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PETITION

of the

NATURAL RESOURCES DEFENSE COUNCIL, INC.

to the

SECRETARY OF HEALTH AND HUMAN SERVICES

REQUESTING
IMMEDIATE SUSPENSION OF APPROVAL OF THE
SUBTHERAPEUTIC USE OF
PENICILLIN AND TETRACYCLINES
IN ANIMAL FEEDS

November 20, 1984

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The Natural Resources Defense Council, Inc. (NRDC) hereby petitions the Secretary of Health and Human Services to suspend immediately approval of the subtherapeutic use of penicillin and tetracyclines in animal feeds, pursuant to Section 512(e)(1) of the Food, Drug and Cosmetic Act, 21 U.S.C. § 360b(e)(1). This section of law authorizes the Secretary of Health and Human Services to suspend approval of an application for use of a new animal drug if "there is an imminent hazard" to the health of man or of the animals for which the drug is intended.

NRDC submits that an imminent hazard to the public health is posed by the subtherapeutic use of penicillin and tetracyclines in animal feeds. Recent studies have confirmed that (1) widespread use of subtherapeutic dosages of these drugs in animal feeds contributes to the development of bacterial resistance to these drugs and (2) the presence in the environment of strains of resistant bacteria to these antibiotic drugs poses a serious threat to the public health.

In 1977, the FDA initiated withdrawal proceedings with respect to its approval of the use of subtherapeutic doses of penicillin and tetracyclines in animal feeds. The withdrawal procedure was, however, held up by, among other things, Congressional advice to the FDA to postpone action until more conclusive studies were completed.

Recently, newly published studies which exist have conclusively confirmed that a serious public health threat exists. In light of these studies, FDA should renew its efforts to ban subtherapeutic

use of these drugs in animal feeds. In the meantime, suspension of approval, pending completion of administrative proceedings for withdrawal, should be ordered.

I. CRITERIA FOR SUSPENSION

The criteria the Secretary has proposed be used in determining whether an "imminent hazard" exists and, consequently, whether approval of a drug application should be suspended pending withdrawal proceedings are:

(A) The likelihood that, after the customary administrative process is completed, the product will be withdrawn from the market;

(B) The severity of the harm that could be caused by the product during the completion of customary administrative proceedings to withdraw the product from the market;

(C) The likelihood that the product will cause such harm while the administrative process is being completed;

(D) The risk to the health of humans or animals currently taking the product that might be occasioned by the immediate removal of the product from the market, taking into account the availability of alternatives to the product and the steps necessary for affected persons to adjust to these other alternatives; and

(E) The availability of other approaches to protect the public health.

44 Fed. Reg. 48,979 (to be codified at 21 C.F.R. §2.1) (proposed August 21, 1979) (proposed rule establishing imminent hazard criteria and procedure).

Similar criteria were employed by then-Secretary Joseph Califano in suspending approval of new human drug applications for phenormin hydrochloride. Order of the Secretary Suspending Approval, New Drug Application for Phenformin (July 25, 1977).

These criteria were upheld in the face of legal challenge. The district court for the District of Columbia, refusing to enjoin enforcement of the Phenformin suspension order, held that the Secretary's criteria properly reflected Congressional intent as to imminent hazard. Forsham v. Califano, 442 F. Supp. 203 (D.D.C. 1977), dismissed as moot per curiam, No. 77-1478 (D.C. Cir. 1979). The district court expressed approval of the Secretary's interpretation of imminent hazard, stating:

> [W]e are not inclined to adopt plaintiff's "crisis" interpretation of imminent hazard. Rather we are more persuaded by defendant's suggested analogy to cases interpreting the imminent hazard provisions of the Federal Insecticide, Fungicide and Rodenticide Act which caution "against any approach to the term imminent hazard...that restricts it to a concept of crisis" and adopt the view that "It is enough that there is substantial likelihood that serious harm will be experienced during any realistic projection of the administrative process." See Environmental Defense Fund v. EPA, 510 F.2d 1292, 1297 (1975); Environmental Defense Fund v. EPA, 465 F.2d 528, 540 (1972).

