JUDGE BERMAN 11 CV 3562

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF NEW YORK

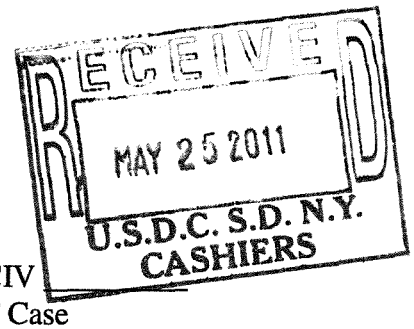
NATURAL RESOURCES DEFENSE COUNCIL, INC.; CENTER FOR SCIENCE IN THE PUBLIC INTEREST; FOOD ANIMAL CONCERNS TRUST; PUBLIC CITIZEN, INC.; and UNION OF CONCERNED SCIENTISTS, INC.,

Plaintiffs,

v.

UNITED STATES FOOD AND DRUG ADMINISTRATION; MARGARET HAMBURG, in her official capacity as Commissioner, United States Food and Drug Administration; CENTER FOR VETERINARY MEDICINE; BERNADETTE DUNHAM, in her official capacity as Director, Center for Veterinary Medicine; UNITED STATES DEPARTMENT OF HEALTH AND HUMAN SERVICES; and KATHLEEN SEBELIUS, in her official capacity as Secretary, United States Department of Health and Human Services,

Defendants.



11 CIV
ECF Case

COMPLAINT FOR DECLARATORY AND INJUNCTIVE RELIEF

INTRODUCTION

1. The misuse and overuse of antibiotics has given rise to a growing and dangerous trend of antibiotic resistance. Increasingly, bacteria are resistant to not one but multiple antibiotics, resulting in infections that are difficult to treat, require longer and more expensive hospital stays, and are more likely to be fatal. The Institute of Medicine of the National Academy of Sciences has warned that "[t]he specter of untreatable infections—a regression to the pre-antibiotic era—is looming just around the corner."

2. Approximately 80 percent of all antibiotics used in the United States today are used in livestock. Most of these drugs are not used to treat disease. Instead, they are given to healthy animals in their feed or water, both to promote faster growth and to prevent infections that tend to occur when animals are kept in cramped, unsanitary conditions. Research has shown that the use of antibiotics in livestock leads to the development of antibiotic-resistant bacteria that can be—and have been—transferred from animals to people through direct contact, environmental exposure, and the consumption and handling of contaminated meat and poultry products.

3. The U.S. Food and Drug Administration (FDA) is charged with regulating the use of antibiotics in livestock. FDA has approved the use of antibiotics in animal feed for nontherapeutic purposes—such as growth promotion and routine disease prevention—since the 1950s. These antibiotics are generally given to animals at "subtherapeutic" levels (i.e., doses too low to treat disease). Many of the antibiotics currently approved for such uses, including penicillin and tetracyclines, are also important in human medicine.

4. The Federal Food, Drug, and Cosmetic Act ("Food and Drug Act"), 21 U.S.C. § 360b(e)(1), requires FDA to withdraw approval for an animal drug if FDA finds that the drug is not shown to be safe for the uses for which it was approved. In 1977, FDA found that certain subtherapeutic uses of penicillin and tetracyclines in animal feed were not shown to be safe. The agency found that these drug uses were contributing to the development of antibiotic-resistant bacteria that could be transferred to humans, a conclusion that later research has reinforced. FDA has never reversed or retracted this conclusion. Instead, it has reiterated its findings in subsequent decades. Nonetheless, despite the statutory requirement that it do so, and the steady accumulation of scientific research establishing the risks posed by the routine, nontherapeutic

use of antibiotics in livestock, FDA has never withdrawn its approvals for subtherapeutic uses of penicillin and tetracyclines.

5. FDA's failure to withdraw approvals for subtherapeutic uses of penicillin and tetracyclines in animal feed constitutes an agency action unlawfully withheld in violation of the Administrative Procedure Act (APA), 5 U.S.C. § 706(1), and the Food and Drug Act, 21 U.S.C. § 360b(e)(1).

6. In 1999 and 2005, Plaintiffs Center for Science in the Public Interest (CSPI), Food Animal Concerns Trust (FACT), Public Citizen, and Union of Concerned Scientists (UCS) submitted citizen petitions ("the Petitions") to FDA requesting that the agency withdraw approvals for nontherapeutic uses of antibiotics in livestock if those antibiotics are also important in human medicine. FDA has never issued a final response to either petition.

7. FDA has unreasonably delayed ruling on the Petitions, in violation of the APA, 5 U.S.C. § 706(1), and the Food and Drug Act's implementing regulations, 21 C.F.R. § 10.30(e)(1).

8. Plaintiffs Natural Resources Defense Council (NRDC), CSPI, FACT, Public Citizen, and UCS seek a judgment declaring that FDA's (1) failure to withdraw approval of subtherapeutic uses of penicillin and tetracyclines in animal feed, and (2) delay in issuing a final response to the Petitions, violate the APA and the Food and Drug Act. Plaintiffs also seek an order compelling FDA to withdraw approval for subtherapeutic uses of penicillin and tetracyclines, unless FDA's findings are reversed in new administrative proceedings, and to respond to the Petitions, all by specific deadlines.

