Erratum: Acquired antibiotic resistance genes: an overview

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A commentary on

Acquired antibiotic resistance genes: an overview

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Dr. Marilyn C. Roberts and Dr. Stefan Schwarz have contacted the authors of the original publication with several comments and suggestions to better harmonize the correct nomenclature of the antibiotic resistance genes, as the gene names were not always correctly presented in the various tables given.

Authors often pick their own gene names which in many cases have been approved for use for other genetically distinct genes or give names to determinants which were already given an approved designated name. Therefore, we (Dr. Marilyn C. Roberts and Dr. Stefan Schwarz and Dr. Henk J. M. Aarts on behalf of the authors of the original publication) would like to present here the correct nomenclature and mechanistic features of the antibiotic resistance genes belonging to the following classes: Aminoglycosides (Table 1), Phenicols (Table 3), Macrolides–Lincosamides–Streptogramins B (Table 4), Quinolones (Table 5), Tetracyclines (Table 6), and Trimethoprim (Table 7). In addition some additional information is given on the various classes of antibiotic resistance genes as also a section regarding the antibiotic class Oxazolidinones has been added. Table 2 was correctly displayed by van Hoek et al. (2011) but has been updated.

To the subsection dealing with the “Resistance mechanisms” of the AMINOGLYCOSIDES we would like to add that to date six additional methylases have been reported, i.e., npmA, rmtA, rmtB, rmtC, rmtD, and rmtE (Courvalin, 2008; Doi et al., 2008; Davis et al., 2010). Furthermore, that within the three major classes (AAC, ANT, and APH) an additional subdivision can be made based on the enzymes’ target sites within the aminoglycoside molecules: i.e., there are four acetyltransferases: AAC(1), AAC(2′), AAC(3), and AAC(6′); five nucleotidytransferases: ANT(2′′), ANT(3′′), ANT(4′), ANT(6), and ANT(9); and seven phosphotransferases: APH(2′′), APH(3′), APH(3′′), APH(4), APH(6), APH(7′′), and APH(9).

To the subsection β-LACTAM, Resistance, mechanisms we would like to add that in recent years acquired genes encoding ESBLs have become a major concern (Bradford, 2001). Over time, the genes for the parent enzymes blaTEM, blaTEM′, blaSHV′′, and blaSHV−1 have undergone point mutations which resulted in amino acid substitutions that changed the substrate spectrum to that of ESBLs, starting with blaTEM′ and blaSHV−2 (Bradford, 2001).

Because chloramphenicol is not an actual antibiotic class the subsection of CHLORAMPHENICOL should be called PHENICOLS. Concerning the history of PHENICOLS, it is worthwhile to know the first antibiotic, chloramphenicol, originally referred to as chloromycetin, was isolated already in 1947 from Streptomyces venezuelae (Ehrlich et al., 1947).

Besides the inactivating enzymes (chloramphenicol acetyltransferases), there are also reports on other phenicol resistance systems, such as the inactivation by phosphotransferases, mutations of the target site, permeability barriers, and efflux systems (Schwarz et al., 2004). Of the latter mechanism, cmIA and floR are the most commonly known genes in Gram-negative bacteria (Bissonnette et al., 1991; Briggs and Fratamico, 1999).

The macrolides (subsection MACROLIDES–LINCOSAMIDES–STREPTOGRAMIN B) have a similar mode of antibacterial action, comparable antibacterial spectra and in part overlapping binding sites at the ribosome as two other antibiotic classes, i.e., lincosamides and streptogramin antibiotics (comprising streptogramin A and B compounds that act synergistically). Consequently, these antibiotics, although chemically distinct, have been clustered together as MLS antibiotics (Roberts, 1996). Macrolides, lincosamides and streptogramins all inhibit protein synthesis by binding to the 50S ribosomal subunit of bacteria (Weisblum, 1995; Roberts, 2002).

To Resistance mechanisms of the subsection MACROLIDES–LINCOSAMIDES–STREPTOGRAMIN B. Shortly after the introduction of erythromycin into clinical setting in the 1950s, bacterial resistance to this antibiotic was reported for the first time in staphylococci (Weisblum, 1995). Since then a large number of bacteria have been identified that are resistant to MLS due to the presence of various different genes. The resistance determinants responsible include rRNA methylases that modify the ribosomal target sites, ABC transporters, and efflux proteins of the Major Facilitator Superfamily, as well as genes for inactivating enzymes (Roberts et al., 1999; Roberts, 2008). The latter group can be further
### Table 1 | Acquired aminoglycoside resistance genes*

| Mechanism | Gene name | Length (nt) | Accession number or reference | Coding region | Genera |
|-----------|-----------|-------------|--------------------------------|---------------|--------|
| ACT       | aac(2′)-Ia | 537         | L06156                         | 264...800     | Providencia |
|           | aac(2′)-Ib | 588         | U41471                         | 265...385     | Mycobacterium |
|           | aac(2′)-Ic | 546         | U72714                         | 373...918     | Mycobacterium |
|           | aac(2′)-Id | 633         | U72743                         | 386...1018    | Mycobacterium |
|           | aac(2′)-Ie | 549         | NC_011896                      | 3039059...3039607 | Mycobacterium |
|           | aac(3)-I  | 465         | AJ877225                       | 5293...5757   | Pseudomonas |
|           | aac(3)-Ia | 534         | X15852                         | 1250...1783   | Acinetobacter, Escherichia, Klebsiella, Salmonella, Serratia, Streptomyces |
|           | aac(3)-Ib | 531         | L06157                         | 555...1085    | Pseudomonas |
|           | aac(3)-Ib | 1005        | AF355189                       | 1435...2439   | Pseudomonas |
|           | aac(3)-Ic | 471         | AJ511268                       | 1295...1765   | Pseudomonas |
|           | aac(3)-Id | 477         | AB114632                       | 104...580     | Proteus, Pseudomonas, Salmonella, Vibrio |
|           | aac(3)-Ie | 477         | AAY463797                      | 8583...9059   | Proteus, Pseudomonas, Salmonella, Vibrio |
|           | aac(3)-If | 465         | AAY84051                       | 61...525      | Serratia, Pseudomonas |
|           | aac(3)-Ig | 477         | CP000282                       | 2333620...2334906 | Saccharophagus |
|           | aac(3)-Ih | 459         | CP000490                       | 509912...510370 | Paracoccus |
|           | aac(3)-Ii | 459         | CP000356                       | 638262...638720 | Sphingopyxis |
|           | aac(3)-Ij | 465         | CP000155                       | 6963012...6963476 | Halella |
|           | aac(3)-Ik | 444         | BX571856                       | 765853...766296 | Staphylococcus |
|           | aac(3)-Il | 861         | X15354                         | 91...951      | Acinetobacter, Enterobacter, Escherichia, Klebsiella, Pseudomonas, Salmonella |
|           | aac(3)-Ib | 810         | M97172                         | 656...1465    | Serratia |
|           | aac(3)-Ic | 861         | X54723                         | 819...1679    | Escherichia |
|           | aac(3)-Id | 861         | EU022314                       | 1...861       | Escherichia |
|           | aac(3)-Ie | 861         | EU022315                       | 1...861       | Escherichia |
|           | aac(3)-Il | 816         | X56652                         | 1124...1939   | Pseudomonas |
|           | aac(3)-Ib | 738         | L06160                         | 984...1721    | Pseudomonas |
|           | aac(3)-Ic | 840         | L06161                         | 106...945     | Pseudomonas |
|           | aac(3)-IIa| 786         | X01385                         | 244...1029    | Escherichia |
|           | aac(3)-IIa| 816         | M88012                         | 193...1092    | Enterobacter, Escherichia, Salmonella |
|           | aac(3)-VIIa| 867       | M22999                         | 493...1359    | Streptomyces |
|           | aac(3)-VIIa| 861       | M55426                         | 466...1326    | Streptomyces |
|           | aac(3)-VIIa| 846       | M55427                         | 274...1119    | Micromonospora |
|           | aac(3)-IXa| 855         | AB028210                       | 2711...3565   | Streptomyces |
|           | aac(3′)-I | 441         | AY553333                       | 1392...1832   | Pseudomonas |
|           | aac(3′)-I | 555         | AJ628983                       | 1985...2539   | Pseudomonas |
|           | aac(3′)-I | 402         | DQ302723                       | 81...482      | Pseudomonas |
|           | aac(3′)-I | 555         | EU912537                       | 2092...2646   | Pseudomonas |
|           | aac(3′)-Ia | 558        | M18967                         | 757...1314    | Citrobacter, Escherichia, Klebsiella, Shigella |
|           | aac(3′)-Ib | 606        | M21682                         | 380...985     | Klebsiella, Proteus, Pseudomonas |
|           | aac(3′)-Ib-cr | 519   | EF636461                       | 1124...1642   | Enterobacter, Escherichia, Klebsiella, Pseudomonas, Salmonella |
|           | aac(3′)-Ic | 441        | M94066                         | 1554...1994   | Serratia |
|           | aac(3′)-Id | 450        | X12618                         | 905...1354    | Klebsiella |
|           | aac(3′)-Ie |            |                               |               |        |
|           | aac(3′)-If | 435        | X55353                         | 279...713     | Enterobacter |

