

Availability of antimicrobial VMPs

experience from the Czech Republic

1st March 2024

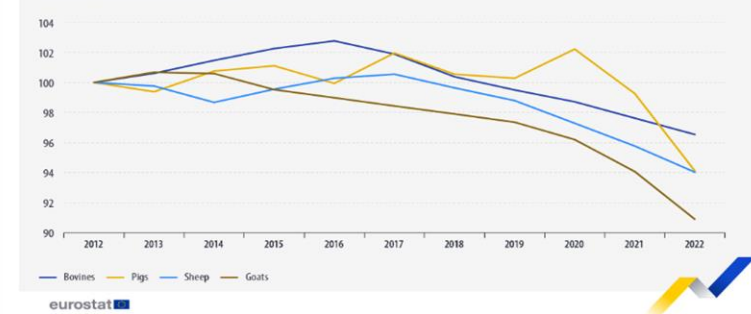


Considering the context ... Not only antimicrobials alone ... Animal health + welfare + One Health + Socio-economic...

Decrease for all livestock species over the past decade

Over the past decade, the livestock population decreased for all species. The goat population experienced the sharpest decline in this period (-9 index points in 2022 compared with 2012). Until 2020, the pig population was an exception to this trend; however, it has since caught up with the rest of the species, with remarkable declines in each of the past two years.

Livestock population in the EU, November/December 2012-2022
(Index 2012=100, based on head of livestock)



Source datasets: [apro_mt_lscatl](#), [apro_mt_lspig](#), [apro_mt_ls sheep](#) and [apro_mt_lsgoat](#)

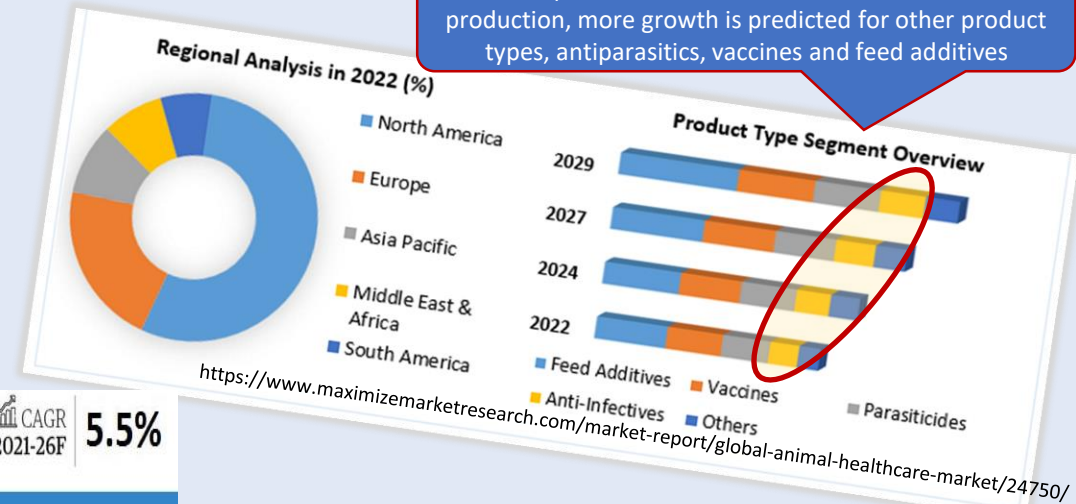


<https://fefac.eu/newsroom/news/the-future-of-livestock-in-the-eu-and-beyond-working-together-towards-ending-polarization-around-animal-husbandry/>

EUROPE VETERINARY VACCINES MARKET

Europe Veterinary Vaccines Market is predicted to grow at a CAGR of around 5.5% during (2021-26)

CAGR 2021-26F **5.5%**



„AHCare“ products: Still some increase of anti-infectives production, more growth is predicted for other product types, antiparasitics, vaccines and feed additives

<https://www.maximizemarketresearch.com/market-report/global-animal-healthcare-market/24750/>

