Utilizzo di antimicrobici negli animali; resistenza batterica e salute pubblica

Angelo Ferrari

Direttore Sanitario

Istituto Zooprofilattico Sperimentale del Piemonte Liguria e Valle d'Aosta

Il Network italiano degli Istituti Zooprofilattici

TOPIC

- ***Uso di antibiotici in ambito veterinario***
- ***Presenza di residui di antimicrobici negli alimenti***
- ***Il fenomeno dell'antibioticoresistenza***

………….DIAMO I NUMERI……….

Patrimonio Zootecnico

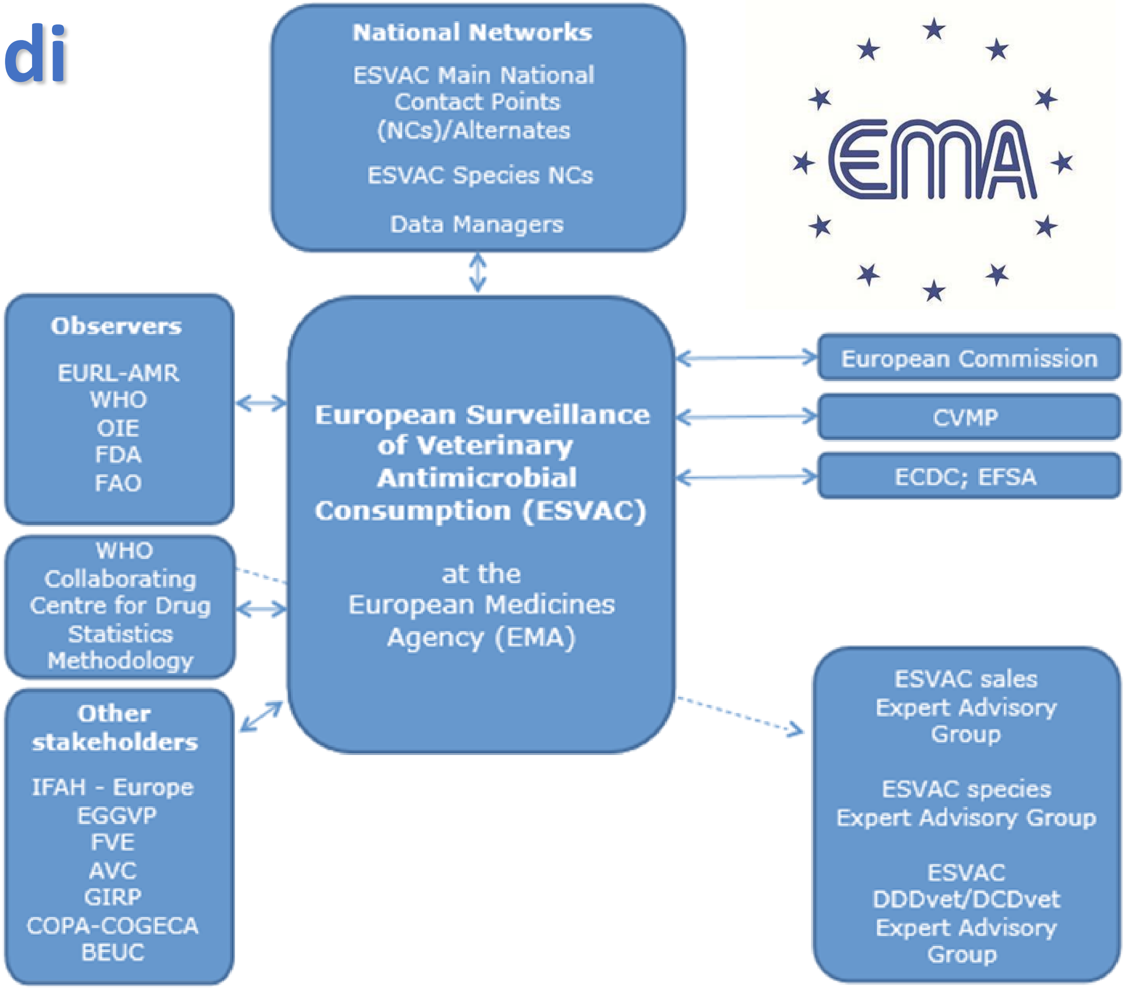
- *5.953.000 di bufali/bovini sul territorio nazionale, circa 12.700 in Liguria*
- *8.076.000 di ovi-caprini sul territorio nazionale, circa 23.400 in Liguria*
- *8.695.000 di suini sul territorio nazionale, circa 1.000 in Liguria*

Animali d'affezione

- *circa 9.500.000 di cani sul territorio nazionale circa 200.000 in Liguria*

Rapporto sui dati di vendita

ESVAC



Fonte: European Medicines Agency, European Surveillance of Veterinary Antimicrobial Consumption, 2017. 'Sales of veterinary antimicrobial agents in 30 European countries in 2015'. (EMA/184855/2017)

Categories of veterinary antimicrobial agents	ATCvet codes
Antimicrobial agents for intestinal use	QA07AA; QA07AB
Antimicrobial agents for intrauterine use	QG01AA; QG01AE; QG01BA; QG01BE; QG51AA; QG51AG
Antimicrobial agents for systemic use	QJ01
Antimicrobial agents for intramammary use	QJ51
Antimicrobial agents for antiparasitic use[1]	QP51AG

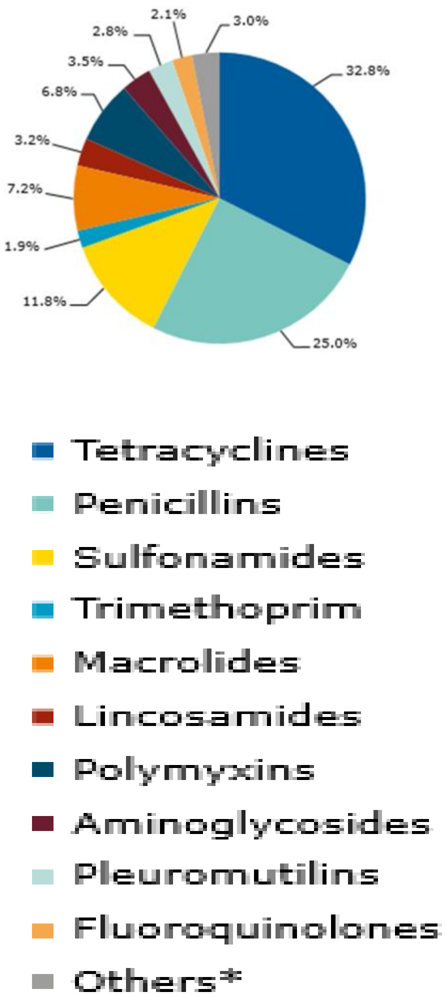
[1] Solely sulfonamides

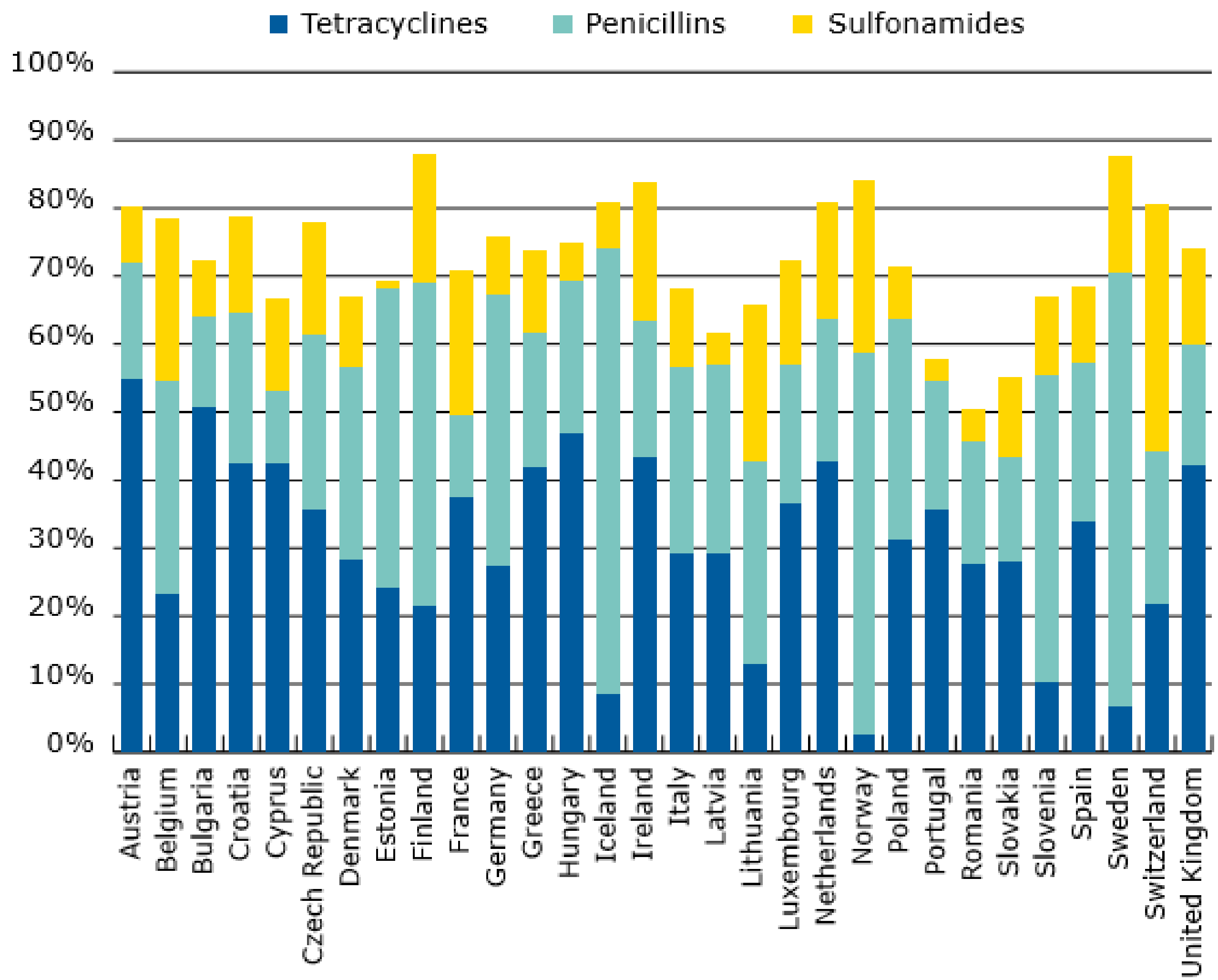
Country	Tablets		All other pharmaceutical forms		Total tonnes
	Tonnes	% of overall sales	Tonnes	% of overall sales	
Austria	0.3	0.6%	48.5	99.4%	48.8
Belgium	1.9	0.7%	258.1	99.3%	260.1
Bulgaria	0.5	1.0%	46.3	99.0%	46.8
Croatia	0.3	1.2%	27.9	98.8%	28.2
Cyprus	0.1	0.1%	46.9	99.9%	46.9
Czech Republic	1.1	2.2%	47.5	97.8%	48.6
Denmark	0.8	0.8%	101.9	99.2%	102.8
Estonia	0.1	1.6%	8.1	98.4%	8.2
Finland	1.7	13.6%	10.6	86.4%	12.3
France	12.3	2.4%	501.5	97.6%	513.8
Germany	7.1	0.8%	851.1	99.2%	858.2
Greece	0.5	0.7%	72.6	99.3%	73.1
Hungary	0.3	0.2%	176.0	99.8%	176.3
Iceland	0.03	5.2%	0.6	94.8%	0.6
Italy	**9.7**	**0.7%**	**1,300.0**	**9.3%**	**1,309.7**
Lithuania	0.04	0.3%	11.9	99.7%	11.9
Luxembourg	0.1	6.2%	1.8	93.8%	1.9
Netherlands	2.8	1.3%	213.7	98.7%	216.5
Norway	0.5	8.8%	5.6	91.2%	6.1
Poland	2.3	0.4%	582.5	99.6%	584.8
Portugal	0.7	0.5%	134.0	99.5%	134.6
Romania	2.3	0.9%	257.2	99.1%	259.6
Slovakia	0.2	1.4%	13.3	98.6%	13.4
Slovenia	0.4	8.1%	4.6	91.9%	5.0
Spain	1.9	0.1%	3,027.8	99.9%	3,029.8
Sweden	0.9	8.8%	9.6	91.2%	10.5
Switzerland	0.1	0.2%	41.2	99.8%	41.3
United Kingdom	12.8	3.1%	394.9	96.9%	407.7
Total 30 countries	**62.4**	**0.7%**	**8,298.9**	**99.3%**	**8,361.3**

