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HEARING TO REVIEW THE ADVANCES OF ANIMAL HEALTH WITHIN THE LIVESTOCK INDUSTRY

HEARING

BEFORE THE

SUBCOMMITTEE ON
LIVESTOCK, DAIRY, AND POULTRY

OF THE

COMMITTEE ON AGRICULTURE
HOUSE OF REPRESENTATIVES

ONE HUNDRED TENTH CONGRESS

SECOND SESSION

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HEARING TO REVIEW THE ADVANCES OF ANIMAL HEALTH WITHIN THE LIVESTOCK INDUSTRY

THURSDAY, SEPTEMBER 25, 2008

HOUSE OF REPRESENTATIVES,
SUBCOMMITTEE ON LIVESTOCK, DAIRY, AND POULTRY,
COMMITTEE ON AGRICULTURE,
Washington, D.C.

The Subcommittee met, pursuant to call, at 10:04 a.m., in Room 1300 of the Longworth House Office Building, Hon. Leonard L. Boswell [Chairman of the Subcommittee] presiding.

Members present: Representatives Boswell, Kagen, Baca, Peterson (*ex officio*), Hayes, Foxx, Smith, and Goodlatte (*ex officio*).

Staff present: Adam Durand, Alejandra Gonzalez-Arias, Chandler Goule, John Konya, John Riley, April Slayton, Rebekah Solem, John Goldberg, Pam Miller, and Jamie Weyer.

OPENING STATEMENT OF HON. LEONARD L. BOSWELL, A REPRESENTATIVE IN CONGRESS FROM IOWA

The CHAIRMAN. The hearing of the Subcommittee on Livestock, Dairy, and Poultry to review the advances of animal health within the livestock industry will come to order.

I appreciate you all being here and I first want to welcome you and thank you for joining us today to discuss a very important issue to rural America and food security across the country. A special thanks to our witnesses for appearing before the Subcommittee today, particularly from my territory, not that everybody is not equally as important of course. But, I want to call attention to Mr. Blair Van Zetten and Dr. Craig Rowles, here not only to represent their respective industries but my home state. Thank you very much for taking the time to come.

Having spent most of my life involved in animal agriculture, and knowing the responsibility of using antibiotics, which I think all farmers do, I understand many of the issues that affect the industry firsthand. I spent most of my youth working in some aspect of livestock production, but when I left the Army and moved back to Iowa to be in farming again, I sat down with a local veterinarian that some of you may know, Dr. McElroy. We discussed the use of antibiotics to treat sick animals, prevent illness and to preserve the health of those animals. As I discussed my experience with producers and veterinarians, I learned this is not the exception but it is the rule that I find that all producers live by. We understand that it is something that is a very useful tool, but we have to use

it carefully, and we have to use it according to the expectations of how to handle those antibiotics. For over 40 years, the U.S. animal agriculture industry has used FDA-approved drugs to ensure we have healthy animals because healthy animals produce healthy food.

Also, I would like to take a moment to highlight very important programs for safe and efficient drug use, the Food Animal Residue Avoidance Databank, known as FARAD, and the Animal Drug User Fee Act, ADUFA. FARAD is a program that has a computer-based decision-support system which provides producers and veterinarians with practical information on how to avoid antibiotic residues in food. FARAD helps protect our food supply yet continually struggles for funding. In Fiscal Year 2008, FARAD received no funding, and this year is in danger of shutting down completely. Ranking Member Hayes and I sent a letter to both USDA and the FDA, in July, regarding this critical issue, and I wanted to once again stress the importance of getting this program funded.

I was pleased this year when Congress passed ADUFA, which also plays a vital role in maintaining a healthy animal agricultural industry. This critical program supports continued improvements of FDA's review program and assists FDA in a timely drug approval process.

I must be cautious when people outside the industry talk about banning antibiotic use in livestock. I believe we must follow a science-based process to ensure that unintended consequences do not put human health at risk. I think a compelling example of this is the Denmark case where the removal of antibiotics for health maintenance or growth purposes resulted not only in the use of more antibiotics to treat animal disease, but also increased animal death and disease. Antibiotic use in livestock has been a hot topic of discussion for years, and this year is no exception.

In recent months, both sides of the Hill have held various hearings over this subject. Today it is my hope that consumers can put their faith in science-based evidence that the use of antibiotics in animal agriculture not only gives us healthy animals but also a safe food supply.

Once again, I would like to thank everyone for joining us here today.

[The prepared statement of Mr. Boswell follows:]

PREPARED STATEMENT OF HON. LEONARD L. BOSWELL, A REPRESENTATIVE IN CONGRESS FROM IOWA

Good morning, I would like to thank everyone for joining us today to discuss a very important issue to rural America and food security across the country. A special thanks to our witness for appearing before the Subcommittee today, particularly Mr. Blair Van Zetten and Dr. Craig Rowles who are here not only to represent their respective industries but also the great State of Iowa.

Having spent most my life involved in animal agriculture and responsibly using antibiotics, I understand many of the issues that affect the industry first hand. I spent most of my youth working in some aspect of livestock production but when I retired from the Army and moved back to Iowa to begin farming I sat down with the local veterinarian—Doc McElroy. We discussed the use of antibiotics to treat sick animals, prevent illness, and to preserve the health of those animals. As I have discussed my experience with producers and veterinarians I learned this is not the exception but the rule.

For over 40 years the U.S. animal agriculture industry has used FDA approved drugs to ensure we have healthy animals. Because healthy animals produce healthy food.

I also would like to take a moment to highlight two very important programs for safe and efficient drug use—the Food Animal Residue Avoidance Databank (FARAD) and the Animal Drug User Fee Act (ADUFA).

FARAD is a program that has a computer-based decision-support system which provides producers and veterinarians with practical information on how to avoid antibiotic residues in food. FARAD helps protect our food supply yet continually struggles for funding. In Fiscal Year 2008, FARAD received no funding and this year is in danger of shutting down completely. Ranking Member Hayes and I sent a letter to both USDA and FDA, in July, regarding this critical issue and I wanted to once again stress the importance of getting this program funding. I was please this year when Congress passed ADUFA, which also plays a vital role in maintaining a health animal agriculture industry. This critical program supports continued improvements of FDA's review program and assists FDA in a timely drug approval process.

I must be cautious when people outside the industry talk about banning antibiotic use in livestock. I believe we must follow a science-based process to ensure that unintended consequences do not put human health at risk. I think a compelling example of this is the Denmark case where the removal of antibiotics for health maintenance or growth purposes resulted not only in the use of more antibiotics to treat animal diseases but also increased animal death and disease.

Antibiotic use in livestock has been a hot topic of discussion for years and this year is no exception. In recent months both sides of the Hill have held various hearings over this subject. Today, it is my hope that consumers can put their faith in science-backed evidence that the use of antibiotics in animal agriculture not only gives us healthy animals but also a safe food supply.

Once again, I would like to thank everyone for joining us here today. At this time I would like to recognize my Ranking Member and good friend Robin Hayes from North Carolina for any opening remarks he would like to make.

The CHAIRMAN. At this time I would like to recognize my Ranking Member and my good friend, Robin Hayes from North Carolina, for any opening remarks that he would like to make. Mr. Hayes.

OPENING STATEMENT OF HON. ROBIN HAYES, A REPRESENTATIVE IN CONGRESS FROM NORTH CAROLINA

Mr. HAYES. Thank you, Mr. Chairman, and you are a good friend and a trusted advisor. I had my sausage yesterday and not today, so I may not be at my peak.

The CHAIRMAN. Oh, okay.

Mr. HAYES. Thank you, Mr. Chairman, for holding this hearing relating to the use of antibiotics in animal agriculture. Agricultural use of antibiotics has received quite a bit of press lately. Unfortunately, the press coverage has not provided the full picture on the issue. It has not given adequate attention to the factual information surrounding the use of antibiotics for animal agriculture, and why it is so important that farmers have the ability to administer antibiotics to their livestock. The veterinary community, as well as farmers and ranchers, can attest to the fact that banning antibiotics will impose substantial cost on producers and provide no quantifiable public health benefit. Farmers have an economic incentive to keep their herd healthy. Obviously, livestock farmers would be discriminating in the frequency and quantity of the antibiotics they administer to prevent the adulteration of their product. At the same time, judicious use of antibiotics is necessary for both prevention and treatment of disease.

One example of how a ban on antibiotics in animal agriculture can negatively impact the health of livestock is the instance that you referred to in Denmark. I won't go into detail. I will insert that

in the record. You are looking at increased death and disease in herds, a 135 percent increase in the amount of antibiotics used to treat animal disease between 1996 and 2005. Denmark is now using more antibiotics for treatment as a result of banning its use for prevention. There is no evidence that we are aware of to demonstrate that the decline in antibiotic resistance in humans is a result of the ban. The net result of the ban is an increase in disease and death in swine herds that discontinued use. Yet there is no evidence to suggest this ban resulted in a reduction of resistance.

Mr. Chairman, many of our colleagues simply have no understanding of the challenges confronting animal agriculture. For them it would seem to be an easy decision to vote for legislation that imposes arbitrary restrictions on food producers under the mistaken assumption that they are helping address concerns in human medicine. Based on the Danish experiments and the balance of today's testimony, I think we can fairly conclude they would be mistaken.

I appreciate you holding the hearing, and I might also add that our purpose is to confirm and reaffirm the quality and safety of the American livestock industry's product. This hearing will create additional oversight but also insight by exchanging ideas, experiences and results of stringent testing and evaluation. So I thank our witnesses and I thank our Chairman. Let us proceed.

[The prepared statement of Mr. Hayes follows:]

PREPARED STATEMENT OF HON. ROBIN HAYES, A REPRESENTATIVE IN CONGRESS FROM NORTH CAROLINA

Thank you, Mr. Chairman, for holding this hearing relating to the use of antibiotics in animal agriculture. Agricultural usage of antibiotics has received quite a bit of press lately. Unfortunately, the press coverage has not provided the full picture on this issue. It has not given adequate attention to the factual information surrounding the use of antibiotics for animal agriculture, and why it is so important that farmers have the ability to administer antibiotics to their livestock.

The veterinary community, as well as farmers and ranchers, can attest to the fact that banning antibiotics will impose substantial costs on producers and provide no quantifiable public health benefit.

