Ministry of Food, Agriculture and Fisheries of Denmark
Danish Veterinary and Food Administration

# Real-time use data collection demonstrates behavioural changes in antimicrobial usage

**Laura Mie Jensen**, Frederik Fabricius, Pia Holm Jul

AACTING, Vienna
1.-2. February 2024
Laura Mie Jensen

# Withdraw of the zinc oxide as medicinal product

Marketing authorizations for veterinary medicinal products containing medicinal zinc oxide must be withdrawn in all EU member states with effect from 26 June 2022 at the latest

EUROPA-KOMMISSIONEN

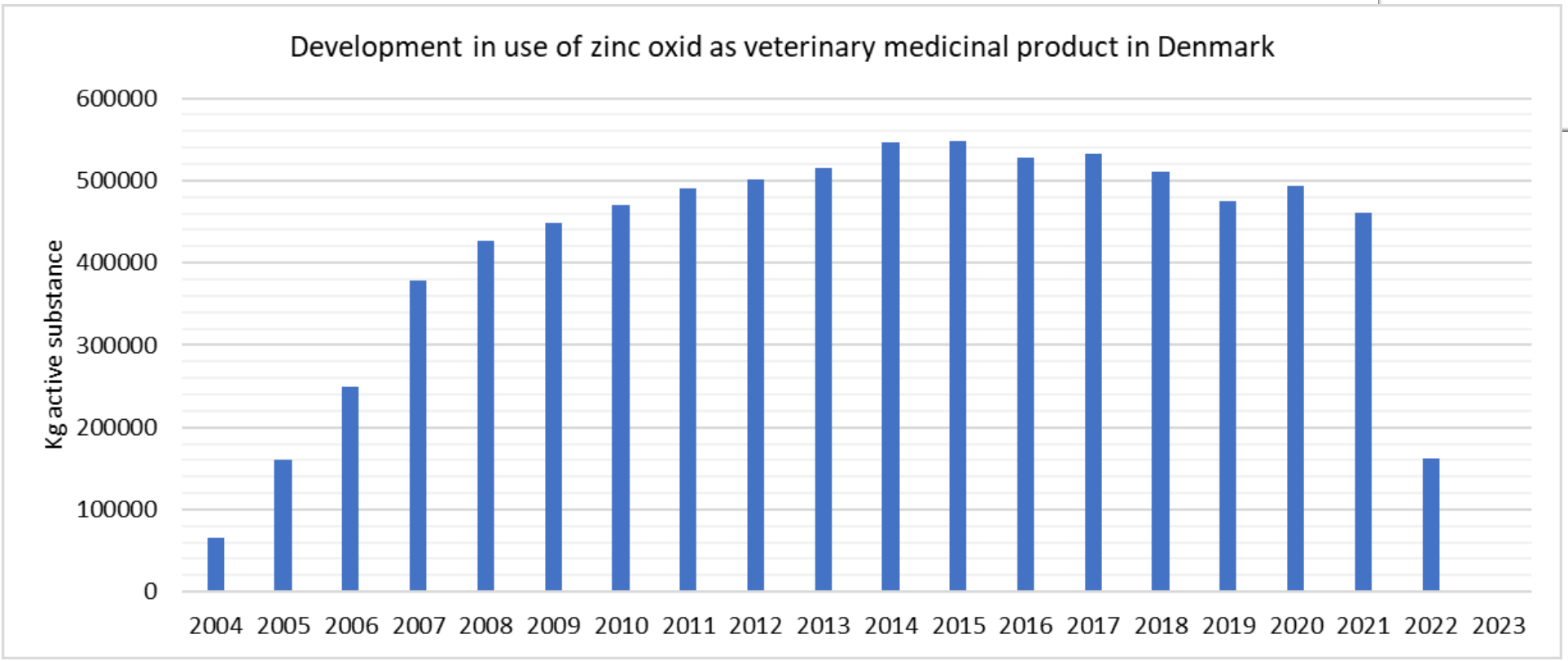
Bruxelles, den 26.6.2017
C(2017) 4529 final

**KOMMISSIONENS GENNEMFØRELSESAFGØRELSE**

**af 26.6.2017**

**om markedsføringstilladelserne for veterinærlægemidler, der indeholder zinkoxid, som indgives oralt til arter bestemt til fødevareproduktion, jf. artikel 35 i Europa-Parlamentets og Rådets direktiv 2001/82/EF**