Fonte: European Medicines Agency, European Surveillance of Veterinary Antimicrobial Consumption, 2017. 'Sales of veterinary antimicrobial agents in 30 European countries in 2015'. (EMA/184855/2017)

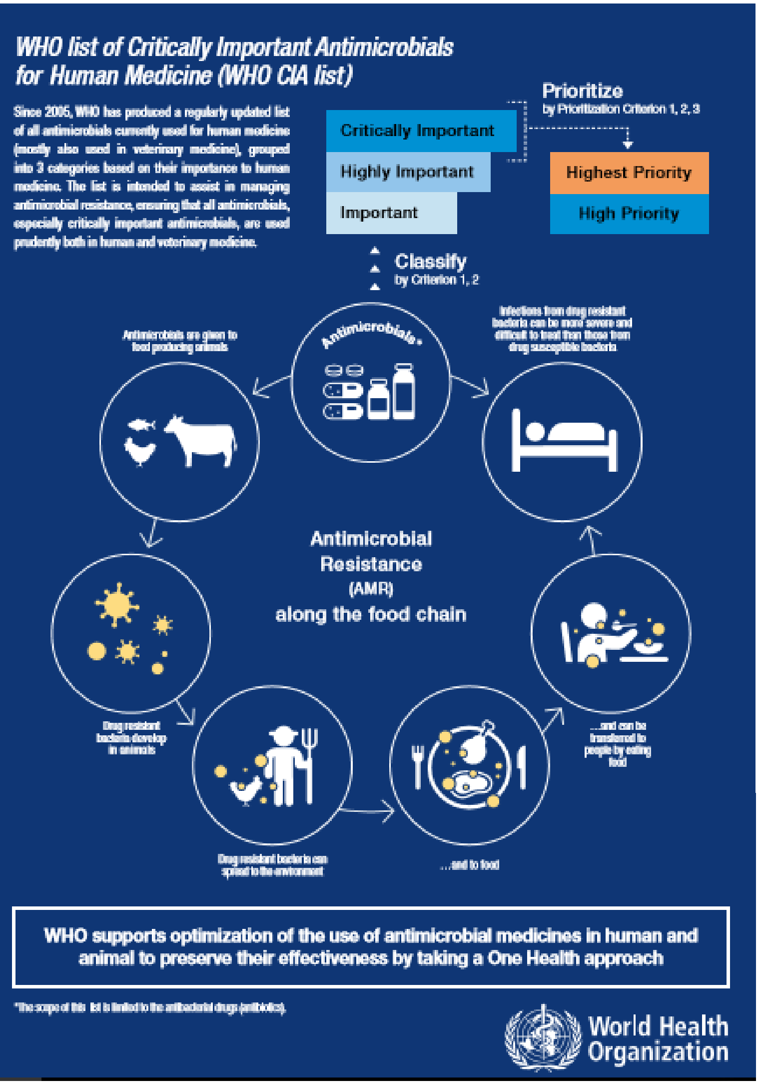
Country	Sales (tonnes) for food-producing animals	PCU (1,000 tonnes)	mg/PCU
Austria	48.5	957	50.7
Belgium	258.1	1,719	150.1
Bulgaria	46.3	380	121.9
Croatia	27.9	274	101.6
Cyprus	46.9	108	434.2
Czech Republic	47.5	698	68.1
Denmark	101.9	2,415	42.2
Estonia	8.1	123	65.2
Finland	10.6	519	20.4
France	501.5	7,147	70.2
Germany	851.1	8,690	97.9
Greece	72.6	1,268	57.2
Hungary	176.0	833	211.4
Iceland	0.6	116	5.0
Ireland	[illegible]	[illegible]	[illegible]
Italy	1,300.0	4,038	322.0
Latvia	6.8	180	37.6
Lithuania	11.9	339	35.1
Luxembourg	1.8	53	34.6
Netherlands	213.7	3,318	64.4
Norway	5.6	1,912	2.9
Poland	582.5	4,193	138.9
Portugal	134.0	997	134.4
Romania	257.2	2,559	100.5
Slovakia	13.3	246	53.8
Slovenia	4.6	173	26.4
Spain	3,027.8	7,532	402.0
Sweden	9.6	808	11.8
Switzerland	41.2	815	50.6
United Kingdom	394.9	6,961	56.7

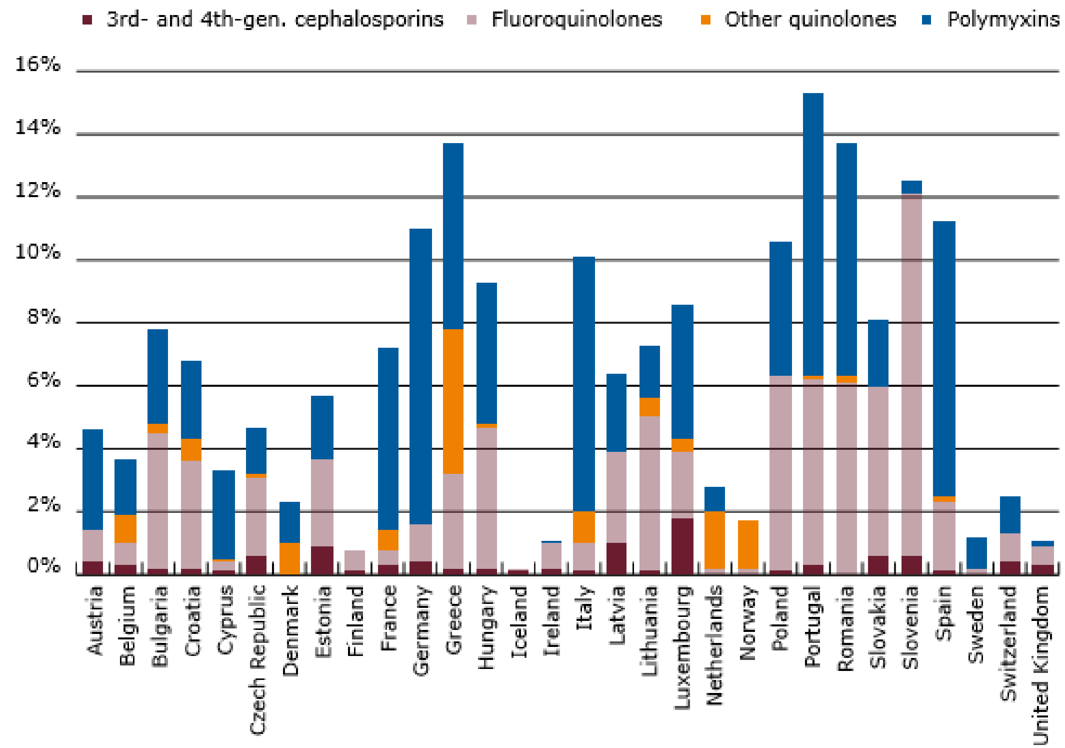
Fonte: European Medicines Agency, European Surveillance of Veterinary Antimicrobial Consumption, 2017. 'Sales of veterinary antimicrobial agents in 30 European countries in 2015'. (EMA/184855/2017)





fonte: European Medicines Agency, European Surveillance of Veterinary Antimicrobial Consumption, 2017. 'Sales of veterinary antimicrobial agents in 30 European countries in 2015'. (EMA/184855/2017)





Antimicrobial class	Criterion (Yes = ●)			
CRITICALLY IMPORTANT ANTIMICROBIALS	C1	C2	P1	P2
HIGHEST PRIORITY				
Highest Priority — *Cephalosporins (3rd, 4th and 5th generation)*	●	●	●	●
Glycopeptides	●	●	●	●
Macrolides and ketolides	●	●	●	●
Polymyxins	●	●	●	●
Quinolones	●	●	●	●

Fonte: European Medicines Agency, European Surveillance of Veterinary Antimicrobial Consumption, 2017. 'Sales of veterinary antimicrobial agents in 30 European countries in 2015'. (EMA/184855/2017)


Piano
Nazionale
Residui
Ministero della Salute
PIANO NAZIONALE INTEGRATO 2015-2018

- **Sostanze vietate o non autorizzate:**
  > MRPL: campione non conforme, distruzione;
  presente: campione conforme, distruzione.

