

Veterinary perspective of tackling AMR: at the national context of the „One Health“ concept



Lucie Pokludová

PRAGUE, 26th Nov 2018

JAMRAI, Ministry of Health CZ

Content

- National Antibiotic programme and Action plan(s)
- „CZ One health“ concept – history and present
- Steps to ensure good practices of use of antimicrobials in veterinary medicine
 - Regulatory/restrictive
 - Positive: education/innovation/communication
- Veterinary antimicrobials consumption – trends
- Target veterinary pathogens monitoring
- Examples from practices
 - Disease prevention /Disease control
 - Diagnostic tools
- Future
- Conclusions

CZ – long-term tradition of „One health“ concept: cooperation HUM-VET

CZ „Antibiotic policy“ started in 90ties,

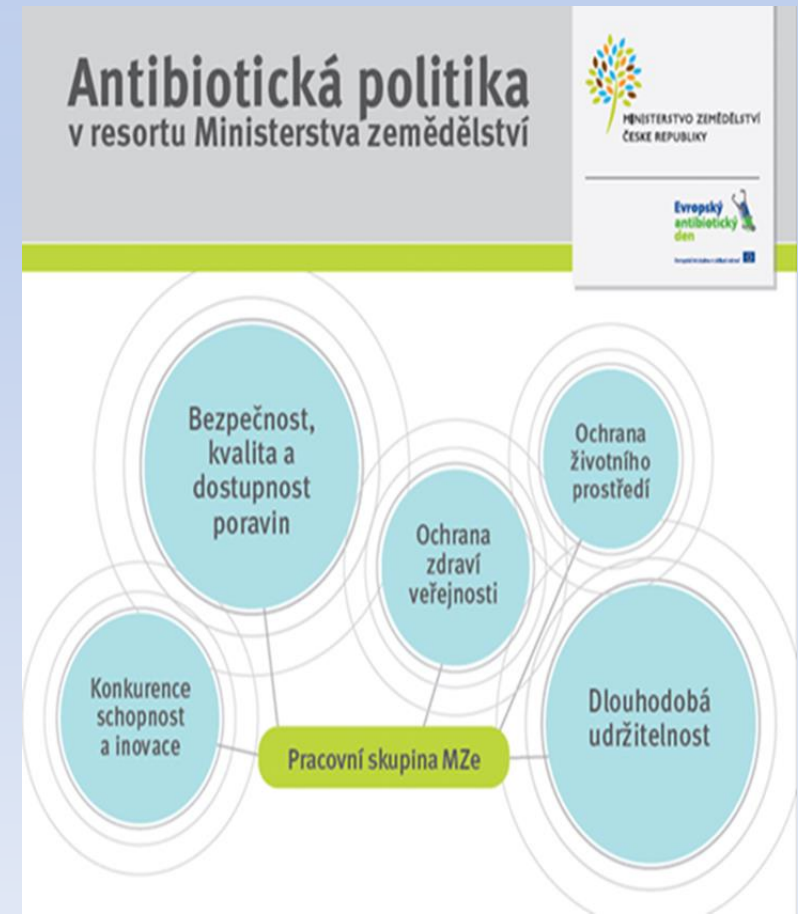
„One health“ = systematic, long term,
Human + veterinary cooperation

**National Antibiotic Policy/Programme
since 1995**

2013 established at the Ministry of Agriculture
Working Group on antimicrobials

Currently **final stage of approval of
Action plan CZ 2019–2022**
within the framework of the National
Antibiotic Programme

First AP in CZ: 2011 – 2013 (hum+ vet)



(First) **Action plan 2011-2013**

Quite ambitious VET PART: **8 priorities of the NAP action plan:**

- 1) Surveillance AMR - HUM/VET: **YES** (zoonotic/indicator)
NO (target vet pathogens)
- 2) Surveillance ATM consumption- HUM/VET: **YES** (since 2003)
- 3) Recommendations – guidance for ATM use and AMR control
(continuing HUM, starting VET) : **NO** (vet ... as very limited national data on AMR vet)
- 4) Indicators of responsible use of antimicrobials: **YES** (CIAs, premixes)
- 5) Supportive measures to promote rational prescription of ATM, control of resistance in primary health care: **PARTIALLY**
- 6) Implementation of programs on use of antimicrobials in hospitals (HUM)
- 7) Mass medial campaigns on responsible use of ATM public targeted **PARTIALLY**
- 8) NAP infrastructure setting/innovation of activity of the antibiotic centers **NO**
- 9) Information support and NAP activities promotion **YES**
- 10) Infections associated with the healthcare (HUM)

Example of „One health cooperation“

„Prudent use regimen“ for specific CIAs established:

- approved in **1998** in CZ,
- enforced by the Decree 344/**2008** + targeted inspections **2013**
- **The most important aspect was „critical importance“ for human medicine**
- Use of the VMP containing these antimicrobials when:
 - Old narrow spectrum antimicrobials not effective
 - Antimicrobials susceptibility testing is performed
- **Cephalosporins 3. / 4.** generations (EFT, CFQ, PER, VEC)
- **(Fluoro) quinolones** (ENR, MAR)
- **Ansamycines** (RIF – class of first line anti TBC)
- **Aminoglycosides** of higher generation (AMI, GEN, KAN)
- **2018 UPDATE:**
 - **Colistin** to be added into the list (despite the fact that **CZvet** consumption is quite low - belong to the countries with less 1 mg/PCU as for vet colistin consumption)

CIAs link to targeted inspections **2013**

Having data from wholesalers =>

demand for identification of the subjects (vets/farms) with

Highest sales (package level)

for the antimicrobials under „prudent use“ regimen

Investigation: Why so high use of CIAs?

- number of animals, farms under the vet care of the highest prescribers)

Checking the on farm log books with treatment records

- for indications, where CIAs used
- for presence of the culturing /AST results (in CZ obligatory by national law since 2008)
- for justification, why not used first choice antimicrobials

First ADVICES: recommendations how to improve

using the (nationally) available tools!