Id. at 208.

To justify invocation of the imminent hazard provision, what must be shown is that there is a substantial likelihood that serious harm would occur pending completion of normal administrative proceedings. The harm need not be immediate. Rather, consideration of the seriousness of the harm extends to "long-term effects that may be initiated during that period, the final anticipated injury from which occurs later." 44 Fed. Reg. at 48,981. The development of antibiotic-resistant strains of bacteria is just such a long-term effect. It is closely analogous to the long-term environmental contamination and carcinogenic risks caused by certain pesticides summarily suspended under the imminent hazard provision of the Federal

Insecticide, Fungicide and Rodenticide Act ("FIFRA"), 7 U.S.C. §136d(c). Several cases approving the application of the imminent hazard provision of that act, e.g., Environmental Defense Fund v. EPA, 510 F.2d 1292 (D.C. Cir. 1975) (aldrin/dieldrin), Environmental Defense Fund v. EPA, 548 F.2d 998 (D.C. Cir. 1976), cert. denied, 431 U.S. 925 (1977) (heptachlor/chlordane), are discussed as precedent in Secretary Califano's Order on phenformin and the proposed rule (44 Fed. Reg. at 48,981).

NRDC submits that the criteria for invoking the "imminent hazard" provision of the Food, Drug and Cosmetic Act, 21 U.S.C. § 360b(e)(1), have been met with respect to the subtherapeutic use of penicillin and tetracyclines in animal feeds. The reasons are set forth below.

II. APPLICATION OF CRITERIA

A. Likelihood of Withdrawal

The first criterion to be used in deciding whether an imminent hazard exists is the likelihood that FDA approval of the drug application will be withdrawn. 44 Fed. Reg. at 48,982. Section 360b(e)(1)(B) requires the FDA to withdraw approval of a new animal drug application when new evidence shows that the drug is not shown to be safe. Because new evidence clearly demonstrates that subtherapeutic use of penicillin and tetracyclines in animal feeds is not shown to be safe, there is a substantial likelihood that the FDA will withdraw its approval.

Indeed, in 1977, based on numerous studies demonstrating the health hazards associated with the subtherapeutic use of penicillin and tetracyclines in animal feeds, the FDA concluded that such use of these antibiotics had not been shown to be safe and proposed to withdraw its approval for such uses. 42 Fed. Reg. 43,772 (Aug. 30, 1977) (penicillin); 42 Fed. Reg. 56,264 (Oct. 21, 1977) (tetracyclines). Since 1977, additional scientific evidence has been gathered which demonstrates overwhelmingly the need for withdrawal.

what evidence

1. FDA Proposed Withdrawal and Findings, 1977

In 1977, based on data it had collected from independent studies and from the drug industry, the FDA found that the use of penicillin and tetracyclines in animal feeds posed a serious human health threat and initiated withdrawal proceedings. The Director of the FDA's Bureau of Veterinary Medicine (now the Center for Veterinary Medicine) presented a detailed analysis of the scientific evidence with respect to penicillin in the notice of opportunity for hearing. 42 Fed. Reg. 43,772 (August 30, 1977). In the summary, the Director concluded:

> Evidence demonstrates that the use of subtherapeutic levels of penicillin and other antibiotics in animal feed contributes to the increase in antibiotic resistant E. coli and in the subsequent transfer of this resistance to Salmonella. Further, many strains of E. Coli and Salmonella infect both man and animals.
>
> The holders of approved NADA's have submitted no evidence to demonstrate that the observed strains of E. Coli and Salmonella in man and animals are mutually exclusive; in fact, the evidence is overwhelming to the contrary. Furthermore, in some cases the R-plasmids as well as the resistance genes from human and animal sources are indistinguishable. Thus, the potential for harm exists, as illustrated by the studies submitted and verified by evidence

> from studies conducted by independent scientists. No evidence has been submitted by any NADA holder to resolve conclusively the safety questions raised by this potential...

