

been deeply discussed (Wright 2010; Perry and Wright 2013; Martinez et al. 2015; Manaia 2017). However, it is the continuous and wide dissemination of the contaminant antibiotic resistome that represents nowadays a major threat for human health. Since the acquisition of ARGs represents an additional cost for the bacterial cell, which may be justified only if it brings a survival advantage, it is believed that it is stimulated by external selective pressures (Goh et al. 2002; Allen et al. 2010; Andersson and Hughes 2014). Among the different selective pressures that are identified (e.g. metals or biocides), antibiotics are those considered the most important selectors for resistance acquisition and maintenance. Indeed, it is impossible to dissociate the evolution of the contaminant resistome from that of antibiotic usage, to which the next section is dedicated.

## 10.5 Evolution of Antibiotics Usage

Since the 1940s the global production and consumption of antibiotics has increased not only due to the rise of the human population but also due to prosperity (CDDEP 2015). It is estimated that during the first decade of the twenty-first century occurred an overall increase of 36% on antibiotic use for human consumption. This percentage corresponds to an average increase from  $5 \times 10^{10}$  to  $7 \times 10^{10}$  standard units, i.e. the number of doses sold, in 71 countries with different incomes (Van Boeckel et al. 2014). In general, the consumption of antibiotics per capita is higher in high-income countries than in middle-income countries. However, in middle-income countries the increase in human antibiotic consumption has been higher than in high-income countries, where, in general, the consumption stabilized or decreased (Van Boeckel et al. 2014). Brazil, Russia, India, China, and South Africa account for 76% increase in antibiotic sales for human consumption (Van Boeckel et al. 2014).

The absence of adequate measures to prevent infectious diseases and the inappropriate antibiotic consumption has probably significantly contributed to the excessive antibiotic use. Indeed, it has been argued that in some low-income countries, antibiotic consumption increase is mainly a compensation of the lack of efficient programs of vaccination and sanitation (Laxminarayan et al. 2016). In turn, inadequate antibiotics prescription is associated with the uncertainty in diagnosis (e.g. frequently to treat upper respiratory tract infections caused by viruses), motivating the prescription of an unnecessary broad-spectrum antibiotic, with an incorrect dosage or duration (Starrels et al. 2009; Om et al. 2016). Notoriously, these situations are not necessarily related with the country development index. In hospitals, the excessive use of broad-spectrum antibiotics is leading to dangerous and almost difficult to treat infections. However, the lack of or delayed access to antibiotics still kills more people than resistant infections (CDDEP 2015).