Natural Resources Defense Council, Inc. et al v. United States Food and Drug Administration et al Doc. 21

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,	)	11 CIV 3562 (THK)
	)	ECF Case
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.	)	

PLAINTIFFS' STATEMENT OF UNDISPUTED MATERIAL FACTS IN SUPPORT OF MOTION FOR SUMMARY JUDGMENT

Plaintiffs Natural Resources Defense Council, Center for Science in the Public Interest (CSPI), Food Animal Concerns Trust (FACT), Public Citizen, and Union of Concerned Scientists (UCS) respectfully submit this Statement of Undisputed Material Facts in support of their Motion for Summary Judgment. This statement is based on the Answer of Defendants United States Food and Drug Administration (FDA); Margaret Hamburg, in her official capacity as Commissioner, FDA; Center for Veterinary Medicine (CVM); Bernadette Dunham, in her

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official capacity as Director, CVM; United States Department of Health and Human Services (HHS); and Kathleen Sebelius, in her official capacity as Secretary, HHS; the concurrently filed Declaration of Jennifer A. Sorenson (Sorenson Decl.); and accompanying exhibits.

Pursuant to Federal Rule of Civil Procedure 56 and this Court's Local Civil Rule 56.1, there is no genuine issue as to the following facts:

Antibiotic Resistance

1. "Antibiotics are drugs used for treating infections caused by bacteria. Also known as antimicrobial drugs, antibiotics have saved countless lives. Misuse and overuse of these drugs, however, have contributed to a phenomenon known as antibiotic resistance. This resistance develops when potentially harmful bacteria change in a way that reduces or eliminates the effectiveness of antibiotics." Decl. of Jennifer A. Sorenson (Sorenson Decl.) Ex. S, at 1; Answer ¶ 1.

2. 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. Amended Complaint ¶ 35; Answer ¶ 35; Sorenson Decl. Ex. X, at 2.

3. 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 also to other chemically related drugs. 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. Amended Complaint ¶ 36; Answer ¶ 36; Sorenson Decl. Ex. T, at 1.

4. 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. Amended Complaint ¶ 38; Answer ¶ 38; Sorenson Decl. Ex. T, at 1. According to FDA, "[w]hen a person is infected with an antibiotic-resistant bacterium, not only is treatment of that patient more difficult, but the antibiotic-resistant bacterium may spread to other people." Sorenson Decl. Ex. S, at 1.

5. 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. Amended Complaint ¶ 38; Answer ¶ 38.

6. FDA considers antibiotic resistance "a serious public health threat" and "a mounting public health problem of global significance." Amended Complaint ¶ 38; Answer ¶ 38; Sorenson Decl. Ex. O, at 3-4.

7. According to FDA, "[p]reserving the effectiveness of current antimicrobials [or antibiotics] . . . [is] vital to protecting human and animal health against infectious microbial pathogens," Sorenson Decl. Ex. R, at 1, and "[d]eveloping strategies for reducing antimicrobial resistance is critically important for protecting both public and animal health." Sorenson Decl. Ex. O, at 3.

8. Because the use of antibiotics "contributes to the emergence of drug resistant organisms," FDA has explained that "these important drugs must be used judiciously in both animal and human medicine to slow the development of resistance. . . . Using these drugs judiciously means that unnecessary or inappropriate use should be avoided." Sorenson Decl. Ex. O, at 3.

9. The Centers for Disease Control and Prevention (CDC), a division of HHS, names antibiotic resistance as one of its "top concerns." Sorenson Decl. Ex. X, at 2.

10. Because antibiotic resistance "threatens our ability to treat disease and to protect the advances made in global health in recent decades," the World Health Organization (WHO) urges that "[w]e must do everything in our power to preserve [antibiotics] for future generations." Sorenson Decl. Ex. BB, at 1.

11. 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." Amended Complaint ¶ 1; Answer ¶ 1; Sorenson Decl. Ex. Z, at 205.

Antibiotics in Livestock

12. FDA reports that 13,067,100 kilograms of antibiotics were sold or distributed for use in food-producing animals in the United States in 2009. Sorenson Decl. Ex. P, at 3. In comparison, 3,316,906 kilograms of antibiotics were sold in the U.S. market for human use in 2009. Sorenson Decl. Ex. Q, enclosure, at 4. Thus, approximately 80 percent of the more than 16 million kilograms of antibiotics sold in the United States in 2009 went to livestock.