42 Fed. Reg. at 43,775.

The Director concluded that subtherapeutic use of penicillin creates a selective pressure on bacteria in animals to develop strains resistant to penicllin and related anti-bacterial drugs. 42 Fed. Reg. at 43,776. These bacteria, present in the animals' systems, are released into the human environment, either through direct contact of humans with farm animal or their feces, or more likely through the presence of the bacteria in animal and dairy food products. 42 Fed. Reg. at 43,776-7.

The Director was further concerned that subtherapeutic use of penicillin in animal feeds might compromise the treatment of animal diseases with antibiotics. 42 Fed. Reg. at 43,787-8. The Director found that studies submitted by industry did not alleviate this concern or show the drug to be safe.

The Director found that subtherapeutic uses of tetracyclines in animal feeds produce effects similar to those produced by penicillin. 42 Fed. Reg. 56,264. The findings as to tetracycline are based on much of the same evidence as, and are substantially similar to those for penicillin. On the basis of these findings, FDA proposed to withdraw approval of most subtherapeutic uses of tetracyclines in animal feeds.

Neither the proposed withdrawal for penicillin nor tetracyclines became final.

2. Recent Scientific Evidence, 1982-1984

(a) O'Brien et al. Study

In 1982, Dr. Thomas O'Brien and his associates at Harvard Medical School reported a study of antibiotic-resistant Salmonella bacteria (Salmonella typhimurium var. copenhagen) taken from people and food animals in several states in the United States.[1] This study isolated from the bacteria the pieces of non-chromosomal genetic material called plasmids which carry antibiotic resistance. Using a new biochemical technique to analyze the plasmids' DNA structure, the O'Brien study could identify related bacterial strains by comparing DNA fragments from plasmids in different bacteria in a variety of host organisms.

The O'Brien study found that plasmids from bacteria obtained from humans were genetically related to plasmids in bacteria isolated from animals. In fact, certain plasmids found in bacteria in human and animals were virtually identical. The similarity between the strain of bacteria and its plasmids from humans and animals in this study provides very strong evidence that antibiotic-resistant bacteria are transmitted between animals and humans on a widespread basis.

The above study also found similar or identical plasmid in bacteria from humans in widely-dispersed geographic locations. They were all identical to a plasmid carried by a single widely dispersed Salmonella strain in animals. The appearance of

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1 O'Brien, et al., Molecular Epidemiology of Antibiotic Resistance in Salmonella from Animals and Human Beings in the United States, 307 New Eng. J. Med. 1 (1982).

similar plasmids in human bacteria in a variety of places among persons having no direct contact with food animals is strong support for the contention that these antibiotic-resistant bacteria are being transmitted from animals to humans through the food chain. The above finding can only be explained by multiple independent incidents of transfer of antibiotic-resistant strain Salmonella from animals to humans.

Do we agree?

(b) Holmberg et al. Study

In 1983, Dr. Scott Holmberg and his associates from the Centers for Disease Control in Atlanta conducted a study of 18 patients from four midwestern states who had contracted infections of Salmonella newport with identical plasmid profiles and multiple antibiotic resistance.[2] Holmberg and his associates concluded that the source of the Salmonella bacteria of all 18 patients was a single beef herd in South Dakota. The only human (six-state area) or animal (United States) isolate of this strain of Salmonella newport in the year before the outbreaks was from dairy cows on a South Dakota farm adjacent to a feedlot beef farm. Several of the 18 persons studied were known to have consumed beef directly from the herd and epidemiological evidence based on the distribution of the meat indicated that other patients also consumed beef which originated from the single feedlot beef farm. The beef herd had been fed subtherapeutic levels of chlortetracycline for over a year before the first human subject became ill.

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2 Holmberg, et al., Drug-Resistant Salmonella from Animals Fed Antimicrobials, 311 New Eng. J. Med. 617 (1984).