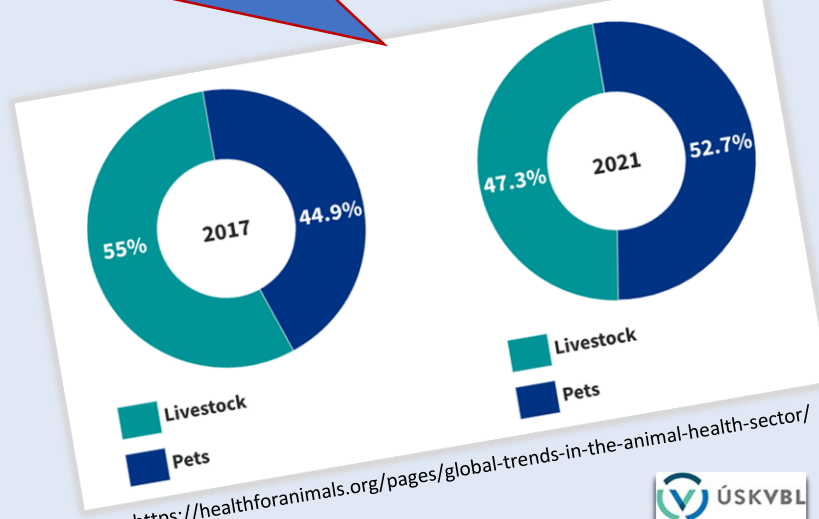
Increase of veterinary injectable devices segment predicted

Prediction 2035: Mostly due to **Companion animals' care**

DRIVERS

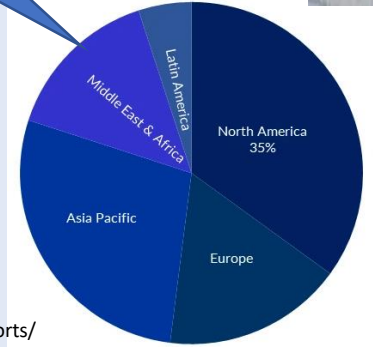
- 01 Increasing awareness about animal health and snowballing incidences of zoonotic and livestock disease.
- 02 Burgeoning investment by the companies in veterinary healthcare.
- 03 Escalating demand for poultry vaccine and upsurge in the number of households owning at least one pet.

„AH Care“ Product sales livestock/pets (2017 vs 2021)



Growth Drivers

- Growing Demand for Animal Healthcare
- Advancements in Technology
- Increasing Prevalence of Zoonotic Diseases
- High Cost of Veterinary Care
- Injuries and Infections due to Needles



<https://www.researchnester.com/reports/veterinary-injectable-devices-market/871>

Approved: 8 November 2023
DOI: 10.2903/j.efsa.2023.8442

SCIENTIFIC REPORT



The European Union One Health 2022 Zoonoses Report

European Food Safety Authority (EFSA) | European Centre for Disease Prevention and Control (ECDC)

<https://healthforanimals.org/pages/global-trends-in-the-animal-health-sector/>



Political / socio-economic context of VMPs availability / affordability – possible major drivers

- Market size / perspective

Current/future EU an attractive market (?)

- Impact of F2F on agriculture/food production – reducing the production
- Antimicrobial policies stronger than outside EU – food and animals import

- Competition

Does competition in the EU fulfill its role (?)

Merges and Acquisitions – are we considering the impact at the EU level?

- Business / investment environment

Is the EU business environment attractive (?)

- Stability/predictability for enterprises
 - (Original) proposal by the EP for the list of antimicrobials reserved for human use
- EU still competitive to other regions? Incentives / subsidies implemented by other countries / regions.

- Red tape status

Is the current level of centralisation / harmonisation still effective?

- Can we effectively take advantage of the skills / knowledge available across the EU?
- Does the system allow new enterprises on the market? Spin-offs/academia/SMEs to bring new ideas/products/competition?

- Incentives

Are incentives provided to the correct objectives / subjects (?)

- E.g. „Old products“ data update – considering all risks (example referral benzyIPNC)
- Building capacity for API manufacture

- Purchase power of customers

Purchase power of customers – perspective (?)

- Pet owners – increasing living costs
- Food producing species – impact of F2F on farming
- Farmer’s position in value chain for agricultural products – decreasing

- Policies in related areas

From socio-economical perspective: Agriculture not that important – decrease in production expected

- Policies leading in fact to more reliance on imports of food from the third countries
- EU economy development has started to lag behind other regions

Factors that can potentially affect availability of VMPs

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No marketing authorisation

=> VMP not placed on the market

Shortages due to:

- Troubles on manufacturers side
 - manufacturing defects
 - shortages of API
 - shortages of packaging material
- Decline of production
- Switch to another VMPs portfolio
- Withdrawals of MA

Market potential/commerciality:

- Small market
- Low economic power of the market
- Shipping/packaging costs
 - Minor species/use
- Legal rules in certain MS as for distribution chain

