tetracyclines (40,6 tons; 19,4%) are the second most used group followed by the sulphonamides and trimethoprim (36,5 tons; 17,5%). 2018 is the sixth year in row where penicillins 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.

Class AB Mg/kg Biomass	2012	2013	2014	2015	2016	2017	2018	'12 » '13	'13 » '14	'14 » '15	'15 » '16	'16 » '17	'17 » '18	2018%
penicillins	40,55	39,88	39,91	38,09	42,03	40,96	35,78	-1,6%	0,1%	-4,6%	10,3%	-2,6%	-12,6%	33,01
tetracyclines	30,98	30,80	29,92	28,49	24,16	27,66	23,95	-0,6%	-2,8%	-4,8%	-15,2%	14,4%	-13,4%	22,10
sulphonam & trimethoprim	42,42	36,79	37,39	35,08	31,64	21,56	17,49	-13,3%	1,6%	-6,2%	-9,8%	-31,8%	-18,9%	16,14
macrolides	8,94	8,64	11,27	10,80	9,57	9,18	8,12	-3,4%	30,5%	-4,2%	-11,4%	-4,0%	-11,5%	7,49
aminosydes	4,09	3,99	4,34	4,47	4,48	4,49	3,94	-2,3%	8,8%	3,1%	0,2%	0,3%	-12,4%	3,63
polymixins	4,74	3,89	2,74	2,25	2,03	1,76	1,69	-18,0%	-29,6%	-17,6%	-9,9%	-13,3%	-4,1%	1,56
fenicols	0,71	0,75	0,78	0,99	1,46	1,50	1,59	5,8%	4,6%	26,5%	47,3%	3,0%	6,1%	1,47
other**	1,27	0,90	0,61	0,57	0,55	0,50	1,05	-28,9%	-32,3%	-6,1%	-3,8%	-9,4%	109,5%	0,97
quinolones	2,07	1,64	1,69	1,92	0,82	0,29	0,44	-21,1%	3,2%	13,7%	-57,5%	-64,2%	50,0%	0,40
cephalosporins 1° & 2° gen	0,35	0,35	0,39	0,37	0,44	0,41	0,37	-1,9%	12,7%	-4,4%	16,3%	-6,7%	-7,8%	0,35
cephalosporins 3° & 4° gen	0,40	0,41	0,38	0,35	0,25	0,09	0,07	3,7%	-7,0%	-9,5%	-28,3%	-65,9%	-19,2%	0,06
Total mg/kg Biomas	136,51	128,02	129,42	123,39	117,43	108,40	94,50	-6,22%	1,09%	-4,66%	-4,83%	-7,69%	-12,83%	100

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

** zink bacitracin, rifaximin, metronidazol, tiamulin
In 2018, the use of the three main compounds (penicillins, tetracyclines, sulphonamides) all reduced very substantially. Only in three antimicrobial classes an increase was seen this year. First of all an increase of 6,1% in use of phenicols was observed. This is in line with previous years where it has been observed that the use of phenicols is growing almost every year. This is mainly due to an increased use of florfenicol and is likely the result of a change towards the use of "yellow" molecules.

In 2018, for the first year a very important increase (+109,5%) in the use of 'others' was observed as well. This is almost entirely due to a very substantial increase in the use of tiamulin, also a yellow categorized antimicrobial.

The most worrisome increase observed in 2018 is this of the quinolones, categorized as "red" antimicrobials, where after two years of very important decreases now an increase with 50% is observed. This increase is entirely due to an increase in the use of flumequine which is mainly applied in poultry. The cephalosporines of the 3rd and 4th generation (the second group of "red" molecules, continue to decrease in use again driven by a continued substantial decrease in use of ceftiofur and to a lesser extend the use of cefquinome (table 5).

The decreased use of polymyxins (almost entirely colistin sulphate) is observed for the sixth year in a row with a decrease of -4,1% in 2018. This is a positive trend given the simultaneous decrease in use of ZnO as an alternative for colistin use in the treatment of post-weaning diarrhoea in piglets, meaning that alternative treatments without use of antibiotics or ZnO may have been used more frequently. When comparing to 2012 (before authorization of ZnO products), polymyxin use has dropped with 64,4%.

AMCRA (centre of expertise on AntiMicrobial Consumption and Resistance in Animals)¹⁴ 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 colour 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 health¹⁵ and the lists produced by the World Animal Health Organization (OIE) indicating the importance of antibacterials for veterinary health¹⁶. 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 3rd and 4th generation and the quinolones.

In figure 19, the evolution of use of the different colour groups of antibacterials over the last 4 years is presented. From this figure it can be seen that the orange group remains 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 2018, a very substantial decrease in the yellow (-11,6%) and orange (-13,5%) groups is observed, whereas the red group shows an increase of +34,4%. The latter increase is entirely due to the increased use in the quinolone group as was discussed already before. In comparison to 2011 (reference year) the reduction of red molecules is still -79,1% which remains below the aim of minus 75% by 2020.

¹⁴ www.amcra.be

¹⁵ http://apps.who.int/iris/bitstream/10665/77376/1/9789241504485_eng.pdf

¹⁶ <u>http://web.oie.int/downld/Antibacterials/OIE_list_Antibacterials.pdf</u>



Figure 19: Evolution in the antibacterial consumption (mg/kg) per antibacterial colour group between 2014 and 2018.