(EØS-relevant tekst)



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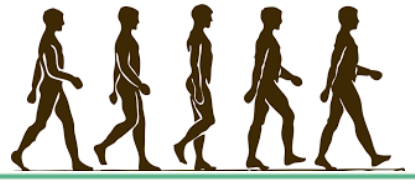
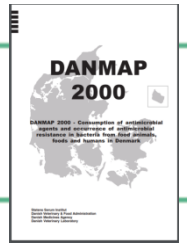
**1994**
Monitoring of all use for humans



**1994**
Herd Advisory Contracts
Vet's: No profit on VMP sale

Det Nationale Antibiotikaråd

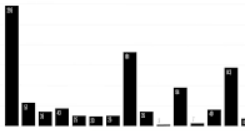



**1995**
DANMAP

**1995-1999**
Industry ban on antimicrobial growth promotors

STOP

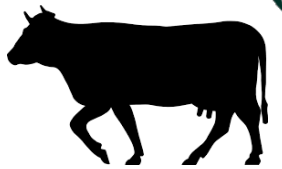
**2000**
National ban on AGP's



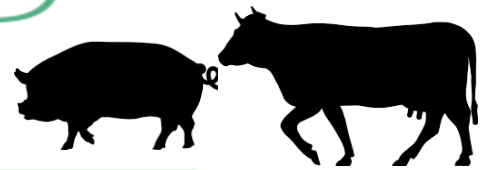
**2000**
VetStat data collection

**2002**
Restriction on CIA: fluoroquinolon

**2010**
Restriction: only simple penicillins for mastitis



**2010**
Yellow card initiative
Benchmarks for pigs and cattle



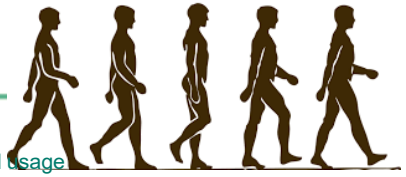
STOP

**2010**
Pig industry ban on CIA: 3rd/4th cephalosporin

**2013**
Tax on antimicrobials

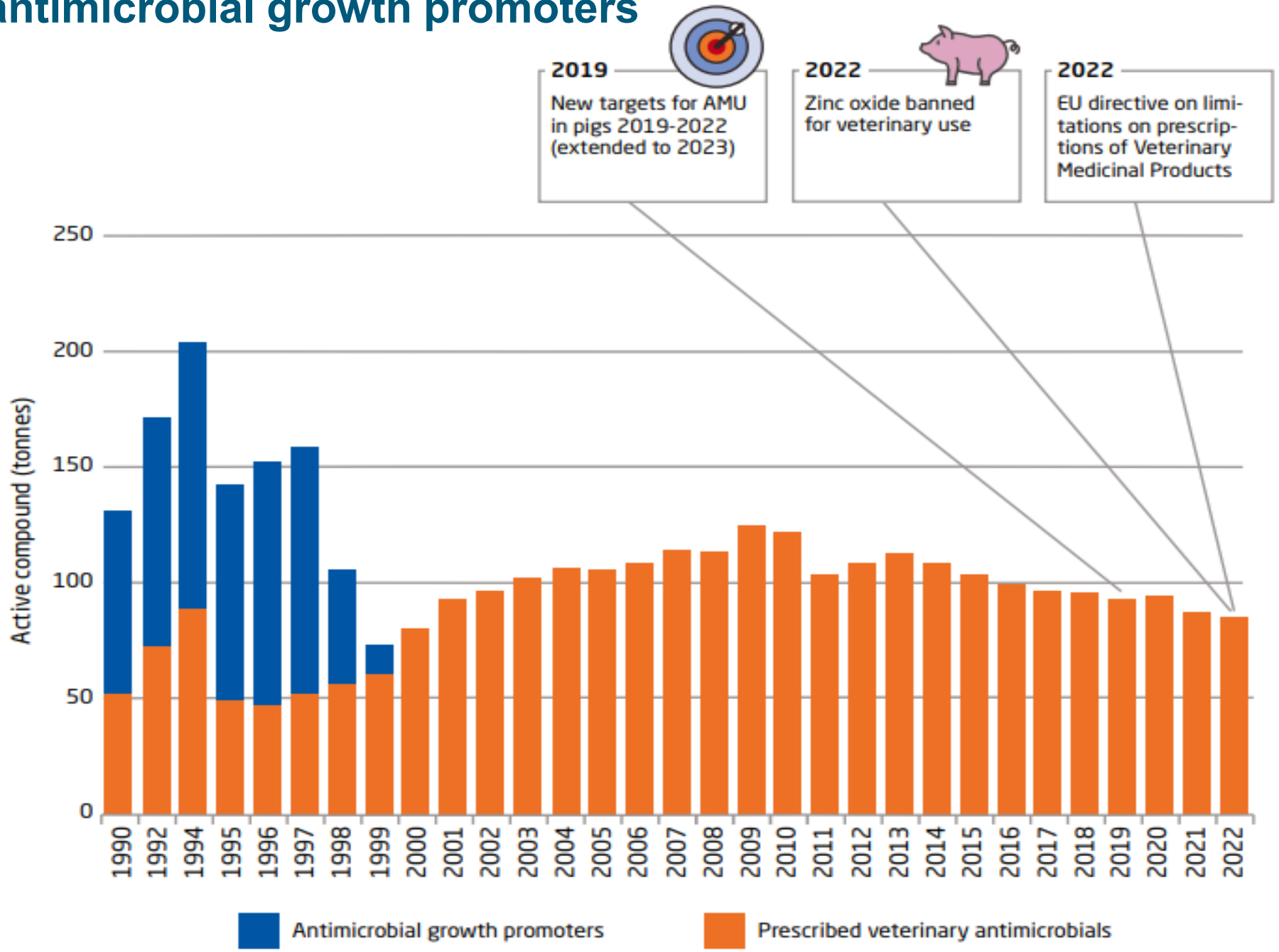
**2016 -2017**
New Yellow Card Initiative for pigs - risk of AMR