Farmers have an economic incentive to keep their herd healthy. Obviously, livestock farmers would be discriminating in the frequency and quantity of the antibiotics they administer to prevent the adulteration of their product. At the same time, the judicious use of antibiotics is necessary for both the prevention and treatment of disease.

One example of how a ban on antibiotics in animal agriculture can negatively impact the health of livestock happened in Denmark.

* * * * *

In the late 1990s, Denmark instituted a voluntary ban on the use of antibiotics for growth promotion in feed; a compulsory ban was initiated in 2000. Since then the pork industry in Denmark, which has about the same number of swine as the State of Iowa, bas experienced the following as a result of this ban:

- Increased death and disease in the swine herds.
- 135% increase in the amount of antibiotics used to *treat* animal disease between 1996 and 2005. So, Denmark is now using more antibiotics for *treatment* as result of banning its use for *prevention*.
- Overall mixed results. Resistance to some antibiotics has decreased, while resistance to others has increased.
- And, there is no evidence that we're aware of to demonstrate a decline in antibiotic resistance in humans as a result of this ban.

The net result of the ban is an increase in disease and death in the swine herds that discontinued use. Yet, there is no evidence to suggest that this ban resulted in a reduction of antibiotic resistance patterns in humans.

* * * * *

Mr. Chairman, many of our colleagues simply have no understanding of the challenges confronting animal agriculture. For them, it would seem to be an easy decision to vote for legislation that imposes arbitrary restrictions on food producers under the mistaken assumption that they are helping address concerns in human medicine.

Based on the Danish experiment and the balance of today's testimony I think we can fairly conclude that they would be mistaken. I appreciate your holding this hearing so that we can all make this point on the record. I yield back.

The CHAIRMAN. Thank you, Mr. Hayes, and thank you for being here. We are going to follow the normal routine, move on to witnesses and welcome any statements that Members want to put into the record. Also, you will be recognized when we get to question time.

[The prepared statements of Mr. Peterson and Mrs. Boyda follow:]

PREPARED STATEMENT OF HON. COLLIN C. PETERSON, A REPRESENTATIVE IN CONGRESS FROM MINNESOTA

First, I want to thank Chairman Boswell for holding this hearing. I also want to recognize two of the witnesses who have Minnesota ties. Dr. Randall Singer is a Professor of Epidemiology at the University of Minnesota's College of Veterinary Medicine and Dr. Christine Hoang, who is here on behalf of the American Veterinary Medical Association, graduated from the University. Thanks to both of you and to all of our witnesses here today.

The livestock industry faces numerous challenges in today's market. Energy and other input prices are squeezing producers. Local, state and Federal regulations and requirements impose all kind of restrictions on their operations. Producers are being blamed by some for increasing antibiotic resistance in humans because they treat their animals with antibiotics.

Like so many issues, the problem of antibiotic resistance is complicated, and there is not a single cause or simple solution. Without a doubt, antibiotic resistance is a serious public health problem, and we need to be sure that we take responsible steps to address it.

The responsible use of antibiotics in animal agriculture decreases mortality rates and disease and increases food safety. The overuse of antibiotics, on the other hand, is clearly not acceptable. Professional associations and industry leaders in animal agriculture must lead in the development of best management practices and guidelines for responsible antibiotic use in livestock, and in educating producers about those practices. I am looking forward to hearing from those groups testifying here today about their education and outreach efforts on this issue and the results they are seeing among producers.

There are some who would like to blame antibiotic resistance in humans on animal agriculture. I want to be clear that banning antibiotics from animal agriculture will have serious consequences and will not solve the problems we are seeing with antibiotic resistance. Without antibiotics, the supply of meat, poultry, dairy and eggs would decline at a time when demand for these products around the world is on the rise. In addition, banning antibiotics in animal agriculture will increase consumers' exposure to pathogens that cause foodborne illnesses and at the same time will increase food costs.

I hope that in the testimony presented here today, we can get a better understanding of where we are in terms of antibiotic resistance in human as well as animal health. I appreciate Dr. Clifford from USDA and Dr. Dunham from FDA for joining us. This is an important issue, and we need to know what the facts are and what the implications would be if we severely restricted or banned the use of antibiotics in animal agriculture.

Chairman Boswell, thank you again for holding this hearing, and I look forward to the testimony from our witnesses.

PREPARED STATEMENT OF HON. NANCY E. BOYDA, A REPRESENTATIVE IN CONGRESS FROM KANSAS

Chairman Boswell and Ranking Member Hayes, thank you for holding this hearing to review animal health. I appreciate the Committee addressing a subject so important to the Second District of Kansas.

Although I am not a Member of the Subcommittee, I wanted to share my support for continued oversight and research into animal research. In particular, more research is needed into the link or lack thereof between antibiotics in animal feed and resistance to antibiotics in humans.

I'd also like to take this opportunity to highlight the important research occurring in Kansas and Missouri and encourage support for H. Res. 829, which recognizes the region from Manhattan, Kansas, to Columbia, Missouri, as the Kansas City Animal Health Corridor. The Animal Health Corridor is home to 45 companies involved in the animal health industry; more than 120 companies involved in the animal health industry are located in Kansas and Missouri, including four of the ten largest global animal health companies and one of the five largest animal nutrition companies.

Several leading veterinary colleges and animal research centers are located in Kansas and Missouri, including the College of Veterinary Medicine and the $54,000,000 Biosecurity Research Institute of Kansas State University and the College of Veterinary Medicine, the College of Agriculture, Food and Natural Resources' Division of Animal Sciences, the $60,000,000 Life Sciences Center, the National Swine Resource and Research Center, and the Research Animal Diagnostic Laboratory of the University of Missouri. Additionally, more than 45 percent of the fed cattle in the United States, 40 percent of the hogs produced, and 20 percent of the beef cows and calves are located within 350 miles of Kansas City. H. Res. 829 would highlight the research taking place in Kansas and Missouri, and encourage more companies to relocate to the area.

Thank you again for allowing me the opportunity to address the Subcommittee.

The CHAIRMAN. We will start with our first panel, and I think we will recognize Dr. Clifford first and then Dr. Dunham. Dr. John Clifford, Doctor of Veterinary Medicine, is the Deputy Administrator, Animal and Plant Health Inspection, U.S. Department of Agriculture, Washington, D.C. So Dr. Clifford, please begin when you are ready, and thank you for your presence.

STATEMENT OF JOHN CLIFFORD, D.V.M., DEPUTY ADMINISTRATOR FOR VETERINARY SERVICES AND CHIEF VETERINARIAN, ANIMAL AND PLANT HEALTH INSPECTION SERVICE, U.S. DEPARTMENT OF AGRICULTURE, WASHINGTON, D.C.; ACCOMPANIED BY ROB HEDBERG, ACTING DIRECTOR, LEGISLATIVE AND GOVERNMENTAL AFFAIRS, COOPERATIVE STATE RESEARCH, EDUCATION, AND EXTENSION SERVICE, U.S. DEPARTMENT OF AGRICULTURE

Dr. CLIFFORD. Thank you, Mr. Chairman. My name is John Clifford. I am the Deputy Administrator for Veterinary Services with the Department of Agriculture's Animal and Plant Health Inspection Service, or APHIS. Thank you for this opportunity to testify before you.

My agency's role in advancing livestock health is multifaceted. At any given time, APHIS is working to safeguard the health of U.S. livestock against foreign animal diseases, eradicate and control diseases that exist in the United States, and conduct surveillance related to issues affecting animal health. Important advances have been realized in all of these areas in recent years to the benefit of the U.S. livestock industry. This morning I would like to highlight for you APHIS's emergency planning and response efforts, the bru-

cellosis program and our efforts related to the use of antibiotics in livestock.

As USDA's Chief Veterinary Officer, I believe one of the most important ways of protecting and advancing livestock health is to ensure that we have a strong system in place to safeguard against animal diseases. Foreign animal disease incursions and other animal health emergencies can have a major impact on America. For example, studies have projected that an outbreak of foot-and-mouth disease contained in California could cost between $6 billion and $14 billion.

The U.S. response to animal health emergencies involves a partnership between Federal, state and industry cooperators. In support of this effort, APHIS develops emergency response plans, operates the nation's repository of vaccines, personal protective equipment and other critical supplies and equipment, and provides laboratory and diagnostic services. Written response plans have been developed and tested for the most dangerous animal diseases that pose a risk to U.S. agriculture including highly pathogenic avian influenza and foot-and-mouth disease. Since its establishment in 2000, the National Animal Health Emergency Response Corps has deployed over 500 volunteers to assist Federal and state responders during animal health emergencies and our National Animal Health Laboratory Network continues to grow with a current total of 58 laboratories in 45 states. All the above preparations have us well positioned to safeguard livestock in the United States.

In the event that a disease of concern is introduced or has existed in the United States, APHIS works with the livestock industry and states to eradicate and control the disease. One of APHIS's longstanding programs is our brucellosis program. This program has been highly effective, and in 1956 we had 124,000 affected herds in the United States as a result of testing. By 1992, that number had dropped to 700. As of today, there are only two known affected domestic cattle herds remaining in the entire United States. Also, annual brucellosis-related losses due to aborted fetuses, reduced breeding efficiency and lowered milk production had decreased from more than $400 million in 1952 to almost zero today.

In addition to safeguarding against diseases that affect livestock health, APHIS also collaborates with other Federal agencies and the livestock industry to conduct surveillance and collect data related to animal health issues such as the use of antibiotics in livestock. One of these cooperative efforts is the National Antimicrobial Resistance Monitoring System, or NARMS. The NARMS was established in 1996 by USDA, the Department of Health and Human Services, as well as other cooperators. That system provides data on the prevalence of antibiotic resistance in animals, humans and retail foods. APHIS contributes by providing isolates from clinically ill animals and isolates from healthy animals on farms. For example, APHIS in collaboration with the U.S. Department of Agriculture's Agricultural Research Service collects samples to be cultured for bacteria, which are subsequently evaluated for antimicrobial drug resistance as part of the NARMS.