A similar graph with products exclusively registered for dogs and cats (Fig. 20) shows a more moderate reduction in use of the red molecules (-1%) and a substantial increase in the use of the yellow molecules of +33%. 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 colour group for compounds exclusively registered for use in dogs and cats between 2014 and 2018.

b) Antibacterial pharmaceuticals



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



c) 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)					Medica	dicated premixes (kg)			
Class	Antimicrobial compound	2014	2015	2016	2017	2018	2014	2015	2016	2017	2018	2014	2015	2016	2017	2018
Cephalosporins 1G	Cephalexin	767,7	740,4	837,3	763,0	720,2	767,7	740,4	837,3	763,0	720,2					
Cephalosporins 1G	Cefalonium	12,3	12,8	12,2	10,2	9,3	12,3	12,8	12,2	10,2	9,3					
Cephalosporins 1G	Cefapirin	12,8	20,7	31,7	44,3	45,3	12,8	20,7	31,7	44,3	45,3					
Cephalosporins 1G	Cefazoline	16,7	15,6	17,7	16,0	7,3	16,7	15,6	17,7	16,0	7,3					
Phenicols	Chloramphenicol	-	-	-	-	-	-	-	-	-	-					
Phenicols	Florfenicol	1.616,1	2.084,5	3.006,5	3.077,5	3.320,7	1.580,3	1.984,1	2.632,3	2.816,2	3.041,5	35,8	100,5	374,1	261,3	279,2
Other	Metronidazole	94,0	92,5	100,5	96,7	234,4	94,0	92,5	100,5	96,7	234,4					
Other	Tiamulin	1.047,6	1.032,3	994,2	879,0	1.901,6	615,7	548,3	640,4	624,6	1.236,0	431,8	484,0	353,8	254,4	665,6
Other	Valnemulin	59,3	11,2	-	0,3	-	-	-	-	-	-	59,3	11,2	-	0,3	-
Other	Zinc bacitracin	39,2	48,6	23,3	28,9	28,2	39,2	48,6	23,3	28,9	28,2					
Penicillines	Benethamine penicillin	8,1	10,2	22,1	33,7	38,2	8,1	10,2	22,1	33,7	38,2					
Penicillines	Cloxacillin	393,4	337,7	286,9	260,0	257,2	393,4	337,7	286,9	260,0	257,2					
Penicillines	Phenoxymethyl- penicillin	378,3	537,0	796,4	864,2	1.078,4	378,3	537,0	796,4	864,2	1.078,4					
Penicillines	Nafcillin	7,1	7,2	6,3	6,0	6,0	7,1	7,2	6,3	6,0	6,0					

Penicillines	Penethamate	6,8	146,1	184,8	235,2	202,0	6,8	146,1	184,8	235,2	202,0					
Penicillines	Procaine benzylpenicillin	10.113,0	10.508,4	10.359,3	9.426,0	9.583,8	10.113,0	10.508,4	10.359,3	9.426,0	9.583 <i>,</i> 8					
Sulpho-namides	Sulfachloor- pyridazine natrium	847,0	1.098,2	1.094,5	1.176,4	1.050,7	847,0	1.098,2	1.094,5	1.176,4	1.050,7					
Sulpho-namides	Sulfadiazine	62.414,9	59.403,3	51.631,2	33.703,6	27.303,7	40.610,9	37.954,0	37.350,2	32.971,4	27.266,8	21.804,0	21.449,3	14.281,0	732,3	36,9
Sulpho-namides	Sulfa- dimethoxine natrium	-	-	-	-	37,7	-	-	-	-	37,7					
Sulpho-namides	Sulfadimidine natrium	0,0	-	-	-	-	0,0	-	-	-	-					
Sulpho-namides	Sulfadoxine	511,7	587,9	922,8	1.174,1	1.238,4	511,7	587,9	922,8	1.174,1	1.238,4					
Sulpho-namides	Sulfamethoxazol	660,9	557,6	785,4	810,8	792,6	660,9	557,6	785,4	810,8	792,6					
Sulpho-namides	Sulfanilamide	-	-	-	-	-	-	-	-	-	-					
Sulpho-namides	Trimethoprim	12.911,8	12.351,8	10.906,3	7.390,8	6.092,7	8.551,0	8.061,9	8.050,1	7.244,4	6.085,3	4.360,8	4.289,9	2.856,2	146,5	7,4
Amino(glyco)- sides	Apramycin	141,6	97,9	79,5	49,5	55,4	54,6	37,0	26,3	12,5	0,2	87,0	60,9	53,2	37,0	55,2
Amino(glyco)- sides	Dihydro- streptomycin	9,0	7,2	6,3	131,7	6,0	9,0	7,2	6,3	131,7	6,0					
Amino(glyco)- sides	Framycetin- sulphate	6,5	6,3	11,3	16,3	17,8	6,5	6,3	11,3	16,3	17,8					
Amino(glyco)- sides	Gentamicin	126,5	129,2	136,1	141,7	172,9	126,5	129,2	136,1	141,7	172,9					
Amino(glyco)- sides	Kanamycin	17,6	23,7	22,7	25,3	53,2	17,6	23,7	22,7	25,3	53,2					
Amino(glyco)- sides	Neomycin	765,9	336,0	683,8	672,9	47,7	765,9	336,0	683,8	672,9	47,7					

