

# OCCURRENCE OF *QAC*E/*QAC*E $\Delta$ 1 GENES AND THEIR CORRELATION WITH CLASS 1 INTEGRONS IN *SALMONELLA ENTERICA* ISOLATES FROM POULTRY AND SWINE

Rungtip Chuanchuen<sup>1</sup>, Sirintip Khemtong<sup>1</sup> and Pawin Padungtod<sup>2</sup>

<sup>1</sup>Faculty of Veterinary Science, Chulalongkorn University, Bangkok;

<sup>2</sup>Faculty of Veterinary Medicine, Chiang Mai University, Chiang Mai, Thailand

**Abstract.** In this study, a total of 122 *Salmonella enterica* isolates from poultry and swine were assessed for susceptibility to clinically important antibiotics and to benzalkonium chloride (BKC). All isolates were examined for the presence of the antiseptic resistance genes *qacE* and *qacE $\Delta$ 1* and *intI1* (class 1 integrase). The *intI1*-positive strains were further investigated for the presence of the 3' conserved region. The results demonstrated widespread distribution of *qacE $\Delta$ 1* (27%) but no isolate with *qacE* was observed. The *intI1* gene was identified in 23 isolates (70%) with *qacE $\Delta$ 1*. All of the *intI1*-positive strains carried *qacE $\Delta$ 1* in 3' conserved segment, confirming that the *qacE $\Delta$ 1* gene is linked to the integrons. Increased MIC value to BKC was independent of the presence of *qacE $\Delta$ 1*, and multiple antibiotic-resistant bacteria were no more tolerant to BKC than the non-multidrug resistant strains, regardless of the presence of *qacE $\Delta$ 1*.

## INTRODUCTION

Disinfectants including quaternary ammonium compounds (QACs) have been introduced into farm environments. A particular concern is that repeated usage of disinfectants may give rise to the selection and persistence of bacteria with reduced susceptibility not only to the antiseptics but possibly to antibiotics as well (Randall *et al*, 2004b).

Benzalkonium chloride (BKC) is a cationic, surface-active QAC commonly used as a farm disinfectant. To date, BKC resistance has been reported in various bacteria, *eg.* *Listeria monocytogenes* (Mereghetti *et al*, 2000) and *Staphylococcus* spp (Bjorland *et al*, 2005) and one of the major mechanisms underlying such resistance is acquisition of resistance

genes (McDonnell and Russell, 1999). *qacE* and *qacE $\Delta$ 1* are genes that confer resistance to QACs and dyes such as ethidium bromide. *qacE $\Delta$ 1*, a mutant version of *qacE*, appears to be partially functional as a multidrug transporter (Kazama *et al*, 1999) and is widely distributed throughout gram-negative bacteria because of its location on the 3' conserved region of class 1 integrons (Paulsen *et al*, 1993).

Class 1 integrons are the most frequently found integrons that are considered to be the major contributors to multidrug resistance in gram-negative bacteria (Fluit and Schmitz, 2004; Hsu *et al*, 2006). The integrons comprise two conserved segments (5' CS and 3' CS) separated by a variable region that usually contains one or more gene cassettes. The 5' CS contains the integrase gene (*intI1*), an integration site (*attI1*), and a promoter ( $P_{ant}$ ) (Fluit and Schmitz, 2004). The 3' CS usually consists of *qacE $\Delta$ 1*, *sul1* that encodes resistance to sulphonamide and ORF5 of unknown

---

Correspondence: Dr Rungtip Chuanchuen, Faculty of Veterinary Science, Chulalongkorn University, Pathumwan, Bangkok 10300, Thailand.  
Tel: 66 (0) 2218-9578; Fax: 66 (0) 2218-9577  
E-mail:rchuanchuen@yahoo.com

function (Paulsen *et al* 1993). The gene cassettes found in the variable regions are mobile and normally encode for antibiotic resistance.

Antibiotic and QAC resistance genes are both carried on class 1 integrons, which raises concerns that QAC exposure resistance may co-select for antibiotic resistance by selecting for class 1 integrons. This provides a potential reservoir of antibiotic-resistant bacteria in QAC-containing environment including animal farms. These particular concerns were supported by a study of the bacterial isolates from QAC-polluted surroundings that showed a link between increased class 1 integron frequency and increased QAC resistance (Gaze *et al*, 2005). However, the dissemination of the *qacE/qacEΔ1* genes and their correlation with class 1 integrons, and antibiotic resistance in *Salmonella* isolates from farms where QACs are widely used have not been reported.

