Preserving antibiotics for human health: banning colistin in Ecuador

Jorge Reyes

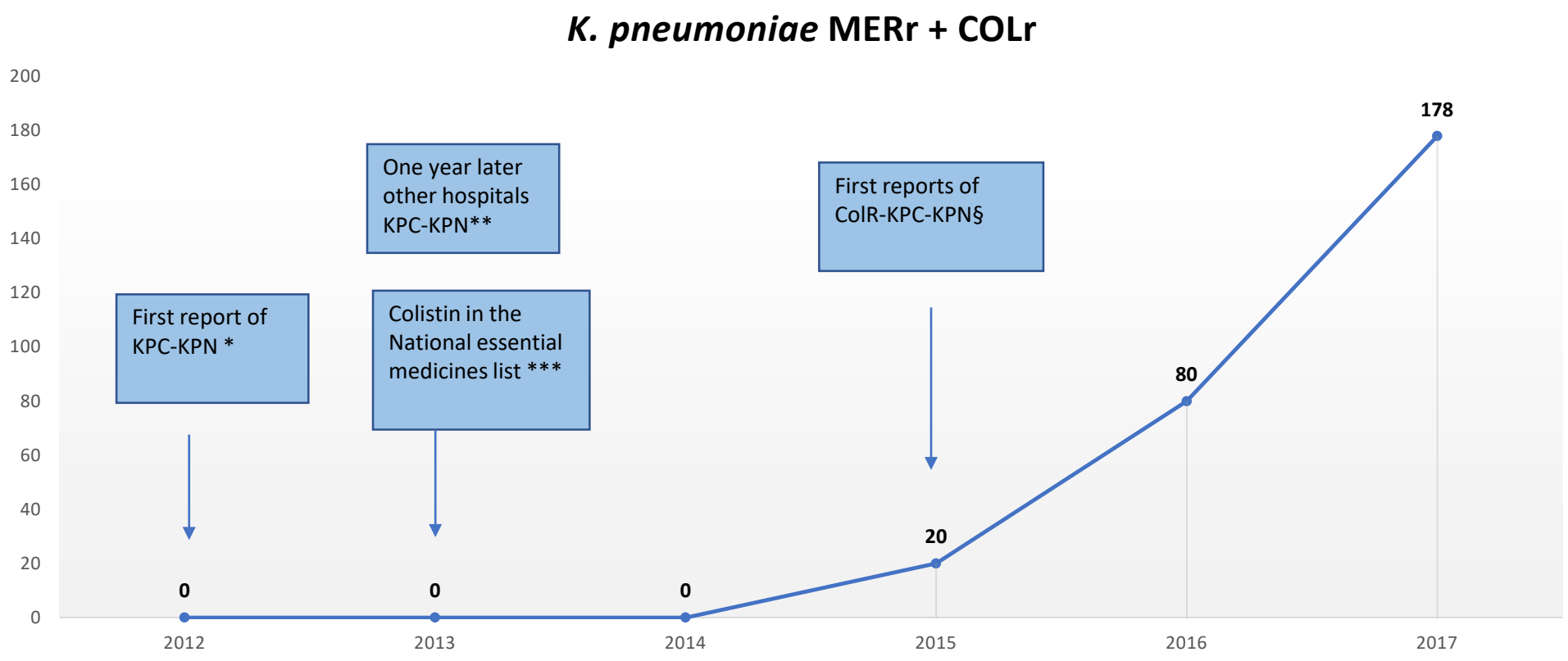
- **Outline:**

1. Colistin in humans
2. Colistin in animals

Colistin in humans

Carbapenem and colistin resistant *Klebsiella pneumoniae* isolates

First reports of KPC-KPN, colistin in the national essential medicines list (EML) and ColR-*K. pneumoniae*