JURISDICTION AND VENUE

9. This Court has jurisdiction pursuant to 28 U.S.C. § 1331.

10. Venue is proper in this Court pursuant to 28 U.S.C. § 1391(e)(3), because Plaintiff NRDC resides and has its principal place of business in this judicial district.

11. This Court may award Plaintiffs all necessary injunctive relief pursuant to the APA, 5 U.S.C. § 706(1), and may award declaratory relief pursuant to the Declaratory Judgment Act, 28 U.S.C. §§ 2201-02.

THE PARTIES

12. Plaintiff NRDC is a nonprofit environmental and public health advocacy organization headquartered in New York, New York, with a national membership of more than 400,000. NRDC engages in research, advocacy, and litigation to improve the regulation of harmful substances in food and consumer products, including drug-resistant bacteria engendered by the misuse and overuse of antibiotics and other antibacterial products. NRDC also works to promote sustainable agricultural practices.

13. Plaintiff CSPI is a science-based nonprofit organization that focuses on nutrition and food safety issues. It is based in Washington, DC. CSPI is supported by about 750,000 American subscribers-members. For more than a decade, CSPI has published reports and articles about the risks of antibiotic use in farm animals.

14. Plaintiff FACT is a nonprofit organization located in Chicago, Illinois, and dedicated to improving the welfare of farm animals, addressing public health problems that come from the production of meat, milk, and eggs, and broadening opportunities for family farmers. FACT conducts on-farm research projects and makes science-based recommendations to agricultural, public health, and environmental organizations and to federal regulatory agencies. Phasing out the routine, nontherapeutic use of medically important antibiotics in livestock has been one of FACT's top priorities for more than a decade.

15. Plaintiff Public Citizen is a national, nonprofit, public interest organization, headquartered in Washington, DC, with approximately 225,000 members and supporters. Since its founding in 1971, Public Citizen has worked before Congress, regulatory agencies, and in the courts to advance the interests of its members on a wide range of consumer protection issues. In particular, Public Citizen's Health Research Group (HRG) promotes research-based, system-wide changes in health care policy and provides oversight concerning drugs, medical devices, doctors, hospitals, and occupational health. HRG works to ban or relabel unsafe or ineffective drugs, and publishes "Worst Pills, Best Pills News," a consumer guide to avoiding drug-induced death or illness. "Worst Pills, Best Pills News" has about 160,000 subscribers.

16. Plaintiff UCS is a science-based nonprofit organization headquartered in Cambridge, Massachusetts, with a national membership of about 79,000. Established in 1969, UCS combines rigorous scientific analysis, innovative policy development, and effective citizen advocacy to achieve practical environmental solutions. Ensuring that all people have food that is produced in a safe and sustainable manner is central to UCS's mission. For over a decade, UCS has worked to eliminate routine, nontherapeutic uses of medically important antibiotics in livestock.

17. Plaintiffs NRDC, CSPI, Public Citizen, and UCS bring this action on their own behalf and on behalf of their members. NRDC's, CSPI's, Public Citizen's, and UCS's memberships include consumers who are concerned about health risks from their exposure to antibiotic-resistant bacteria in meat and poultry products. FDA's failure to withdraw approval for subtherapeutic uses of penicillin and tetracyclines in animal feed increases the likelihood that these members will be exposed to antibiotic-resistant bacteria. These bacteria may cause infections that are difficult or impossible to treat, or they may transfer resistance traits to other,

more dangerous bacteria. At least one of Plaintiffs' members has already suffered from an antibiotic-resistant infection that was difficult to treat and required a prolonged hospital stay.

18. Plaintiff FACT brings this action on its own behalf. Plaintiffs CSPI, FACT, Public Citizen, and UCS have been injured by FDA's unreasonable delay in issuing a final response to the Petitions filed with the agency in 1999 and 2005. FDA's long delay has deprived CSPI, FACT, Public Citizen, and UCS of (1) a decision on the merits of the Petitions and (2) the opportunity to seek judicial review of that decision, if necessary.

19. Defendants FDA and Margaret Hamburg, in her official capacity as Commissioner of FDA, are charged by the Food and Drug Act with protecting the public health by ensuring that veterinary drugs are safe. The Food and Drug Act requires FDA to withdraw approval of new animal drugs that are not shown to be safe.

20. Food and Drug Act implementing regulations and the APA require Defendants FDA and Hamburg to rule on citizen petitions within a reasonable period of time.

21. Defendants Center for Veterinary Medicine (CVM) and Bernadette Dunham, in her official capacity as Director of CVM, are charged by the Food and Drug Act and its implementing regulations with withdrawing approval of new animal drugs that are not shown to be safe.