**2017**
National One Health Strategy



# Phasing out antimicrobial growth promoters

Graphics from DANMAP, 2022
(www.danmap.org)

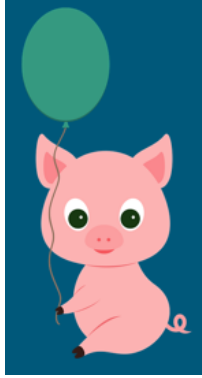


# Intervention triggers shift – 'Balloon effect'

Ministry of Environment and Food of Denmark
Danish Veterinary and Food Administration

## The 'balloon effect' – intervention triggers shift between antimicrobial classes

How interventions on one substance effect other substances – for gastrointestinal disorders in weaner pigs



AACTING, Bern

1.-2. July 2019
Laura Mie Jensen

**The 'balloon effect' – intervention triggers shift between antimicrobial classes** - How interventions on one substance effect other substances – for gastrointestinal disorders in weaner pigs

**Laura Mie Jensen**[1] and Elisabeth Okholm Nielsen[1]
[1]Danish Veterinary and Food Administration;

The 'Yellow card' initiative with threshold values for pigs has been in place in Denmark since 2010. In 2015 it was decided to promote a more prudent use. Differentiation between antimicrobial classes in the 'Yellow card' initiative was chosen as the regulatory framework, and the technical dose values were weighted into three categories in 2016 and modified in 2017. The three categories are: **a)** Flouroquinolones, 3.-4. gen. cephalosporins and colistin – factor 10, **b)** Tetracyclines – factor 1.5 and **c)** Other antimicrobials – factor 1.0. The use of fluoroquinolones and 3rd/4th generation cephalosporins is negligible in Denmark; therefore in reality only colistin is weighted with a factor 10. The 'balloon effect' of the intervention on tetracyclines and colistin is investigated in this paper.

Tetracyclines and colistin are mostly used for gastroenteric disorders in weaner pigs. The intervention resulted in an immediately change of the consumption. Tetracycline was reduced from app. 12 tons to app. seven tons active compound from 2016 to 2018 and colistin dropped from app. one tons to less than one kg active compound. In both cases an obvious 'balloon effect' was observed. 'Balloon effect' is when the reduction of one antimicrobial class results in a similar increase in another. Like when you squeeze on a balloon, the air pops up in different places. The reduction in tetracyclines resulted in a marked increase in macrolides, whereas the reduction in colistin was shifted to an increase in aminoglycosides – hence 'balloon effect'.