***Iñiguez D. 2012. **Zurita J 2013 *** Ministry of Health 2013 § INSPI-LIP 2018.**

Molecular mechanisms for colistin resistance in KPC -producing *K. pneumoniae*

ST	Strain code	Location	Source	MIC µg/mL BMM COL	Carbapenemase	*mcr* 1-5	*MgrB*	*PhoQ*	*crrAB*	*PhoP*	*PmrA*	*PmrB*	*pmrD*
258 (N=2)	L6	ICU	Tracheal	16	KPC-2	Neg.	F28C*	WT	Pos	WT	WT	R256G* Deleterious	
	L35	Internal medicine	Blood	16	KPC-2	Neg.	F28C	WT		WT	WT	R256G* Deleterious	
25 (N=2)	L73	ICU	Tracheal	16	KPC-2	Neg.	WT	WT		WT	WT	WT	
	L71	Urology	Blood	32	KPC-2	Neg.	WT	WT		WT	WT	WT	
39 (N=2)	L5	Traumatology	blood	16	KPC-2	Neg.	WT	WT		WT	WT	WT	
	L17	Emergency	Tracheal	32	KPC-2	Neg.	Insertional inactivation, IS*kpn*14 + nt72 and + nt73	WT		WT	WT	WT	
15	L53	ICU	Blood	Emergency	KPC-2	Neg	F28C*	WT	---------	WT	WT	T246A*	WT
3023	L70	Cardiology	Catheter	32	KPC-2	Neg	Insertional inactivation, IS*1* n+117	WT	------	WT	I66M**	WT	WT

Reyes J. et al. 2018

Risk factors and clinical outcomes - ColR-KPC-KPN

	CONTROLS N=59 (%)	CASES N=24 (%)	p-value	OR
Age (years), mean, ±DS,	53.2, 20.5, (16-87)	53.25, 17.9, (20-80)	0.99	
Hospitalization days, mean, ±DS	48.5 (37.5-59.4)	56.5 (41.5-71.6)	0.15	
Mortality	25 (44.6)	14 (58.3)	0.33	
Mechanical ventilation	34 (57.63)	18 (75)	0.14	2.21 (0.76-6.35)
Central catheter	31 (52.54)	19 (79.17)	0.03	3.4 (1.13-10.4)
Peripheral venous catheter	41 (69.49)	22 (91.67)	0.03	4.85 (1.02-22.7)
Urinary catheter	29 (49.15)	20 (83.33)	0.004	5.2 (1.6-16.9)
Use of antibiotics 6 months	16 (27.1)	14 (58.3)	0.01	3.8 (1.4-10)
β-lactam/β-lactamase inhibitor	32 (54.2)	9 (37.5)	0.23	0.50 (0.2-1.33)
Carbapenems	47 (79.7)	20 (83.3)	1.0	1.27 (0.36-4.44)
Colistin	38 (64.4)	18 (75)	0.44	1.66 (0.57-4.8)
Tigecycline	20 (33.9)	12 (50)	0.22	1.95 (0.74-5.1)

Reyes J. et al. 2019.

Use of colistin in Ecuador. Example of a high complexity hospital

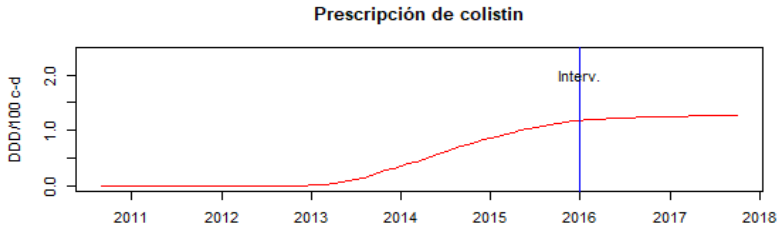
- **Use of colistin in public hospitals . Units/year :**
- 2017: 15.924
- 2018: 16.523

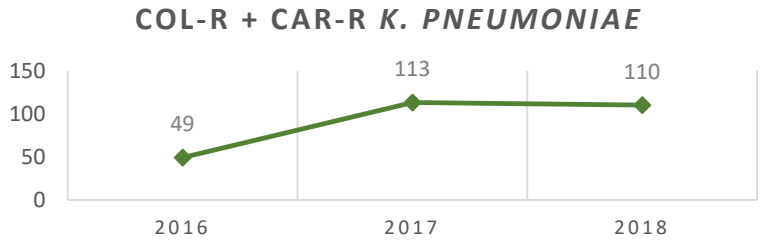
Health Observatory - Universidad Central del Ecuador.