The Holmberg study has extraordinary significance for illustrating the risk to human health from the use of antimicrobials in animal feed. This is the first definitive study to directly link subtherapeutic use of antibiotics in animals to human disease and death (one of the 18 subjects in Holmberg's study died from Salmonella infection). The Holmberg study demonstrates that antimicrobial-resistant bacteria in animals can be transmitted to and colonize in humans. Before now, this contention was probably the most disputed of all the steps involved in establisning the human health risks associated with the feeding of antimicrobials to animals. 42 Fed. Reg. at 43,776.

Another important finding of the Holmberg study is the observation that many patients had been taking antibiotics for treatment of minor infections a few days prior to being hospitalized for salmonellosis. It is well-known that antibiotics can facilitate infection with resistant organisms because they inhibit sensitive bacterial flora of the host, enabling the invading resistant strains to gain a foothold and proliferate. Thus, individuals who harbor asymtomatic infection from antibiotic-resistant bacteria are at higher risk of gastrointestinal infection, since antibiotics are used commonly in therapeutic treatment for a variety of bacterial infections in the general population.

(c) Holmberg, Wells and Cohen Study

In a recently published paper,[3] Holmberg, Wells and Cohen of the Centers for Disease Control examined the origin and severity of antibiotic-resistant strains of bacteria responsible for 52 reported Salmonella outbreaks over a 12-year period. They report that multiple drug-resistant isolates have accounted for a steadily increasing percentage of human Salmonella infections and now represent approximately 20 to 30 percent of identified cases.[4] Because the increase of resistant bacteria is rapidly diminishing the effectiveness of doses for human use, there is a greater urgency for action to halt the proliferation of resistant bacteria. They reported, on the basis of epidemiological investigation, that of the 38 outbreaks of Salmonella infection from an identified source or mode of transmission, 69% of the resistant strains and 38% of the sensitive strains were of food-producing animal origin. The study also found that "[t]he case fatality rate for patients with identified infections with multiply resistant Salmonella was 4.2 percent, 21 times higher than the case fatality rate associated with antimicrobial-sensitive Salmonella infections."[5] The conjunction of the mortality rate for persons suffering from resistant Salmonella with the increasing frequency of resistant Salmonella make it urgent that action be taken to abate the spread of resistant bacteria.

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3 Holmberg, Wells and Cohen, Animal-to-Man Transmission of Antimicrobial-Resistant Salmonella: Investigations of U.S Outbreaks, 1971-1983, 225 Science 833 (1984).

4 Id.

5 Id.

3. Conclusion

There is overwhelming evidence to support withdrawal of subtherapeutic uses of penicillin and tetracyclines in animal feed. Therefore, the first criterion of suspension, the likelihood of withdrawal, is met.

B. Severity of Harm

The second criterion to be used in determining whether use of a drug constitutes an imminent hazard is the severity of the harm that could be caused by the product pending the completion of customary administrative proceedings to withdraw the product from the market.

On the basis of recent scientific evidence it can be established that hundreds of human deaths each year and several hundred deaths prior to the completion of withdrawal proceedings could result from subtherapeutic use of penicillin and the tetracyclines in animal feed.

It has been known for some time that subtherapeutic use of penicillin and tetracyclines in animal feed exerts selective pressure on animal bacterial populations, creating large reservoirs of strains of bacteria resistant to these and closely related antibiotics.[6] Salmonella bacteria resistant to one or more antibiotics are responsible for the majority of human deaths

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6 Sun, M., Use of Antibiotics in Animal Feed Challenged, 226 Science 144 (1984).

from Salmonella infection.[7] Dr. Holmberg's recent study shows that 69% of all multiply resistant Salmonella outbreaks in humans are traceable to animal sources, either animal-source food or live animals.[8] Given the selective pressure for the proliferation of resistant strains cited before, these findings clearly implicate subtherapeutic use of antibiotics in animal feed with human disease. In the discussion of likelihood of harm which follows, we discuss the number of deaths which could be associated with continued subtherapeutic use of these antibiotics in animal feed pending completion of withdrawal proceedings.

