Supplementary Material

 Supplementary Table 1. Main antimicrobials used in treatment of swine enteric colibacillosis

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| --- | --- | --- |
| **Antimicrobial/ Prescribing categorya** | **Administration and dosage (mg/kg body weight)** | **Adminsitration in enteric colibacillosis** |
| **Injection** | **In water** | **In feed** |
| **TETRACYCLINE / Class One – Use with Prudence**  |
| **Chlortetracycline**  | NA | 22  | NA | Orally |
| **Oxytetracycline** | 3-5 | NA | NA | IM |
|  **SULFONAMIDE/** **Class One – Use with Prudence** |
| Trimethoprim | 15  | 30 | 15 | IM and orally |
| **SYNTHETIC PENINCILLINS/ Class One/Two – Use with Prudence/Caution** |
| Amoxicilin | 7 | 20 | 15-20 | IM and orally |
| Amoxicilin plus Clavulanic acid | 7.5 + 1.75 | NA | NA | IM |
| **AMINOGLYCOSIDES/ Class Two – Use with Caution** |
| Neomycin | NA | 11 | 11 | Orally |
| Apramycin  | NA | 7.5-12.5 | 4-8 | Orally |
| Spectinomycin | NA | 10-50 | 1.1-2.2 | Orally |
| Gentamicin | 1 | 0.5+0.5+0.5 | NA | IM/Orally |
| **FLUOROQUINOLONES/ Class Three – Restrict use** |
| Enrofloxacin | 2.5 | NA | NA | IM |
| **CEPHALOSPORINS/ Class Three – Restrict Use** |
| Ceftiofur | 3 | NA | NA | IM |
| Cefquinome | 1-2 | NA | NA | IM |
| **POLYMIXIN/ Class Three – Restrict use** |
| Colistin sulphateb | NA | 100.00 IU/Kg body weight | 100.00 IU/Kg body weight | Orally |
| **QUINOXALINESc/Not included in prescribing category list** |
| Carbadox | NA | NA | 50 | Orally |
| Olaquindox 10% | NA | NA | 100000/kg | Orally |

Abbreviation: IM (intramuscular); NA (not applicable). Notes: a Prescribing guidance note for the use of antimicrobials under the cascade. Class 1 – refers to standard prescribing within responsible use guidelines. Class 2 – not to be used unless sensitivity tests or clinical experience has proven that first-choice antimicrobials are not effective. Class 3 – products of last resort; only to be used when no other options are available and supported by laboratory sensitivity tests or in extreme circumstances when all else has failed. b The use of colistin in Europe varies widely between countries. Countries with intensive livestock production can have a level of practice below 1 mg/PCU (e.g. Denmark and the UK) or much higher, up to 20 to 25 mg/PCU (Italy and Spain). Furthermore, some countries like USA and Canada never approved colistin usage in animal feed (Kumar et al., 2020). c The authorization of carbadox and olaquindox as feed additives was withdrawn in the European Union in 1999.

Supplementary Table 2. List of current vaccines available in the market used in the control of swine enteric colibacillosis

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| Vaccines | Dosage | Typology of vaccine | Manufacturer |
| Porcilis® coli(F4ab, F4ac, F5, F6, LT) | 2 mL | Vaccine to provide passive immunity to the progeny against *Escherichia coli* and *Clostridium perfringens* in pigs (live attenuated) | *MSD Animal Health* |
| Porcilis® 2\*4\*3((K88, K99, F41 e 987P) | 2 mL | Vaccine to provide passive immunity to the progeny against *E. coli*and *C.perfringens* in pigs (live attenuated) | *MSD Animal Health* |
| SUISENG® Coli/C (F4ab, F4ac, F5, F6, LT) | 2 mL | Inactivated vaccine against neonatal colibacillosis and Clostridium infections in swine, in injectable suspension (live attenuated) | *HIPRA* |
| PILI SHIELD®(K99, K88, 987P e F41) | 2 mL | Inactivated (live attenuated) | *VETFARMA* |
| SERKEL GASTRO RV®(K88, 987P, K99, F41) | 2 mL | Inactivated (live attenuated) | *Vencofarma* |
| COLIDEX-C(K88, K99, F41, P987, LT, Sta, VT, Hly) | 4 mLfor adults and 1 mL for piglets | Inactivated vaccine against neonatal and post-weaning diarrhea in piglets caused by *E. coli* and *Clostridium perfringens* type C. (live attenuated) | *CZ - VACCINES* |
| Enteroporc Coli(F4ab, F4ac, F5, F6) | 2 mL | Neonatal piglet colibacillosis vaccine (recombinant, inactivated) (live attenuated) | *Ceva Salud Animal* |
| Coliprotec F4/F18(F18ac, F4ac) | 2 mL | Live attenuated | *Prevtec microbia* |
| Entero-Vac  | (100/500) dose | Avirulent live *Escherichia coli* vaccine recommended as an aid in the prevention of enteritis caused by K88 and *E. coli* in swine | *ARKO Laboratories* |
| Edema-Vac  | (100/500) dose | Avirulent live culture to the prevention of edema disease caused by F18-positive *E. coli* | *ARKO Laboratories* |
| Prosystem RCE | 2 mL | Intramuscular injectable vaccine with four major *E. coli* pilus antigens (K88, K99, F41 and 987P) | *Merck Animal Health* |
| Prosystem CE | 2 mL | Intramuscular injectable vaccine with four major *E. coli* pilus antigens (K88, K99, F41 and 987P) | *Merck Animal Health* |
| Neocolipor(F4ab (K88ab), F4ac (K88ac), F4ad (|K88 ad) F5 (K99) F6 (987P) and F41) | 2 mL | Live attenuated vaccine that contains inactivated strains of *E. coli* | Merial |
| LitterGuard®(K99, K88, 987P, F41) | 2 mL | Live attenuated vaccine that contains chemically inactivated strains of *E. coli.* | Zoetis |
| LitterGuard® LT-C | 2 mL | Live attenuated vaccine that contains chemically inactivated strains of *E. coli* and gives protection against beta toxin produced by *Clostridium perfringens* Type C  | Zoetis |