Consumo de colistin en el HCAM por servicios

2013					
Servicios	Cirugía	Clínica	Emergencia	Pediatría	Terapia Intensiva
Unid. prescritas	150	127	11	48	243
Pacientes	4	7	2	1	14
USD	$ 12,226.50	$ 10,351.77	$ 896.61	$ 3,912.48	$ 19,806.93
2014					
Unid. prescritas	1,180	414	140	22	1,291
Pacientes	41	15	11	2	60
USD	$ 69,683.00	$ 23,080.84	$ 10,248.00	$ 574.42	$ 80,452.81
2015					
Unid. prescritas	1,222	1,026	55	81	2,899
Pacientes	160	62	7	5	26
USD	$ 20,390.56	$ 16,560.32	$ 973.02	$ 1,206.90	$ 48,159.70
2016					
Unid. prescritas	1,006	966	15	191	4,267
Pacientes	39	80	5	23	149
USD	$ 14,989.40	$ 14,393.40	$ 223.50	$ 2,845.90	$ 63,578.29
2017					
Unid. prescritas	1,468	1,360	12	326	4,224
Pacientes	83	46	7	45	128
USD	$ 18,693.85	$ 18,219.07	$ 147.59	$ 3,766.70	$ 52,972.61
2018					
Unid. prescritas	1,359	1,358	21	252	2,403
Pacientes	44	74	6	18	109
USD	$ 11,491.16	$ 11,481.15	$ 177.50	$ 2,131.02	$ 20,314.38