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Factors that could help:

- Marketing authorization
 - (including relevant package sizes)
- Multilingual packages
 - (harmonised text/ pictograms)
- Legal rules in certain MS as for permission for market entry in a language other than official in MS (e.g. if small volumes marketed per year / immediate packages in EN/DE in CZ)
- Provide list of essential „antimicrobials“ (or generally VMPs) with commented alternatives
- **Using cascade rules** (according legislative)
 - ... Nationally could be stricter rules for antimicrobials: (EU) 2019/6 Art 107/7
- Precise/legally valid – but as well flexible system of import of VMPs =>

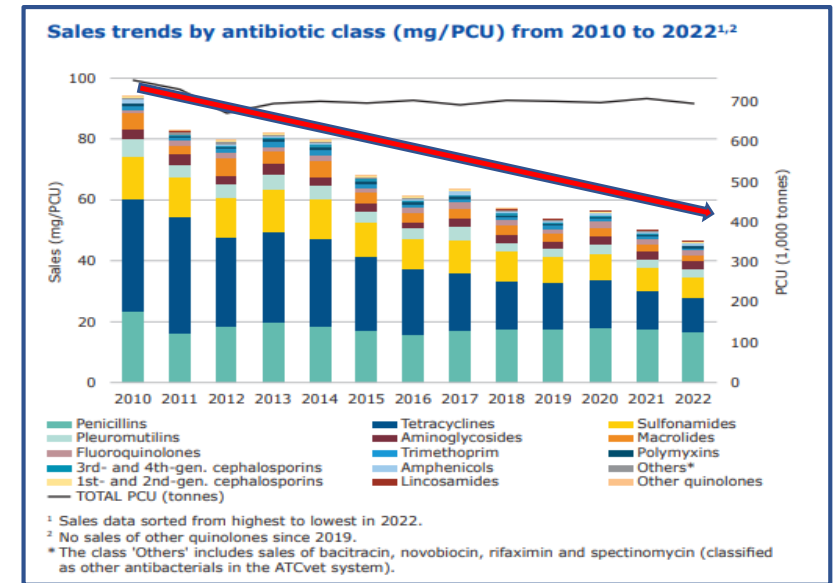
Necessary prerequisite is to have the VMP on EU market (manufacturing capacity + API availability for Europe!)

CZ: Trend in withdrawal of the MA

Since 2010 approx 50% decrease of sales of antimicrobials in CZ

Total 91 withdrawn antimicrobials containing VMPs in 5 year period in CZ

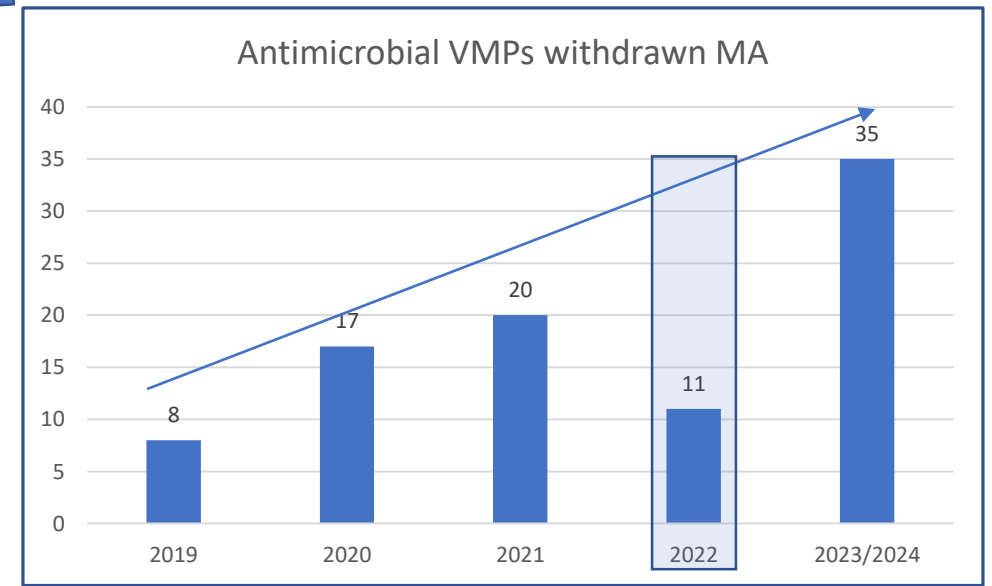
- Within year 2022/2023:
 - total 46 antimicrobials
 - total 26 immunologicals
 - other VMPs linked to infectious diseases prevention, therapy (incl adjuvant therapy) as well (e.g. ZnO and NSAIDs)!



