

(VRE). Only two years later, the percentage of VRE dropped about 50% (van den Bogaard et al. 2000).

#### 24.4.2 Manure Application

Potential pathways for resistance dissemination do not only exist within animal husbandry, but resistant bacteria can also be spread onto crop fields via the application of manure. Typically, this fertilizer is of animal origin, but as discussed above, sewage sludge is also used as manure to some degree, although regulations around this practice differ vastly between countries (Kelessidis and Stasinakis 2012). There is a large body of literature showing that manure applied to fields contains antibiotic-resistant bacteria and resistance genes (Heuer et al. 2011; Munir and Xagorarakis 2011; Wichmann et al. 2014; Ruuskanen et al. 2016). In addition, it has been repeatedly shown that these bacteria persist in soils for extended amounts of time (Rahube et al. 2014; Riber et al. 2014; Chen et al. 2016) and that the application of manure also increases the frequency of horizontal gene transfer in soils (Jechalke et al. 2013; Ross and Topp 2015). It has even been suggested that application of manure increases the resistance frequencies of the indigenous soil bacteria (Udikovic-Kolic et al. 2014).

#### 24.4.3 Agriculture in Developing Countries

Agriculture practices differ substantially in industrialized countries, but the span of different ways to do agriculture may be even greater in the developing parts of the world. In addition, there are very different farm sizes, ranging from essentially single household supplies to industrialized plantations managed using large numbers of generally low-paid workers. This also leads to very different scenarios for chemical use. Smaller farms may not have the resources to use virtually any chemicals, including antibiotics, for their crops or animals. At the same time, there are often limited regulations (or limited enforcement of regulations), prompting wealthier farmers to use antibiotics in excessive quantities. These differences lead to a situation where much of farmed animals and land are not exposed to any significant quantities of antibiotics (or other co-selective agents), but with specific local settings that can be subjected to exposure with excessive quantities of antimicrobial compounds. Further complicating this picture is that some antibiotics, including sulfonamides, are widely and cheaply available in many low- and middle-income countries, which has led to widespread and largely uncontrolled use in both humans and animals (Pruden et al. 2013). It is likely that this has contributed to the wide-reaching incidence of resistance genes toward these antibiotics in humans and animals, both locally and globally (He et al. 2014; Pal et al. 2016). In addition, the infrastructure for