Amino(glyco)sid es	Paromomycin	2.690,6	2.368,1	1.878,4	1.807,1	2.510,2	2.690,6	2.368,1	1.878,4	1.807,1	2.510,2					
Amino(glyco)- sides	Spectinomycin	5.224,8	6.471,5	6.437,2	6.380,4	5.361,0	4.959,9	6.217,7	6.320,8	6.360,6	5.356,6	264,9	253,7	116,4	19,8	4,4
Macrolides	Clindamycin	148,1	144,1	142,7	121,2	135,8	148,1	144,1	142,7	121,2	135,8					
Macrolides	Erythromycin	0,6	0,9	-	-	-	0,6	0,9	-	-	-					
Macrolides	Gamithromycin	20,2	20,3	32,9	29,8	39,3	20,2	20,3	32,9	29,8	39,3					
Macrolides	Lincomycin	4.803,0	5.631,8	4.582,0	4.990,6	4.378,7	4.538,0	5.378,0	4.465,6	4.970,8	4.374,3	265,0	253,7	116,4	19,8	4,4
Macrolides	Pirlimycin	0,4	0,4	0,2	-	-	0,4	0,4	0,2	-	-					
Macrolides	Spiramycin	75,5	248,0	195,4	183,7	160,0	75,5	248,0	195,4	183,7	160,0					
Macrolides	Tildipirosin	39,6	44,5	48,9	48,5	49,2	39,6	44,5	48,9	48,5	49,2					
Macrolides	Tilmicosin	4.380,1	4.159,7	3.785,5	3.160,2	2.824,7	2.467,2	2.540,3	2.637,1	2.344,6	2.113,7	1.912,9	1.619,4	1.148,4	815,6	711,0
Macrolides	Tulathromycin	100,7	111,1	133,1	142,2	128,1	100,7	111,1	133,1	142,2	128,1					
Macrolides	Tylosin	13.475,3	12.041,0	10.581,1	9.839,8	9.181,1	12.201,5	11.151,5	10.149,1	9.600,2	9.040,3	1.273,9	889,5	432,0	239,5	140,9
Macrolides	Tylvalosin	275,7	377,9	259,8	330,2	60,5	275,7	377,9	259,8	330,2	46,2					14,4
Other	Rifaximin	23,1	24,8	21,4	20,7	21,3	23,1	24,8	21,4	20,7	21,3					
Penicillines	Amoxicillin	71.420,3	68.574,8	74.840,9	72.929,0	63.182,0	58.319,6	55.025,1	64.267,8	61.549,1	53.406,1	13.100,7	13.549,7	10.573,1	11.380,0	9.775,9
Penicillines	Amoxicillin-clav	215,1	222,2	244,3	257,6	230,0	215,1	222,2	244,3	257,6	230,0					
Penicillines	Ampicillin	234,7	233,3	297,8	302,8	356,3	234,7	233,3	297,8	302,8	356,3					
Polymyxins	Colistin-sulphate	5.658,1	4.755,6	4.195,0	3.613,9	3.524,9	4.693,9	4.060,3	3.719,4	3.156,1	3.134,9	964,3	695,3	475,6	457,8	390,0
Polymyxins	Polymyxine B sulphate	1,0	0,9	0,8	0,8	0,7	1,0	0,9	0,8	0,8	0,7					
Tetracyclines	Chlor- tetracycline	633,1	588,2	717,2	664,9	738,5	510,8	526,1	680,1	664,9	738,5	122,3	62,1	37,1	-	-
Tetracyclines	Doxycyclin	50.664,6	49.134,3	38.130,4	46.540,0	39.821,8	43.263,6	42.364,9	33.120,0	41.705,1	34.070,8	7.401,0	6.769,4	5.010,4	4.834,9	5.751,0

Tetracyclines	Oxytetracycline	10.603,4	10.369,3	11.052,0	9.552,0	9.448,8	10.259,4	10.199,8	10.926,9	9.448,0	9.444,8	344,0	169,5	125,1	104,0	4,0
(Fluoro)quino- Iones	Danofloxacin	69,1	60,0	42,5	12,0	8,4	69,1	60,0	42,5	12,0	8,4					
(Fluoro)quino- Iones	Difloxacin	0,7	-	-	-	-	0,7	-	-	-	-					
(Fluoro)quino- Iones	Enrofloxacin	1.411,2	1.280,7	719,3	306,5	305,4	1.411,2	1.280,7	719,3	306,5	305,4					
(Fluoro)quino- Iones	Flumequine	1.564,5	2.197,5	610,6	176,0	519,5	1.564,5	2.197,5	610,6	176,0	519,5					
(Fluoro)quino- Iones	Ibafloxacin	0,0	-	-	-	-	0,0	-	-	-	-					
(Fluoro)quino- Iones	Marbofloxacin	438,2	504,0	306,6	99,0	75,3	438,2	504,0	306,6	99,0	75,3					
(Fluoro)quino- Iones	Orbifloxacin	3,4	3,1	3,0	2,7	2,9	3,4	3,1	3,0	2,7	2,9					
(Fluoro)quino- Iones	Pradofloxacin	4,7	3,4	2,9	2,5	2,1	4,7	3,4	2,9	2,5	2,1					
Cephalosporins 3G	Cefoperazon	5,5	6,5	5,9	5,0	5,4	5,5	6,5	5,9	5,0	5,4					
Cephalosporins 3G	Cefovecin	9,3	9,1	9,3	9,0	9,1	9,3	9,1	9,3	9,0	9,1					
Cephalosporins 3G	Cefquinome	180,7	179,9	132,6	89,2	75,6	180,7	179,9	132,6	89,2	75,6					
Cephalosporins 4G	Ceftiofur	598,4	537,1	366,6	71,4	53,3	598,4	537,1	366,6	71,4	53,3					

ANTIMICROBIAL USE DATA

Notifications

Veterinarians

Farms

Notifications in Sanitel-Med in 2018

171 942

5289

312

Table 6 shows per species the number of farms which had notifications (incl. ZnO) in Sanitel-Med in 2018, the total number of notifications and the number of veterinarians that made the notifications. The pig sector clearly is the largest sector in all terms. The veal sector is the smallest sector in terms of active veterinarians and number of farms; in terms of notifications however, it equals the poultry sector. It must be noted that the sum of the veterinarians per species does not equal the total number, meaning that some veterinarians have notifications for different species.