The less severe harm associated with nonfatal cases of infection with antibiotic-resistant strains of Salmonella should also be weighed in the imminent hazard determination. The resistance to antibiotics in these cases results in difficulty of treatment when indicated and consequently in longer duration of the illness and its symptoms. Further, there is evidence that treatment of other diseases with antibiotics may cause resistant Salmonella to predominate in an individual's system and result in the symptomatic expression of an otherwise asymptomatic infection.[9]

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7 Holmberg, supra, p. 10, 225 Science at 335.

8 Id. at 334.

9 Holmberg, supra p. 8, 311 New Eng. J. Med. 617.

C. Likelihood of Harm

The third component of the imminent hazard determination is the likelihood that the product will cause serious harm while the administrative process is being completed. The administrative process of withdrawal of the new animal drug approvals of penicillin and tetracyclines has already taken several years. Completion of this administrative process could take another three years.[10]

A preliminary risk analysis, outlined below, projects a mortality rate of between 100 and 300 deaths per year linked to subtherapeutic animal feed uses of penicillin and tetracyclines. In addition, over 2,700 reports of Salmonella cases and over 270,000 unreported cases of Salmonella infection may be associated on an annual basis with the use of penicillin and tetracyclines in animal feeds. These data demonstrate that there is a substantial likelihood of serious harm to the public health being caused while withdrawal proceedings are completed.

1. Estimated Annual Mortality Linked to Animals Fed Subtherapeutic Doses of Penicillin and Tetracyclines in Animal Feed

(a) Method 1

According to the Centers for Disease Control, approximately 40,000 cases of Salmonella infection in humans are reported each

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10 Letter from Alair Townsend, Assistant Secretary for Management and Budget, HHS, to Hon. Jamie I. Whitten, Chairman, House Committee on Appropriations (June 23, 1981).

year in the United States.[11] Since 20-30% of Salmonella strains isolated from humans are resistant to one or more antibiotics,[12] a conservative estimate of the number of cases due to resistant strains of Salmonella bacteria is 8,000 (20%). Of these, an estimated 336 cases may be fatal, assuming a 4.2% fatality rate for resistant Salmonella infections.[13] Since 69% of reported Salmonella outbreaks involving antibiotic-resistant strains are traceable to animal sources, of the estimated 336 deaths from resistant bacteria 69%, or 232, are attributable to resistant bacteria from animal sources. Penicillin and tetracyclines constitute approximately 50% of all antibiotics produced in the United States.[14] We can assume that a similar proportion of penicillin and tetracyclines is used in the livestock industry (although the percentage may in fact be higher) since approximately half the antibiotics produced in the United States is

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11 Personal communication with Scott D. Holmberg, M.D., Enteric Diseases Branch, Centers for Disease Control, Atlanta, Georgia. This estimate is supported by the figure of 35,625 cases reported in 1981, up 10,000 from ten years earlier, reported by Riley, Importance of Host Factors in Human Salmonellosis Caused by Multiresistant Strains of Salmonella, 149 J. of Infectious Diseases at 878 (1980).

12 Holmberg, supra p.10, 225 Science at 833.

13 Id.

14 Personal communication with Edward Capeuchelli, Energy and Chemical Division, U.S. Trade Commission, Washington, D.C. In 1982, penicillin (9,507,000 lbs) and tetracycline (7,243,000 lbs) accounted for a total of 51.5% of the 32,518,000 lbs. of antibiotics produced in the U.S.

used in the animal livestock industry.[15] Next, since subtherapeutic antibiotic use constitutes most of all antibiotic use for animals, we assume that this use is responsible for virtually all antibiotic resistance among animal bacterial populations.[16] Thus, if half the resistant strains of Salmonella from animal sources have emerged under the selective pressure of subtherapeutic use of penicillin and tetracyclines, it is estimated that 116 (0.5 x 232) Salmonella deaths each year are associated with subtherapeutic use of these antibiotics.