- **Farmaci autorizzati (con LMR)**
  > CCalfa LMR: campione non conforme, distruzione;
  < CCalfa LMR: campione conforme, può esser commercializzato; eventuale non conformità derivante da mancata compilazione del registro dei trattamenti, da verificare a seguito di farmacosorveglianza

- **Coccidiostatici e Contaminanti:**
  solo se **(quantità – incertezza di misura) > LM**: campione non conforme, distruzione.

CATEGORIA B

Ricerca Residui	Ricerca Residui
B1: tetracicline	B2a: avermectine
B1: chinolonici	B2a: benzimidazolici
B1: sulfamidici	B2a: avermectine
B1: macrolidi	B2a: levamisolo
B1: penicilline	B2b: coccidiostatici
B1: cefalosporine	B2d: butirrofenoni
B1: amminoglicosidi	B2d: beta-bloccanti
B1: lincomicina	B2e: FANS
B1: polimixine	B2f: chinossaline
B1: pleuromotiline	B3e: coloranti vietati
B2a: benzimidazolici	

NUOVE Ricerche 2017

Dapsone in ovicaprini, equini e latte: IZS LT.
Cefalosporine in muscolo bovino, suino e equino: IZS LER.
Amminoglicosidi in muscolo, latte, uova e miele: IZS LER.
Colistina in bovini, ovicaprini, conigli, equini: IZS LER.

Lincomicina in muscolo bovino: IZS LER.
Pleuromotiline in muscolo suinovolatili e conigli: IZS LER.
Sulfamidici in muscolo equino: IZS PLVA.
Macrolidi in latte e miele: IZS LER.

Levamisolo in fegato suino e ovicaprino: IZS PLVA.
Carbammati in bovini, suini, ovicaprini e miele: IZS LER.
CAF in uova di quaglia: IZS PLVA

Fonte: M. Gili, Torino 7 aprile 2017. PRISA 2017: DAL TERRITORIO AL LABORATORIO

Il Piano Nazionale Residui

Multiresiduo - multiclasse

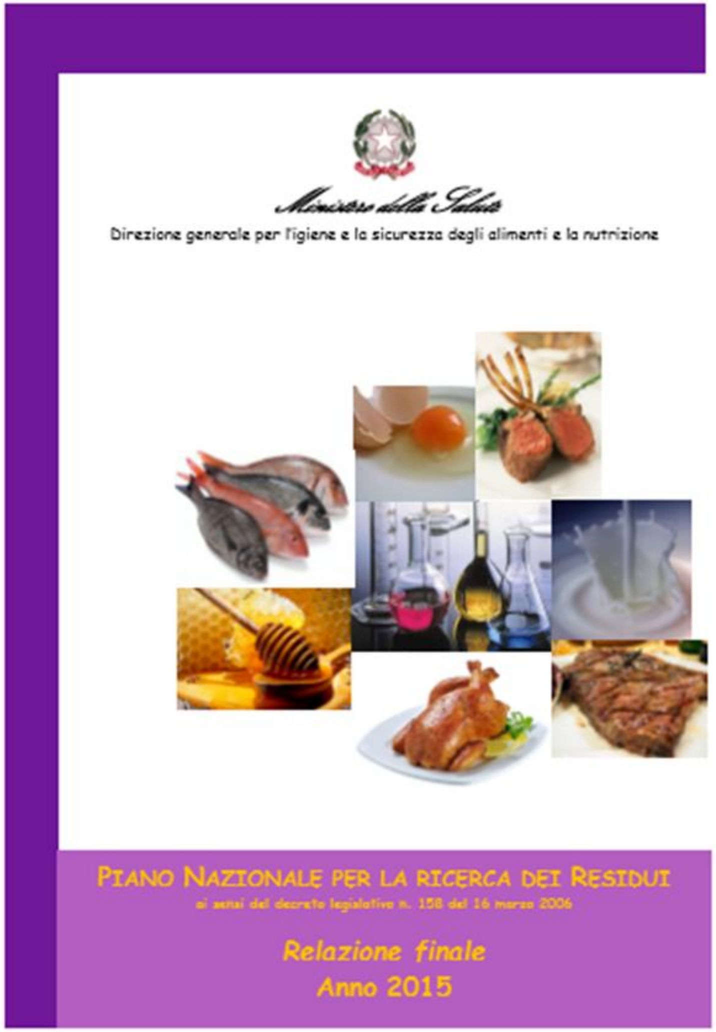
Per dare un SERVIZIO EFFICACE il laboratorio deve utilizzare metodi in grado di rilevare il maggior numero di componenti di una classe di farmaci

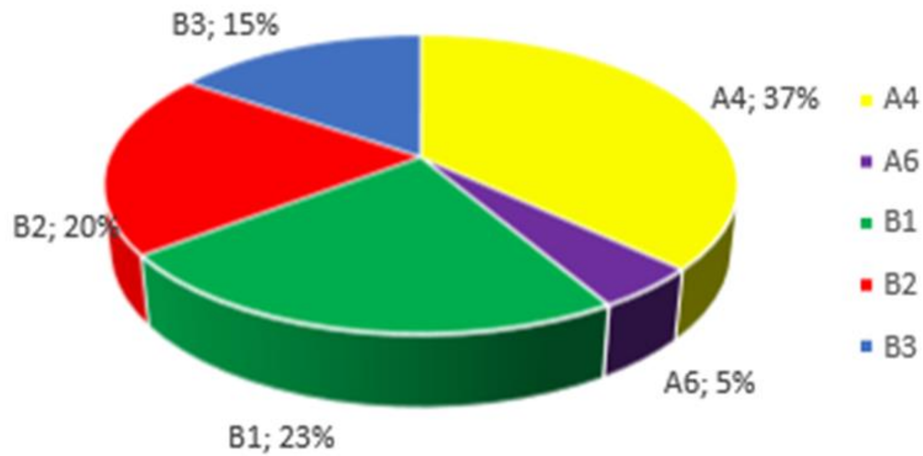
today - multiresiduo

o meglio ancora il maggior numero di classi di farmaci

tomorrow - multiclasse

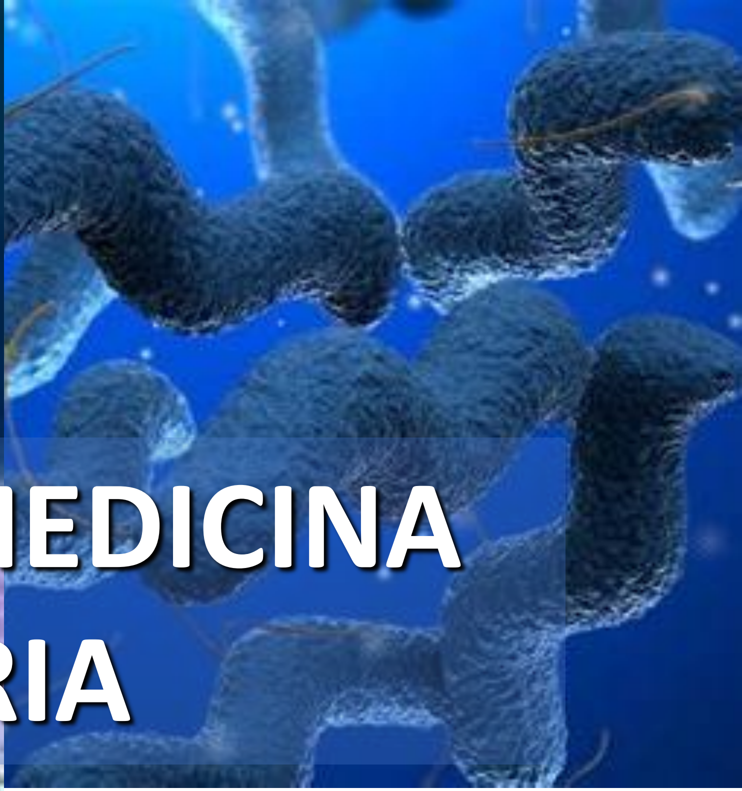
utilizzando tecniche in **ALTA RISOLUZIONE**