(Continued)
Table 1 | Continued

| Mechanism            | Gene name | Length (nt) | Accession number or reference | Coding region | Genera                        |
|----------------------|-----------|-------------|-------------------------------|---------------|-------------------------------|
| aac(6')-I-g          | 438       | L09246      | 544…981                       | Acinetobacter |
| aac(6')-I-h          | 441       | L29044      | 352…792                       | Acinetobacter |
| aac(6')-I-i          | 549       | L12710      | 169…717                       | Enterococcus  |
| aac(6')-I-j          | 441       | L29045      | 260…700                       | Acinetobacter |
| aac(6')-I-k          | 438       | L29510      | 369…806                       | Acinetobacter |
| aac(6')-I-l          | 522       | Z54241      | 530…1051                      | Acinetobacter, Citrobacter |
| aac(6')-I-m          | 537       | AF337947    | 1215…1751                     | Escherichia   |
| aac(6')-I-n          | 573       | Wu et al., 1997 |                           | Citrobacter   |
| aac(6')-I-o          | 552       | AF047556    | 127…678                       | Klebsiella, Salmonella |
| aac(6')-I-p          | 441       | AF031326    | 1…441                         | Acinetobacter |
| aac(6')-I-q          | 441       | AF031327    | 1…441                         | Acinetobacter |
| aac(6')-I-r          | 441       | AF031328    | 1…441                         | Acinetobacter |
| aac(6')-I-s          | 441       | AF031329    | 1…441                         | Acinetobacter |
| aac(6')-I-t          | 441       | AF031330    | 1…441                         | Acinetobacter |
| aac(6')-I-u          | 441       | AF031331    | 1…441                         | Acinetobacter |
| aac(6')-I-v          | 441       | AF031332    | 1…441                         | Acinetobacter |
| aac(6')-I-w          | 441       | AF144880    | 3452…3979                     | Salmonella    |
| aac(6')-I-x          | 438       | AF140221    | 390…851                       | Stenotrophomonas |
| aac(6')-I-y          | 438       | NC_003197   | 1707358…1707795  | Salmonella    |
| aac(6')-I-30         | 435       | AB119105    | 1…435                         | Acinetobacter |
| aac(6')-I-31         | 552       | AB104852    | 1935…2486                     | Pseudomonas, Salmonella |
| aac(6')-I-32         | 556       | AB462903    | 1200…1751                     | Pseudomonas   |
| aac(6')-I-33         | 519       | EU886977    | 544…1110                      | Pseudomonas   |
| aac(6')-I-34         | 555       | AE879608    | 1524…2078                     | Salmonella    |
| aac(6')-I-35         | 555       | EF614235    | 2247…2801                     | Pseudomonas   |
| aac(6')-I-36         | 555       | G0337064    | 1203…1757                     | Pseudomonas   |
| aac(6')-I-37         | 555       | M29695      | 707…1261                      | Aeromonas, Klebsiella, Pseudomonas, Salmonella |
| aac(6')-I-38         | 543       | L06163      | 532…1074                      | Pseudomonas   |
| aac(6')-I-l          | 582       | AF162771    | 62…643                        | Enterobacter, Klebsiella, Pseudomonas |
| aac(6')-I-39         | 435       | X55353      | 279…713                       | Enterobacter  |
| aacA29               | 381       | AY139599    | 768…1148                      | Unknown       |
| aacA43               | 564       | HQ247816    | 639…1202                      | Klebsiella    |
| aprM                 | 822       | FN806789    | 2858…3682                     | Staphylococcus |
| sat2                 | 525       | X51546      | 518…1042                      | Acinetobacter, Enterobacter, Escherichia, Klebsiella, Proteus, Pseudomonas, Salmonella, Shigella, Vibrio |
| sat3                 | 543       | Z48231      | 221…763                       | Escherichia   |
| sat4                 | 543       | X92945      | 38870…39412                   | Campylobacter, Enterococcus, Staphylococcus, Streptococcus |
| aac(6')-aph(2')      | 1440      | M13771      | 304…1743                      | Enterococcus, Lactobacillus, Staphylococcus, Streptococcus |
| ACT–PHT              |           |             |                               |                |
| aac(6')-aph(2')      | 543       | X92945      | 38870…39412                   | Campylobacter, Enterococcus, Staphylococcus, Streptococcus |
| MET                  | 774       | AY220558    | 1978…2751                     | Acinetobacter, Citrobacter, Enterobacter, Escherichia, Klebsiella, Salmonella, Serratia |
| npmA                 | 660       | AB261016    | 3069…3728                     | Escherichia   |
| Mechanism | Gene name | Length (nt) | Accession number or reference | Coding region | Genera |
|-----------|-----------|-------------|-------------------------------|--------------|--------|
| rmtA      | 756       | AB120321    | 6677...7432                  | Pseudomonas  |
| rmtB      | 756       | AB103506    | 1410...2165                  | Enterobacter, Escherichia, Klebsiella, Pseudomonas, Serratia |
| rmtC      | 846       | AB194779    | 6903...7748                  | Proteus, Salmonella |
| rmtD      | 744       | DO914960    | 8889...9632                  | Klebsiella, Pseudomonas |
| rmtD2     | 744       | HQ401565    | 14139...14882                | Citrobacter, Enterobacter |
| rmtE      | 822       | GU021947    | 55...876                     | Escherichia |
| NUT       | aadA1     | 972         | X02340                       | Acinetobacter, Aeromonas, Enterobacter, Escherichia, Klebsiella, Proteus, Pseudomonas, Salmonella, Shigella, Vibrio |
|           | aadA1b    | 792         | M95287                       | Pseudomonas, Serratia |
|           | aadA2     | 780         | X68227                       | Acinetobacter, Aeromonas, Citrobacter, Enterobacter, Escherichia, Klebsiella, Proteus, Pseudomonas, Salmonella, Shigella, Staphylococcus, Vibrio, Yersinia |
|           | aadA3     | 792         | AF047479                     | Escherichia |
|           | aadA4     | 789         | Z50802                       | Acinetobacter, Aeromonas, Escherichia, Pseudomonas, |
|           | aadA5     | 789         | AF137361                     | Acinetobacter, Aeromonas, Escherichia, Pseudomonas, Salmonella, Shigella, Staphylococcus, Vibrio |
|           | aadA6     | 846         | AF140629                     | Pseudomonas |
|           | aadA7     | 798         | AF224733                     | Escherichia, Salmonella, Vibrio |
|           | aadA8     | 792         | AF326210                     | Klebsiella, Vibrio |
|           | aadA8b    | 792         | AM040708                     | Escherichia |
|           | aadA9     | 837         | AJ420072                     | Corynebacterium |
|           | aadA10    | 834         | U37105                       | Pseudomonas |
|           | aadA11    | 846         | AY144590                     | Pseudomonas, Riemerella |
|           | aadA12    | 792         | AY666771                     | Escherichia, Salmonella, Yersinia |
|           | aadA13    | 798         | AY713504                     | Escherichia, Pseudomonas, Yersinia |
|           | aadA14    | 786         | AJ884726                     | Pasteurella |
|           | aadA15    | 792         | DQ393783                     | Pseudomonas |
|           | aadA16    | 846         | EU675686                     | Escherichia, Klebsiella, Vibrio |
|           | aadA17    | 792         | FJ460181                     | Aeromonas |
|           | aadA21    | 792         | AY171244                     | Salmonella |
|           | aadA22    | 792         | AM261837                     | Escherichia, Salmonella |
|           | aadA23    | 780         | AJ809407                     | Salmonella |
|           | aadA24    | 780         | AM711129                     | Escherichia, Salmonella |
|           | aadC      | 477         | V01282                       | Staphylococcus |
|           | aadD      | 771         | AF181950                     | Staphylococcus |
|           | aadE      | 543         | X04555                       | Acinetobacter, Enterobacter, Escherichia, Klebsiella, Proteus, Pseudomonas, Salmonella, Serratia, Shigella, Vibrio |
|           | ant(6)-la | 771         | AJ506108                     | Bacillus |
|           | ant(6)-la | 759         | M98270                       | Pseudomonas |
|           | ant(6)-la | 756         | AY114142                     | Pseudomonas |
|           | ant(6)-la | 909         | AF330699                     | Enterococcus, Staphylococcus |
|           | ant(6)-la | 858         | FN594949                     | Campylobacter |
|           | ant(9)-la | 783         | X02588                       | Enterococcus, Staphylococcus |
|           | ant(9)-la | 768         | M69221                       | Enterococcus, Staphylococcus |

