

## ANTIBIOTIC RESISTANCE AND DAIRY PRODUCTION - FREQUENTLY ASKED QUESTIONS\* -

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### What are antibiotics?

Antibiotics are chemicals that result in *bacterial cell death or inhibition of bacterial cell growth*. Antibiotics are produced naturally by bacteria and fungi, and are manufactured by pharmaceutical companies for their use as treatments for infectious bacterial diseases in humans, animals and plants<sup>[1]</sup>. Antibiotics do not include disinfectants, antiseptics or ionophores (e.g. the feed additive Rumensin®), and are *not prescribed or effective for the treatment of fungal, viral or parasitic infections*.

### What is antibiotic resistance?

Antibiotic resistance (AR) is a *naturally occurring process* where previously susceptible bacteria develop the ability to resist the effects of an antibiotic. *Antibiotic resistance is not gained by the host (cow or human) but by the bacteria*. It is widely believed that the extensive use of human and veterinary antibiotics has increased the prevalence of antibiotic resistant bacteria <sup>[1-4]</sup>.

### What are antibiotic resistant bacteria and antibiotic resistance genes?

Antibiotic resistant bacteria (ARB) are bacteria that have the ability to resist the effects of an antibiotic. Antibiotic resistance genes (ARG) are genes naturally present in bacterial populations and give bacteria the ability to resist the effects of an antibiotic(s).

### How do bacteria become ARB and how does AR proliferate? (Figure 1.)

1. ARB are naturally present in low quantities in the environment.
2. Exposure to antibiotics that are administered or present as residues in the environment will limit the growth and survival of non-resistant bacteria, while ARB will be unaffected.
3. Exposure to antibiotics thus selects for ARB which by passing ARG onto their offspring will increase the abundance of ARB populations overtime.
4. ARG can also be passed from ARB to unrelated bacteria through processes collectively called 'horizontal gene transfer.' Once acquired, these unrelated bacteria will gain AR and can then pass ARG on to their offspring or to other unrelated bacteria. Horizontal transfer of ARG from one bacteria to another can occur in human and cow digestive tracks, manure, anaerobic digesters, wastewater treatment plants, and in soil and water<sup>[3,5]</sup>.

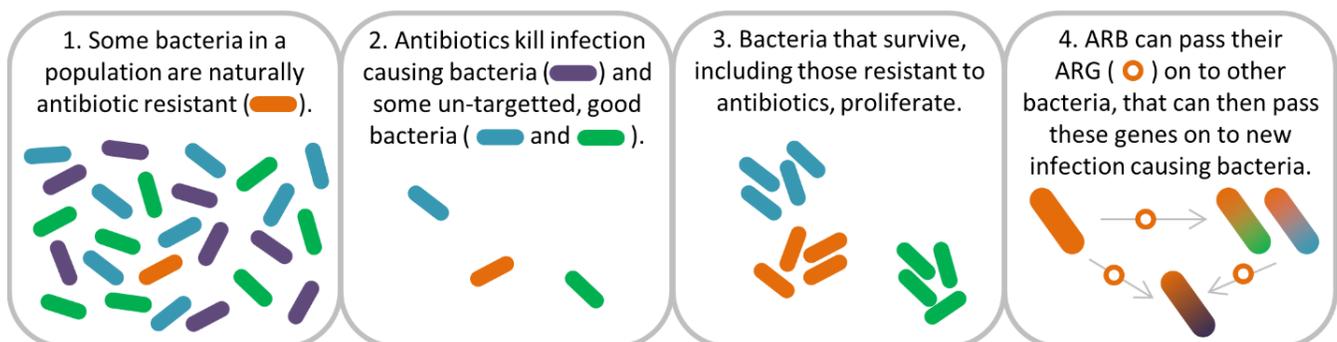


Figure 1. How AR occurs<sup>[6]</sup>.