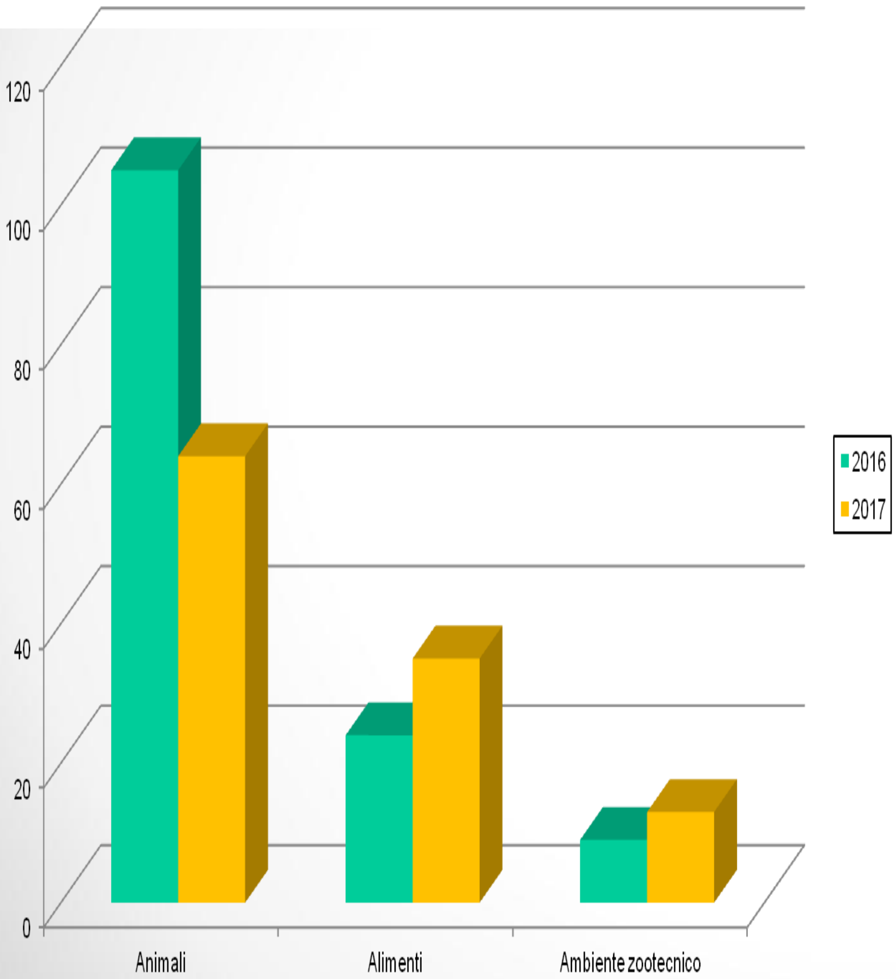


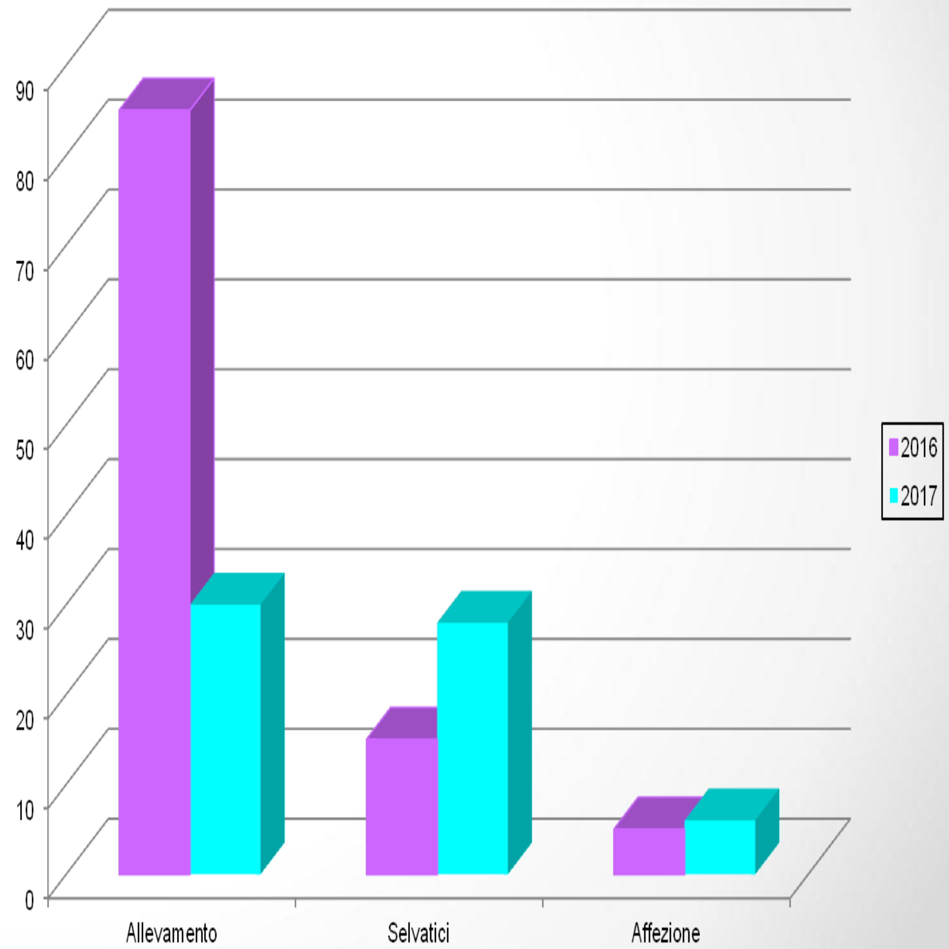
Fonte: Ministero della Salute

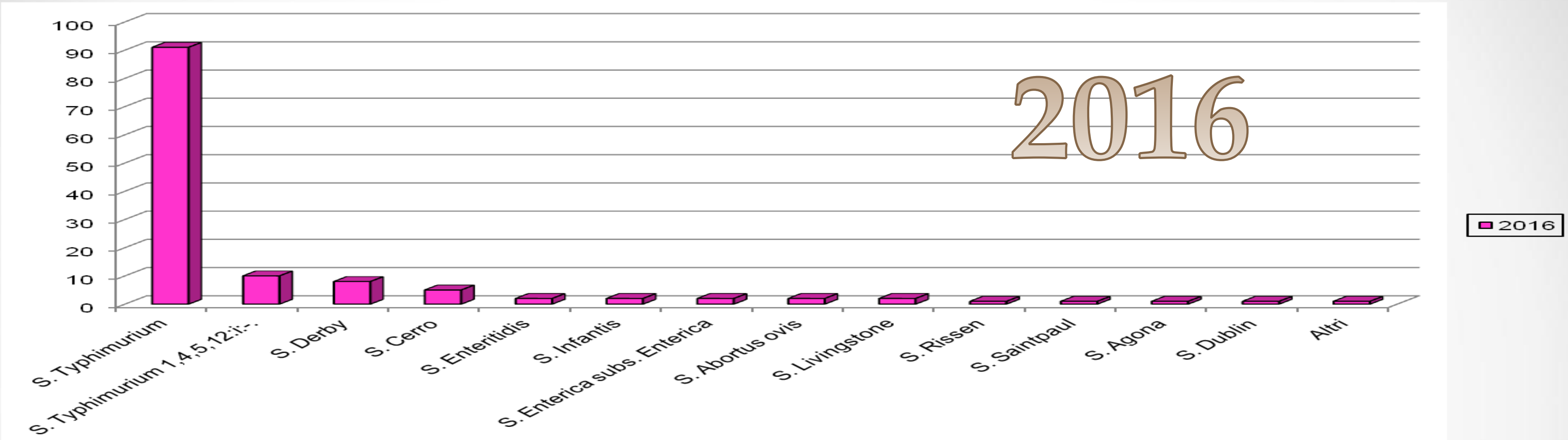
ANTIBIOTICI IN MEDICINA VETERINARIA

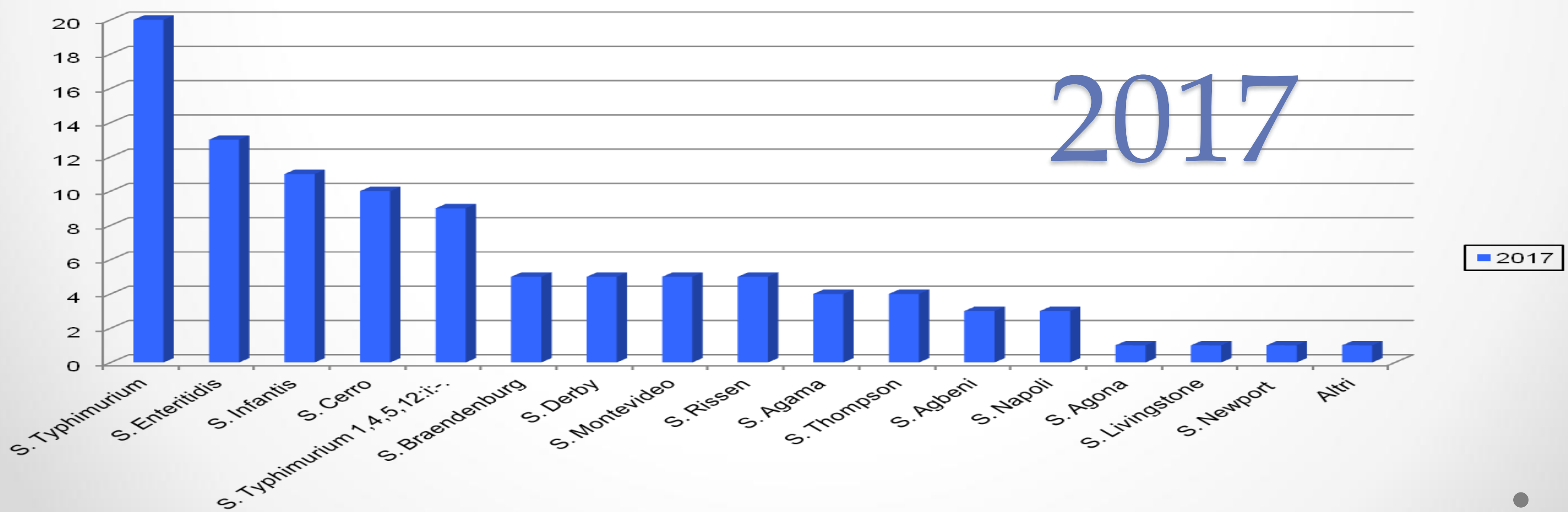


Origine ceppi – Salmonella spp.