(Continued)
| Mechanism | Gene name | Length (nt) | Accession number or reference | Coding region | Genera |
|-----------|-----------|-------------|--------------------------------|---------------|--------|
| spc, see ant(9)-la | | | | | |
| sph | 801 | X64335 | 6657…7354 | Escherichia, Pseudomonas, Salmonella |
| str | 849 | X92846 | 18060…18908 | Enterococcus, Staphylococcus, Lactococcus |
| NUT-ACT | ant(3’)-Ih-aac(6’)-Iid | 1392 | AF453998 | 3555…4946 | Serratia |
| PHT | aph(2”)-Ib | 900 | AF337947 | 272…1171 | Enterococcus, Escherichia |
| | aph(2’)-lc | 921 | U51479 | 196…1116 | Enterococcus |
| | aph(2’)-Id | 906 | AF016483 | 131…1036 | Enterococcus |
| | aph(2’)-Ie | 906 | AY743255 | 131…1036 | Enterococcus |
| | aph(3’)-Ia | 816 | J01839 | 1162…1977 | Escherichia, Klebsiella, Pseudomonas, Salmonella |
| | aph(3’)-Ic | 816 | M20305 | 779…1594 | Escherichia |
| | aph(3’)-Id | 816 | X625115 | 410…1225 | Acinetobacter, Citrobacter, Escherichia, Klebsiella, Salmonella, Serratia, Yersinia |
| | aph(3’)-Ia | 795 | X57709 | 1…795 | Escherichia, Pseudomonas, Salmonella |
| | aph(3’)-Ib | 807 | X90856 | 388…1194 | Pseudomonas |
| | aph(3’)-Ic | 813 | AM743169 | 2377498…2378310 | Stenotrophomonas |
| | aph(3’)-IIa | 795 | M26832 | 604…1398 | Bacillus, Campylobacter, Enterococcus, Staphylococcus, Streptococcus |
| | aph(3’)-IIb | 789 | X03364 | 277…1065 | Bacillus |
| | aph(3’)-IIc | 807 | K00432 | 307…1113 | Streptomyces |
| | aph(3’)-IIc | 795 | S81599 | 282…1076 | Micromonospora |
| | aph(3’)-Vb | 780 | X07753 | 103…882 | Acinetobacter, Pseudomonas |
| | aph(3’)-Vb | 780 | AJ627643 | 4934…5713 | Alcaligenes |
| | aph(3’)-IIa | 753 | M29953 | 131…1036 | Campylobacter |
| | aph(3’)-VIIa | 804 | AF182845 | 1…804 | Streptomyces |
| | aph(3’)-VIIb | 795 | Y18050 | 4758…5552 | Achromobacter, Citrobacter, Pseudomonas |
| | aph(3’)-Ia | 819 | M16482 | 501…1319 | Streptomyces |
| | aph(3’)-Ib | 801 | AB366441 | 11310…12110 | Enterobacter, Escherichia, Klebsiella, Pasteurella, Pseudomonas, Salmonella, Shigella, Yersinia, Vibrio |
| | aph(4’)-Ia | 1026 | V01499 | 231…1256 | Escherichia |
| | aph(4’)-Ib | 999 | X03615 | 232…1230 | Streptomyces |
| | aph(6’)-Ia | 924 | AY791801 | 1…924 | Streptomyces |
| | aph(6’)-Ib | 924 | X05648 | 382…1305 | Streptomyces |
| | aph(6’)-Ic | 801 | X01702 | 485…1285 | Escherichia, Pseudomonas, Salmonella |
| | aph(6’)-Id | 837 | M28829 | 866…1702 | Enterobacter, Escherichia, Klebsiella, Pasteurella, Pseudomonas, Salmonella, Shigella, Yersinia, Vibrio |
| | aph(7´)-Ia | 999 | X03615 | 232…1230 | Streptomyces |
| | aph(9’)-Ia | 996 | U94857 | 151…1146 | Legionella |
| | aph(9’)-Ib | 993 | U70376 | 7526…8518 | Streptomyces |

Note: *Last update: January 6th 2012. This table was adapted from Elbourne and Hall (2006), Magnet and Blanchard (2005), Partridge et al. (2009), Ramirez and Tolmansk (2010), Shaw et al. (1993), Vakulenko and Mobashery (2003), and data provided by B. Guerra, B. Aranda, D. Avsaroglu, B. Ruiz del Castillo, and R. Helmut, on behalf of the Med-Vet Net (EU Network of Excellence) WP29 Project Group. The data were collected within the subproject “AMe’s,” with following participants representing their institutions: Agnes Perry Guyomard (ANSES), Dik Mewius (CIVI), Yvonne Agero (DTU), Katie Hopkins (HPAI), Silvia Herrera (ISCIII), Alessandra Carattoli (ISS), Antonio Battisti (IIS-Rome), Stefano Lollai (IIS-Sardegna), Lotte Jacobsen (SSI), Béla Nagy (VMRI), M. Rosario Rodicio and M. C. Mendoza (University of Oviedo, UK), Luis Martinez-Martinez (University Hospital of Valdecilla, HUV), and Bruno Gonzalez-Zorn (UCM).

ACT: Acetyltransferase; MET: Methyltransferase; NUT: Nucleotidyltransferase; PHT: Phosphotransferase.

*Although the sat genes are not aminoglycoside resistance determinants, they encode streptothricin-acetyltransferases, for convenience they are included in this table.
Table 2 | β-lactamases and ESBLs families.

| Amber class A | Number of variants* | Amber class B | Number of variants* | Amber class C | Number of variants* | Amber class D | Number of variants* |
|---------------|---------------------|---------------|---------------------|---------------|---------------------|---------------|---------------------|
| β-lactamases and ESBLs | | β-lactamases and MBLs | | β-lactamases and ESBLs | | β-lactamases and ESBLs | |
| blaACI | 1 | blaB | 13 | blaACC | 5 | ampH | 1 |
| blaAER | 1 | blaCGB | 2 | blaACT | 14 | ampS | 1 |
| blaAST | 1 | blaDIM | 1 | blaADC | 54 | blaLCR | 1 |
| blaBEL | 3 | blaER | 1 | blaBIL | 1 | blaRPS | 1 |
| blaBES | 1 | blaGM | 1 | blaBUT | 2 | blaROXa | 247 |
| blaBIC | 1 | blaGOB | 18 | blaCFLa | 1 | lpxA | 1 |
| blaBPS | 5 | blaBMP | 37 | blaCMG | 1 | | |
| blaCARB | 14 | blaND | 7 | blaCMY | 92 | | |
| blaCA | 1 | blaJOHN | 1 | blaDHA | 8 | | |
| blaCGA | 1 | blaMUS | 1 | blaFOX | 10 | | |
| blaCDO | 5 | blaDOM | 6 | blaLAT | 1 | | |
| blaCMX | 2 | blaDM | 1 | blaLEN | 26 | | |
| blaCTX-M | 130 | blaDMX | 1 | blaMIR | 5 | | |
| blaDES | 1 | blaDNS | 1 | blaMIR | 1 | | |
| blaERP | 1 | cepA | 34 | blaMOK | 8 | | |
| blaFAR | 1 | | 7 | blaOCH | 7 | | |
| blaHONa | 6 | cfla | 16 | blaOXPa | 16 | | |
| blaHES | 22 | cepA | 8 | blaOXPB | 20 | | |
| blaHFA | 8 | immH | 1 | blaOXY | 23 | | |
| blaHMI | 3 | immS | 1 | blaRNU | 1 | | |
| blaKLUAd | 12 | | | blaZEG | 1 | | |
| blaKLUCd | 2 | | | cepH | 1 | | |
| blaKLUG | 1 | | | | | | |
| blaKLUY | 4 | | | | | | |
| blaKHCa | 12 | | | | | | |
| blaKUT | 6 | | | | | | |
| blaMAL | 2 | | | | | | |
| blaMOR | 1 | | | | | | |
| blaMCa | 1 | | | | | | |
| blaPERa | 7 | | | | | | |
| blaPA | 1 | | | | | | |
| blaSE | 4 | | | | | | |
| blaRHN | 2 | | | | | | |
| blaROB | 1 | | | | | | |
| blaRE | 1 | | | | | | |
| blaSC | 1 | | | | | | |
| blaSO | 1 | | | | | | |
| blaSHV | 166 | | | | | | |
| blaSEM | 3 | | | | | | |
| blaTEM | 201 | | | | | | |
| blaTLA | 1 | | | | | | |
| blaTMA | 1 | | | | | | |
| blaVEB | 7 | | | | | | |
| blaZ | 1 | | | | | | |
| cdiA | 1 | | | | | | |
| cfxA | 6 | | | | | | |
| cumA | 1 | | | | | | |
| hupA | 1 | | | | | | |
| penA | 1 | | | | | | |

*Last update: June 8th 2012.

aAccording to http://www.lahey.org/Studies.

GES and IBC-type ESBLs have all been renamed as blaGES according to Weldhagen et al. (2006).

According to http://www.pasteur.fr/ip/easy/site/go/03b-00002u-03q/beta-lactamase-enzyme-variants.

According to http://www.lahey.org/Studies.

