

# Belgian Veterinary Surveillance of Antibacterial Consumption National consumption report 2021

Publication: 29 June 2022

## **SUMMARY**

This annual BelVet-SAC report is now published for the 13<sup>th</sup> time and describes the antimicrobial use (AMU) in animals in Belgium in 2021 and the evolution since 2011. For the fourth year this report combines sales data (collected at the level of the wholesalers-distributors and the compound feed producers) and usage data (collected at farm level). This allows to dig deeper into AMU at species and farm level in Belgium.

With a **consumption of 81,2 mg antimicrobial/kg biomass in 2021** a decrease of **-8,4** % in comparison to 2020 is observed. The decrease is seen in **pharmaceuticals (-7** % **mg/kg) and antibacterial premixes (-12,9** % **mg/kg).** After a year of standstill in 2020 this reduction connects again with the descending trend, observed between 2014 and 2019. Overall, a **cumulative reduction of -44,6** % **since 2011** is achieved.

In 2021, total sales data were 50,3 tonnes higher than total usage data notified in SANITEL-MED, which is a remarkable increase compared to 2020 (38,7 tonnes) and 2019 (34,6 tonnes). As the usage data do not cover all animal species, a big part of the difference is likely explained by usage in the non-included species or categories, most importantly bovines but also other poultry categories and companion animals, horses, rabbits, turkeys, ... However, non-compliance with the notification of use in the currently compulsory animal categories may also account for a difference between sales and use. Therefore the growing gap between the two data sources is worrisome and requires further follow up.

When looking at the **evolution in the number of treatment days (BD**<sub>100</sub>) **at the species level**, as calculated from the SANITEL-MED use data, a substantial decreased use is observed in all species. For **pigs a decrease of -15,3** % was registered, **for veal calves the decrease mounted to -19,4** % and for **poultry the largest decrease with -40,7** % **was observed**. These results are in line with the evolution in the sales data although the observed reductions in use are substantially higher. This is linked to the growing gap between sales and use data as described above.

The farm-level results per animal category in the pig sector show overall positive results. For the suckling piglets a median BD $_{100}$  of 1,73 is seen which is a decrease of -4,2% compared to 2020. In weaned piglets a median of 14,18 is obtained which is a decrease of -22,0% compared to 2020. Also in fatteners a decrease of -15,4% is observed (median BD $_{100}$  of 2,47 compared to 2,92 in 2020). In pigs for breeding the median BD $_{100}$  was 0,32 compared to 0,42 in 2020 which is a decrease of -23,3%. Although all these results are positive the obtained reductions are not yet sufficient for some farms. In 2023 the action values for BD $_{100}$  in piglets and fatteners will be adjusted downwards and with the current antibacterial use approximately 20% of the farms will end up in the red zone. Therefore immediate actions are needed especially in the highest using groups. In broilers, big improvements were made in 2021 with a reduction of the median BD $_{100}$  from 5,40 to 3,49 which is change of -35,3%. Moreover it is good to see that less than 1% of farms, using antibacterials in broilers, are currently above the current action BD $_{100}$ -value (= red zone) and only 3% are above the action BD $_{100}$ -value as foreseen to be implemented at the end of 2024. Likewise, 80% of farms, using antibacterials in broilers, are situated in the green zone. Also in laying hens the median BD $_{100}$  has decreased from 1,68 to 1,53 (reduction of -8,9%). Finally in veal calves, the median farm level BD $_{100}$  also reduced from 20,33 to 16,26 which corresponds to a reduction of -20,0%. However, still more than 10% farms, using antibacterials in veal calves, were in the red zone and 30% of farms would be red with the current results when the action BD $_{100}$ -value will be adjusted beginning of 2023.

In dairy cattle it is positive to observe that the average intramammary antimicrobial use per milk cow is decreasing for the second year in a row. Yet when zooming in a little more in detail it is remarkable to see that this decrease is mainly due to a decrease in use of antimicrobial applicators in lactating cows and not due to a decrease in dry cow applicators. In dogs and cats the volume of antibacterial products in 2021 has increased with +4,0 % in comparison to 2020. Compared to 2014 the total increase of sales of antibacterial substances solely authorised for use in dogs and cats is +28,0 %. With the absence of an accurate estimate of the evolution in the total dog and cat population (denominator) it remains difficult to interpret this evolution but it clearly does not offer a positive feeling. On the contrary, in 2021 the use of critical important antimicrobials (red molecules) in dogs and cats decreased spectacularly with -67 % (from 214 kg of active substance in 2020 to 71 kg in 2021). This is mainly due to a decreased use of enrofloxacin.

With regard to the general reduction target formulated by AMCRA (-50 % by 2020), despite the substantial reduction obtained in 2021, this goal has still not been fully achieved: a total reduction of -44,6 % compared to 2011 was obtained. On the other hand, the new decrease observed in the use of antibacterial premixes means the original reduction target (-50 %) was by far maintained. Furthermore, use of the "red" molecules, after the disappointing increase in 2020, decreased again very

substantially with -42,8 % in 2021. In comparison to 2011 (reference year) the reduction of red molecules in 2021 is -82,9 % which is largely below the reduction goal of -75 % by 2020.

With the start of 2021, a **renewed Covenant** between the sectors, AMCRA and competent authorities was signed. The new Covenant includes a **reduction goal of the total antibacterial use of up to -65% by 2024** compared to the reference year 2011. Achieving this will require continuous and additional efforts to be made. With regard to the additional reduction targets agreed to in the new Covenant, the 2021 results suggests these will likely be achieved, if the current efforts are maintained. Indeed, the **cumulative reduction of the use of antibacterial premixes of -74,2% in comparison to 2011 already almost equals the goal of -75% by 2024**. And as noted, with the achieved reduction in the use of red products, the -75% compared to 2011 is largely maintained. Finally, colistin use in 2021 landed at a level of 1,17 mg/kg biomass which approaches the goal of less than 1 mg/kg biomass set in the AMCRA 2024 goals. Only the goal of having maximum 1% of farms with alarm use remains a difficult challenge which will require a lot of work.

#### Conclusion

The 2021 antibacterial product sales and use data fortunately show that due to joint efforts, the results scrambled back up after the setback of 2020. It is clear that close surveillance and a joint effort from all stakeholders is mandatory to press on to achieve and maintain the reduction goals for 2024. Especially in view of the reduction paths, efforts are necessarily, if not urgently, required in order to decrease the number of red farms.

## **SAMENVATTING**

Dit 13<sup>de</sup> BelVet-SAC rapport beschrijft de resultaten van het antibioticumgebruik bij dieren in België in 2021 en de evolutie sinds 2011. Voor het vierde jaar op rij combineert het rapport zowel gegevens over de verkoop (verzameld ter hoogte van de groothandelaars-verdelers en mengvoederfabrikanten) als gegevens over gebruik (verzameld op het niveau van de veehouderij) wat toelaat om het gebruik meer in detail te bestuderen per diercategorie.

Met een **consumptie van 81,2 mg antibiotica/kg biomassa** werd in 2021 **een daling van -8,4** % opgetekend in vergelijking met 2020. Deze daling was verdeeld over de **'pharmaceuticals' (-7** % **mg/kg) en de antibacteriële premixen (-12,9** % **mg/kg).** Na een jaar van stilstand (2020) word met deze daling terug aangeknoopt met de dalende trend waargenomen tussen 2014 en 2019. De **cumulatieve reductie sinds 2011 bedraagt nu -44,6** %.

In 2021 was het verschil tussen het totale volume antibiotica in de verkoopgegevens en het volume van gebruiksgegevens geregistreerd via SANITEL-MED 50,3 ton wat aanzienlijk meer is dan in 2020 (38,7 ton) en 2019 (34,6 ton). Aangezien de gebruiksgegevens niet alle diersoorten omvatten kan een groot deel van dit verschil worden verklaard door het gebruik in de niet ingesloten diersoorten met in het bijzonder rund maar ook verschillende pluimvee categorieën, kleine huisdieren, paarden, konijnen, kalkoenen ... Maar ook het niet correct of volledig registreren van het gebruik bij de diersoorten waar het verplicht is om het gebruik te registreren kan aanleiding geven tot dit groeiende verschil. Deze toenemende trend is dan ook zorgwekkend en vergt een grondige opvolging.

Bekijken we de **evolutie** in het aantal behandeldagen (BD<sub>100</sub>) op het niveau van de diersoort, berekend uit de SANITEL-MED gebruiksgegevens, dan zien we een substantiële daling in alle opgevolgde diersoorten. Bij varkens bedroeg de daling -15,3 %, voor vleeskalveren was dat -19,4 % en voor pluimvee werd een daling van -40,7 % waargenomen. Deze resultaten zijn in lijn met de daling van de verkoopcijfers maar zijn wel meer uitgesproken wat mede een verklaring voor is voor de groeiende kloof tussen de verkoop- en gebruikscijfers.

Als we naar de resultaten op bedrijfsniveau per diercategorie kijken, uitgedrukt in de mediane BD100, zien we in de varkenssector een positieve trend in alle diercategorieën. Bij de zuigende biggen is de mediane BD<sub>100</sub> gedaald met -4,2 % ten opzichte van 2020 naar een niveau van 1,73. In de gespeende biggen is de mediane BD<sub>100</sub> nu 14,18 wat een daling van -22,0 % is. Ook in de vleesvarkens wordt een daling van -15,4 % vastgesteld (mediane BD<sub>100</sub> van 2,47 in vergelijking tot 2,92 in 2020). In de zeugen was de mediane BD<sub>100</sub> gelijk aan 0,32 in vergelijking met 0,42 in 2020 wat een daling van -23,3 % is. Ondanks deze positieve trends zijn de waargenomen reducties nog niet voldoende voor sommige bedrijven. In 2023 zal de actiewaarde voor de BD<sub>100</sub> in biggen en vleesvarkens verder verlaagd worden waardoor met het huidig antibioticagebruik ongeveer 20 % van de bedrijven in de rode zone zullen belanden. Als gevolg hiervan zijn er dringend acties nodig in de bedrijven met het grootste gebruik. In de vleeskippen zijn er grote verbeteringen gerealiseerd in 2021 met een reductie van de mediane BD<sub>100</sub> van 5,40 naar 3,49 wat een daling van -35,3 % betekend. Bovendien is het goed om zien dat minder dan 1 % van de bedrijven boven de huidige BD<sub>100</sub> actiewaarde zitten (= in de rode zone) en slechts 3 % boven de BD<sub>100</sub> actiewaarde zoals voorzien in 2024. Op dit moment zit reeds 80 % van de braadkippenbedrijven in de groene zone. Ook op de leghennenbedrijven is de BD<sub>100</sub> gedaald van 1,68 tot 1,53 wat een daling van -8,9 % inhoudt. Tenslotte is in de vleeskalveren de mediane  $BD_{100}$  gedaald van 20,33 tot 16,26 wat overeenkomt met een daling van 20 %. Maar hier zitten nog steeds 10 % van de bedrijven in de rode zone en zullen 30 % van de bedrijven in de rode zone zitten met de aangepaste actiewaardes die vanaf begin 2023 van kracht worden.

In de melkveehouderij is het positief om vast te stellen dat het gebruik van intramammaire producten voor het tweede jaar op rij daalt. Wanneer we wat meer inzoomen is het opmerkelijk om vast te stellen dat deze daling voornamelijk een gevolg is van een daling van het gebruik van uierpreparaten voor de behandeling van klinische mastitis en niet door een daling in het gebruik van droogzetpreparaten. In honden en katten is het gebruik van antibacteriële producten met +4,0 % gestegen in vergelijking met 2020. In vergelijking met 2014 is dit al een toename van +28,0 %. Door de afwezigheid van een goed zicht op de totale populatie honden en katten is het moeilijk om in te schatten of deze stijging een gevolg is van de toename van de populatie dan wel van het gebruik van antibiotica. Maar het is duidelijk geen positieve evolutie. Wat betreft het gebruik van de rode antibiotica in honden en katten is wel een spectaculaire daling van -67 % waarneembaar en dit voornamelijk door een daling in het gebruik van enrofloxacine.

Als we deze resultaten uitzetten tegenover de AMCRA 2020 reductiedoelstellingen dan zien we dat, ondanks de belangrijke daling van dit jaar, het doel van 50 % reductie van het totaal gebruik tegen 2020 nog steeds niet volledig werd gerealiseerd is. Op dit moment zitten we aan een daling van -44,6 %. Aan de andere kant is de nieuwe daling in het gebruik van

antibacteriële premixen wel ruim voldoende om de doelstelling van een daling van -50 % verder te bestendigen. Ook het gebruik van de "rode" moleculen is in 2021 sterk gedaald met -42,8 % in vergelijking met 2020. In vergelijking met het referentiejaar 2011 is de daling nu reeds -82,9 % wat ruimschoots het doel van -75 % overstijgt.

In 2021 werd een nieuw convenant ondertekend tussen alle betrokken sectoren, AMCRA en de bevoegde overheden. In dit convenant zijn nieuwe reductiedoelstellingen opgenomen waarbij wordt gestreefd naar een reductie van het totaal antibioticagebruik van -65 % in vergelijking met 2011. Om dit doel te bereiken zullen blijvende inspanningen noodzakelijk zijn. De andere doelstellingen die in het nieuwe convenant zijn afgesproken, -75 % reductie in gebruik van antibacteriële premixen tegen 2024 (nu al -74,2 %), het behouden van minimaal 75 % minder gebruik van rode producten en het reduceren van het colistinegebruik tot minder dan 1 mg/kg biomassa (nu nog 1,17 mg/kg) zijn binnen handbereik. Enkel de doelstelling om per diersoort maximaal 1 % van de bedrijven in de rode zone te hebben blijft een hele uitdaging waar nog hard zal aan gewerkt moeten worden.

#### Conclusie

De resultaten van de antibioticumverkoop en gebruiksdata in 2021 tonen gelukkig dat, als gevolg van gezamenlijke inspanningen, de resultaten terug in de positieve richting evolueren na de terugval in 2020. Het blijft evenwel duidelijk dat een goede opvolging en verdere acties in alle sectoren noodzakelijk blijven om de doelstellingen voor 2024 te realiseren. In het bijzonder zijn, met het oog op de reductiepaden, dringend bijkomende maatregelen noodzakelijk om het aantal bedrijven met een hoog gebruik te doen dalen.

# **RÉSUMÉ**

Ce 13e rapport BelVet-SAC décrit les résultats de l'utilisation des antibiotiques chez les animaux en Belgique en 2021 et l'évolution depuis 2011. Pour la quatrième année d'affilée, le rapport combine à la fois les données de vente (compilées au niveau des grossistes-répartiteurs et des fabricants d'aliments composés) et les données d'utilisation (compilées au niveau de l'élevage), ce qui permet d'étudier plus en détail l'utilisation par catégorie d'animaux.

Avec une consommation de 81,2 mg d'antibiotiques/kg de biomasse, on constate en 2021 une baisse de -8,4 % par rapport à 2020. Cette baisse s'observe au niveau des produits pharmaceutiques (-7 % mg/kg) et des prémélanges antibactériens (-12,9 % mg/kg). Après un an de statu quo (2020), on retrouve donc une tendance à la baisse observée entre 2014 et 2019. La réduction cumulative depuis 2011 est donc aujourd'hui de -44,6 %.

En 2021, la différence entre le volume total d'antibiotiques dans les données de vente et le volume des données d'utilisation enregistrées via SANITEL-MED était de 50,3 tonnes, soit une hausse significative par rapport à 2020 (38,7 tonnes) et 2019 (34,6 tonnes). Étant donné que les données d'utilisation n'incluent pas toutes les catégories d'animaux, cette différence peut en grande partie s'expliquer par l'utilisation dans les catégories d'animaux non incluses, notamment les bovins, mais aussi différentes espèces de volailles, les petits animaux domestiques, les chevaux, les lapins, les dindes... Mais cette différence croissante peut également s'expliquer par l'enregistrement incorrect ou incomplet de l'utilisation pour les catégories d'animaux soumises à l'obligation d'enregistrer l'utilisation. Cette tendance à la hausse est dès lors préoccupante et nécessite un suivi approfondi.

Si nous examinons l'évolution du nombre de jours de traitement (BD<sub>100</sub>) au niveau de l'espèce d'animaux, calculée à partir des données d'utilisation SANITEL-MED, nous observons une diminution substantielle dans toutes les catégories d'animaux suivies. En ce qui concerne les porcs, on observe une baisse de -15,3 %, tandis que pour les veaux de boucherie, la diminution est de -19,4 % et pour les volailles de -40,7 %. Ces résultats sont conformes à la baisse des chiffres de vente mais sont plus marqués, ce qui peut également expliquer le fossé croissant entre les données de vente et d'utilisation.