22. Defendants United States Department of Health and Human Services (HHS) and Kathleen Sebelius, in her official capacity as Secretary of HHS, are charged with responsibility for the implementation and administration of relevant provisions of the Food and Drug Act.

23. For the purposes of this Complaint, Defendants FDA, Margaret Hamburg, CVM, Bernadette Dunham, HHS, and Kathleen Sebelius shall individually and collectively be referred to as "FDA."

STATUTORY AND REGULATORY FRAMEWORK

Withdrawal of New Animal Drug Applications

24. The Secretary of HHS, "through the Commissioner" of FDA, 21 U.S.C. § 393(d)(2), regulates antibiotics in animal feed as "new animal drugs" under section 512 of the Food and Drug Act, 21 U.S.C. § 360b.

25. FDA is required to withdraw its existing approval of a new animal drug application if new information shows that the drug is not shown to be safe:

> The Secretary *shall*, after due notice and opportunity for hearing to the applicant, issue an order withdrawing approval of an application . . . if the Secretary finds . . . that experience or scientific data show that such drug is unsafe for use under the conditions of use upon the basis of which the application was approved . . . ; [or] that new evidence not contained in such application . . . evaluated together with the evidence available to the Secretary when the application was approved, *shows that such drug is not shown to be safe for use under the conditions of use upon the basis of which the application was approved* . . . .

21 U.S.C. § 360b(e)(1) (emphasis added).

26. The Commissioner of FDA has delegated several responsibilities under 21 U.S.C. § 360b to the Director of CVM, formerly known as the Bureau of Veterinary Medicine. As of 1977, the Commissioner had delegated to the Director the authority to "issue notices of an opportunity for a hearing on proposals to refuse approval or to withdraw approval of new animal drug applications." 21 C.F.R. § 5.84 (1977). This delegation is now contained in FDA's Staff Manual Guides. *See* FDA, Staff Manual Guides § 1410.503 (2011).

Citizen Petitions

27. FDA's regulations allow citizens to petition FDA to "issue, amend, or revoke a regulation or order, or to take or refrain from taking any other form of administrative action." 21 C.F.R. § 10.25.

28. FDA must rule on each petition filed. 21 C.F.R. § 10.30(e)(1); *see id.* § 10.30(e)(2)(iii); *id.* § 10.30(e)(3).

29. The Commissioner must respond within 180 days of receipt of the petition by approving, denying, or providing a tentative response to the petition, indicating why the agency has not yet been able to reach a decision on the petition. 21 C.F.R. § 10.30(e)(2). In a tentative response, the Commissioner "may also indicate the likely ultimate agency response, and may specify when a final response may be furnished." *Id.* § 10.30(e)(2)(iii).

30. The Commissioner "may grant or deny such a petition, in whole or in part, and may grant such other relief or take other action as the petition warrants." 21 C.F.R. § 10.30(e)(3). The petitioner must be "notified in writing of the Commissioner's decision." *Id.*

THE FACTS

Human Health Risks Posed by Antibiotics in Animal Feed

31. Livestock producers have been adding low doses of antibiotics to the feed of healthy animals since the 1950s. One reason they do so is that subtherapeutic doses of antibiotics appear to promote faster animal growth on less feed.

32. Another reason livestock producers give subtherapeutic doses of antibiotics to herds of healthy animals is to prevent diseases that tend to occur when animals are kept in cramped, unsanitary conditions. Researchers have observed that the beneficial effects of the subtherapeutic use of antibiotics in livestock are less pronounced in clean, healthful, and stress-free environments.

33. Today, approximately 80 percent of all antibiotics used in the United States are used in livestock.

34. The majority of the antibiotics used in livestock—according to the best estimates, about 83 percent—are administered flock- or herdwide at low levels for nontherapeutic purposes, such as growth promotion and routine disease prevention. According to FDA, the use of antibiotics in entire herds or flocks of animals over extended periods of time poses a qualitatively higher risk to public health than the short-term use of such drugs in individual animals or targeted groups of animals. This litigation does not concern targeted, short-term uses of antibiotics to treat animals that are already sick.

35. It has long been understood that bacteria are capable of developing resistance to antibiotics. Natural selection plays an important role in the development of antibiotic resistance. When an antibiotic drug is introduced to a population of bacteria, the bacteria that are susceptible to the drug die off, but bacteria that are resistant to the drug survive and reproduce, increasing the proportion of resistant bacteria in the population.

36. Through a variety of mechanisms, bacteria may become resistant to multiple classes of antibiotics. For example, the use of any one drug may select for groups of genes that provide resistance not only to the original drug but to other chemically related drugs as well. Bacteria can also transfer resistance traits to other bacteria, allowing bacteria that have never been exposed to antibiotics to become resistant to them. Bacteria can transfer resistance genes to bacteria in different species and genera, and from bacteria that do not cause human illness to bacteria that do.