Poultry and swine are the major-food producing animals in Thailand. These food animals are the common reservoirs of *Salmonella enterica*, an important food-borne pathogen having well characterized multidrug resistance. Disinfectants containing BKC have been commonly used in poultry and pig farms in Thailand. However, the susceptibility of *Salmonella* to BKC and its contribution to multidrug resistance phenotype by co-selection of class 1 integrons have never been reported. Therefore, the purpose of this study was to assess the susceptibility of *Salmonella* isolated from poultry, swine and their farm environment to BKC and relevant antibiotics. The occurrence of *qacE* and *qacEΔ1* genes and their association with class 1 integrons, BKC susceptibility and antibiotic resistance were also examined.

## MATERIALS AND METHODS

### Bacterial strains, media and growth conditions

A total of 122 *S. enterica* isolates representing 24 serotypes were obtained from

samples (feces, rectal swabs, drinking water and feed) collected from poultry and swine during 2004-2006. BKC was occasionally in use in all of the farms but its application was not systematically recorded. All strains were recovered by using methods described in ISO6579 (ISO, 2002). Serotypes of *Salmonella* isolates were determined by slide agglutination using the Kauffman-White serotyping schemes (Popoff and LeMinor, 1992). Specific antiserum was obtained from S&A REAGENTS LAB (Bangkok, Thailand). All bacterial strains were stored as 20% glycerol stocks at -80°C. Bacteria were grown on Luria-Bertani (LB) media (Difco, BD Diagnostic Systems, MD, USA) or Muller Hinton agar (MHA; Difco) at 37°C. *Pseudomonas aeruginosa* strain P90 and P87 was used as a positive control for *qacE* and *qacEΔ1*, respectively. *P. aeruginosa* ATCC 27853, *E. coli* ATCC 25922 and *S. aureus* ATCC 29213 were used as quality control organisms for determination of minimum of inhibitory concentrations (MICs).

### Antimicrobial agents and MIC determinations

Antimicrobial agents used in this study were purchased from Sigma-Aldrich (St Louis, MO, USA). MICs were determined by two-fold agar dilution technique according to Clinical and Laboratory Standards Institute (CLSI, formerly NCCLS) (NCCLS, 2002). BKC was dissolved in sterile distilled water and Mueller-Hinton agar plates were prepared that contained this disinfectant in two-fold serial dilutions ranging from 0.5 to 256 µg/ml. Multidrug resistance (MDR) was defined as isolates being resistant to 2 or more different classes of antibiotics (Hsu *et al* 2006; Weill *et al*, 2006).

### PCR amplification and DNA sequencing

Location of primers on class 1 integrons is shown in Fig 1. Template DNA was prepared by the whole cell lysate procedure as described elsewhere (Leverstein-van Hall *et al*, 2002). *int11* was amplified by using primers intF (5'- CCT GCA CGG TTC GAA TG-3') and

intR (5'- TCG TTT GTT CGC CCA GC-3). For amplification of *qacE*, *qacED1* and 3' CS, forward primer *qacEF* (5'-TAA GCC CTA CAC AAA TTG GGA GAT AT-3) was used in combination with reverse primer *qacER* (5'-TTA GTG GGC ACT TTG CTT TGG AAA G-3), *qacEΔ1R* (5'-GCC TCC GCA GCG ACT TCC ACG-3') and *sulR* (5'-GGG TGC GGA CGT AGT CAG C-3'), respectively. PCR was performed using Eppendorf® MasterMix (Eppendorf, Hamburg, Germany) according to the manufacturer's instructions. PCR reaction conditions for *qacE* and *qacEΔ1* were an initial denaturation at 95°C for 5 minutes, and 30 cycles of denaturation for 45 seconds at 95°C, primer annealing for 45 seconds at 67°C, and extension for 45 seconds at 72°C and a final extension for 10 minutes. *int11* and 3' CS were amplified using the same denaturation conditions, except that the annealing condition was changed to 50°C for 45 seconds and the extension time was changed to 1 minute. PCR products were purified using QIAQuick Gel Extraction kit (Qiagen, CA, USA) and representative DNA samples were submitted for sequencing at Macrogen (Seoul, South Korea).