Si nous observons les résultats au niveau de l'exploitation par catégorie d'animaux, exprimés dans le BD<sub>100</sub> médian, nous constatons, pour le secteur porcin, une tendance positive dans toutes les catégories d'animaux. Concernant les porcelets allaités, le BD<sub>100</sub> médian a baissé de -4,2 % par rapport à 2020 pour atteindre 1,73. Chez les porcelets sevrés, le BD<sub>100</sub> médian est à présent de 14,18, soit une diminution de -22,0 %. Dans le secteur des porcs de boucherie aussi, on observe une baisse de -15,4 % (BD<sub>100</sub> médian de 2,47 par rapport à 2,92 en 2020). Chez les truies, le BD<sub>100</sub> médian était de 0,32 par rapport à 0,42 en 2020, soit une diminution de -23,3 %. Malgré ces tendances positives, les réductions observées ne sont pas encore suffisantes pour certaines exploitations. En 2023, la valeur d'action pour le BD100 chez les porcelets et les porcs à l'engraissement continuera de diminuer, si bien qu'avec l'utilisation actuelle des antibiotiques, quelque 20 % des exploitations se retrouveront en zone rouge. Il est par conséquent urgent d'agir dans les exploitations où l'usage des antibiotiques est le plus élevé. Dans le secteur des poulets de chair, des améliorations majeures ont été réalisées en 2021, avec un BD<sub>100</sub> médian passé de 5,40 à 3,49, soit une baisse de -35,3 %. En outre, on se réjouit de voir que moins d'1 % des exploitations se situe au-delà de la valeur d'action BD<sub>100</sub>actuelle (= zone rouge) et que seuls 3 % sont au-dessus de la valeur d'action BD<sub>100</sub> prévue en 2024. À l'heure actuelle, déjà 80 % des exploitations de poulets de chair sont en zone verte. Dans les exploitations de poules pondeuses, le BD100 a baissé de 1,68 à 1,53, soit une diminution de -8,9 %. Enfin, chez les veaux d'engraissement, le BD<sub>100</sub> médian est passé de 20,33 à 16,26, ce qui correspond à une baisse de 20,0 %. Ce secteur compte néanmoins toujours 10 % d'exploitations en zone rouge et ce pourcentage passera à 30 % suite aux valeurs d'action adaptées qui entreront en vigueur début 2023.

Dans les exploitations laitières, un élément positif que nous constatons est que l'usage de produits intramammaires est en diminution pour la deuxième année d'affilée. Si nous examinons les chiffres de plus près, nous pouvons remarquer que cette baisse s'explique principalement par une diminution de l'utilisation de préparations mammaires pour le traitement de la mastite clinique et non par une diminution de l'utilisation de préparations pour le tarissement. Chez les chiens et chats, l'utilisation de produits antibactériens a augmenté de +4,0 % par rapport à 2020. Par rapport à 2014, l'augmentation est de +28,0 %. En l'absence d'une bonne vue d'ensemble de la population totale des chiens et chats, il est difficile de juger si cette hausse est due à une augmentation de la population ou de l'utilisation des antibiotiques. Mais ce n'est manifestement pas une évolution positive. En ce qui concerne l'utilisation des antibiotiques rouges chez les chiens et chats, on peut observer une diminution spectaculaire de -67 %, ce principalement en raison d'une baisse de la consommation d'enrofloxacine.

Si nous comparons ces résultats aux objectifs de réduction de l'AMCRA 2020, on constate que, malgré la baisse importante de cette année, l'objectif d'une réduction de 50 % de la consommation totale d'ici 2020 n'a toujours pas été entièrement atteint. La réduction est à ce jour de -44,6 %. D'un autre côté, la nouvelle diminution de l'utilisation des prémélanges antibactériens est largement suffisante pour maintenir l'objectif de réduction de 50 %. Par ailleurs, l'utilisation des molécules « rouges » a connu une forte baisse en 2021 (-42,8 % par rapport à 2020). Comparée à l'année de référence 2011, la diminution est à présent de -82,9 %, dépassant ainsi largement l'objectif de -75 %.

En 2021, une nouvelle convention a été signée entre tous les secteurs concernés, l'AMCRA et les autorités compétentes. Cette convention contient de nouveaux objectifs visant à réduire la consommation totale d'antibiotiques de -65 % par rapport à 2011. Pour atteindre cet objectif, les efforts devront se poursuivre. Les autres objectifs convenus dans la nouvelle convention, à savoir une réduction de -75 % de l'utilisation des prémélanges antibactériens à l'horizon 2024 (-74,2 % actuellement), maintenir au moins 75 % d'utilisation en moins des antibiotiques rouges et la réduction de l'utilisation de la colistine à moins de 1 mg/kg de biomasse (1,17 mg/kg actuellement) sont à portée de main. Seul l'objectif d'avoir maximum 1 % d'exploitations en zone rouge par catégorie d'animaux reste un vrai défi qui nécessitera encore de nombreux efforts.

#### Conclusion

Les résultats des données sur les ventes et l'usage des antibiotiques en 2021 montrent heureusement que, grâce aux efforts conjugués de chacun, les résultats évoluent à nouveau dans un sens positif après la diminution en 2020. Il demeure toutefois évident qu'un bon suivi et de nouvelles actions restent indispensables dans tous les secteurs pour atteindre les objectifs de 2024. En particulier, compte tenu des trajectoires de réduction, des mesures supplémentaires sont nécessaires de toute urgence pour réduire le nombre d'exploitations à forte consommation 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.

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 twelfth BelVet-SAC report gives an overview of the consumption of antibacterial products in veterinary medicine in Belgium in 2021 and describes evolutions in use since 2011.

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Funded by: Federal Agency for Medicines and Health products

Suggested citation: Belgian veterinary surveillance on antimicrobial consumption report 2021 (BELVETSAC 2021). Brussels: Federal Agency For Medicines and Health Products.

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## **ANTIMICROBIAL SALES DATA**

## **Data collection**

#### a) Antibacterials for veterinary use

#### i. Antibacterial pharmaceuticals

Sales data of all veterinary medicinal products in all pharmaceutical formulations containing antibacterial active substances and authorized on the Belgian market were aggregated. These data were asked from the 21 wholesaler-distributors that are licensed and actively supply veterinarians and pharmacies in Belgium with veterinary medicines during the observation period. The wholesalers-distributors are obliged by law (article 12 sexies, Law on medicines 25<sup>th</sup> March 1964; Articles 221 and 228 Royal Decree 14<sup>th</sup> 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. December 2021 to upload the required data via a secured web-application (www.belvetsac.ugent.be). The required data consisted of all veterinary antibacterial products sold in the year 2021 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 veterinary medicinal products authorized and marketed on the Belgian market was provided, together with their market authorization holder and national code, pharmaceutical formulation and package form. The wholesaler-distributor only needed to provide the number of packages sold for each product for the given year.

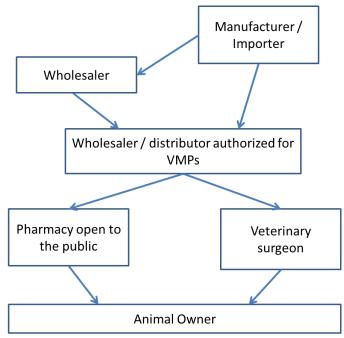


Figure 1. Distribution of veterinary medicinal products (VMPs) in Belgium.

# ii. Antibacterial premixes

As antibacterial premixes can be purchased by feed mills directly from the manufacturers or wholesalers (not necessarily through wholesaler-distributors) (fig. 2) data on medicated feed were collected separately. This was done by contacting all

Belgian compound feed producers that are licensed and active to produce medicated feed¹ (n=45). The feed mills were asked by letter dd. December 2021 to upload the required data, on legal basis of article 12 sexies Law on medicines 25<sup>th</sup> March 1964; Article 221 and 228 Royal Decree 14<sup>th</sup> December 2006 on medicines for human and veterinary use. This data on medicated feed delivered at Belgian farms in 2020 was also submitted via the secure web-application². Producers of medicated feed were asked to provide data on the use of antibacterial premixes as well as ZnO containing premixes for the year 2021. A list of authorised and marketed antibacterial premixes was provided. Antibacterial and ZnO premixes can only be incorporated into medicated feed on prescription of a veterinarian.

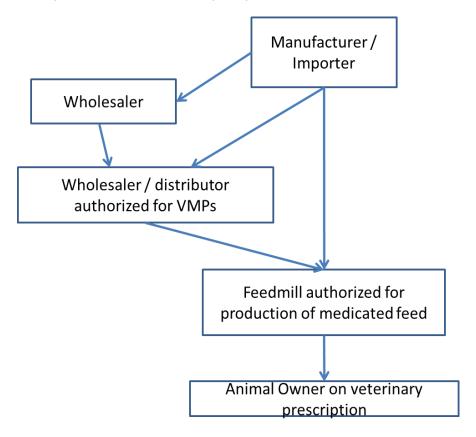


Figure 2. Distribution of veterinary premixes in Belgium.

# 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.

The BelVet-SAC data collection covers all veterinary antibacterial medicines (Table 1). No antibacterial products are excluded which is in contrast to the ESVAC reporting system where antibacterial products for dermatological use and for use in sensory organs are excluded. This explains why sales 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.

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<sup>&</sup>lt;sup>1</sup> http://www.favv-afsca.be/bo-documents/Inter R0-1002 3 dierlijke producten erkende bedrijven.PDF

<sup>&</sup>lt;sup>2</sup> www.BELVET-SAC.ugent.be

Table 1. Groups of antibacterial agents covered in the data collection and corresponding ATCvet codes.

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

## b) Animal population

Animal population data to calculate the produced biomass were derived from the Eurostat website<sup>3</sup>.

From these animal population data, the biomass (in kg) was calculated, according to Grave<sup>4</sup> et al., (2010), as the sum of the amount of meat from 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 (European Surveillance of Veterinary Antibacterial Consumption) recommendations. This additional information consisted of:

- the different antibacterial active 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 reporting

Through this extra information, the number of packages sold can be converted to the amount of active substance sold.

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.

<sup>&</sup>lt;sup>3</sup> http://ec.europa.eu/eurostat/data/database

<sup>&</sup>lt;sup>4</sup> 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

As in the previous reports (BELVET-SAC 2007-2019)<sup>5</sup>, yearly sales figures were put versus biomass as a yearly adjusted denominator according to the methodology described by Grave et al. (2010). The animal species included represent 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 products also covers the sales 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 industry<sup>6</sup>. 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.

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<sup>&</sup>lt;sup>5</sup> http://www.belvetsac.ugent.be/