In 2003, APHIS, ARS and USDA's Food Safety Inspection Service undertook a pilot project that was designed to complement

NARMS. This pilot project was the Collaboration in Animal Health and Food Safety Epidemiology and it was established to examine bacterial resistance to antimicrobial drugs on farms and to evaluate the potential for resistant organisms to persist in food products from the animals under study. The project was concluded in 2005.

In closing, I believe we will continue to see advances within animal health and the livestock industry. Partnerships with the livestock industry, states and other stakeholders will continue to be critical in realizing advances in our livestock industry.

Thank you for the opportunity to testify this morning, and I will be pleased to answer any of your questions.

[The prepared statement of Dr. Clifford follows:]

PREPARED STATEMENT OF JOHN CLIFFORD, D.V.M., DEPUTY ADMINISTRATOR FOR VETERINARY SERVICES AND CHIEF VETERINARIAN, ANIMAL AND PLANT HEALTH INSPECTION SERVICE, U.S. DEPARTMENT OF AGRICULTURE, WASHINGTON, D.C.

Chairman Boswell, Ranking Member Hayes, thank you for the opportunity to testify before the Committee this morning. My name is Dr. John Clifford and I am the Deputy Administrator for Veterinary Services with the Department of Agriculture's (USDA) Animal and Plant Health Inspection Service (APHIS). In this position, I also serve as USDA's Chief Veterinary Officer.

Today, the Committee is looking at an important issue—advances of animal health within the livestock industry. We at USDA are actively engaged in developing and utilizing innovative methods to provide leadership on food, agriculture, natural resources, and related issues based on sound public policy, the best available science, and efficient management.

In furtherance of this mission, APHIS is the agency within USDA responsible for protecting and promoting U.S. agricultural health, administering the Animal Welfare Act, and carrying out wildlife damage management activities. Within APHIS, Veterinary Services protects and improves the health, productivity, quality, and marketability of animals, animal products, and veterinary biologics in the United States. Partnerships with the livestock industry, as well as other global and domestic stakeholders, are critical in accomplishing this mission.

At any given time, my agency is working on multiple priorities in order to ensure the health of our nation's domestic animal resources. These priorities include safeguarding against foreign animal diseases, emergency planning and preparedness, animal disease eradication and control, and monitoring and surveillance for animal diseases. I am very pleased to provide the following outline of some of the advances that have been realized in these important areas.

Foreign Animal Diseases

While I am going to look broadly at several components of USDA's programs that assist in advancing livestock health, including several of those that look at the use of antibiotics in production practices, I want to start with an area that is critical to me as the Chief Veterinary Officer. In my mind, one of the most important ways of protecting and advancing livestock health is to ensure we have a strong system for preventing and responding to animal diseases.

Foreign animal diseases (FAD) represent an ongoing threat to human health and to the health of the U.S. agricultural industry. We expect that these diseases will continue to be of major concern because of increased trade and increased movement of people, animals, and pathogens. This fiscal year, we expect U.S. agriculture exports to reach approximately $114 billion, making it the highest export sales in a 12 month period ever in our history. U.S. agriculture imports are rising as well—increasing from nearly $58 billion in 2005 to an estimated $79 billion this fiscal year. APHIS works diligently with state animal health officials and veterinary professionals to protect U.S. agriculture from the introduction of animal diseases and to identify, control, and eradicate animal diseases and diminish their impact.

Efforts to detect FAD events in the United States include surveillance in disease-specific programs, reporting by producers and private veterinarians, and field investigations conducted by specially trained Federal, state, and private accredited veterinarians. Additional detection efforts include state diagnostic laboratory surveillance, in which routine cases that are subsequently considered "suspicious" for FADs are reported to Federal and state animal health authorities for further investigation.

Early identification and quick response in the FAD investigations are critical steps to ensuring that any further spread is minimized.

Several important events have occurred globally over the last few years involving foreign animal diseases, including foot-and-mouth disease (FMD) and exotic Newcastle disease. A few of these events have highlighted the importance of our emergency preparedness and response capabilities. Most recently, highly pathogenic avian influenza (HPAI) subtype H5N1 virus has captured global attention as a potential human and animal health threat.

Preventing, preparing for, and responding to potential outbreaks of avian influenza (AI) require collaboration on the broadest scale. Successfully protecting avian health depends on our ability to work together effectively—across all levels of government, with private industry and the public, and around the world. This includes working with the World Organization for Animal Health (OIE), which sets international standards concerning diseases that affect human and animal health, the United Nations' Food and Agriculture Organization (FAO) and World Health Organization (WHO).

Internationally, we are collaborating with a variety of partners to control, and eradicate HPAI in those countries where it currently exists, and to prevent its introduction into the United States and other areas. For example, APHIS works with its partners to identify reservoirs of the disease and develop biosecurity recommendations for farmers; conduct intensive diagnostic training sessions to expand international diagnostic resources; and offer funding, technical expertise, and equipment to countries affected by or at risk for HPAI.

On the domestic front, APHIS has partnered with other Federal and state agencies and the commercial poultry industry in conducting surveillance efforts for AI for many years. APHIS implemented strategies to strengthen existing AI surveillance where necessary in 2006, and continued the enhanced surveillance efforts in 2007. We also increased our AI preparedness by refining our response plans and strengthening existing core programs in 2007.

Because of heightened animal- and public-health concerns, the poultry industry and state and Federal animal-health regulatory agencies are continuing efforts to increase biosecurity measures and conduct extensive surveillance for HPAI, as well as certain subtypes of low pathogenic avian influenza (LPAI), in commercial poultry, live-bird markets, and poultry raised in non-confinement operations. The H5 and H7 subtypes of LPAI are of concern because they have the potential to mutate into highly pathogenic forms. This is why we established regulations for a new monitoring and control program for the H5 and H7 subtypes for LPAI in 2006.

In addition, in partnership with the U.S. Department of the Interior's U.S. Geological Survey and U.S. Fish and Wildlife Service, APHIS' Wildlife Services program monitors wild birds for AI. Bird banding data are used in conjunction with U.S. Census of Agriculture data to rank counties with a high prevalence of domestic poultry production and relatively high numbers of migrant waterfowl to identify areas of critical concern and overlap between commercial poultry production and concentrations of migratory waterfowl.

We at APHIS are proud of the success of our AI prevention efforts to date. And it is worth reminding ourselves that, in addition to routinely addressing outbreaks of LPAI, the United States has effectively eradicated outbreaks of HPAI in three past instances, in 1924, 1983, and 2004.

Emergency Planning and Preparedness

Foreign animal disease incursions, as well as other animal health emergencies, can have a major impact on America's infrastructure, animal and public health, food safety, economy, and export markets. For example, an outbreak of FMD in the United States could have significant economic impacts. There are many susceptible animals in the United States, including 96 million cattle, 61 million swine, and almost nine million sheep and goats. The 2001 outbreak in the United Kingdom cost an estimated £8 billion ($13 billion) and reduced the British gross domestic product by 0.2 percent. Studies have projected a cost of between $6 and $14 billion for a U.S. outbreak contained to California. The impact comes primarily from lost international trade, followed by costs directly associated with the eradication effort including the expenses of depopulation, indemnity, carcass disposal, and cleaning and disinfecting. In addition there are direct and indirect costs related to lost production, unemployment, and losses in related businesses.

APHIS' Veterinary Services (VS) program is charged with preventing animal health emergencies in the United States, rapidly detecting such emergencies should they occur, and responding effectively to control or eradicate them.

The U.S. emergency response to animal health emergencies involves a partnership between various Federal, state, tribal, local, industry, and other private-sector co-

operators. Written response plans and guidelines address all areas of an emergency response, such as the initial field investigation; local disease control and eradication activities; emergency management, including line of command, planning, logistics, and resources; and interagency coordination. Written response plans have been developed for the most dangerous animal diseases that pose a risk to U.S. agriculture, including HPAI and foot-and-mouth disease.

Disease outbreaks throughout the past several years have demonstrated the critical need for surge capacity personnel during an animal health emergency. In 2000, APHIS created the National Animal Health Emergency Response Corps (NAHERC) to provide a volunteer reserve of veterinary professionals to assist Federal and state responders during an animal health emergency. In 2001, 145 NAHERC members deployed to the FMD outbreak in the United Kingdom. In 2003, 340 NAHERC personnel assisted in the exotic Newcastle disease outbreak in California and 71 NAHERC personnel responded to a LPAI outbreak in Virginia. Their efforts were critical in protecting the nation's livestock from these diseases.

During an emergency, APHIS is responsible for rapidly deploying critical veterinary supplies and personal protective equipment for workers from the National Veterinary Stockpile (NVS). The NVS was established in February 2004 through Homeland Security Presidential Directive—9 (HSPD–9). HSPD–9 reflects concerns that terrorists could simultaneously, and in multiple locations, release catastrophic animal diseases. The mission of the NVS is to deliver critical veterinary supplies nationwide within 24 hours.

In 2007, the NVS continued expanding its capabilities. It acquired personal protective equipment and antiviral medications against AI to protect 3,000 responders, portable vaccine storage containers for field use, emergency air and ground transportation contracts to ensure deployment within 24 hours, and satellite phones to provide reliable emergency voice and data communications, anywhere, anytime. It also established commercial partnerships with all-hazard response companies to provide large numbers of trained, experienced personnel with equipment to help states depopulate, dispose, and decontaminate if they do not have enough of their own personnel. Looking forward, the NVS is working with the Department of Homeland Security to acquire next-generation FMD vaccines and to quickly deliver current vaccines should an FMD emergency occur.

Laboratory and diagnostic services are an essential component of the U.S. emergency response to animal health emergencies. The National Animal Health Laboratory Network (NAHLN) is part of a national strategy to coordinate the activities of Federal, state, and university laboratories providing critical animal disease surveillance and testing. The NAHLN is a cooperative effort between two U.S. Department of Agriculture (USDA) agencies—APHIS and a portion of the Cooperative State Research, Education, and Extension Service's (CSREES) Integrated Activities program—and the American Association of Veterinary Laboratory Diagnosticians.

The USDA Homeland Security Office established the NAHLN as part of a national strategy to coordinate and link the testing capacities of the Federal veterinary diagnostic laboratories with the extensive infrastructure (facilities, professional expertise, testing capacity, and support) of state and university veterinary diagnostic laboratories. This network enhances the nation's early detection of, response to, and recovery from animal health emergencies, including emerging diseases and FADs that threaten the nation's food supply and public health.