Secondly PENALTIES

If not improved or serious disturbances of law (e.g. insufficient records, no AST results, extremely frequent prescriptions of CIAs) => penalty

One of indicator of responsible use of
ATM according AP 2011-2013

Steps to ensure good practices of use of antimicrobials in VET (I)

- **Antimicrobials as POMs:** ATM VMPs in all pharmaceutical forms
- **„Prudent use regimen“** in VMPs containing CIAs
- **Marketing authorisation + availability** (whole portfolio including first line antimicrobials)
- **Distribution and supply** by authorised channels only – traceability (unique CZ code of VMPs/packages)
- **GMP for medicated feedingstuffs**
- **Regular inspections:**
 - In vets, pharmacies, wholesalers ...
 - **based on risk assessment/analysis:**
 - residues, supply of VMPs, CIAs overuse ...
 - ISCVBM, SVA

Risks/evidence based approach
of inspections AP 2019-2022

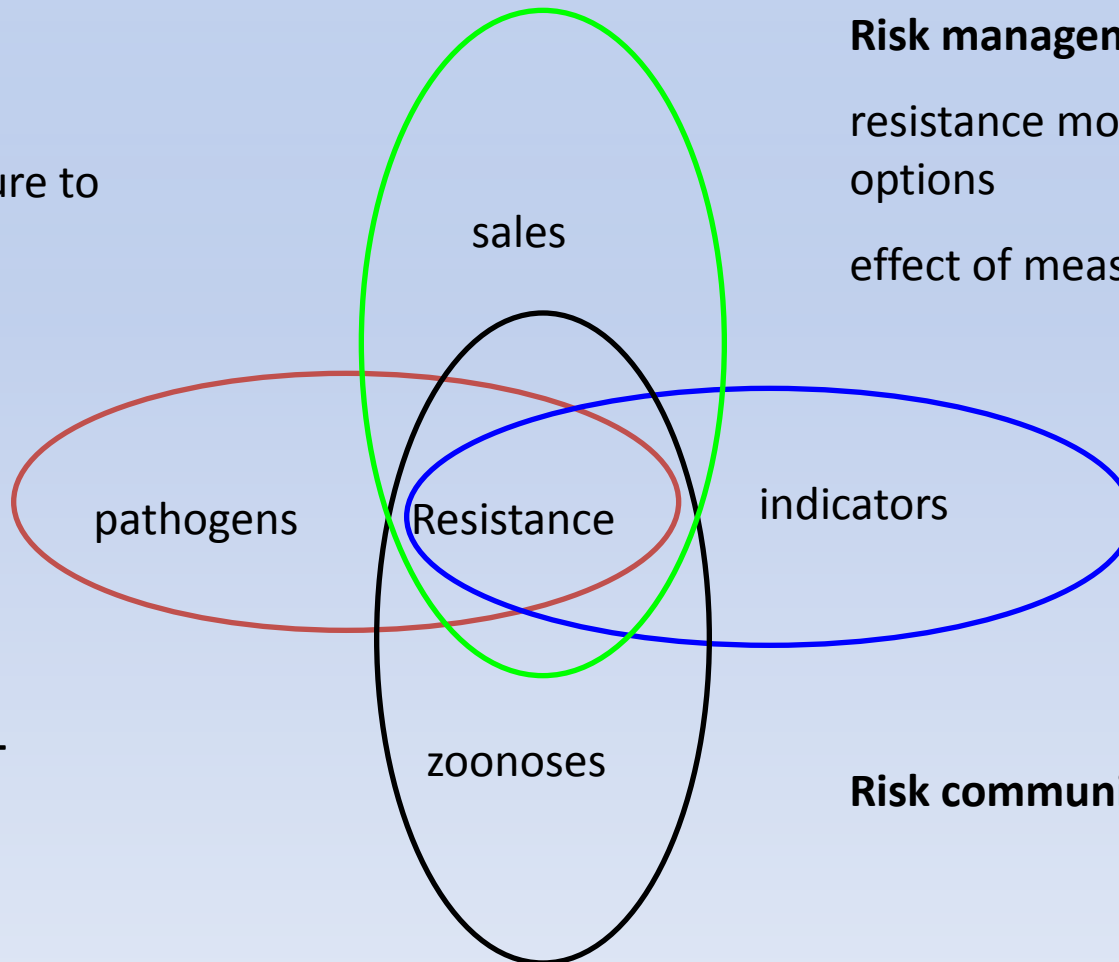
Key elements of info for **risk analysis** come from **monitoring**

Risk assessment:

sales vs. exposure to
ATM

Risk management:

resistance monitoring
options
effect of measures



Surveillance – monitorings:

Risk communication

Link between human and vet medicine

Steps to ensure good practices of use of antimicrobials in VET (II)

Continuing AP 2011-2013 ... improvement planned AP 2019 - 2022

– Education

- All SPCs readily available on line : **web app/Android mob app**
- Special part of web : FOR VETS (e.g. Info on CIAs, PHV ...)
- Vets/farmers specific trainings/workshops
- Webinars

– Inovations

- „on farm testing sets“ – mastitis/cattle
- METRICULT – unique sampling system
- MICs unique microplates for target vet pathogens AST
- Indication/use of VMPs – electronical tool (cattle)

– Communication – vet/farmers/public


Education: vets

- Cooperation with Chamber of Vet Surgeon
- Lectures to vet (once year/regionally; iscvbm)
- Publication in „Zvěrokruh“ ... e.g. in cooperation with ISCVBM
 - e.g. Prescription habits survey CZ and EU
 - Off label use of VMPs
- Publication in (VRI, VFU, ISCVBM, specialists)
 - „Veterinářství“
 - „Veterinary Clinic“
 - „Acta Veterinaria Brno“
- Lectures (Aviary, Porcine, Buitarics... specialists)
- VRI: „VÚVeL FEST“
- Webinar Chamber of Veterinary Surgeons
 - „Responsible user of antimicrobials“



Example: Summer school of mastitis

Target audience
students/vets/ but also farmers/staff on farms



TV, press ... communication !