**Statistical analysis**

All statistical analysis was carried out using STATA software Version 8.0 (STATA Corp, College Station, TX, USA). Pearson  $\chi^2$  tests of independence were used to determine the association between MIC for BKC and the presence of *qacEΔ1* and the association between *qacEΔ1* and the presence of class 1 integrons. Association between resistance to multiple antibiotics in the *Salmonella* isolates and susceptibility to BKC was determined using Mantel-Haenzel  $\chi^2$  test controlling for the presence of *qacEΔ1*.

**RESULTS**

A hundred and one isolates (83%) were resistant to antibiotics: ampicillin (65, 53.3%);

Table 1  
Antibiotic resistance of *Salmonella* isolates (n = 122).

Antibiotic resistance pattern	No. of isolates (%)
AMP	1(0.8)
STR	3(2.5)
SUL	7(5.7)
TET	3(2.5)
TRI	1(0.8)
AMP-STR	1(0.8)
AMP-SUL	6(4.9)
STR-SUL	3(2.5)
STR-TET	3(2.5)
SUL-TET	1(0.8)
AMP-CHP-TET	1(0.8)
AMP-STR-SUL	2(1.6)
AMP-SUL-TET	1(0.8)
CHP-STR-SUL	1(0.8)
CHP-SUL-TRI	1(0.8)
STR-SUL-TET	1(0.8)
STR-SUL-TRI	2(1.6)
SUL-TET-TRI	4(3.3)
AMP-CHP-STR-TET	1(0.8)
AMP-STR-SUL-TET	5(4.1)
AMP-SUL-TET-TRI	1(0.8)
CHP-STR-SUL-TRI	1(0.8)
CHP-SUL-TET-TRI	1(0.8)
STR-SUL-TET-TRI	3(2.5)
AMP-CHP-STR-SUL-TET	8(6.6)
AMP-CHP-STR-TET-TRI	2(1.6)
AMP-CHP-SUL-TET-TRI	1(0.8)
AMP-GEN-SUL-TET-TRI	3(2.5)
AMP-STR-SUL-TET-TRI	2(1.6)
CHP-STR-SUL-TET-TRI	1(0.8)
AMP-CHP-STR-SUL-TET-TRI	12(9.8)
AMP-GEN-STR-SUL-TET-TRI	4(3.3)
AMP-CHP-GEN-STR-SUL-TET	5(4.1)
AMP-CHP-GEN-STR-TET-TRI	1(0.8)
AMP-CHP-GEN-SUL-TET-TRI	1(0.8)
AMP-CHP-GEN-STR-SUL-TET-TRI	7(5.7)
Total	101 (82.8)

AMP, ampicillin; CHP, chloramphenicol; GEN, gentamicin; STR, streptomycin; SUL, sulfamethoxazole TET, tetracycline; TRI, trimethoprim

chloramphenicol, (44, 36.1%); gentamicin (21, 17.2%); tetracycline (72, 59%); trimethoprim (48, 39.3%); streptomycin (68, 55.7%) and sulfamethoxazole (84, 68.9%) (Table 1). Eighty-

six isolates (70%) were multiresistant. The antibiotic-resistance patterns were also analyzed. All of the isolates could be grouped into 36 resistance patterns (Table 1). The most frequent multiple resistance pattern was AMP-CHP-STR-SUL-TET-TRI (10%).

For susceptibility to BKC, the MIC distributions are shown in Table 2. All of the isolates had MICs ranging from 8 to 256 µg/ml. Fifty-five percent of the isolates tested showed MICs of 128-256 µg/ml.