37. Studies have shown, for example, that the use of tetracycline in swine may promote increased bacterial resistance not only to tetracycline but also to other medically important drugs, including penicillins, cephalosporins, and aminoglycosides. The use of penicillins, such as amoxicillin and ampicillin, has been shown to promote bacterial resistance to

cephalosporins (in a study of swine) and aminoglycosides and fluoroquinolones (in a laboratory study). Aminoglycosides, cephalosporins, and fluoroquinolones are among the few treatments available for serious human infections caused by bacteria that can be transferred from animals to humans.

38. According to FDA, "[a]ntimicrobial [or antibiotic] resistance, and the resulting failure of antimicrobial therapies in humans, is a mounting public health problem of global significance." Draft Guidance No. 209, at 4 (2010). People who contract antibiotic-resistant infections are more likely to have longer hospital stays, may be treated with less effective and more toxic drugs, and may be more likely to die as a result of the infection. In 2009, Cook County Hospital and the Alliance for the Prudent Use of Antibiotics estimated that antibiotic-resistant infections from all sources cost Americans between $16.6 and $26 billion every year.

39. It is widely agreed that the overuse of antibiotics in livestock is helping fuel the rapid proliferation of antibiotic-resistant bacteria in animals and humans. HHS has concluded that "there is a preponderance of evidence that the use of antimicrobials in food-producing animals has adverse human consequences." In a 2004 report, the U.S. General Accounting Office (GAO) observed that "[m]any studies have found that the use of antibiotics in animals poses significant risks for human health, and some researchers contend that the potential risk of the transference is great for vulnerable populations," while only a "small number of studies contend that the health risks of the transference are minimal." In its comments on the report, HHS urged GAO to note that the only article cited in the report as arguing that the risks were minimal was written by an advisory group to the Animal Health Institute, an industry association representing pharmaceutical companies.

40. As FDA has explained, "[a]ntimicrobial use in animals can contribute to the emergence of antimicrobial resistance which may be transferred to humans, thereby reducing the effectiveness of antimicrobial drugs for treating human disease." For this reason, "FDA believes it is critically important that antimicrobial drugs be used as judiciously as possible in an effort to minimize resistance development."

41. Studies show that the use of antibiotics in livestock, including nontherapeutic uses in feed, leads to the development of antibiotic-resistant bacteria in the animals receiving the antibiotics. These bacteria include common sources of foodborne illness in humans, such as *Salmonella*, *Campylobacter*, and *E. coli*. It is well documented that antibiotic-resistant bacteria, including *Salmonella*, *Campylobacter*, and *E. coli*, have been transferred from animals to people.

42. Although the nontherapeutic use of antibiotics in livestock may present risks to animal health as well as human health, this Complaint focuses exclusively on risks to human health.

43. Researchers have focused most often on the transfer of antibiotic-resistant bacteria from animals to humans through the consumption or handling of contaminated meat. Data collected by the National Antimicrobial Resistance Monitoring System indicate that retail meat products are frequently contaminated by *Salmonella*, *Campylobacter*, *E. coli*, and other bacteria that are resistant to multiple classes of antibiotics. Various epidemiological studies have confirmed that these bacteria have been transferred to humans.

44. A study published earlier this year reported that nearly half of the meat and poultry products sampled in five U.S. cities contained drug-resistant strains of *Staphylococcus aureus*, the type of bacteria that commonly causes staph infections. More than half of those bacteria were resistant to multiple classes of antibiotics. Research has shown that veal calves

treated with antibiotics are more likely to carry methicillin-resistant *S. aureus* than calves not treated.

45. Humans can also be exposed to antibiotic-resistant bacteria from animals in other ways. For example, there are several documented cases of the transfer of drug-resistant bacteria from livestock to farmworkers and others who came in contact with the animals. There may also be environmental exposure pathways: a recent study found that bacteria collected in waterways downstream of concentrated animal feeding operations were more than twice as likely to be resistant to multiple antibiotics than bacteria in waterways that were not agriculturally impaired.

46. Many organizations that have studied the human health risks linked to the use of antibiotics in livestock, such as the World Health Organization and the Institute of Medicine, have recommended that livestock producers be prohibited from using antibiotics for growth promotion if those antibiotics are also used in human medicine. Other nations have already acted on these recommendations: In Australia and Japan, penicillins and tetracyclines cannot be used for growth promotion. New Zealand prohibits using antibiotics for growth promotion if they are related to antibiotics used in human medicine. The European Union has banned the use of all antibiotics for growth promotion since 2006.

47. Denmark banned the use of antibiotics for growth promotion in broiler chickens and adult swine in 1998, and in young swine in 1999. Danish government and industry data collected since then show that antibiotic-resistant bacteria in livestock and in meat products have declined, and livestock production has increased.

FDA's Failure to Withdraw Approval of
Penicillin and Tetracyclines in Animal Feed

48. FDA first approved the use of penicillin as an animal feed additive in 1951. Today, penicillin may be used for growth promotion in chickens, turkeys, and swine. 21 C.F.R. § 558.460.