(b) Method 2

An alternative method of risk estimate is based on the actual mortality incidence from Salmonella infections. According to statistics compiled by the Centers for Disease Control, between 1,000 and 1,500 deaths each year are associated with Salmonella outbreaks in the United States.[17] The recent Holmberg, et al., study indicates that 76.5% of all fatal

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15 National Academy of Sciences, The Effects on Human Health of Subtherapeutic Use of Antimicrobials in Animal Feeds 7-8 (1980).

16 The remaining use of antibiotics in animals is for therapeutic treatment which is episodic in nature and of limited duration. It is reasonable to assume that such use does not contribute significantly, if at all, to the longterm, sustained development of antibiotic-resistant bacterial strains in animals.

17 Private communication with Scott D. Holmberg, M.D., Enteric Diseases Branch, Centers for Disease Control, Atlanta, Ga.

Salmonella infections are associated with resistant bacteria.[18] Application of this percentage to the lower estimate of 1,000 Salmonella fatalities per year gives an estimate of 756 deaths per year from resistant strains of Salmonella. As in the first method of analysis, the number of fatal resistant infections traceable to animal sources is estimated based on the finding that 69% of multiply resistant Salmonella outbreaks are traceable to animal sources, giving a figure of 528 deaths per year. As in the previous analysis, it is assumed that penicillin and tetracyclines constitute 50% of the antibiotics used subtherapeutically in animal feed and that virtually all antibiotic-resistant strains of Salmonella of animal origin are linked to subtherapeutic use of antibiotics in animal feed. Thus, an estimated one-half of the 528 fatalities from infections by resistant strains result from subtherapeutic use of penicillin and tetracyclines, or 264 deaths per year.

2. Estimated Annual Morbidity Linked to Animals Fed Subtherapeutic Doses of Penicillin and Tetracyclines in Animal Feed

Resistant strains of bacteria emerging in animal populations given subtherapeutic amounts of penicillin and tetracyclines in animal feed could be responsible for an estimated 270,000 non-fatal cases of Salmonella each year. In these 270,000 cases the

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18 Holmberg, supra p. 10, 225 Science 833-834. Holmberg found 13 deaths from 312 Salmonella cases associated with resistant bacteria and 4 deaths from 1,912 Salmonella cases associated with sensitive strains. Thus, out of a total of 2,224 cases, 13 out of 17 deaths, or 76.5% were associated with resistant Salmonella strains.

resistance of the bacteria to antibiotic treatment may increase the duration of the illness and its symptoms. This estimate is arrived at by means of the following analysis. Approximately 40,000 cases of Salmonella bacterial infection are reported each year.[19] An estimated 20% of these cases, or 8,000 cases, are infections by resistant strains of bacteria.[20] Of these estimated 8,000 reported cases of infection by resistant Salmonella, 69% or 5,520, can be attributed to animal sources, and 50% or 2,760, of these are attributed to bacterial strains whose resistance is a result of subtherapeutic use of penicillin and tetracyclines in animal feeds.[21] Since only approximately 1% of all cases of Salmonella infection are clinically reported,[22] the 2,760 figure is multiplied by one hundred, giving an estimate of over 270,000 cases of non-fatal salmonellosis each year due to strains whose resistance is associated with the subtherapeutic use of penicillin and tetracyclines in animal feeds.

D. Risk To Human or Animal Health of Suspending Subtherapeutic Uses of Penicillin and Tetracyclines in Animal Feeds

The fourth criterion used in deciding whether an imminent hazard exists is the risk to the health of humans or animals that would result from the immediate removal of the drug. No significant risk would be associated with suspending approval of

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19 Supra, p. 13.

20 Supra, p. 14.

21 Id.

22 Private communication with Scott D. Holmberg, M.D., Enteric Branch, Centers for Disease Control, Atlanta, GA.

subtherapeutic uses of penicillin and tetracyclines in animal feed. No potential health risks to humans have been discussed in the literature. The health risk to animals can be greatly minimized, or even eliminated, by use of substitute antibiotics and better farming practices.