Twenty-seven percent of the *Salmonella* strains possessed *qacEΔ1* and none of them harbored *qacE*. Association of the occurrence of *qacEΔ1* with the distributions of MICs for BKC and resistance to antibiotics is presented in Table 2. Thirty of 33 isolates (91%) with the *qacEΔ1* gene had MICs for BKC of 64-256 µg/ml, compared to 56 out of 89 isolates (62%) without *qacEΔ1* gene. To explore the link between *qacEΔ1* and class 1 integrons, the presence of *int11* and 3' CS were determined in the *qacEΔ1*-containing isolates (Table 3). The *int11* genes were observed in 23 (70%) of the *qacEΔ1*-positive strains. All of these *int11*-positive strains were additionally positive for 3' CS and *qacEΔ1* which were located upstream of *sul1* as confirmed by PCR using *qacEF* and *sul1R* primers. Since class 1 integrons lacking the typical 3' CS also exist, the presence of *int11* was additionally investigated in the

strains without *qacEΔ1*, but the *int11* gene was not detected in the *qacEΔ1*-negative strains (data not shown). Nucleotide sequencing of amplified products confirmed the high specificity of all primers used in this study and no differences were observed, compared to the published sequences (data not shown).

Statistical analysis showed that having high MICs for BKC was not significantly associated with the presence of *qacEΔ1* ( $p=0.176$ ). Multiple antibiotic-resistant *Salmonella* isolates were not less susceptible to QACs than those non-multidrug resistant strains even though *qacEΔ1* was present ( $p=0.458$ ). However, the presence of *qacEΔ1* was associated to the presence of *int11* ( $p<0.001$ ).

## DISCUSSION

The majority of *Salmonella* isolates had MICs for BKC of 128-256 µg/ml, which is comparable to those previously reported for *Salmonella* by Aarestrup and Hasman (2004). Braoudaki and Hilton (2005) demonstrated that exposure to sublethal concentration of BKC selected for *S. Enteritidis* with reduced susceptibility to BKC from 32 to 256 µg/ml. However, based on the results of this study, we can not conclude whether the *Salmonella* isolates in this study acquired resistance to BKC or not.

Table 2  
Distributions of MIC for BKC, resistance to antibiotics and the presence of *qacEΔ1* among *Salmonella* isolates (n = 122).

<i>Salmonella</i> <sup>a</sup>	MIC (µg/ml)						Total (%)
	256	128	64	32	16	8	
Number	34(27.9) <sup>b</sup>	33(27.1)	19(15.6)	22(18.1)	1(0.8)	13(10.7)	122(100)
<i>qacEΔ1</i>	13(10.7)	8(6.6)	9(7.4)	2(1.6)	1(0.8)	0	33(27)
MDR	27(22.1)	28(23.0)	16(13.1)	14(11.5)	1(0.8)	0	86(70.5)

<sup>a</sup>None of the isolates carried *qacE* genes; <sup>b</sup>Number (%); MDR, multidrug resistance

Table 3  
MIC of BKC, antibiotic resistance pattern and association with class 1 integrons among *Salmonella* isolates containing *qacEΔ1*.