Tuble 0. Humber	ormoundatio		iis unu	vetermana	115 0010	innotineation	is per u	initial spee		inter mean	12010.
	TOTAL		PIG	ì		POULT	ſRY	VEA	L		
	n	AB n	%	ZnO n	%	Total n	%	AB n	%	AB n	%

4

12

34

134 991

4 280

259

79

81

83

18 058

751

63

10,5

14

20

18 893

258

20

11

5

6

Table 6. Number of potifications and farms and veterinarians with potifications per animal species in Sanitel-Med in 2018

Weight-based analysis of a	ntimicrobial use

127 395

4 276

258

This weight-base analysis is primarily meant to make the comparison between the usage data and the sales data. It also includes a weight-based comparison among the different sectors as well as their 2017-2018 evolution in mg/kg.

a) Total antimicrobial usage versus antimicrobial sales in 2018

74

81

83

7 596

621

107

In total, antimicrobial use data covered 78% of tonnes active substance according to the sales data in 2018, with 77% coverage for pharmaceuticals and 92% coverage for premixes medicated with antibacterials (Figure 23). This means that in absolute amounts there is a difference of 42,6 tonnes between sales and use data for 2018.



Figure 23. Comparison of tonnes active substance used (Sanitel-Med¹¹⁷) and sold (BelVet-SAC) in 2018.

¹⁷ The Sanitel-Med data include the self-defined products (SDPs), which are products imported for use through cascade.

b) Tonnes used in the different animal species/categories in 2018

Figure 24 summarizes the use in tonnes of antibacterial products in all Sanitel-Med animal categories. Figure 25 gives more details for pigs, with the distinction between pharmaceuticals and antibacterial premixes, as well as including ZnO.

Most tonnes were used in pigs and more specifically in fatteners (accounting for 41,1% of tonnes used and 32,2% of tonnes sold in 2018) and weaners (26,0% of tonnes used; 20,4% of tonnes sold). Weaners used two thirds of antibacterial premix and when including the ZnO premix, weaners used most tonnes of antibacterial products of all categories. ZnO usage data covered 93,3% of ZnO sales data. In poultry (14,7% of tonnes used; 11,5% of tonnes sold) and veal calves (13,6% of tonnes used; 10,7% of tonnes sold), a comparable number of tonnes was used. Use in breeding pigs, suckling piglets and laying hens together accounted for <5% of tonnes used and sold. Broilers accounted for 98% of the total use in poultry.



Figure 24. Tonnes of antibacterial products (incl. SDPs) used in 2018 per Sanitel-Med animal category.



Figure 25. Tonnes of antibacterial products (incl. SDPs) used per pig category in 2018, with used tonnes ZnO added.

c) Sales data coverage according to antibacterial class in 2018

When breaking down the total usage data in the different antibacterial classes, coverage of sales data was particularly high for polymyxins and penicillins (Table 7). In contrast, coverage was (very) low for cephalosporins, aminosides, phenicols and quinolones. This shows that currently these molecules are predominantly used in animal species not covered in Sanitel-Med. The seemingly low coverage of aminosides usage data is partly due to the fact that the spectinomycin used via lincomycinspectinomycin combination products is shown as a separate category and not included in the aminosides category as for the sales data.

Expressed in tonnes, penicillins and tetracyclines were the most used classes in pigs and veal calves. In poultry lincomycinspectinomycin combination products were the second most used class, after penicillins. Further analysis shows that the penicillins are predominantly extended spectrum molecules.

	Sales 2018				Use	2018			
	Ton	Total ton	% sales	Pig ton	% sales	Poultry ton	% sales	Veal ton	% sales
Penicillins	74,7	63,2	85	46,3	62	10,2	14	6,6	9
Tetracyclines	50,0	37,7	75	28,4	57	1,8	4	7,5	15
Trim-sulfa	36,5	25,7	70	20,8	57	3,7	10	1,1	3
Macrolides*	17,0	13,1	77	5,7	34	3,2	19	4,2	24
Aminosides	8,2	1,3	16	0,2	3	0	0	1,1	14
Polymixins	3,5	3,2	92	2,9	83	0,1	2	0,3	7
Phenicols	3,3	1,4	43	1,3	38	<0,01	<0,1	<0,01	<0,1
Other**	2,2	1,4	65	1,4	65	0	0	<0,01	<0,1
Quinolones	0,92	0,44	48	0,01	2	0,39	42	0,04	4
Cephalosporins	0,92	<0,01	<0,1	<0,01	<0,1	0	0	<0,01	<0,1
Linco-spectino***	-	7,5	-	3,6	-	3,8	-	0,1	-

 Table 7. Total tons per antibacterial class sold in 2018 (Sales 2018) and total tons used in pigs, poultry and veal calves (Use 2018, incl. SDPs). Next to the tonnes used by each species the % this covers of the sales data (%sales) is shown.

* Use data include the single substance lincosamide-products but exclude combination products with lincomycin.

** Use data include pleuromutilins and all combination products that are not trim-sulfa or linco-spectino.

*** The sales data add the quantity of lincomycine used in combination products to the macrolides, whereas the quantity of spectinomycine in combination products is added to the aminosides.

d) Use of critical substances

A very small quantity of cephalosporins 3G/4G was used, and this was only in pigs (Figure 26). (Fluoro)quinolones were more used, especially in poultry (100% in broilers). As noted in the sales data, this was largely due to the use of flumequine, being the most used substance in pigs and veal as well.

Remarkably, almost a quarter of veal farms with notifications had at least one notification of fluoroquinolone use in 2018; for broilers this was 16% (Figure 26).

As noted in the sales data, usage data of fluroquinolones in broilers increased in 2018 compared to 2017 (data not shown). It also slightly increased in veal, while decreasing in pigs. While still a small amount of 3G/4G cephalosporins were used in veal in 2017, this decreased to zero in 2018 (data not shown).