**\*This document was prepared for the use of dairy farms.**

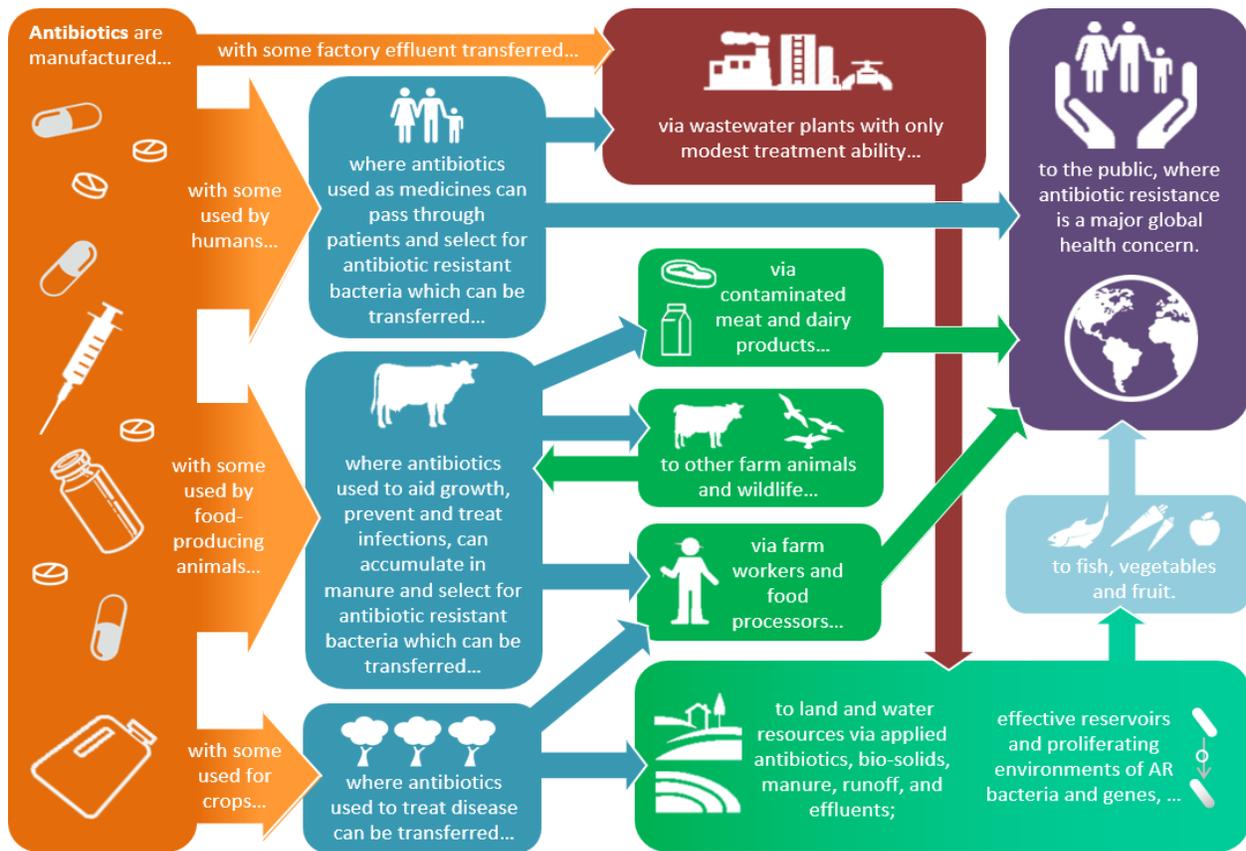
It is intended to provide a brief list of facts about antibiotic resistance as it relates to dairy production.

### Why is AR important to dairy?

Antibiotics are critical therapeutics used to *treat* bacterial infections in dairy cattle. Lost efficacy of these medicines due to AR could increase the difficulty and cost of treatment<sup>[7]</sup>, adding expense to production.