Strain	Serotype	BKC MIC (μg/ml)	<i>int1</i> <sup>a</sup>	3' CS <sup>a</sup>	Antibiotic resistance pattern
SA012	<i>S. Weltevreden</i>	256	+	+	AMP-CHP-GEN-STR-SUL-TET-TRI
SA014	<i>S. Anatum</i>	256	+	+	AMP-GEN-STR-SUL-TET-TRI
SA015	<i>S. subspecies I</i>	128	-	-	AMP-CHP-GEN-SUL-TET-TRI
SA016	<i>S. Stanley</i>	64	+	+	AMP- STR-SUL-TET-TRI
SA021	<i>S. subspecies I</i>	256	+	+	AMP-CHP-GEN- STR-SUL-TET-TRI
SA022	<i>S. Albany</i>	128	+	+	AMP-CHP- STR-SUL-TET-TRI
SA023	<i>S. Albany</i>	128	+	+	AMP-CHP- STR-SUL-TET-TRI
SA032	<i>S. Typhimurium</i>	32	-	-	SUL
SA034	<i>S. Give</i>	128	+	+	AMP-CHP- STR-SUL-TET-TRI
SA035	<i>S. Albany</i>	64	+	+	AMP-CHP- STR-SUL-TET-TRI
SA036	<i>S. Albany</i>	64	+	+	AMP-CHP- STR-SUL-TET-TRI
SA039	<i>S. Kingston</i>	64	+	+	AMP-CHP- STR-SUL-TET-TRI
SA040	<i>S. Eppendrof</i>	256	+	+	AMP-GEN-SUL-TET-TRI
SA041	<i>S. subspecies I</i>	64	+	+	AMP-CHP-GEN- STR-SUL-TET-TRI
SA044	<i>S. Kedougou</i>	256	+	+	AMP-CHP- GEN-STR-SUL-TET
SA046	<i>S. Kentucky</i>	64	+	+	AMP-GEN-SUL-TET-TRI
SA 047	<i>S. Madjorio</i>	64	-	-	AMP-SUL-TET-TRI
SA048	<i>S. Schwarzengrund</i>	64	+	+	AMP-SUL-TET-TRI
SA058	<i>S. Rissen</i>	128	+	+	SUL-TET
SA072	<i>S. Albany</i>	64	+	+	AMP- STR-SUL-TET-TRI
SA074	<i>S. subspecies I</i>	128	+	+	AMP-CHP-GEN- STR-SUL-TET-TRI
SA079	<i>S. Stanley</i>	128	-	-	AMP-CHP- STR-SUL-TET-TRI
SA096	<i>S. Anatum</i>	256	-	-	STR-TET
SA097	<i>S. Emek</i>	256	+	+	STR-SUL-TRI
SA098	<i>S. Emek</i>	256	+	+	STR-SUL-TRI
SA100	<i>S. subspecies I</i>	256	-	-	AMP- STR-SUL-TET
SA104	<i>S. Orion</i>	256	+	+	AMP- STR-SUL-TRI
SA107	<i>S. Singapore</i>	256	-	-	STR-SUL
SA108	<i>S. Stanley</i>	256	+	+	CHP- STR-SUL-TET-TRI
SA109	<i>S. Stanley</i>	256	+	+	AMP-CHP- STR-SUL-TET-TRI
SA115	<i>S. Weltevreden</i>	128	-	-	STR-SUL-TET-TRI
SA124	<i>S. Enteritidis</i>	32	-	-	STR
SA128	<i>S. Typhimurium</i>	16	-	-	STR-SUL-TET-TRI

<sup>a</sup>+ (plus), positive result; - (minus), negative result

AMP, ampicillin; CHP, chloramphenicol; CIP, ciprofloxacin, GEN, gentamicin; TET, tetracycline; TRI, trimethoprim; SUL, sulfamethoxazole

Class 1 integrons associated with *qacEΔ1* and *sul1* have been commonly detected in clinical isolates of *Salmonella* (Randall *et al*, 2004a,b; Hsu *et al*, 2006; Vo *et al*, 2006), which is in agreement with findings of this

study. Most of the *qacEΔ1*-positive strains contained *int1*. All of the *qacEΔ1* genes in these strains appeared upstream of *sul1*, indicating that the integrons from *Salmonella* isolates usually contain the typical 3' con-

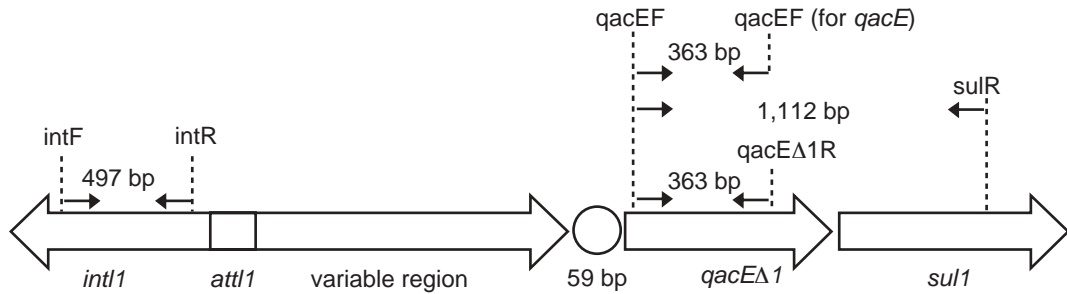


Fig 1—Schematic presentation of class 1 integrons showing location of the primers and the resulting amplicons. The arrows indicate the direction of primers. The vertical-dashed lines indicate location of primers.

served region. Therefore, exposure to BKC, which is a substrate for *qacEΔ1*, has the potential to coselect for antibiotic resistance. Integrons that contain *qacE* but lack *sul1* are predominant in environmental isolates (Kazama *et al*, 1998) including those from aquatic environment (Gaze *et al* 2005). However, isolates with *qacE* were not observed in this study. The difference in the basic structure of class 1 integrons identified in clinical and environmental isolates may mirror differences in the selective pressure. Clinical isolates are generally exposed to sulphonamides, and thus, there is a need for a *sul1* gene cassette to integrate into integrons (Gaze *et al* 2005). Support of this notion is the observation that all *int11*-positive strains were resistant to sulphonamide (Table 3).

