(*Fusarium* patch, anthracnose, and dollar spot) and ornamental plants (mildew and rusts). Tebuconazole and propiconazole are used to prevent wood decay by some fungi (e.g. *Gloeophyllum trabeum* and *Poria* spp.). They can be used in combination with copper carbonate and are the main components of copper organic wood preservatives used in industry to pressure-treat timbers, such as those used in fencing, cladding, plywood, roofing, and garden decking. Copper triazole combination preservatives are widely marketed in North America and across Europe. Wood preservatives containing propiconazole and tebuconazole are also available for domestic use. Propiconazole is registered for use in adhesives, paints, leather, paper, and textiles and is available in the UK as the active ingredient in an antifouling agent, biocidal paints and surface biocides (U.S. Forest Service, 2016; U.S. EPA, 2006; ECDC, 2013; Eurostat, 2001).

The widespread use of azoles has been defended by industry. A modeling study done by the wheat industry estimated that if azoles were not used on crops, such as wheat in Europe, there would be a drop in domestic wheat production, estimated to be about 9.8 million tons in 2013 (from 141.1 to 131.3 tons) and possibly 18.6 million tons in 2020 (from 152.4 to 133.8 tons), with the EU potentially ceasing to be a net wheat exporter and with possible impacts on global food security (ECPA, 2012).

From a resistance perspective, however, it appears that azole resistance has evolved in the environment and may be driven by the selective pressure of azole fungicides (Hof, 2001; Verweij *et al.*, 2009; Mortensen *et al.*, 2010; Chowdhary *et al.*, 2013; Parker *et al.*, 2014; Bromley *et al.*, 2014; Bowyer and Denning, 2014). One report noted that although evidence supporting this hypothesis is growing, the link between the environmental use of azole fungicides and the development of azole resistance in *Aspergillus* spp. is not yet proven. Nevertheless, the following observations support an environmental route of azole resistance development (ECDC, 2013). First, azole resistance was observed relatively frequently in azole naive patients. In a Dutch culture–based survey in seven university medical centers, 64% (14/22) of patients with azole-resistant *Aspergillus* spp. disease were azole naive at the time the resistant isolate was cultured, and the resistance mechanism(s) observed in these strains was consistent with environmental acquisition rather than from human-to-human transmission (van der Linden *et al.*, 2013). Notably, several studies from European countries (Netherlands, Denmark, Norway, UK, Italy) have shown that *A. fumigatus* isolates from environmental samples may be resistant to medical triazoles, which is consistent with the fact that azole fungicides used in agriculture have a similar molecular structure to medical azoles (including propiconazole, tebuconazole, epoxiconazole, difenoconazole, and bromuconazole) (ECDC, 2013).

NEED FOR IMPROVED USAGE AND RESISTANCE SURVEILLANCE DATA

Worldwide, antimicrobial (antibiotics and antifungal) usage data are limited. Although areas such as Europe, Canada, the United States, Australia and some other developed countries regularly produce usage data, they are often many years out of date and provide little information on the details about which antibiotics are used in which agricultural sector. Furthermore, some emerging nations, such as China and Brazil, are huge food producers and agricultural users of antimicrobials, yet very limited surveillance data are available. What information is available, suggests high volumes of sulfonamides, tetracyclines, and fluoroquinolones (enrofloxacin, fleroxacin, and norfloxacin) are used (Graham *et al.*, 2014; FAOSTAT, 2015; Van Boeckel *et al.*, 2015; Collignon and Voss, 2015; Krishnasamy *et al.*, 2015; Zhang *et al.*, 2015).

THE WHO LIST OF CRITICALLY IMPORTANT ANTIMICROBIALS

The WHO has developed criteria to rank antimicrobials according to their importance in human medicine. The WHO list of critically important antibiotics was developed to provide a tool for risk management strategies and to focus resources to address antimicrobial usage in agriculture and veterinary medicine. The list was first developed in Canberra in 2005, substantially revised in Copenhagen in 2007 and in Oslo in 2011, and most recently revised in Bogota in 2013 (WHO, 2011; WHO, 2013; Collignon *et al.*, 2009). The antibiotic classes categorized as critically important, highly important and important are given in Table 2.2.

POTENTIALLY EFFECTIVE ACTIONS TO REDUCE ANTIMICROBIAL USAGE IN AGRICULTURE

Three principles to minimize the risk of development and spread of antibiotic resistant bacteria related to food animals are as follows:

Antibiotics that are critically important or last-line antibiotics for serious human infections should not be used in food production animals or agriculture or at least should have major restrictions imposed on their use.

The use of antibiotics for prophylactic purposes in animals should be kept to a minimum, with the current usage levels reduced. Other nonantibiotic methods to prevent animal infections should be developed and emphasized.

Antibiotics should not be used as growth promoters in agriculture.