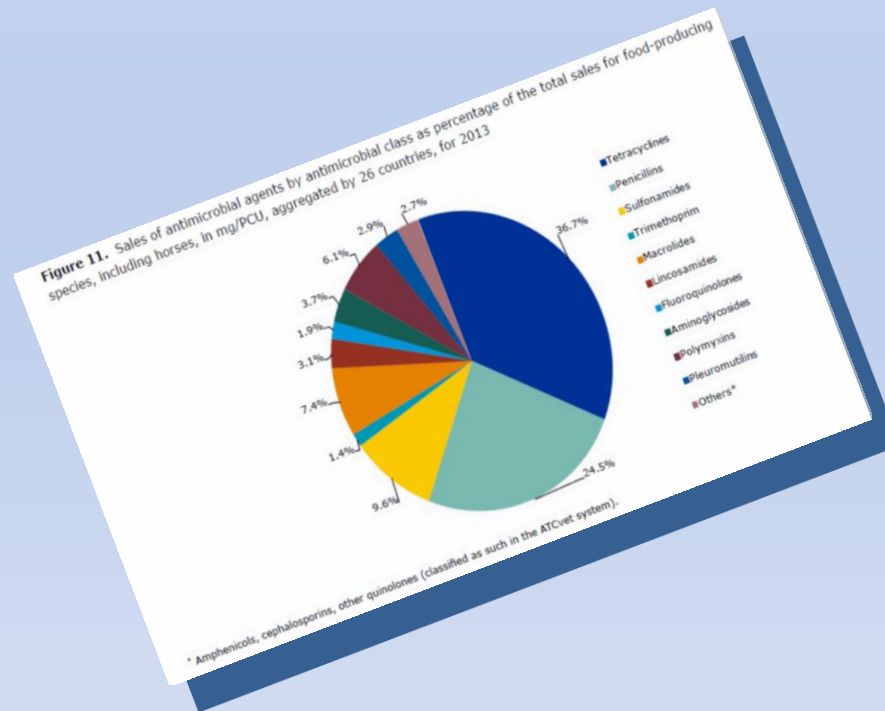


... more examples on further slides

Campaigns (EAAD)



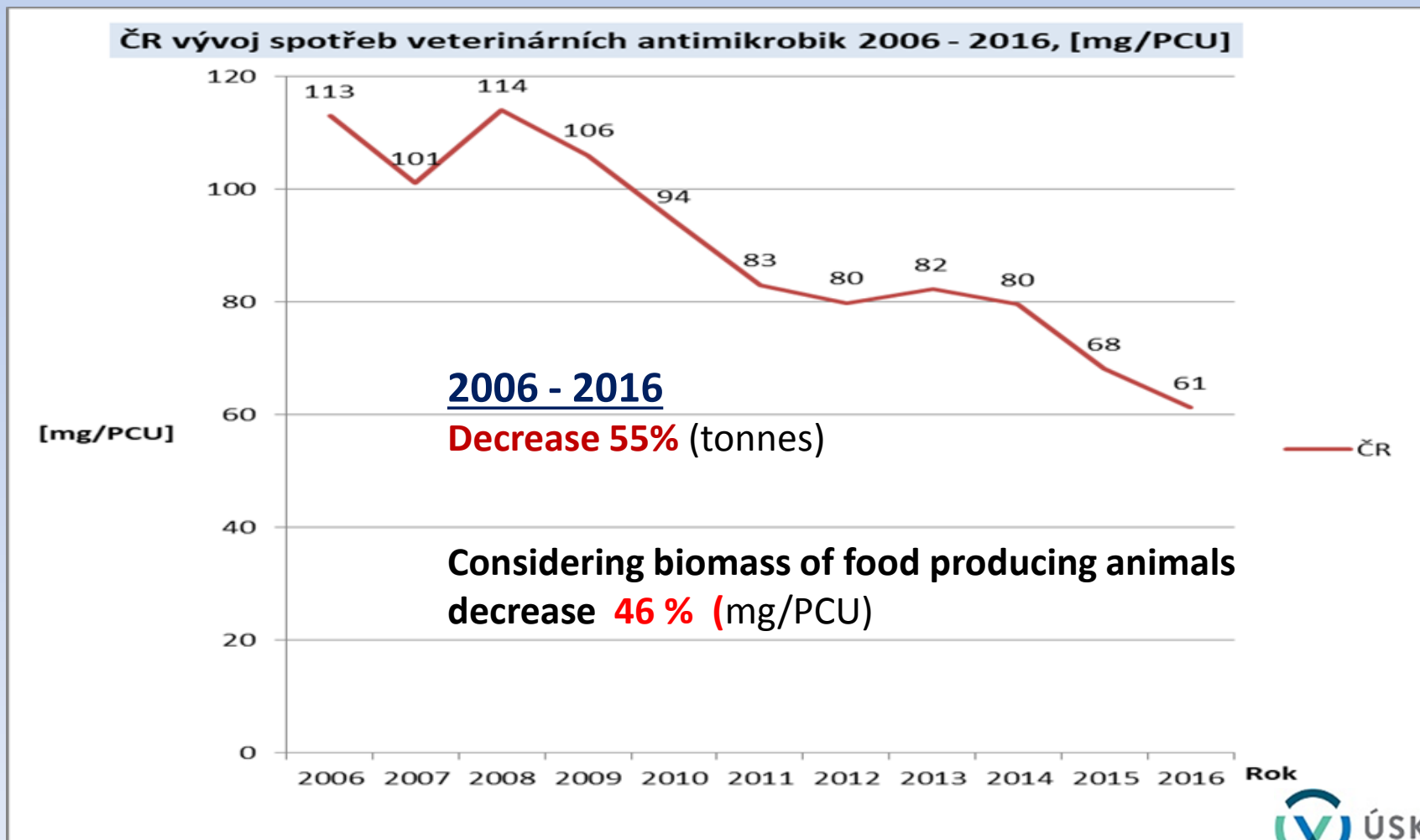
Is there any evidence that steps, mentioned above, work ?