### What are the potential pathways that antibiotic resistance may spread?

The proliferation of antimicrobial resistance has been attributed to the extensive use (and misuse) of human, veterinary and crop antibiotics and inadequate mitigation by municipal wastewater treatment plants (WWTP) and manure treatment systems. Even when used correctly, antibiotic residues, ARB and ARG may accumulate in sewage and manure<sup>[3,5]</sup>. Typical WWTP and manure systems are not designed specifically to treat antibiotics, ARB or ARG, and when processed materials have been tested, residues are often detected. As a result of land application of WWTP biosolids and manure, WWTP discharges directly into waters of the State, and application of antibiotics to crops, antibiotics, ARB and ARG may enter the environment, where they may spread via multiple pathways, including contaminated foods, to the public<sup>[3]</sup> (**Figure 2**).



**Figure 2. Potential pathways for the spread of AR from human & livestock sources** [8].

### Is antibiotic usage by dairy operations a main cause of AR?

There is evidence that antibiotic use in food-producing animals may lead to AR in animal and human pathogens<sup>[2]</sup>, and elevated levels of AR can be associated with dairies<sup>[9]</sup>. However, there is no evidence suggesting dairy is a main or sole cause of AR with many domestic (i.e. humans and companion animals), hospital, industrial (i.e. antibiotic manufacturing) and agricultural (i.e. livestock, poultry, aquaculture, fruit production) sources recognized<sup>[3]</sup>. According to the 2011 review by Stephen Oliver et al. *“there are no studies that show that use of antimicrobials to treat mastitis in dairy cows has resulted in the emergence and establishment of dominant antimicrobial resistant clonal types in both human and dairy cattle populations”*<sup>[10]</sup>. Recent work shows that while ARG profiles of *Salmonella* isolates from humans and dairy cows do overlap, the ARG profiles of isolates from humans are more diverse and include > 20 ARG not detected in bovine *Salmonella* isolates<sup>[11]</sup>.

### **How significant is the use of antibiotics by dairy farms?**

Based on the most recent USDA study representing 79.5% of US dairy operations and 82.5% of US dairy cows; to prevent disease and promote healthy growth, 90.1% of US dairy operations practiced dry cow therapy, 18.2% fed antibiotics in heifer rations, and 57.5% fed medicated milk replacer to unweaned calves. Therapeutically, antibiotics were used by ~85% of US dairy operations to treat mastitis and by over 50% of farms to treat respiratory, reproductive and lameness in cows. More than 60% used antibiotics to treat respiratory problems in weaned calves and heifers, and to treat respiratory problems and diarrhea in unweaned calves<sup>[12]</sup>. Considerable discrepancy exists over exact antibiotic usage by animal agriculture however<sup>[5,11]</sup>. Recent 2015 estimates indicate that ~40% of the antibiotics manufactured in the U.S., or ~20.3 million lbs. of the ~50 million lbs. produced annually (value excludes ionophores), are used by the livestock and poultry industries<sup>[13]</sup>. While the FDA is tracking data for animal agriculture, data is lacking on the antibiotic usage of humans, companion animals, aquaculture and crop production. Though reliable estimates for the total amount of antibiotics used specifically by the dairy industry have not yet been released by the FDA, dairy is estimated to be minor consumer of antibiotics compared to other livestock and poultry sectors<sup>[14]</sup>. Note: the FDA has begun collecting antibiotic usage data by livestock sector, and this data should be available in the next reporting cycle<sup>[13]</sup>.

### **Are antibiotics broken down by the cow?**

Based on data from multiple livestock types, 30 to 90% of a properly administered antibiotic dose can be excreted in urine and feces depending on the antibiotic<sup>[15,16,17]</sup>. Regarding intramammary treatments, ~50% of a properly administered dose can be excreted in cow's milk<sup>[18]</sup>. Excretion rates will depend on the drug, time since administration, and animal physiology.