Saladin et al., 2002; Olson et al., 2005.
| Mechanism | Group | Gene | Gene(s) included | Length (nt) | Accession number | Coding region | Genera |
|-----------|-------|------|------------------|------------|------------------|---------------|--------|
| Efflux    | Type E-1 | cmlA1 | cmlA, cmlA2, cmlA4, cmlA5, cmlA6, cmlA7, cmlA8, cmlA10, cmlB | 1260 | M64556 | 601…1860 | Acinetobacter, Aeromonas, Arcanobacterium, Enterobacter, Escherichia, Klebsiella, Laribacter, Pseudomonas, Salmonella, Serratia, Staphylococcus |
|           | Type E-2 | cmlI | – | 903 | M22614 | 427…1335 | Escherichia |
|           | Type E-3 | floR | cmlA-like, flo, p-plo, cmlA9 | 1215 | AF071555 | 4445…5659 | Acinetobacter, Aeromonas, Bordetella, Escherichia, Pasteurella, Salmonella, Stenotrophomonas, Vibrio |
|           | Type E-4 | fexA | – | 1428 | AJ549214 | 177…1604 | Bacillus, Staphylococcus |
|           | Type E-5 | cml | – | 1179 | X59968 | 508…1686 | Streptomyces |
|           | Type E-6 | cmlv | – | 1311 | U09991 | 28…1338 | Streptomyces |
|           | Type E-7 | cmrA | cmr | 1176 | Z12001 | 993…2168 | Rhodococcus |
|           | Type E-8 | cmr | cmx | 1176 | U85507 | 3518…4693 | Corynebacterium |
|           | – | cmlB1 | – | 1266 | AM296481 | 776…2041 | Bordetella |
|           | – | fexB | – | 1410 | JN192453 | 10637…12046 | Enterococcus |
|           | – | pexA | – | 1248 | HM537013 | 24055…25302 | Uncultured |
| Inactivating enzyme | Type A-1 | catA1 | cat, catI, pp-cat | 660 | V00622 | 244…903 | Acinetobacter, Corynebacterium, Escherichia, Klebsiella, Salmonella, Shigella, Aeromonas, Agrobacterium, Escherichia, Haemophilus, Legionella, Klebsiella, Photobacterium, Salmonella, Vibrio |
|           | Type A-2 | catA2 | cat, catII | 642 | X53796 | 187…828 | Aeromonas, Agrobacterium, Escherichia, Klebsiella, Salmonella, Shigella |
|           | Type A-3 | catA3 | cat, catIII | 642 | X07848 | 272…913 | Actinobacillus, Edwardsiella, Klebsiella, Mannheimia, Pasteurella, Shigella |
|           | Type A-4 | cat | – | 654 | M11587 | 880…1533 | Proteus |
|           | Type A-5 | cat | – | 663 | P20074 | 1002758…100320 | Streptomyces |
|           | Type A-6 | cat86 | – | 663 | K00544 | 145…807 | Bacillus |
|           | Type A-7 | cat(pC221) | cat, catC | 648 | X02529 | 2267…2914 | Bacillus, Enterococcus, Lactobacillus, Staphylococcus, Streptococcus |
|           | Type A-8 | cat(pC223) | cat | 648 | AY355285 | 1000…1647 | Enterococcus, Lactococcus, Listeria, Staphylococcus |
|           | Type A-9 | cat(pC194) | cat, cat-TC | 651 | NC_002013 | 1260…1910 | Bacillus, Enterococcus, Lactobacillus, Staphylococcus, Streptococcus |
|           | Type A-10 | cat | – | 687 | AY238971 | 1055…1741 | Bacillus |
|           | Type A-11 | catP | catD | 624 | U15027 | 2953…3576 | Clostridium, Neisseria |
|           | Type A-12 | catS | – | 492 | X74948 | 1…492 | Streptococcus |
|           | Type A-13 | cat | – | 624 | M35190 | 309…932 | Campylobacter |
|           | Type A-14 | cat | – | 651 | S48276 | 479…1129 | Listonella, Photobacterium, Proteus, Vibrio |
|           | Type A-15 | catB | – | 660 | M93113 | 145…804 | Clostridium |
|           | Type A-16 | catQ | – | 660 | M55620 | 459…1118 | Clostridium |

(Continued)
Table 3 | Continued

| Mechanism | Group | Gene | Gene(s) included | Length (nt) | Accession number | Coding region | Genera |
|------------|-------|------|------------------|-------------|------------------|--------------|--------|
| Type B-1   | catB1 | cat  | —                | 630         | M58472           | 148…777      | Agrobacterium |
| Type B-2   | catB2 | —    | —                | 633         | AF047479         | 5957…6589    | Acinetobacter, Aeromonas, Bordetella, Escherichia, Klebsiella, Pasteurella, Pseudomonas, Salmonella |
| Type B-3   | catB3 | catB4, catB5, catB6, catB8 | 633         | AJ009818      | 883…1515        | Acinetobacter, Aeromonas, Bordetella, Comamonas, Enterobacter, Escherichia, Klebsiella, Kluvyera, Morganella, Proteus, Pseudomonas, Salmonella, Serratia, Stenotrophomonas |
| Type B-4   | catB7 | —    | 639              | AF036933    | 177…815         | Pseudomonas   |
| Type B-5   | catB9 | —    | 630              | AF462019    | 27…656          | Vibrio        |
| Type B-6   | catB10| —    | 633              | AJ878850    | 1197…1829       | Pseudomonas   |
| rRNA       | —     | cfr$^+$ | —              | 1050        | AJ579365         | 6290…7339    | Bacillus, Enterococcus, Escherichia, Jeotgalicoccus, Macroccocus, Proteus, Staphylococcus |

Note: *Last update: December 16th 2011. Adapted from Partridge et al. (2009), Roberts and Schwarz (2009), Schwarz et al. (2004), and nucleotide BLAST searches.
$^+$ Partial sequence.

The multidrug resistance gene cfr confers resistance against phenicols, lincosamides, oxazolidinones, pleuromutilins, and streptogramin A (see Table 4; Kehrenberg et al., 2007).

Table 4 | Acquired macrolide-lincosamide-streptogramin B (MLS) resistance genes*.

| Mechanism | Gene | Gene(s) included | Length (nt) | Accession number | Coding region | Genera |
|------------|------|------------------|-------------|------------------|--------------|--------|
| Efflux     | car(A)| —                | 1656        | M80346           | 411…2066     | Streptomyces |
|            | imr(A)| —                | 1446        | X59926           | 318…1763     | Streptomyces |
|            | isa(A)| abc-23           | 1497        | AY225127         | 41…1537      | Enterococcus |
|            | isa(B)| orf3             | 1479        | AJ579365         | 4150…5628    | Staphylococcus |
|            | isa(C)| —                | 1479        | HM990671         | 5193…6671    | Gardnerella, Streptococcus |
|            | isa(E)| —                | 1485        | JQ861959         | 6673…8157    | Enterococcus, Staphylococcus |
|            | mef(A)| mef(E)           | 1218        | U70055           | 314…1531     | Acinetobacter, Bacteroides, Citrobacter, Clostridium, Corynebacterium, Enterococcus, Enterobacter, Escherichia, Fusobacterium, Gemella, Haemophilus, Klebsiella, Lactobacillus, Micrococcus, Morganella, Neisseria, Pantoea, Providencia, Proteus, Ralstonia, Rothia, Pseudomonas, Salmonella, Serratia, Staphylococcus, Streptococcus, Stenotrophomonas, Ureaplasma |
|            | mef(B)| —                | 1230        | FJ196385         | 11084…12313  | Escherichia |
|            | msr(A)| msr(B), msr(SA)  | 1467        | X52085           | 343…1809     | Corynebacterium, Enterobacter, Enterococcus, Gemella, Pseudomonas, Staphylococcus, Streptococcus, Ureaplasma |
|            | msr(C)| —                | 1479        | AY004350         | 496…1974     | Enterococcus |
|            | msr(D)| mel, orf5        | 1464        | AF274302         | 2462…3925    | Acinetobacter, Bacteroides, Citrobacter, Clostridium, Corynebacterium, Enterococcus, Enterobacter, Escherichia, Gemella, Fusobacterium, Klebsiella, Morganella, Neisseria, Proteus, Providencia, Pseudomonas, Ralstonia, Staphylococcus, Streptococcus, Serratia, Stenotrophomonas, Ureaplasma |

