Comments of Food Antimicrobial Concerns Trust (FACT) and Health Watch USA for the September 26, 2018 meeting of the Presidential Advisory Council on Combatting Antibiotic-Resistant Bacteria (PACCARB)

Food Animal Concerns Trust (FACT) and Health Watch USA appreciate the opportunity to comment to PACCARB. We ask that PACCARB review the use of over-the-counter (OTC) polymyxins in humans and animals and recommend that the Food and Drug Administration (FDA) consider prohibiting the OTC use of these vital drugs in humans and prohibit their use in food producing animals altogether. Polymyxins are drugs of last resort that are used in patients when no other drug will work. The U.S. Centers for Disease Control and Prevention (CDC) has described resistance to polymyxins as one of two resistance mechanisms of greatest concern.[1] The World Health Organization (WHO) in 2017 included polymyxins among a handful of "reserve group antibiotics" that should only be used in specific setting where other antibiotics would not work.[2] Despite their incredible importance in fighting otherwise untreatable infections in humans, topical polymyxin antibiotics are widely available without a prescription and can easily be purchased in most pharmacies. Polymyxin use in food animals has been linked to the global spread of transferable polymyxin resistance in food animals. We believe that these uses of polymyxins are inappropriate and federal action is required to prevent them.

Since the 1970s, due to toxicity, polymyxins have rarely been used systemically in humans, and so have been relegated to use in topical applications. Today, there are hundreds of these topical products on the shelves containing polymyxin B, to be used without medical supervision or even demonstration of medical need. Unlike prescription drugs, FDA does not approve OTC products prior to marketing and the only restriction concerning their sale is that they have to comply with OTC regulations (monographs) regarding indications, labeling, administration, and formulation.[3] These regulations, written in 1987, allow polymyxin B to be legally marketed as part of double or triple combination topical therapies in combination with bacitracin, neomycin sulfate, oxytetracycline, or some combination of these drugs.

Polymyxins are also widely used in food animal production across the globe. In the US, they are currently found in an OTC eye ointment for cattle and sheep. Polymyxins are also approved by FDA for use in chicken and turkey hatcheries but these products are not currently marketed. Outside the U.S., polymyxins are commonly administered in the feed

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[1] CDC. Notes from the Field: Pan-Resistant New Delhi Metallo-Beta-Lactamase-Producing Klebsiella pneumoniae — Washoe County, Nevada, 2016. Available from: https://www.cdc.gov/mmwr/volumes/66/wr/mm6601a7.htm

[2] WHO. The Selection and Use of Essential Medicines, WHO Technical Report Series – 1006. Available from: http://www.who.int/medicines/publications/essentialmedicines/trs-1006-2017/en/

[3] FDA. Over-the-Counter (OTC) Drug Monograph Process. Available from: https://www.fda.gov/drugs/developmentapprovalprocess/howdrugsaredevelopedandapproved/ucm317137.htm

and water of food animals to promote growth and prevent disease. This use in food animals is likely transferring resistance from animals to human.[4]

In the U.S., products containing polymyxins lack strong evidence supporting safety and effectiveness for current OTC uses in humans. The regulation authorizing the topical use of polymyxin B in combination with other antimicrobials was written in 1987.[5] The regulation does not address polymyxin resistance and at that time, FDA did not consider polymyxins to be antibiotics of last resort for multidrug resistant infections. The FDA also did not require evidence from head-to-head controlled trails comparing the effectiveness of topical first aid combination therapies with and without the addition of polymyxin B.

With the global spread of multi-drug resistant gram-negative infections, doctors have had to turn to the use of polymyxins despite their toxicity.[6] The recent change of polymyxins from drugs used primarily in food animals and for preventing infections in minor wounds to a drug of last resort for treating life threatening infections in humans warrants a re-examination of these non-critical uses. Given the importance of these drugs, it is essential that their use be appropriately supervised by healthcare providers and limited to circumstances under which both efficacy and safety are well established.

We therefore ask that PACCARB consider potential steps to identify and restrict unnecessary polymyxin use in humans and animals by asking the FDA to reconsider the evidence base supporting the current regulation of these products. Specifically we ask PACCARB to recommend that FDA review the OTC and food animal uses of these drugs and consider requiring prescriptions for all uses in humans and prohibit their use in food animal altogether.

Thank you so much for your time.

Food Animal Concerns Trust

Health Watch USA

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[4] Webb et al. Illustrative examples of probable transfer of resistance determinants from food animals to humans: Streptothricins, glycopeptides, and colistin. F1000Res. 2017 Oct 5;6:1805. doi: 10.12688/f1000research.12777.1. eCollection 2017.

[5] Federal Register 52(238):46983-47364.

[6] Michalopoulos and Karatza. Multidrug-resistant Gram-negative infections: the use of colistin. Expert Review of Anti-infective Therapy 8(9): 1009-1017.