1. Risks to Animal Health

It has been claimed that subtherapeutic doses of antibiotics are fed to farm animals in order to (1) prevent disease outbreaks among livestock, (2) increase feed efficiency (weight gain per unit of food) and (3) promote growth.[23]

Withdrawing subtherapeutic uses of penicillin and tetracyclines would serve to eliminate these intended benefits. Decreased feed efficiency and slower growth are purely economic effects. They pose no health risks to the animals. The sole health risk to animals, then, is the hypothetical increased likelihood of disease. This risk is not severe, since diseased animals, whether or not they are already receiving low levels of antibiotics, are typically treated with therapeutic doses of antibiotics. NRDC is not advocating a ban on treatment of actual disease with antibiotics. Additionally, it is increasingly recognized by the livestock industry that antibiotics at any dose level do not treat infection caused by resistant organisms.

Two effective alternatives exist to minimize the incidence of illness among farm animals. The first and simplest alterna-

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23 Office of Technology Assessment, U.S. Congress, Drugs in Livestock Feed, Vol. I: Technical Rept. 5 (1979).

tive is for farmers to substitute other antibiotics for penicillin and tetracyclines in animal feeds. Alternative antibiotics currently used in animal feeds include bacitracin, nitrofurazone, banbermycin, novobiocin, monensin, tylosin and others.[24]

Though some have argued that the substitutes for penicillin and tetracyclines are not as effective, there is substantial evidence that they are effective. For example, tylosin and bacitracin are considered excellent substitutes for tetracyclines and penicillin in swine, chicken and turkeys.[25] In the case of pork and beef, tylosin and bacitracin are considered viable substitutes.[26]

Another method of reducing the incidence of disease in farm animals would involve altering farming practices. Intensive farming practice confines animals, usually with very little room for each animal, for most or all of their lives, and rigidly controls their diet, thereby altering their physical and behavioral characteristics. The confinement and crowding creates a great deal of stress for animals, and this stress increases the risk of disease. Since the animals are so crowded, disease spreads quickly. Many farmers who practice this type of animal

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24 Report of the Comptroller General of the United States, U.S. General Accounting Office: Need To Establish Safety And Effectiveness of Antibiotics Used In Animal Feeds 4 (1977). Haysten, I. et al., Effect of Banbermycin and Tylosin on Performance of Growing-Finishing Swine, 50 J. Animal Sciences 484 (1980).

25 Headley, J.C., Economic Aspects of Drug and Chemical Additives, p. 30, paper commissioned for OTA study, supra, p. 18.

26 Id.

husbandry may feel that it is necessary to administer subtherapeutic doses of antibiotics in order to counteract these disease-producing and disease-spreading influences. Even so, death losses have increased due to confinement systems, at least in hog farming,[27] and this can often be attributed to bacterial resistance to antibiotics being used in a futile attempt to control infections.

Non-intensively farmed animals are not confined as much, may have access to the outdoors and are weaned later. Each of these practices lessens the stress on the animals. This type of farming is relatively low cost, since the farmer need not buy the expensive facilities and equipment needed by the confinement farmer.[28]

Finally, unsanitary conditions cause the animals to be even more stressed, and antibiotic need is, therefore, greater. Only a small number of farms may actually have these conditions, but there is concern that some use of antibiotics may be covering up for bad practices.[29] In these cases, better sanitation could minimize the animal health risk posed by removal of antibiotics.

For farms with less intensive animal-raising practices and good management, subtherapeutic levels of antibiotics may not be

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27 Statement of Charles Henry Hassebrook, Center for Rural Affairs, Walthill, Nebraska, before the House Committee on Interstate and Foreign Commerce, Subcommittee on Health and the Environment, Serial No. 96-169, June 12 and 24, 1980.