Will this trend continue or will be more steep?

Afraid from more steep trend in withdrawal is based on following facts:

- Further decrease of use of antimicrobials
- Low commercial interest to supply small market ... further promoted by fact that:
 - Some MAHs perform now very thorough analysis of costs linked with updating product texts to be in line with Reg (EU) 2019/6 requirements and new QRD templates and those VMPs, for which sales are low are therefore put under the scrutiny, if invest effort (human/budgetary resources to them) => already indicated further MA withdrawal
- Production of API outside of EU ... EU market is becoming „too small“ as markets outside of EU with higher AM consumption bringing more profit and therefore will be preferably supplied with antimicrobial VMPs

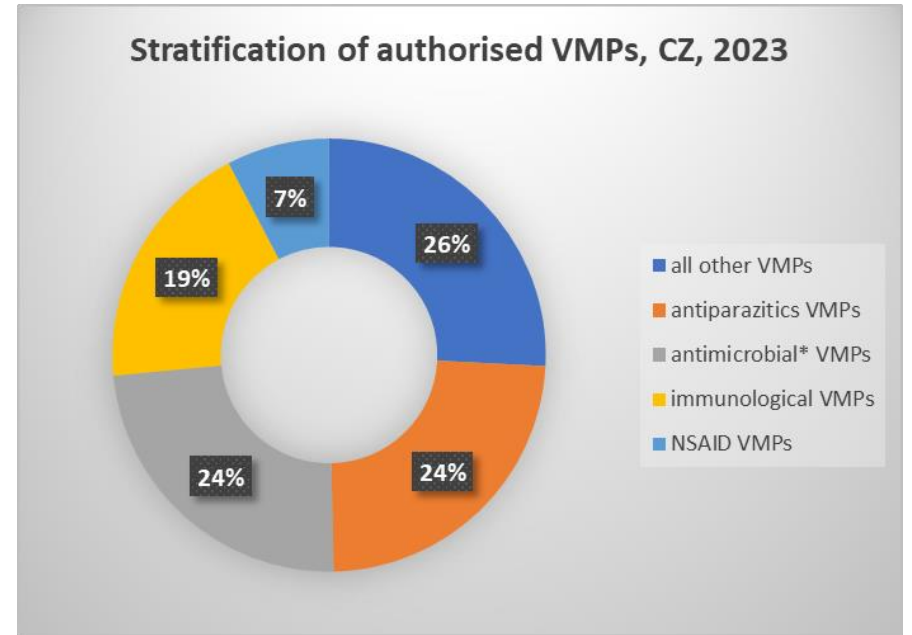


Note: 2023/2024 (some MA withdrawn at the end of 2023 and formal procedure finished in first days of 2024)

VMPs with marketing authorisations valid in 2023 (CZ)

Proportion of **authorised** VMPs (according MA numbers; till 31.12. 2023)

2 100	all VMPs
500	antimicrobial* VMPs
501	antiparasitic VMPs
396	all immunological VMPs
161	NSAID VMPs
542	others



all other VMPs	542
antiparasitics VMPs	501
antimicrobial* VMPs	500
immunological VMPs	396
NSAID VMPs	161

* Incl antimycotics, without sole antiprotozoals (76 VMPs, included under antiparasitics - QP ATCvet)