13. Of the antibiotics sold for use in livestock, 11,766,613 kilograms, or 90 percent, were sold for administration via animal feed or water, rather than by injection. Sorenson Decl. Ex. Q, at 1.

14. According to the Institute of Medicine, the majority of antibiotics used in animal husbandry in the United States are used for growth promotion or preventive therapy in healthy animals. Sorenson Decl. Ex. Z, at 207. These antibiotics are generally given to animals at "subtherapeutic" levels, or in doses too low to treat disease. Sorenson Decl. Ex. H, at iii n.1; Penicillin-Containing Premixes (Penicillin Notice), 42 Fed. Reg. 43,772, 43,773 (Aug. 30, 1977), Ex. A to Sorenson Decl.

15. Since the 1950s, FDA has approved some antibiotics for growth promotion indications in livestock. Some of the antibiotics that were originally approved for growth promotion may be important to human medicine. Answer ¶ 3.

16. Antibiotics used for growth promotion "are typically administered through the feed or water on a herd- or flock-wide basis and are approved for such uses as increasing rate of weight gain or improving feed efficiency." Sorenson Decl. Ex. O, at 4. The approved dose of an antibiotic for growth promotion is typically lower than the approved dose for a disease indication. Answer ¶ 3; Penicillin Notice, 42 Fed. Reg. at 43,773.

17. Administering medically important antimicrobial drugs to entire herds or flocks of food-producing animals (e.g., for growth promotion) poses a qualitatively higher risk to public health than administering such drugs to individual animals or targeted groups of animals. Answer ¶ 34.

18. Since the 1950s, FDA has approved some antibiotics for disease prevention in livestock. Some of the antibiotics that were originally approved for disease prevention may be important to human medicine. Answer ¶ 3.

19. According to the Institute of Medicine, "it has been noted that subtherapeutic antibiotics are most effective in animals under the stress of inadequate nutrition and suboptimal sanitary conditions . . . ; therefore, improved hygiene and changes in animal husbandry practices to control disease could potentially eliminate the need for growth promoters." Sorenson Decl. Ex. Z, at 208.

20. According to FDA, 610,514 kilograms of penicillins were sold or distributed for use in food-producing animals in the United States in 2009. Thus, penicillins accounted for approximately 4.7 percent of all antibiotics sold for use in livestock. Sorenson Decl. Ex. P, at 3.

21. According to FDA, 4,611,892 kilograms of tetracyclines were sold or distributed for use in food-producing animals in the United States in 2009. Thus, tetracyclines accounted for approximately 35.3 percent of all antibiotics sold for use in livestock. Sorenson Decl. Ex. P, at 3.

Human Health Risks Posed by the Use of Antibiotics in Livestock

22. FDA has classified penicillins and tetracyclines as "highly important" to human medicine. Sorenson Decl. Ex. M, at 28-29, 30, 32.

23. 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. Amended Complaint ¶¶ 2, 74; Answer ¶¶ 2, 74; Sorenson Decl. Ex. Y, at 11, 17-23, 89; *id.* Ex. Z, at 207; *id.* Ex. W, cover letter, at 1; Penicillin Notice, 42 Fed. Reg. at 43,776-78; Tetracycline (Chlortetracycline and Oxytetracycline)-Containing Premixes (Tetracyclines Notice), 42 Fed. Reg. 56,264, 56,268-70 (Oct. 21, 1977), Ex. B to Sorenson Decl.

24. 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. Sorenson Decl. Ex. W, cover letter, at 1; Answer ¶ 41. These bacteria include *Salmonella*, *Campylobacter*, and *E. coli*, all of which may cause foodborne illness in humans. Sorenson Decl. Ex. Y, at 11, 17-23.

25. 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. Amended Complaint ¶ 73; Answer ¶¶ 37, 73.