<sup>&</sup>lt;sup>6</sup> www.bfa.be

#### ANTIBACTERIAL USE DATA

## **Data collection in Sanitel-Med**

## a) Notifications of antibacterial use at farm-level

Since 27 February 2017, veterinarians are legally obliged (Royal Decree of 02.07.2017 modifying Royal Decree 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 raising 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 of the legally obliged animal species that could be selected until 2021 are

```
    Pigs:

            sows (PIGB);
            gilts (PIGI);
            fattening pigs (PIGF);
            weaned piglets (PIGLW);
            suckling piglets (PIGLU)

    Poultry:

            broilers (BROIR);
            laying hens (LAYIH)

    Veal:

            Veal calves (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 code key. As for the antibacterial 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 (incl. quantities lower than 1). For premixes, either the number of packages or the kg premix needs to be registered and 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 14<sup>th</sup> 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(s) responsible for the completeness, correctness and timeliness of the registrations.

Reprising Figure 1 explaining the origin of the antibacterial 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 or more years, 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 'sales data' described previously.

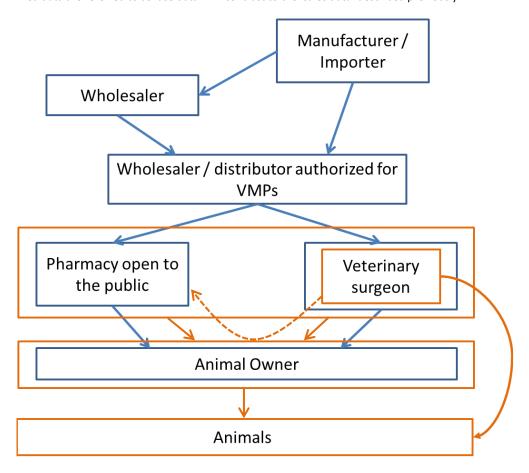


Figure 3. Origin of Sanitel-Med data concerning farm-level use of antibacterial pharmaceuticals. Veterinarians can directly administer antibacterials to the animals, deliver the antibacterials to the farmer after which the farmer administers them to the animals or prescribe the antibacterials which can then be bought in a pharmacy (dashed line) of from a feed mill (in case of premixes, not shown in the figure).

A 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).

# b) Number of animals present at farm level

The number of animals present at each farm is needed to calculate the animal mass 'at risk of treatment' at the farm (cfr. further, Calculation of the indicator  $BD_{100}$ ). The number is deduced from identification and registration data present in the

SANITEL<sup>7</sup> -database (owned and managed by the Federal Agency for the Safety of the Food Chain (FASFC)) or, specifically for poultry farms for the year 2018, from SANITEL-data combined with data from the yearly 'Biosecurity-survey' organized by the FASFC.

#### i. Veal calf farms

The average number of calves present at each farm is calculated per semester, as the average over the six corresponding monthly numbers of animals. From January 2018 till July 2019, the monthly number of animals was calculated as the average occupation number taking into account the number of arrivals, births, departures and deaths per month on the farm as notified in SANITEL. From August 2019 onwards, the monthly number of animals is calculated as the average of the number of calves notified as present in SANITEL each 1st, 11th and 21st day of each month and the 1st day of the subsequent month.

#### ii. Poultry farms

As of 2019, the SANITEL-capacity data of a poultry facility are calculated as the sum of the SANITEL-capacity data of the corresponding poultry sanitary units in that facility.

For 2018, preference was given to the yearly FAFSC 'Biosecurity-survey' capacity numbers above SANITEL-data. These are either a separate capacity for broilers and laying hens on a facility, a total capacity for broilers and laying hens on a facility, or a total capacity for either broilers or laying hens on a facility. If for a given facility 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.

# iii. Pig farms

The 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  $\# sucklers = \# sows \times 30/12$ . The number of gilts is added to the number of sows if these are present at the farm; if not, gilts are counted as fattening pigs. No separate antibacterial use analysis is done for gilts.

## 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, Quality control for defining the yearly reference populations for benchmarking). Being 'active' is encoded as a separate feature in SANITEL at sanitary unit level. A list of active farms is accessible to AMCRA as a report, based on a query developed and maintained by the FAMHP, that can be exported by AMCRA through a secured online business object tool provided by the FAFSC.

## d) Veterinary contract

A list with all agreement roles stopped, begun or active since 01/04/2017 between the so-called herd veterinarians and farms, containing the start and end dates of each agreement, is accessible to AMCRA as a report, based on a query developed and maintained by the FAMHP, that can be exported by AMCRA through a secured online business object tool provided by the FAFSC.

<sup>&</sup>lt;sup>7</sup> http://www.afsca.be/dierlijkeproductie/dieren/sanitel/

# **Data analysis**

The analysis of the Sanitel-Med data is split up into three parts:

- The first part focusses on the coverage of the antibacterial sales data by the Sanitel-Med use data; the latter concern only 'numerator data' (the quantities of antibacterials used); a denominator is not taken into account.
- The second part focusses on the evolution of the Sanitel-Med use data at the species-level, based on the number
  of treatment days calculated with a species-specific denominator.
- The third part focusses on the Sanitel-Med use data at the farm-level, based on the number of treatment days calculated with a farm-specific denominator.

For the first and second part of the analyses, the data were subjected to quality controls for possibly erroneous notifications (see further, Quality control for possibly erroneous notifications). Hence, the analyses include all numerator data (all notifications) submitted to Sanitel-Med, except those that were considered erroneous and have not been confirmed as being correct. For the third part, the data were additionally subjected to the farm-level quality controls for defining the reference populations for benchmarking (see further, Quality control for defining the yearly reference populations for benchmarking).

#### a) Determination of the numerator

#### i. Mg active substance used

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

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

For pharmaceuticals, 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 unit<sup>8</sup>. If the product contains more than one active substance, the calculation is done for each substance and the sum is made.

For premixes, if the number of packages or the kg medicated feed in combination with the parts-per-million is registered, these are first recalculated to the kg premix used. From the kg premix used, the active substance used is calculated by multiplying with the mg active substance per kg premix, taken from the SPC.

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, and recalculated to kg or tonnes used.

## ii. Number of DDDA<sub>bel</sub> used

The DDDA<sub>bel</sub> (the Defined Daily Dose Animal for Belgium) is the daily dose (in mg) per kg live bodyweight for products administered orally of through injection, and the daily dose (in mg) per animal for products administered locally or topically. This is calculated per notification using the formula

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

The DDDA<sub>bel</sub>-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 species<sup>9</sup>. The lists also contain the LA<sub>bel</sub> (Long-acting factor defined for Belgium) of each product. This LA<sub>bel</sub> factor corrects the longer duration of action of certain

<sup>&</sup>lt;sup>8</sup>https://www.amcra.be/swfiles/files/Principes%20voor%20bepalen%20van%20DDD-bel%20op%20productniveau(2) 109.pdf

<sup>9</sup> https://www.amcra.be/nl/analyse-antibioticagebruik/

products in the calculation of the BD<sub>100</sub> (cfr. further, Calculation of the indicator BD<sub>100</sub>). For not-long-acting products, the LA<sub>bel</sub> equals 1. The procedures for determining the DDD<sub>bel</sub> and LA<sub>bel</sub> values are also available on the AMCRA website  $^{10}$ .

#### b) Determination of the denominator

#### i. Animals and kg at risk per species at national level

The national number and kg animal at risk (for antibacterial treatment) per species is calculated from the yearly average number of animals present per animal category, consulted in the Statbel database <sup>10</sup>. The categories included from that database and the standard weights (source: EMA 2013 <sup>11</sup>) to calculate the corresponding kg at risk are shown below:

Piglets of <20 kg	12 kg	Laying hens	2 kg	Bovines < 1 year to be	80 kg
Pigs 20-50 kg + fatteners	50 kg	Broilers	1 kg	slaughtered as calves	
Breeding pigs >50 kg	220 kg				

#### ii. Kg at risk per animal category at farm level

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

kg animals at risk = number of animals  $\times$  estimated standard weight (kg) at treatment

The following estimated standard weights at treatment are used (source: EMA 2013 11):

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				

#### c) Indicators

#### i. Mg used

To make a comparison between the yearly antibacterial sales data, which include all animal species, and the Sanitel-Med use 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. BD100

To compare and follow up on the use 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:

$$\mathit{BD}_{100} = \left[ \left( ^{\#DDDA_{bel}} \middle/_{kg \ animals \ at \ risk} \times days \ at \ risk \right) \times \mathit{LA}_{bel} \right] \times 100$$

 $^{10}\,\underline{\text{https://statbel.fgov.be/nl/themas/landbouw-visserij/land-en-tuinbouwbedrijven\#figures}}$ 

https://www.ema.europa.eu/en/documents/scientific-guideline/revised-european-surveillance-veterinary-antimicrobial-consumption-esvac-reflection-paper-collecting\_en.pdf

To obtain a result per combination of farm and animal category, the  $BD_{100}$  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  $BD_{100}$  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  $BD_{100}$  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. further, Quality control for defining the yearly reference populations for benchmarking).

#### i. BD100-species

The  $BD_{100}$ -species is calculated with the  $BD_{100}$  formula but with numerator and denominator data at species level. It is per species the sum of:

- BD<sub>100</sub>-species<sub>mg/kg</sub>: in the numerator the total #DDDA<sub>bel</sub>\*LA<sub>bel</sub> used for products administered orally or through injection and in the denominator the animal weight (in kg) at risk.
- BD<sub>100</sub>-species<sub>mg/animal</sub>: in the numerator the total #DDDA<sub>bel</sub>\*LA<sub>bel</sub> used for products administered locally or topically and in the denominator the number of animals at risk.

# d) Antibacterial use by the contract veterinarian

The part of the antibacterial use (excl. ZnO) at farm level by the contract veterinarian was calculated by linking the responsible veterinarian for a use notification in Sanitel-Med to the veterinarian having a contract with the farm at the document date.

# **Quality control for possibly erroneous notifications**

The notified quantity of antibacterials is considered possibly erroneous in the following cases:

- Notifications for pigs:
  - The quantity is greater than one of a multi-package product for injection;
  - The quantity is greater than 100 of a product for injection;
  - $\circ$  The BD<sub>100</sub> calculated for a notification is higher than 350 for PIGF; higher than 1300 for PIGLW; higher than 100 for PIGB;
  - The premix ppm is unlikely low or high (based on the product-specific SPC's).
- Notifications for poultry:
  - The quantity is greater than 50;
  - The BD<sub>100</sub> calculated for a notification is higher than 500.
- Notifications for veal calves:
  - o The quantity is greater than one of a multi-package product for injection;
  - o The quantity is greater than 50 of a product for injection;
  - The BD<sub>100</sub> calculated for a notification is higher than 500.

# Quality control for defining the yearly reference populations for benchmarking

The yearly reference population for benchmarking is used to study the distribution of the  $BD_{100}$  in an animal category and its evolution over several years, and it is per animal category defined as the group of farms that, for the whole year under consideration

- were 'active' (see below, point a)
- had no 'errors' in their Sanitel-Med notifications (see below, point b)
- fulfilled the conditions with respect to 'minimum herd size and empty stables' (see below, points c and d).

In the reference populations, a further distinction is made between zero-use farms and use-farms (see below, point e).

# a) Active during the whole year

A farm is eligible for inclusion in the benchmarking reference population when it was encoded active during the whole year. For poultry farms, more specifically, at least one sanitary unit needed to have been active during the whole year for the facility to be included. 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 the year considered) or having a recent count date (i.e. count date in the year considered) but with all counts in that year equalling zero, were excluded. Veal calf farms encoded as 'active', yet not having any registration in Sanitel-Med and having zero animals in the year considered, were excluded.

## 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 erroneous (see higher, *Quality control for possibly erroneous notifications*).

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

Pig farms with recent count data equalling zero for two consecutive trimesters, poultry farms with facility capacities equalling zero at the start of two consecutive trimesters and veal calf farms with at least one semester without animals were excluded from the benchmarking reference population.

#### d) Minimum herd size requirements

For the data until 2020 included, a minimum herd size was 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 benchmarking reference population. Veal calf farms with animal numbers below the minimum for at least one semester were excluded from the reference population.

From 2021 onwards, these criteria were no longer taken into account to define the benchmarking populations.

# e) Zero-use and use farms

A zero-use farm is defined as a farm that has no notifications in Sanitel-Med in a given period. For pigs farms, this is at species level (no notifications in the period in all categories present at the farm). For farms with broilers, laying hens and veal calves, it is at animal category level (no notifications in the period in that category).