*S. enterica* strains positive for *qacEΔ1* but without *int11* were also identified. Carriage of *qacEΔ1* gene may be on other elements or integrated into the chromosome. These non-integron-associated *qacEΔ1* genes contribute to the development of reduced susceptibility to BKC of *Salmonella*. It may partly explain the persistence of this pathogen in laying and broiler flocks through many flock cycles, despite cleaning and disinfection have been performed after depopulation (Gradel *et al*, 2005). Further studies to localize the gene are warranted and will help to explain their significance.

Due to the concern that multiple antibi-

otic resistance bacteria are simultaneously resistant to QACs because of the presence of integrons, emphasis should be placed on associations between the multiple antibiotic resistance and the presence of *qacEΔ1*. The results showed that the isolates with multiple antibiotic-resistant phenotypes did not have higher MICs for BKC than those with non-multiple antibiotic resistance, which is consistent to a previous study of clinical isolates from human patients (Kucken *et al*, 2000). This dissociation suggests that multidrug efflux systems do not play an important role as the common cross-resistance mechanism.

As a whole, no correlation between increased MIC value to BKC and the presence of *qacEΔ1* was observed. This finding was similar to the previous report in human isolates (Kucken *et al* 2000). However, when *qacEΔ1* was present, 91% strains had high MICs for BKC, indicating that the gene may well be contributing to reduced susceptibility to BKC, when it is present. It is unlikely that only one resistance mechanism would satisfactorily explain the resistance to any antimicrobial agents (Gilbert and McBain, 2003). Indeed, reduced susceptibility to QACs may be reminiscent of co-expression of resistance mechanisms (McDonnell and Russell, 1999).

In view of the results obtained, it should be noted that class 1 integrons and multidrug resistance are widely spread among *Salmonella* of farm animal origins. Interestingly, all

of the *intI1*-positive isolates were resistant to at least one antibiotic, particularly streptomycin, trimethoprim and ampicillin, in agreement with the previous reports that *aad*, *dfra* and *bla* genes are often cassettes of class 1 integrons (Hsu *et al*, 2006). These results warrant further experiments, currently in progress, to identify the gene cassettes in the integrons and to determine their transfer ability.

#### ACKNOWLEDGEMENTS

We are grateful to Dr Chanwit Tribudharat, Mahidol University, Bangkok, Thailand for donating *P. aeruginosa* strains P90 and P87 and Cindy Loui, UC Berkeley, CA, USA for assistance in the preparation of this manuscript. This work was supported in part by the Thai Government Research Fund of the fiscal year 2006.