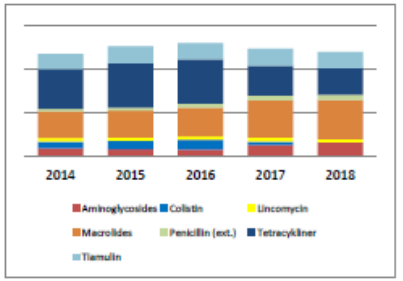



**Figure 1.** The most used antimicrobials for weaner pigs - gastroenteric disorder - kg-doses (y-axis not shown)

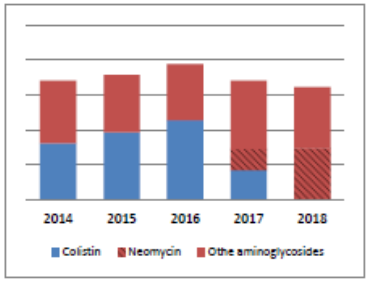
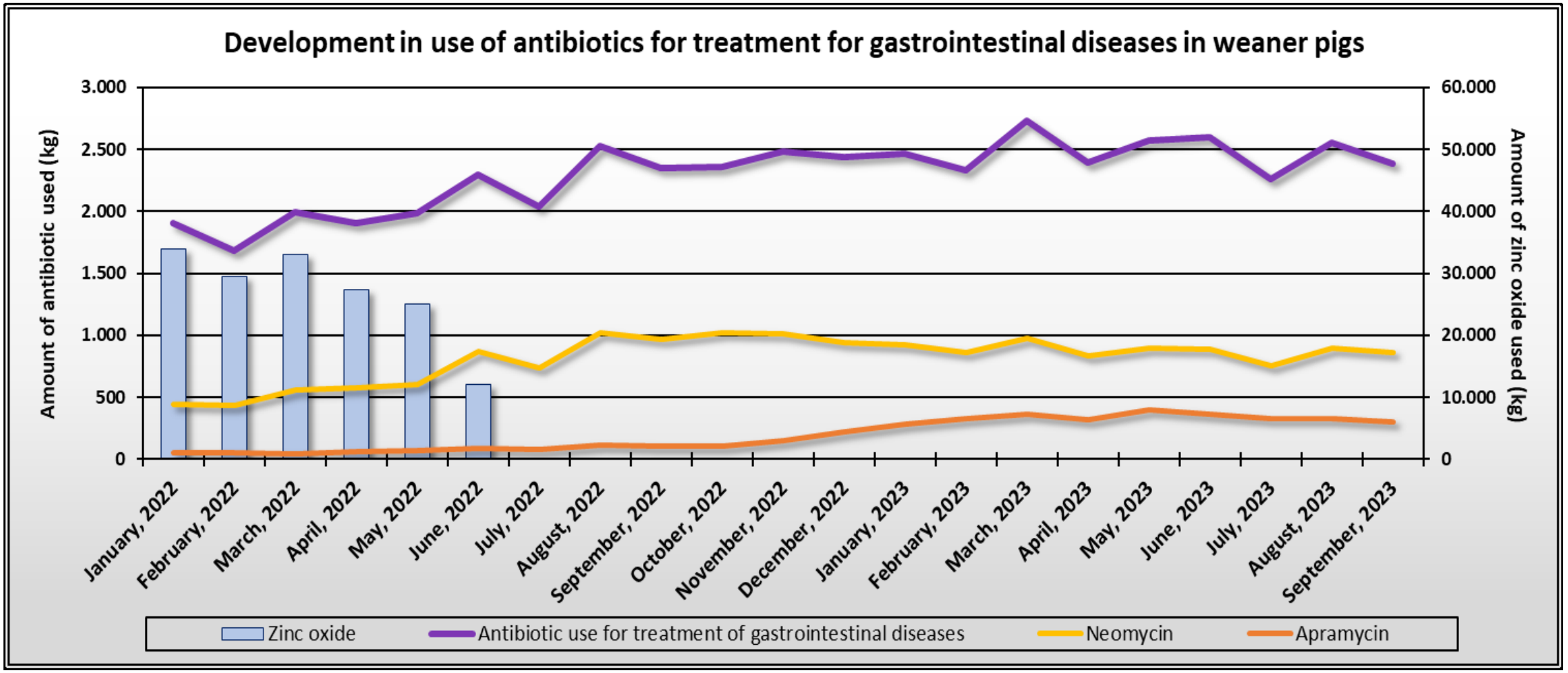



