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Capital Office
1875 Connecticut Ave., N.W.
Washington, DC 20009
(202) 387-3500
Fax 202-234-6049
www.edf.org

April 6, 1999

Dockets Management Branch (HFA-305),
Food and Drug Administration
5630 Fishers Lane, Room 1061
Rockville, MD 20852

RE: Docket No. 98D-1146 - Discussion Paper: "A Proposed Framework for Evaluating and Assuring the Human Safety of the Microbial Effects of Antimicrobial New Animal Drugs Intended for Use in Food-Producing Animals."

Via Facsimile: (301) 827-6870

To Whom It May Concern:

These comments are submitted with regard to the Food and Drug Administration's (FDA's) "Proposed Framework for Evaluating and Assuring the Human Safety of the Microbial Effects of Antimicrobial New Animal Drugs Intended for Use in Food Producing Animals" (64 Fed. Reg. 887, Jan. 6, 1999). The proposed Framework (1) describes a pre-approval system under which FDA will consider the potential of new uses of antibiotics in animal agriculture to exacerbate problems of antibiotic resistance in human pathogens, and (2) outlines requirements for post-approval studies and monitoring of resistance levels for new uses of antibiotics in animal agriculture. As discussed below, we are pleased that FDA is beginning to consider antibiotic resistance resulting from antibiotic use in animal agriculture. Nevertheless, the proposed Framework is extremely weak and needs to be substantially revised in order to protect the efficacy of antibiotics vital to human health.

FDA should restrict the use of antibiotics in food-animal production based on concerns about antibiotic resistance.

We support FDA for beginning to consider antibiotic resistance before approving new antibiotics for use in food-animal production. As described in the proposed Framework and in numerous scientific reports, the evolution of antibiotic resistance by bacteria poses a serious threat to human health. In response to heavy use of antibiotics, strains of many disease-causing bacteria are losing their susceptibility to the antibiotics formerly used to treat them. As a result, literally untreatable bacterial infections could

National Headquarters

257 Park Avenue South
New York, NY 10010
(212) 505-2100

5655 College Ave.
Oakland, CA 94618
(510) 658-8008

1405 Arapahoe Ave.
Boulder, CO 80302
(303) 440-4901

2500 Blue Ridge Rd.
Raleigh, NC 27607
(919) 881-2601

44 East Avenue
Austin, TX 78701
(512) 478-5161

Project Office

6 Faneuil Hall Marketplace
Boston, MA 02109
(617) 723-2996

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become common in the future. Recently, a number of reports by leading experts have urged sharp reductions in uses of antibiotics in agriculture (e.g. WHO 1997, Levy 1998, Witte 1998).

We strongly agree with FDA that uses of antibiotics in animal agriculture should be evaluated and, as appropriate, restricted in order to assure that these uses do not threaten human health by promoting the spread of antibiotic resistance. We strongly advocate that FDA make decisions in favor of protecting human health when there are tradeoffs between human health and perceived economic advantages for current systems of intensive animal production. Unfortunately, as discussed below, the proposed Framework favors animal agriculture at the expense of human health.

The proposed Framework will only be risk-based if it is applied to existing as well as to new uses of antibiotics.

FDA asserts that the proposed Framework "sets out a conceptual risk-based framework for evaluating the microbial safety of antimicrobial drugs intended for use in food-producing animals." Taking a narrow view, FDA's proposed Framework can be considered a risk-based approach for evaluating new uses of antibiotics in food-animal production, in that FDA's proposed actions are related to the extent of human health risks from particular new uses of antibiotics in animal agriculture.