Figure 26. Kg used of the 'red molecules' (fluoro)quinolones and 3G/4G cephalosporins in pigs, poultry and veal calves in 2018, and the % of farms with notifications that used these critical substances.

Colistin was used at least once in 2018 on more than 50% of veal farms with notifications (Figure 27). Also approx. one third of pig farms used colistin. Remarkably, of the pig farms using colistin in weaned piglets 32% also used ZnO in weaned piglets. Colistin use was lowest in poultry, with 94% of kg used being in laying hens.



Figure 27. Kg used of polymyxins (colistin) in in pigs, poultry and veal calves in 2018, and the % of farms with notifications that used colistin.

Although sales data show a decrease for colistin, usage increased for all three species (data not shown). Possibly, a stocking effect plays a role in this phenomenon.

e) Mg/kg per species in 2017 and 2018

To make a better comparison of usage in the different sectors the mg antibacterials used per species was standardised with the produced biomass per species. This was also calculated for 2017, to illustrate the evolution at sector level.

This shows a substantial different picture than when looking at tonnes alone. Veal calves appear by far the largest using sector, before pigs and poultry (Table 8). The mg/kg in pigs approximates the general sales result (108,5 mg/kg in 2017; 94,6 mg/kg in 2018) the most, which can be explained by the fact that pigs form the largest part of both the numerator and denominator in the sales data.

Remarkably, usage decreased substantially in pigs (-8,3% mg/kg) but increased substantially in both poultry (+13,8%) and veal calves (+17,6%). This is an encouraging result for the pig sector but quite a disappointing result for the poultry and veal sector. The fact that pigs have the biggest impact on the total AMU sales data largely explains the positive result for the latter.

		-				-				
		2017			2018		% difference 2018 – 2017			
	PIG	POULTRY	VEAL	PIG	POULTRY	VEAL	PIG	POULTRY	VEAL	
mg used (x 10 ⁹)	117,4	20,1	17,9 ¹	110,6	23,2	20,01	-5,8%	+15,4%	+11,7%	
Kg biomass (x 10 ³)	1 044 560	463 390	62 483	1 073 120	469 590	59 359	+2,7%	+1,3%	-5,0%	
mg/kg	112,4	43,4	287,0	103,1	49,4	337,7	-8,3%	+13,8%	+17,6%	

Table 8. Mg active substance^{*} / kg biomass used in 2017 and 2018 in pigs, poultry and veal calves.

* As the comparability of the SDP data for veal calves in 2017 and 2018 could not be guaranteed, they were excluded from the mg active substance calculations.

In the dose-based analysis below, the results are looked at in more detail for the different animal categories and in terms of treatment days (BD₁₀₀).

Dose-based analysis of antimicrobial use

a) Core reference population for benchmarking

After applying the quality control procedures, 3597 pig farms, 857 poultry farms and 195 veal calf farms were found eligible to be included in the 2017-2018 core reference populations for benchmarking. Table 12 shows the number of farms in the reference population of each animal category.

Table 12. Number of farms per animal category that were part of the 2017-2018 Sanitel-Med core reference populations for benchmarking.

		PIC	GS	POL	VEAL		
	Fatteners	Weaners	Sucklers	Sows/boars	Broilers	Laying hens	Veal calves
n farms	3355	1447	1452	1452	671	188	195

b) BD₁₀₀-distribution per animal category in the core reference population

i. Summary for 2018

Figure 28 represents the distributions of the BD₁₀₀ over the farms belonging to the core reference population for each animal category as a box-and-whisker-plot. This illustrates that usage is situated predominantly in three animal categories: weaners, veal calves and broilers. As expected from previous results (scientific papers as well as results from data collection systems in other countries, e.g. the Netherlands), the distributions are right-skewed, with a long tail towards the high-users end.



Figure 28. Box-plots representing the BD₁₀₀ distribution over all farms raising animals of the different categories. Outliers are not shown. The median values are provided next to the lines in the boxes, and the average values next to or above the crosses. SDPs were included in the calculation.

ii. Evolution 2017-2018 per animal category

The graphs below show for each animal category separately the distribution of the BD₁₀₀-values per farm in the core reference population for 2017 (blue) and 2018 (red), together with some important descriptive parameters of the distributions (Figure 29-35). It must be noted that the number of farms with zero use was not extrapolated for 2017, hence is based on 10 months data.

Fattening pigs: in 2018, on 50% of the farms a fattening pig was treated with antibacterial products for less than 2,84% of its time present, whereas on 10% of farms, a fattening pig is treated for more than 10,7% of its time present (Figure 29). The distribution shows usage decreased between 2018 and 2017, with 1,4% based on the median BD₁₀₀-value. The % decrease is slightly more pronounced towards the high-users. Total treatment days decreased with -4,4%.



Figure 29. Distribution of the BD₁₀₀-values per farm in the reference population for fattening pigs in 2017 (blue) and 2018 (red), descriptive parameters of this distribution and % difference (% diff) between 2018 and 2017.

<u>Weaned piglets:</u> in 2018, on 50% of farms a weaned piglet was treated with antibacterial products for less than 16,57% of its time present, whereas on 10% of farms, a weaned piglet was treated for more than 69% of its time present (Figure 30). The distribution shows usage also decreased between 2018 and 2017, with 6% based on the median BD₁₀₀-value. The % decrease was more pronounced towards the high-users. Total treatment days decreased with almost 11%.



Figure 30. Distribution of the BD₁₀₀-values per farm in the reference population for weaned piglets in 2017 (blue) and 2018 (red), descriptive parameters of this distribution and % difference (% diff) between 2018 and 2017.

