



August 30, 2010

The Honorable Margaret A. Hamburg, MD  
Commissioner  
c/o Division of Dockets Management (HF A305)  
U.S. Food and Drug Administration  
5630 Fishers Lane  
Room 1061  
Rockville, MD 20852

ATTN: Comment Docket No. FDA-2010-D-0094

Dear Commissioner Hamburg and Principal Deputy Commissioner Sharfstein:

Here are my comments on scientific evidence relating to the consequences of antimicrobial use in food-producing animals, research needs and shortfalls in response to the Draft Guidance, “The Judicious Use of Medically Important Antimicrobial Drugs in Food-Producing Animals.”

### **Overview**

The document summarizes 14 past key scientific reports on the consequences of use of antimicrobial drugs in food-producing animals, and relates their findings to the emerging policies of the FDA on such use.

It might be helpful to number the past key scientific reports to facilitate referring to particular ones in subsequent discussions.

### **Omission**

The fourth cited report refers to the second of the two studies of the problem that FDA funded circa 1980 to examine the problem, the Seattle-King County Study: “Surveillance of the Flow of Salmonella and Campylobacter in a Community” by FDA. There is no mention of the first study, however, which seems a significant omission. This was a collaborative project of Brigham and Women’s Hospital and Harvard Medical School, Miriam Hospital and Brown University, the National Veterinary Services Laboratory in Ames Iowa and public health laboratories of Massachusetts, California and Wisconsin.

This study, funded under contracts (223-78-3015 and 223-79-7060) from the FDA published its findings as the lead article of the New England Journal of Medicine July 1 1982<sup>1</sup> The study found specific plasmids expressing multiple antibiotic resistance genes in *salmonella* that were endemic in food-producing animals, and then found identical plasmid molecules in similar *salmonella* infecting humans in the 3 states in which it surveyed human infections. The publication effectively ended the prior contention that antibiotic resistance in animals was unconnected to that in humans, and so reopened discussion of antibiotic use in animals. It also modeled and emphasized the need for integrated surveillance of antibiotic resistant

bacteria in animals and humans, and so prompted deliberations that led to the founding of the NARMS project.

**Progression**

The reviewed reports from the U.S generally progress over the forty years they cover, from the clear recommendations of the 1970 FDA Task Force Report but rather inconclusive first (1980) report of the U.S. National Academy of Sciences to the 2003 report of the Institute of Medicine (IOM) and the 2004 report of the US Government Accountability Office (GAO) that cite detailed growing evidence of the harm to human health of unessential antibiotic use in animals. They also reflect the general lag in recognition of the problem by the US as compared to Europe. The first report cited in the draft, the 1969 “Swann Report” from the UK, with its very direct evidence, and the later European ban on antibiotic use for growth promotion both reflect a greater sense of urgency to address the problem in Europe than in the US.

**Inaction**

The reviewed reports from the U.S. also reflect the remarkable failure of the FDA and other U.S. health agencies over those decades (NIH, NSF, etc.) to support any science that might improve understanding of these complex health-related issues. Support for research in antibiotic resistance generally was until recently similarly neglected by all of the agencies. The FDA funded each of the two circa 1980 studies mentioned above for moderate amounts for several years each, with no follow-on funding for either. For comparison try to imagine which of all the advances in understanding and treatment of cancer or heart disease we would have if there had been no sustained research or career investigators in those fields. What happened, in effect, was that one or more of the meetings issuing the reports reviewed in this document was convened every decade or so to review the evidence on the subject, only to find that there wasn’t much because no agency had supported any science to develop such evidence.

Lack of support for science to guide policy on these issues has been partly improved over the last decade by the establishment of the NARMS program conjointly by the FDA, CDC, and USDA. The idea was that each of these agencies would utilize its special resources and skills to develop ongoing, integrated and insightful surveillance of antibiotic resistance in animals and humans in the U.S. and so generate new understanding for its management. Ongoing it has been and annual reports dutifully accumulate from each component, but integrated much less so. Each uses testing and data systems that are mutually compatible to facilitate data merger and cross analyses, but it isn’t clear that there have been any or any creative use of any insights such cross analyses might produce. Especially absent seem the delineation and tracing through animal and human isolates of genotypically confirmed distinctive phenotypes that represent and track cross-species outbreaks, of the kind that first brought attention to the problem three and four decades ago.

**Conclusion**

The Draft Guidance moves from its summaries of these scientific reports to statements of the FDA’s current activities, its two recommended principles and its conclusion. This transition is concise, easily followed and, after decades of wide ranging controversy, notable for its understated simplicity. Use of medically important antimicrobials in food-producing

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animals should be only for the health of the animals and so only with veterinary oversight or consultation. Growth promotion use, while unmentioned directly presumably to minimize up-front controversy, is thus presumably (and importantly) to be excluded. The difficulty of obtaining such veterinary involvement in the real world is acknowledged, but cooperation and openness in working it forward is sought.

1. (O'Brien TF, Hopkins JD, Gillece ES, Medeiros AA, Kent RL, Blackburn BO, Holmes M, Reardon JP, Vergeront JM, Schell WL, Christenson E, Bissett ML, Morse Ev. Molecular epidemiology of antibiotic resistance in salmonella from animals and human beings in the United States. New Engl J Med 1982; 307:1-6.)

Thank you for your consideration of these comments.

Sincerely,

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Vice President, APUA  
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