## **RESULTS**

#### ANTIBACTERIAL PRODUCTS SALES DATA

# Response rate and data validation

All of the 20 wholesaler-distributors, requested to deliver their sales data on veterinary antibacterial products sold in 2021, responded. One indicated to have stopped activities therefore data were collected from 19 wholesaler-distributors. Of the 44 contacted compound feed producers, licensed for the production of medicated feed, 33 indicated to have produced medicated feed and 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 %.

This year, the internal data validation step recognized three odd reports originating from wholesalers distributers. All of them were contacted to confirm / update the provided data. In one wholesaler-distributor there was indeed an internal mistake in the provided data and a new dataset was uploaded. For the two other wholesaler-distributors the change in sales volumes were due to changes in the market (stopping of the activities of one wholesaler-distributors in 2020 and one in 2021).

# 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 2012 according to the commented compendium of the Belgian Centre for Pharmacotherapeutic Information<sup>12</sup>.

Table 2. Armatorium of antibacterial products on the Belgian market from 2012 to 2021.

	2012	2013	2014	2015	2016	2017	2018	2019	2020	2021
Number of Antibacterial pharmaceuticals on the market	308	294	298	339	329	323	325	326	308	327
Number of Antibacterial premixes on the market	22	23	21	21	19	16	18	13	15	14
Total number of Antibacterial products on the market	330	317	319	360	348	339	343	339	323	341

The only new antibacterial products registered on the market in the last 9 years are products containing 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. It is remarkable to see that the number of registered products is increasing although the total sales volumes are decreasing.

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<sup>12</sup> www.bcfi-vet.be

# Animal biomass produced in Belgium

The produced biomass was calculated based on the Eurostat data for the years 2016-2021 as described above (Table 3).

Table 3. Animal biomass produced in Belgium from 2016 to 2021.

Animal biomass	2016	2017	2018	2019	2020	2021
Meat (tonnes)						
Pork	1 060 540	1 044 560	1 073 120	1 038 916	1 098 710	1 140 740
Beef	278 360	281 540	277 310	263 749	254 500	247 060
Poultry	461 250	463 390	469 590	447 786	448 970	455 120
Sheep/goat	3 020	3 230	3 090	3 010	2 830	3 050
Total biomass from meat production	1 803 170	1 792 720	1 823 110	1 753 487	1 805 010	1 845 970
Dairy cattle						
Dairy cattle (number)	529 780	519 160	529 250	537 960	541 090	537 250
Dairy cattle metabolic weight (tonnes)	264 890	259 580	264 625	268 980	270 545	268 625
Total biomass (tonnes)	2 068 060	2 052 300	2 087 735	2 022 450	2 075 555	2 114 595
Evolution since previous year	-2,09 %	-0,76 %	+ 1,73 %	-3,13 %	+2,63 %	+1,88 %

An **increase in biomass production of +1,88** % is observed between 2020 and 2021. Compared to the reference year 2011 an increase of + 3,6 % is observed in the total biomass production in Belgium mainly due to an increase in dairy cattle and broiler production.

# Total sales of antibacterial drugs for veterinary use in Belgium

The total sales of antibacterial products for veterinary use in Belgium is presented in Figure 4 in tonnes of active substance per year since 2011 (reference year for all reduction initiatives in Belgium). The total amount is subdivided into antibacterial compounds contained in pharmaceuticals (all pharmaceutical formulations except premixes) and antibacterial compounds contained in premixes incorporated into medicated feed intended to be used in Belgium.

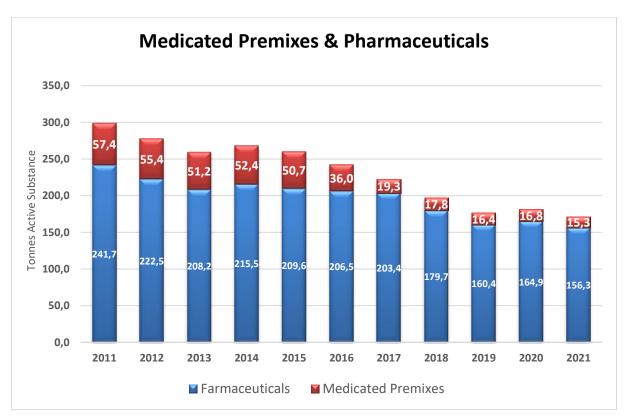


Figure 4. Total national sales of antibacterial compounds for veterinary use in Belgium for the years 2011-2021 (tonnes active substance).

Between 2020 and 2021, there was a **decrease of -5,6** % in the total sales of antibacterial products in veterinary medicine in Belgium (171 595,5kg in 2021 versus 181 749,6 kg in 2020). The use of antibacterial **pharmaceuticals decreased with -5,3** % between 2020 and 2021, and the use of **antibacterial premixes decreased with -8,9** %. After the small increase in 2020 we see again a decrease in the total sales numbers. **Since 2011 (reference year for reduction initiative) a decrease of -42,6** % **is realized in absolute volumes.** 

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

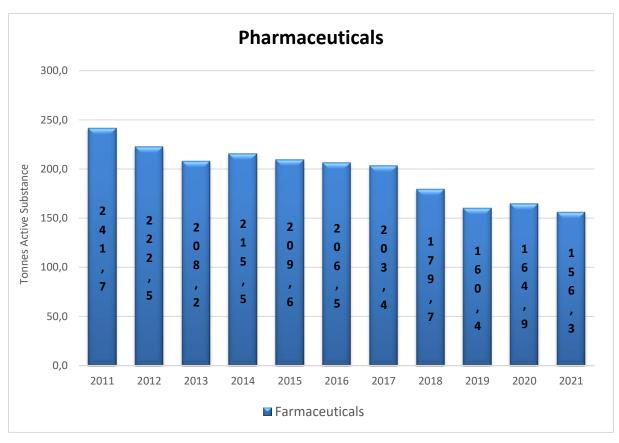


Figure 5. National sales of antibacterial pharmaceuticals for veterinary use in Belgium for the years 2011-2021 (tonnes active substance).

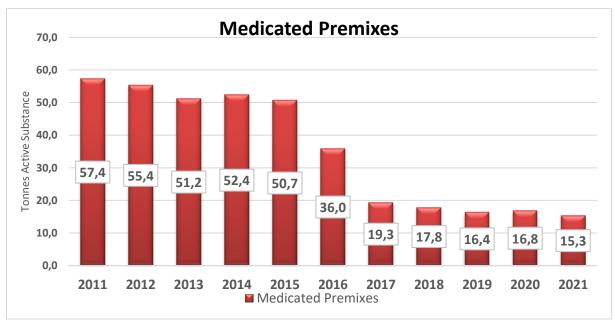


Figure 6. National consumption of antibacterial premixes in Belgium for the years 2011-2021 (tonnes active substance)

Since 2011 the data collection system allows to differentiate the animal species of destination for the antibacterial premixes. In 2021, 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 was allowed. After an increased use between 2013 (use during only one quarter) and 2015 a first decrease was observed in 2016 and continued since. In 2021 the use of ZnO was totally stopped as is presented in figure 7.

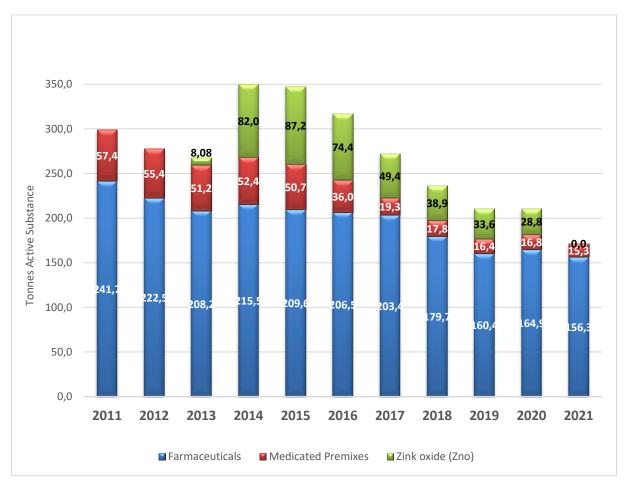
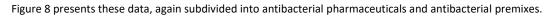


Figure 7. Total national sales of antibacterial compounds for veterinary use in Belgium plus the sales of ZnO for the years 2011-2021 (tonnes active substance).

# **Antibacterial sales versus biomass**

As described above, the total biomass production in 2021 in Belgium has increased with +1,9 % in comparison to 2020. As a consequence the decreasing trends in sales observed in absolute values (kg) is strengthened by the fact that this decreased volume of antibacterial products is used in an increased population. For 2020, the mg of active substance used in relation to a kg biomass produced was 88,6 mg/kg whereas in 2021 this is 81,2 mg/kg. This means a decrease of -8,4 % in comparison to 2020. Split up between the different pharmaceutical forms (premix vs other forms), a decrease of -7,0 % is observed in the antibacterial pharmaceuticals and -12,9 % in the antibacterial premixes.



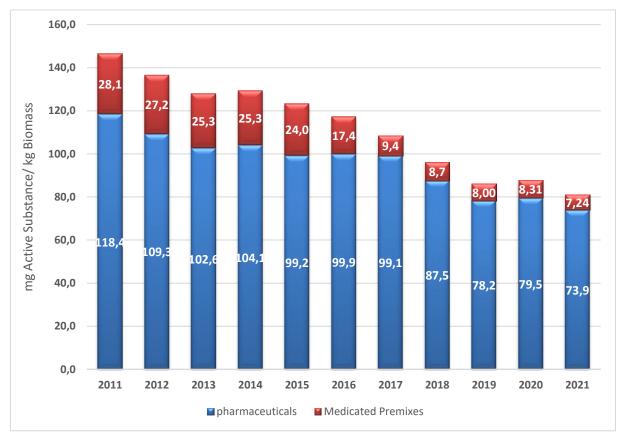


Figure 8. Total mg of active substance used per kg biomass produced in Belgium for 2011-2021.

With the **decrease of -8,4**% in the amount of antimicrobials used per kg biomass in 2021 the descending trend, observed between 2014 and 2019, is followed again. When using 2011 as a reference (see AMCRA 2020 objectives), **a cumulative reduction of -44,6**% **is achieved**, distributed in a reduction of -37,6% in antibacterial pharmaceuticals and -74,2% in antibacterial medicated premixes (Fig. 9).

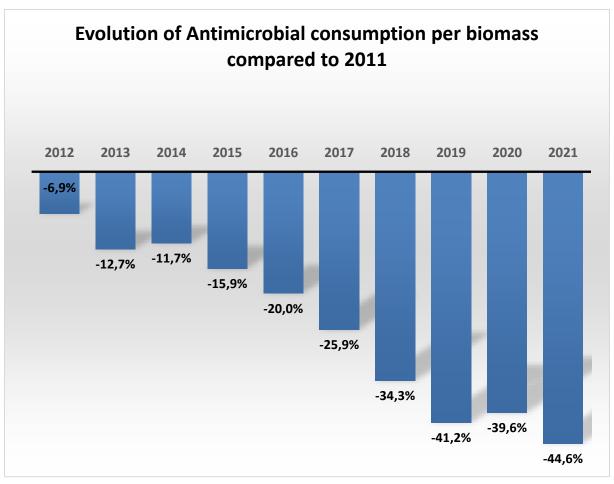


Figure 9. Evolution of antibacterial product sales per kg biomass produced in Belgium with 2011 as reference year.

# 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 sales 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 2021, the eleventh ESVAC report, presenting results on antibacterial usage in 31 EU/EEA countries up to the year 2020 was released<sup>13</sup>. In this report the **antibacterial consumption in animals up to 2020 is presented in relation to the animal production in the country.** 

In figure 10 the results of the 31 participating countries are presented in mg active substance sold 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.

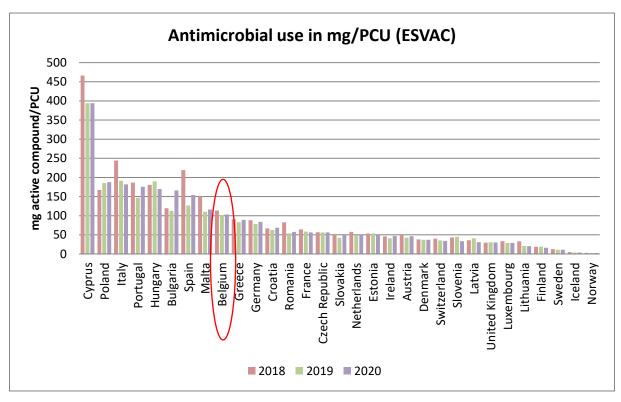


Figure 10. Overall sales of antibacterial compounds for food-producing species, including horses, in mg/PCU, per country between 2018-2020 (source: 10<sup>th</sup> and 11<sup>th</sup> ESVAC reports on Sales of veterinary Antibacterial agents).

When looking at figure 10, it can be observed that Belgium resides at the ninth position in terms of antibacterial usage expressed in mg/PCU in 2020. 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).

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https://www.ema.europa.eu/en/veterinary-regulatory/overview/antimicrobial-resistance/europeansurveillance-veterinary-antimicrobial-consumption-esvac#annual-report-on-sales-of-veterinary-antimicrobialmedicinal-products-section

It is remarkable to see that although the mean value of use in Europe has decreased from 109,5 mg/PCU in 2013 to 82,4 mg/PCU in 2020, the median value has only reduced from 66,0 mg/PCU to 51,9 mg/PCU indicating that the reduction is mainly achieved by a reduction in use by the highest users.

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 further reductions are required to achieve the same levels.

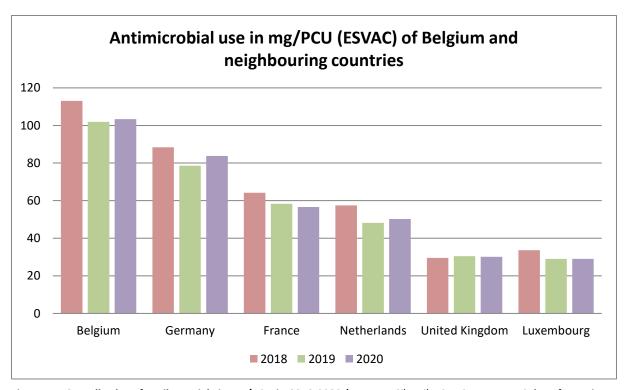


Figure 11. Overall sales of antibacterials in mg/PCU in 2018-2020 (source: 10<sup>th</sup>-11<sup>th</sup> ESVAC report on Sales of veterinary Antibacterial agents) for Belgium and neighbouring countries.

# Species specific antibacterial use

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

In 2021, antibacterial products authorised only for use in pigs are most used (32,8 %) followed by antibacterial products authorised for both pigs and cattle (23,5 %). The third most used antibacterial pharmaceuticals are the ones registered for pigs and poultry (17,2 %).

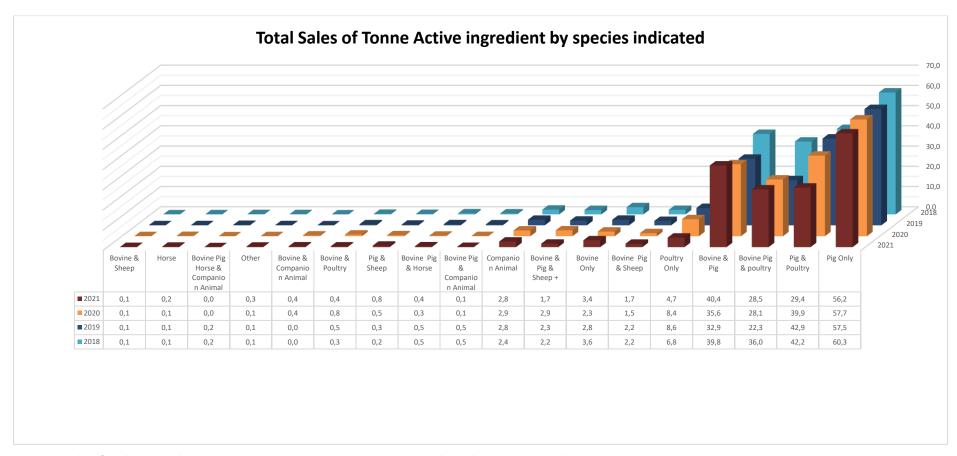


Figure 12. Sales of antibacterial pharmaceuticals and premixes per target species, evolution between 2018 and 2021.

# **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 sales of intramammary products

In Figure 13 an overview is given of the sales of intramammary products for prevention and treatment of udder infections in the last five years separated into the classes of active substances and related to the biomass of dairy cows present in that year.

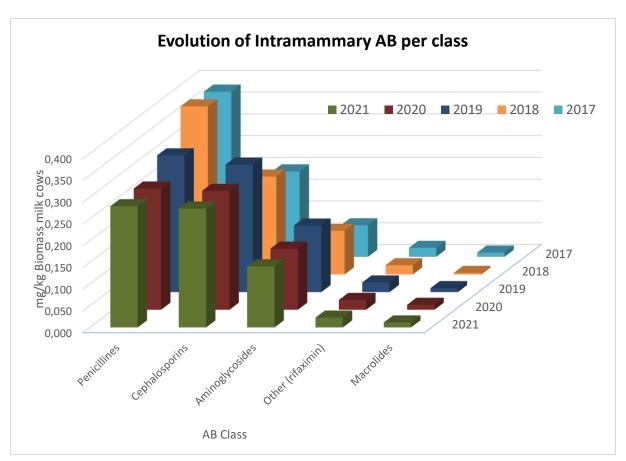


Figure 13. Evolution in sales of antibacterials for intramammary use between 2017 and 2021.

In Figure 14 the evolution in overall sales per kg biomass over the last five years of all products for intramammary use is presented.

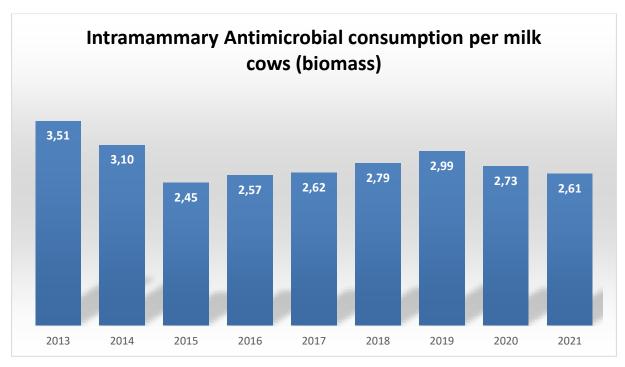


Figure 14. Evolution in sales of antibacterial products for intramammary use expressed in mg per kg biomass of dairy cattle between 2013 and 2021.

From the results of figure 14 it can be seen that the use of intramammary preparations was substantially reduced between 2013 and 2015 (-30 %), however since 2015 it has steadily increased again (+22 %) until 2019. Since 2020 a decrease is observed now for two years in a row.

# b) Number of DC and LC injector per dairy cow.

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

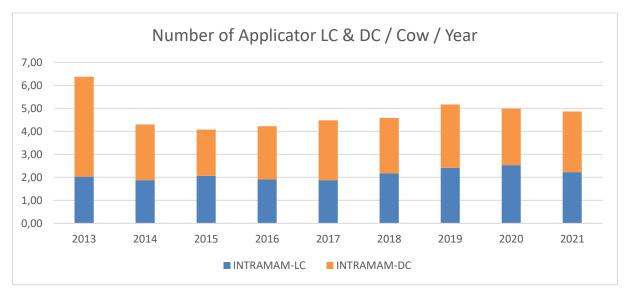


Figure 15. Evolution in use of number of intramammary preparations used per cow present over the last 9 years.

Also from the number of applicators used per cow per year a substantial reduction in sales of intramammary applicators was observed between 2013 and 2015 which is mainly due to a reduction of the sales of DC applicators. Between 2015 and 2019 a steady increase in the sales of DC applicators was observed. In 2020 a reduction in the sales of DC applicators was seen whereas in 2021 this increased again. The number of applicators sold for the treatment of mastitis cases showed a decrease in 2021 for the first time after 4 years of increase.

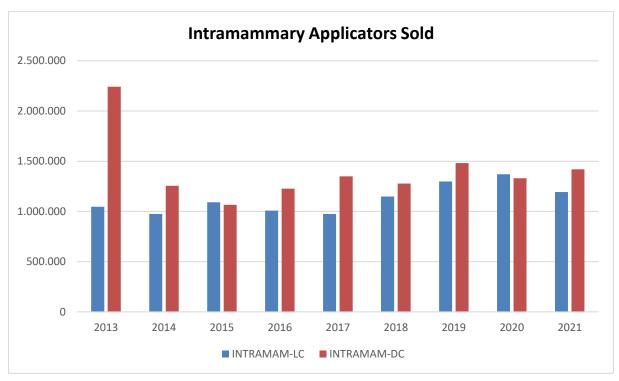


Figure 16. Number of intramammary preparations sold for dry cow therapy (DC) and treatments of lactating cows (LC) over the last 9 years.

# Antibacterial pharmaceuticals in dogs and cats

In 2021 2757,9 kg of active substance was sold as preparations that are solely authorised for use in dogs and cats, this is an increase of +4,0 % in comparison to 2020. Compared to 2014 the total increase of sales of antibacterial substances solely authorised for use in dogs and cats is + 28,0 %. It is noteworthy however 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.

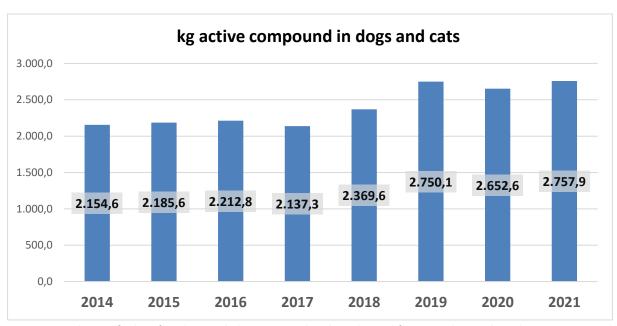


Figure 17. Evolution of sales of antibacterial pharmaceuticals only authorised for use in dogs and cats between 2014 and 2021.

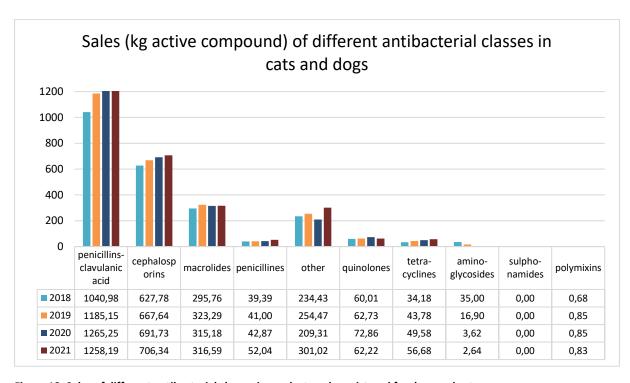


Figure 18. Sales of different antibacterial classes in products only registered for dogs and cats.

Penicillin/clavulanic acid is the most used antibacterial compound in dogs and cats, followed by cephalosporins of the 1° and 2° generation and macrolides. In the cephalosporins of the 1° and 2° generation a continued increase is observed since 2018

due to an increased use in cefalexin, a narrow spectrum cephalosporin. The increased use in "others" is due to an increase in use of metronidazole, administered in combination with spiramycin.

# Antibacterial sales per class of antibacterial compound

# a) Total sales (antibacterial pharmaceuticals and premixes)

In Figure 19 and table 4 the total sales of antibacterial active substances per class (ATC level 3 or 4) is presented.

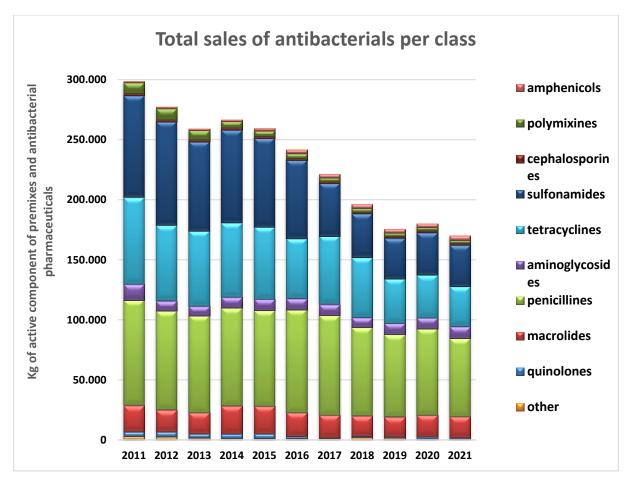


Figure 19. Total sales of antibacterial active substances per class from 2011 to 2021.

In 2021, the most sold group of antibacterial compounds remained the penicillins (65,3 tonnes; 38,1 %). The sulphonamides and trimethoprim (34,6 tonnes; 20,2 %) are the second most sold group closely followed by the tetracyclines (33,5 tonnes; 19,5 %)

In table 4, the evolution of the sold products per antimicrobial class in mg/kg biomass in the last 5 years is presented.

Table 4. The evolution of sales (mg/kg biomass) per antibacterial class since 2015.

Class AB Mg/kg biomass	2016	2017	2018	2019	2020	2021	'16 » '17	'17 » '18	'18 » '19	'19 » '20	'20 » '21	2021 %
Penicillins & clavulanic acid	42,03	40,96	35,78	34,63	35,37	31,59	-2,6 %	-12,6 %	-3,2 %	2,1 %	-10,7 %	38,93
Sulphonamids & Trimethoprim	31,64	21,56	17,49	16,69	17,06	16,36	-31,8 %	-18,9 %	-4,5 %	2,2 %	-4,1 %	20,16
Tetracyclines	24,16	27,66	23,96	18,35	17,26	15,83	14,4 %	-13,3 %	-23,4 %	-5,9 %	-8,3 %	19,51
Macrolides	9,57	9,18	8,12	8,09	8,75	8,36	-4,0 %	-11,5 %	-0,4 %	8,1 %	-4,4 %	10,31
Polymixins	2,03	1,76	1,69	1,50	1,33	1,17	-13,3 %	-4,1 %	-11,2 %	-11,3 %	-12,3 %	1,44
Aminosides	4,48	4,49	3,93	4,71	4,41	4,65	0,3 %	-12,6 %	20,0 %	-6,5 %	5,5 %	5,74
Quinolones	0,82	0,29	0,44	0,48	0,66	0,36	-64,2 %	50,0 %	10,0 %	36,2 %	-45,9 %	0,44
Other**	0,55	0,50	1,05	0,82	0,47	0,37	-9,4 %	109,5 %	-21,4 %	-42,7 %	-22,1 %	0,45
Phenicols	1,46	1,50	1,59	1,56	1,57	1,81	3,0 %	6,1 %	-1,8 %	0,3 %	15,4 %	2,23
Cephalosporins 1° & 2° G	0,44	0,41	0,37	0,52	0,62	0,60	-6,7 %	-7,8 %	38,1 %	19,8 %	-3,9 %	0,73
Cephalosporins 3° & 4° G	0,25	0,09	0,07	0,07	0,07	0,06	-65,9 %	-19,2 %	-2,6 %	2,3 %	-13,3 %	0,07
Total mg/kg biomass	117,43	108,40	94,50	87,43	88,56	81,15	-7,69 %	-12,83 %	-7,48 %	1,29 %	-8,37 %	100
Total biomass (cfr. Grave et al., 2010)*	2.065.040	2.052.300	2.087.735	2.022.450	2.075.555	2.114.595	-0,62 %	1,73 %	-3,13 %	2,63 %	1,88 %	

<sup>\*</sup> 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

<sup>\*\*</sup> zinc bacitracin, rifaximin, metronidazole, tiamulin