49. FDA first approved the use of chlortetracycline as an animal feed additive in 1951, and it approved such use of oxytetracycline as early as 1954. Currently, chlortetracycline and oxytetracycline are approved as growth promoters in chickens, turkeys, swine, cattle, and sheep. 21 C.F.R. §§ 558.128, 558.450.

50. In the mid-1960s, FDA became concerned that the long-term use of antibiotics in animals might pose threats to human and animal health. In 1970, the agency convened a Task Force to study the issue; it staffed the Task Force with scientists from FDA, the National Institutes of Health, the U.S. Department of Agriculture, the Center for Disease Control, universities, and industry. *See* Removal of Obsolete Regulations, 68 Fed. Reg. 47,272, 47,273 (Aug. 8, 2003); Antibiotic and Sulfonamide Drugs in Animal Feeds, 37 Fed. Reg. 2444, 2444 (Feb. 1, 1972).

51. The Task Force concluded that (1) the use of antibiotics in animal feed, especially at subtherapeutic levels, favors the development of antibiotic-resistant bacteria; (2) animals receiving antibiotics in their feed may serve as a reservoir of antibiotic-resistant pathogens, which can produce human infections; (3) the prevalence of bacteria carrying transferable resistance genes for multiple antibiotics had increased in animals, and the increase was related to the use of antibiotics; (4) antibiotic-resistant bacteria had been found on meat and meat products; and (5) the prevalence of antibiotic-resistant bacteria in humans had increased. *See* Antibiotic and Sulfonamide Drugs in Animal Feeds, 37 Fed. Reg. at 2444-45.

52. The Task Force recommended, *inter alia*, that (1) antibiotics used in human medicine be prohibited from use in animal feed unless they met safety criteria established by FDA and (2) several specific drugs, including tetracycline and penicillins, be reserved for therapy unless they met safety criteria for subtherapeutic use. *See id.* at 2445.

53. In response to the "significant questions" raised by the Task Force's findings, in 1973 FDA issued a regulation providing that the agency would propose to withdraw all approvals for subtherapeutic uses of antibiotics in animal feed unless drug sponsors and other interested parties submitted data within the next two years "which resolve[d] conclusively the issues concerning [the drugs'] safety to man and animals . . . under specific criteria" established by FDA. *See* Antibiotic and Sulfonamide Drugs in the Feed of Animals, 38 Fed. Reg. 9811, 9813 (Apr. 20, 1973) (codified at former 21 C.F.R. § 135.109; renumbered as 21 C.F.R. § 558.15).

54. One of the "most important" of the human and animal health safety criteria that FDA established for drug safety evaluations under the regulation dealt with the transfer of drug resistance: "An antibacterial drug fed at subtherapeutic levels to animals must be shown not to promote increased resistance to antibacterials used in human medicine. Specifically, increased multiple resistance capable of being transferred to other bacteria in animals or man should not occur." Penicillin-Containing Premixes ("Penicillin Notice"), 42 Fed. Reg. 43,772, 43,774-75 (Aug. 30, 1977). Additional criteria focused on the effects of subtherapeutic antibiotics on the *Salmonella* reservoir in livestock, whether antibiotic use increases the pathogenicity of bacteria, and the presence of antibiotic residues in food products. *See id.* at 43,774.

55. After evaluating the information collected under 21 C.F.R. § 558.15, FDA concluded that, at least with respect to penicillin and certain uses of tetracyclines, the drug sponsors had failed to demonstrate that using the drugs subtherapeutically in animal feed was

safe. Accordingly, the Director of FDA's Bureau of Veterinary Medicine issued notices of opportunity for hearing on proposals to withdraw all uses of penicillin in animal feed, *see* Penicillin Notice, 42 Fed. Reg. at 43,772, and nearly all subtherapeutic uses of tetracyclines in animal feed, with limited exceptions, *see* Tetracycline (Chlortetracycline and Oxytetracycline)-Containing Premixes ("Tetracyclines Notice"), 42 Fed. Reg. 56,264, 56,264 (Oct. 21, 1977).

The Penicillin Notice

56. In the Penicillin Notice, the Director reported that "[n]one of the specified human and animal health safety criteria [for the subtherapeutic use of penicillin] have been satisfied." 42 Fed. Reg. at 43,775. With respect to the criterion dealing with the transfer of drug resistance, for example, the Director surveyed the available data and found that (1) the pool of bacteria carrying transferable resistance genes was increasing; (2) the increase was due in part to the subtherapeutic use of penicillin in animal feed; and (3) antibiotic-resistant bacteria were transferred from animals to humans as a result of direct human-animal contact, the consumption of contaminated food, and the widespread presence of resistant bacteria in the environment. Studies submitted by or on behalf of the drug sponsors failed to rebut these findings. *Id.* at 43,781.

57. Following an extensive analysis, the Director indicated that he was "unaware of evidence that satisfies the requirements for the safety of penicillin-containing premixes [i.e., feed supplements] as required by section 512 of the Federal Food, Drug, and Cosmetic Act and § 558.15 of the agency's regulations." Penicillin Notice, 42 Fed. Reg. at 43,792. He proposed to "withdraw approval of new animal drug applications . . . for all penicillin-containing premixes intended for use in animal feed on the grounds that . . . new evidence shows that the penicillin-

containing products have not been shown to [be] safe for subtherapeutic use" as required by the Food and Drug Act. *Id.* at 43,772.