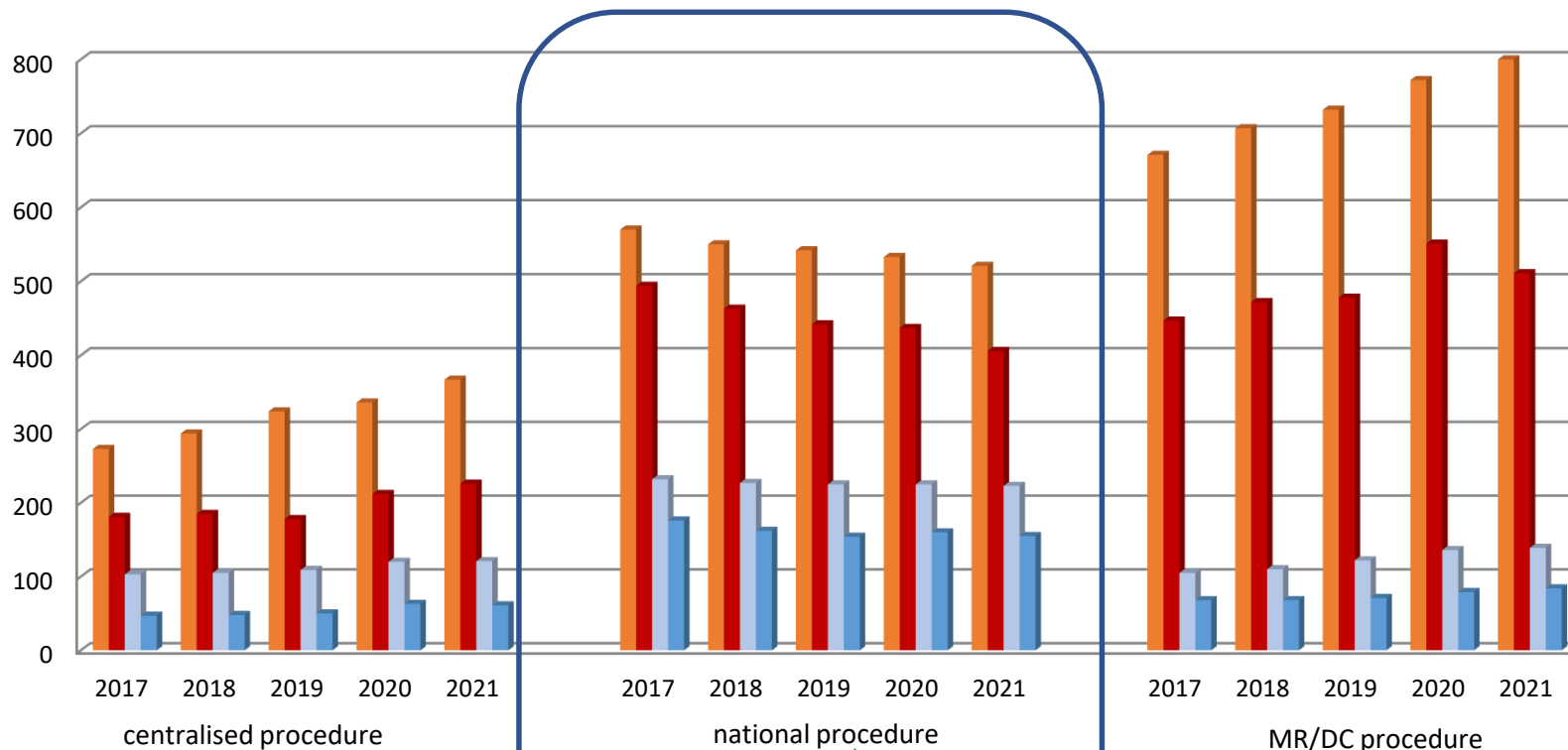
Stratification by authorisation procedure

National	Imuno/159
MRP/SRP/DCP	Imuno/129 (69/3/57)
Central	Imuno/108

Antimicrobial/207
Antimicrobial/254 (54/1/199)
Antimicrobial/38

Comparison of authorised VMPs market availability within different procedures of MA (Czech Republic)

Numbers of authorised and marketed products by procedure over 5 years



Highest **proportion** of marketed VMPs those authorised nationally

Due to increasing numbers of MA via **DCP/MRP in pharmaceuticals =>** DCP/MRP started to prevail those VMPs authorised via NP (and CP):
2021: 511 (MRP/DCP) > 406 (NP) >> 226 (CP)

Immunologicals: nationally authorised are mostly marketed:
2021: 223 (NP) > 139 (MRP/DCP) > 121 (CP)

- Pharmaceuticals authorised
- Pharmaceuticals marketed
- Immunological authorised
- Immunologicals marketed

Pharmaceuticals:
54.9% - 66.3 %
marketed

Immunologicals:
45.6% - 52.5 %
marketed

Pharmaceuticals:
77.9% - 86.7 %
marketed

Immunologicals:
68.4% - 75.9 %
marketed

Pharmaceuticals:
63.9% - 71.4 %
marketed

Immunologicals:
58.1% - 64.8 %
marketed

Trends in antimicrobial active substances portfolio (CZ)