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| Genetic target | Chemistry of antisense oligonucleotide | Reference (s) |
| *acpP* (acyl carrier protein; fatty acid biosynthesis) | Peptide-peptide nucleic acid (PNA) conjugate | **(Good et al., 2001; Tan et al., 2005; Nikravesh et al., 2007)**  |
| Phosphorodiamidate morpholino (PMO) | **(Geller et al., 2003, 2005; Deere et al., 2005)** |
| dendron–PNA conjugates | **(Iubatti et al., 2022)** |
| *rpoD**(*[RNA polymerase](https://www.sciencedirect.com/topics/biochemistry-genetics-and-molecular-biology/rna-polymerase) primary) |  Conjugated peptide [nucleic acids](https://www.sciencedirect.com/topics/materials-science/nucleic-acids) (PPNAs) | **(Bai et al., 2012)** |
| *gyrA* (DNA gyrase; DNA replication) | Peptide- Phosphorodiamidate morpholino (PMO) conjugate | **(Rao et al., 2008)** |
| *rne*(essential endoribonuclease RNase E) | Locked nucleic acid (LNA) gapmers | **(Goddard et al., 2021)** |
| *mazEF*(toxin-antitoxin complex) | Peptide nucleic acid (PNA) | **(Równicki et al., 2018)** |
| *hipBA* (toxin-antitoxin complex) | Peptide nucleic acid (PNA) | **(Równicki et al., 2018)** |
| *marORAB* (antibiotic resistance operon) | Phosphorothioate (PS) | **(White et al., 1997)** |
| *mcr-1* (colistin resistance) | Peptide nucleic acids (PNAs) | **(Wang et al., 2020)** |
|  *acrB* (efflux pump responsible) | liposome phosphorothioate (PS)-conjugate  | **(Meng et al., 2012)** |
| *ribF* (riboflavin biosynthesis) | 2′-alkyl modification and phosphorothioate (PS) | **(Traykovska and Penchovsky, 2022)** |

**Supplementary Table 3.** Chemistry of antisense oligonucleotide used to different genetic target of *E. coli*

**Supplementary Table 4.** Aptamers used to different genetic target of *Escherichia coli*

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| --- | --- | --- | --- |
| Aptamer | Type | Target | Reference(s) |
| P12-31 | DNA | Meningitis/sepsis associated *E. coli* (MNEC) | **(Marton et al., 2016)** |
| E18R, E-5, E-11, E-12, E-16, E-17, E-18, E-19, AM-6 | DNA | *E. coli* O157:H7 | **(Amraee et al., 2017; Siddiqui and Yuan, 2021)** |
| Apt B12, Apt 7, 19, 31 and 37 | DNA | *E. coli* K88 | **(Li et al., 2011; Peng et al., 2014)** |
| E1, E2, E10, E12 | DNA | *E. coli* ATCC 8739 | **(Kim et al., 2013; Chung et al., 2015; Guo et al., 2016; Jin et al., 2017)** |
| Apt 7, 19, 31 and 37 | DNA | *Shiga toxin 1 & 2 subtypes* | **(Kaur et al., 2020)** |

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