**Figure 2.** Colistin and aminoglycosides of that neomycin used for weaner pigs - gastroenteric disorder - kg-doses (y-axis not shown)

Figure 1 and 2 demonstrates the 'balloon effect' of the intervention. A marked reduction in the use of tetracyclines (40 %) was replaced by an increased use of macrolides (35%, Figure 1). In Figure 2 the reduction and shift between colistin and aminoglycosides, mostly neomycin, is demonstrated. Neomycin was reintroduced to the Danish market in 2017, and seems to be used as an alternative for colistin. The almost complete phase out of colistin has resulted in an increased use of aminoglycoside between 2016 and 2018 of 101 % (Figure 2).

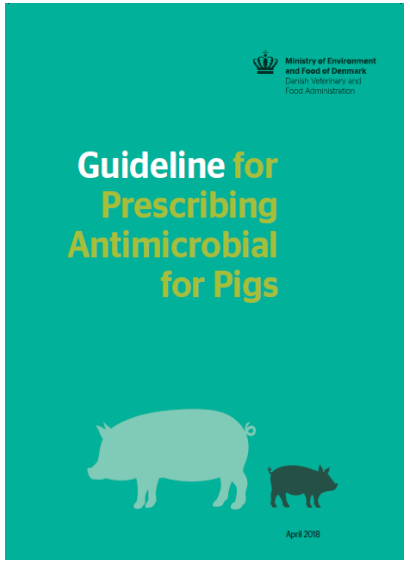
**Conclusion**
The intervention has triggered a shift between antimicrobial classes. If the access of an important antimicrobial is limited, the consumption may shift to another class or active substance, based on availability and cost-effectiveness and the use is therefore not only reduced but also replaced. An intervention may in some cases result in a total swap hence, the 'balloon effect'.

# Development in use of antimicrobial treatment after withdraw of zinc oxide



# Guideline for prescribing antimicrobial for piges in Denmark

| The Danish Veterinary and Food Administration Recommendations | Antimicrobial |
|---|---|
| **GROUP 1**<br>First line antimicrobials. To be used when a veterinarian has determined that an antimicrobial treatment is necessary | • Florphenicol<br>• Lincomycin<br>• Macrolides<br>(e.g. tylosin, tylvalosin, tilmicosin, tildipirosin, tulathromycin, gamithromycin)<br>• Neomycin<br>• Penicillins, narrow-spectrum<br>(e.g. benzylpenicillin, benethaminpenicillin, phenoxymethylpenicillin)<br>• Penicillins, broad-spectrum<br>(e.g. amoxycillin, ampicillin possibly with clavulanic acid)<br>• Pleuromutilins<br>(e.g. tiamulin, valnemulin)<br>• Sulfonamides<br>(e.g. sulfadizine, sulfadimidine, sulfadoxine possibly in combination with trimethoprim)<br>• Spectinomycin<br>• Streptomycin |
| **GROUP 2**<br>Alternative antimicrobials when first line antimicrobials are not effective | • Apramycin<br>• Gentamicin<br>• Tetracycline<br>(e.g. chlortetracycline, oxytetracycline, doxycy |
| **GROUP 3**<br>These antimicrobials should not be used in pigs | • 3rd and 4th generation cephalosporins<br>(e.g. ceftiofur, cefquinome)<br>• Colistin<br>• Fluoroquinolones<br>(e.g. enrofloxacin) |