Fuente: MIS-AS400 HCAM. Autor: H Romo

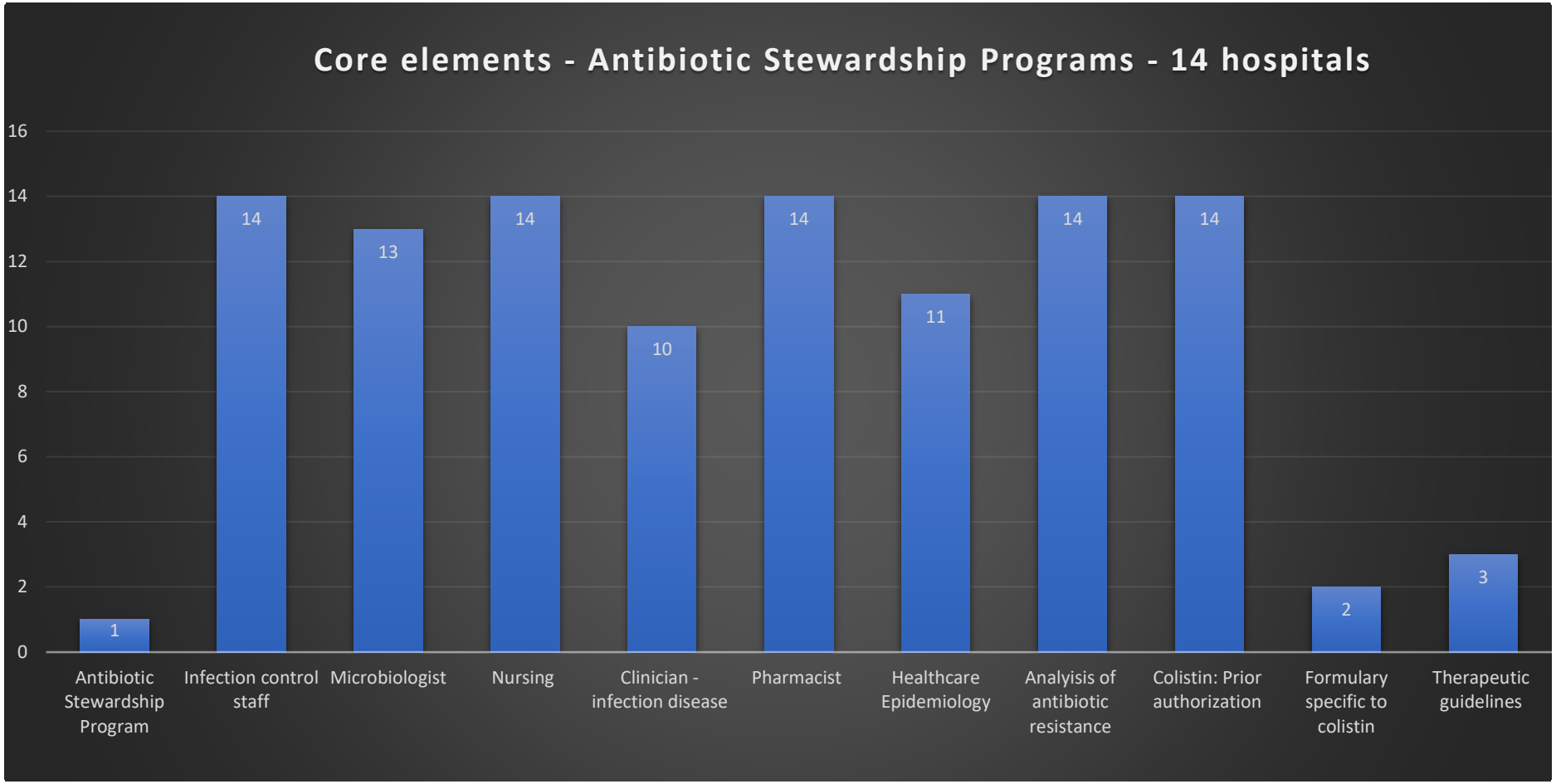




- High use of colistin in the Intensive Care Unit
- Increase of colistin precription and ColR.-KPN

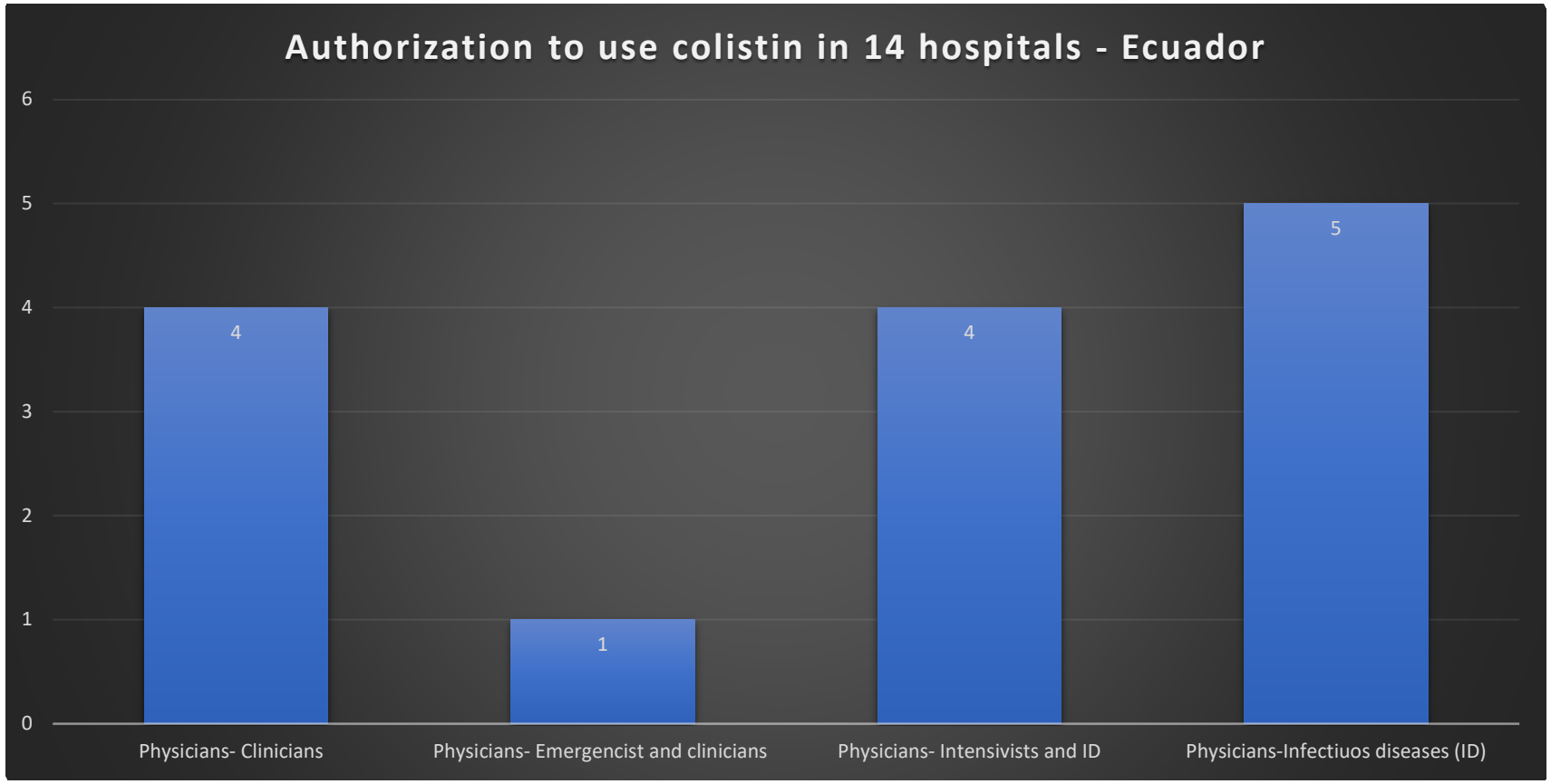
Romo H. et al. 2019.