26. Data collected by the National Antimicrobial Resistance Monitoring System (NARMS) in 2009 indicate that *Salmonella* was present on 21.0% of retail chicken breast samples and 14.4% of retail ground turkey samples. Sorenson Decl. Ex. V, at 20 tbl.3. Nearly half (48.4%) of the *Salmonella* on chicken breasts and more than a quarter (26.3%) of the *Salmonella* from ground turkey was resistant to three or more classes of antibiotics. *Id.* at 8; 30 tbl.8. Tetracycline resistance was common among *Salmonella* isolates from chicken and turkey products (59.9% and 65.3%, respectively), while resistance to ampicillin (an antibiotic in the penicillin class), was only slightly less common, at 45.8% of chicken *Salmonella* and 57.9% of turkey *Salmonella*. *Id.* at 23 tbl.5.

27. The NARMS *2009 Retail Meat Report* shows that *Campylobacter*, including the *Campylobacter jejuni* and *Campylobacter coli* species, was present on 44.1% of retail chicken breasts tested. Sorenson Decl. Ex. V, at 8, 20 tbl.3. Nearly half (46.2%) of the *C. jejuni* isolates and more than a third (38.0%) of the *C. coli* isolates were resistant to tetracycline. *Id.* at 42 tbl.13.

28. The 2009 NARMS report indicates that *E. coli* was highly prevalent on all retail meat types tested: chicken breasts (87.5%); ground turkey (85.0%); ground beef (68.6%); and pork chops (40.8%). Sorenson Decl. Ex. V, at 20 tbl.3. Multidrug resistance was most prevalent among *E. coli* isolates from chicken breasts (37.5%) and ground turkey (66.3%). *Id.* at 70 tbl.24. Approximately 56.2% of *E. coli* isolates from ground turkey were resistant to ampicillin, while 82.0% were resistant to tetracycline. *Id.* at 64 tbl.22.

29. According to the U.S. Government Accountability Office (GAO), epidemiologic studies suggest that antibiotic-resistant *E. coli* bacteria have been transferred from animals to humans, and studies that include molecular subtyping demonstrate that antibiotic-resistant

Salmonella and *Campylobacter* bacteria have been transferred from animals to humans through the consumption or handling of contaminated meat. Sorenson Decl. Ex. Y, at 17-23.

30. 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. Amended Complaint ¶ 45; Answer ¶ 45.

31. According to GAO, "[r]esistant bacteria may . . . be spread to fruits, vegetables, and fish products through soil, well water, and water runoff contaminated by waste material from animals harboring these bacteria." Sorenson Decl. Ex. Y, at 11.

32. 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. Amended Complaint ¶ 75; Answer ¶ 75.

33. FDA has concluded that "the overall weight of evidence available to date supports the conclusion that using medically important antimicrobial drugs for production purposes [in livestock] is not in the interest of protecting and promoting the public health." Sorenson Decl. Ex. O, at 13; *id.* Ex. R, at 2.

34. FDA recognizes that "[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." Sorenson Decl. Ex. U, at 2; Amended Complaint ¶ 40; Answer ¶ 40. "FDA believes it is critically important that antimicrobial drugs be used as judiciously as possible in an effort to minimize resistance development." Sorenson Decl. Ex. U, at 2; Amended Complaint ¶ 40; Answer ¶ 40.

35. HHS has concluded that "there is a preponderance of evidence that the use of antimicrobials in food-producing animals has adverse human consequences." Sorenson Decl. Ex. Y, at 89; Amended Complaint ¶ 39; Answer ¶ 39.

36. In a 2004 report, 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." Sorenson Decl. Ex. Y, at 23; Amended Complaint ¶ 39; Answer ¶ 39.

37. In its comments on the 2004 GAO 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. Sorenson Decl. Ex. Y, at 89; Amended Complaint ¶ 39; Answer ¶ 39.

38. According to CDC, there is "strong scientific evidence of a link between antibiotic use in food animals and antibiotic resistance in humans," including "multiple North American studies describing how: [u]se of antibiotics in animals results in resistant bacteria in food animals; [r]esistant bacteria are present in the food supply and transmitted to humans; [and] [r]esistant bacteria result in adverse human health consequences (such as increased hospitalizations). . . . [T]here is a compelling body of evidence to demonstrate this link." Sorenson Decl. Ex. W, cover letter, at 1.