### **How does manure treatment & storage affect AR?**

The fate of antibiotic residues, ARB and ARG during dairy manure treatment has not been thoroughly explored. Based on available research from dairy and other livestock systems, some mitigation of antibiotic residues, ARB and ARG occurs over time during composting, anaerobic digestion, and storage, depending on the antibiotic, manure characteristics, treatment process and conditions<sup>[3]</sup>. Generally, longer, aerobic and higher temperature treatment conditions result in increased degradation of these compounds, cells and genes. Work is currently underway to better understand the fate of these potential contaminants as they are treated by different farm manure systems with results and Fact Sheets summarizing the state-of-the-knowledge available in 2018.

### **What happens to AR after field application of manure?**

Due to the physical, chemical and biological differences of soils, there is no simple fate of antibiotic residues, ARB and ARG in the field. Typically some breakdown of antibiotics occurs in soil environments after manure spreading, but ARB may survive for weeks and ARG may persist for longer<sup>[5]</sup>. More-soluble antibiotics are generally more biodegradable, but more mobile in the environment. Less-soluble antibiotics, along with some ARB and ARG, can persist bound to soils, organic matter and sand. Dissolved or suspended to these substrates, these residues, cells and genes can move in drainage and ground waters to surface waters. In soils and water, antibiotic residues can enable proliferation of ARB and thus manure spreading may increase the potential for natural systems to become reservoirs of antibiotic resistance<sup>[4,5]</sup>.

### **What is the risk?**

- ARG may persist in environmental bacterial populations for decades<sup>[3]</sup>.
- In some cases, AR pathogens from livestock production have been linked to human illness<sup>[2,8]</sup>.
- Though there is no evidence for widespread increases in antibiotic resistance among mastitis pathogens, AR bovine mastitis causing pathogens have been detected<sup>[19]</sup>.
- The efficacy of certain antibiotics might be lost.

## What will the future bring?

Prompted by the National Action Plan for Combating Antibiotic-Resistant Bacteria<sup>[20]</sup>, the U.S. Food and Drug Administration has been refining its regulation of antibiotic usage in livestock animals to promote more judicious use and better protect animal and human health. Specifically, the Administration's aim is to "phase out the use of medically important antimicrobials in food animals for production purposes (e.g., to enhance growth or improve feed efficiency), and to bring the therapeutic uses of such drugs (to treat, control, or prevent specific diseases) under the oversight of licensed veterinarians"<sup>[21]</sup>. The Veterinary Feed Directive (VFD) changes, effective January 2017 are part of this effort and can be learned about in the Oct. 13<sup>th</sup>, 2016 PRO-DAIRY e-Alert ([link](#))<sup>[22]</sup>.

## What should I do?

While there may be the potential to improve manure management systems (i.e. composting, storage, anaerobic digestion) to adequately mitigate antibiotic residues, ARB and ARG before land application, *currently the best way to reduce the release of antibiotics, and generation of ARB and ARG from a farm is to optimize and reduce the use of antibiotics*<sup>[3,5]</sup>. This can be accomplished by improving animal husbandry, farm hygiene and working with your veterinarian to promote animal health, improve treatment protocols, and record keeping to optimize antibiotic use, limit the use of non-therapeutic antibiotics, and avoid the use of 'critically important antimicrobials' for human health<sup>[3]</sup>. Critically important antimicrobials are antibiotics that are 1) "the sole, or one of limited available therapy, to treat serious human disease", and 2) "used to treat diseases caused by either: organisms that may be transmitted to humans from non-human sources or, human diseases caused by organisms that may acquire resistance genes from nonhuman sources"<sup>[23]</sup>. Critically important antibiotics include fluoroquinolones (e.g. enrofloxacin), beta-lactams (e.g. ceftiofur, penicillin), and macrolides (e.g. tulathromycin), and highly important antibiotics include tetracyclines (e.g. oxytetracycline) and sulfonamides (e.g. sulfadimethoxine). The complete list of critically important antimicrobials can be found at the World Health Organization<sup>[23]</sup>.

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