The Tetracyclines Notice

58. The Director undertook a similar analysis, and reached similar conclusions, in the Tetracyclines Notice. For purposes of the notice, FDA treated chlortetracycline, oxytetracycline, and tetracycline identically because it concluded there was no scientific basis for treating them otherwise. *See* Tetracyclines Notice, 42 Fed. Reg. at 56,266. The Director found that "the results of the studies submitted and the data available are clear—the affected parties have failed to show that extensive subtherapeutic use of the tetracyclines is safe." *Id.* at 56,267.

59. The Director proposed retaining seven limited subtherapeutic uses of tetracyclines then considered "unique" and "essential," primarily for the control of specific diseases. Tetracyclines Notice, 42 Fed. Reg. at 56,287. He then proposed to withdraw "all approvals for tetracycline-containing premix products intended for subtherapeutic uses in animal feed, other than those cited, . . . on the grounds that they have not been shown to be safe." *Id.* at 56,288.

Further Research

60. Shortly after FDA issued the two notices of opportunity for hearing, the House Committee on Appropriations requested that FDA, before taking action on its withdrawal proposals, conduct further research on the question whether the subtherapeutic use of antibiotics in animal feed presents a threat to human health. *See* H.R. Rep. No. 95-1290, at 99-100 (1978). In response, FDA contracted with the National Academy of Sciences (the "National Academy") to assess the human health consequences of the subtherapeutic use of penicillin and tetracyclines in animal feeds by evaluating existing data, and to recommend areas for additional research.

61. The resulting report by the National Academy, published in 1980, did not conclude that using antibiotics subtherapeutically in animal feed was safe. The Academy recommended additional epidemiological studies.

62. Soon thereafter, the House Committee on Appropriations requested that FDA undertake additional research in response to the 1980 report of the National Academy, and that in the meantime FDA continue to hold its penicillin and tetracyclines proposals in abeyance. *See* H.R. Rep. 96-1095, at 105-06 (1980). The following year, the Senate Committee on Appropriations made the same request. *See* S. Rep. No. 97-248, at 79 (1981). FDA contracted with the Seattle-King County Department of Public Health and the Institute of Medicine for further research.

63. The Seattle-King County study, published in 1984, contained several important findings that supported FDA's concerns about the risks posed by antibiotics in animal feed. For example, the study found that *Campylobacter* bacteria were likely transferred from chickens to humans through the consumption of poultry products; that samples of such bacteria taken from poultry products and humans exhibited "surprisingly high" and "similar" patterns of tetracycline resistance; and that drug-resistant *Campylobacter* could likely transfer resistance genes to other bacteria.

64. The 1988 report of the Institute of Medicine, like the studies before it, could not conclude that the subtherapeutic use of antibiotics in animal feed was safe. The Institute found several sources of "indirect evidence implicating subtherapeutic use of antimicrobials in producing resistance in infectious bacteria that causes a potential human health hazard."

65. By 1988, FDA had completed the research requested by the congressional appropriations committees. As a result of that research, FDA "did not conclude that the

continued subtherapeutic use of penicillin and the tetracycylines [*sic*] in animal feed is safe." Removal of Obsolete Regulations, 68 Fed. Reg. at 47,275.

66. FDA has never rescinded or altered its 1977 findings that subtherapeutic uses of penicillin and tetracyclines in animal feed are not shown to be safe. As recently as 2003, FDA confirmed that the 1977 Penicillin and Tetracyclines Notices "remain pending." *Id.* In 1983, FDA denied a request by drug sponsors that it withdraw the penicillin and tetracyclines proposals. The agency explained that "[t]he Director has not changed his earlier conclusion that the available scientific information warrants the proposed actions. . . . The notices of opportunity for hearing represent the Director's formal position that use of the drugs *is not shown to be safe*." Penicillin and Tetracycline in Animal Feeds, 48 Fed. Reg. 4554, 4555-56 (Feb. 1, 1983) (emphasis added).

67. In 2004, FDA sent letters to several manufacturers of approved animal feed products containing penicillin and tetracyclines, explaining that the administrative record did not contain sufficient information to alleviate FDA's concerns about "the use of these products and their possible role in the emergence and dissemination of antimicrobial resistance." FDA reported that it had conducted a qualitative risk assessment and concluded that the products fell into "Category 1," or "high" risk, and use of the products for growth promotion was therefore not appropriate. FDA invited the manufacturers to meet with the agency to discuss its findings.

Nonbinding Guidance

68. Rather than act on its 1977 findings and withdraw approval of subtherapeutic uses of penicillin and tetracyclines in animal feeds, FDA has issued a series of nonbinding guidance documents.