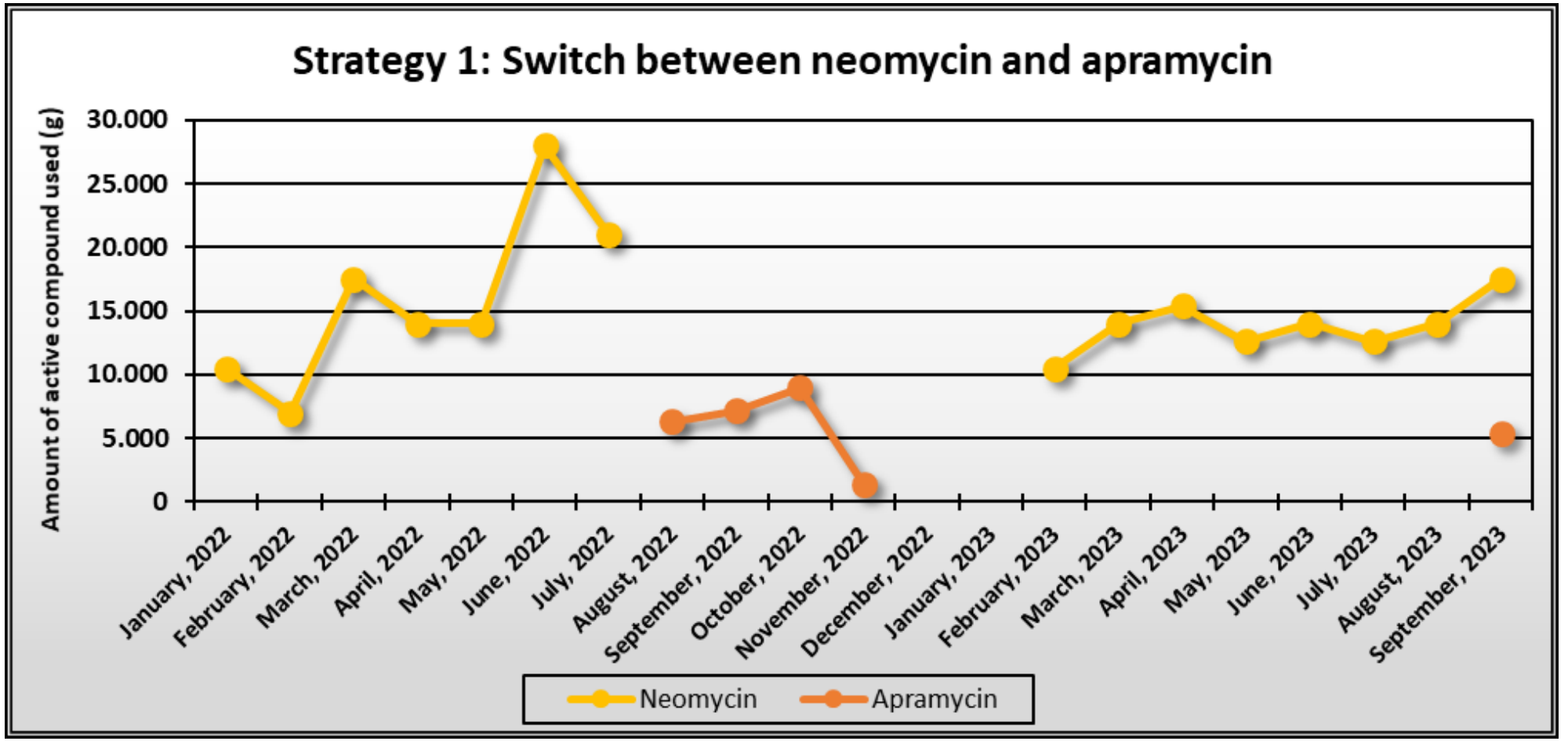



**Sensitivity of Important Intestinal Bacteria to Different Antimicrobials***
**First choice antimicrobials are highligted in bold green.**