In 2002, APHIS and CSREES initiated the network by entering into cooperative agreements with 12 state and university veterinary diagnostic laboratories. These were funded by the Department of Homeland Security. APHIS now contracts with 54 state and university diagnostic laboratories to assist with testing and surveillance; the number of NAHLN facilities totals 58 laboratories in 45 states, which includes those 54 laboratories plus the National Veterinary Services Laboratories (NVSL), the Department of the Interior (DOI) laboratory in Madison, WI; and the Food Safety and Inspection Service (FSIS) laboratory in Athens, GA. All of the above preparations have us well positioned to respond to animal health emergencies and to safeguard the animal health in the United States.

Animal Disease Eradication and Control Programs

In the event diseases are introduced or have existed in the United States, a key component of APHIS' VS program is its role in eradicating, controlling, or preventing diseases that threaten the biological and commercial health of U.S. livestock and poultry industries. Diseases targeted in VS eradication programs include scrapie in sheep and goats, tuberculosis in cattle and cervids, pseudorabies and brucellosis in swine, and brucellosis in cattle and bison.

APHIS' animal disease control and eradication programs generally include many of the same features. The programs center on regulatory measures that include, for

example, quarantines to stop the movement of possibly infected or exposed animals; the establishment of state statuses, including regions or zones located therein that allow us to fight infection while enabling commerce to continue; testing and examination to detect infection; destruction of infected (sometimes exposed) animals to prevent further disease spread; treatment to eliminate parasites; vaccination in some cases; and cleaning and disinfection of contaminated premises. Advancements in these program areas have come through exhaustive work with states and industry over the years. There have been successes in several key eradication programs.

Pseudorabies

One eradication program that has seen significant advances over the years is the pseudorabies program. Pseudorabies emerged as an economically important disease of swine in the late 1960s. After a virulent strain of pseudorabies virus (PRV) caused concentrated outbreaks in the Midwest in the 1970s, the Livestock Conservation Institute (now the National Institute for Animal Agriculture) set up a task force in the 1980s that defined two state stages and established the National Pseudorabies Control Board to oversee and determine the status of each state. In 1989, APHIS published the program standards for a plan to eradicate pseudorabies from commercial swine production by 2000. By 1999, the U.S. infection rate was down to less than one percent of all swine herds (about 1,000 herds), and the Accelerated Pseudorabies Eradication Program was established to remove the last infected domestic commercial herds through depopulation by the end of 2004, but accomplished this by early 2003.

Conducted in cooperation with state governments and swine producers, the National Pseudorabies Eradication Program eliminated pseudorabies from domestic commercial herds in all states, Puerto Rico, and the U.S. Virgin Islands by the end of 2004. As documented in the Pseudorabies Program Standards, program measures are based on prevention, vaccination (now largely discontinued), disease surveillance, and eradication. Primary program activities include surveillance, herd certification, and herd cleanup.

Currently, there are no known domestic production swine herds infected with PRV in the United States. Nationally, 18 transitional herds, which are any herds with pigs that were exposed to feral or wild pigs, were disclosed through surveillance as infected with PRV during FY 2007. All herds were depopulated promptly. Complete epidemiologic investigations of all cases disclosed no evidence that infection had spread from the infected transitional herds to any contact herds. Extensive surveillance activities over the past 3 years also suggest that no commercial production farms have been infected.

A comprehensive surveillance plan for PRV, specifically for rapidly detecting PRV introduction into commercial swine, was completed in 2007. Although pseudorabies has been eradicated from commercial production swine, it is still endemic in feral swine and can be found occasionally in transitional swine herds. The distribution of feral swine continues to expand, with an estimated three million to four million feral swine now located in at least 35 states. Therefore, surveillance for PRV continues to be a priority for APHIS, particularly with respect to addressing the new challenge of wildlife disease reservoirs in feral swine populations. This prioritization of pseudorabies is consistent with the sense of Congress in the Food, Conservation, and Energy Act of 2008 (P.L. 110–246, 122 Stat. 1651) that pseudorabies eradication is a high priority the Secretary of Agriculture should carry out under the Animal Health Protection Act (7 U.S.C. 8301 *et seq.*).

Brucellosis

Another animal disease eradication program that I would like to highlight for you is the brucellosis program. USDA has been working with state and industry cooperators to eradicate brucellosis for many years. The disease affects numerous species of animals, including humans, and is caused by the bacteria *Brucella abortus*. Cattle, bison, and elk are especially susceptible to the disease.

The Brucellosis Eradication Program was launched on a national scale in 1934, and a cooperative effort among the Federal Government, states, and livestock producers began in 1954. All states participate in APHIS' Cooperative State-Federal Brucellosis Eradication Program and are assigned a brucellosis classification by APHIS. These classifications—Class Free, Class A, Class B, and Class C—are based on herd prevalence rates for the disease and require various levels of movement restrictions and surveillance activities. Most importantly to cattle producers, restrictions on moving cattle interstate become less stringent as a state approaches or achieves Class Free classification.

The program has been highly effective. In 1956, 124,000 affected herds were found in the United States as a result of testing. By 1992, this number had dropped to

700, and as of today, there are only four known affected domestic cattle or bison herds remaining in the entire United States. Currently, 49 states, Puerto Rico, and the U.S. Virgin Islands are considered free of brucellosis. Montana is the last remaining Class A status state. I am also pleased to report that annual brucellosis-related losses due to aborted fetuses, reduced breeding efficiency, and lowered milk production have decreased from more than $400 million in 1952 to almost zero today.

The Greater Yellowstone Area (GYA), which encompasses approximately 20 million acres in three states, is the last known reservoir of brucellosis in wild elk and bison in the United States. While management of the disease is our approach for the near term, our long term goal is to eliminate brucellosis from GYA wildlife, along with protecting the elk and bison populations from the disease. I should note that brucellosis in elk is widespread across the entire GYA, and indications are that all disease transmissions from wildlife to cattle in the GYA have come from elk. Transmission can occur through direct contact between infected elk or bison and non-infected cattle if they are allowed to co-mingle. Approximately 90 percent of GYA elk fall under state jurisdiction during the summer season.

Surveillance testing of wild bison from the Yellowstone herd indicates that approximately 50 percent of the bison in the 2 million acre Park have been exposed to and are potentially infected with the disease. This disease reservoir poses a risk to cattle that graze on lands adjacent to the Park.

APHIS works with the GYA States, the cattle industry, and the National Park Service to address the risk of brucellosis transmission from wildlife leaving the Park to cattle that graze in surrounding areas. Our sister agency within USDA, the U.S. Forest Service, also plays a key role in managing the public lands on the Gallatin National Forest, adjacent to Yellowstone National Park in Montana. The current Interagency Bison Management Plan carefully balances the need to preserve the Yellowstone bison herd with the need to prevent the spread of brucellosis from bison to cattle.

USDA and the Department of the Interior (DOI) believe the next step is to develop a long-term plan for the elimination of brucellosis from the GYA. USDA and DOI have agreed to a draft a Greater Yellowstone Interagency Brucellosis Committee (GYIBC) Memorandum of Understanding and have forwarded it to the Governors of Idaho, Montana, and Idaho for their review and signature.

Monitoring and Surveillance for Diseases That Affect Production and Marketing

A key role of APHIS is the monitoring and surveillance for diseases of major impact on animal production and marketing. This includes monitoring animal health and production trends; facilitating the use of new technologies for early and rapid disease detection, response, and data analysis; and capturing, analyzing, interpreting, and disseminating data using standardized methods.

National Animal Identification System (NAIS)

One of our more recently developed technologies for swift and effective disease response is the National Animal Identification System, or NAIS. NAIS is a modern, streamlined information system that helps producers and animal health officials respond quickly and effectively to animal disease events in the United States. from the beginning, NAIS has been a cooperative effort among states, APHIS, and industry.

There are three components of NAIS—premises registration, animal identification, and animal tracing. Through NAIS, APHIS' ultimate, long-term goal is to have the capacity to identify all premises and animals that have had contact with a FAD or domestic animal disease of concern within 48 hours after its discovery.

Our initial focus in developing NAIS has been to encourage farmers and ranchers to register their premises. Registering premises provides animal health officials with the key information needed to conduct disease investigations quickly and efficiently. To date, more than 482,000 premises had been registered within the states, tribes and territories. This total represents more than 34 percent of the estimated number of premises nationwide. Thanks to the support and outreach efforts of our state and industry partners, NAIS continues to build momentum.

APHIS is also working to accelerate participation in the animal-identification component of the system. In terms of animal tracing, we've established 14 state and private databases to keep track of animal movements. We've also developed a system that will allow authorized state and Federal animal health officials to request information from these databases during an animal disease event.

By working together with the public and with our partners, we will continue to increase our ability to respond to animal diseases and guarantee that we are successful in protecting the health and marketability of American agriculture.

Data Collection and Other Activities Related to the Use of Antibiotics in Livestock

Another area where APHIS, along with other agencies with the USDA, has contributed to advances in the livestock industry is in the collection of data related to animal health issues using standardized methods. Over the past several years, one such issue that has captured national attention is the use of antibiotics in livestock.

As you may know, several Federal agencies have in place programs to learn more about, track, and reduce antimicrobial resistance in animals. Many of these activities are joint activities among several Federal agencies and are supported by the agricultural industries. In fact, in 1999, the U.S. Interagency Task Force on Antimicrobial Resistance was created to develop a national plan to combat antimicrobial resistance. The Task Force is co-chaired by the Centers for Disease Control and Prevention, the Food and Drug Administration (FDA), and the National Institutes of Health and also includes USDA, the Agency for Healthcare Research and Quality, the Health Care Financing Administration, the Health Resources and Services Administration, the Department of Defense, the Department of Veterans Affairs, and the Environmental Protection Agency. Within USDA, agencies that have contributed to the Task Force activities include APHIS, the Agricultural Research Service (ARS), the Food Safety and Inspection Service (FSIS), and CSREES.