69. In 2003, FDA issued Guidance for Industry No. 152. The guidance recommended a risk assessment approach that drug sponsors could use to evaluate the safety of antimicrobial new animal drugs with regard to their microbiological effects on bacteria of human health concern. Guidance No. 152 made clear that "FDA's guidance documents, including this guidance, do not establish legally enforceable responsibilities." Guidance No. 152, at 2.

70. In 2010, FDA issued Draft Guidance No. 209, expected to be finalized in 2011, which concludes that "using medically important antimicrobial drugs for production purposes [i.e., increasing rate of weight gain or improving feed efficiency] is not in the interest of protecting and promoting the public health." Draft Guidance No. 209, at 13. The guidance recommends that medically important antibiotics be used in food-producing animals (1) only when necessary to ensure the animals' health and (2) only with veterinary oversight. *See id.* at 16-17. Like other FDA guidance documents, Draft Guidance No. 209 does "not establish legally enforceable responsibilities." *Id.* at 2.

71. Today, the science supporting FDA's 1977 findings is stronger than ever. In recognition of the "[m]ounting evidence suggest[ing] a relationship between antimicrobial use in animal husbandry and an increase in bacterial resistance in humans," the Institute of Medicine now recommends that FDA "ban the use of antimicrobials for growth promotion in animals if those classes of antimicrobials are also used in humans." FDA has not done so.

Harm to Plaintiffs from FDA's Failure to Withdraw
Approval of Penicillin and Tetracyclines in Animal Feed

72. According to figures released by FDA in 2010, penicillins now account for approximately 4.7 percent of total antibiotic use in U.S. livestock, and tetracyclines account for approximately 35.3 percent. Most of this use is nontherapeutic.

73. The use of penicillin and tetracyclines in animal feed promotes the development of antibiotic-resistant bacteria in livestock. These bacteria may be resistant not only to penicillin or tetracyclines but also to other medically important drugs.

74. Antibiotic-resistant bacteria may be transferred from animals to humans through the consumption and handling of contaminated meat products. Data collected by the National Antimicrobial Resistance Monitoring System demonstrate that *Salmonella*, *Enterococcus*, and *E. coli* bacteria collected from retail meat and poultry samples are frequently resistant to penicillins and tetracyclines, and *Campylobacter* bacteria so collected is often resistant to tetracyclines.

75. Antibiotic-resistant bacteria that have been transferred from animals to humans may cause drug-resistant infections, or they may transfer resistance traits to other bacteria that can cause infections.

76. The health of Plaintiffs' members is continually threatened by their exposure to meat and poultry products contaminated with bacteria resistant to penicillins, tetracyclines, and other antibiotics, including aminoglycosides and cephalosporins.

77. The risk that Plaintiffs' members will be exposed to bacteria resistant to penicillins, tetracyclines, or other antibiotics through the consumption or handling of contaminated meat products is traceable to FDA's failure to comply with its statutory duty to withdraw approval for subtherapeutic uses of penicillin and tetracyclines in animal feed.

78. If FDA were to withdraw approval for subtherapeutic uses of penicillin and tetracyclines in animal feed, the prevalence of bacteria in livestock with resistance to those drugs would stop increasing, and would likely decrease. As a result, Plaintiffs' members would face a reduced risk of contracting a drug-resistant infection from consuming or handling meat products.

Citizen Petitions Filed with FDA in 1999 and 2005

79. On March 9, 1999, CSPI, FACT, Public Citizen, and UCS submitted a petition to FDA requesting that the agency "rescind approvals for subtherapeutic uses in livestock of any antibiotic used in (or related to those used in) human medicine."

80. The petition summarized the supporting science, and explained that:

(A) Subtherapeutic antibiotics are used widely in livestock.
(B) Subtherapeutic antibiotic use in livestock leads to the selection of antibiotic-resistant bacteria.
(C) Antibiotic-resistant bacteria can be transferred between animals and from animals to people.
(D) Antibiotic-resistant bacteria may transfer resistance genes to other bacteria.
(E) Subtherapeutic antibiotic use may select for multi-drug-resistant bacteria that can cause infections that are difficult to treat.
(F) Subtherapeutic antibiotic use jeopardizes therapeutic options in veterinary and human medicine.
(G) Expert committees and leading scientists support a phase-out of subtherapeutic antibiotic use in livestock.
(H) Authoritative scientific bodies such as the U.S. Centers for Disease Control and Prevention and the World Health Organization consider it a human health risk to permit subtherapeutic use in livestock of antibiotics that are used in (or related to those used in) human medicine.

81. The petition also addressed the modest economic and environmental impacts of the proposed withdrawals. As evidence, the petition cited the National Academy's estimate that elimination of *all* subtherapeutic use of antibiotics in livestock would lead to approximately $4.84 to $9.72 a year in higher costs for consumers. The petition also pointed to the experiences of countries such as Sweden and Denmark, which have successfully eliminated some uses of antibiotics in livestock.