(Continued)
Table 4 | Continued

| Mechanism | Gene | Gene(s) included | Length (nt) | Accession number | Coding region | Genera |
|------------|------|------------------|------------|-----------------|---------------|--------|
| Inactivating enzyme<sup>a</sup> | msr(E) | mel | 1476 | AY522431 | 20650...22125 | Acinetobacter, Citrobacter, Escherichia, Klebsiella, Mannheimia, Pasteurella, Serratia |
| Inactivating enzyme<sup>a</sup> | ole(B) | – | 1710 | L36601 | 1421...3130 | Streptomyces |
| Inactivating enzyme<sup>a</sup> | ole(C) | – | 978 | L06249 | 1528...2505 | Streptomyces |
| Inactivating enzyme<sup>a</sup> | smr(B) | – | 1653 | XG3451 | 558...2210 | Streptomyces |
| Inactivating enzyme<sup>a</sup> | tlc(C) | – | 1647 | M5743 | 277...1923 | Streptomyces |
| Inactivating enzyme<sup>a</sup> | vga(A) | vga | 1569 | M90056 | 909...2477 | Staphylococcus |
| Inactivating enzyme<sup>a</sup> | vga(A)<sub>LC</sub> | vga | 1569 | DQ823382 | 1...1569 | Staphylococcus |
| Inactivating enzyme<sup>b</sup> | vgb(B) | – | 1659 | U82085 | 629...2287 | Enterococcus, Staphylococcus |
| Inactivating enzyme<sup>b</sup> | vga(C) | – | 1569 | NC_013034 | 12570...14138 | Staphylococcus |
| Inactivating enzyme<sup>b</sup> | vga(D) | – | 1578 | GQ205627 | 1394...2971 | Enterococcus |
| Inactivating enzyme<sup>b</sup> | vga(E) | – | 1575 | FR772051 | 8741...10315 | Staphylococcus |
| Inactivating enzyme<sup>b</sup> | ere(A) | – | 1221 | AY183453 | 2730...3950 | Achromobacter, Aeromonas, Citrobacter, Enterobacter, Escherichia, Klebsiella, Proteus, Pseudomonas, Serratia, Salmonella, Staphylococcus, Stenotrophomonas |
| Inactivating enzyme<sup>b</sup> | ere(B) | – | 1260 | X03988 | 383...1642 | Acinetobacter, Citrobacter, Enterobacter, Escherichia, Klebsiella, Proteus, Pseudomonas, Staphylococcus |
| Inactivating enzyme<sup>c</sup> | vgb(A) | vgb | 900 | M20129 | 641...1540 | Enterococcus, Staphylococcus |
| Inactivating enzyme<sup>c</sup> | vgb(B) | – | 888 | AF015628 | 399...1286 | Staphylococcus |
| Inactivating enzyme<sup>c</sup> | lnu(A) | lni(A), lin(A) | 486 | M14039 | 413...898 | Clostridium, Lactobacillus, Staphylococcus |
| Inactivating enzyme<sup>c</sup> | lnu(B) | lin(B) | 804 | AJ238249 | 127...930 | Clostridium, Enterococcus, Staphylococcus, Streptococcus |
| Inactivating enzyme<sup>c</sup> | lnu(C) | – | 495 | AY928180 | 1150...1644 | Haemophilus,Streptococcus |
| Inactivating enzyme<sup>c</sup> | lnu(D) | – | 495 | EF452177 | 19...513 | Streptococcus |
| Inactivating enzyme<sup>c</sup> | lnu(F) | lin(F), lin(G), linF | 822 | EU118119 | 1030...1851 | Escherichia, Salmonella |
| Inactivating enzyme<sup>d</sup> | var(A) | – | 660 | L07778 | 258...917 | Staphylococcus |
| Inactivating enzyme<sup>d</sup> | var(B) | – | 639 | U19459 | 67...705 | Enterococcus, Staphylococcus |
| Inactivating enzyme<sup>d</sup> | var(C) | – | 639 | AF015628 | 1307...1945 | Staphylococcus |
| Inactivating enzyme<sup>d</sup> | var(D) | sat(A) | 630 | L12033 | 162...791 | Enterococcus |
| Inactivating enzyme<sup>d</sup> | var(E) | sat(G), var (E-3)–var(E-8) | 645 | AF139725 | 63...707 | Enterococcus, Lactobacillus |
| Inactivating enzyme<sup>d</sup> | var(F) | – | 666 | AF170730 | 70...735 | Yersinia |
| Inactivating enzyme<sup>d</sup> | var(H) | var(G) | 651 | GQ205627 | 3037...3687 | Enterococcus |
| Inactivating enzyme<sup>d</sup> | mph(A) | mph(K) | 906 | D16251 | 1626...2831 | Aeromonas, Escherichia, Citrobacter, Enterobacter, Klebsiella, Pantoae, Pseudomonas, Proteus, Serratia, Shigella, Stenotrophomonas |
| Inactivating enzyme<sup>d</sup> | mph(B) | mph(B) | 909 | D85892 | 1159...2067 | Escherichia, Enterobacter, Proteus, Pseudomonas |
| Inactivating enzyme<sup>d</sup> | mph(C) | mph(BM) | 900 | AF167161 | 5665...6564 | Staphylococcus, Stenotrophomonas |
| Inactivating enzyme<sup>d</sup> | mph(D) | – | 840<sup>5</sup> | AB048951 | 1...840 | Escherichia, Klebsiella, Pantoae, Proteus, Pseudomonas, Stenotrophomonas |
| Inactivating enzyme<sup>d</sup> | mph(E) | mph1, mph2 | 885 | DQ839391 | 12873...13757 | Acinetobacter, Citrobacter, Escherichia, Klebsiella, Mannheimia, Pasteurella, Serratia |
| Inactivating enzyme<sup>d</sup> | mph(F) | mph(B), mph(E) | 900 | AM206957 | 4187...5086 | Unknown |
| rRNA methylase | cfr<sup>6</sup> | – | 1050 | AM408573 | 10028...11077 | Bacillus, Enterococcus, Escherichia, Jeotgalicoccus, Macrooccus, Proteus, Staphylococcus |
| rRNA methylase | erm(A) | erm(TR) | 732 | X03216 | 4551...5282 | Aggregatibacter, Bacteroides, Enterococcus, Helcococcus, Peptostreptococcus, Prevotella, Staphylococcus, Streptococcus |

(Continued)
Table 4 | Continued

| Mechanism | Gene(s) included | Length (nt) | Accession number | Coding region | Genera |
|------------|------------------|-------------|------------------|---------------|--------|
| **erm(B)** | **erm(2), erm(AM), erm(AMR), erm(BC), erm(BP), erm(Z), erm(BZ1, BZ2), erm(IP), erm(erm80)** | 738 | M36722 | 714…1451 | Aggregatibacter, Acinetobacter, Aerococcus, Arcanobacterium, Bacillus, Bacteroides, Citrobacter, Corynebacterium, Clostridium, Enterobacter, Escherichia, Eubacterium, Enterococcus, Fusobacterium, Gemella, Haemophilus, Klebsiella, Lactobacillus, Micrococcus, Neisseria, Pantoeae, Pedicoccus, Peptostreptococcus, Porphyromonas, Proteus, Pseudomonas, Ruminococcus, Rothia, Serratia, Staphylococcus, Streptococcus, Ureaplasma, Treponema, Wolinella |
| **erm(C)** | **erm(IM), erm(M)** | 735 | M19652 | 988…1722 | Aggregatibacter, Actinomyces, Arcanobacterium, Bacillus, Bacteroides, Clostridium, Corynebacterium, Escherichia, Eubacterium, Enterococcus, Haemophilus, Lactobacillus, Macroccocus, Micrococcus, Neisseria, Prevotella, Peptostreptococcus, Staphylococcus, Streptococcus, Wolinella |
| **erm(D)** | **erm(J), erm(K)** | 864 | M29832 | 430…1293 | Bacillus, Salmonella |
| **erm(E)** | **erm(E2)** | 1146 | X51891 | 190…1335 | Bacteroides, Eubacterium, Fusobacterium, Ruminococcus, Saccharopolyspora, Shigella, Streptomyces |
| **erm(F)** | **erm(FS), erm(FU)** | 801 | M14730 | 241…1041 | Aggregatibacter, Actinomyces, Bacteroides, Capnocytophaga, Clostridium, Corynebacterium, Eubacterium, Enterococcus, Fusobacterium, Gardnerella, Haemophilus, Lactobacillus, Mobiluncus, Neisseria, Porphyromonas, Prevotella, Peptostreptococcus, Ruminococcus, Shigella, Selenomonas, Staphylococcus, Streptococcus, Treponema, Veillonella, Wolinella |
| **erm(G)** | – | 735 | M15332 | 672…1406 | Bacillus, Bacteroides, Catenibacterium, Lactobacillus, Prevotella, Porphyromonas, Staphylococcus |
| **erm(H)** | **car(B)** | 900 | M16503 | 244…1143 | Streptomyces |
| **erm(I)** | **mdm(A)** | – | – | – | Streptomyces |
| **erm(N)** | **trl(D)** | 876 | X97721 | 160…1035 | Streptomyces |
| **erm(O)** | **irm, smr(A)** | 783 | M74717 | 40…822 | Streptomyces |
| **erm(Q)** | – | 774 | L22689 | 262…1035 | Aggregatibacter, Bacteroides, Clostridium, Staphylococcus, Streptococcus, Wolinella |
| **erm(R)** | – | 1023 | M11276 | 333…1355 | Aeromicrobium, Arthrobacter |
| **erm(S)** | **erm(SF), trl(D)** | 960 | M19269 | 460…1419 | Streptomyces |
| **erm(T)** | **erm(GT), erm(LF)** | 735 | M64090 | 168…902 | Enterococcus, Lactobacillus, Staphylococcus, Streptococcus |
| **erm(U)** | **irm(B)** | 837 | X62867 | 361…1197 | Streptomyces |
| **erm(V)** | **erm(SV)** | 780 | U69450 | 397…1176 | Eubacterium, Fusobacterium, Streptomyces |
| **erm(W)** | **myr(B)** | 936 | D14532 | 1039…1974 | Micromonospora |
| **erm(X)** | **erm(CD), erm(Y)** | 855 | M36726 | 296…1150 | Arcanobacterium, Blidobacterium, Corynebacterium, Propionibacterium |
| **erm(Y)** | **erm(GM)** | 735 | AB014481 | 556…1290 | Staphylococcus |
| **erm(Z)** | **srm(D)** | 849 | AM709763 | 2817…3665 | Streptomyces |
| **erm(30)** | **pikR1** | 1011 | AF079138 | 1283…2293 | Streptomyces |
| **erm(31)** | **pikR2** | 969 | AF079138 | 154…1122 | Streptomyces |
| **erm(32)** | **trl(B)** | 843 | AJ009971 | 1790…2632 | Streptomyces |

(Continued)
Table 4 | Continued

| Mechanism | Gene | Gene(s) included | Length (nt) | Accession number | Coding region | Genera |
|-----------|------|------------------|-------------|------------------|---------------|--------|
| erm(33)   | –    | 732              | AJ313523    | 163...894        | Staphylococcus|        |
| erm(34)   | –    | 846              | AY234334    | 355...1200       | Bacillus      |        |
| erm(35)   | –    | 801              | AF319779    | 33...833         | Bacteriodes   |        |
| erm(36)   | –    | 846              | AF462611    | 186...1031       | Micrococcus   |        |
| erm(37)   | erm(MT) | 540       | AE000516    | 2229013...2229552| Mycobacterium|        |
| erm(38)   | –    | 1161             | AY154657    | 63...1223        | Mycobacterium|        |
| erm(39)   | –    | 741              | AY487229    | 2153...2893      | Mycobacterium|        |
| erm(40)   | –    | 756              | AY570506    | 2035...2790      | Mycobacterium|        |
| erm(41)   | –    | 522              | EU590124    | 258...779        | Mycobacterium|        |
| erm(42)   | erm(MII) | 906       | FR734406    | 1...906          | Mannheimia, Pasteurella, Photobacterium|        |

Note: *Last update: January 6th 2012. Adapted from http://faculty.washington.edu/marilynr/

§Partial sequence.