Continuing - sales data before and within AP 2011-2013 ...
Improvement planned - species use data AP 2019 - 2022

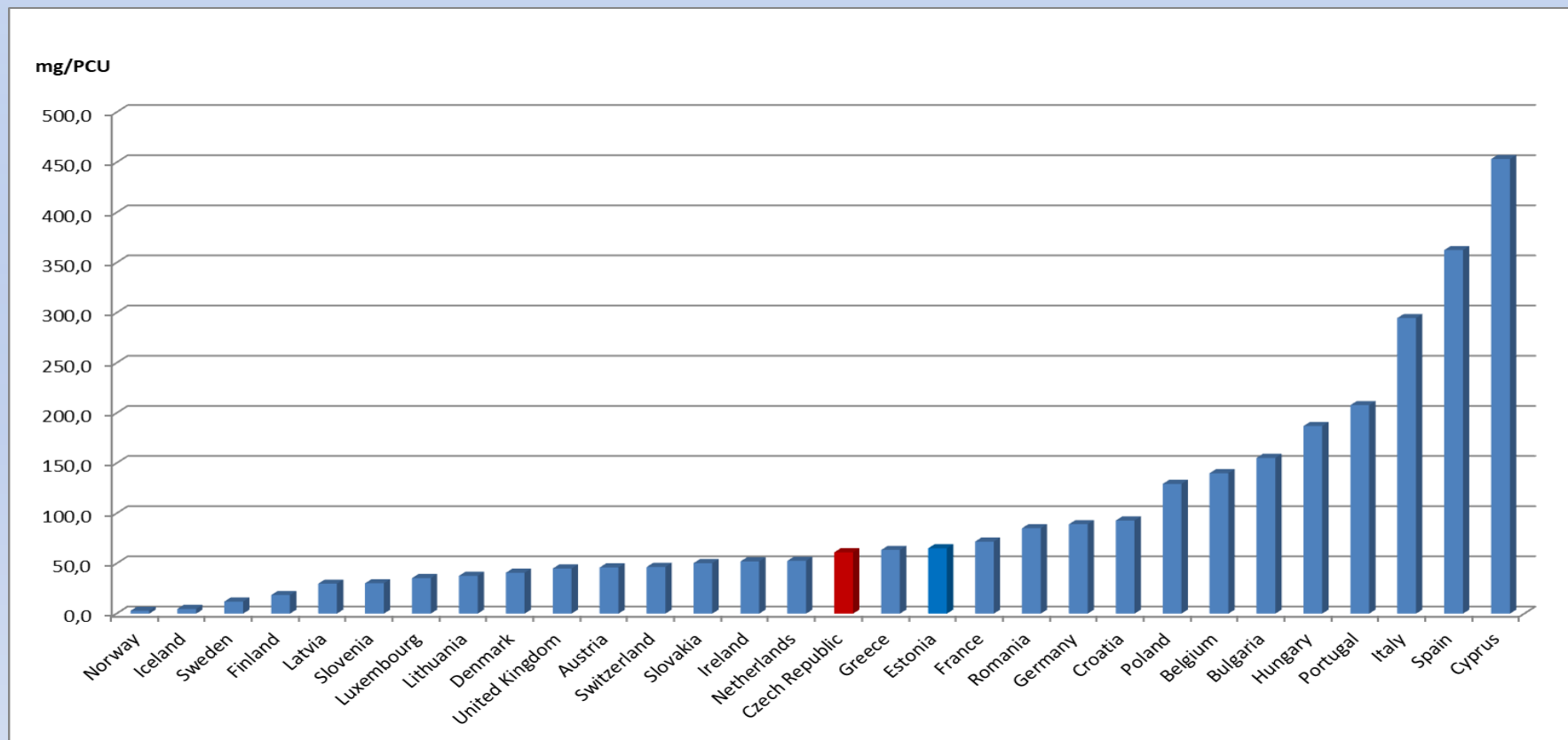
CZ: Consumption of vet ATM decreases

ČR vývoj spotřeb veterinárních antimikrobik 2006 - 2016, [mg/PCU], dle dat nahlášených do projektu ESVAC											
Roky	2006	2007	2008	2009	2010	2011	2012	2013	2014	2015	2016
mg/PCU	113	101	114	106	94	83	80	82	80	68	61



Is it possible to compare with other MSs?

Data on sales vet ATM Considering biomass of food producing animals [mg/PCU] - 2016