The first is surveillance. In 1996, HHS and USDA, in cooperation with several state and local health departments, established the National Antimicrobial Resistance Monitoring System—NARMS. The goal of the system is to provide data on the prevalence of antibiotic resistance in animals, humans, and retail foods. This monitoring system has been operating for about 10 years and has provided critical information on emerging resistance trends. USDA supports NARMS through three of its agencies. FSIS contributes isolates from its regulatory program for *Salmonella* and isolates of *Campylobacter* from its microbiological baseline data collection surveys. APHIS contributes isolates from clinically ill animals and isolates from healthy animals on farms. And, ARS conducts all testing and analysis of isolates collected by USDA. The impact of NARMS has been to assist the FDA in regulatory decision making on animal antimicrobial drugs, practitioners on prudent use practices, and commodity organizations on quality improvement.

In addition, APHIS has been collecting an increasing amount of data on production practices and samples containing bacteria that have been used to evaluate levels and impacts of antimicrobial use on livestock operations throughout the United States. This data and the samples are collected through the National Animal Health Monitoring System (NAHMS), which conducts national studies on the health and health management of United States domestic livestock and poultry populations. Bacterial isolates gathered via NAHMS have been tested for antibiotic resistance and included in the NARMS. The data collected yielded information on, among other things, the types of antimicrobials used to treat various common diseases in animal populations, how producers decide to treat and what to treat with, how antimicrobial drugs are delivered to the animals (via feed, water, or parenterally), and primary influencers on the antimicrobial drug decision-making process. All of these factors are critical to understanding the ways to optimize antimicrobial drug use in animal populations.

APHIS, in collaboration with ARS, has also been collecting samples to be cultured for bacteria as part of the NAHMS program, which are subsequently evaluated for antimicrobial drug resistance as part of the NARMS program. These studies provide information on the extent of antimicrobial drug resistance among potential foodborne pathogens and commensal organisms in livestock populations. Such information is critical to risk assessments that evaluate the potential for transfer of the resistant organism or resistance determinants through the food chain. To date, the NAHMS program has collected antimicrobial drug use and antimicrobial drug resistance data from 11 studies conducted between 1994 and 2008.

Finally, in 2003, APHIS, ARS, and FSIS undertook a pilot project that was designed to complement the NARMS and the NAHMS. The mission of the Collaboration in Animal Health and Food Safety Epidemiology (CAHFSE) was to monitor bacterial resistance to antimicrobial drugs on farms over time and to evaluate the potential for resistant organisms to persist in food products from animals from the farms under study. Health and health management data were collected on the same operations where repeated samples were collected over time. The CAHFSE project was concluded in 2005.

In addition to the data collection and surveillance activities that we are involved in, I would also like to mention two additional activities that other USDA agencies

participate in with respect to the use of antibiotics in livestock: (1) Research and (2) prevention and control.

In terms of research, ARS conducts hypothesis-driven research on various topics relevant to use of antibiotics in livestock. This includes research on the mechanisms of resistance development and transfer of resistance genes; the potential mitigation for resistance alternatives for antibiotic use in livestock; and alternatives to antibiotics for subtherapeutic use and potential interventions for foodborne pathogens that could affect resistance development. ARS also develops technologies for the detection and characterization of antibiotic resistance genes in foodborne pathogens, such as *Salmonella, Campylobacter,* and *E. coli.*

In addition to ARS' research, a growing segment of CSREES' directed funding had been dedicated to research on antimicrobial resistance. from 1999–2008 there have been over thirty research, education and extension competitive grants funded by CSREES in the area of antibiotic resistance. The competitive grants, totaling over $17 million, were funded primarily through the National Integrated Food Safety Initiative, the National Research Initiative's (NRI) Epidemiological Approaches for Food Safety, and the NRI Microbiological Approaches for Food Safety; three flagship competitive grant programs administered by CSREES. These grants were funded at various land grant universities, professional societies, and other 4 year universities throughout the country. The research focuses on a variety of foodborne pathogens as they relate to antimicrobial/antibiotic resistance including *Listeria monocytogenes, Salmonella, E. coli, E. coli O157:H7,* and *Campylobacter*. Many of these studies are ongoing.

Prevention and control is an area of emphasis within USDA, both domestically and internationally. On the domestic front, I would like to highlight that, while the FDA regulates the use of drugs given to food animals—including determining what drugs are permitted, what they can be used for, and setting the tolerance levels for those drugs in food animal tissues—FSIS is responsible for verifying the tolerance levels for antibiotics set forth by FDA. To accomplish this, FSIS collects samples of meat, poultry, and egg products at federally-inspected establishments and analyzes these samples at FSIS laboratories for chemical residues of veterinary drugs, among other things.

Since 1967, FSIS has administered the National Residue Program (NRP) to collect data on chemical residues in domestic and imported meat, poultry, and egg products. The NRP is designed to provide a structured process for identifying and evaluating compounds of concern by production class, statistical analyses of compounds of concern, appropriate regulatory follow-up of reports of violative tissue residues, and collection, analyses, and reporting of the results of these activities. When a violation of tolerance levels is found, FSIS notifies FDA of the violation and assist in obtaining the names of producers and other parties involved in offering animals for sale.

Internationally, USDA has also taken an active role in the development of harmonized approaches and guidance on the use of antibiotics. For example, representatives from the USDA, including ARS and FSIS, are part of the ad hoc Intergovernmental Task Force on Antimicrobial Resistance that was established by the twenty-ninth Session of the Codex Alimentarius Commission. Its mandate is to develop science-based guidance, taking full account of its risk analysis principles and the work and standards of other relevant international organizations, such as FAO, WHO, and OIE. The intent of this guidance is to assess the risks to human health associated with the presence in food and feed including aquaculture and the transmission through food and feed of antimicrobial resistant microorganisms and antimicrobial resistance genes and to develop appropriate risk management advice based on that assessment to reduce such risk. The first session of the Task Force was held in October 2007. The session was very productive and resulted in the development of three project documents on risk assessment, risk management and risk profiling based upon project proposals submitted in response to the Circular Letter request for proposals for new work. The next session is scheduled for this fall.

Conclusion

As the comments above indicate, we have made tremendous progress in collaborating with our partners in the U.S. Government and industry that have a stake in protecting public and animal health. Expanding current partnerships with the livestock industry, as well as other global and domestic stakeholders, will continue to be critical in realizing advances of animal health within the livestock industry and ensuring the health of our nation's domestic animal resources.

The CHAIRMAN. Well, thank you, Dr. Clifford, and I think we will go ahead and ask Dr. Dunham to share, and then we will come to questions following that.

But before Dr. Dunham delivers her testimony on behalf of the Food and Drug Administration, I feel it necessary to express a concern and frustration with the FDA that I have. This hearing was originally planned for June 24 but had to be postponed because we couldn't get a witness from the Center for Veterinary Medicine. It is my full belief that someone from the CVM, Center for Veterinary Medicine, would be the most qualified to discuss advances in animal health within the livestock industry, hence the title of this hearing. Today the FDA has provided us with such a witness. However, in comparing the testimony that was delivered by Dr. Linda Tolson on June 24 to the Senate Health Committee and the testimony delivered today by Dr. Dunham, they seem to be the same. The testimony spends nearly 95 percent of its time talking about public health and completely ignores the topic of the hearing of advances in animal health within the livestock industry. Now, I understand the FDA has a message they want to get across but not taking the subject of this hearing seriously is a concern.

Dr. Dunham, please begin when you are ready.

STATEMENT OF BERNADETTE DUNHAM, D.V.M., PH.D., DIRECTOR, CENTER FOR VETERINARY MEDICINE, FOOD AND DRUG ADMINISTRATION, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, ROCKVILLE, MD

Dr. DUNHAM. Thank you very much. Good morning, Mr. Chairman, Members of the Subcommittee. I am Dr. Bernadette Dunham, Director of the Center for Veterinary Medicine at the Food and Drug Administration. Thank you for the opportunity to discuss FDA's role with regard to antimicrobial resistance.

Preserving the effectiveness of existing antimicrobial drugs, and encouraging the continued development of new ones, are vital to protecting human and animal health against infectious microbial pathogens. Approximately two million people acquire bacterial infections in U.S. hospitals each year and 90,000 die as a result. About 70 percent of those infections are resistant to at least one drug. The trends towards increasing numbers of infections and increasing drug resistance show no sign of abating. Resistant pathogens lead to higher healthcare costs because they often require more expensive drugs and extended hospital stays. Resistant infections impact clinicians practicing in every field of medicine, including veterinarians.

The problem is not limited to hospitals or traditional healthcare settings. Community-acquired infections are also frequently resistant to multiple antimicrobial drugs such as community-acquired methicillin resistant *Staphylococcus aureus,* common respiratory pathogens including *Streptococcus pneumoniae,* and gram-negative bacilli, which can affect humans through contaminated food.

Many factors contribute to the spread of antimicrobial resistance. In some cases, doctors prescribe antimicrobials too frequently or inappropriately. Sometimes patients do not complete the prescribed course of an antimicrobial, making it more likely that surviving microbes will develop resistance. Antimicrobial use in animals may

contribute to the emergence of resistant microorganisms that can infect people. Through international trade and travel, resistant microbes can spread quickly worldwide.

Antimicrobial agents have been used in human and veterinary medicine for more than 50 years with tremendous benefits to both human and animal health. However, after several decades of successful antimicrobial use, we continue to see the emergence of multi-resistant bacterial pathogens which are less responsive to therapy. The emergence of antimicrobial resistant bacterial populations is a complicated phenomenon and is attributed in part to the combined impact of the various uses of antimicrobial drugs in both humans and animals.

FDA co-chairs, along with the Centers for Disease Control and Prevention and the National Institutes of Health, the U.S. Interagency Task Force on Antimicrobial Resistance, which was created in 1999 to develop a national plan to combat antimicrobial resistance. In 2001, the Task Force published the *Public Health Action Plan to Combat Antimicrobial Resistance.* The Action Plan provides a blueprint for specific coordinated Federal actions to address the emerging threat of antimicrobial resistance. It reflects a broad-based consensus of Federal agencies, which was reached with input from state and local health agencies, universities, professional societies, pharmaceutical companies, healthcare delivery organizations, agricultural producers, consumer groups and other stakeholders. The Action Plan has four major components: surveillance, prevention and control, research, and product development.