The multidrug resistance gene cfr confers resistance against phenicols, lincosamides, oxazolidinones, pleuromutilins, and streptogramin A (see Table 3; Kehrenberg et al., 2007).

Table 5 | Acquired quinolone resistance genes.

| Gene | Length (nt) | Accession number | Coding region | Genera |
|------|-------------|------------------|---------------|--------|
| qepA | 1536        | AB263754         | 7052...8587   | Escherichia |
| qepA2| 1536        | EU847537         | 1672...3207   | Escherichia |
| qnrA1a| 657    | AY070235         | 303...959     | Citrobacter, Escherichia, Klebsiella, Proteus |
| qnrA2a| 657    | AY675584         | 1...657       | Klebsiella, Shewanella |
| qnrA3a| 657    | DQ058661         | 1...657       | Shewanella |
| qnrA4a| 657    | DQ058662         | 1...657       | Shewanella |
| qnrA5a| 657    | DQ058663         | 1...657       | Shewanella |
| qnrA6a| 657    | DQ151889         | 1...657       | Proteus |
| qnrA7a| 657    | GQ463707         | 1...657       | Shewanella |
| qnrB1a| 645    | DQ351241         | 37...681      | Klebsiella |
| qnrB2a| 645    | DQ351242         | 1...645       | Citrobacter, Enterobacter, Klebsiella, Salmonella |
| qnrB3a| 645    | DQ303920         | 37...681      | Escherichia |
| qnrB4a| 645    | DQ303921         | 4...648       | Citrobacter, Enterobacter, Escherichia, Klebsiella |
| qnrB5a| 645    | DQ303919         | 37...881      | Salmonella |
| qnrB6a| 645    | EF520349         | 37...881      | Enterobacter, Panthoea |
| qnrB7a| 645    | EU043311         | 1...645       | Enterobacter, Klebsiella |
| qnrB8a| 645    | EU043312         | 1...645       | Citrobacter |
| qnrB9a| 645    | EF526508         | 1...645       | Citrobacter |
| qnrB10a| 645   | DQ631414         | 37...681      | Citrobacter, Enterobacter, Klebsiella |
| qnrB11a| 645   | EF653270         | 4...648       | Citrobacter |
| qnrB12a| 645   | AM774474         | 2435...3079   | Citrobacter |
| qnrB13a| 645   | EU273756         | 37...681      | Citrobacter |
| qnrB14a| 645   | EU273757         | 37...681      | Citrobacter |
| qnrB15a| 645   | EU302865         | 37...681      | Citrobacter |
| qnrB16a| 645   | EU136183         | 37...681      | Citrobacter |
| qnrB17a| 645   | AM919398         | 37...681      | Citrobacter |
| qnrB18a| 645   | AM919399         | 37...681      | Citrobacter |
| qnrB19a| 645   | EU432277         | 1...645       | Escherichia, Klebsiella, Salmonella |
| qnrB20a| 645   | AB379831         | 37...681      | Escherichia |
| qnrB21a| 645   | FJ611948         | 1...645       | Escherichia |
Table 5 | Continued

| Gene      | Length (nt) | Accession number | Coding region | Genera       |
|-----------|-------------|------------------|---------------|--------------|
| qnrB22\(^a\) | 645         | FJ81621           | 37...681      | Citrobacter  |
| qnrB23\(^a\) | 645         | FJ81622           | 37...681      | Citrobacter  |
| qnrB24\(^a\) | 645         | HM192542          | 37...681      | Citrobacter  |
| qnrB25\(^a\) | 645         | HQ172108          | 1...645       | Citrobacter  |
| qnrB26\(^a\) | 645         | HM439644          | 1...645       | Citrobacter  |
| qnrB27\(^a\) | 645         | HM439641          | 1...645       | Citrobacter  |
| qnrB29\(^a\) | 645         | HM439649          | 37...681      | Citrobacter  |
| qnrB30\(^a\) | 645         | HM439650          | 37...681      | Citrobacter  |
| qnrB31\(^a\) | 645         | HQ418999          | 1...645       | Klebsiella   |
| qnrB32\(^a\) | 645         | JN173054          | 37...681      | Citrobacter  |
| qnrB33\(^a\) | 645         | JN173055          | 36...680      | Citrobacter  |
| qnrB34\(^a\) | 645         | JN173056          | 39...683      | Citrobacter  |
| qnrB35\(^a\) | 645         | JN173057          | 2307...2951   | Citrobacter  |
| qnrB36\(^a\) | 645         | JN173058          | 37...681      | Citrobacter  |
| qnrB37\(^a\) | 645         | JN173059          | 36...680      | Citrobacter  |
| qnrB38\(^a\) | 645         | JN173060          | 2307...2951   | Citrobacter  |
| qnrB39\(^a\) | 645         | NZ_ABWL02000005   | –             | –            |
| qnrB40\(^a\) | 645         | JN166689          | 16...660      | Citrobacter  |
| qnrB41\(^a\) | 645         | JN166690          | 37...681      | Citrobacter  |
| qnrB42\(^a\) | 645         | JN680743          | 1...645       | Klebsiella   |
| qnrB43\(^a\) | 644         | JQ349152          | 37...680      | Escherichia  |
| qnrB44\(^a\) | 644         | JQ349153          | 37...680      | Escherichia  |
| qnrB45\(^a\) | 644         | JQ349152          | 37...680      | Escherichia  |
| qnrB46\(^a\) | 644         | JQ349154          | 37...680      | Escherichia  |
| qnrB47\(^a\) | 644         | JQ349155          | 37...680      | Escherichia  |
| qnrB48\(^a\) | 645         | JQ762640          | 37...681      | Citrobacter  |
| qnrB49\(^a\) | 645         | JQ582718          | 37...681      | Citrobacter  |
| qnrB50–qnrB51 not public yet |
| qnrB52\(^a\) | 645         | EF488762          | 1...645       | Proteus      |
| qnrB53\(^a\) | 645         | HQ704413          | 37...681      | Klebsiella   |
| qnrB54–qnrB59 not public yet |
| qnrC\(^a\) | 666         | EU917444          | 1717...2382   | Proteus      |
| qnrD\(^a\) | 645         | EU692908          | 1...645       | Escherichia, Morganella, Proteus, Providencia, Salmonella |
| qnrS1\(^a\) | 657         | AB187515          | 9737...10393  | Enterobacter, Escherichia, Klebsiella, Proteus, Salmonella, Shigella |
| qnrS2\(^a\) | 657         | DQ485530          | 1...657       | Aeromonas, Salmonella |
| qnrS3\(^a\) >656 | 657     | EU077611          | <1...656      | Escherichia  |
| qnrS4\(^a\) | 657         | FJ418153          | 1...657       | Salmonella   |
| qnrS5\(^a\) | 657         | HQ631377          | 1...657       | Aeromonas    |
| qnrS6\(^a\) | 657         | HQ631376          | 1...657       | Aeromonas    |
| qnrS7–qnrS8 not public yet |

*Last update: July 8th 2012. According to http://www.lahey.org/qnrStudies* and nucleotide BLAST searches.

The most common mechanism of MLS\(_B\) resistance is due to the presence of rRNA methylases, encoded by the *erm* genes. These enzymes methylate the adenine residue(s) resulting in MLS\(_B\) resistance. The methylated adenine(s) prevents the drugs from binding to the 50S ribosomal subunit. The other two mechanisms efflux and enzymatic inactivation result in resistance to only 1 or 2 classes of antibiotics belonging to the MLS group.

There are currently 77 MLS resistance genes recognized. A new MLS gene must have <79% amino acid identity with all previously characterized MLS genes before receiving a unique name (Roberts et al., 1999; Roberts, 2008). For an actual list of the MLS acquired resistance genes we refer to the website of Dr. Marilyn Roberts, http://faculty.washington.edu/marilynr/.

