UPDATE – Antibiotics

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In my presentation, I'd like to provide an update on the recent issues concerning the use of subtherapeutic antibiotics in animal feeds. Part of the presentation will be devoted to a discussion of the scientific and regulatory history of the use of penicillin and tetracyclines in animal feeds and the rest will be devoted to the renewed public concern over illegal residues in meat.

In 1949, Dr. Thomas Jukes discovered that feeding the fermentation products from antibiotic production caused chicks and pigs to grow faster. Soon the addition of low levels of antibiotics in animal feeds was common practice. Today it is a major use of antibiotics. It is estimated that from 40% to 48% of all antibiotics produced in the U.S. are fed to animals. Manufacturers continue to invest up to 7.5 years and $15 million in the development of a new feed antibiotic. The total market for antibiotics in animal feeds is estimated at more than $290 million a year.

Shortly after the discovery and use of antibiotics, scientists learned that bacteria could develop resistance to them. Not only could this resistance be passed down through generations of bacteria, but the resistance could be passed between different kinds of bacteria. The genes which code for resistance are located on little pieces of DNA called R-plasmids. The R-plasmids can transfer between types of bacteria because they are not located in the nucleus of the bacteria, but rather float freely in the body of the bacteria. The significance is that bacteria can become resistant to antibiotics they've never been exposed to or to more than one antibiotic at a time.

Scientists and medical experts recognized this characteristic of bacteria as presenting a problem in the direct treatment of human disease with antibiotics. Some scientists believe, however, that the subtherapeutic use of antibiotics in food animals adds a theoretical risk to public health by allowing humans to come in contact with resistant bacteria.

The theoretical risk has two scenarios:

1. That resistant, pathogenic animal bacteria will infect humans and cause disease;
2. That resistant animal bacteria will pass their R-plasmids to human pathogenic bacteria.

Public health concern over the possible risk involved in the use of antibiotics in food animals was stimulated in 1965 in Great Britain. There, an outbreak of salmonella in dairy calves spread to humans. The outbreak lasted several years with thousands of animal deaths and seven human fatalities. In the process of trying to treat sick animals, the salmonella strain became resistant to eight different drugs. This led to the now-famous Swann Committee and its report. Contrary to popular opinion, the Swann report did not call for the "ban" of subtherapeutic use of all antibiotics, only those used in human medicine. These products, however, could be used at therapeutic levels under a veterinary prescription.

In the wake of the British action, FDA, in 1970, established a task force to study the use of antibiotics in animal feeds. The task force suggested that restrictions be placed on products that could not meet certain guidelines for safety and efficacy. FDA regulations, now in effect, specify that a product used in feed for longer than two weeks must meet certain criteria relating to the antibiotic's ability to cause the emergence of resistant bacteria and the effects of that resistant strain. Manufacturers of penicillin and the tetracyclines were required to submit data on their products. FDA felt that the data submitted did not meet the safety criteria and the Commissioner called for additional review. Notices of opportunity for hearing were published on proposals to ban the subtherapeutic use of penicillin and severely restrict tetracyclines in feed.

At this point Congress stepped in. The scientific community was divided as to whether the use of subtherapeutic antibiotics presented a health risk. Congress directed FDA to contract with the National Academy of Sciences to study the issue and mandated that FDA proceed no further with the proposals to withdraw the approvals for penicillin and tetracyclines until the study had been completed. While the NAS stated that the proper studies needed to provide definitive proof of a hazard may not be possible to perform, it did suggest certain types of studies that may provide some more clues. These studies included comparisons between vegetarians and non-vegetarians, studies of abbatoir workers, etc.

The research that FDS eventually contracted for was an epidemiological study performed at the Seattle-King County Hospital. The study consisted of two parts. In the first, the hospital conducted a detailed survey of the cases of salmonella and campylobacter enteritis diagnosed in members of a Seattle group health association. In the second part, the hospital sampled food (red meat and poultry) to determine bacterial contamination. The study found that campylobacter enteritis was responsible for over ⅔ of the enteritis cases and that the bacterium is a common contaminant.

Public attention to the issue intensified when a report by Dr. Scott Holmberg et al. from the Centers for Disease Control was published in the September 6, 1984 *New England Journal of Medicine*. The report purported to prove the link between the subtherapeutic use of antibiotics and illness

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in humans. Eighteen people in four states became ill with a drug-resistant strain of salmonella that had the same plasmid profile, or fingerprint, as a strain found in a dairy calf on a farm next to a feedlot in South Dakota. The study attempted to show a connection between hamburger produced from the cattle at the South Dakota feedlot and the eighteen salmonella cases.

After the release of the Holmberg report, the Natural Resources Defense Council filed an Imminent Hazard Petition with HHS. On January 2, 1985, at the request of HHS Secretary Heckler, FDA held a hearing to gather evidence. The petition asked for an immediate ban on the subtherapeutic uses of penicillin and the tetracyclines in animal feeds. Representatives of the product manufacturers, the Animal Health Institute, consumer groups, animal rights activists, food animal producers and independent scientists testified. Our understanding is that the FDA Commissioner is in the process of making his recommendation to Mrs. Heckler. It is possible that she will announce her decision by this fall.

As a result of the media attention generated by this controversy, the agricultural animal producer groups reviewed their positions on the feeding of antibiotics to animals.