Monitoring of Antibiotic Stewardship Programs implementation in 14 public hospitals to improve the use of colistin.



Reyes J. et al. 2019.

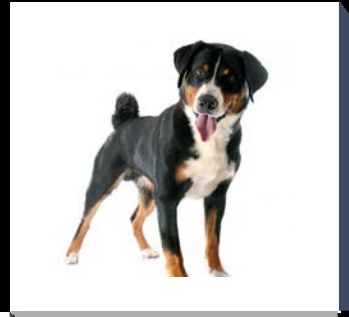
Physicians authorized to prescribe colistin in 14 public hospitals



Reyes J. et al. 2019

Colistin in animals

Presence of the *mcr-1* gene in *E. coli* isolates



Strain origin	Antimicrobial resistance	MLST	PCR	Plasmid Inc group										
		ST	*bla* genes	HI1	I2	N	FIA	FIB	I1γ	FIIS	R	X1	Y	FII
Chicken	COL, CRO, CIP	3941	$bla_{CTX-M-65}$	-	+	-	+	-	+	-	-	-	-	-
Turkey	COL, CRO, CIP	1630	bla_{TEM-1}; $bla_{CTX-M-65}$	+	-	-	-	-	+	-	-	-	-	-
Dog1	COL, SAM, CRO, CIP	2170	bla_{TEM-1}; $bla_{CTX-M-3}$	-	+	-	-	+	+	+	-	-	+	+
Dog2	COL, SAM, CRO, CIP, GN	2170	bla_{TEM-1}; $bla_{CTX-M-3}$	-	-	-	-	-	+	-	-	-	-	-
Child*	COL, CAZ, CRO, FEP, CIP	609 [13]	$bla_{CTX-M-55}$ [13]	-	+	+	-	-	+	-	+	+	-	-

79 COL, colistin; SAM, ampicillin/sulbactam; CAZ, ceftazidime; CRO, ceftriaxone; FEP, cefepime; GN, gentamicin; CIP, ciprofloxacin.

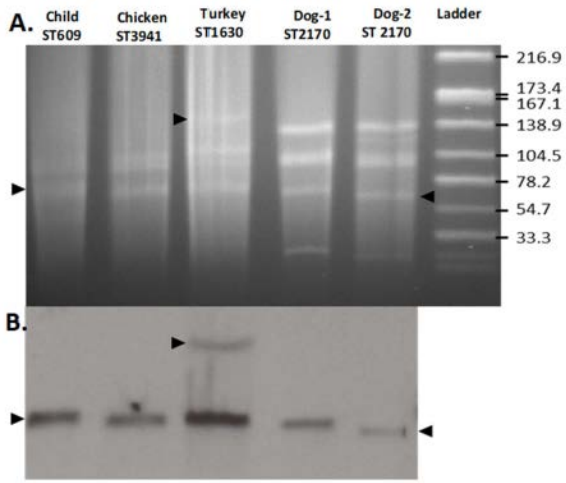
Epidemiol. Infect. (2016), **144**, 2967–2970. © Cambridge University Press 2016
doi:10.1017/S0950268816001369

SHORT REPORT

Colistin-resistant *Escherichia coli* clinical isolate harbouring the *mcr-1* gene in Ecuador

D. ORTEGA-PAREDES[1], P. BARBA[1] AND J. ZURITA[1,2]*

[1] *Unidad de Investigaciones en Biomedicina, Zurita & Zurita Laboratorios, Quito, Ecuador*
[2] *Facultad de Medicina, Pontificia Universidad Católica del Ecuador, Quito, Ecuador*



Source: Zurita J. . 2018. INSPI-Agrocalidad.

Source: Loaiza F. – Reyes J. 2018. INSPI-Agrocalidad.

