1981). Overall, the net benefit associated with growth promoter use was estimated to be only 1% to 3% for weight gain and/or improved feed efficiency, with these benefits potentially outweighed by the cost of increased bacterial resistance in both animals and humans. Based on these analyses and public health concerns, a number of major U.S. poultry producers have now decided to cease using antibiotics as growth promoters (Perdue Foods, 2015; Tysons Foods, 2015). Other major food purchasers and retailers are now increasingly adopting improved antibiotic usage policies in their purchasing contracts (Zuraw, 2014; McDonald's Corporation, 2015; Huffstutter, 2015).

Despite these gains in terms of the ban of antibiotic usage for growth promotion in the EU, antibiotics continue to be used in large amounts in many EU countries for prophylaxis and therapeutic purposes (DANMAP, 2014; EFSA and ECDC, 2015; ECDC *et al.*, 2015). In the Netherlands there appeared to be a much higher relative use of antibiotics in food animals than in other European countries (Mevius and Heederik, 2014; Grave *et al.*, 2012; Wageningenur, 2016). Notably, however, a large proportion of the ESBL *E.coli* bacteremia isolates isolated from humans were recently shown to contain antibiotic-resistance genes or were bacterial clones that were very similar to what was found in poultry in the same region (Leverstein-van Hall *et al.*, 2011; Willemsen *et al.*, 2015; Jakobsen *et al.*, 2010; Overdevest *et al.*, 2011). After government and agriculture sector involvement, the Netherlands recently reduced by more than 50%, the total amount of antibiotics used in food animals (from 561 tons in 2000 to 244 tons in 2012). Similar to ceasing antibiotic growth promotors, this change was achieved without any obvious marked economic or production problems (Mevius and Heederik, 2014; Wageningenur, 2016). Australia has maintained very low rates of resistance in human bacterial isolates to fluoroquinolones and close to zero resistance rates in food animals for fluoroquinolone resistance in *E.coli*, *Salmonella* and *Campylobacter* isolates. A major factor contributing to this is considered to be the banning of fluoroquinolone use in food animals and strict restrictions on imported fresh meats. Despite this ban, Australia has continued to increase its very high levels of meat production and food animal numbers (FAOSTAT, 2015; JETACAR, 1999; Cheng *et al.*, 2012). These examples suggest that societies can markedly decrease the total antibiotic usage volumes in food animals without major economic consequences, while potentially also achieving safer animal-derived food products and reduced emergence of resistance in animals and humans.

For some antibiotics that are extensively used for prophylactic purposes in certain farm animals (e.g. pigs and chicken), a reduction in use can be achieved by the introduction of new innovations, such as vaccines, modification of diets (including use of probiotics), changed animal husbandry practices and research directed to the prevention of these infections, such as farm design to improve on-farm infection control. For example, in chickens, continuous infeed antibiotics are frequently used to prevent necrotizing enterocolitis due to *Clostridia perfringens,* yet changes in animal husbandry practices and diet can prevent this infection without the use of prophylactic antibiotics and with an increase in the total number of chickens produced annually (Aarestrup *et al.*, 2008).

The risk of antimicrobial-resistant bacteria or -resistance genes being transmitted to humans via the food chain has been documented but has been difficult to quantify. In developed countries almost all *Campylobacter* spp. and *Salmonella* spp. are likely acquired by humans from food animals, predominantly via foods. *C. difficile* can also be transferred from food animals to humans. More important, resistance genes can be acquired by human gut flora from bacteria of animal origin, where the gene either originated or was significantly amplified (Le Hello *et al.*, 2013; Su *et al.*, 2011; Swann, 1969; WHO, 1998; Ho *et al.*, 2011; Price *et al.*, 2012; Gupta *et al.*, 2003; Mølbak, 2005; Collignon, 2009; Guerra *et al.*, 2014). In 2003 in Canada and the United States , the third-generation cephalosporin ceftiofur was used in an off-label manner for routine administration/injection into chicken eggs or into 1-day-old meat chickens in hatcheries to attempt to prevent some *E.coli* infections. In Québec, a surveillance program demonstrated a marked increase in the prevalence of resistance to third-generation cephalosporins among *Salmonella enterica* serotype *heidelberg* from humans and chicken (from approximately 30% in 2003 to 48% in early 2005). A survey of antimicrobial use in Québec hatcheries confirmed that in 2004, all chicken hatcheries switched from using gentamicin and ceftiofur in an alternating manner to the exclusive use of ceftiofur. In early 2005, Québec hatcheries voluntarily stopped using ceftiofur. This was followed by a dramatic decline in the prevalence of third-generation cephalosporin resistance in this serotype from both humans and chicken (retail and abattoir meat). Similar trends in ceftiofur resistance were observed among *E.coli* isolates from retail chicken. When the industry subsequently reintroduced an alternating ceftiofur regimen, a resurgence in resistance to cephalosporins among *S. heidelberg* isolates was observed (Dutil *et al.*, 2010).

ANTIMICROBIAL USE IN AQUACULTURE

Large amounts of antibiotics are used in aquaculture but there is generally poor documentation of the antibiotic types or quantities. World aquaculture production is rapidly increasing, with countries in Asia accounting for over 80% of the total production. The antibiotics are most often given as medicated feed or by adding antimicrobial agents directly to the water ("immersion therapy")—commonly used agents include amoxicillin, ampicillin, chloramphenicol, erythromycin, streptomycin, furazolidone, nitrofurantoin, oxolinic acid, enrofloxacin, ciprofloxacin, flumequine, tetracyclines, and sulfonamides (Le Hello *et al.*, 2011; WHO, 2006; Angulo, 1999; Duran and Marshall, 2005; FAO, 2007; Collignon, 2013b). In addition, large amounts of antibiotics are added into waterways via the run-off from aquaculture farms that contains fish feed. In many developing countries, aquaculture