82. On April 7, 2005, FACT and UCS submitted a second petition to FDA. The petition requested that the FDA Commissioner "withdraw approvals for herdwide/flockwide uses of [specific] antibiotics in chicken, swine, and beef cattle for purposes of growth promotion

(including weight gain and feed efficiency) and disease prevention and control (except for non-routine use where a bacterial infection has been diagnosed within a herd or flock)." The petition covered penicillins, tetracyclines, aminoglycosides, streptogramins, macrolides, lincomycin, and sulfonamides. It did not cover any uses of those drugs for disease treatment.

83. The second petition analyzed the listed antibiotics under the risk assessment approach developed by FDA in Guidance No. 152. The petition demonstrated that herdwide or flockwide uses of the listed drugs—all of which were classified by FDA as "critically important" or "highly important" for human health—were inconsistent with the agency's own risk management criteria.

84. FDA has never issued a final response to either the 1999 or 2005 petition.

85. The agency issued tentative responses to the 1999 petition in 1999 and 2001. The second tentative response, dated February 28, 2001, explained that FDA "cannot yet issue a final response" to the petition because the withdrawal of a new animal drug application involves multiple steps, and agency resources are limited.

86. FDA issued a tentative response to the 2005 petition on October 4, 2005. The agency essentially reiterated its response to the 1999 petition, and also mentioned its development of nonbinding guidance for evaluating the safety of antimicrobial drug use in food-producing animals.

87. FDA is required by Food and Drug Act implementing regulations to make a final decision on all citizen petitions. FDA's long delay in ruling on the Petitions is unreasonable.

Harm to Plaintiffs from FDA's Delay in Issuing
a Final Response to the Citizen Petitions

88. In over twelve years, CSPI, FACT, Public Citizen, and UCS have not received a final response to their 1999 petition. FACT and UCS have waited more than six years for a final

response to their 2005 petition. FDA's delay has injured CSPI, FACT, Public Citizen, and UCS by depriving them of (1) a decision on the merits of the Petitions and (2) the opportunity to seek judicial review of that decision, if necessary.

89. While CSPI, FACT, Public Citizen, and UCS await a final decision on the Petitions, the health of CSPI's, Public Citizen's, and UCS's members is continually threatened by their exposure to meat and poultry products contaminated with bacteria resistant to medically important antibiotics.

90. A final response either granting or denying the Petitions would redress CSPI, FACT, Public Citizen, and UCS's injuries by either (1) granting them the relief they seek or (2) giving them an opportunity to seek judicial review of a denial of the Petitions.

FIRST CLAIM FOR RELIEF

91. Plaintiffs incorporate by reference all preceding paragraphs.

92. The Food and Drug Act requires FDA to withdraw approval of a new animal drug application if it finds that new evidence shows that the drug is not shown to be safe for the uses for which it was approved. *See* 21 U.S.C. § 360b(e)(1).

93. FDA found in 1977 that all subtherapeutic uses of penicillin in animal feed, and certain subtherapeutic uses of tetracyclines, have not been shown to be safe. FDA has never retracted those findings, it has reaffirmed them, and the scientific evidence supporting them is stronger now than ever.

94. For more than thirty years, FDA has failed to comply with its statutory duty, after notice and opportunity for hearing, to withdraw approval of subtherapeutic uses of penicillin and tetracyclines in animal feed.

95. FDA's failure to withdraw approval constitutes an agency action unlawfully withheld in violation of the APA, 5 U.S.C. § 706(1), and the Food and Drug Act, 21 U.S.C. § 360b(e)(1).

SECOND CLAIM FOR RELIEF

96. Plaintiffs incorporate by reference all preceding paragraphs.

97. FDA has delayed unreasonably in issuing a final response to the Petitions submitted in 1999 and 2005.

98. FDA's failure to issue a final response constitutes an agency action unreasonably delayed in violation of the APA, 5 U.S.C. § 706(1), and the Food and Drug Act's implementing regulations, 21 C.F.R. § 10.30(e)(1).

REQUEST FOR RELIEF

Plaintiffs request that this Court enter judgment against FDA as follows:

A. Declaring that FDA's failure to withdraw approval of subtherapeutic uses of penicillin and tetracyclines in animal feed is unlawful, pursuant to the APA, 5 U.S.C. § 706(1), and the Food and Drug Act, 21 U.S.C. § 360b(e)(1);

B. Declaring that FDA's delay in issuing a final response to the Petitions is unreasonable and not in accordance with law, pursuant to the APA, 5 U.S.C. § 706(1), and the Food and Drug Act's implementing regulations, 21 C.F.R. § 10.30(e)(1);

C. Compelling FDA to withdraw approval for subtherapeutic uses of penicillin and tetracyclines in animal feed, unless FDA's findings are overturned in new administrative proceedings, by a Court-ordered deadline;

D. Compelling FDA to issue a final response to the Petitions, by a Court-ordered deadline;

E. Awarding Plaintiffs their reasonable costs and attorneys' fees; and

F. Granting such other and further relief as the Court deems just and proper.

Dated: New York, New York
May 25, 2011

Respectfully submitted,

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