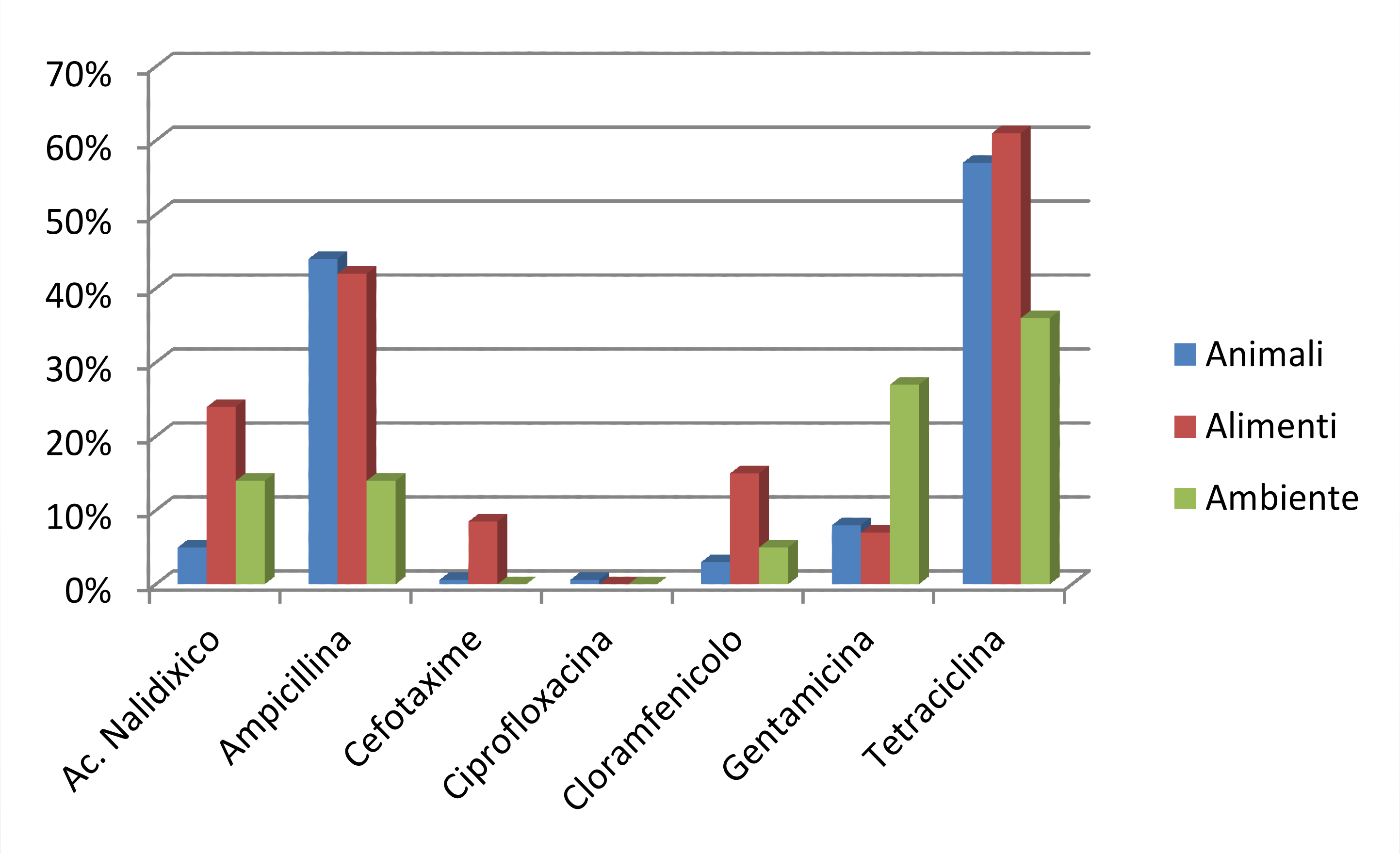





2016
100
90
80
70
60
50
40
30
20
10
0
S.Typhimurium
S.Typhimurium 1,4,5,12:i:-.
S.Derby
S.Cerro
S.Enteritidis
S.Infantis
S.Enterica subs.Enterica
S.Abortus ovis
S.Livingstone
S.Rissen
S.Saintpaul
S.Agona
S.Dublin
Altri
2016

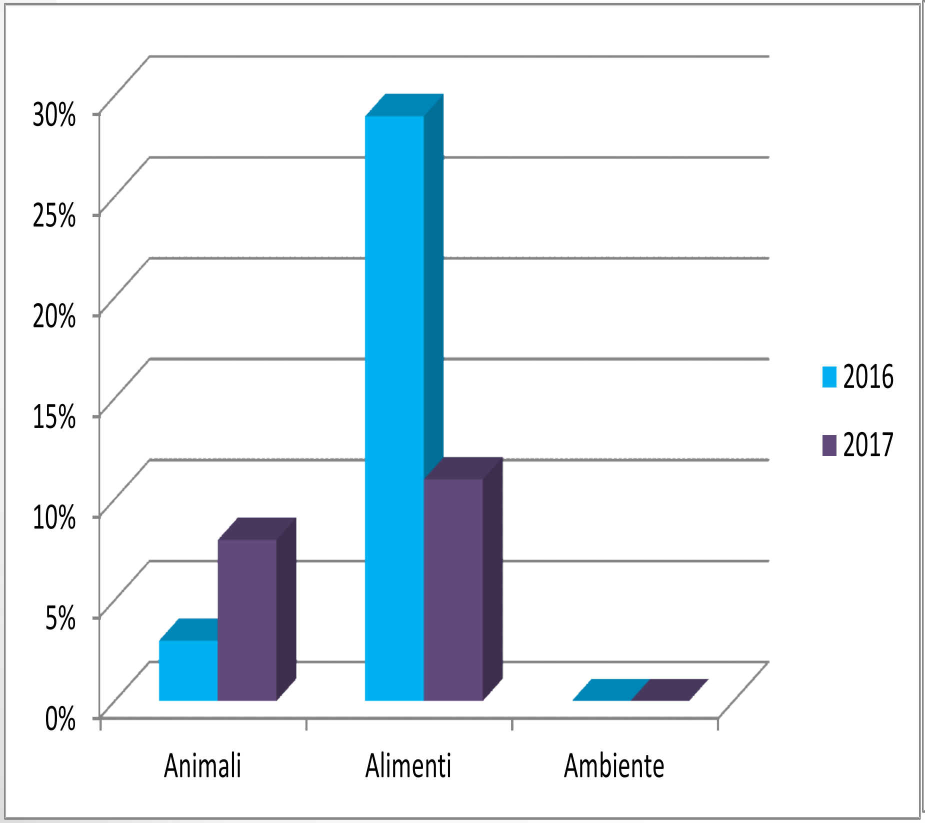

2017
20
18
16
14
12
10
8
6
4
2
0
S.Typhimurium
S.Enteritidis
S.Infantis
S.Cerro
S.Typhimurium 1,4,5,12:i:-.
S.Braendenburg
S.Derby
S.Montevideo
S.Rissen
S.Agama
S.Thompson
S.Agbeni
S.Napoli
S.Agona
S.Livingstone
S.Newport
Altri
2017

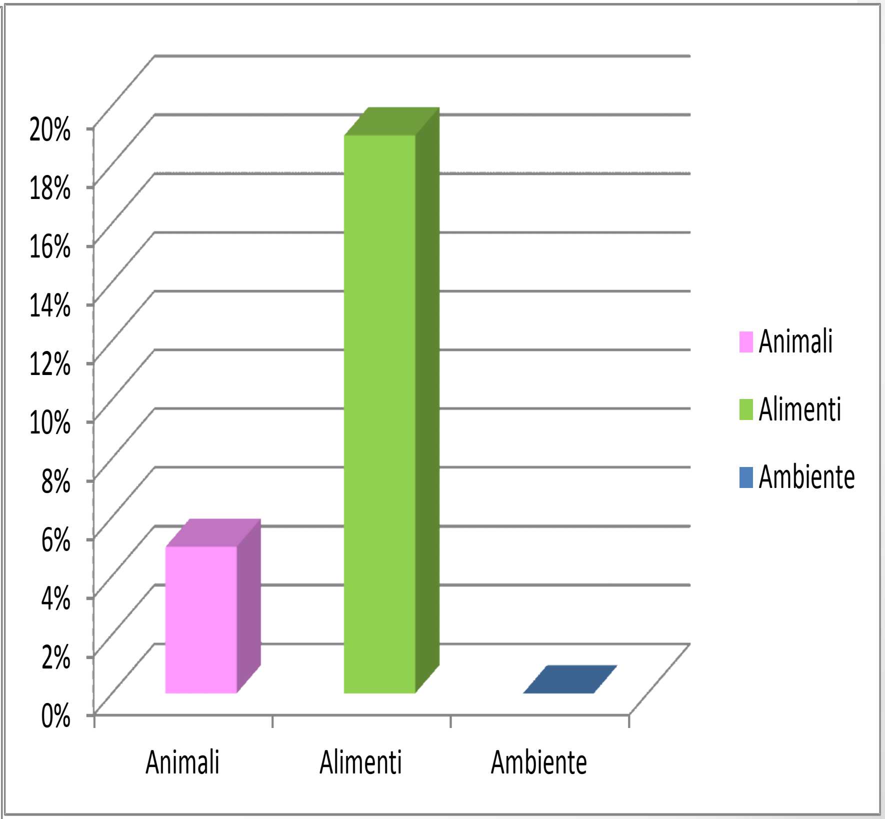
% di Resistenza ceppi Salmonella spp. isolati da animali, da alimenti e da ambiente, 2016-2017



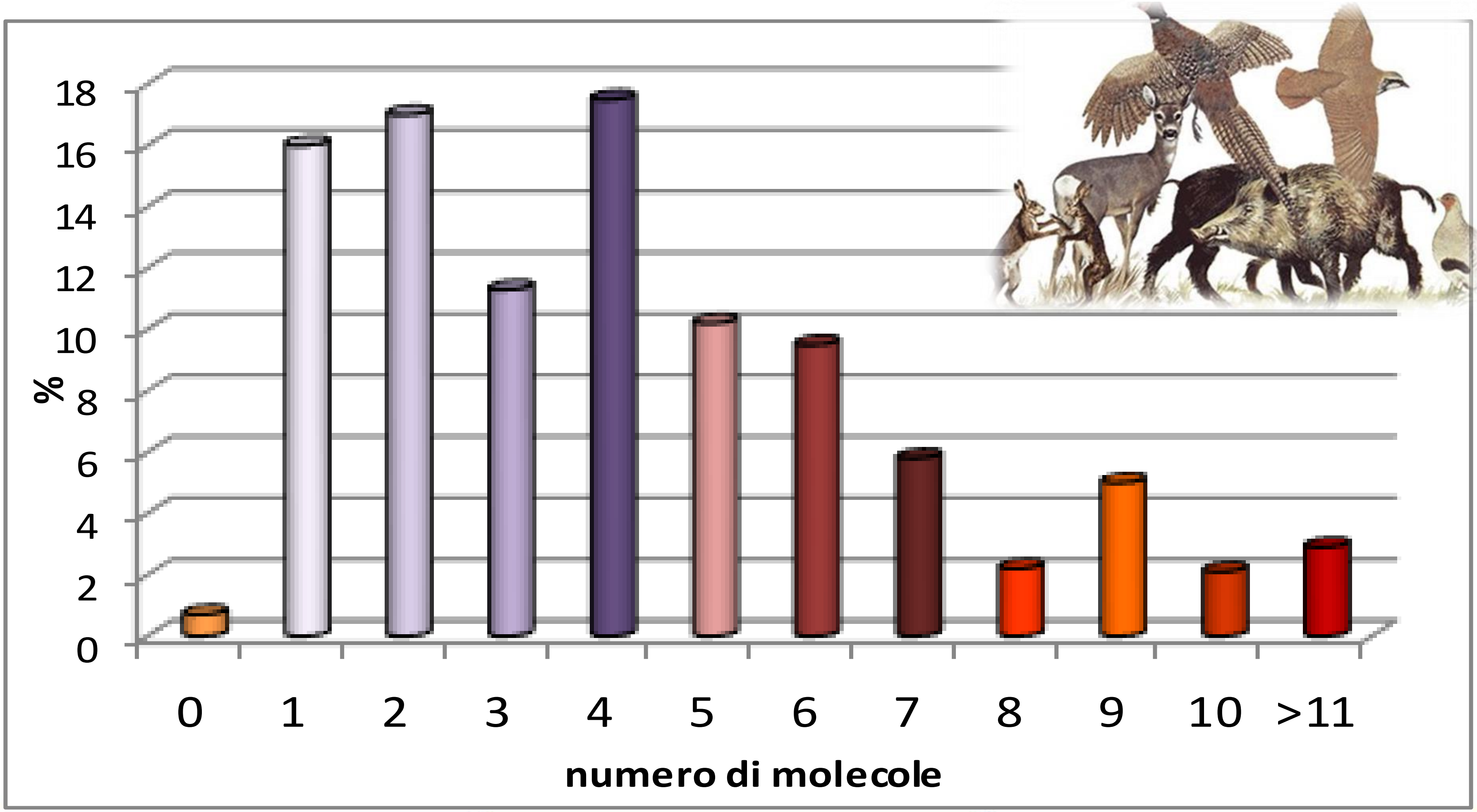
Ceppi multiresistenti (≥ 3 resistenze) - Salmonella spp.