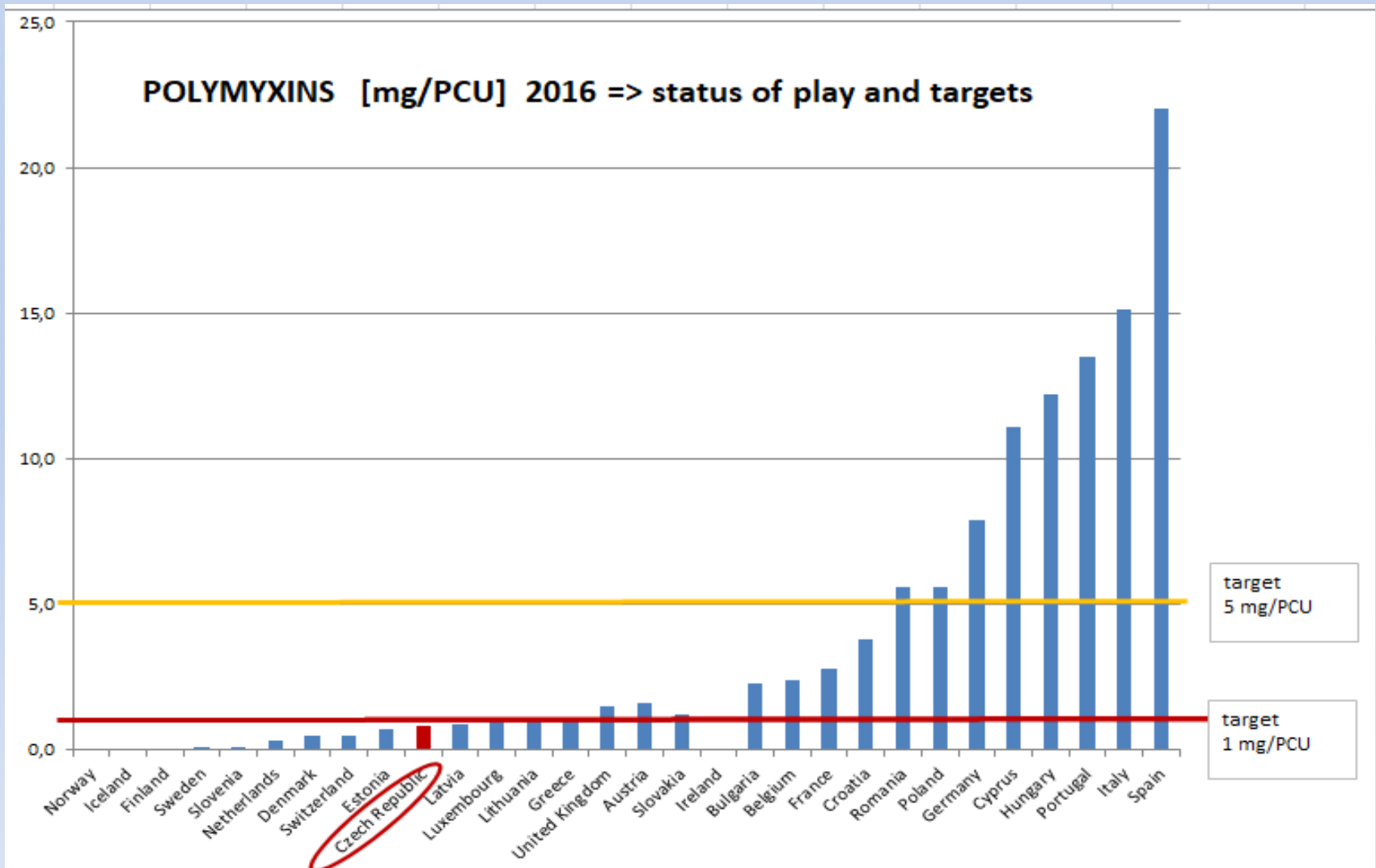


- Data should be interpreted with caution! Demography of species of animals kept, husbandry systems, climate, portfolio of ATM available/used ... more in oral explanation

ESVAC: Sales of veterinary antimicrobial agents in 30 EU/EEA countries in 2016

http://www.ema.europa.eu/docs/en_GB/document_library/Report/2018/10/WC500236750.pdf