Since 1996, FDA has actively addressed the issue of antimicrobial resistance. For example, FDA's Center for Veterinary Medicine is addressing potential human health risks associated with the use of antimicrobial drugs in food-producing animals. As part of the new animal drug approval process, CVM developed and implemented an approach for assessing antimicrobial resistance concerns associated with the use of antimicrobial drugs intended for use in food-producing animals. This approach uses risk assessment methodologies to assess the potential human health impact from the proposed antimicrobial use in animals and outlines risk management strategies that may be applied. CVM is also applying the basic principles of this approach to an ongoing review of currently approved antimicrobial drugs. CVM believes that, while these potential public health concerns must be addressed, it is critical that veterinarians continue to have access to effective antimicrobial drugs for the treatment, control and prevention of disease in animals.

Other key components of CVM's strategy for addressing antimicrobial resistance include robust research and monitoring programs, as well as educational outreach activities. CVM is actively conducting research to advance our understanding of antimicrobial resistance mechanisms and to support our regulatory decisions. CVM is the lead coordinator of the National Antimicrobial Resistance Monitoring System, referred to as NARMS. It is a multifaceted monitoring system that takes advantage of the expertise and resources of a number of Federal agencies and state public health laboratories. NARMS data provide regulatory officials and the veterinary medical community with critical information to help

assess the risk associated with antimicrobial use in food animal production. CVM continues to collaborate with veterinary and animal producer associations to develop and distribute guidelines on the judicious use of antimicrobial drugs in food-producing animals.

FDA'S other Centers are also actively working on antimicrobial resistance. FDA's Center for Drug Evaluation and Research has launched several initiatives to address antimicrobial resistance, including regulating drug labels, emphasizing the prudent use of systemic antibacterial drugs in humans, and revising its guidance to industry on the development of drugs for the treatment of bacterial infections.

FDA's Center for Biologics Evaluation and Research is focused on the development and continued availability of effective vaccines. Prevention of infections through the use of vaccines has markedly decreased antimicrobial resistance by reducing or nearly eliminating some types of infections. Vaccines also contribute to the control of resistance by reducing the need for antimicrobials.

In addition, development of increasingly sensitive diagnostic assays for detection of resistance allows for rational, targeted antibiotic use. FDA's Center for Devices and Radiological Health leads several efforts to clarify regulatory requirements to both industry and the scientific community on clearance of diagnostic tests for use in antimicrobial resistance initiatives.

In conclusion, I would like to mention that USDA and FDA are cosponsoring a meeting this afternoon to discuss agenda items and to present draft U.S. positions on them for the upcoming second session of the Codex ad hoc Intergovernmental Task Force on Antimicrobial Resistance to be held in Korea, October 20 through 24, 2008. The public meeting will be held at our Rockville facility in Maryland between 1 and 3 p.m. this afternoon. The antimicrobial resistance task force was established in 2006 to develop science-based guidance to be used to assess the risks to human health associated with the presence in food and feed, including aquaculture, and the transmission through food and feed of antimicrobial resistance microorganisms and genes. FDA will continue to work with Federal, state, local and foreign government officials, medical professionals including the veterinary community, the regulated industry and all of our FDA stakeholders in developing sound strategies to address and advance both human and animal health.

Thank you for the opportunity to discuss FDA's role with regard to antimicrobial resistance, and I would be happy to answer any of your questions.

[The prepared statement of Dr. Dunham follows:]

PREPARED STATEMENT OF BERNADETTE DUNHAM, D.V.M., PH.D., DIRECTOR, CENTER FOR VETERINARY MEDICINE, FOOD AND DRUG ADMINISTRATION, U.S. DEPARTMENT OF HEALTH AND HUMAN SERVICES, ROCKVILLE, MD

Introduction

Good morning, Mr. Chairman and Members of the Subcommittee. I am Bernadette Dunham, D.V.M., Ph.D., Director of the Food and Drug Administration's (FDA or the agency) Center for Veterinary Medicine (CVM), which is a part of the Department of Health and Human Services (HHS). Thank you for the opportunity to discuss FDA's role with regard to antimicrobial resistance.

Preserving the effectiveness of current antimicrobials, and encouraging the continued development of new ones, are vital to protecting human and animal health against infectious microbial pathogens. Approximately two million people acquire

bacterial infections in U.S. hospitals each year, and 90,000 die as a result. About 70 percent of those infections are associated with bacterial pathogens displaying resistance to at least one antimicrobial drug. The trends toward increasing numbers of infection and increasing drug resistance show no sign of abating. Resistant pathogens lead to higher health care costs because they often require more expensive drugs and extended hospital stays. The problem is not limited to hospitals. Resistant infections impact clinicians practicing in every field of medicine, including veterinarians. Community-acquired infections are also frequently resistant to multiple antimicrobial drugs, such as community-acquired methicillin-resistant *Staphylococcus aureus* (CA–MRSA), common respiratory pathogens including *Streptococcus pneumoniae,* and gram-negative bacilli, which can infect humans through contaminated food.

In my testimony, I will provide background information on antimicrobial resistance, discuss FDA's involvement with the Interagency Task Force on Antimicrobial Resistance, and describe FDA's actions to combat resistance and promote product development.

Background

Antimicrobial drugs are used to treat infections caused by microorganisms. The term "antimicrobial" refers broadly to drugs with activity against a variety of microorganisms including bacteria, viruses, fungi, and parasites (such as malaria). The term "antibacterial" refers to drugs with activity against bacteria in particular. Another term commonly used to describe an antibacterial drug is "antibiotic." This term refers to a natural compound produced by a fungus or another microorganism that kills bacteria that cause disease in humans or animals. Some antibacterial drugs are synthetic compounds; *i.e.,* they are not produced by microorganisms. Though these do not meet the technical definition of antibiotics, they are referred to as antibiotics in common usage.

Antimicrobial resistance is the ability of bacteria or other microbes to resist the effects of a drug. Antimicrobial resistance occurs when bacteria change in some way that reduces or eliminates the effectiveness of drugs, chemicals, or other agents designed to cure or prevent infections.

Many factors contribute to the spread of antimicrobial resistance. In some cases, doctors prescribe antimicrobials too frequently or inappropriately. Sometimes patients do not complete the prescribed course of an antimicrobial, making it more likely that surviving microbes will develop resistance. Antimicrobial use in animals may contribute to the emergence of resistant microorganisms that can infect people. Through international trade and travel, resistant microbes can spread quickly worldwide.

Antimicrobial agents have been used in human and veterinary medicine for more than 50 years, with tremendous benefits to both human and animal health. Many infections that were fatal, or left individuals with severe disabilities, are now treatable or preventable. However, because resistance to antimicrobial drugs is expected to occur with their use, it is essential that such drugs be regulated and used judiciously to delay the development of resistance. Misuse and overuse of these drugs contribute to an even more rapid development of resistance. After several decades of successful antimicrobial use, we have seen and continue to see the emergence of multi-resistant bacterial pathogens, which are less responsive to therapy. Antimicrobial-resistant bacterial populations are emerging because of the combined impact of the various uses of antimicrobial drugs, including their use in humans and animals. All of these pathways are not yet clearly defined or understood.

New classes or modifications of older classes of antimicrobials over the past 6 decades have been matched slowly but surely by the systematic development of new bacterial resistance mechanisms. As of today, antimicrobial resistance mechanisms have been reported for all known antibacterial drugs that are currently available for clinical use in human and veterinary medicine. In some cases, strains have been isolated that are resistant to multiple antibacterial agents.

U.S. Interagency Task Force on Antimicrobial Resistance

To address these challenges, the U.S. Interagency Task Force on Antimicrobial Resistance was created in 1999 to develop a national plan to combat antimicrobial resistance. FDA co-chairs the task force, along with the Centers for Disease Control and Prevention (CDC) and the National Institutes of Health (NIH).

The Task Force also includes the Agency for Healthcare Research and Quality (AHRQ), Centers for Medicare and Medicaid Services (CMS), the Health Resources and Services Administration (HRSA), the Department of Agriculture (USDA), the Department of Defense, the Department of Veterans Affairs, and the Environmental

Protection Agency. In 2001, the U.S. Agency for International Development joined the Task Force to help address global antimicrobial resistance issues.

Public Health Action Plan To Combat Antimicrobial Resistance

In 2001, the Task Force published the "Public Health Action Plan to Combat Antimicrobial Resistance" (Action Plan). The Action Plan provides a blueprint for specific, coordinated Federal actions to address the emerging threat of antimicrobial resistance. It reflects a broad-based consensus of Federal agencies, which was reached with input from consultants from state and local health agencies, universities, professional societies, pharmaceutical companies, healthcare delivery organizations, agricultural producers, consumer groups, and other members of the public.

The Action Plan has four major components: surveillance, prevention and control, research, and product development. Highlights of the Action Plan include:

Surveillance. Information and statistics about the emergence and spread of resistant microbes and the use of antimicrobial drugs can help experts interpret trends and identify strategies to prevent or control antimicrobial resistance. CDC is working with state health departments and other Task Force members to design and implement a strategy to coordinate national, regional, state, and local surveillance efforts. In addition, FDA, CDC, and USDA developed and expanded systems to monitor patterns of antimicrobial resistance among foodborne bacteria in human medicine, in agriculture, and in retail meat.

Prevention and Control. Research shows that controlling the use of antibacterial drugs can help reduce the incidence of antimicrobial resistance. In 2003, FDA partnered with CDC on its launch of its *Get Smart: Know When Antibiotics Work* campaign. The goal of the campaign is to educate consumers and healthcare professionals on the appropriate use of antibiotics. In partnership with doctors and other medical professionals, CDC has developed clinical guidelines for health professionals on how best to use antimicrobials and supports pilot projects to identify effective strategies to promote appropriate antimicrobial drug use. FDA has promulgated labeling regulations for the appropriate use of systemic antibacterial drugs in humans. CVM has developed, in conjunction with stakeholders, in-depth antimicrobial prudent use principles for beef, dairy, swine, poultry, and more recently, aquatic veterinarians.