In 2021, the sale of almost all different antimicrobial groups, including the 3 main compounds (penicillins, sulphonamides and tetracyclines) decreased. The only two groups that increased are the phenicols and the aminosides. After the disappointing small increase in use of cephalosporins of the  $3^{\circ}$  and  $4^{\circ}$  generation in 2020 again an important decrease (-13,3%) is observed this year. The same is observed for the use of quinolones where a spectacular decrease of -45,9% is seen in 2021. The decrease in 2021 is largely due to the reduced used of flumequine (which is mainly applied in poultry) completed by a moderate decrease in the use of enrofloxacin and marbofloxacin (table 5).

The use of polymyxins (almost entirely colistin sulphate) continues to decrease in 2021 with another -12,3 %. This is a positive trend given the simultaneous phasing out of ZnO as an alternative for colistin in the treatment of post-weaning diarrhoea in piglets. When comparing to 2012 (before authorization of ZnO products), polymyxin use has dropped with -75.4 %.

AMCRA (centre of expertise on AntiMicrobial Consumption and Resistance in Animals)<sup>14</sup> 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 make a differentiation in terms of their importance for human and animal health. The ranking of importance is based on the WHO list on antibacterial compounds with importance for human health<sup>15</sup> and the lists produced by the World Animal Health Organization (OIE) indicating the importance of antibacterial substances for veterinary health<sup>16</sup>. When creating 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, polymyxins, aminoglycosides, tetracyclines and 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 conditions. This group contains the cephalosporins of the 3<sup>rd</sup> and 4<sup>th</sup> generation and the quinolones.

In figure 20, the evolution of use of the different colour groups of antibacterial substances over the last 5 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 2021, the use of yellow molecules decreased with -4,0 %. The use of orange molecules also reduced substantially with -8,2 %. The use of the red molecules, after the disappointing increase in 2020, decreased again very substantially with -42,8 %. In comparison to 2011 (reference year) the reduction of red molecules in 2021 is -82,9 % which is largely below the reduction goal of minus 75 % by 2020 and 2024.

<sup>&</sup>lt;sup>14</sup> www.amcra.be

<sup>&</sup>lt;sup>15</sup> http://apps.who.int/iris/bitstream/10665/77376/1/9789241504485 eng.pdf

<sup>&</sup>lt;sup>16</sup> http://web.oie.int/downld/Antibacterials/OIE list Antibacterials.pdf

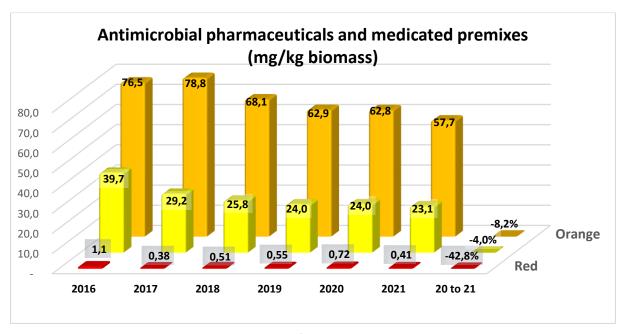


Figure 20: Evolution in the antibacterial consumption (mg/kg) per AMCRA colour code between 2016 and 2021.

A similar graph with products exclusively authorised for dogs and cats (Fig. 20) shows a small decrease in use of orange products and an increase in use of yellow products. The use of red molecules decreased very substantially in 2021 (-67 %) and this is mainly due to a decreased use of enrofloxacin.

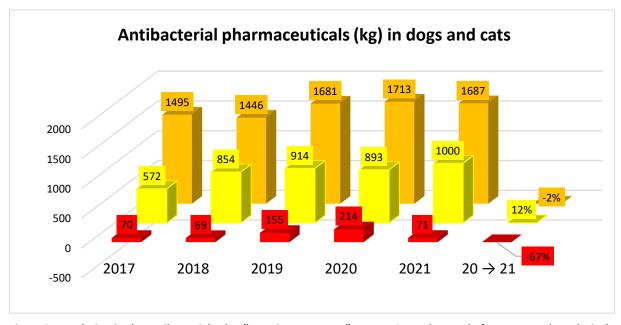


Figure 21: Evolution in the antibacterial sales (kg active compound) per AMCRA colour code for compounds exclusively authorised for use in dogs and cats between 2017 and 2021.

# b) Antibacterial pharmaceuticals

In Figure 22 the sales of antibacterial compounds per class (ATC level 3 or 4) is presented for the pharmaceuticals.

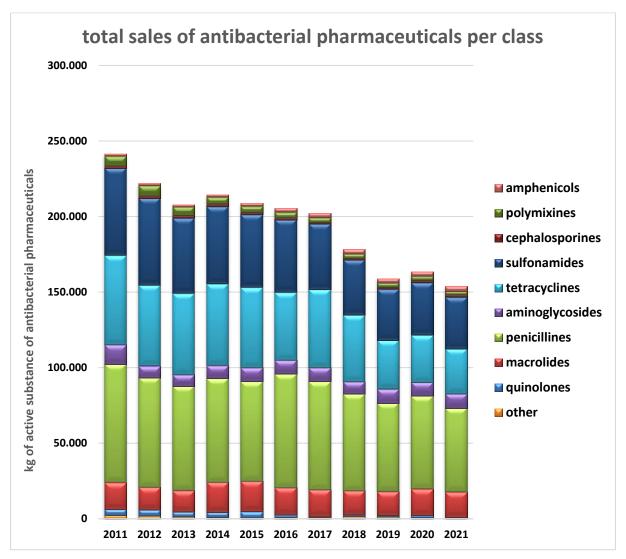


Figure 22. Sales of antibacterial pharmaceuticals per class of antibacterial compounds between 2011 and 2021.

# c) Antibacterial premixes

In Figure 23 the sales of antibacterial compounds per class (ATC level 3 or 4) is presented for the antibacterial premixes.

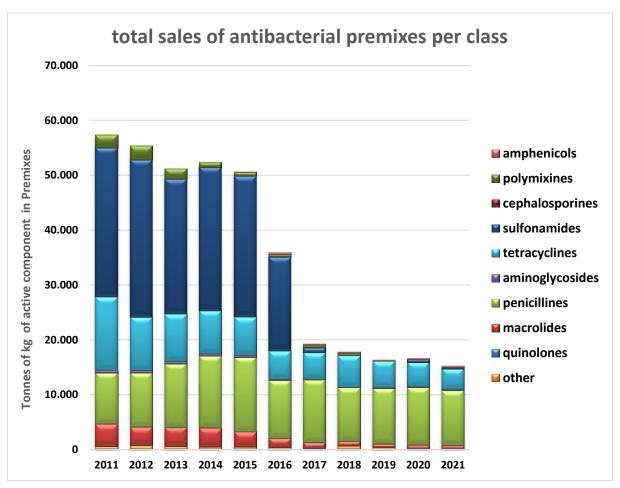


Figure 23. Sales of antibacterial premixes per class of antibacterial compounds between 2011 and 2021.

# Sales per antibacterial active substance

Table 5 gives the amounts sold per individual active substance, grouped per antibacterial class.

Table 5. Sales per antibacterial active substance.

		Total Kg				Antib	acterial pha	rmaceutica	ls (kg)	Antibacterial premixes (kg)			
Class	Antibacterial compound	2018	2019	2020	2021	2018	2019	2020	2021	2018	2019	2020	2021
cephalosporins 1G	<mark>cefalexin</mark>	720,2	993,2	1.239,4	1.193,3	720,2	993,2	1.239,4	1.193,3				
cephalosporins 1G	<mark>cefalonium</mark>	9,3	8,7	10,8	8,9	9,3	8,7	10,8	8,9				
cephalosporins 1G	<mark>cefapirin</mark>	45,3	41,3	28,3	48,5	45,3	41,3	28,3	48,5				
cephalosporins 1G	<mark>cefazolin</mark>	7,3	3,2	7,7	8,3	7,3	3,2	7,7	8,3				
fenicols	<u>chlooramphenicol</u>	-	-	-	-	-	-	-	-				
fenicols	Florphenicol	3.320,7	3.159,5	3.253,1	3.823,6	3.041,5	2.916,5	2.984,2	3.521,6	279,20	243,00	268,92	302,00
other	metronidazol	234,4	254,5	218,1	301,0	234,4	254,5	218,1	301,0				
other	tiamulin	1.901,6	1.362,2	706,2	408,2	1.236,0	1.007,8	565,0	314,2	665,60	354,40	141,13	94,00
other	valnemulin	-	-	-	-	-	-	-	-	-	-		
other	zinc bacitracin	28,2	25,4	32,1	46,1	28,2	25,4	32,1	46,1				
penicillines	<mark>cloxacillin</mark>	257,2	183,8	151,1	116,7	257,2	183,8	151,1	116,7				
penicillines	Phenoxymethylpenicillin	1.078,4	1.424,4	1.512,4	520,7	1.078,4	1.424,4	1.512,4	520,7				
penicillines	Nafcillin	6,0	7,3	8,9	8,6	6,0	7,3	8,9	8,6				
penicillines	Benethamine penicillin	38,2	58,6	63,8	79,7	38,2	58,6	63,8	79,7				
penicillines	penethamate	202,0	198,6	175,4	147,1	202,0	198,6	175,4	147,1				
penicillines	procaine benzylpenicillin	9.583,8	7.013,7	7.050,7	7.483,5	9.583,8	7.013,7	7.050,7	7.483,5				
sulphonamides	sulphachloropyridazine sodium	1.050,7	458,5	775,1	215,0	1.050,7	458,5	775,1	215,0				
sulphonamides	sulphadiazine	27.303,7	25.602,3	26.647,7	25.115,9	27.266,8	25.602,3	26.113,0	24.895,0	36,88	-	534,69	220,94

sulphonamides	sulphadimethoxine sodium	37,7	32,0	3,4	0,1	37,7	32,0	3,4	0,1				
sulphonamides	sulphadimidine sodium	-	-	-	-	-	-	-	-				
sulphonamides	sulphadoxine	1.238,4	816,4	935,8	1.104,8	1.238,4	816,4	935,8	1.104,8				
sulphonamides	sulphamethoxazole	792,6	1.222,8	1.141,6	2.379,7	792,6	1.222,8	1.141,6	2.379,7				
sulphonamides	sulphanilamide	-	-	-	-	-	-	-	-				
sulphonamides	trimethoprim	6.092,7	5.632,4	5.902,7	5.771,2	6.085,3	5.632,4	5.795,8	5.727,0	7,38	-	106,94	44,19
amino(glyco)sides	apramycin	34,0	102,1	372,6	1.026,5	0,2	-	296,1	787,3	33,80	102,05	76,47	239,13
amino(glyco)sides	dihydrostreptomycine	6,0	8,5	9,3	13,9	6,0	8,5	9,3	13,9				
amino(glyco)sides	gentamicin	172,9	170,7	188,9	189,0	172,9	170,7	188,9	189,0				
amino(glyco)sides	kanamycin	53,2	102,0	83,8	67,1	53,2	102,0	83,8	67,1				
amino(glyco)sides	neomycin	47,7	34,0	23,1	32,6	47,7	34,0	23,1	32,6				
amino(glyco)sides	paromomycin	2.510,2	2.502,5	2.401,4	2.570,7	2.510,2	2.502,5	2.401,4	2.570,7				
amino(glyco)sides	spectinomycin	5.361,0	6.589,9	6.047,6	5.909,8	5.356,6	6.589,3	6.046,5	5.909,8	4,40	0,55	1,09	-
amino(glyco)sides	Framycetin sulphate	17,8	24,3	26,4	33,2	17,8	24,3	26,4	33,2				
macrolides	clindamycin	135,8	136,3	149,5	147,0	135,8	136,3	149,5	147,0				
Macrolides	erythromycin	-	-	-	-	-	-	-	-				
Macrolides	gamithromycin	39,3	36,7	16,2	14,3	39,3	36,7	16,2	14,3				
Macrolides	lincomycin	4.378,7	5.066,7	4.659,0	3.867,9	4.374,3	5.066,2	4.657,9	3.867,9	4,40	0,55	1,09	-
Macrolides	pirlimycin	-	-	-	-	-	-	-	-				
Macrolides	spiramycin	160,0	187,0	165,9	169,6	160,0	187,0	165,9	169,6				
Macrolides	tilmicosin	2.824,7	2.918,8	3.258,1	2.383,2	2.113,7	2.372,8	2.659,7	1.902,6	711,00	546,00	598,45	480,60
Macrolides	tulathromycin	128,1	119,5	114,6	146,0	128,1	119,5	114,6	146,0				
Macrolides	tylosin	9.181,1	7.808,5	9.750,6	10.934,3	9.040,3	7.674,8	9.664,9	10.759,3	140,85	133,75	85,68	175,00
Macrolides	tildipirosin	49,2	47,2	37,3	20,6	49,2	47,2	37,3	20,6				
Macrolides	tylvalosin	60,5	39,2	3,3	0,3	46,2	37,5	-	-	14,37	1,70	3,32	0,34

other	rifaximin	21,3	22,3	22,6	21,2	21,3	22,3	22,6	21,2				
penicillines	amoxicillin	63.182,0	60.560,0	63.913,0	57.935,0	53.406,1	50.419,1	53.430,0	47.928,0	9.775,90	10.140,83	10.482,96	10.007,05
penicillines	Amoxicillin-clavulanic acid	230,0	279,3	280,5	296,4	230,0	279,3	280,5	296,4				
penicillines	Ampicillin	356,3	312,0	262,5	213,2	356,3	312,0	262,5	213,2				
polymyxins	Colistin sulphate	3.524,9	3.033,4	2.761,1	2.466,8	3.134,9	2.961,9	2.754,9	2.466,8	390,00	71,54	6,17	-
polymyxins	Polymyxin B sulphate	0,7	1,0	1,0	0,8	0,7	1,0	1,0	0,8				
tetracyclines	chlortetracycline	738,5	634,8	686,5	610,1	738,5	634,8	686,5	610,1	-	-		
tetracyclines	doxycyclin	39.843,2	30.687,1	27.830,0	26.707,7	34.070,8	25.872,1	23.321,6	22.957,7	5.772,35	4.815,00	4.508,47	3.750,00
tetracyclines	oxytetracycline	9.448,8	5.786,7	7.316,8	6.161,1	9.444,8	5.786,7	7.316,8	6.161,1	4,00	-	-	
cephalosporins 3G	cefoperazon	5,4	4,2	3,6	3,5	5,4	4,2	3,6	3,5				
cephalosporins 3G	cefovecin	9,1	9,4	9,8	9,0	9,1	9,4	9,8	9,0				
cephalosporins 3G	cefquinome	75,6	75,3	85,3	78,1	75,6	75,3	85,3	78,1				
cephalosporins 4G	ceftiofur	53,3	46,4	43,4	34,9	53,3	46,4	43,4	34,9				
(fluoro)quinolones	danofloxacin	8,4	6,5	7,3	5,8	8,4	6,5	7,3	5,8				
(fluoro)quinolones	difloxacin	0,0	0,0	0,0	0,0	0,0	0,0	0,0	0,0				
(fluoro)quinolones	enrofloxacin	305,4	375,7	421,4	294,6	305,4	375,7	421,4	294,6				
(fluoro)quinolones	flumequin	519,5	516,5	845,0	375,5	519,5	516,5	845,0	375,5				
(fluoro)quinolones	ibafloxacin	-	-	-	-	-	-	-	-				
(fluoro)quinolones	marbofloxacin	75,3	70,2	81,6	70,4	75,3	70,2	81,6	70,4				
(fluoro)quinolones	orbifloxacin	2,9	3,2	3,9	3,3	2,9	3,2	3,9	3,3				
(fluoro)quinolones	pradofloxacin	2,1	1,8	2,1	1,3	2,1	1,8	2,1	1,3				

## ANTIBACTERIAL USE DATA

## **Notifications in Sanitel-Med**

Table 6 shows the number of notifications in Sanitel-Med in 2021 (accession date: 20/04/2022), the number of farms for which notifications were done and the number of veterinarians that did the notifications, in total and per species. The therapeutical use of ZnO was no longer allowed in 2021, but a few notifications were still registered in the first two weeks of 2021, completely ceasing after that. The pig sector remained the largest sector in all terms and the veal sector remained the smallest sector, yet with a slightly higher number of notifications compared to the poultry sector. As in the previous years, the sum of the veterinarians per species does not equal the total number, meaning that some veterinarians did notifications for multiple species also in 2021.

Table 6. Number of notifications and farms and veterinarians with notifications per animal species in Sanitel-Med in 2021.

	TOTAL			PIC	<b>3</b>			POUL	ΓRY	VEAL	
	n	AB n	%	ZnO n	%	Total n	%	AB n	%	AB n	%
Notifications	147 228	113 802	77,3	7	<0,1	113 809	77,3	16 444	11,2	16 975	11,5
Farms	4 883	3 998	81,9	7	0,1	3998	81,9	759	15,5	249	5,1
Veterinarians	272	218	80,1	4	1,5	218	80,1	52	19,1	19	7,0

Since first reporting these data in 2018, the number of notifications has decreased with 14 %, whereas the numbers of farms and vets with notifications decreased with 8 % and 13 % respectively (data not shown). It is not clear whether this decreasing trend has multiple causes, but some likely are the general decrease in use of antibacterials over the years and a decrease in the number of active farms, especially in the pig sector; also an increase in the lack of compliance with the law cannot be ruled out.

# Sanitel-Med coverage of sales data

## a) General

The mass antibacterials calculated from all Sanitel-Med notifications in 2021 covered only 71 % of the mass according to the 2021 Belgian sales data as presented earlier in this report. The coverage was 68 % for pharmaceuticals and 93 % for premixes medicated with antibacterials (Figure 23). This represents a noteworthy decrease in the coverage result compared to the previous years, with an additional 'deficit' of approx. 10 tonnes (Figure 24).

Just as it has so far been unclear what is causing, in general, the (variation in the) difference between the sales and use data, at present one can only guess at the cause of this remarkable 'additional' difference, given that in terms of data collection nothing obvious has changed. Indeed, there are no indications to suspect the quality of the collected data, neither sales nor usage, has deteriorated to such an extent that this could lead to such a difference. The cause is therefore most likely to be sought in the context in which animal husbandry and veterinary antibiotic use take place, and one possible explanation might be the new veterinary legislation that was due to come into effect beginning of 2022. Fears of adverse effects on the purchase and/or use of antibiotics – justified or not – could have prompted veterinarians to replenish their stock over the course of 2021. If that is the case, then next year an inverse effect should be observable in the sales data.

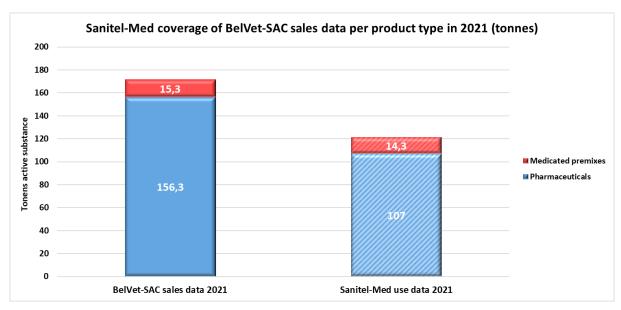


Figure 23. Comparison of tonnes active substance used (Sanitel-Med) in 2021 with the Belgian sales data for 2021, distinguishing among medicated premixes and pharmaceuticals.

It must be noted that the coverage result is slightly confounded because Sanitel-Med accepts notifications from products not authorised for sale in Belgium (notified as Self Defined Products – SDPs). The part SDPs make up from the Sanitel-Med total tonnes slightly decreased to approx. 1,2 tonnes in 2021 (Figure 24). Virtually all of this use is due to the cascade use of Neosol 100 % (injectable solution) even though in comparison to previous years the usage of more non-authorised products was notified, including Penstrep-ject (injectable solution), Tulissin (injectable solution) and Trisulmix (soluble powder for oral use).

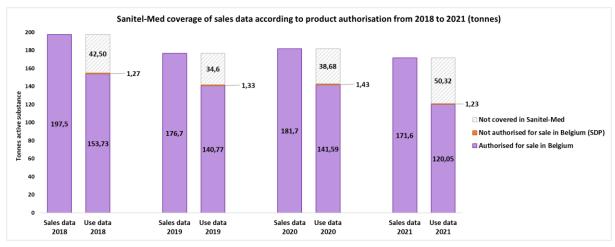


Figure 24. Comparison of tonnes active substance used (Sanitel-Med) from 2018 to 2021 with the corresponding Belgian sales data for those years, distinguishing based on authorisation of the products for sale in Belgium. The part of the sales data not covered by Sanitel-Med data is also shown.

In the following analyses, SDPs are always included in the Sanitel-Med data unless stated otherwise.

## b) Per species/animal category

In 2021, pigs for fattening and weaned piglets remained the animal categories with the largest mass of antibacterials used, even increasing their relative importance to almost 70 % of tonnes used (Figure 25). With the disappearance of ZnO, fatteners rose to the first place as users of the highest total mass of antibacterials. This indicates that the therapeutical use of ZnO in weaned piglets was not replaced by the use of colistin or another antibacterial product. In most pig categories, both use of premixes and pharmaceuticals decreased, except for the fatteners, where the tonnes premixes slightly increased from 4,9 tonnes in 2020. In poultry, after the dramatic increase in tonnes pharmaceuticals used in 2020 in laying hens, 2021 saw a halving of the used tonnes in this category. Tonnes used in veal calves further decreased.

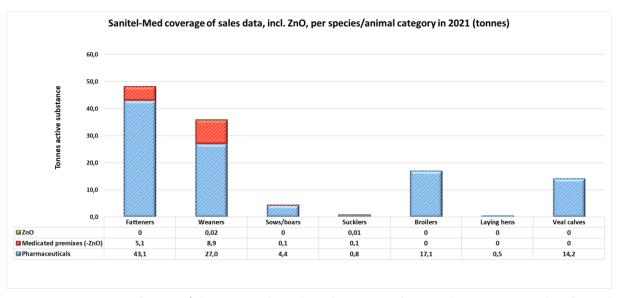


Figure 25. Tonnes active substance of pharmaceuticals, medicated premixes and ZnO used in 2021 per Sanitel-Med animal category.