Colistin – lives saving ATM in human: CZ vet

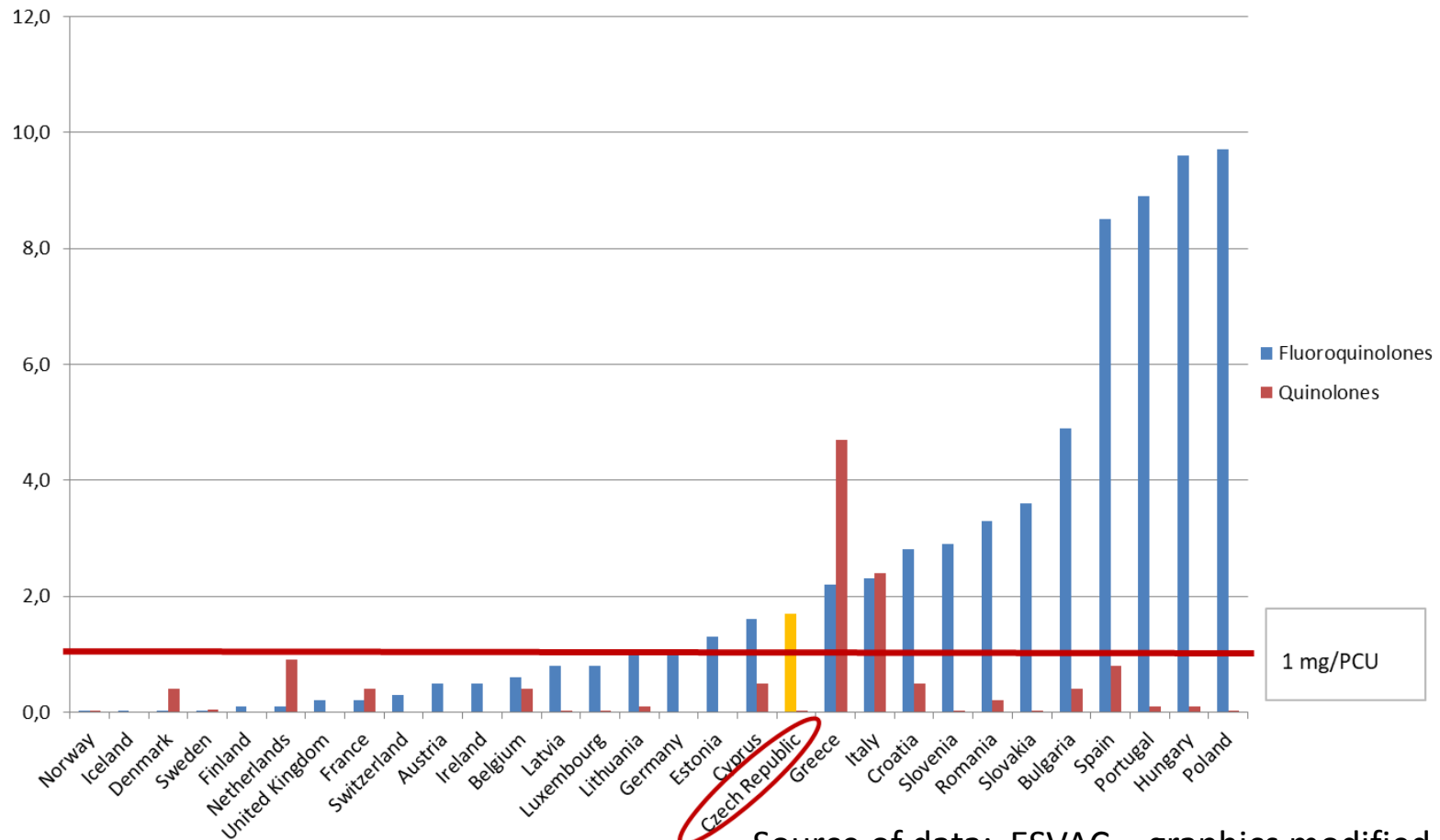


Source of data: ESVAC – graphics modified

FQ/Q – still space for improvement: CZ vet

AP 2011-2013 not succeed fully ... improvement planned AP 2019 - 2022

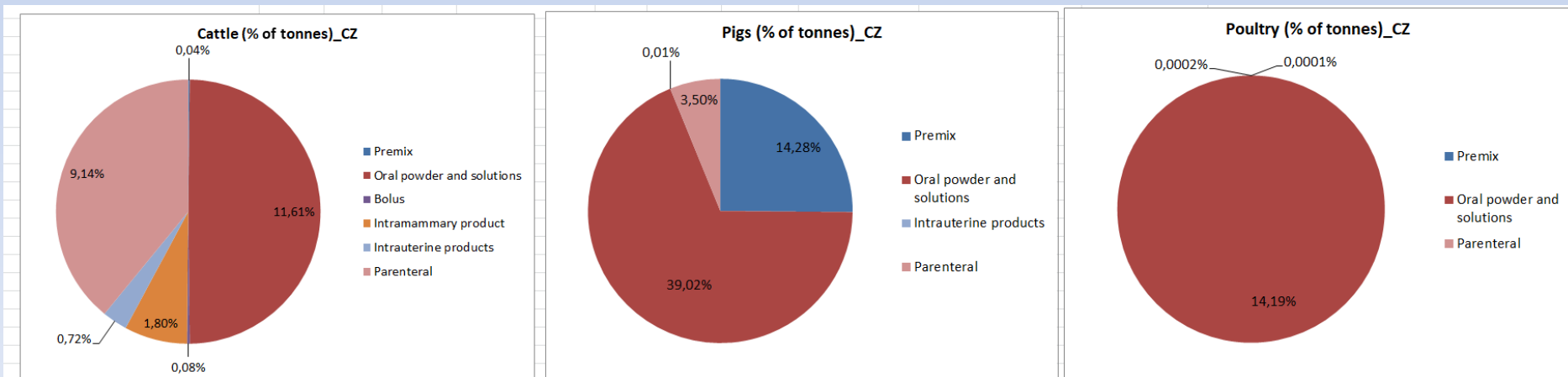
Fluoroquinolones/Quinolones [mg/PCU] 2016 => status of play



Source of data: ESVAC – graphics modified

CZ participation in EMA recent pilot project: stratification per animal species

- 6 piloting countries (AT, CZ, DK, ES, FR, NL)
- CZ data as qualified estimations + data from big producers
- Exercise to learn/prepare for the future VMP regulation requirements



When we want to do things reasonably- we need to know local situation !



**Monitoring zoonotic /indicator bacteria
(EU harmonised, EFSA)**

Continuing - AP 2011-2013

CZ monitoring of target vet pathogens

Not achieved in AP 2011-2013 ... but operational since III/2015

National program of antimicrobial resistance monitoring of pathogens with vet importance (I)

- Established in 2015 (III-2015 first samples analysed)
 - Since 2017 – extended genotyping – e.g. ESBLs, AmpC, resistance to colistin in G- and MRSA, multiresistance strains
- Specific diagnostic sets (microplates)
 - Gram positive pathogens
 - Gram negative pathogen
 - Veterinary specific pathogens
- Range of antimicrobials – adapted to authorised products
- Standardised interpretation criteria (CLSI, EUCAST, marketing authorisation data, other sources)
- Clinical isolates from cattle, pigs and poultry

Species of bacteria involved

- **Cattle (non - mastitis):**

- *Mannheimia haemolytica*
- *Pasteurella multocida*
- *Escherichia coli*
- *Histophilus somni*

- **Cattle (mastitis):**

- *Streptococcus agalactiae*
- *Streptococcus dysgalactiae*
- *Streptococcus uberis*
- *Staphylococcus aureus*,
- *Escherichia coli*,
- *Klebsiella* spp.
- *Raoultella* spp.

- **Pigs:**

- *Actinobacillus pleuropneumoniae*
- *Pasteurella multocida*
- *Escherichia coli*
- *Streptococcus suis*
- *Staphylococcus hyicus*

- **Poultry :**

- *Escherichia coli*
- *Pasteurella multocida*
- *Enterobacter* spp.
- *Enterococcus* spp.
- *Staphylococcus aureus*

Who is involved and how

Ministry of Agriculture - WG on AMR – 2014/15

Stakeholders agreed on necessity of project , voluntary base and principles of confidentiality (not publishing husbandry details)

State Veterinary Administration

- Leader of project
- Budgetary resource for MICs testing
- Validation of the data
- 2015/2016 **reports**

State Veterinary Institutes (SVI - Praha, Jihlava, Olomouc)

- Perform susceptibility testing/interpret results/fill the database

Antibiotic centre for Veterinary Clinical Practice (since 2017, Jihlava)

- Since 2017 **reports I and II**

Veterinary Research Institute

- Microplates development, production, validation

Institute for State Control of Veterinary Biologicals and Medicines

- Cooperation on the settings of antimicrobials tested - based on available antimicrobial contained in authorised VMPs

Veterinarians + farmers

Collection of samples, payment for identification



National program of antimicrobial resistance monitoring in veterinary important pathogens (II)

- Results available at:

- <https://www.svscr.cz>

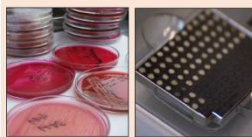
- https://www.svujihlava.cz/intranet/publikace/Zprava_cast_I_NAP_2017.pdf



NÁRODNÍ PROGRAM SLEDOVÁNÍ REZISTENCÍ K ANTIMIKROB U VETERINÁRN VÝZNAMNÝCH



NÁRODNÍ PROGRAM SLEDOVÁNÍ REZISTENCÍ K ANTIMIKROBÍKŮM U VETERINÁRNĚ VÝZNAMNÝCH PATOGENŮ



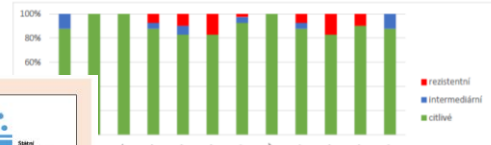
za rok 2017 část II.