In addition to the subsection of QUINOLONES currently five families of *qnr* genes have been reported; *qnrA* (7 subtypes), *qnrB* (59 subtypes), *qnrC* (1 subtype), *qnrD* (1 subtype), and *qnrS* (8 subtypes) (Jacoby et al., 2008; Cattoir...
### Table 6 | Acquired tetracycline resistance genes*

| Mechanism | Gene | Length (nt) | Accession number | Coding region | Genera |
|-----------|------|-------------|------------------|---------------|--------|
| Efflux    | otr(B) | 1692 | AF079900 | 40…1731 | Mycobacterium, Streptomyces |
|           | otr(C) | 1056 | AY509111 | 224…1379 | Streptomyces |
|           | tcr   | 1539 | D38215  | 516…2054 | Streptomyces |
|           | tet   | 1200 | X00006  | 1328…2527 | Acinetobacter, Aeromonas, Alcaligenes, Bordetella, Chryseobacterium, Citrobacter, Edwardsiella, Enterobacter, Escherichia, Flavobacterium, Klebsiella, Laribacter, Plesiomonas, Proteus, Pseudomonas, Salmonella, Serratia, Shigella, Variorox, Veillonella, Vibrio |
|           | tet(A) | 1263 | L20800  | 1063…2325 | Clostridium |
|           | tet(B) | 1206 | J01830  | 1608…2813 | Aeromonas, Actinobacillus, Aeromonas, Aggregatibacter, Brevundimonas, Citrobacter, Enterobacter, Erwinia, Escherichia, Haemophilus, Klebsiella, Mannheimia, Moraxella, Neisseria, Pantoea, Pasteurella, Photobacterium, Plesiomonas, Proteus, Providencia, Pseudomonas, Roseobacter, Salmonella, Serratia, Shigella, Treponema, Vibrio, Yersinia |
|           | tet(C) | 1191 | X01654  | 86…1276 | Aeromonas, Bordetella, Chlamydia, Citrobacter, Enterobacter, Escherichia, Francisella, Halomonas, Klebsiella, Proteus, Pseudomonas, Roseobacter, Salmonella, Serratia, Shigella, Vibrio |
|           | tet(D) | 1185 | X65876  | 1521…2705 | Aeromonas, Alteromonas, Citrobacter, Edwardsiella, Enterobacter, Escherichia, Halomonas, Klebsiella, Morganella, Pasteurella, Photobacterium, Proteus, Salmonella, Shewanella, Shigella, Vibrio, Yersinia |
|           | tet(E) | 1218 | L06940  | 21…1238 | Aeromonas, Alcaligenes, Escherichia, Flavobacterium, Plesiomonas, Proteus, Providencia, Pseudomonas, Roseobacter, Serratia, Vibrio |
|           | tet(G) | 1128 | AF071555 | 6644…7771 | Acinetobacter, Brevundimonas, Escherichia, Fusobacterium, Mannheimia, Ochrobactrum, Pasteurella, Proteus, Providencia, Pseudomonas, Roseobacter, Salmonella, Shewanella, Vibrio, Yersinia |
|           | tet(H) | 1203 | U00792  | 716…1918 | Acinetobacter, Actinobacillus, Histophilus, Mannheimia, Moraxella, Pasteurella, Psychrobacter |
|           | tet(J) | 1197 | AF038993 | 1084…2280 | Escherichia, Morganella, Proteus |
|           | tet(K) | 1380 | M16217  | 305…1684 | Bacillus, Clostridium, Enterococcus, Eubacterium, Haemophilus, Lactobacillus, Listeria, Mycobacterium, Nocardia, Peptostreptococcus, Staphylococcus, Streptococcus, Streptomyces |
|           | tet(L) | 1377 | D00006  | 189…1565 | Acinetobacter, Actinobacillus, Actinomyces, Bacillus, Bifidobacterium, Citrobacter, Clostridium, Enterobacter, Escherichia, Flavobacterium, Fusobacterium, Geobacillus, Kurthia, Lactobacillus, Listeria, Mannheimia, Morganella, Mycobacterium, Nocardia, Ochrobactrum, Oceanobacillus, Paenibacillus, Pasteurella, Pediococcus, Peptostreptococcus, Proteus, Pseudomonas, Rhahnella, Salmonella, Sporosarcina, Staphylococcus, Streptococcus, Streptomyces, Variorox, Veillonella, Virgibacillus |
|           | tet(V) | 1260 | AF030344 | 462…1721 | Mycobacterium |
|           | tet(Y) | 1176 | AF070999 | 1680…2855 | Aeromonas, Escherichia, Photobacterium |
|           | tet(Z) | 1155 | AF121000 | 11880…13034 | Corynebacterium, Lactobacillus |
|           | tet(S) | 1165 | AF909887 | 1130…3214 | Agrobacterium |
|           | tet(X) | 1233 | AJ280203 | 1651…2883 | Aeromonas, Gallibacterium |
|           | tet(Y) | 1224 | AJ420072 | 22940…24163 | Arthrobacter, Corynebacterium |
|           | tet(Z) | 1231 | AF353562 | 2213…3322 | Stenotrophomonas, Vibrio |
|           | tet(A) | 1353 | AY825285 | 1…1353 | Staphylococcus |
|           | tet(B) | 1188 | AY473590 | 749…1936 | Acinetobacter, Alcaligenes, Brevundimonas, Enterobacter, Providencia, Stenotrophomonas |
|           | tet(C) | 1221 | AM419751 | 14211…15431 | Clostridium |
|           | tet(D) | 1182 | AY264780 | 1825…3006 | Serratia |
|           | tet(E) | 1267 | EU523697 | 687…1973 | Bacillus, Microbacterium, Micrococcus, Paenibacillus, Pseudomonas, Staphylococcus |

(Continued)
Another mechanism of conferring resistance to quinolones is represented by the plasmid-borne gene qepA, which codes for an efflux pump that can export hydrophilic fluoroquinolones, e.g., ciprofloxacin and enrofloxacin (Périchon et al., 2007; Yamane et al., 2007). A variant of this resistance pump, QepA2, was identified in an E. coli isolate from France (Cattoir et al., 2008).

Regarding TETRACYCLINE, Resistance mechanisms, currently there are 45 different acquired tetracycline resistance determinants recognized (Roberts, 1996, 2005; Brown et al., 2008) (Table 6). For an up-to-date list of the acquired tetracycline resistance genes, we refer to the website of Dr. Marilyn Roberts, http://faculty.washington.edu/marilynr/. Among these, 26 of the tet genes, 2 of the otr genes and the only tcr determinant code for efflux pumps, whereas 11 tet genes and 1 otr gene code for ribosomal protection proteins (RPPs). The enzymatic inactivation mechanism can be attributed to 3 tet genes. The tet(U) determinant represents an unknown tetracycline resistance mechanism.

Table 6 | Continued

| Mechanism               | Gene   | Length (nt) | Accession number | Coding region | Genera                                                                 |
|-------------------------|--------|-------------|------------------|---------------|------------------------------------------------------------------------|
| Enzymatic               | tet(43)| 1560        | GO244501         | 60…1619       | Uncultured                                                            |
|                         | tet(X)| 1167        | M37699           | 586…1752      | Bacteroides, Pseudomonas, Sphingobacterium                            |
|                         | tet(34)| 465         | AB061440         | 306…770       | Aeromonas, Pseudomonas, Serratia                                      |
|                         | tet(37)| 327         | AF540889         | 1…327         | Uncultured                                                            |
| Ribosomal protection    | otr(A)| 1992        | X53401           | 348…2340      | Bacillus, Mycobacterium, Streptomyces                                  |
|                         | tetB(P)| 1959       | L20800           | 2309…4267     | Clostridium                                                           |
|                         | tet(M)| 1920        | U08812           | 1981…3900     | Clostridium, Bacteroides, Capnocytophaga, Clostridium, Eubacterium, Fusobacterium, Gardnerella, Gemella, Granulicatella, Haemophilus, Kingella, Klebsiella, Kurthia, Lactobacillus, Lactococcus, Listeria, Microbacterium, Mycoplasma, Neisseria, Paenibacillus, Pantoaea, Pasteurella, Peptostreptococcus, Photobacterium, Prevotella, Pseudoalteromonas, Pseudomonas, Ralstonia, Selenomonas, Serratia, Shewanella, Staphylococcus, Streptococcus, Streptomyces, Ureaplasma, Veillonella, Vibrio |
|                         | tet(O)| 1926        | X71523           | 362…2287      | Actinobacillus, Aerococcus, Anaerovibrio, Bifidobacterium, Butyryrivibrio, Campylobacter, Clostridium, Eubacterium, Fusobacterium, Gardnerella, Lactobacillus, Mitsuokella, Mobiluncus, Neisseria, Peptostreptococcus, Porphyromonas, Prevotella, Ruminococcus, Selenomonas, Streptococcus, Subdoligranulum, Veillonella |
|                         | tet(Q)| 1956        | L42544           | 478…2433      | Lactobacillus, Streptococcus                                          |
|                         | tet(W)| 1920        | AJ222769         | 3687…5606     | Acidaminococcus, Actinomyces, Arcanobacterium, Bacillus, Bacteroides, Bifidobacterium, Butyryrivibrio, Clostridium, Fusobacterium, Gardnerella, Lactobacillus, Mitsuokella, Mobiluncus, Neisseria, Peptostreptococcus, Porphyromonas, Prevotella, Ruminococcus, Selenomonas, Streptococcus, Streptomyces, Subdoligranulum, Veillonella |
|                         | tet(32)| 1920       | DQ647324         | 181…2100      | Eubacterium, Streptococcus                                            |
|                         | tet(36)| 1923       | AJ514254         | 2534…4456     | Bacteroides, Clostridium, Lactobacillus                               |
|                         | tet(44)| 1923       | FN594949         | 25245…27167   | Campylobacter, Clostridium                                            |
|                         | tet  | 1920       | M74049           | 343…2261      | Streptomyces                                                          |
|                         | tet(U)| 318        | U01917           | 413…730       | Enterococcus, Staphylococcus, Streptococcus                            |

Note: *Last update: January 6th 2012. Adapted from http://faculty.washington.edu/marilynr/. The efflux genes tet(45) and tet(46) have been named but not yet published.
### Table 7 | Acquired trimethoprim resistance genes.