In general, the producer groups feel that subtherapeutic antibiotics are useful and needed tools of production and that no hard scientific evidence exists to indicate a hazard to the public health. The National Cattlemen's Association, however, departed slightly from this common stand when, on April 19, 1985, it recommended to its members that they discontinue low-level, continuous feeding of tetracyclines for growth promotion and feed efficiency. NCA emphasized that this decision was made to prevent erosion of consumer confidence in the safety and wholesomeness of beef, not because the association felt there was a question of safety of these products. In conjunction with this announcement, NCA strongly urged FDA to make a decision on the issue.

AHI has also called on the U.S. Food and Drug Administration to complete its review of the available scientific data and issue a statement that will reassure both livestock producers and the consuming public. AHI knows of no scientific data that demonstrate a hazard to human health resulting from the low-level administration of antibiotics to livestock.

The whole debate, of course, hinges on the existence of a human health risk. Toward this end, several pharmaceutical companies have joined together to fund studies similar to those suggested by the National Academy of Science in 1980. Two of the studies, one in Boston, the other in California, are comparing the type of gut flora and resistance patterns found in vegetarians and non-vegetarians. The people participating in the studies were chosen so that any differences found in their gut flora can be attributed to the presence or absence of meat in their diet. The third study compares the types and resistance patterns of bacteria in urinary tract infections of slaughterhouse workers with bacteria from the animals. This study is trying to determine if constant, direct exposure to resistant bacteria of animal origin would have any effect on the bacteria involved in human urinary infections. The studies are proceeding very well and results are expected in the third quarter of this year.

If the FDA administrative procedures necessary to ban or restrict subtherapeutic pencillin and tetracyclines were to proceed, Congress may not be willing to wait for protracted FDA hearings. Thus, it is possible, though unlikely, that Congress will force a decision sooner. Congressman James Weaver (D-OR) has already introduced a bill in the House of Representatives which would ban the subtherapeutic use of antibiotics certified for human use and ban the subtherapeutic use of any antibiotic if it was shown to select for cross-resistance to any antibiotic certified for human use. It is possible Congressman Berkley Bedell (D-IA) will hold a Congressional hearing this fall on the use of antibiotics in animal feeds.

Illegal Residues

I'd like to discuss now the problem of illegal residues in meat. In 1977, the Food Safety and Inspection Service (FSIS) uncovered a very high incidence of illegal antibiotic residues in several species of animals presented for slaughter. For instance, the rate in swine was 13%. The residues in swine and bob veal calves were primarily sulfas. The swine residues were coming from the carry-over of powdered sulfas in mixing equipment and the veal calf residues were coming from the use of sulfa boluses immediately prior to slaughter.

USDA's FSIS and the Extension Service (ES) signed a joint agreement in 1978 to study the problem and find solutions. Part of that effort was a massive educational program for producers to help them implement management practices to prevent illegal residues. As part of this program, the Residue Avoidance Program Task Force was formed. The task force was made up of representatives of several branches of USDA, the Center for Veterinary Medicine at FDA and the various producer groups. These groups helped plan the educational program and, to a large extent, were responsible for dissemination of the material.

One of the group's accomplishments is the development of the Food Animal Residue Avoidance Database or FARAD. The purpose of the database is to make information on food animal residue avoidance available to the people most in need of it – producers, veterinarians or extension agents. The database is organized to help professionals provide information to producers that will help them prevent residue problems and correct any that may arise.

Following the implementation of the education program and FARAD, the level of illegal residues dropped significantly. Much of this drop was attributed to producer awareness of the problem and the use of the USDA-developed screening tests such as the Calf Antibiotic Sulfa Test or CAST, the Sulfa Swab Test or SST, or the Swab Test on Premises or STOP test. By 1981, the incidence of illegal sulfa residues in swine dropped to 5% overall and to 2% in some states.

Unfortunately, in the last few months, USDA has seen the rate of violative residues rise. Their response has been, in the case of bob-veal calves, to issue an interim rule to intensify in-plant testing procedures for detecting violative residues and provide for a voluntary certification program for veal producers. The interim rule requires that a certain number of calves from each lot must be tested for violative residues, using the CAST test. Under the certification pro-

gram, the producer certifies that his calves have not been treated with antibiotics, or, if they have, that the proper withdrawal period has passed. Up to three calves in each certified lot will be given the CAST test to verify the certification. Should any of the certified calves test positive, all subsequent calves from that producer must be tested.

In the case of swine, the Food Safety Inspection Service published a "notice of intent to institute proposed rulemaking" on May 20, 1985. In a plan outlined in the publication, the in-plant inspector will randomly select one or two lots of swine to be retained and tested. The proposed rule also sets forth various methods of disposing of violative carcasses. It leaves open the possibility for a voluntary certification program for swine, similar to the veal program.

AHI has for years worked closely with USDA's Food Safety Inspection Service and the producer groups to promote proper drug use. Each year we send news kits to more than 250 magazine editors. The kits contain feature stories on proper drug use and public service ads which we ask editors to insert in their magazines. In a recent survey of editors, of those responding, 86 percent told us they use our information in their publications.

In this very brief report, I've tried to update you on some of the scientific and regulatory challenges facing the meat industry. Concern has been expressed about public health aspects from the feeding of subtherapeutic levels of penicillin and the tetracyclines. The Department of Health and Human Services will make a determination about the use of these products. The Department of Agriculture has expressed its concern over the recent increase in illegal residues of sulfas. It plans to begin rulemaking to create an impetus for reduction of these illegal residues. None of these problems are easy to solve and we can expect the public debate on these issues to go for some time.