Other reports of *mcr-1*-harboring *E. coli*:

*Poultry farms - “broiler farms”

**Pigs

§Colonization in humans

***Vinueza et al. 2019. **Yamamoto et al. 2019. §Villacís J. Reyes J. et al. 2019**

Ecuadorian Government Resolution

February 2019

“The manufacture, formulation, importation, trade, registration and use of products containing colistin is prohibited”

“The marketing authorization of all products containing colistin is canceled”

AGENCIA DE REGULACIÓN Y CONTROL FITO Y ZOOSANITARIO

Toda una Vida

EL GOBIERNO DE TODOS

RESOLUCIÓN 0003

EL DIRECTOR EJECUTIVO DE LA AGENCIA DE REGULACIÓN Y CONTROL FITO Y ZOOSANITARIO - AGROCALIDAD

CONSIDERANDO:

RESUELVE

Artículo 1.- Se prohíbe la fabricación, formulación, importación, comercialización, registro y uso de productos que contengan el ingrediente activo colistina (polimixina E) o cualquiera de sus sales como parte de su formulación para uso o consumo animal.

Artículo 2.- Se cancela el registro de todos los productos que contenga el ingrediente activo *colistina (polimixina E)* o cualquiera de sus sales como parte de su formulación para uso o consumo animal, de conformidad con el Anexo 1, mismo que forma parte integrante de la presente resolución.

Problems related to the document

- 1.- Colistin used to treat infections
- 2.- Antibiotics (colistin) used as growth promoters
- Economic impact related to swine and poultry production

Table 1. Antimicrobial additives used in pigs farm as prophylactics in group A.

Growth phase	Age (days)	Antimicrobial	Dose, ppm	Administration via
0	21 ├ 28	Tilmicosin	200	Food
		Colistin	40	Food
1	29 - 34	Tiamulin	150	Food
		Chlortetracycline	450	Food
2	35 - 45	Tiamulin	150	Food
		Chlortetracycline	450	Food
3	45 - 70	Tiamulin	150	Food
		Chlortetracycline	450	Food
4	70 - 85	Chlortetracycline	450	Food
5	123 - 139	Chlortetracycline	450	Food
2	37 - 40	Trimetoprim-sulfamethoxazole	25mg/Kg/PV	Water
3	45 - 47	Doxicycline	10mg/Kg/PV	Water

Loaiza F. et al 2018

Antibiotics (colistin) used as growth promoters

- Strategies:

Last Tuesday, a workshop was held on food safety. The following stakeholders were involved:

a) Government institutions: Agrocalidad, Senescyt, Ministry of health

b) Academic institutions (Public and private universities)

c) Industry (swine and poultry production) ¡¡¡ this is the challenge !!!

Objective: Find alternatives to growth promoters

GOBIERNO DE LA REPÚBLICA DEL ECUADOR

*SECRETARÍA DE EDUCACIÓN SUPERIOR, CIENCIA, TECNOLOGÍA E INNOVACIÓN * AGENCIA DE REGULACIÓN Y CONTROL FITO Y ZOOSANITARIO

INVITAN A USTED

Al taller para promover los estudios en inocuidad alimentaria

Fecha: Martes, 7 de mayo de 2019
Hora: 8:30 a 12:30
Lugar: Sala de reuniones de uso múltiple (3er piso)
Ministerio de Transporte y Obras Públicas
Calle Juan León Mera N26-220 y Av. Orellana
Quito - Ecuador

AGENCIA DE REGULACIÓN Y CONTROL FITO Y ZOOSANITARIO

AGENCIA DE REGULACIÓN Y CONTROL FITO Y ZOOSANITARIO – AGROCALIDAD

COORDINACIÓN GENERAL DE INOCUIDAD DE ALIMENTOS

Desarrollo de investigación, como una herramienta para la mitigación de contaminantes.

Organizador:	Agencia de Regulación y Control Fito y Zoosanitario - AGROCALIDAD Secretaría de Educación Superior, Ciencia, Tecnología e Innovación - SENESCYT
Lugar:	Sala de Reuniones de Uso Múltiple (3er piso) del Ministeriode Transporte y Obras Públicas
Fecha:	07 de mayo de 2019
Hora:	08H30 – 12H30

Conclusions

- Colistin resistant isolates are problem in public health
- The use of colistin is increasing in human and animals
- It is necessary to work together human and animal health to control the use of colistin

- Thank you …