2017 - 2023, CZ

- Availability of the **active substances** (individual antimicrobials) stable
- 60 antimicrobials (2017) => 58 antimicrobials (2023)
- Antimicrobial classes still well represented => portfolio of antimicrobials for major species available, for minor species lost of flumequin
 - **2 antimicrobials lost**
 - **FLUMEQUIN (QUINOLONE) ... MA withdrawn**
 - FQs still available ENROFLOXACIN ... MARBOFLOXACIN (only INJ), PRADOXACIN (only TAB)
 - but VMP containing (fluoro) quinolones **no more available for certain species ... fish, goat, sheep**
 - **SULFADIMETHOXINE (other SULPHONAMIDES available)**
 - still available other sulphonamides

Real availability of antimicrobial VMPs on CZ market (2023): **centrally** authorised

Centrally authorised **38 AM** VMPs (status 31.12. 2023)

No AMEG „**D**“ antimicrobials authorised via CP!

From 38 AM centrally authorised **52.6%** available in CZ (2023):

- 15 systemic (ATC_{vet} QJ; from these):

- 2 cephalosporins 3rd gen
- 2 pradofloxacin
- 7 tulathromycin (generic!) containing VMPs (in total 10 macrolides)
- 1 florfenicol (fixed combination + NSAID)

- 5 topical (ATC_{vet} QS; mostly fixed combinations)

4 **HPCIA*** AMEG B

10 **CIA*** AMEG C

1 **HIA*** AMEG C

Real availability of antimicrobial VMPs (MRP/DCP/SRP) 2023

- Portfolio of available antimicrobials covers AMEG categories B-C-D
- CZ, 2023: 254 authorised / 151 marketed => **59.4 %**

Real availability of antimicrobial VMPs (national authorised)

- Portfolio of available antimicrobials covers AMEG categories B-C-D
- 207 authorised / 160 marketed => **77,3 %** (2023)

MRP/DCP/Nationally authorised ... shortages/non-availability appeared (e.g. necessity of import + if small volumes marketed per year / immediate packages in EN; or ask for keeping of already marketed batches in old QRD templates => needs for individual cases assessment/check) :

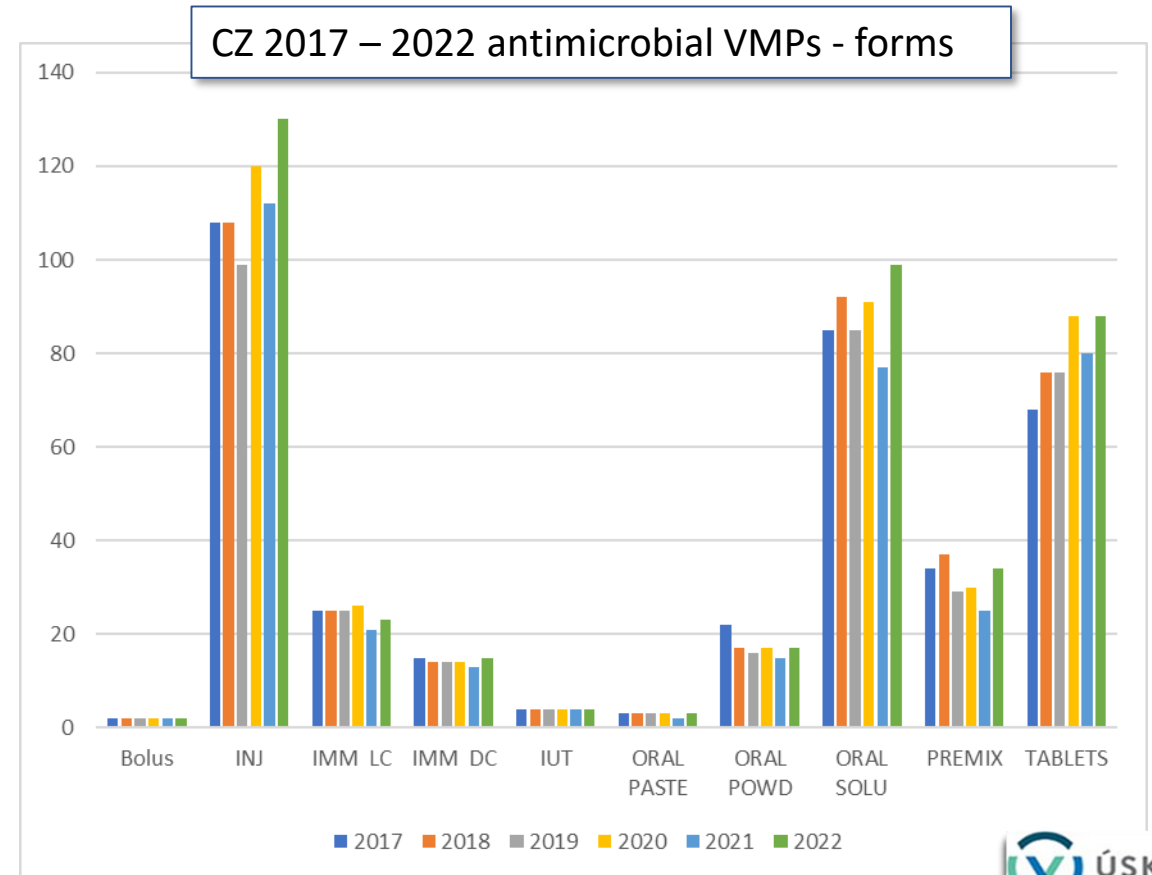
2022: 19 antimicrobial VMPs ; 8 vaccines