Measures that reduce the need for antimicrobial use also serve to reduce the emergence of antimicrobial-resistant microorganisms. Prevention of bacterial infections through the use of vaccines has effectively eliminated or markedly decreased the problem of resistance in organisms such as *Haemophilus influenzae* type b (virtually eliminated in the U.S. while still a problem in other parts of the world) and *Streptococcus pneumoniae,* also known as pneumococcus. Published research has confirmed that the latter pneumococcal vaccine has lowered common infections that are often treated with antimicrobials. Prevention of viral infections through the use of vaccines can also indirectly help reduce antibiotic use and minimize the emergence of antibiotic-resistant microorganisms. For example, viral infections, such as respiratory infections due to influenza, often lead to unnecessary antimicrobial use and are sometimes complicated by serious secondary infections caused by bacteria such as staphylococcus or pneumococcus. In addition, development of increasingly sensitive diagnostic assays for detection of resistance allows for rational targeted antimicrobial use.

Research. The Action Plan promotes expanding existing research in antimicrobial resistance and related fields in an effort to improve treatments and outcomes. NIH is leading a team of agencies to provide the research community with new information and technologies, including genetic blueprints for various microbes, to identify targets for desperately needed new diagnostics, treatments, and vaccines to combat the emergence and spread of resistant microbes. NIH supports clinical studies to test new antimicrobials and novel approaches to treating and preventing infections caused by resistant pathogens. NIH also continues to support and evaluate the development of new rapid diagnostic methods related to antimicrobial resistance, in conjunction with FDA's Center for Devices and Radiological Health (CDRH). In addition, AHRQ funds various studies on the use of antimicrobial drugs and antimicrobial resistance, including ongoing research on reducing unnecessary prescribing of antimicrobials to children. FDA's Center for Biologics Evaluation and Research (CBER) conducts research that facilitates vaccine development for diseases in which resistance is an issue, such as malaria, staphylococcus (MRSA), and enteric diseases.

Product development. As antimicrobial drugs lose their effectiveness, new products must be developed to prevent, rapidly diagnose, and treat infections.

The priority goals and action items in the product development focus area of the Action Plan address ways to:

- Ensure researchers and drug developers are informed of current and projected gaps in the arsenal of antimicrobial drugs, vaccines, and diagnostics, and of potential markets for these products;
- Stimulate development of priority antimicrobial products for which market incentives are inadequate, while fostering their appropriate use;
- Optimize the development and use of veterinary drugs and related agricultural products that reduce the transfer of resistance to pathogens that can infect humans; and
- Facilitate development of effective prophylactic vaccines: in particular, focusing on vaccines against microbes that are known to develop antimicrobial resistance (*e.g.,* MRSA), thereby reducing the need for antimicrobials and the occurrence of antimicrobial resistant strains.

The task force is currently updating the Action Plan for the next 5 years.

FDA Accomplishments on Antimicrobial Resistance

Since 1996, FDA has actively addressed the issue of antimicrobial resistance. As an agency composed of several product centers, FDA has addressed antimicrobial resistance through a variety of initiatives, primarily through four key areas: surveillance, product development, education, and research.

- **Surveillance:** Monitoring and surveillance of antimicrobial resistance and then promptly and effectively responding to current threats from drug resistance.
- **Product Development:** Facilitating and encouraging development and appropriate use of products, including new drugs and vaccines, and improved, more timely tests for infectious diseases.
- **Education:** Facilitating the safe and effective use of antimicrobials and thus prolonging the life of these products by helping improve the quantity and quality of information available to consumers and health professionals regarding antimicrobial resistance and principles of appropriate usage. In addition, FDA has an important role in informing the public and healthcare professionals both through educational outreach and by assuring useful and accurate product labeling and appropriate marketing.
- **Research:** Maximizing and coordinating FDA's scientific research to address needs in antimicrobial resistance.

Specific activities by the various Centers within FDA include the following:

Center for Veterinary Medicine (CVM)

CVM is addressing potential human health risks associated with the use of antimicrobial drugs in food-producing animals. CVM's approach uses risk assessment methodologies to quantify the human health impact from antimicrobial use in animals, in conjunction with robust monitoring, research, and risk management. CVM is actively conducting research to advance our understanding of antimicrobial resistance mechanisms and to support our regulatory decisions. The agency also continues to participate in public meetings with stakeholders to provide educational outreach activities and to strengthen and promote science-based approaches for managing the potential human health risks associated with the use of antimicrobial drugs in food-producing animals.

One of the key components of CVM's strategy to assess relationships between antimicrobial use in agriculture and subsequent human health consequences is the National Antimicrobial Resistance Monitoring System (NARMS). CVM is the lead coordinator of NARMS. NARMS is a multi-faceted monitoring system that takes advantage of the expertise and resources of a number of Federal agencies and state public health laboratories. NARMS data provide regulatory officials and the veterinary medical community with critical information to help assess the risk associated with antimicrobial use in food animal production.

As part of the new animal drug approval process, CVM developed and implemented an approach for assessing antimicrobial resistance concerns associated with the use of antimicrobial drugs intended for use in food-producing animals. This approach uses risk assessment methodologies to assess the potential human health impact from the proposed antimicrobial use in animals and outlines risk management strategies that may be applied. In 2003, FDA published Guidance for Industry #152 ("Evaluating the Safety of Antimicrobial New Animal Drugs with Regard to their Microbiological Effects on Bacteria of Human Health Concern"). Guidance #152 provides recommendations to drug sponsors on the use of a qualitative risk assessment

approach for evaluating the likelihood that an antimicrobial drug used to treat a food-producing animal may cause an antimicrobial resistance problem in humans. The risk assessment approach recommended in the guidance considers a broad set of information, including the importance of the drug in question to human medicine. This information is collectively considered in determining whether the proposed antimicrobial product will pose a risk to public health.

CVM is also applying the basic principles of this approach to an ongoing review of currently approved antimicrobial drugs. While potential public health concerns must be addressed, it is critical that veterinarians continue to have access to effective antimicrobial drugs for the treatment, control, and prevention of disease in animals.

CVM continues to collaborate with veterinary and animal producer associations to develop and distribute guidelines on the judicious use of antimicrobial drugs in food-producing animals.

Center for Drug Evaluation and Research (CDER)

CDER has launched several initiatives to address antimicrobial resistance. Through CDER's initiatives, FDA has issued drug labeling regulations emphasizing the prudent use of systemic antibacterial drugs in humans. The regulations encourage healthcare professionals to prescribe these antibacterial drugs only when clinically necessary and to counsel patients about the proper use of such drugs and the importance of taking them as directed.

Over the last several years, CDER has been evaluating the design of clinical trials that are used to study the safety and efficacy of drugs for the treatment of a variety of infections. CDER recognizes the importance of ensuring that antibacterial drugs are approved based on sound, informative clinical trials, because the clinical use of marginally effective antimicrobials can contribute to the development of antimicrobial resistance. For milder infections that are often self-resolving over time, we are recommending different types of studies than what were used in the past. The agency is doing this in order to have studies that have the capacity to provide informative data to assess an antimicrobial drug's effects in these milder conditions. It is essential that clinical trials evaluating a new drug be performed in a manner that allows for assessment of the benefits and the risks of the drug in the condition under study. A better assessment of the benefits that a drug may provide and balancing these benefits with risks should provide better quality information on antimicrobial drugs to foster appropriate use and ideally reduce inappropriate use that is also contributing to the development of resistance.

To that end, CDER has been revising its guidance to industry on the development of drugs for the treatment of bacterial infections. Since October 2007, CDER has issued four such guidance documents. In January of this year, FDA co-sponsored a workshop with the Infectious Diseases Society of America to discuss clinical trial designs for community acquired pneumonia (CAP). The agency also convened an advisory committee meeting in April 2008 to get additional advice and the agency is now writing a draft guidance document that will provide the agency's thinking on informative trial designs in CAP. By providing these draft guidance documents on developing drugs for these conditions we have provided some clarity on the types of study designs that will be informative in these conditions.

Most of the discussion of drug development has focused on resistance in common bacterial infections, but resistance is also a problem in conditions such as tuberculosis (TB), fungal infections, and malaria. CDER has participated in a working group with other representatives from FDA and the European Medicines Agency to discuss strategies for developing drugs for TB. CDER also published a draft guidance document describing approaches to the development of drugs for malaria in June of 2007.

Appropriate use of antimicrobial drugs is guided not only by understanding the safety and effectiveness of risks and benefits of these drugs, but also by having information on whether a particular drug is active against a patient's infection when culture results are available. Laboratory testing to assess whether a bacterial isolate is "susceptible" to a particular antimicrobial drug can provide such information. There are a number of antibacterial drug labels that are in need of updating of the information on susceptibility testing. FDA recently published a draft guidance document on "Updating Labeling for Susceptibility Test Information in Systemic Antibacterial Drug Products and Antimicrobial Susceptibility Testing Devices" (published June 2008). This draft guidance, in compliance with section 1111 of the Food and Drug Administration Amendments Act of 2007 (FDAAA), describes options for updating the antibacterial susceptibility testing information in antibacterial drug product labeling and we believe could facilitate the timely updating of this information.

Section 1112 of FDAAA requires FDA to convene a public meeting to consider "which serious and life threatening infectious diseases, such as diseases due to gram-negative bacteria and other diseases due to antibiotic-resistant bacteria, [would] potentially qualify for available grants and contracts under section 5(a) of the Orphan Drug Act . . . or other incentives for development." In compliance with Section 1112 of FDAAA, FDA held a public hearing on April 28, 2008, to discuss, in part, potential incentives to encourage pharmaceutical companies to develop new antimicrobial drugs.

Center for Biologics Evaluation and Research (CBER)

Research and regulatory efforts have contributed to the development and continued availability of effective vaccines which have eliminated or markedly decreased antimicrobial resistance by reducing or even nearly eliminating some types of infections. Other vaccines contribute by reducing the need for use of antimicrobials. CBER has initiated a new research program to facilitate vaccine development to prevent MRSA and has ongoing research programs to foster the development of vaccines to prevent other frequent infectious diseases problems such as *Salmonella* or *E. coli* gastroenteritis, and TB, as multidrug-resistance has emerged as a national and international threat to health. In addition, CBER works with sponsors to develop safe and effective vaccines against emerging infectious diseases problems. Additional efforts at CBER address new diagnostic tests and evaluation of emerging technologies and test kits for detecting bacteria as it relates to transfusion medicine, mechanisms of resistance, alternative therapies for highly resistant organisms, and regulatory pathways to assess the potential value of probiotics to help reduce the development and spread of antimicrobial-resistant bacteria.