Taking a broader view of the problem of antibiotic resistance, however, leads to the conclusion that the proposed Framework is not risk-based. More than 40 percent of the total volume of antibiotics in the United States are now used in animal agriculture, and the greatest risk to human health comes from existing rather than new uses of antibiotics in animal agriculture. Yet these existing use of antibiotics in agriculture are virtually ignored by the proposed Framework. We urge FDA to address existing uses of antibiotics in food-animal production, as well as prospective uses. In particular, we urge the agency to implement the March 1999 petition by the Center for Science in the Public Interest, the Environmental Defense Fund, the Union of Concerned Scientists, Food Animals Concerns Trust, and Public Citizen's Health Research Group, to end existing uses of antibiotics in animals feeds consistent with recommendations by the World Health Organization (WHO 1997) and the U.S. Centers for Disease Control and Prevention.

FDA's proposed scheme for categorizing antibiotics does not adequately protect human health.

As part of FDA's proposed Framework, the agency proposes to place antibiotics into one of three categories according to their relative importance in human medicine. FDA would then subject new uses of antibiotics in each of the proposed categories to certain use restrictions and post-approval requirements. Use of antibiotics in Category I, for example, would be subject to far greater restrictions than the use of antibiotics in Category III.

In principle, the establishment of such categories by FDA is a reasonable method to facilitate agency decision-making. As proposed, however, FDA's categorization scheme does not adequately protect against bacterial resistance to antibiotics important to human medicine. FDA's proposed Category I includes antibiotics that are "Essential for the treatment of a serious or life-threatening disease in humans for which there is no satisfactory alternative therapy." In other words, Category I includes antibiotics for which the loss of bacterial susceptibility would likely result in human deaths. Yet, FDA proposes to allow Category I antibiotics to be used in food-animal production, as long as steps are taken to limit the spread of bacterial resistance. But, even limited use of Category I antibiotics will increase the risk that bacteria will evolve resistance to them, thus jeopardizing human lives. Instead of risking the future efficacy of antibiotics critical to human health, we urge that FDA not permit the use of Category I antibiotics in food-animal production.

Similarly, we urge that FDA revise the standards for Category II and III antibiotics. Category II includes antibiotics important for the treatment of human disease, but for which "satisfactory alternative therapies exist." These drugs should be subject to the restrictions and post-approval requirements now proposed for Category I antibiotics. Category III now includes antibiotics that are not a first choice for treating human infections and drugs that are not used in human medicine. We urge that Category III is subdivided, so that antibiotics used in human medicine are subject to greater restrictions and post-approval requirements than those not used in human medicine.

FDA should require that drug-sales information be submitted to the agency.

The efforts of scientists at FDA and other institutions to correlate the evolution of resistance in bacteria with the use of antibiotics in agriculture are now severely hampered by drug manufacturers' refusal to divulge information on antibiotic sales. Under the proposed Framework, FDA would require that detailed drug sales information be submitted as part of "drug experience reports." Drug sales information is vital to improved understanding of the evolution of antibiotic resistance and to the effectiveness of post-approval monitoring for resistance. We therefore strongly support FDA's proposal to require the submission of drug sales information. We also urge that FDA make drug sales information publicly available to the fullest extent allowed by law, thus allowing researchers and others to have access to it.

Thank you for your consideration.

Sincerely,

Organizations

Rebecca Goldberg, Ph.D.
Senior Scientist
Environmental Defense Fund
257 Park Avenue South
New York, NY 10010

Amy Little
Executive Director
Loni Kemp
Co-Chair
National Campaign for Sustainable Agriculture
P.O. Box 396
Pine Bush, NY 12566

Jean Halloran, Director,
Consumer Policy Institute/Consumers Union.
101 Truman Avenue,
Yonkers, NY 10703

Robert K. Musil, Ph.D.
Executive Director
Physicians for Social Responsibility
1101 14th Street NW Suite 700
Washington, DC 20005

Richard A. Levinson, MD, DPA
American Public Health Association
1015 15th Street, N.W.
Washington, DC 20005-2605

Sarah Newport
Friends of the Earth
1025 Vermont Avenue, NW Suite 300
Washington, D.C. 20005