<u>Suckling piglets:</u> in 2018, on 50% of farms a suckling piglet was treated with antibacterial products for less than 1,83% of its time present, whereas on 10% of farms, a suckling piglet is treated for more than 14,34% of its time present (Figure 31). The distribution shows usage decreased between 2018 and 2017. The decrease was most pronounced of all pig categories, with

a 18% decrease of the median BD_{100} -value. The % decrease was more pronounced towards the high-users, with the P90 dropping with almost 30%. Total treatment days decreased with more than a quarter.



Figure 31. Distribution of the month-average BD₁₀₀-values per farm in the reference population for suckling piglets in 2017 (blue) and 2018 (red), descriptive parameters of this distribution and % difference (% diff) between 2018 and 2017.

Breeding pigs: in 2018, on 50% of farms a sow/boar was treated with antibacterial products for less than 0,28% of its time present, whereas on 10% of farms, a sow/boar was treated for more than 2,12% of its time present (Figure 32). Again, less farms recorded zero use in 2018 than in 2017 but again the distribution parameters show usage decreased between 2018 and 2017, with 3,4% based on the median BD₁₀₀-value. Also here, the % decrease was more pronounced towards the high-users, with the P90 decreasing with 13,8%.



Figure 32. Distribution of the month-average BD₁₀₀-values per farm in the reference population for sows/boars in 2017 (blue) and 2018 (red), descriptive parameters of this distribution and % difference (% diff) between 2018 and 2017.

Broilers: in 2018, on 50% of farms a broiler is treated with antibacterial products for less than 5,35% of its time present, whereas on 10% of farms, a broiler is treated for more than 16,68% of its time present (Figure 33). Despite the fact that more farms recorded zero use in 2018 than in 2017 and the median BD_{100} -value decreased with 2%, the distribution still shows use increased between 2018 and 2017. The mean, P75 and P90 all increased, the P90 even with 12%, and also the total treatment days increased with 6,5%



Figure 33. Distribution of the month-average BD₁₀₀-values per farm in the reference population for broilers in 2017 (blue) and 2018 (red), descriptive parameters of this distribution and % difference (% diff) between 2018 and 2017.

Laying hens: Based on the Sanitel-Med core reference population, more than 50% of farms (between 65% and 70%, data not shown) do not treat laying hens with antibacterial products (Figure 34). Use in laying hens is generally very low and appeared to further decrease in 2018.



Figure 34. Distribution of the month-average BD₁₀₀-values per farm in the reference population for laying hens in 2017 (blue) and 2018 (red), descriptive parameters of this distribution and % difference (% diff) between 2018 and 2017.

<u>Veal calves</u>: veal calf farms have the highest basic level of antimicrobial use. There are almost no farms without use of antibacterial products, and in 2018 a veal calf was treated on 50% of farms for more than approx. 28% of its time present. On 10% of farms, a veal calf is treated for more than almost 50% of its time present (Figure 35). The distribution of the use over the farms slightly narrowed between 2017 and 2018, with a slight shift to the right, meaning usage in the core reference group generally increased.



Figure 35. Distribution of the month-average BD₁₀₀-values per farm¹ in the reference population for veal calves in 2017 (blue) and 2018 (red), descriptive parameters of this distribution and % difference (% diff) between 2018 and 2017. ¹ As the comparability of the SDP data for veal calves in 2017 and 2018 could not be guaranteed, they were excluded from the BD₁₀₀ calculations. As a consequence, the mean and median values for 2018 differ slightly from those shown in figure 28.

c) Antibacterial classes and AMCRA colour codes in 2018 and 2017 in the core reference population

Figure 36 shows, for the different animal species, the number of treatment days with the different antibacterial classes and the proportions this represent in the total treatment days per species.

In pigs, broad-spectrum penicillins are most frequently used, followed by tetracyclines, colistin, macrolides and trimethoprimsulphamide products. These five classes account for >90% of treatment days. Except for pleuromutilins, the number of treatment days decreased for all classes, resulting in a total decrease in treatment days in pigs of 12%.

Further analysis per pig category (data not shown) learns that more than 70% of all treatment days with broad-spectrum penicillins is in weaned piglets, while tetracyclines are more evenly distributed over weaners (approx. 50%) and fatteners (approx. 40%). More than 85% of treatment days with colistin is in weaners; weaners also have the highest % of treatment days with macrolides, although sucklers have an almost equal portion (approx. 40%). The only class not used most frequently in weaners (45%) are the trim-sulpha products, which have a slightly higher use in fatteners (46%).

In veal calves, not broad-spectrum penicillins but tetracyclines were the most used antibacterial class. Also macrolides were frequently used. These three classes accounted for more than 80% of treatment days. Number of treatment days increased for some antibacterial classes while it decreased for others.

In poultry, broad-spectrum penicillins appear to be by far the most applied antibacterial class, with tetracyclines and trimsulpha completing the top-three. Lincomycin-spectinomycin products are the fourth most frequently used. Treatment days increased for almost all classes, resulting in a total increase of 6% of treatment days.

As shown previously (Table 10), use of (fluoro)quinolones strongly increased in poultry in 2018, which is also visible in an increased number and proportion of treatment days (> 2% of treatment days in 2018).



Figure 36. Number of treatment days with the different antibacterial classes and percentage of the total number of treatment days per species in 2017 and 2018. Numbers/percentages not shown are classes where use was below 1% of treatment days in 2017 and 2018.

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 tenth time and describes the antibacterial use in animals in Belgium in 2018 and the evolution since 2011.

For the first time this report combines sales data (collected at the level of the wholesaler-distributors and the compound feed producers) and usage data (collected at herd level). This allows to dig deeper into AMU at species and herd level in Belgium.