4.2. Procento rezistentních/citlivých kmenů

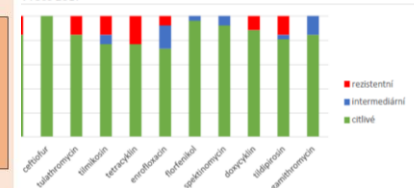
4.2.1. Procento rezistentních/citlivých kmenů z chovu skotu

Zastoupení rezistentních, intermediálních a citlivých izolátů jednotlivých původců detekovaných v chovech skotu je znázorněno v grafech č. 1 – 6.

Graf č. 1: Zastoupení rezistentních a citlivých kmenů *Pasteurella multocida* izolovaných v chovech skotu v roce 2017



4.2.2. Procento rezistentních a citlivých kmenů *Mannheimia haemolytica* izolovaných v chovech skotu v roce 2017



4.3.2 Fenotypové vlastnosti izolátů z chovu prasat

Výsledky fenotypových vlastností izolátů z chovu prasat jsou uvedeny v tabulkách č. 14 – 17.

Tabulka č. 14: Výsledky fenotypových vlastností izolátů *Actinobacillus pleuropneumoniae* v roce 2017

ANTIMIKROBIKUM	počet izolátů	MIC ₅₀ mg/L	MIC ₉₀ mg/L	C (%)	I (%)	R (%)
Penicilin	27	0,5	1	-	-	nehodnoceno
Ampicilin	27	0,5	1	77,8	14,8	7,4
Ceftiofur	27	<= 0,125	0,25	96,3	0	3,7
Tulathromycin	27	32	128	88,9	-	11,1
Tilmikosin	27	8	16	92,6	-	7,4
Tiamulin	27	16	16	92,6	-	7,4
Tetracyklin	27	<= 0,5	<= 0,5	96,3	3,7	0
Enrofloxacin	27	<= 0,06	0,25	92,6	7,4	0
Florfenikol	27	0,25	0,5	100	0	0
Spektinomycin	27	128	>128	7,4	18,5	74,1
Doxycyklin	27	<= 0,5	1	100	-	0
Tildipirosin	27	8	16	92,6	-	7,4
Gamthromycin	27	2	4	-	-	nehodnoceno

Tabulka č. 15: Výsledky fenotypových vlastností izolátů *Pasteurella multocida* v roce 2017

ANTIMIKROBIKUM	počet izolátů	MIC ₅₀ mg/L	MIC ₉₀ mg/L	C (%)	I (%)	R (%)
Penicilin	31	0,125	0,25	90,3	6,5	3,2
Ampicilin	31	0,25	0,5	90,3	6,5	3,2
Ceftiofur	31	<= 0,125	<= 0,125	100	0	0
Tulathromycin	31	<= 1	2	96,8	0	3,2
Tilmikosin	31	8	16	93,5	-	6,5
Tiamulin	31	32	32	3,2	25,8	71,0
Tetracyklin	31	<= 0,5	8	74,2	9,7	16,1
Enrofloxacin	31	<= 0,06	0,125	100	0	0
Florfenikol	31	0,5	0,5	100	0	0
Spektinomycin	31	32	64	77,4	19,4	3,2
Doxycyklin	31	<= 0,5	1	90,3	-	9,7
Tildipirosin	31	2	4	90,3	-	9,7
Gamthromycin	31	1	1	-	-	nehodnoceno



Odbor ochrany zdraví a pohody zvířat

Národní program sledování rezistencí k antimikrobiikům u veterinárně významných patogenů

informační brožura č. 02/2017



Links to international activities

Cooperation with VETCAST-I

VETCAST = Veterinary Committee for Antimicrobial Susceptibility Testing
http://www.eucast.org/ast_of_veterinary_pathogens/

DATA NEEDED FOR INTERPRETATIVE, VET SPECIFIC, EU CRITERIA !

- Some of **MIC profiles** from CZ target pathogen monitoring useful for the project
- Susceptibility to tetracyclines (TC, DOX) data already **provided by DK, SE, NL, IT and CZ** to VETCAST:
 - **Already processed:** *E.coli*, *Klebsiella* (different species), *Enterobacter* (different species)
 - **Further provided:** *Streptococcus* (different species), *Actinobacillus pleuropneumoniae*, *Histophilus somni*



Joint Action
Antimicrobial Resistance and
Healthcare-Associated Infections

Co-funded by the
Health Programme
of the European Union

WP7.4 Joint Meeting

06/09/2018

Rodolphe Mader
ANSES

Meeting objectives

- Start a collaboration between the human and veterinary sector for the surveillance and monitoring of AMR
- Description of the main challenges for an integrated surveillance of AMR in diseased patients and animals
- Find solutions for keeping a relevant One Health approach
- Think about the next work steps of our collaboration

Importance of international context:

- EU Action plan ... CZ Action Plan(s) quite in line with
- New VMP /MF regulations ... pros/cons for the future
- OIE activities (AMU data collection) ... CZ provides the data
- Codex Alimentarius TFAMR – CZ actively participates by written comments on both GLs (Code of Practice ... GL on Surveillance)

Example: projects for practice

Example: Dairy cattle

- MIC tests – mastitis
- Rapid diagnostic/bacteria detecting tests
- Example of specific sampling system
- Tools useful for farm management:
 - **Disease** recording/database linked with
 - **Treatment/VMPs** use recording
- Summary linked to **National Antibiotic Programme**



MICROMAST
MicroMast je kultivační set pro rychlou farmaci diagnostiku původců mastitid.

Přínosy:

- Jednoduchost provedení.
- Snížení spotřeby antibiotik.
- Zvýšení účinnosti léčby, snížení brádky.
- Více mléka v dojílce.
- Rychlé očištění stáda.
- Vychytí výsledky v managementu stáda.
- Uchování kultury ke stanovení citlivosti k antimikrobiálním látkám.
- Zapřehování bez antibiotik.