| Gene       | Sub-family | Gene(s) included | Length (nt) | Accession number | Coding region | Genera                                                                 |
|------------|------------|------------------|-------------|------------------|---------------|------------------------------------------------------------------------|
| dfrA1      | dfrA1-group| dhfrIb, dfr1, dhfr| 474         | X00926           | 236…709       | Actinobacter, Enterobacter, Escherichia, Klebsiella, Laribacter, Morganella, Pasteurella, Proteus, Pseudomonas, Salmonella, Serratia, Shigella, Vibrio |
| dfrA2      | –          | –                | 489         | J03306           | 103…591       | Salmonella                                                            |
| dfrA5      | dfrA1-group| dhfrV, dfrV      | 474         | X12868           | 1306…1779     | Actinobacter, Aeromonas, Comamonas, Enterobacter, Escherichia, Klebsiella, Pseudomonas, Salmonella, Vibrio                    |
| dfrA6      | dfrA1-group| dfrVI            | 474         | Z86002           | 336…809       | Proteus                                                               |
| dfrA7      | dfrA1-group| dfrVII, dfrVII, dfrA17 | 474 | X58425           | 594…1067      | Actinobacter, Escherichia, Proteus, Salmonella, Shigella                |
| dfrA8      | –          | –                | 510         | U10186           | 711…1220      | Escherichia                                                           |
| dfrA9      | –          | –                | 534         | X57730           | 726…1259      | Escherichia                                                           |
| dfrA10     | –          | –                | 564         | L06418           | 5494…6057     | Actinobacter, Escherichia, Klebsiella, Salmonella                      |
| dfrA12     | dfrA12-group| dhfrXII, dfr12   | 498         | Z21672           | 310…807       | Actinobacter, Aeromonas, Citrobacter, Edwardsiella, Enterobacter, Escherichia, Klebsiella, Proteus, Providencia, Pseudomonas, Serratia, Salmonella, Staphylococcus, Stenotrophomonas |
| dfrA13     | dfrA12-group| –                | 498         | Z50802           | 718…1215      | Escherichia                                                           |
| dfrA14     | dfrA1-group| dhfrIb           | 474         | Z50805           | 72…545        | Actinobacter, Aeromonas, Escherichia, Klebsiella, Salmonella, Vibrio   |
| dfrA15     | dfrA1-group| dhfrXVb          | 474         | Z83311           | 357…830       | Actinobacter, Enterobacter, Escherichia, Klebsiella, Morganella, Proteus, Pseudomonas, Vibrio                              |
| dfrA16     | dfrA1-group| dhfrXVI, dfr16   | 474         | AF174129         | 1352…1825     | Aeromonas, Escherichia, Klebsiella, Salmonella                         |
| dfrA17     | dfrA1-group| dhfrXVII, dfr17  | 474         | AB126604         | 98…571        | Actinobacter, Enterobacter, Escherichia, Klebsiella, Klyvera, Laribacter, Pseudomonas, Salmonella, Serratia, Shigella, Staphylococcus, Stenotrophomonas |
| dfrA18     | –          | dfrA19           | 570         | AJ310778         | 7004…7573     | Enterobacter, Klebsiella, Salmonella                                   |
| dfrA20     | –          | –                | 510         | AJ605332         | 1304…1813     | Pasteurella                                                           |
| dfrA21     | dfrA12-group| dfrxii          | 498         | AY552589         | 1…498         | Escherichia, Klebsiella, Salmonella                                   |
| dfrA22     | dfrA12-group| dfr22, dfr23    | 498         | AJ628423         | 325…822       | Escherichia, Klebsiella, Serratia                                    |
| dfrA23     | –          | –                | 561         | AJ46361          | 6743…7303     | Salmonella                                                            |
| dfrA24     | –          | –                | 558         | AJ972619         | 83…640        | Escherichia                                                           |
| dfrA25     | dfrA1-group| –                | 459         | DQ267940         | 54…512        | Citrobacter, Klebsiella, Salmonella, Serratia                          |
| dfrA26     | –          | –                | 552         | AM403715         | 303…854       | Escherichia                                                           |
| dfrA27     | dfrA1-group| dfr              | 474         | EU675686         | 2543…3016     | Aeromonas, Escherichia, Klebsiella, Serratia, Vibrio                  |
| dfrA28     | dfrA1-group| –                | 474         | FM877476         | 116…589       | Aeromonas                                                             |
| dfrA29     | –          | dfrVII, dfrA7    | 472         | AM237806         | 615…1086      | Salmonella                                                            |
| dfrA30     | –          | dhfrV            | 474         | AM997279         | 705…1178      | Klebsiella                                                            |
| dfrA31     | –          | dfr6             | 474         | AB200915         | 1832…2305     | Escherichia, Vibrio                                                   |
| dfrA32     | dfrA1-group| –                | 474         | GU067642         | 535…1008      | Laribacter, Salmonella                                                 |
| dfrA33     | dfrA12-group| –                | 498         | FM957884         | 88…585        | Unknown                                                               |
| dfrB1      | –          | dhfrIa, dhfr2a   | 237         | U36276           | 717…953       | Aeromonas, Bordetella, Escherichia, Klebsiella, Pseudomonas            |
| dfrB2      | –          | dhfrIb, dhfr2b   | 237         | J01773           | 809…1045      | Escherichia                                                           |
| dfrB3      | –          | dhfrIc, dhfr2c   | 237         | X72585           | 5957…6193     | Aeromonas, Enterobacter, Escherichia, Klebsiella                      |
| dfrB4      | –          | dfr2d            | 237         | AJ429132         | 69…305        | Aeromonas, Escherichia, Klebsiella                                    |
| dfrB5      | –          | dfr2e            | 237         | AY943084         | 2856…3092     | Pseudomonas                                                            |
| dfrB6      | –          | –                | 237         | DQ274503         | 394…630       | Salmonella                                                            |
| dfrB7      | –          | –                | 237         | DQ993182         | 244…480       | Aeromonas                                                             |
| dfrB8      | –          | –                | 249         | GU295656         | 1048…1296     | Aeromonas                                                             |

(Continued)
mechanism since its sequence does not appear to be related to either efflux or RPPs, nor to the inactivation enzymes. The efflux and RPP encoding genes are found in members of Gram-positive, Gram-negative, aerobic, as well as anaerobic bacteria. In contrast, the enzymatic tetracycline inactivation mechanism has so far only been identified in Gram-negative bacteria. The tet(M) has the broadest host range of all tetracycline resistance genes, whereas tet(B) gene has the widest range among the Gram-negative bacteria. In recent years published data indicate that there are increasing numbers of Gram-negative bacteria that carry tet genes originally identified in Gram-positive bacteria (Roberts, 2002).

To the subsection TRIMETHOPRIM, Resistance mechanisms. Initially, the acquired DHFRs fell into two distinct families A and B, encoded by the *dfra* and *dfrb* genes (Howell, 2005). Up to now 6 plasmid-mediated families can be distinguished with relatively few *dfr* determinants originating from Gram-positive bacteria (Table 7). The *dfrk* and *dfra28* genes are the newest additions to the trimethoprim resistance determinant family (Kadlec and Schwarz, 2009; Kadlec et al., 2011). In contrast to the latest reported DHFRs, the oldest families, *dfra* and *dfrb*, each contain several members (Roberts, 2002; Levings et al., 2006). For example, the *dfra* group accommodates over 30 published genes; however, unpublished, *dfra* variants are also present in the public DNA libraries and some genes apparently have changed nomenclature (Table 7).

Furthermore, we suggest an additional section concerning oxazolidinones.

**OXAZOLIDINONES**

**HISTORY AND ACTION MECHANISM**

Linezolid is to date the only FDA-approved oxazolidinone (Shaw and Barbachyn, 2011). It was approved in 2000 for the treatment of serious infections caused by Gram-positive bacteria resistant to other antibiotics, such as vancomycin-resistant enterococci (VRE) and methicillin-resistant *Staphylococcus aureus* (MRSA) (Long and Vester, 2012). As such linezolid is considered one of the last resort antimicrobial agents in human medicine. It has not been approved for use in veterinary medicine. Oxazolidinones bind at the P site of the ribosome and inhibit the formation of the initiation complex, which consists of mRNA, f-Met tRNA, and the 50S ribosomal subunit (Shaw and Barbachyn, 2011; Long and Vester, 2012).

### RESISTANCE MECHANISM

Various mutations located in the peptidyl transferase loop of domain V of 23S rRNA as well as mutations in the genes for the ribosomal proteins L3 and L4, all associated with resistance to oxazolidinones, have been identified (reviewed by Long and Vester, 2012). A single gene, *cfr*, has been identified to confer transferable resistance to oxazolidinones. This gene codes for a methyltransferase that targets A2503 in 23S rRNA (Kehrenberg et al., 2005). Besides oxazolidinone resistance, it also confers resistance to phenicols, lincosamides, pleuromutilins, and streptogramin A antibiotics. Although initially identified in coagulase-negative staphylococci of animal origin, the gene *cfr* has now been detected in a wide variety of staphylococci of human and animal origin, including a Panton-Valentine leukocidin-positive MRSA USA300 (Shore et al., 2010) and livestock-associated MRSA ST398 (Kehrenberg et al., 2009). More recently, the *cfr* gene has also been identified in *Bacillus* spp. (Dai et al., 2010) and *Enterococcus faecalis* (Liu et al., 2012), but also in Gram-negative bacteria, such as *Proteus vulgaris* (Wang et al., 2011) and *Escherichia coli* (Wang et al., 2012). Plasmids and insertion sequences seem to play an important role in the spread of this gene across species and genus boundaries.

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