28 Id.

29 Green, Feed Additives: A Crutch for Poor Management? Feedstuffs, Feb. 18, 1980, 36.

necessary. If they can still decrease the extent of disease, then effective substitutes for penicillin and tetracyclines are available. NRDC is, therefore, convinced that there is no significant health risk to animals associated with banning subtherapeutic doses of penicillin and tetracyclines from animal feed. On the contrary, there is a positive benefit, since if the animals should become ill, there is at least the chance of treating them if the causative agent is a sensitive bacterial strain.

In conclusion, the risk to animal health from suspension is not as severe nor as important as the human health risk from continued application of these antibiotics in animal feed.

2. Risks To Human Health

NRDC has found no evidence or even suggestions in the medical and public health literature that withdrawal of penicillin and tetracyclines from subtherapeutic uses in animal feeds would result in risks to human health. The only effect on humans would be economic. A number of studies have modelled production and prices of meat if various combinations of antibiotics are banned from animal feed. Results indicate that economic losses to consumers will be felt mostly in the first few

years of a ban[30] and that, over the longer term, use of existing alternatives to these antibiotics would substantially mitigate the economic effects on consumers.[31]

Since the average citizen consumes almost three times the amount of meat per year that the U.S. Department of Agriculture considers necessary to meet nutritional standards,[32] the difference of a few less pounds of meat or a few extra dollars per year per person cannot be considered a human health risk. Economic hardship may be felt by the low-income members of society, but no evidence suggests that this presents a health problem, given the fact that most food prices will not be affected by a ban, and the impact of slightly nigher meat prices is, for the most part, temporary.

A conceivable risk to human health could be that of eating meat from an animal which became ill as a result of withdrawing subtherapeutic use of penicillin and tetracyclines. First, using alternate antibiotics and improved farming practices, a farmer can control disease in the great majority of animals. If an animal does become ill, the farmer can treat the animal with therapeutic doses of antibiotics, a standard practice whose effectiveness would actually be increased by the proposed ban.

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30 U.S. Dept. of Agriculture, Economic Effects of a Prohibition on the Use of Selected Animal Drugs 2 (1978).

31 Headley, supra p. 19, at 30-31.

32 Council for Agricultural Science and Technology, Antibiotics in Animal Feeds 34 (1981).

E. The Availability of Other Approaches to Protect the Public Health

The fifth and final criterion for a finding of imminent hazard is the lack of other suitable approaches to protect the public.

NRDC has found no mention in the literature of effective alternatives, or, indeed, any alternatives to protect the public health other than a ban on subtherapeutic uses of penicillin and tetracyclines in animal feed. While the only conceivable possibility would be an extensive public education campaign on careful food and meat handling, this approach presents a number of difficulties. First, developing and implementing a large-scale education program would be more time consuming and less effective than an immediate ban in preventing unnecesary deaths and illness. Second, antibiotic-resistant bacteria, like other bacteria, can be transferred from animals to humans without the humans having direct contact with the animals. Humans can contract bacteria from utensils and kitchen counters that were at one point in contact with the animal or its by-products, such as the raw meat. Therefore, even careful handling of meat would be unlikely to eliminate completely the risk of bacterial transfer from animals to humans. Finally, a public education program would be expensive and resource-intensive, cancelling out some of the economic arguments against banning subtherapeutic uses of penicillin and tetracyclines in animal feed. NRDC concludes that a public education campaign would be an unsatisfactory option, leaving no alternative to a ban.

III. CONCLUSION

In view of the likelihood that FDA will utlimately withdraw approval, the severe harm that is likely to occur pending completion of withdrawal proceedings, the insignificant risk to human or animal health from suspension and the lack of effective alternatives to protect the public health, NRDC respectfully requests that you act immediately to suspend approval of subtherapeutic use of penicillin and tetracyclines in animal feeds.

Respectfully submitted,

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The undersigned certify that, to the best of their knowledge and belief, this petition includes all data and information on which the petition relies, and that it includes representative data and information known to the petitioners that are unfavorable to the petition.

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