Odborné poradenství:
MUDr. Josef Prošek, Ph.D.
+420 775 956 986
josef.prosek@gmail.com
www.josefprosek.cz

Balení:
Zkoumavka, sterilní klička, dezinfekční ubrousek,
řísavčová Petriho miska o 90 mm se třemi různými páněmi.
Pánev „A“ slouží k zachytu G⁻ bakterií.
Pánev „B“ je pánev obecná, která umožňuje zachytit G⁻ i G⁺ bakterie.
Pánev „C“ slouží k zachytu G⁺ bakterií.



METRICULT
Souprava na odběr vzorku pro vyšetření endometritid u dojnic.

- Zaručuje nekontaminovaný odběr vzorku
- Vhodná i pro vyšetření klisven
- Neomezuje plodnost

Souprava na odběr vzorku je složena:

- 1 z jednorázového kufříku pro zavedení odliškového temporu špičička k odběru mikrobiologického vzorku z důlního dipnce, bez rizika mikrobiologické kontaminace z prostředí počasí vyšetřovaného zvířete
- 2 ze žilnovek s transportním mediem Amies pro přípravu vzorku do laboratorika k mikrobiologickému vyšetření

Prvotní cíle odliškového vzorku na 90% jistě lze provést, je odlišný vzorek a dříve než kontaminace z prostředí zvířete dipnce. Ten vzorek byl dříve pro nepřesné vyšetření laboratorika v 10% - 20% případů. Aktuálně provedeno na 100% a zejména odlišná souprava jako patent č. 305628.

Zabudovat kufřík (Bifida tempor) je z biologicky odbořitelého materiálu.

60 cm

Více informací na www.laboratorika.cz

Example: prevention + control

Complexity of the issues to be solved:

One part: Health status of the herd:

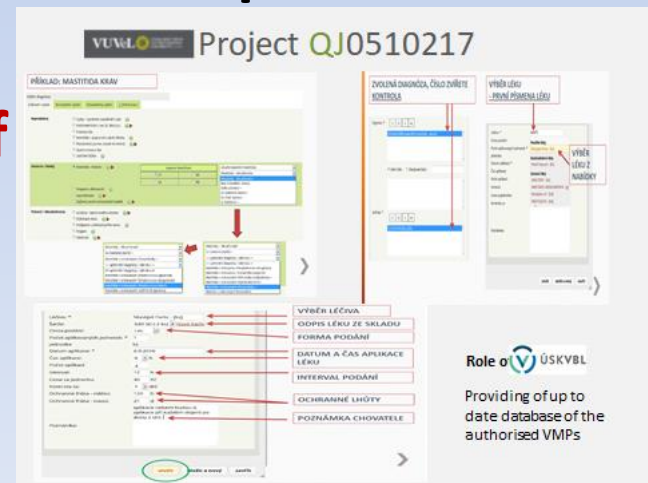
Electronical tool/system of dairy herd management enabling e.g.

Disease diagnostics and electronic recording

- Use of ICAR system of classification of diagnosis

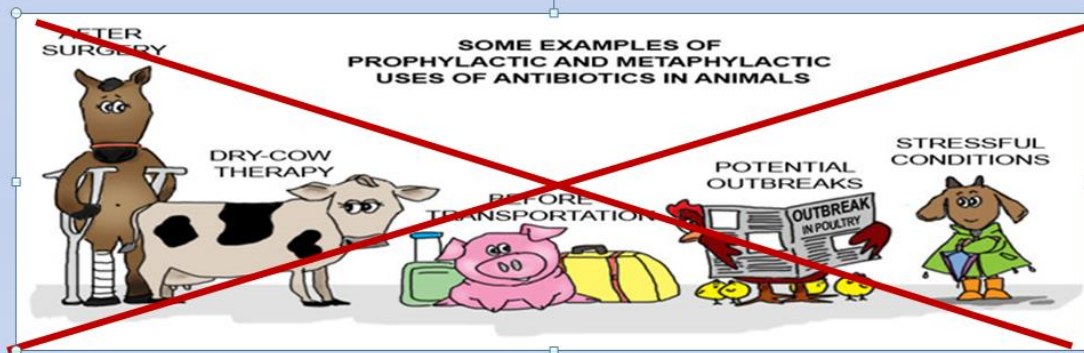
Monitoring of use of veterinary medicinal products:

- Vaccines
- **Antimicrobials => monitoring of on farm USE**
- NSAIDs
- Other VMPs ...



Future projects - vet

Pressure on minimising the practices, that can be solved by alternative tools other than antimicrobials



Specific targets - programmes to minimise the use of CIAs

Steps for future

- Good husbandry practices and welfare conditions as pre-requisite of the good health animal status
 - Health programmes for herds/flocks
 - Search for „alternatives“ that fit the local conditions
(vakcíny, fágy, imunomodulátory, probiotika, prebiotika, bylinné preparáty, vitamíny, minerály ...)
- Use evidence based approaches to set reasonable local policies
(monitoring data needed)



- Avoid routine preventive use of antimicrobials (... ad VMP reg)
 - Minimise the need for treatment and metaphylaxis



All these steps should in fact lead to healthy, well kept animals =>
help **to keep/advance good quality of food** and
decrease the need for use and finally the use of antimicrobials



Minimising the selective pressure for AMR

Conclusion:

Healthy and well cared animals do not need antimicrobials !

TARGET: decrease NEED of use ATM in vet med
FUTURE: avoid/strictly limit use of CIAs for human med in vet med

- Systematic work of Min Agri and NCAs (ISCVBM, SVA, MVA, SVI ...)
- Increasing awareness, responsibility and cooperation of VETs, FARMERS, FOOD PRODUCERS, OWNERS of pets
- Health and welfare improvement - livestock animals
- Increase of availability of scientific proof of evidence for evidence based correct decisions on rational/responsible use of antimicrobials
- Increase of awareness of public on AMR

Tackling AMR should be done carefully and **should be tailored on local conditions** - some experiences/systems can be exchanged and shared

Measures setting rather „**bottom up**“ using „**puzzle system**“

Thank you for your attention

**On behalf of the „team of stakeholders“ and
with big thanks people in everyday practice**

Questions and Comments welcomed

Contact/presenting person address:

pokludova@uskvbl.cz