Antibiotici considerati: Ac. Nalidixico, Ampicillina, Cefotaxime, Ciprofloxacina, Cloramfenicolo, Gentamicina, Tetraciclina





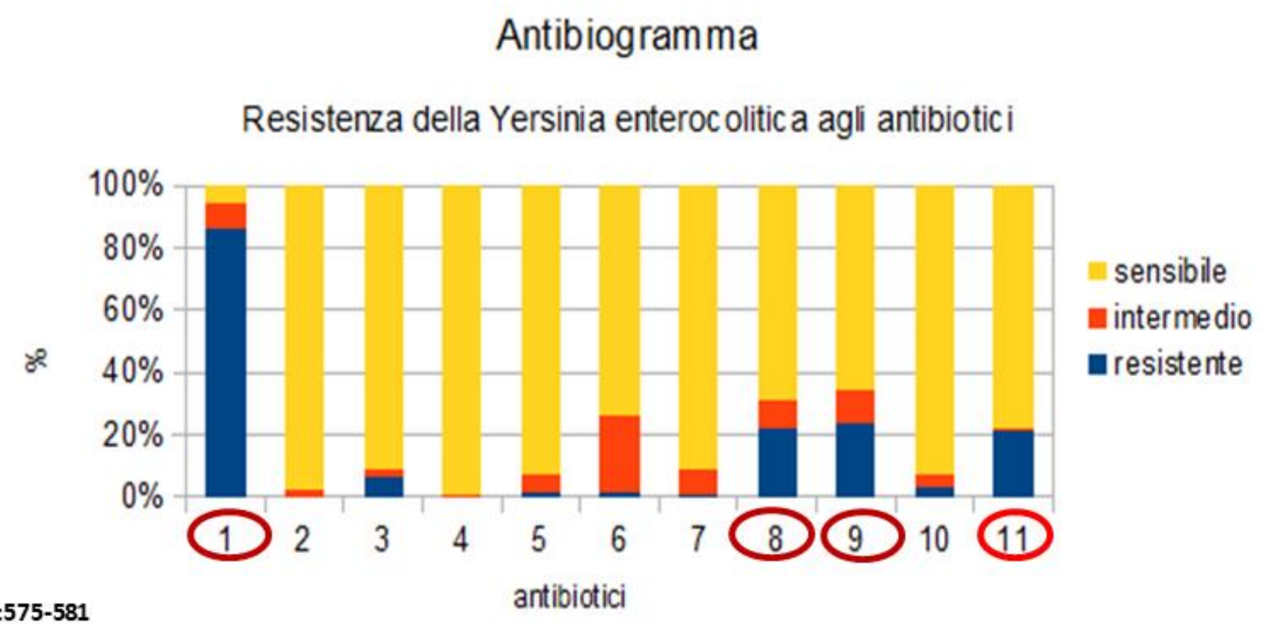
Salmonella e Antibioticoresistenza



Yersinia enterocolitica e Antibioticoresistenza

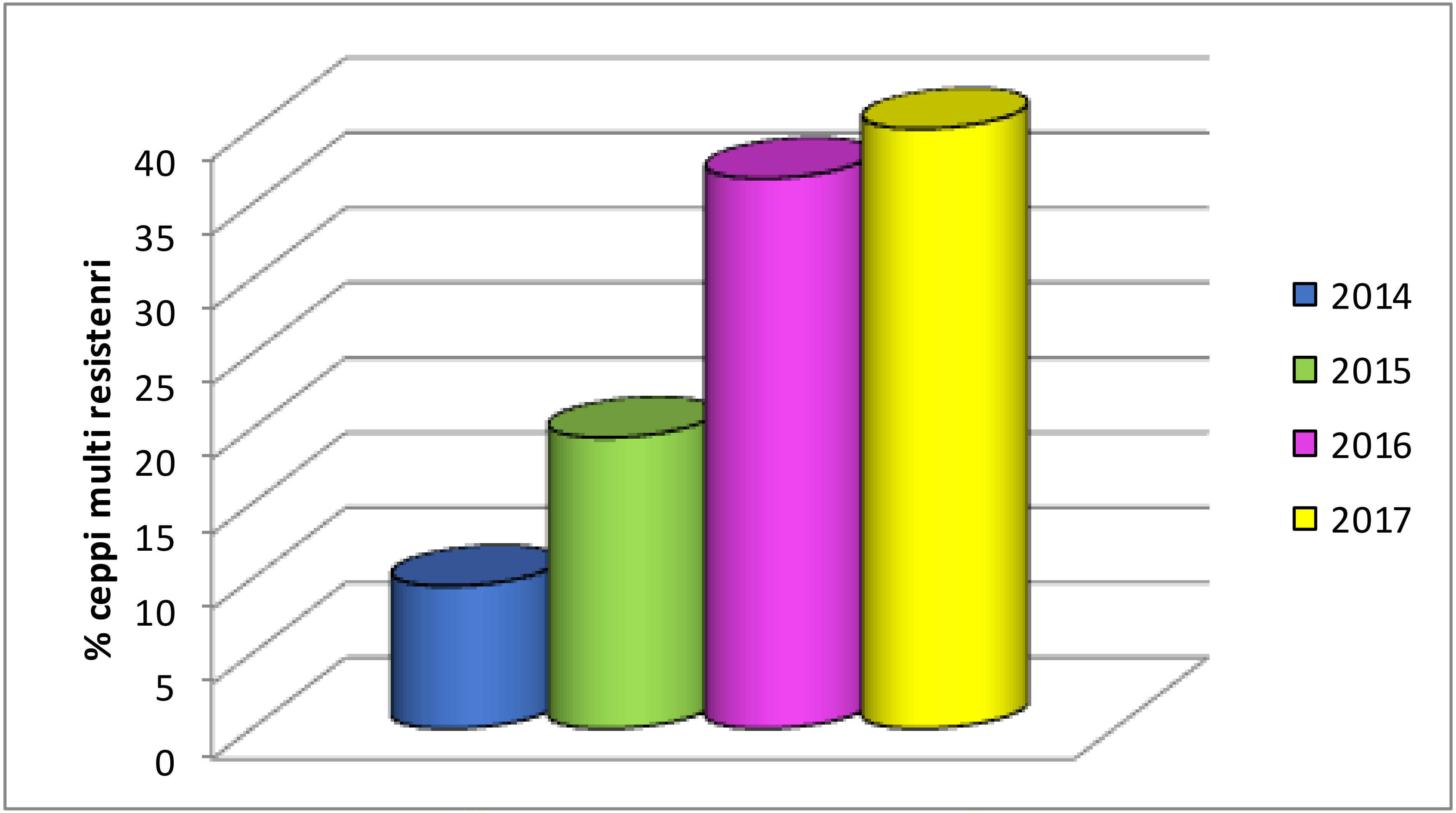
testata la sensibilità alle seguenti molecole:

1-Triple-Sulfa
2-Sulfameto + Trimethoprim
3-Tetraciclina
4-Ampicillina
5-Cloranfenicolo
6-Streptomicina
7-Ceftiofur
8-Enrofloxacina
9-Gentamicina
10-Kanamicina
11-Sulfissoxazolo