2023: 10 antimicrobial VMPs ; 5 vaccines

Trends in consumption of antimicrobial VMPs according pharmaceutical forms/routes of administrations

Consumption by forms/routes (in columns numbers of VMPs (counted as MA numbers) marketed i.e. available across years

FORM	2017	2018	2019	2020	2021	2022
Bolus	2	2	2	2	2	2
INJ	108	108	99	120	112	130
IMM LC	25	25	25	26	21	23
IMM DC	15	14	14	14	13	15
IUT	4	4	4	4	4	4
ORAL PASTE	3	3	3	3	2	3
ORAL POWD	22	17	16	17	15	17
ORAL SOLU	85	92	85	91	77	99
PREMIX	34	37	29	30	25	34
TABLETS	68	76	76	88	80	88



- **Injectables** (increase – long term trend continuing)
- **Tablets increase** (should be evaluated together with trends of generics as well as trend of HMPs)
- **Oral powder + premix long term decrease** pronounced significance especially in long term, but 2022 back to higher proportion (pig sector, ban of ZnO?)
- **Oral solutions - oscillation**
- **Other forms stable trends in assessed time period**

Availability of antimicrobials: example



- **Rabbits** (as an example of minor species, CZ):
 - CZ: Several VMPs authorised (nationally, MRP/DCP or even CP MIA)
 - But low/no availability of VMPs in CZ for indication ERE (necrotic enteritis)
 - Special licence - exemptions (imports from other MSs in previous years)
 - Issue have started in 2022 when availability of 2 VMPs was lost (last packages imported to CZ expired and no other available even in other MSs/EU market)
 - Once population of animals is below of the threshold of „economical interest“
 - hardly to be organized import + mixing into medicated feed
 - Situation improved since 2Q 2023 with generic VMP authorisation in Spain => but still need to issue exemption (CZ Law on pharmaceuticals + organise import + mixing into MF in licensed feed mill)

Shortages/lack of availability of antimicrobials: some examples from MSs

- Injectables (shortages):
 - SUL/TRI
 - PNC (or PNC/DHSTM)
 - AMO/CLA
- Orally administered aminoglycosides
 - NEO
 - APR
 - PAR
- MSs with very low use of AMEG „B“ category antimicrobials
 - Lack of availability of VMPs (injectable) containing CEF 3/4 and FQ to treat serious cases
⇒ need for import from countries where sales are high(er)

Some countries also reported (within ESVAC reports) Sales (consumption) of antimicrobials based on special licence => Table 2 in ESVAC reports, examples those reporting and with low consumption of antimicrobials :

	2020	2021	2022
Iceland	11.1%	15.5%	30%
Norway	6.9%	18.9%	11.2%
Sweden	10.2%	10.9%	13.6%
Finland	5.7%	8%	8%
Latvia		3.4%	6.75%

Some answers ?