Ed Hopkins
Sierra Club
408 C Street, NE
Washington, DC 20002

Margaret Janes DVM
Potomac Headwaters Resource Alliance, HC
67 Box 27aa
Mathias, WV 26812

Gail Eisnitz
Chief Investigator
Humane Farming Association
PO Box 2013
Bigfork, MT 59911

Susan Studer
Community Outreach Coordinator
Ohio Environmental Council
1207 Grandview Ave. Suite 201
Columbus, OH 43212

Ronnie Cummins
Campaign for Food Safety
860 Hwy 61
Little Marais, MN. 55614

Mark Ritchie
President
Institute for Agriculture and Trade Policy
2105 First Ave. South
Minneapolis, MN 55404

Lisa Lefferts
Science Advisor
Mothers and Others for a Livable Planet
5280 Rockfish Valley Highway
Faber, VA 22938

Nancy Raeder
Co-Chair
Concerned Citizens Committee of SE Ohio
13744 CR 11
Caldwell, OH 43724-9537

Mary Gibson
SOS (Sick of Stench)
P.O. Box 315
Louisville, OH 44641

Ed Luersman
President
Ohio Family Farm Coalition
1601 Rd 24
Fort Jennings, OH 45844

Richard Hill
President
Save the Valley, Inc.
P.O. Box 813
Madison, IN 47250

Alfredo Quarto
Executive Director
Mangrove Action Project
PO Box 1854
Port Angeles, WA 98362-0279

Patricia Kemp
Executive Director
Florida Consumer Action Network
4100 W Kennedy Boulevard #128
Tampa FL 33609

Kirsten Bryant
Watchdog Campaign Coordinator
The Alabama Environmental Council
2717 7th Avenue S #207
Birmingham, AL 35233

Peter Rosset
Director
Food First/Institute for Food & Development Policy
398 60th Street
Oakland, CA 94618

Barbara Vlamis
Executive Director
Butte Environmental Council
116 W. Second Street, Suite 3
Chico, CA 95928

Frankie M. Summers, Ed.D.
Spokesperson
Kearny County Alliance,
Rural Route 1, Box 24-A
Lakin, KS, 67860

Linda D. Appelgate
Executive Director
Iowa Environmental Council
711 East Locust Street
Des Moines, IA 70309

John Runkle
Past President
Conservation Council of North Carolina
PO Box 3793
Chapel Hill, NC 27515

Jean Halloran, Director,
Consumer Policy Institute/Consumers Union.
101 Truman Avenue,
Yonkers, NY 10703

Individuals

Jack L. Paradise, M.D.
Children's Hospital of Pittsburgh
3705 Fifth Ave.
Pittsburgh, PA 15213

Dr. Guenther Stotzky
Department of Biology
New York University
New York, NY 10003

Garret M. Ihler, Ph.D., M.D.
Tom & Jean McMullen Professor of Genetics
Reviews Editor, FEMS Microbiology Letters
Department of Medical Biochemistry and Genetics
Texas A&M College of Medicine

Robert E. Rutkowski, Esq.
2527 Faxon Court
Topeka, KS 66605-2086

Patty Cantrell
Michigan Land Use Institute
Economic Analyst
P.O. Box 228
Benzonia, MI 49616

Joyce C. Lashof, MD
Professor Emerita School of Public Health
Univ. of California, Berkeley, Ca.
601 Euclid Ave.
Berkeley, CA. 94708

Joe Rudek, Ph.D.
North Carolina Environmental Defense Fund
2500 Blue Ridge Road, Suite 330
Raleigh, NC 27607

Hank Stoddard, DVM, DTVM
Shamrock Veterinary Clinics and Fisheries
Box 1620
Cross City, FL 32628

Peter Weyer, Ph.D.
Program Coordinator
Center for Health Effects of Environmental Contamination
The University of Iowa
100 Oakdale Campus, N203 OH
Iowa City, IA 52242-5000