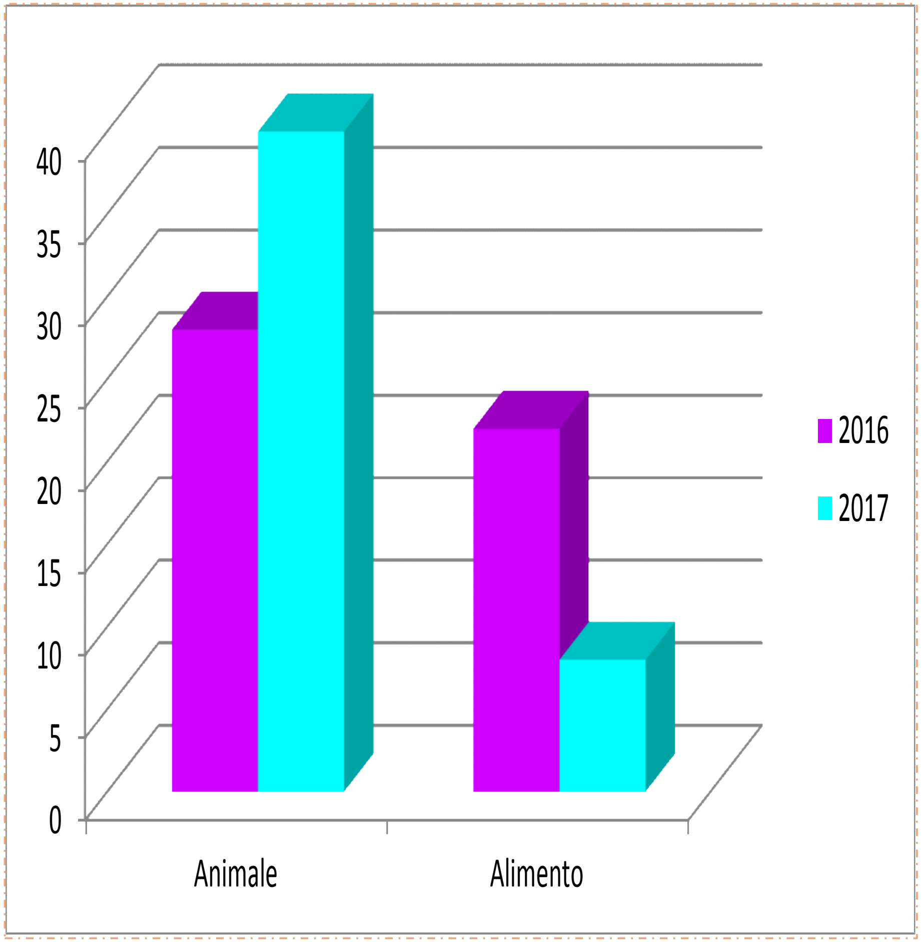


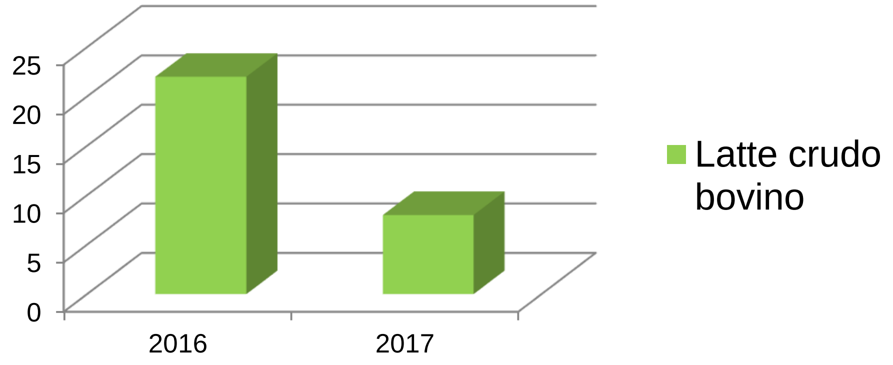
Bonke et al., 2011. Microbial drug resistance. 17:575-581

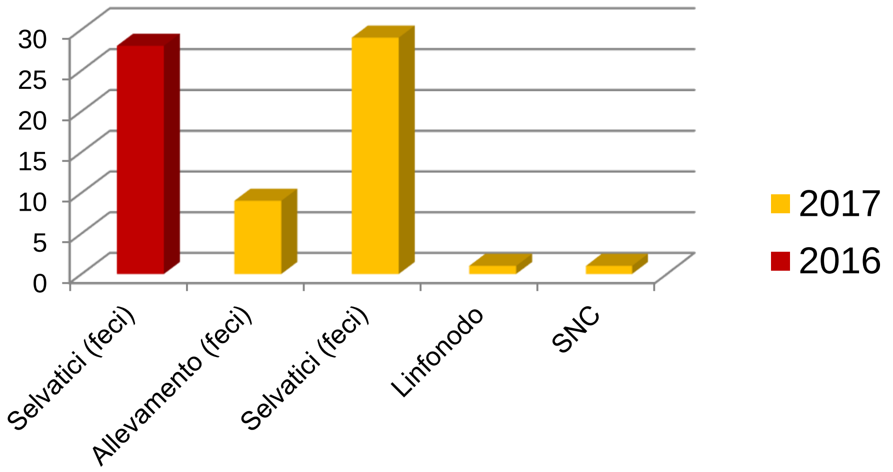
Yersinia enterocolitica e Antibioticoresistenza



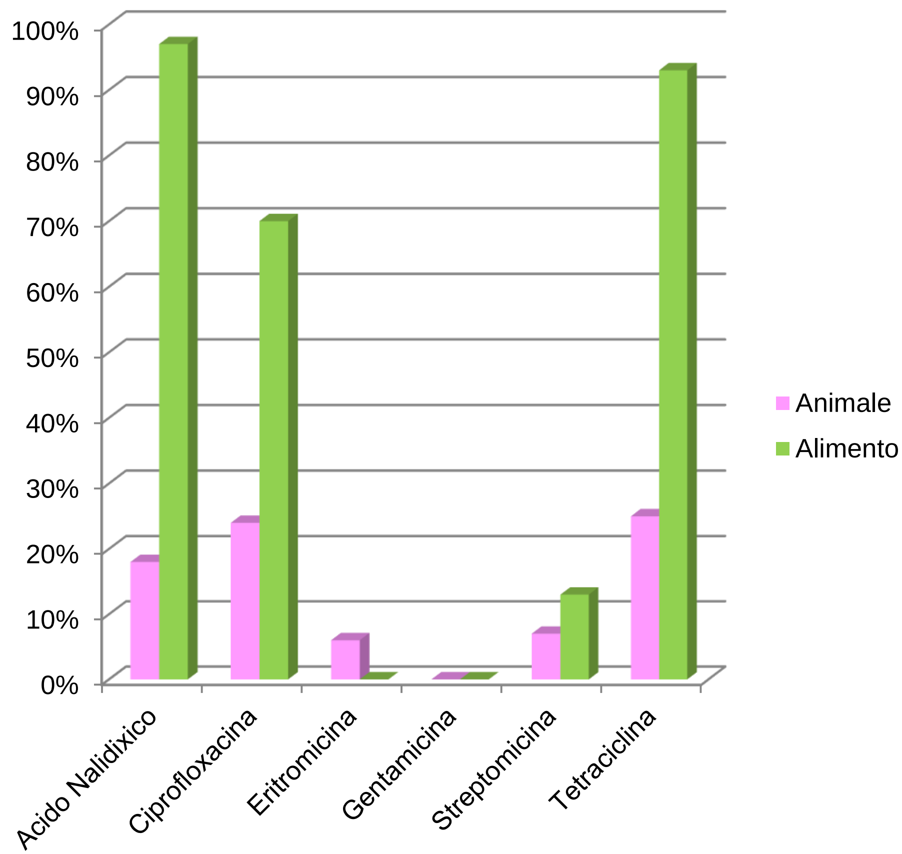
Origine ceppi – *Campylobacter* spp.

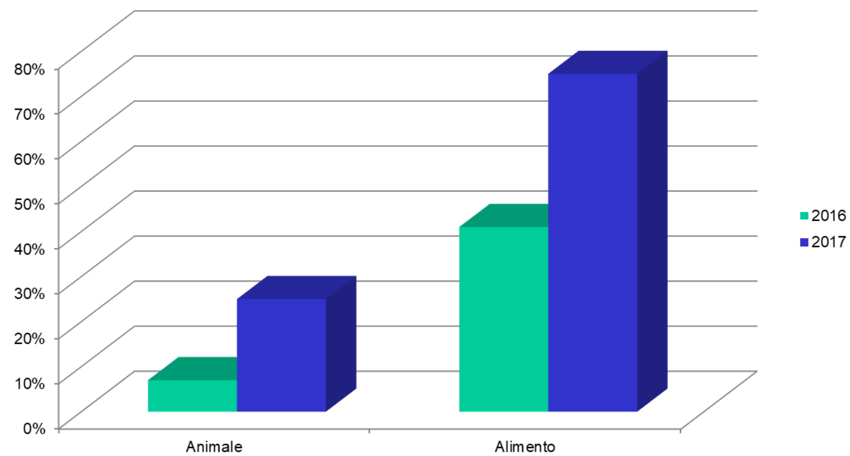


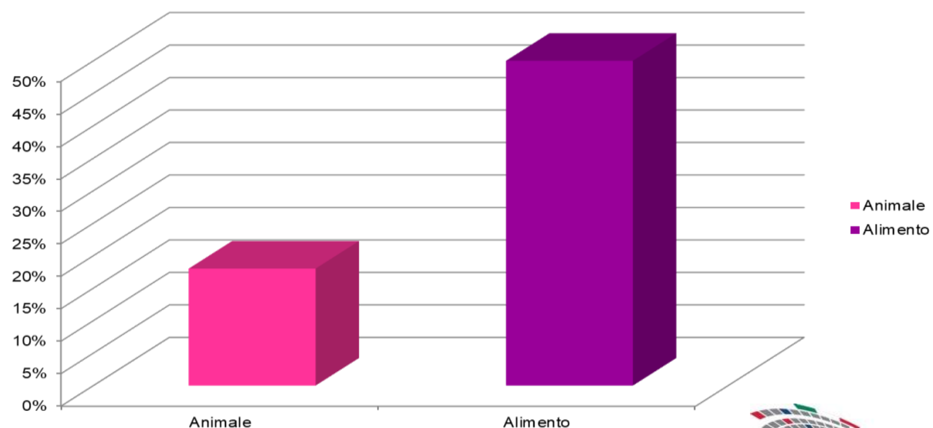




% di Resistenza ceppi *Campylobacter* spp. di origine animale e alimentare







Il test di sensibilità agli antibiotici (MIC) è stato eseguito presso il Laboratorio Nazionale di Riferimento per Campylobacter, IZSAM

IZSAM G.CAPORALE TERAMO

COSA STIAMO FACENDO???

1. *La ricetta elettronica*
2. *Miglioramento del benessere degli animali in produzione zootecnica*
3. *Utilizzo di immuno-modulanti*
4. *Utilizzo di molecole alternative*
5. *Selezione di razze resistenti*

La ricetta elettronica

COSA STIAMO FACENDO???

1. ***La ricetta elettronica***
2. ***Miglioramento del benessere degli animali in produzione zootecnica***
3. ***Utilizzo di immuno-modulanti***
4. ***Utilizzo di molecole alternative***
5. ***Selezione di razze resistenti***

BENESSERE ANIMALE

Lo stress è un influsso ambientale che sovraccarica i sistemi di controllo e regolazione dell'organismo.

Animale stressato

↓

Animale immunosoppresso

↓

Antibiotico ad uso veterinario ← *Rischio di malattia*

↓

Antibiotico ad uso umano/veterinario ← *Rischio Zoonosi*

↓

Rischio per la salute umana

- ***Produce meno***

- ***Produce alimenti di qualità inferiore***

Es. ***Bovina da latte***

a seguito di stress da caldo presenta calo della produzione di latte e peggioramento della qualità in termini di grasso e proteine con aumento delle cellule somatiche.