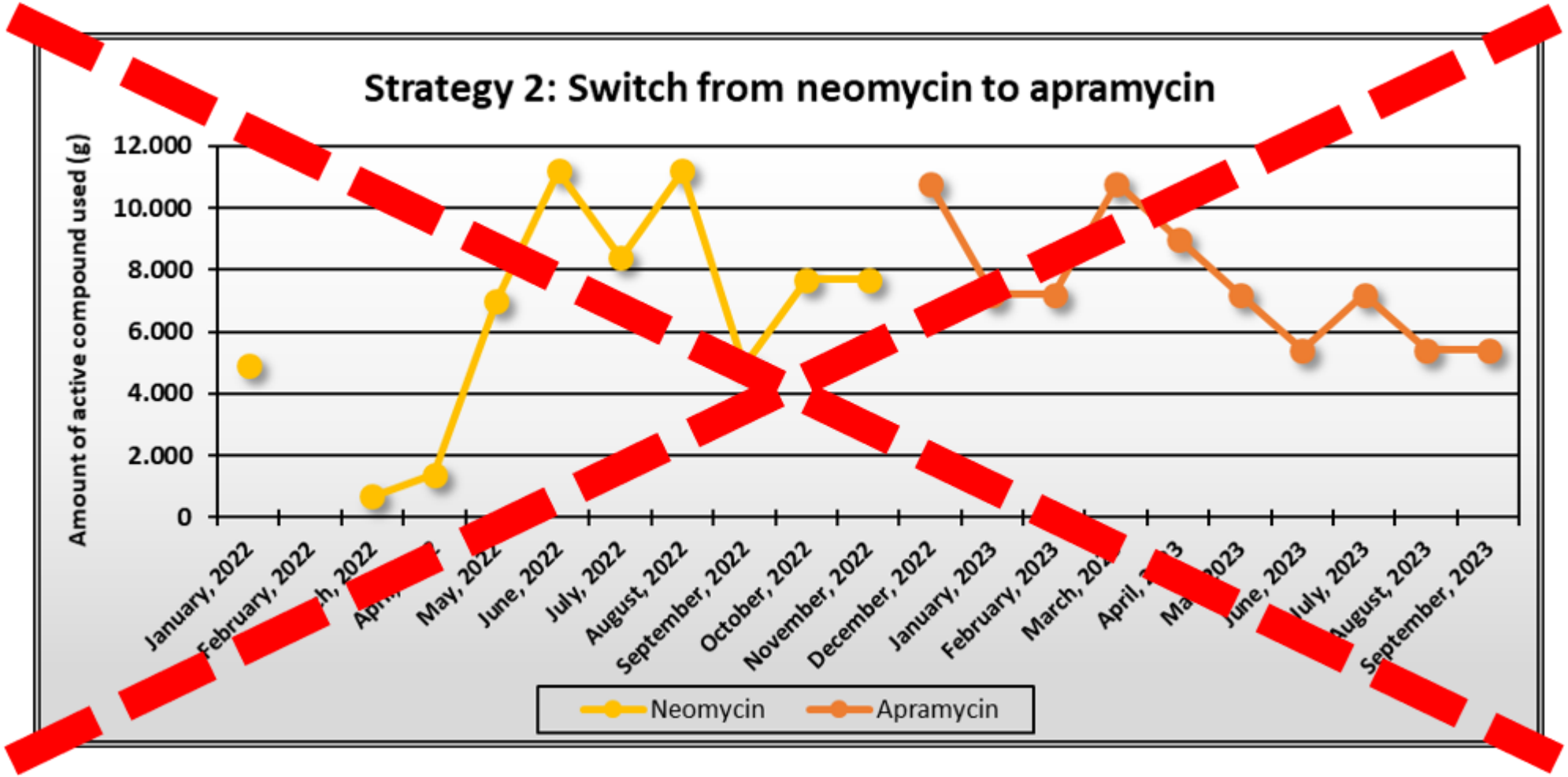
| Porcine intestinal bacteria | Sensitive (>75%) | Intermediate sensitivity | Less sensitive/resistant |
|---|---|---|---|
| **L. intracellularis** | Tiamulin<br>Valnemulin | Tylosin<br>Tylvalosin<br>Tetracyklin | Lincomycin |
| **B. pilosicoli** | Tiamulin<br>Tylvalosin<br>Valnemulin<br>Tetracycline | | Tylosin |
| **E. coli **** | Amoxicillin/ clavulanic acid<br>Florfenicol<br>Neomycin<br>Apramycin<br>Colistin<br>Gentamicin | Ampicillin<br>Spectinomycin<br>TMP-sulfa<br>Streptomycin<br>Tetracycline | |

* Data from sensitivity testing of pathogenic bacteria in pig in Denmark can be found on the homepage of Danish Technical University
** It is recommended that E. coli (F4 and F18) is examined for resistance for optimal treatment outcome

# Switch between neomycin and apramycin



# Switch from neomycin to apramycin



# The use of real-time data – results in small-scale interventions

- With access to real-time data on use of antibiotics, the DVFA was able to identify challenges from the withdrawal of medicinal zinc early.
- This enabled the DVFA to quickly reach out to stakeholders and engage into dialog on possible interventions.
- The data also serves as early-warning to steer risk assessment and management.
- Real-time use data also supplements AMR surveillance data as changes in treatment strategy can reveal resistance bacteria on the farms.
- Main challenge: political mandate and support is required to implement effective interventions that can successfully reduce unwanted use.

**➔ Conclusion: real-time use data can support timely interventions and steer risk assessment and management**

# Thank you!

vetstat.fvst.dk