As always, in the sales data, 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. Furthermore, we have to take into account that it is not 100% 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. However, also the contrary may happen, i.e. veterinarians from neighbouring countries using products in Belgium that are not included in the BelVet-SAC sales data. The usage data might help to shed some light on this. Indeed, cascade use ('import') is requested to be registered in Sanitel-Med as 'Self Defined Products' and in 2018 approx. one ton of SDPs (predominantly Neosol 100%) was registered. Still, sales data were 42,6 tons higher than usage data (not corrected for SDPs). As the usage data do not cover all animal species, most of this difference will be explained by usage in the non-included species, most importantly bovines but also companion animals, horses,... It can also not be excluded that some usage is not registered in Sanitel-Med for the currently obliged animal categories. The data-collection is still relatively new and it likely takes time to get all veterinarians involved, especially those who have small practices. Adequate sensibilisation and controls should therefore further ensure the completeness of the collected usage data.

With -12,8% mg antimicrobial/kg biomass in comparison to 2017, 2018 marks the largest reduction in total sales of antimicrobials for animals in Belgium since 2011. This obviously continues the decreasing trend of the previous years, resulting in a cumulative reduction of -35,4% since 2011. In contrast to 2016 and 2017, where the majority of the reduction in AMU was linked to a reduction in antimicrobial premixes, the reduction in 2018 is more balanced over a **reduction in pharmaceuticals (-13,2% mg/kg) and antibacterial premixes (-9,2% mg/kg).** It is speculated that the large reduction observed in 2018 might partly be due to the effect of extra stock (of pharmaceuticals) taken during 2017 by wholesalers-distributors and veterinarians in anticipation of the increase in the antimicrobial tax for Marketing Authorisation Holders, which became effective on the 1st of April 2018. This is supported by the usage data: when comparing the extrapolated total Sanitel-Med usage data for 2017 with the 2017 sales data, a difference of approx. 67 tonnes is observed, much higher than in 2018.

As expected from previous studies, from the biomass distribution and from the stratification exercises based on the species, the usage data now unambiguously confirm that the total AMU in animals is in large part determined by the pig sector and more specifically, by the fatteners and the weaners. Together, they accounted for 67% of tonnes used and 53% of tonnes sold in 2018. Broilers and veal calves accounted for 15% and 14% of tonnes used (approx. 11% of tonnes sold), respectively, and the remaining animal categories for only 4%.

Considering the large reduction observed in total AMU in 2018, it is not surprising that also in the **pig sector a substantial reduction of -8,3% mg/kg between 2017 and 2018** is observed. Translated to BD₁₀₀ in the core reference group this results in **decreases of the median BD₁₀₀ of -1,4% in fatteners, -6% in weaners, -18% in sucklers and -3% in pigs for breeding**. In 2018, on a majority of farms, fatteners were treated with antibacterials for less than 3% of their time, sucklers for less than 2% and pigs for breeding for less than 0,3%. These are encouraging results for the pig sector, which has already put a lot of efforts in reducing their antibacterial use before 2018, starting with a private data-collection system (AB Register) already in 2014 and having also bore the entire weight of the antibacterial premix reduction up to 2017. Yet, challenges remain: despite the achieved reductions, the weaners remain a problem, begin among the three highest using categories with a median BD₁₀₀ of 16,57. On 25% of farms, a weaner is treated for more than 38% of its time, and on 10% of farms even for more than 69% of its time. Also in the other pig categories, there is still a long tail towards the high-using farms, showing potential for further reductions. Being the sector with the largest portion of total AMU, it will be important that pigs sustain their efforts in the coming years, especially in weaners.

Even though broilers and veal calves account for a smaller part of the tonnes antibacterials used, the increase of respectively +13,8% mg/kg and +17,7% mg/kg for these sectors are quite disappointing results. The results for broilers might still appear rather modest, with a mg/kg result substantially below that of pigs and veal calves and a decrease of the median BD₁₀₀ with

2%, resulting in a broiler being treated for less than approx. 5% of its time on a majority of broiler farms. However, this must be interpreted with care: due to the enormous weight gain rate of broilers, the ESVAC standard weight used for the calculation of the BD₁₀₀ in broilers (1 kg) is relatively advantageous compared to the ESVAC standard weight used for veal calves (80 kg) and weaners (12 kg), in terms of the actual weight at the presumed time of treatment (most treatments occur in the first week). That there is a very high use in broilers at young age is reflected in the antimicrobial resistance levels in broilers, which are known from previous years to be highest of all species. **Together with the increase in use of fluoroquinolones in 2018**, **these should be alarming results for the poultry (broiler) sector, requiring urgent measures for reduction in the coming years.**

Veal calves, finally, are known to be a difficult sector in terms of AMU. This is confirmed by the baseline level of AMU, which is highest in veal calves compared to all other animal categories (median use of almost 28% of the time). Yet the fact that there is still a large variation between farms shows the big potential for reducing the use at the sector level. As for broilers, **the veal calf sector is urged to take measures to reverse the increasing trend in the coming years.**

When comparing the results achieved in 2018 with the three AMCRA 2020 reduction targets, the goal of reducing the overall AMU in animals with 50% by 2020 has not been achieved yet, however the objective becomes in range with still 14,6% to reduce over the next two years. It is anticipated that the herd level data-collection and benchmarking through the Sanitel-Med and AB register systems, in combination with multiple other initiatives such as herd health plans, continuous education, increased biosecurity,.... will provide invaluable support to achieve this goal. Indeed, while (a large) part of the pig sector has been receiving benchmarking reports since 2014, this only started in the course of 2018 for poultry and veal calves.