(rather from expert point of view)

- **MSs level:**

- Work on priority indications/per species a identification of the gaps in availability of VMPs
 - preventive (e.g. **vaccines**) +
 - therapeutic (**antimicrobials**)

- **Regional level:**

- Work on sharing of data for countries with similarities (e.g. language DE/AT ... FR/BE ... CZ/SK/PL)

- **European level:**

- Stable and predictable „environment“
- Promotion of professional skills => need for strengthening educational capacities in technical, pharma technologies and pharmacology => bringing API and medicinal products manufacturing back to EU
- Leaders „medicines“ experts (and not only economists/lawyers)
- Identify priority VMPs to be available
- Not forgetting AMEG „D“ antimicrobials
- Start to cooperate with human thinking on threat of zoonosis

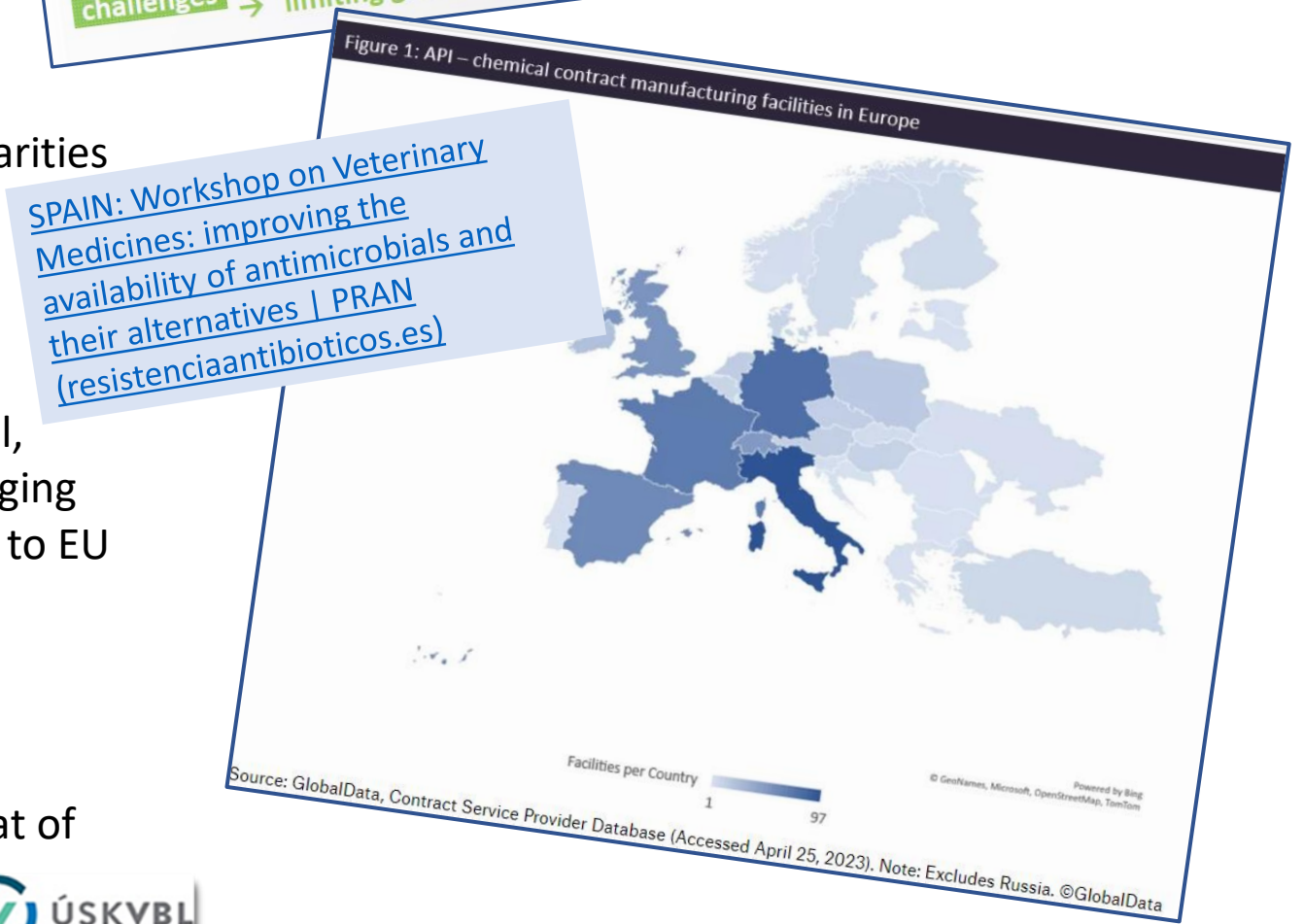
9 > animal & human have to share a single pharmacopeia

HEALTH challenges

- > sharing anti-infectious drugs
- > global management of pathogen resistance to anti-infectious drugs

→ promoting a prudent & sustainable use of anti-infectious drugs

→ limiting growth-promoter use and preventive use of antibiotics





Thank you for your attention!

Questions/comments ?