Diminuita resa alla caseificazione →

L'ESEMPIO DELLA BOVINA DA LATTE

Le bovine ad alta produzione di latte sono più suscettibili alle malattie infettive (es. mastite), stress metabolico (es. cheto-acidosi)

1. *ispezione clinica tempestiva;*
2. *valutazione dei parametri di benessere degli animali;*
3. *Uso di test predittivi basati sulla funzionalità del sistema immunitario.*

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Strategies for reduced antibiotic usage in dairy cattle farms

Erminio Trevisi [a], Alfonso Zecconi [b], Simone Cogrossi [a], Elisabetta Razzuoli [c], Paolo Grossi [a], Massimo Amadori [c,*]

[a] Istituto di Zootecnica, Facoltà di Scienze Agrarie, Alimentari e Ambientali, Università Cattolica del Sacro Cuore, 29122 Piacenza, Italy
[b] Dept. Veterinary Sciences and Public Health - Università degli Studi di Milano, 20133 Milano, Italy
[c] Laboratory of Cellular Immunology, Istituto Zooprofilattico Sperimentale della Lombardia e dell'Emilia-Romagna, 25124 Brescia, Italy

ARTICLE INFO

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Antibiotics
Usage
Disease resistance
Predictive parameters

ABSTRACT

The need for antibiotic treatments in dairy cattle farms can be reduced by a combined intervention scheme based on: (1) timely clinical inspections, (2) the assessment of animal-based welfare parameters, and (3) the use of predictive laboratory tests. These can provide greater insight into environmental adaptation of dairy cows and define animals at risk of contracting disease. In the long-term, an improved disease control justifies the adoption of such a combined strategy. Many antibiotic treatments for chronic disease cases are often not justified with a cost/benefit analysis, because the repeated drug administration does not give rise to the expected outcome in terms of animal health. In particular, compared with untreated cases, antibiotics may not lead to greater cure rates for some forms of mastitis. Lastly, a substantial reduction of antibiotic usage in dairy farms can be achieved through the proper use of immunomodulators, aimed at increasing immunocompetence and disease resistance of cows.

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Research in Veterinary Science

journal homepage: www.elsevier.com/locate/rvsc

Metabolic stress and inflammatory response in high-yielding, periparturient dairy cows

E. Trevisi [a], M. Amadori [b,*], S. Cogrossi [a], E. Razzuoli [b], G. Bertoni [a]

[a] Istituto di Zootecnica, Facoltà di Agraria, Università Cattolica del Sacro Cuore, 29122 Piacenza, Italy
[b] Laboratory of Cellular Immunology, Istituto Zooprofilattico Sperimentale della Lombardia e dell'Emilia-Romagna, 25124 Brescia, Italy

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Stress
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Acute phase protein

ABSTRACT

Increased disease rates are commonly reported among high-yielding dairy cows in the transition period, extending from 3 weeks before to 3 weeks after calving, and characterized by the occurrence of an inflammatory response in terms of both positive and negative acute phase proteins (APP+ and APP–). To determine the above inflammatory response, the authors had developed the Liver Functionality Index (LFI), which defines the above condition on the basis of some APP– responses (albumin, cholesterol *sensu stricto* + bilirubin) during the first month of lactation. In this respect, low LFI values are associated to a high inflammatory response and vice versa. The relationship between LFI and inflammatory cytokine response was investigated from day –28 to day +28 with respect to calving in 12 periparturient dairy cows showing the six highest and six lowest LFI values within a cohort of 54 high-yielding dairy cows. The hypothesis being tested was that LFI and APP– on the whole could be used as readout of successful vs. non-successful adaptation to the transition period, with a strong association to disease occurrence. In fact, low LFI cows experienced many more disease cases (13 vs. 3 in high LFI Group) and related drug treatments till day +28. Interleukin-6 (IL-6) serum concentrations were always higher in low LFI cows ($P < 0.05$ on day +28). The greater IL-6 levels were correlated with higher ceruloplasmin (APP+) and lower lysozyme serum concentrations ($P < 0.05$ and < 0.1, respectively). This latter finding was correlated with a clear role *in vitro* of lysozyme in a dose-dependent modulation of the inflammatory response of swine intestinal epithelial cells and bovine peripheral blood mononuclear cells. Hematological examinations showed no significant differences between the two groups under study. On the whole, our results indicate that LFI and LFI-related parameters could be used to identify cows at risk in the transition period toward an improved farm management. Also, our study indicates that disease cases in periparturient, high-yielding dairy cows are correlated with signs of accentuated IL-6 response and other markers of inflammatory phenomena. These likely start in the late lactation period or around dry-off, as suggested by our prepartal data, and proceed at much greater levels after calving.

Valutazione della funzionalità epatica
(1 mese lattazione)

↓

APP-
(albumina, colesterolo, bilirubina)

↓

Animali con basso indice epatico
(Incremento IL-6, ceruloplasmina e diminuzione del lisozima)

↓

rischio di malattia nel periparto

La valutazione di questi parametri permette:

- *valutare il rischio di sviluppare malattia nel periparto*
- *migliore gestione degli animali in allevamento*
- *prevenzione delle malattie condizionate*
- *diminuzione del ricorso agli antibiotici*

IMMUNO-MODULANTI

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EXTENDED ABSTRACT

Clinical chemistry parameters of piglets at weaning are modulated by an oral, low-dose interferon-α treatment

E. Razzuoli • S. Dotti • I. L. Archetti • M. Amadori

Utilizzo di IFN-α a basso dosaggio

- 1 UI/Kg p.v. somministrati con acqua da bere nei 10 giorni successivi allo svezzamento;
- Miglioramento dei parametri correlati alla risposta infiammatoria;
- Miglioramento degli incrementi ponderali;
- Nessun caso di malattia post-svezzamento

IMMUNO-MODULANTI

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Evaluation of interleukin-2 treatment for prevention of intramammary infections in cows after calving

Alfonso Zecconi [a,*], Renata Piccinini [a], Silvia Fiorina [a], Luca Cabrini [a], Valentina Daprà [a], Massimo Amadori [b]

[a] *Dpt.Animal Pathology, Hygiene and Health, Università degli Studi di Milano 20133, Milano, Italy*
[b] *Dpt. Animal Welfare and Immunoprophylaxis, Istituto Zooprofilattico Sperimentale della Lombardia e dell' Emilia-Romagna, 25124 Brescia, Italy*

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Abstract

A low-dose treatment based on interleukin-2 (IL-2) was investigated for preventing mastitis in dairy cows. The treatment consisted of a single dose of IL-2 injected into the skin region drained by the supramammary lymph node 3–5 days after calving. The study included 45 cows (23 treated and 22 controls) from three commercial dairy herds. The results showed that the treatment had no side effects. The treatment with IL-2 induced the significant increase of several milk markers related to leukocyte and epithelial cell functions, i.e. SCC (somatic cell counts), serum amyloid A (SAA), lactoferrin and NAGase. The increased concentration of milk markers suggested also an activity of IL-2 on epithelial cells, resulting in a higher resistance to invading pathogens. Indeed, the increased efficiency of cells in the udder is supported by the higher frequency of healthy quarters observed in the treated group until day 17–19 after calving, in comparison with the control one.

Utilizzo di IL-2 a basso dosaggio

- 1 pg/Kg p.v. somministrati nel linfonodo sopra-mammario 3-5 giorni dopo il parto;
- Miglioramento dei parametri correlati alla funzionalità cellulare;
- Maggior resistenza ai patogeni;
- Diminuzione casi mastite.

MOLECOLE ALTERNATIVE

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KeAi CHINESE ROOTS GLOBAL IMPACT

Review Article

Essential oils as alternatives to antibiotics in swine production

Faith A. Omonijo [a], Liju Ni [a, b], Joshua Gong [c], Qi Wang [c], Ludovic Lahaye [d], Chengbo Yang [a, *]

[a] Department of Animal Science, University of Manitoba, Winnipeg, MB R3T 2N2, Canada
[b] Shanghai Lab-Animal Research Center, Shanghai 201203, China
[c] Guelph Food Research Centre, Agriculture and Agri-Food Canada, Guelph, ON N1G 5C9, Canada
[d] Jefo Nutrition Inc., Saint-Hyacinthe, QC J2S 7B6, Canada

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ABSTRACT

This review article summarizes the efficacy, feasibility and potential mechanisms of the application of essential oils as antibiotic alternatives in swine production. Although there are numerous studies demonstrating that essential oils have several properties, such as antimicrobial, antioxidative and anti-inflammatory effects, feed palatability enhancement and improvement in gut growth and health, there is still a need of further investigations to elucidate the mechanisms underlying their functions. In the past, the results has been inconsistent in both laboratory and field studies because of the varied product compositions, dosages, purities and growing stages and conditions of animals. The minimal inhibitory concentration (MIC) of essential oils needed for killing enteric pathogens may not ensure the optimal feed intake and the essential oils inclusion cost may be too high in swine production. With the lipophilic and volatile nature of essential oils, there is a challenge in effective delivery of essential oils within pig gut and this challenge can partially be resolved by microencapsulation and nanotechnology. The effects of essential oils on inflammation, oxidative stress, microbiome, gut chemosensing and bacterial quorum sensing (QS) have led to better production performance of animals fed essential oils in a number of studies. It has been demonstrated that essential oils have good potential as antibiotic alternatives in feeds for swine production. The combination of different essential oils and other compounds (synergistic effect) such as organic acids seems to be a promising approach to improve the efficacy and safety of essential oils in applications. High-throughput systems technologies have been developed recently, which will allow us to dissect the mechanisms underlying the functions of essential oils and facilitate the use of essential oils in swine production.

Olii essenziali

Due principali classi di molecole:

- Terpeni
  (es. Timolo e Cavacrolo)
- Fenilpropanoidi (es. Eugenolo)

Alcune proprietà:

- Attività antimicrobica
  (Gam- e Gram +)
- Effetto anti-infiammatorio
- Effetto antiossidante
- Coccidiostatici

SELEZIONE GENETICA

Journal of Fish Diseases 2014 doi:10.1111/jfd.12193

Association of a specific major histocompatibility complex class IIβ single nucleotide polymorphism with resistance to lactococcosis in rainbow trout, *Oncorhynchus mykiss* (Walbaum)

S Colussi, M Prearo, S A Bertuzzi, T Scanzio, S Peletto, L Favaro, P Modesto, M G Maniaci, G Ru, R Desiato and P L Acutis
Istituto Zooprofilattico of Piemonte, Liguria and Valle d'Aosta – Via Bologna, Turin, Italy

Lattococcosi

- Malattia batterica causa di gravi perdite negli allevamenti di trote
- Vaccinazione ed uso di antibiotici
- Possibilità di selezionare animali resistenti
- Lo studio evidenzia resistenza alla malattia in soggetti che presentano l'aplotipo 25 per il MHCII (cruciale la presenza di fenilalanina in posizione 47).

GRAZIE PER L'ATTENZIONE !

..Meglio vivere una vita da sani e morire malati che non vivere una vita da malati e morire da sani!