39. Many organizations that have studied the human health risks linked to the use of antibiotics in livestock, such as WHO 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. Amended Complaint ¶ 46; Answer ¶ 46; Sorenson Decl. Ex. Z,

at 209-11; *id.* Ex. AA, at 2. Eight years ago, the Institute of Medicine explained that "[t]he total burden of human illness due to resistant bacteria that have been transferred from animals to humans is unknown, but the guiding principle should be that we must do what the available evidence suggests will help stem the tide of increasing resistance before it is too late," and "[t]o do nothing is, in effect, to allow the continued evolution of antimicrobial-resistant microbes, which poses serious near- and long-term threats to global health." Sorenson Decl. Ex. Z, at 209.

40. According to the Institute of Medicine, the "main argument" against a ban on the subtherapeutic use of antibiotics for growth promotion in the United States is an economic one. Sorenson Decl. Ex. Z, at 208.

41. The European Union, Australia, and New Zealand prohibit the use of penicillin and tetracyclines for growth promotion indications, and Japan prohibits the use of penicillin for growth promotion indications. Answer ¶ 46.

42. Denmark discontinued 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. Amended Complaint ¶ 47; Answer ¶ 47; Sorenson Decl. Ex. CC, at 40-41.

43. According to CDC, "[i]n general, subtherapeutic use has been shown to lead to an increase in resistant strains in animals. The European experience demonstrates that it is possible to stop these uses, reduce overall use of antibiotics in animals, reduce resistant circulating bacteria that can infect humans, and not have industry or consumers affected by decreased production or increased costs." Sorenson Decl. Ex. W, enclosure, at 3.

FDA's Failure to Withdraw Approvals for Penicillin and Tetracyclines in Animal Feed

44. FDA approved the use of penicillin as an animal feed additive in the 1950s. Today, penicillin may be used for growth promotion in chickens, turkeys, and swine. 21 C.F.R. § 558.460; Amended Complaint ¶ 48; Answer ¶ 48.

45. FDA approved the use of chlortetracycline and oxytetracycline as an animal feed additive in the 1950s. Currently, chlortetracycline and oxytetracycline are approved as growth promoters in chickens, turkeys, swine, cattle, and sheep. 21 C.F.R. §§ 558.128, 558.450; Amended Complaint ¶ 49; Answer ¶ 49.

46. 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, CDC, universities, and industry. *See* New Animal Drugs; Removal of Obsolete and Redundant Regulations, 68 Fed. Reg. 47,272, 47,273 (Aug. 8, 2003), Ex. E to Sorenson Decl.; Antibiotic and Sulfonamide Drugs in Animal Feeds, 37 Fed. Reg. 2444, 2444 (Feb. 1, 1972), Ex. C to Sorenson Decl.; Amended Complaint ¶ 50; Answer ¶ 50.

47. 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.

48. 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.

49. 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. 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), Ex. D to Sorenson Decl.

50. 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 Notice, 42 Fed. Reg. at 43,774-75.

51. 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 (now CVM) issued notices of opportunity for hearing on proposals to withdraw approvals for all uses of penicillin in

animal feed, *see* Penicillin Notice, 42 Fed. Reg. at 43,772, and, with limited exceptions, all subtherapeutic uses of tetracyclines in animal feed, *see* Tetracyclines Notice, 42 Fed. Reg. at 56,264.

The Penicillin Notice

52. 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, 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. *See id.* at 43,781.

53. 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

54. 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.

55. With limited exceptions, the Director proposed to withdraw "all approvals for tetracycline-containing premix products intended for subtherapeutic uses in animal feed . . . on the grounds that they have not been shown to be safe." Tetracyclines Notice, 42 Fed. Reg. at 56,288. The Director carved out limited exceptions related to "unique, essential" drug uses, primarily for the control of specific diseases. *Id.* at 56, 287.

Further Research

56. 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).

57. In response, FDA contracted with the National Academy of Sciences 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. 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. Sorenson Decl. Ex. F, at 53; Amended Complaint ¶ 61; Answer ¶ 61.

58. 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. No. 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).

59. FDA contracted with the Seattle-King County Department of Public Health and the Institute of Medicine for further research. 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 transfer resistance genes to other bacteria. Sorenson Decl. Ex. G, at 3, 169.

60. 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." Sorenson Decl. Ex. H, at 194.