# c) Per antibacterial class

Table 7. Total tonnes per antibacterial class sold in 2021 (Sales 2021) and total tonnes used in pigs, poultry and veal calves (Use 2021). Next to the tonnes used by each species the % this covers of the sales data (% sales) is shown.

	Sales 2021				Use 2021	1			
	Tonne	Total tonne	% sales	Pig tonne	% sales	Poultry tonne	% sales	Veal tonne	% sales
Penicillins	66,8	49,5	74	41,7	62	3,8	6	4,0	6
Tetracyclines	33,5	24,5	73	18,9	<i>57</i>	1,3	4	4,2	13
Sulphonamides	34,6	20,6	60	15,9	46	3,0	9	1,7	5
Macrolides	17,7	15,1	85	6,0	34	6,1	34	3,1	17
Aminosides	9,8	6,8	69	3,1	31	2,8	28	1,0	10
Polymixins	2,5	2,1	84	1,8	73	0,2	10	<0,1	1
Phenicols	3,8	2,0	51	1,7	44	<0,1	<1	0,3	7
Other	0,8	0,4	50	0,4	50	-	-	-	-
Quinolones	0,8	0,3	45	<0,1	<1	0,3	41	<0,1	4
Cephalosporins	1,4	<0,1	1	<0,1	<1	-	-	<0,1	<1

Along with the abovementioned increased difference between tonnes sold and tonnes used, overall coverage results decreased as expected, with clear drops in some of the main antibacterial classes in 2021 compared to previous years. For example, coverage of penicillins so far has always been approx. 85 %, while reaching only 74 % in 2021 (Table 7). This was for a large part driven by a remarkable decrease of penicillin use in poultry. Also coverage of macrolides' sales by the use data decreased remarkably, from above 95 % to mere 85 % in 2021. Here, less use in pigs and veal calves appear to be the main drivers.

Whereas use of aminosides and phenicols increased in 2021 (see also Table 4), the coverage by the Sanitel-Med use data decreased, indicating that the increase in 2021 is to be found in other animal categories or still has another cause. Use of quinolones decreased along with the general sales result, with a coverage remaining below 50 %.

# Use of critical substances in the Sanitel-Med animal species

After the large increase in the mass of (fluoro)quinolones used in poultry in 2020, a sharp decrease occurred in 2021 (Figure 26a), reaching the level of 2019. The % of farms using these products decreased likewise. In veal, the kg (fluoro)quinolones used also decreased, however, this was accompanied by a remarkable increase in the % of veal calf farms using these products, reaching almost 25 %. These are inverse trends compared to last year, yet pointing to the fact that on an increasing number of veal calf farms, health problems emerge in a limited number of animals that require use of these veterinary 'last resort' products. Even though this suggests good veterinary practice, the veal calf sector is encouraged to keep track of this trend, to avoid a further increase of the need to use these products.

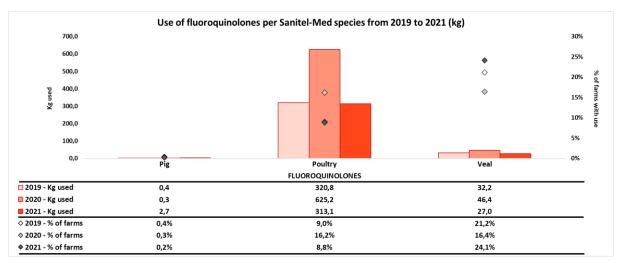


Figure 26a. Kg used of the (fluoro)quinolones in pigs, poultry and veal calves from 2019 to 2021, and the % of farms with notifications of use of these critical substances.

The use of (fluoro)quinolones remained stable at a very low level in pigs, whereas the use of cephalosporins 3G/4G completely ceased in 2021 (Figure 26b).

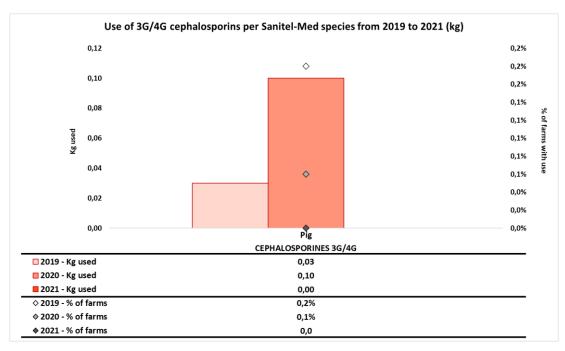


Figure 26b. Kg used of the 3<sup>rd</sup> and 4<sup>th</sup> generation cephalosporins in pigs from 2019 to 2021, and the % of farms with notifications of use of these critical substances.

As in previous years, pigs remained the species with the largest use of colistin, although the used mass as well as the % of farms with notifications using this substance continued to decrease (Figure 27). Used mass colistin also decreased in veal calves with a slight increase the % of farms using colistin. In poultry, use of colistin (in laying hens) slightly decreased again.

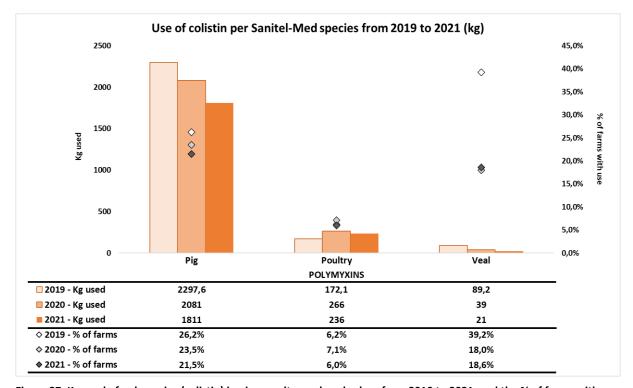


Figure 27. Kg used of polymyxins (colistin) in pigs, poultry and veal calves from 2019 to 2021, and the % of farms with notifications of use of colistin.

# Species-level antibacterial use

# a) BD<sub>100</sub>-species

Table 8 shows the evolution of the (kg) animals at risk of treatment per species at national level between 2018 and 2021. This is the denominator for the  $BD_{100}$ -species. For 2021 the data for 2020 needed to be used, since the data were not available in time for the publication of the present report on 2021.

Table 8. Number and kg animals at risk from 2018 till 2021\* in pigs, poultry and veal calves.

	-	Animals at	risk (x 10³)		-	Kg at ris	k (x 10³)	
	2018	2019	2020	2021*	2018	2019	2020	2021*
PIGS	6 209	6 085	6 218	6 218	318 869	311 901	316 048	316 048
POULTRY	43 624	44 902	49 016	49 016	54 921	55 860	60 838	60 838
VEAL CALVES	170	171	171	171	13 629	13 717	13 718	13 718

<sup>\*</sup> The final data for 2021 were not available yet (date last consultation: 15/06/2022). Data of 2020 were used.

In Table 9 the evolution of daily doses used per species at national level is presented. This is the numerator for the  $BD_{100}$ -species. A distinction is made between products for which the doses are expressed as mg/animal (products for local or topical use) and for which doses are expressed as mg/kg (products for systemic use). While there was a small increase in the amounts of local/topical products used in 2021 compared to 2020, the amounts of systemic products used drastically decreased in all species.

Table 9. Doses used of products administered locally or topically versus orally or through injection from 2018 till 2021 in pigs, poultry and veal calves.

	n DDD	A <sub>bel</sub> × LA <sub>bel</sub>	(locally/top	ically)	n DDDA <sub>bel</sub> × LA <sub>bel</sub> (x10 <sup>3</sup> ) (orally, injection)						
	2018	2019	2020	2021	2018	2019	2020	2021			
PIGS	592 087	497 942	554 535	555 001	8 290 387	7 645 507	7 404 517	6 270 840			
POULTRY	0	0	0	0	1 139 190	1 088 496	1 144 132	677 832			
VEAL CALVES	2 032	3 260	3 238	3 994	1 408 190	1 114 885	1 106 732	891 389			

The resulting BD<sub>100</sub>-species, expressing the treatment days out of 100 days based on the total, national amount of daily doses antibacterials used per species and the total, national mass animals at risk per species, decreased with -15,3 % for pigs, -40,7 % for poultry and -19,4 % veal calves between 2020 and 2021, amounting to a total decrease compared to 2018 of -23,6 % for pigs, -46,3 % for poultry and -37,1 % for veal calves (Figure 28). Yet, as in the previous years, the use in veal calves remained far higher than that in pigs and poultry.

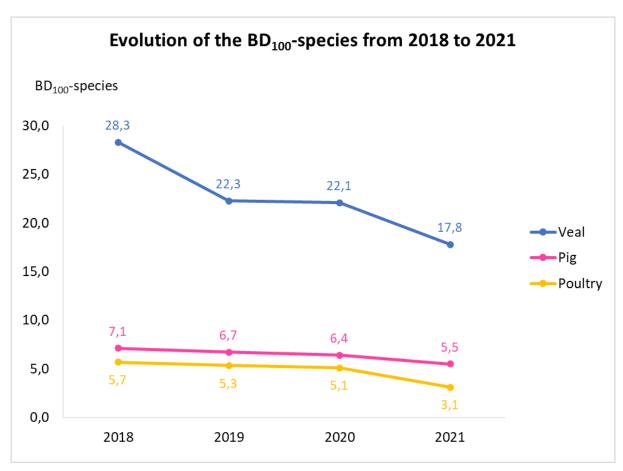


Figure 28. Antibacterial use (BD<sub>100</sub>-species) from 2018 to 2021 in pigs, poultry and veal calves.

# Farm-level antibacterial use

# a) 2021 reference populations for benchmarking

The number of farms per Sanitel-Med animal category that, after applying the farm-level quality controls, were found eligible to be included in the 2021 reference populations for benchmarking are presented in Table 10. Overall, a total of 4623 pig farms, 987 poultry farms and 242 veal calf farms could be included in the 2021 reference populations. It must be noted that compared to previous years the number of pig farms is far higher (4017 in 2020). This is due to a revision of the criteria for inclusion, as the constraints on farm size have been removed. However, as can be noted from the increase in the number of zero-use farms, most of the 'new benchmark IN' farms appear not to use antibacterials. This does not affect the follow-up of the results over the years, as zero-use farms are excluded for these analyses.

Table 10. Number of farms and zero-use farms per Sanitel-Med animal category that were part of the 2021 reference populations for benchmarking.

		PI	GS		POL	JLTRY	· VEAL CALVES
	Sucklers	Weaners	Fatteners	Breeders	Broilers	Laying hens	VEAL CALVES
n farms	1 665	1 704	4 280	1 666	774	214	242
n zero-use farms¹	270	138	827	267	112	142	1

<sup>&</sup>lt;sup>1</sup> For pigs, zero-use is at farm level (hence, if four animal categories are present at the farm, zero-use is only when there is no AMU in all four categories), whereas for poultry and veal calves, it relates to the animal category.

## b) Farm-level antibacterial use in 2021

Below the distribution of the farm-level  $BD_{100}$  in the 2021 reference population of each Sanitel-Med animal category is shown as a box-plot with the median use indicated (Figure 29). Note that the zero-use farms (see Table 10) were excluded from the reference populations to produce the box-plots. Use remained highest in veal calves and weaners, while use in broilers approached that in fatteners. The right-skewed distribution with 'tails' of high users remained in all categories.

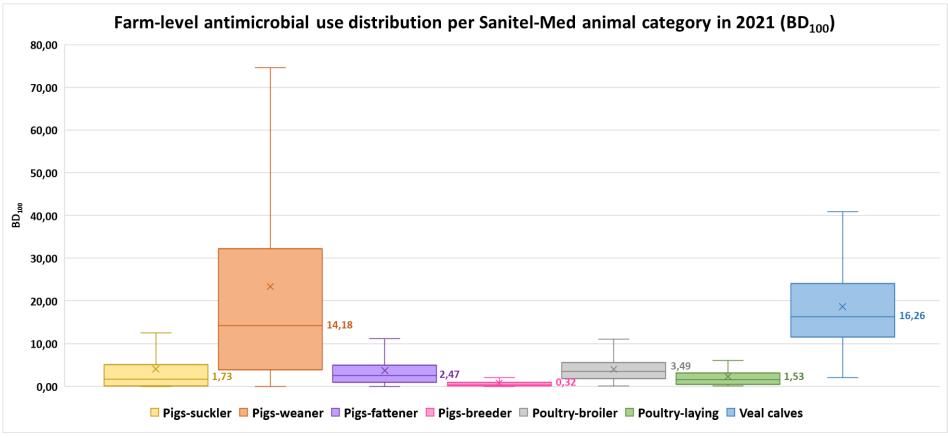


Figure 29. Box-plots representing the BD<sub>100</sub>-distribution in the 2021 reference population of each Sanitel-Med animal category. Outliers are not shown, zero-use farms (see Table 10) were excluded. The median values are provided next to the lines in the boxes.

## c) Evolution of farm-level antibacterial use from 2018 to 2021

#### i. Summary

The evolution of the median farm-level BD<sub>100</sub> in the benchmark reference populations from 2018 to 2021 shows a drastic decrease over this period in most Sanitel-Med animal categories, with highest reductions in broilers and veal calves, which was achieved especially in 2021 (Figure 30). The increase in the laying hens must be interpreted with caution, as there has been an decrease in 2021 compared to 2020, and the exclusion of the zero use farms goes beyond the fact that around two thirds of laying hen farms do not use antibacterials at all. Hence, overall this is a very good result that should fuel all sectors to sustain their efforts, as the overall national targets still remain fairly out of reach.

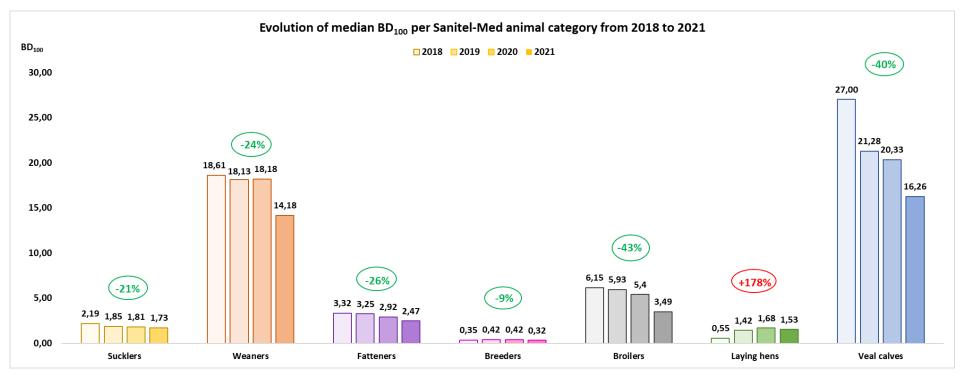


Figure 30. Evolution of the median of the BD<sub>100</sub>-distribution in the reference populations for 2018, 2019, 2020 and 2021 of each Sanitel-Med animal category. Zero-use farms per year were excluded for the analysis.

In the next sections more details of the evolution in the benchmarking reference groups' distributions of antibacterial use are provided, as well as the threshold values that have been outlined for the antibacterial use reduction paths that apply as of 2021 (Tables 11-17).

#### ii. Suckling piglets

Table 11a. Parameters describing the distributions of the farm-level antimicrobial use in the reference populations for benchmarking of suckling piglets from 2018 to 2021 and % difference (% diff) over the years.

Parameters BD <sub>100</sub>	2018	2019	2020	2021	% diff 20-21	% diff 18-21
Mean	5,41	4,89	4,63	4,06	-12,31 %	-24,95 %
P25	0,18	0,16	0,25	0,15	-40,22 %	-17,22 %
P50	2,19	1,85	1,81	1,73	-4,23 %	-20,96 %
P75	6,44	5,76	5,51	5,11	-7,26 %	-20,61 %
P90	13,30	12,4	12,33	9,78	-20,68 %	-26,46 %
Sum	7855	6876	6531	5664	-13,28 %	-27,89 %
Total n farms	1580	1534	1559	1665	ND	ND
% farms with zero use <sup>1</sup>	8,2 %	8,3 %	9,6 %	16,2 %	ND	ND

<sup>&</sup>lt;sup>1</sup> Zero use farms were not included in the data for determining the parameter values.

Table 11b. The thresholds of the BD<sub>100</sub> reduction path 2021-2024 for suckling piglets.

Date of application	Attention value	Action value
01/01/2021	2	10
01/01/2023	2	6
01/01/2024	2	5

As illustrated in Table 11a, the decrease of the antibacterial use in suckling piglets in 2021 was situated throughout the entire benchmarking population of farms. For the first time since following up, there were (slightly) less than 10 % farms, using antibacterials in suckling piglets, in the red zone. However, still over 20 % of farms would be red with the current results when the action  $BD_{100}$ -value will be adjusted to 6 within half a year from the publication of this report (Table 11b). Moreover, only around 54 % of farms, using antibacterials in suckling piglets, are currently below the attention  $BD_{100}$ -value (data not shown).

### iii. Weaned piglets

Similarly to sucklers, the decrease of the antibacterial use in weaned piglets in 2021 was situated throughout the entire benchmarking population of farms (Table 12a). The P90 approached the action  $BD_{100}$ -value but still around 12 % of farms, using antibacterials in weaned piglets, were in the red zone according to the current action value (data not shown). However, the adjustment to an action  $BD_{100}$ -value of 40 would find 19 % farms being red (Table 12b). In addition, just below 50 % of farms, using antibacterials in weaned piglets, are currently below the attention  $BD_{100}$ -value.

Table 12a. Parameters describing the distributions of the farm-level antimicrobial use in the reference population for benchmarking of weaned piglets from 2018 to 2021 and % difference (% diff) over the years.

Parameters BD <sub>100</sub>	2018	2019	2020	2021	% diff 20-21	% diff 18-21
Mean	29,06	26,97	27,36	23,36	-14,62 %	-19,61 %
P25	5,06	5,61	5,17	3,89	-24,67 %	-23,04 %
P50	18,61	18,13	18,18	14,18	-21,98 %	-23,79 %
P75	39,66	36,46	37,96	32,25	-15,05 %	-18,69 %
P90	69,15	60,83	63,67	53,74	-15,60 %	-22,28 %
Sum	44700	40648	41759	36576	-12,41 %	-18,17 %
Total n farms	1608	1578	1597	1704	ND	ND
% farms with zero use <sup>1</sup>	4,4 %	4,5 %	4,4 %	8,1 %	ND	ND

 $<sup>^{\</sup>rm 1}$  Zero use farms were not included in the data for determining the parameter values.

Table 12b. The thresholds of the BD<sub>100</sub> reduction path 2021-2024 for weaned piglets.

Date of application	Attention value	Action value
01/01/2021	14	50
01/01/2023	14	40
31/12/2024	14	30

# iv. Fattening pigs

Table 13a. Parameters describing the distributions of the farm-level antimicrobial use in the reference population for benchmarking of fattening pigs from 2018 to 2021 and % difference (% diff) over the years.

Parameters BD <sub>100</sub>	2018	2019	2020	2021	% diff 20-21	% diff 18-21
Mean	4,91	4,88	4,4	3,69	-16,14 %	-24,85 %
P25	1,2	1,29	1,16	0,922	-20,38 %	-23,17 %
P50	3,32	3,25	2,92	2,466	-15,40 %	-25,72 %
P75	6,64	6,50	5,93	5,014	-15,40 %	-24,49 %
P90	11,28	10,72	10,18	8,4354	-17,12 %	-25,22 %
Sum	17197	16715	15307	12727	-16,86 %	-25,99 %
Total n farms	3813	3717	3790	4280	ND	ND
% farms with zero use <sup>1</sup>	8,1 %	7,8 %	8,3 %	19,3 %	ND	ND

<sup>&</sup>lt;sup>1</sup> Zero use farms were not included in the data for determining the parameter values.

Table 13b. The thresholds of the  $\ensuremath{\mathsf{BD}_{100}}$  reduction path 2021-2024 for fattening pigs.

Date of application	Attention value	Action value
01/01/2021	2,7	9
01/01/2023	2,7	6
01/01/2024	2,7	6

Also the decrease of the antibacterial use in fatteners in 2021 was situated throughout the entire benchmarking population of farms (Table 13a). For the first time since following up, there were less than 10 % farms, using antibacterials in fatteners, in the red zone. However, still 19 % of farms would be red with the current results when the action  $BD_{100}$ -value will be adjusted to 6 (Table 13b). Moreover, only around 53 % of farms, using antibacterials in fatteners, are currently below the attention  $BD_{100}$ -value (data not shown).