#### REFERENCES

- Aarestrup FM, Hasman H. Susceptibility of different bacterial species isolated from food animals to copper sulphate, zinc chloride and antimicrobial substances used for disinfection. *Vet Microbiol* 2004; 100: 83-9.
- Bjorland J, Steinum T, Kvitle B, Waage S, Sunde M, Heir E. Widespread distribution of disinfectant resistance genes among staphylococci of bovine and caprine origin in Norway. *J Clin Microbiol* 2005; 43: 4363-68.
- Braoudaki M, Hilton AC. Mechanisms of resistance in *Salmonella enterica* adapted to erythromycin, benzalkonium chloride and triclosan. *Int J Antimicrob Agents* 2005; 25: 31-7.
- Fluit AC, Schmitz FJ. Resistance integrons and super-integrons. *Clin Microbiol Infect* 2004; 10: 272-88.
- Gaze WH, Abdousslam N, Hawkey PM, Wellington EM. Incidence of class 1 integrons in a quaternary ammonium compound-polluted environment. *Antimicrob Agents Chemother* 2005; 49: 1802-07.
- Gilbert P, McBain AJ. Potential impact of increased use of biocides in consumer products on prevalence of antibiotic resistance. *Clin Microbiol Rev* 2003; 16: 189-208.
- Gradel KO, Randall L, Sayers AR, Davies RH. Possible associations between *Salmonella* persistence in poultry houses and resistance to commonly used disinfectants and a putative role of *mar*. *Vet Microbiol* 2005; 107: 127-38.
- Hsu SC, Chiu TH, Pang JC, Hsuan-Yuan CH, Chang GN, Tsen HY. Characterisation of antimicrobial resistance patterns and class 1 integrons among *Escherichia coli* and *Salmonella enterica* serovar Choleraesuis strains isolated from humans and swine in Taiwan. *Int J Antimicrob Agents* 2006; 27: 383-91.
- ISO. Microbiology of food and animal feeding stuffs- Horizontal method for the detection of *Salmonella* spp. 4<sup>th</sup> ed. ISO6579. 2002.
- Kazama H, Hamashima H, Sasatsu M, Arai T. Distribution of the antiseptic-resistance genes *qacE* and *qacE* delta 1 in gram-negative bacteria. *FEMS Microbiol Lett* 1998; 159: 173-8.
- Kazama H, Hamashima H, Sasatsu M, Arai T. Characterization of the antiseptic-resistance gene *qacE* delta 1 isolated from clinical and environmental isolates of *Vibrio parahaemolyticus* and *Vibrio cholerae* non-O1. *FEMS Microbiol Lett* 1999; 174: 379-84.
- Kucken D, Feucht H, Kaulfers P. Association of *qacE* and *qacE* delta1 with multiple resistance to antibiotics and antiseptics in clinical isolates of Gram-negative bacteria. *FEMS Microbiol Lett* 2000; 183: 95-98.
- Leverstein-van Hall MA, Box AT, Blok HE, Paauw A, Fluit AC, Verhoef J. Evidence of extensive interspecies transfer of integron-mediated antimicrobial resistance genes among multidrug-resistant Enterobacteriaceae in a clinical setting. *J Infect Dis* 2002; 186: 49-56.
- McDonnell G, Russell AD. Antiseptics and disinfectants: activity, action, and resistance. *Clin Microbiol Rev* 1999; 12: 147-79.
- Mereghetti L, Quentin R, Marquet-Van Der Mee N, Audurier A. Low sensitivity of *Listeria monocytogenes* to quaternary ammonium compounds. *Appl Environ Microbiol* 2000; 66: 5083-86.
- NCCLS. Performance standards for antimicrobial

- disk and dilution susceptibility tests for bacteria isolated from animals; Approved Standard-Second edition. NCCLS document M31-A2. PA, USA: NCCLS, 2002.
- Paulsen IT, Littlejohn TG, Radstrom P, *et al.* The 3' conserved segment of integrons contains a gene associated with multidrug resistance to antiseptics and disinfectants. *Antimicrob Agents Chemother* 1993; 37: 761-68.
- Popoff M, LeMinor L. Antigenic formulas of the *Salmonella* serovars. 7 ed. Paris: Institut Pasteur, 1992.
- Randall LP, Cooles SW, Osborn MK, Piddock LJ, Woodward MJ. Antibiotic resistance genes, integrons and multiple antibiotic resistance in thirty-five serotypes of *Salmonella enterica* isolated from humans and animals in the UK. *J Antimicrob Chemother* 2004a; 53: 208-16.
- Randall LP, Cooles SW, Piddock LJ, Woodward MJ. Effect of triclosan or a phenolic farm disinfectant on the selection of antibiotic-resistant *Salmonella enterica*. *J Antimicrob Chemother* 2004b; 54: 621-7.
- Vo AT, van Duijkeren E, Fluit AC, *et al.* Antibiotic resistance, integrons and *Salmonella* genomic island 1 among non-typhoidal *Salmonella* serovars in The Netherlands. *Int J Antimicrob Agents* 2006; 28: 172-9.
- Weill FX, Guesnier F, Guibert V, *et al.* Multidrug resistance in *Salmonella enterica* serotype Typhimurium from humans in France (1993 to 2003). *J Clin Microbiol* 2006; 44: 700-8.