61. FDA has not concluded that the subtherapeutic use of penicillin and tetracyclines in animal feed is safe. Removal of Obsolete Regulations, 68 Fed. Reg. at 47,275; Answer ¶ 65.

62. FDA has never revoked the 1977 notices of opportunity for hearing containing the agency's findings that subtherapeutic uses of penicillin and tetracyclines in animal feed are not shown to be safe. Amended Complaint ¶ 66; Answer ¶ 66.

63. FDA's 1977 Penicillin and Tetracyclines Notices are still pending. Answer ¶ 68.

64. FDA has not withdrawn approvals for penicillin and tetracyclines as proposed in the 1977 notices of opportunity for hearing. Answer ¶ 4.

65. 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." Sorenson Decl. Ex. N, at 1-2. 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. *Id.* at 3.

Nonbinding Guidance

66. 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." Sorenson Decl. Ex. M, at 2.

67. In 2007, the House Committee on Appropriations expressed concern that FDA's Guidance No. 152 "does not assign enough weight to the impact of microbial resistance to drugs that are highly important to human medicine but are not used to treat foodborne illnesses," because "[t]ransferred resistance from antimicrobials used in animals produced for food can also render critically important human antibiotics ineffective." H.R. Rep. No. 110-258, at 98-99 (2007). Because the Committee was "concerned that simply satisfying the requirements of the guidance document is not adequate to protect human health," the Committee "directed FDA to reevaluate the basis on which it makes such decisions and to provide a report to the Committee by November 1, 2007." *Id.* at 99.

68. 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." Sorenson Decl. Ex. O, at 13. The Draft Guidance recommends that medically important antibiotics be used in food-producing animals (1) only when necessary to ensure the animals' health, and not to promote growth or improve feed efficiency, and (2) only with veterinary oversight. *Id.* at 16-17. Like other FDA guidance documents, Draft Guidance No. 209 does "not establish legally enforceable responsibilities." *Id.* at 2.

69. In 2011, the Senate Committee on Appropriations recommended that "FDA examine medically important antimicrobial drugs currently approved for use in food-producing animals and take steps to assure that such products are aligned with current safety standards." S. Rep. No. 112-73, at 80 (2011).

Citizen Petitions Filed with FDA in 1999 and 2005

70. 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." Sorenson Decl. Ex. I, at 1-2.

71. 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 CDC and WHO 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. *Id.* at 9-25.

72. 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 $9.72 a year in higher costs for consumers. Sorenson Decl. Ex. I, at 33. The petition also pointed to the experiences of countries such as Sweden and Denmark, which have successfully eliminated some uses of antibiotics in livestock. *Id.* at 33-34.

73. 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)." Sorenson Decl. Ex. K, at 1. The petition covered penicillins, tetracyclines, aminoglycosides, streptogramins, macrolides, lincomycin, and sulfonamides. *Id.* It did not cover any uses of those drugs to treat disease in animals. *Id.* at 2.

74. 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. *Id.* at 10-16.

75. FDA has never issued a final response to either the 1999 or 2005 petition. Amended Complaint ¶ 87; Answer ¶ 87.

76. FDA issued tentative responses to the 1999 petition in 1999 and 2001. The second tentative response, dated February 28, 2001, acknowledged concern about "the role that antimicrobial drug use in food-producing animals plays in the emergence of antimicrobial drug resistant bacteria," and asserted that, "[t]o address these issues, the FDA is undertaking an extensive process to evaluate issues related to the use of antimicrobial drugs in both humans and animals, and to develop policies that protect public health." Sorenson Decl. Ex. J, at 3. The agency cited its efforts to develop guidance documents for industry. *Id.*

77. FDA issued a tentative response to the 2005 petition on October 4, 2005. The agency again recognized "the need to address concerns related to the role that antimicrobial drug use in food-producing animals plays in the emergence and selection of antimicrobial drug resistant bacteria," and explained that, "[t]o address these public health concerns, the FDA has developed a regulatory strategy that includes Guidance #152 . . . . Like all FDA guidance documents, Guidance #152 does not establish legally enforceable responsibilities." Sorenson Decl. Ex. L, at 2.

Dated: October 6, 2011

Respectfully submitted,

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