It is also very promising to see that in 2018, even after largely achieving the goal of reducing the use of **antibacterial premixes** with 50% by 2017, a further reduction in the use of antibacterial premixes is achieved, now already **resulting in a cumulative reduction of -69,6% in comparison to 2011**. This suggests that the downward trend is sustainable. 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. On top of these results, **the use of ZnO in therapeutic doses continues to decrease with another -21,3% in 2018**. As in previous years, this decrease is coinciding with a further decrease of the polymyxin use of -4,1% in 2018, resulting in a use of 1,56 mg/kg biomass. The European objective in this regard is to obtain an overall result of below 1 mg/kg biomass. The cumulative reduction in polymyxin use since 2011 is now -64,4%.

The details of the use of the different antibacterial classes show – as in previous years – that penicillins (33,0%) form the largest group of consumed antimicrobials, followed by tetracyclines (22,1%) and the sulphonamides (16,1%). For the majority of the antibacterial classes, a decrease in sales was observed in 2018, most pronounced for the cephalosporines of the 3° and 4° generation (-19,2%), but also very substantial for sulphonamides (-18,9%) and the tetracyclines (-13,4%). This year a remarkable increase of +109,5% is seen in the use of "others" which is the group of zinc bacitracin, rifaximin, metronidazole and tiamulin. This increase is almost entirely due to the increased use of tiamulin. This may be linked to an observed increase in dysentery infections in pigs for which tiamulin is often the only remaining therapeutic choice. The increased use of quinolones with 50% is worrisome. This increase is entirely due to an increase in the use of flumequine which is mainly applied in poultry. However, the usage data showed that fluoroquinolone usage also increased in veal calves. The fact that 25% of veal farms used fluoroquinolones in 2018 should likewise raise concern.

In regard to the different AMCRA colour classes, use of "yellow" (-12%) and "orange" (-14%) classes substantially reduced. Yet the use of the "red" products increased (+35%) after a very spectacular drop in 2016 and 2017. Although this (relatively high) proportional increase should be related to the currently low level of absolute use and did not put at risk the reduction target of -75% by 2020 (which was already achieved in 2017) it is an evolution that merits close surveillance. As noted above, this increase is entirely linked to the increased use in fluoroquinolones and more specifically the flumequine. It is anticipated that this will be a onetime event, having evaded from the results next year.

Comparing the Belgian sales data with the results of other European countries and especially our neighbouring countries clearly shows there is still a substantial gap to be bridged. Yet it should be taken into account that the European data (ESVAC) are published with a two year delay (latest EU data are from 2016) and therefore do not take into account the very substantial reductions achieved in 2017 and 2018 in Belgium.

When finally looking at the species not included in the Sanitel-Med usage data, the evolution in the use of intramammary products (cattle) is interesting. This use of intramammary products substantially decreased (-30,1%) between 2013 and 2015,

yet has gradually increased again in the last 3 years. This suggests that the data collection and benchmarking of AMU at herd level in dairy cattle may become very helpful. Also in antimicrobials only registered for use in dogs and cats a substantial increase in use (+12,0%) is observed in 2018. As we have no detailed data on the evolution of the population of dogs and cats in Belgium as well as on the prescription or usage habits of the companion animal veterinarians, it is difficult to speculate on the reasons for this increase.

CONCLUSION

This report shows quite promising results again with the achievement of two out of the three quantitative goals (use of premixes and use of critically important antimicrobials) already. 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. The pig sector is encouraged to sustain its efforts, while the broiler and veal calf sector are urged to increase their efforts.

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. We would like to thank Gudrun Sommereyns from the Belgian Centre for Pharmacotherapeutic

APPENDIX

APPENDIX A. ATC-VET CODES INCLUDED IN THE DIFFERENT CLASSES OF ANTIBACTERIAL PRODUCTS

Class of Antibacterials	ATCvet codes included							
	QJ01FF01							
	QJ01GB03; QJ01GB90							
	QS01AA11							
	QD06AX04							
Aminoglycosides	Q\$02AA14; Q\$02AA57							
Aminogrycosides	QG51AA04							
	QA07AA06							
	QJ51RG01							
	QJ51CE59							
	QJ01XX04							
	QJ01XX10							
Other	QJ01XQ01; QJ01XQ02							
other	QJ51XX01							
	QJ01RA04							
	QJ01DB01							
	QJ01DD90; QJ01DD91							
	QJ51DB01; QJ51DB04; QJ51DB90							
Cephalosporins	QJ01DE90							
cephalospornis	QJ51DE90							
	QG51AX02							
	QJ51DD12							
	QJ51RD01							
Amphenicols	QJ01BA90							
	QS01AA01							
	QJ01FA02; QJ01FA90; QJ01FA92; QJ01FA91; QJ01FA94; QJ01FA95							
Macrolides	QJ01FF02; QJ01FF52							
	QJ51RF03							
	QJ51FF90							
	QJ01CA01; QJ01CA04; QJ01CA51							
	QJ51RC26							
Penicillins	QJ01CR02							
	QJ51CF02							
	QJ01CE02; QJ01CE09; QJ01CE30; QJ01CE90							
	QJ51CA51							
Polymyxins	QJ01XB01							

	QA07AA10					
	Q\$02AA11					
Pyrimidines	QJ01EW10; QJ01EW13					
r yrinnancs	QJ01EA01					
Quinolones	QJ01MA90; QJ01MA92; QJ01MA93; QJ01MA94; QJ01MA95; QJ01MA96					
Quintiones	QJ01MB07					
Sulphonamides and trimethoprim	QJ01EW09; QJ01EW11; QJ01EW12					
Supronamides and trimethophin	QJ01EQ03					
tetracyclines	QJ01AA02; QJ01AA03; QJ01AA06					
icti acyclines	QD06AA02; QD06AA03					