#### v. Breeding pigs

Table 14a. Parameters describing the distributions of the farm-level antimicrobial use in the reference population for benchmarking of breeding pigs from 2018 to 2021 and % difference (% diff) over the years.

Parameters BD <sub>100</sub>	2018	2019	2020	2021	% diff 20-21	% diff 18-21
Mean	0,96	0,93	0,93	0,73	-21,51 %	-23,96 %
P25	0,06	0,09	0,10	0,07	-28,64 %	18,33 %
P50	0,35	0,42	0,42	0,32	-23,26 %	-8,57 %
P75	1,07	1,09	1,11	0,90	-19,25 %	-16,12 %
P90	2,15	2,24	2,34	1,75	-25,04 %	-18,56 %
Sum	1399	1315	1282	1002	-21,84 %	-28,38 %
Total n farms	1580	1529	1554	1666	ND	ND
% farms with zero use <sup>1</sup>	8,2 %	7,9 %	9,2 %	16,0 %	ND	ND

<sup>&</sup>lt;sup>1</sup> These zero use farms were not included in the data for determining the parameters.

Table 14b. The thresholds of the BD<sub>100</sub> reduction path 2021-2024 for breeding pigs.

Date of application	Attention value	Action value
01/01/2021	0,28	1,65
01/01/2023	0,28	1,65
01/01/2024	0,28	1,65

As in the other pig categories, 2021 saw an overall decrease of the antibacterial use in the benchmarking population of farms with breeding pigs (Table 14a). Yet, still 11 % of farms, using antibacterials in breeding pigs, were in the red zone (data not shown). The action value remains stable for the coming years (Table 14b). Unfortunately, so far only 47 % of farms, using antibacterials in breeding pigs, were in the green zone (data not shown).

In conclusion for the pig sector, the situation is positive as to the result for 2021 compared to 2020 yet worrying in terms of the reduction paths and the foreseen downward adjustment of the action  $BD_{100}$ -values in piglets and fatteners. At the moment of publication of this report, this adjustment is only six months away and only if the efforts done in 2021 are continued in 2022, a possibly unworkable situation (of approx. 20 % red farms) might be averted. In addition, the national goal of 65 % reduction in antibacterial use in 2024 compared to 2011 was proposed with the assumption of at least 75 % of farms with antibacterial use under the respective attention values. also from that point of view, a lot of progress remains to be made.

#### vi. Broilers

Table 15a. Parameters describing the distributions of the farm-level antimicrobial use in the reference population for benchmarking of broilers from 2018 to 2021 and % difference (% diff) over the years.

Parameters BD <sub>100</sub>	2018	2019	2020	2021	% diff 20-21	% diff 18-21
Mean	8,12	7,47	6,99	3,96	-43,35 %	-51,23 %
P25	3,23	2,82	2,40	1,85	-22,99 %	-42,78 %
P50	6,15	5,93	5,40	3,49	-35,29 %	-43,22 %
P75	11,47	10,44	10,49	5,54	-47,19 %	-51,68 %
P90	16,91	16,13	15,18	7,67	-49,48 %	-54,64 %
Sum	5141	4659	4487	2624	-41,52 %	-48,96 %
Total n farms	728	728	742	774	ND	ND
% farms with zero use <sup>1</sup>	13,0 %	14,3 %	13,5 %	14,5 %	ND	ND

<sup>&</sup>lt;sup>1</sup> Zero use farms were not included in the data for determining the parameter values.

Table 15b. The thresholds of the  $\ensuremath{\mathsf{BD}}_{100}$  reduction path 2021-2024 for broilers.

Date of application	Attention value	Action value
01/01/2021	6	14
01/01/2023	5	12
31/12/2024	5	10

Spectacular decreases were obtained in broilers in 2021, throughout the entire benchmarking population of farms (Table 15a). Less than 1 % of farms, using antibacterials in broilers, is currently above the current action  $BD_{100}$ -value and only 3 % are above the action  $BD_{100}$ -value as foreseen to be implemented at the end of 2024 (Table 15b). Likewise, 80 % of farms, using antibacterials in broilers, has achieved an antibacterial use below the attention value and already 70 % below the future attention value. These are highly positive results and considering that efforts have only quite recently been stepped up, it might be suspected further reductions might be easily achieved.

# vii. Laying hens

The farm-level use for laying hens decreased in 2021 but considered over the past four years it dramatically increased (Table 16a). It must of course be noted that this sector is by far most affected by the exclusion of the zero use farms as is done for the current analyses, with only 34 % of laying hen farms notifying antibacterial use in 2021.

Table 16. Parameters describing the distributions of the farm-level antimicrobial use in the reference population for benchmarking of laying hens from 2018 to 2021 and % difference (% diff) over the years.

Parameters BD <sub>100</sub>	2018	2019	2020	2021	% diff 20-21	% diff 18-21
Mean	1,29	1,95	2,64	2,31	-12,50 %	79,07 %
P25	0,27	0,39	0,61	0,46	-24,59 %	70,37 %
P50	0,55	1,42	1,68	1,53	-8,90 %	178,27 %
P75	1,35	3,24	2,68	3,19	19,15 %	136,54 %
P90	3,05	4,6	6,88	5,30	-22,91 %	73,89 %
Sum	84	131	211	166	-21,33 %	97,62 %
Total n farms	197	197	206	214	ND	ND
% farms with zero use <sup>1</sup>	67,0 %	66,0 %	61,2 %	66,4 %	ND	ND

<sup>&</sup>lt;sup>1</sup> Zero use farms were not included in the data for determining the parameter values.

Table 15b. The thresholds of the  $BD_{100}$  reduction path 2021-2024 for laying hens.

Threshold values <sup>1</sup>		
Attention value	0	
Action value	3	

<sup>&</sup>lt;sup>2</sup> These values were agreed in consultation with the sector. An evolution in time of these values (reduction path) is not foreseen.

In conclusion for the poultry sector, the results are very good, even though progress remains to be made in laying hens. It can be considered to even formulate more ambitious goals for the coming years, considering the ease and speed with which progress has been made in only 1 year.

#### viii. Veal calves

As in the other species, the result of the veal calf sector is generally positive (Table 17a). However, still slightly more than 10% farms, using antibacterials in veal calves, were in the red zone and 30% of farms would be red with the current results (data not shown) when the action  $BD_{100}$ -value will be adjusted within half a year after the publication of this report (Table 17b). Positive on the other hand is that almost 70% of veal calf farms are below the current attention  $BD_{100}$ -value; however, the attention  $BD_{100}$ -value foreseen to be implemented at the end of 2024 is currently achieved by merely 28% of the farms (data not shown).

Table 17a. Parameters describing the distributions of the farm-level antimicrobial use in the reference population for benchmarking of veal calves from 2018 to 2020 and % difference (% diff) over the years.

Parameters BD <sub>100</sub>	2018	2019	2020	2021	% diff 20-21	% diff 18-21
Mean	29,6	22,69	22,65	18,68	-17,53 %	-36,89 %
P25	19,73	15,17	14,45	11,52	-20,29 %	-41,63 %
P50	27	21,28	20,33	16,26	-20,01 %	-39,76 %
P75	39,13	28,20	28,39	24,02	-15,39 %	-38,62 %
P90	47,27	36,16	38,93	31,86	-18,17 %	-32,60 %
Sum	7046	5400	5458	4501	-17,53 %	-36,12 %
Total n farms	240	239	242	242	ND	ND
% farms with zero use <sup>1</sup>	0,8 %	0,4 %	0,4 %	0,4 %	ND	ND

<sup>&</sup>lt;sup>1</sup> Zero use farms were not included in the data for determining the parameter values.

Table 17b. The thresholds of the  $BD_{100}$  reduction path 2021-2024 for veal calves<sup>1</sup>.

Date of application	Attention value	Action value
01/01/2021	20	30
01/01/2023	16	22
31/12/2024	12	18

<sup>&</sup>lt;sup>1</sup> Recalculated with a standard treatment weight of 80 kg.

In conclusion the result of the veal calf sector is generally positive. However, still slightly more than 10 % farms, using antibacterials in veal calves, were in the red zone and 30 % of farms would be red with the current results when the action  $BD_{100}$ -value will be adjusted within half a year from the publication of this report. Positive on the other hand is that almost 70 % of veal calf farms are below the attention  $BD_{100}$ -value.

## d) Percentage of alarm users in different species

A rough estimation of the number of alarm users at the end of 2021 shows that we are far from the desired 1 % end of 2024 for pigs (approx. 9 % alarm users end of 2021) and veal calves (approx. 13 % of alarm users end of 2021), whereas for broilers we are currently on track (approx. 0,4 % alarm users end of 2021).

However, this is without taking into account the foreseen reductions in the coming two years (beginning of 2023 and beginning/end of 2024, see figure 31). With current AB use the number of red farms will substantially increase, and so will the potential alarm users, in pigs and veal calves, whereas in poultry it will be important to maintain and preferably improve the situation, providing some margin.

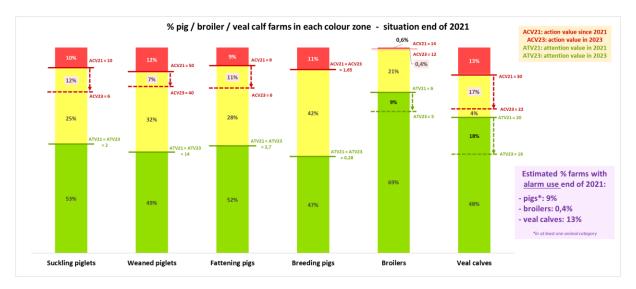


Figure 31. Distribution of the percentage of farms in the different MCRA color zones and the expected evolution with the foreseen changing benchmark values.

Hence, we urge all stakeholders to take their responsibility and increase their efforts to achieve the desired goals. Specifically, focus should be on

- 1) Continuing to work on the development of a solid, concerted (legal) framework for follow-up of alarm users, as a means of stimulating the farms that have so far resisted and/or failed to implement measures to reduce their continued or repeated high use of antibiotics.
- 2) Creating stimuli for farms to achieve and maintain an antibiotic use below the attention values.
- 3) Limiting the uncertainty surrounding the number of 'zero use' farms and the difference between 'sales' and 'use' data by increasing the level of control on the accurate registration of the antibiotic use by all veterinarians obliged to do so.

#### e) Distribution of use according to veterinary contract

As in 2020, there were big differences in 2021 between the three sectors in the role of the contract veterinarian (the veterinarian charged with the epidemiological surveillance) in terms of antibacterial use (Figure 30). The differences even became more pronounced, with higher percentages in all sectors of farms with either all or none of the antibacterial use done by the contract veterinarian.

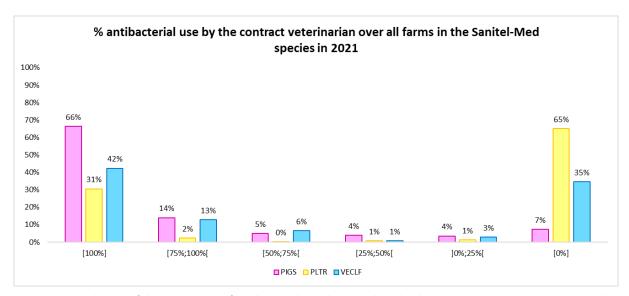


Figure 32. Distribution of the percentage of antibacterial use that was done by the contract veterinarian on pig, poultry and veal calf farms in 2021. Six intervals are shown: 100 % of use was done by the contract vet, between 75 % and 100 %, between 50 % and 75 %, between 25 % and 50 %, between 0 % and 25 %, and 0 %.

## f) Farm-level use of the various antibacterial classes

In pigs, the total number of treatment days decreased but the proportion remained rather stable for all major antibacterial classes compared to 2020 (Figure 33). There seems to be a small decrease in the proportion of tetracyclines and a slight increase in the proportion of macrolides. Relatively speaking, the increases in the proportions of aminoglycosides and amphenicols are most remarkable.

In poultry, the main trend was the drastic decrease in the total number of treatment days with broad-spectrum penicillins, as a result of which the proportion of this class decreased as well while proportions of most other classes increased – even if the absolute number of treatment days of most these classes decreased. Use of lincosamides as single treatments (so not in combination with spectinomycin) almost disappeared.

In veal calves, the situation was more like in pigs, with the decrease rather 'evenly' spread across antibacterial classes and proportions remaining relatively stable, even though the importance of broad-spectrum penicillins appears to increase while that of macrolides appears to decrease. Notably, there was a strong increase in the use of trimethoprim-sulphamides products.

As noted in the previous BelVet-SAC report, relative stability of the used antibacterial classes is important in light of the follow up of the reduction paths.

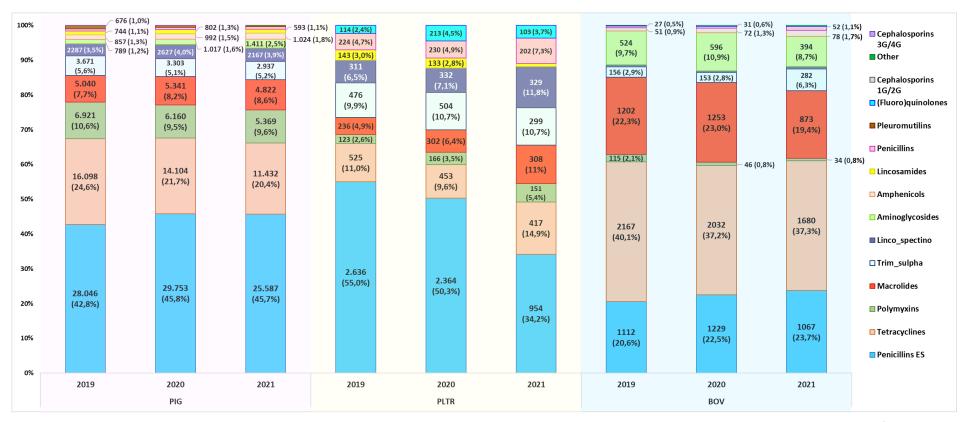


Figure 33. Number of treatment days with the different antibacterial classes and percentage of the total number of treatment days per species in 2019, 2020 and 2021. Numbers/percentages not shown are classes where use was below 1 % of treatment days.

## **DISCUSSION**

In the context of the increasing (awareness on) antibacterial resistance development, comparable data and monitoring of evolutions of antibacterial consumption (AMU) are of utmost importance. This annual BelVet-SAC report is now published for the thirteenth time and describes the AMU in animals in Belgium in 2021 and the evolution since 2011. For the fourth year this report combines sales data (collected at the level of the wholesaler-distributors and the compound feed producers) and usage data (collected at farm level). This allows to dig deeper into AMU at species and farm level in Belgium.

## A growing gap between sales and usage data

As always, in the sales data, the dependency on the biomass factor influences 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 2021 approximately 1,2 ton of SDPs (predominantly Neosol 100 %) was registered, this number has been more or less constant over the last four years varying between 1,2 and 1,4 tonnes. In 2021, sales data were 50,3 tonnes higher than usage data (not corrected for SDPs), which is a remarkable increase compared to 2020 (38,7 tonnes) and 2019 (34,6 tonnes). As the usage data do not cover all animal species, a big part of the difference is likely explained by usage in the non-included species or categories, most importantly bovines but also other poultry categories and companion animals, horses, rabbits, turkeys, ... However, non-compliance with the notification of use in the currently compulsory animal categories may also account for a difference between sales and use. Therefore the growing gap between the two data sources is worrisome. At present one can only guess at the cause of this remarkable 'additional' difference, given that in terms of data collection nothing obvious has changed. One possible explanation might be the new veterinary legislation that came into force beginning of 2022. Fears of adverse effects on the purchase and/or use of antibiotics – justified or not – could have prompted veterinarians to replenish their stock over the course of 2021. If that is the case, next year an inversed effect should be observable in the sales data. In any case, the increased gap between sales and use data is definitely something that needs to be followed up, confirming also the ongoing need for sensibilisation and control regarding accurate notification

## > A motivating reduction in mg/kg biomass antibiotics sold

With a **consumption of 81,2 mg antimicrobial/kg biomass in 2021** a decrease of **-8,4** % in comparison to 2020 is observed. The decrease in 2021 is seen in both **pharmaceuticals (-7** % **mg/kg) and antibacterial premixes (-12,9** % **mg/kg).** After a year of standstill in 2020 this reduction connects again with the descending trend, observed between 2014 and 2019. Overall, a **cumulative reduction of -44,6** % **since 2011** is achieved. In absolute values this corresponds to a reduction of more than 10 tonnes of active substance (171 595,5 kg in 2021 versus 181 749,6 kg in 2020). Compared to 2011 a reduction of 127,5 tonnes of active substance has already been realized, corresponding to a reduction of -42,6 %.

