

Title: Extended-spectrum cephalosporin resistance in *Salmonella* Heidelberg isolated from Argentinian poultry farms

Authors: Johana E. Dominguez^{1,2*}, Pablo Chacana¹, Mariana Herrera³, Gabriel O. Gutkind^{2,4}, Elsa C. Mercado¹, José Di Conza^{2,4}

Institutions: ¹Instituto de Patobiología, Centro de Investigación en Ciencias Veterinarias y Agronómicas, Instituto Nacional de Tecnología Agropecuaria (INTA), Nicolás Repetto y De los Reseros s/n, 1686, Hurlingham, prov. Buenos Aires, Argentina;

²Consejo Nacional de Investigaciones Científicas y Técnicas, Rivadavia 1917 (1033), Ciudad Autónoma de Buenos Aires, Argentina;

³Dirección de Laboratorios (DILAB), Servicio Nacional de Sanidad Animal (SENASA), Talcahuano 1660, Martínez, prov. Buenos Aires, Argentina;

⁴Facultad de Farmacia y Bioquímica, Universidad de Buenos Aires, Junín 954, 1113 Ciudad Autónoma de Buenos Aires, Argentina.

*e-mail: dominguez.elizabeth@inta.gob.ar

Summary: In the last years, *Salmonella enterica* serovar Heidelberg (SH) has become one of most frequently recovered serovars from broiler farms in Argentina. Resistance to various antimicrobial agents, including extended-spectrum cephalosporins (ESC) has been found among SH isolates thus demanding a more profound study of the mechanisms involved in order to contribute to the rational use of antimicrobials to treat salmonellosis in poultry. The aim of this study was to determinate the resistance to ESC on SH recovered from poultry farms located in two different geographical regions from Argentina. Susceptibility profile was analyzed in a selected group of 39 strains of SH by disk diffusion susceptibility test which comprised the analysis of ampicillin (AMP), cephalotin (CEP), cefuroxime (CXM), cefotaxime (CTX), ceftazidime (CAZ), ceftriaxone (CRO), ceftiofur (CFT), cefepima (FEP) and cefoxitina (FOX). Phenotypic screening for extended spectrum β -lactamases (ESBL) or plasmid AmpC β -lactamases (AmpCp) were performed by synergy tests using cefotaxime/clavulanic acid, ceftadizime/clavulanic acid or phenylboronic acid (PBA) containing disks, respectively. Genetic markers were characterized by PCR using specific primers. Most of genes were identified by sequencing. Twenty-one isolates were found to be resistant to AMP, CEP, CXM and third generation cephalosporins and 12/21 of these strains were also resistant to FEP but remained susceptible to FOX. Furthermore, ESBL confirmatory test was positive for all of them. The ESBLs were characterized as members of CTX-M-9 group (n = 8) and CTX-M-2 group (n= 4). The remaining strains (9/21) were resistant to FOX but remained susceptible to FEP. Synergy was observed between PBA and both CAZ and CTX disks, thus suggesting the presence of an AmpCp. Finally, CMY-2 was identified in these 9 isolates. In the context of the One Health principle established by the WHO and OIE, the increased use of cephalosporins to treat bacterial infections in food animals and the consequent emergence of resistance to this antimicrobial has obvious implications in public health. For example, ceftriaxone is the drug of first choice to treat severe salmonellosis in humans. Since poultry has been historically considered as a main source of salmonellosis in humans, further studies should be done to understand the increasing relevance of SH in the farms and the impact that ESC resistant strains may have on both public and veterinary health.

Keywords: *Salmonella* Heidelberg, Poultry, Argentina, extended-spectrum cephalosporins.

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