### Highly favourable reductions of the AMU in the Sanitel-Med species

As in 2020, the total AMU in animals in 2021 is in large part determined by the pig sector and more specifically, by the fatteners and the weaners. Together, they accounted for almost 70 % of tonnes used. Broilers and veal calves accounted for 14 % and 12 % of tonnes used, respectively, and the remaining animal categories (sows/boars; sucklers; layers) for less than 5 %. After the dramatic increase in tonnes pharmaceuticals used in 2020 in laying hens, 2021 saw a halving of the used tonnes in this category. With specific regards to the use of critical antibacterials, favourable results are seen in calves and more spectacularly in poultry with a return to 2019 levels after the dramatic increase in quinolone use in 2020. In veal calf farms, an increase in number of farms using quinolones is seen. Combined with the decreased mass of quinolones used in that animal category, this suggest good veterinary practice, though the sector is encouraged to dig deeper into the cause for the need to use these molecules and to aim higher on prevention.

When looking at the evolution in the number of treatment days (BD<sub>100</sub>) at the species level, as calculated from the SANITEL-MED use data a substantial decreased use is observed in 2021 in all species compared to 2020. For pigs a decrease of -15,3 % was registered, for veal calves the decrease mounted to -19,4 % and for poultry the largest decrease with -40,7 % was

**observed**. These results are in line with the evolution in the sales data although the observed reductions in use are substantially higher. This is linked to the growing gap between sales and use data as described above. Nonetheless, the results are encouraging for all sectors. Especially in the poultry sector, where reductions were limited in the past year, this big improvement obtained this year is to be applauded. It is plausible that this big jump forward is linked to the introduction of the 10 point action plan in the poultry sector in 2020. A comparable effect was seen in the veal sector some years ago when also this sector introduced an action plan.

The farm-level pig results per animal category in the pig sector show overall positive results. For the suckling piglets a median  $BD_{100}$  of 1.73 is seen which is a decrease of -4,4 % compared to 2020. In weaned piglets a median of 14.18 is obtained which is a decrease of -22,0 % compared to 2020. Also in fatteners a decrease of -15,4 % is observed (median  $BD_{100}$  of 2,47 compared to 2,92 in 2020). In pigs for breeding the median  $BD_{100}$  was 0,32 compared to 0,42 in 2020 which is a decrease of -23,3 %. Although all these results are positive the obtained reductions are not yet sufficient for some farms. In 2023 the action values for  $BD_{100}$  in piglets and fatteners will be adjusted downwards and with the current situation approximately 20 % of the farms will end up in the red zone. Therefore immediate actions are needed especially in the highest using groups. Moreover, the national goal of 65 % reduction in antibacterial use in 2024 compared to 2011 was proposed assuming that at least 75 % of farms with antibacterial use are in the green zone. Also from that point of view, a lot of progress remains to be made.

In broilers, big improvements were made in 2021 with a reduction of the median  $BD_{100}$  from 5,40 to 3,49 which is a change of -35,3 %. Moreover it is good to see that less than 1 % of farms, using antibacterials in broilers, are currently above the current action  $BD_{100}$ -value (= red zone) and only 3 % are above the action  $BD_{100}$ -value as foreseen to be implemented at the end of 2024. Likewise, 80 % of farms, using antibacterials in broilers, are situated in the green zone. Also in laying hens the median  $BD_{100}$  has decreased from 1,68 to 1,53 (reduction of -8,9 %). Given the big improvements made in 1 year time in the poultry sector it can be considered to even formulate more ambitious goals for the coming years.

Finally in veal calves, the median farm level BD<sub>100</sub> also reduced from 20,33 to 16,26 which corresponds to a reduction of 20,0 %. However, still more than 10 % farms, using antibacterials in veal calves, were in the red zone and 30 % of farms would be red with the current results when the action BD<sub>100</sub>-value will be adjusted beginning of 2023. Positive on the other hand is that almost 70 % of veal calf farms are already in the green zone and almost 50 % already achieve the attention BD<sub>100</sub>-value foreseen to be implemented at the end of 2024. Notwithstanding these positive evolutions in the veal calf sector the AMU data in this sector still remains the highest of all sectors and therefore needs to be further reduced.

Remarkably, in the three Sanitel-Med species the differences observed in 2020, in terms of how much AMU is attributable to the farm contract veterinarian compared to (an)other veterinarian(s), became even more consolidated in 2021. In the majority of the pig farms, all notifications are made solely by the contract veterinarian whereas in the poultry sector, for 65 % of the farms, 0 notifications can be attributed to the contract veterinarian. This result is probably caused by the fact that many poultry veterinarians no longer have a contract as a natural person (rather, the contract is drawn up with the veterinary practice) while the notifications in Sanitel-Med likely are done with their personal vet code. In 2022 the benchmarking system for veterinarians will be changed to assure a better reflection of the reality.

## Mixed results in cattle and companion animals

For other species such as cattle, horses and companion animals no herd or animal level use data are yet available in Sanitel-Med. Yet the BelVet-SAC sales data do allow to get a rough estimate of the antimicrobial use evolutions in these species. In dairy cattle it is positive to observe that the average intramammary antimicrobial use per milk cow is decreasing for the second year in a row. Yet when zooming in a little more in detail it is remarkable to see that this decrease is mainly due to a decrease in use of antimicrobial applicators in lactating cows and not due to a decrease in dry cow applicators. This needs to be carefully considered within the dairy cattle sector, as most of the antibiotic reduction in this sector is expected to be achievable by reducing the systematic use of antibiotics at dry-off and during lactation.

In dogs and cats the volume of antibacterial products in 2021 has increased with +4,0 % in comparison to 2020. Compared to 2014 the total increase of sales of antibacterial substances solely authorised for use in dogs and cats is +28,0 %. With the absence of an accurate estimate of the evolution in the total dog and cat population (denominator) it remains difficult to interpret this evolution yet it does not provide a very positive feeling. On the contrary, in 2021 the use of critical important

antimicrobials (red molecules) in dogs and cats decreased spectacularly with -67 % (from 214 kg of active substance in 2020 to 71 kg in 2021). This is mainly due to a decreased use of enrofloxacin.

#### The overall reduction is apparent in most antibacterial classes, including the most critical

The details of the sales of the different antibacterial classes show – as in previous years – that penicillins (38.9 %) form the largest group of consumed antimicrobials, followed by the sulphonamides (20,2 %) and the tetracyclines (19,5 %). Fortunately the overall observed decrease is spread over the majority of the different antimicrobial classes resulting in a decreased use for all classes except the aminosides and the phenicols. Especially promising is the substantial decrease in the sales of critically important antibacterial compounds as seen for the quinolones and cephalosporins of the 3<sup>rd</sup> and 4<sup>th</sup> generation (resp. -45,9 % and -13,3 % in kg/kg biomass compared to 2020). Also the sales of colistin is further decreasing; since 2012 (before authorization of ZnO products), colistin sales have dropped with -75.4 %. This evolution is remarkable in the light of the fact that also the sales and use of ZnO has reduced substantially in the last years and is now fully ended in 2021. Hence, the therapeutical use of ZnO in weaned piglets has not been replaced by the use of colistin or another antibacterial product.

#### In a European context Belgium is improving yet still lagging behind

Comparing the Belgian sales data with the results of other European countries, and especially our neighbouring countries, shows that we are catching up, even if there is still a substantial gap to be bridged and despite the expected slight increase in antibacterial sales in 2021. None the less Belgium has still the highest usage (expressed in mg/pcu) of all our neighbouring countries according to the ESVAC report. Yet it should be reminded that the European data for 2021 (ESVAC) will published by the end of 2021 and therefore do not take into account the reductions achieved in 2021 in Belgium, as covered by the current report.

## The results in light of the 2020 reduction targets: almost there

With regard to the general reduction target formulated by AMCRA (-50 % by 2020), despite the substantial reduction obtained in 2021, this goal has still not been fully achieved: a total reduction of -44,6 % compared to 2011 was obtained. On the other hand, the new decrease observed in the use of antibacterial premixes means the original reduction target (-50 %) was by far maintained. Furthermore, use of the "red" molecules, after the disappointing increase in 2020, decreased again very substantially with -42,8 % in 2021. In comparison to 2011 (reference year) the reduction of red molecules in 2021 is -82,9 % which is largely below the reduction goal of minus 75 % by 2020. The restoration of the Royal Decree articles on the conditions for use of critically important antibacterial compounds at the end 2020 might have contributed to this result. Satisfyingly, use of "yellow" (-4,0 %) and "orange" (-8,2 %) antibacterial classes also reduced, albeit moderately, compared to 2020.

#### The results in light of the 2024 reduction targets: increased efforts are required!

With the start of 2021, a **renewed Covenant** between the sectors, AMCRA and competent authorities was signed, expressing not only the will to continue the good work of the past years but also strengthening the sense of urgency to take further actions. The new Covenant includes a **reduction goal up to 65 % by 2024** (compared to the reference year 2011)<sup>17</sup>. This further stresses the need for continuous and additional efforts to be made, such as expanding herd level data-collection and benchmarking through the Sanitel-Med and AB Register systems, in combination with multiple, stewardship-oriented initiatives such as herd health plans, continuous education, increased biosecurity, ...

The herd-level data collection in pigs, broilers, laying hens and veal calves, already existing for multiple years, have led to the establishment of sector-specific reduction paths as a central strategy to support achieving the national reduction target(s). These reduction paths are deemed ambitious yet realistic and, foremost, essential to get the sectors moving towards the required further reductions of AMU. Despite the positive species- and farm-level AMU results in 2021, it must be stressed that increased efforts will be needed. In half a year from the publication of this report, a first downward step of the action

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<sup>&</sup>lt;sup>17</sup> https://www.amcra.be/nl/visie-2024/

BD<sub>100</sub>-values will be taken, and based on the 2021 results this would impact a considerable number of farms. All involved parties are encouraged to further implement their plans and ambitions, especially focussing on the framework for follow-up of alarm-users, as this is expected to be critical for success. Yet, it also needs to be underlined again that the final aim should be to achieve acceptable AMU, below the BD<sub>100</sub>-attention values, on as much farms as possible.

With regard to the additional reduction targets for 2024, the 2021 results suggests these will likely be achieved, if the current efforts are maintained. Indeed, the cumulative reduction of the use of antibacterial premixes of -74.2 % in comparison to 2011 already almost equals the goal of -75 % by 2024. And as noted, with the achieved reduction in the use of red products, the -75 % compared to 2011 is largely maintained. Finally, colistin use in 2021 landed at a level of 1,17 mg/kg biomass which approaches the goals of less than 1 mg/kg biomass set in the AMCRA 2024 goals.

## CONCLUSION

The 2021 antibacterial product sales and use data fortunately show that due to joint efforts, the results scrambled back up after the setback of 2020. It is clear that close surveillance and a joint effort from all stakeholders is mandatory to press on to achieve and maintain the reduction goals for 2024. Especially in view of the reduction paths, efforts are necessarily, if not urgently, required in order to decrease the number of red farms.

#### **ACKNOWLEDGEMENTS**

Belgian wholesaler-distributors and compound feed producers are much obliged for their cooperation and for providing the data on the consumption of antimicrobials in animals in Belgium. All veterinarians and third party organisations who provide data to the SANITEL-MED system are acknowledged for their efforts. We would like to thank Gudrun Sommereyns from the Belgian Centre for Pharmacotherapeutic Information for providing the information on the commercialised medicinal products.

# **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
	QS02AA14; QS02AA57
Aminoglycosides	QG51AA04
	QA07AA06
	QJ51RG01
	QJ51CE59
	QJ01XX04
	QJ01XX10
Other	QJ01XQ01; QJ01XQ02
other	QJ51XX01
	QJ01RA04
	QJ01DB01
	QJ01DD90; QJ01DD91
	QJ51DB01; QJ51DB04; QJ51DB90
Canhalasnarins	QJ01DE90
Cephalosporins	QJ51DE90
	QG51AX02
	QJ51DD12
	QJ51RD01
Amphenicols	QJ01BA90
Amphenicois	QS01AA01
	QJ01FA02; QJ01FA90; QJ01FA92; QJ01FA91; QJ01FA94; QJ01FA95
Macrolides	QJ01FF02; QJ01FF52
iviaci oliues	QJ51RF03
	QJ51FF90
	QJ01CA01; QJ01CA04; QJ01CA51
	QJ51RC26
Penicillins	QJ01CR02
. Chichinis	QJ51CF02
	QJ01CE02; QJ01CE09; QJ01CE30; QJ01CE90
	QJ51CA51
Polymyxins	QJ01XB01

	QA07AA10
	QS02AA11
Pyrimidines	QJ01EW10; QJ01EW13
	QJ01EA01
Quinolones	QJ01MA90; QJ01MA92; QJ01MA93; QJ01MA94; QJ01MA95; QJ01MA96
	QJ01MB07
Sulphonamides and trimethoprim	QJ01EW09; QJ01EW11; QJ01EW12
	QJ01EQ03
tetracyclines	QJ01AA02; QJ01AA03; QJ01AA06
	QD06AA02; QD06AA03