Center for Devices and Radiological Health (CDRH)

CDRH leads several efforts to clarify regulatory requirements to both industry and the scientific community on clearance of diagnostic tests for use in antimicrobial resistance initiatives. For example, CDRH assisted device manufacturers to get an alternative method for detecting vancomycin resistant *Staphylococcus aureus* to market and assured timely introduction of this critically important new product through use of its expedited review process. CDRH has published guidance documents to ensure the safe and effective use of in vitro diagnostics for detecting novel influenza A or A/B viruses from human specimens. CDRH recently cleared a new assay developed by CDC for the detection of human infection with H5 Avian Influenza virus. CDRH also recently cleared a rapid test for confirming methicillin resistant *Staphylococcus aureus,* a rapid DNA test for detecting Group B Streptococcus in pregnant women, and a rapid test for detecting Shiga toxins one and two produced by *E. coli* in stool specimens to aid in the diagnosis of diseases caused by enterohermorrhagic *E. coli* infections.

Conclusion

In conclusion, I would like to note that USDA and FDA are cosponsoring a meeting this afternoon to discuss agenda items and to present draft U.S. positions on them for the upcoming second session of the Codex ad hoc Intergovernmental Task Force on Antimicrobial Resistance (AMR) to be held in Korea, October 20–24, 2008. The public meeting will be held at CVM's Rockville, Maryland, offices between 1:00 and 3:00 p.m. today. This AMR Task Force was established in 2006 to develop science-based guidance to be used to assess the risks to human health associated with the presence in food and feed, including aquaculture, and the transmission through food and feed of antimicrobial resistant microorganisms and genes. FDA will continue to work with Federal, state, local and foreign government officials, medical professionals including the veterinary community, the regulated industry and all of FDA's stakeholders, in developing sound strategies to address and advance both human and animal health.

Thank you for the opportunity to discuss FDA's activities with regard to antimicrobial resistance. I would be happy to answer any questions.

The CHAIRMAN. Well, thank you very much. I appreciate you being here and your statement.

In taking note of the written testimony presented by the second panel, who will be talking to us shortly about their concern about the importance of FARAD, as I stated earlier, on July 10, Representative Hayes and I sent a letter to both USDA and FDA stressing the importance of the program, and also to provide emergency funding to keep the program operating. Over 2 months later,

here we are with no response from either agency, so what is the status of the funding for this program, either of you?

Dr. DUNHAM. As you know, this program has actually been based within USDA CSREES for a very long time. With the 2008 Consolidated Appropriations Act, USDA did not receive any appropriated funds to support the FARAD program, and we are currently working with a lot of the stakeholders to look at some potential, alternative mechanisms that may be available to assist with this program. I do agree that it is a very important program, and we are certainly hoping to be able to get back to you with some very positive results.

The CHAIRMAN. Dr. Clifford?

Dr. CLIFFORD. Mr. Chairman, I have with me today Rob Hedberg, the Acting Director for Legislative and Governmental Affairs from CSREES, and I would ask that he respond to this question.

The CHAIRMAN. Okay. State your name, please.

Mr. HEDBERG. My name is Rob Hedberg, and again, I am Acting Director of Legislative and Governmental Affairs for the USDA Cooperative State Research, Education, and Extension Service. Unfortunately, we do fully understand your concerns about the FARAD program. We have been active in management of this program for many years. We recognize the letter of the request for $2.5 million to provide bridge funding for this program, but the reality is that the program was last appropriated in 2006, and since then there were no funds provided in appropriations in 2007 or 2008. It has been pointed out for 2008, funds were provided by both FDA and USDA CSREES to provide just short of $1 million, which was bridge funding to keep the doors open until now, but unfortunately, our situation at USDA is, we do not have the funds available to continue support of this program. If funds are appropriated for this program, we would gladly continue our administration of it through CSREES.

The CHAIRMAN. Well, I appreciate you saying that. Of course, we are all aware that you have within the agency transferred money around where you see priorities and so on. I appreciate that, and I hope that we will get something that we can share with the appropriate appropriators, if you will, a play on words, regarding what you have just shared with us. Thank you very much.

Mr. HEDBERG. You are welcome. Thank you.

The CHAIRMAN. Another question, if I could. In the decade that the National Antimicrobial Resistance Monitoring System, NARMS, has been enacted, what have you learned about the scope of antimicrobial resistance? How rapid has resistant bacteria increased in agriculture?

Dr. DUNHAM. The NARMS program has been very effective and helpful as we tried to follow this very complex issue—where do you see and how do you see antimicrobial resistance developing. This has allowed us to team with the CDC and USDA to take a look at samples that have been taken from the slaughter facilities; and to follow these through, as we do at FDA, to take a look at the final retail meat products that are in the market. From that, we have been able to, now—courtesy of the technology and the DNA fingerprinting—indicate if we are seeing any resistant serovars,

specifically looking along the lines of *Salmonella* and *Campylobacter*. As we are able to track that, we can see if there are indications of some resistance developing, and that allows us then to take a look in the science to make new decisions as to how we may or may not take action. So it has been very helpful and we are hoping to see this expand. We had an external science board review recently complete an overview of the NARMS and they were very impressed and pleased with that, so we are hoping to see this grow. Thank you, sir.

The CHAIRMAN. Thank you.

Dr. Clifford?

Dr. CLIFFORD. Mr. Chairman, I definitely agree with Dr. Dunham. These types of things are very useful. We need to use appropriate science and collection of data to be able to make decisions about animal health as well as human health and public safety. So we find these types of things to be very effective in helping address and answer these types of questions that are before you.

The CHAIRMAN. Well, thank you, and before I ask Mr. Hayes to participate, I think it is safe for me to say that you agree that healthy animals produce healthy food. In your opinion, does the Denmark case highlight the benefits of both therapeutic and growth antibiotics? What comment might you make about the Denmark example?

Dr. CLIFFORD. I am sorry, Mr. Chairman. Could you repeat that question, please?

The CHAIRMAN. In your opinion, does the Denmark case highlight the benefits for both therapeutic and growth antibiotics?

Dr. CLIFFORD. Absolutely. It certainly does. We feel that the therapeutic use of antibiotics is extremely important in animal health as well as the prevention and the prophylactic use of antibiotics.

Dr. DUNHAM. I think with the Denmark situation, we further did see just how antibiotics are being used and the importance of antibiotics to sustain the health of our animals. I think part of what we saw was when there was a removal of the antibiotics, the therapeutic need was clear. And the catch is, what we are looking at is how a veterinarian will take a look at the animals and be able to decide, from their own training and understanding of disease, when to intervene to treat, control and prevent disease, and that it is very important to keep our animals healthy. I think what we saw in the long run after the Denmark study was, at the time they did a complete ban, it clearly showed us that the antibiotics were working to address a pathogen and they ended up coming back with the therapeutic use of that drug. At that time we probably saw just where that was important. Weanling pigs, for example, will outbreak with diarrheal disease if you are not able to intervene and treat those animals.

The CHAIRMAN. Thank you. I will have some more questions, but I would like to yield to Mr. Hayes.

Mr. HAYES. Thank you, Mr. Chairman.

Dr. Clifford, as you suggest, disease prevention is much more economical than treatment. In the context of the debate over the judicious use of animal health tools in livestock production, would the

Department support or oppose legislation which arbitrarily prohibits the use of essential animal health tools by veterinarians?

Dr. CLIFFORD. The Department believes that, and APHIS—actually I represent APHIS here today—would believe that it is important, very important for veterinarians and animal health professionals to have the opportunity to apply these drugs as necessary for therapeutic and prophylactic use in the field. It is extremely important, yes.

Mr. HAYES. So you would oppose a ban.

Dr. Dunham, in later testimony, Dr. Singer suggests that the risk assessment process currently used by FDA should be modified to take into consideration the impact of implementing specific interventions to reduce human and animal health risk. To what extent do you consider risk mitigation strategies when conducting your assessment?

Dr. DUNHAM. When we go through our drug review approval process, we are looking to ensure that that drug will be safe and effective, and we look at the data that is given to us by the companies to assess that. At the time that you are looking at anything post our approval process, for example, if you were to look at risk mitigation within a slaughter plant—what is being used to handle the carcass, what is being used if you did irradiation before you packaged the meat—any of those interventions are something that would not be something we could take a look at as we are looking from the pharmaceutical company's review of data provided to us for the approval of that drug to be used in the animal for safety and effectiveness. We don't control those other interventions so it makes it very difficult for us to assess that. So we come back, first of all, with that product and the science that we look at to determine safety and effectiveness of that product being used in that animal. And for that reason, then we can approve that product for its safety and effectiveness. Then we do a post-surveillance monitoring of that afterwards to see if we are having any adverse reaction in the animal, and at the same time looking at any data to see, are we finding any problems with resistance.

Mr. HAYES. I think that was a really good answer. I am not sure so much depth that I can get it. To boil it down, do you feel like the processes that we are using now are a reasonable and safe way to address the issue of prevention *versus* mitigation?

Dr. DUNHAM. Yes, sir. As we at the FDA are looking at that product to determine if it is going to meet our approval standards, then we do base all of that with our scientific critique and review. I am very confident, by the time we do put our stamp on it to say this drug is approved for that use in that species and that indication, that yes, we are very happy with that process.

Mr. HAYES. Thank you.

Dr. Clifford, would you agree?

Dr. CLIFFORD. Yes, I do.

The CHAIRMAN. Thank you, Mr. Hayes.

The chair recognizes Mr. Kagen from Wisconsin for 5 minutes.

Mr. KAGEN. Thank you, Mr. Chairman, and thank you both for appearing here before us this morning, and Dr. Clifford, I want to give you an opportunity here to identify, let me just assume that you don't want Congress to begin to practice veterinary medicine

by dictating what drugs should or should not be used. Would that be a fair assumption?

Dr. CLIFFORD. Yes, Congressman, it would be. I would not want that dictated by Congress. I think it is appropriate as animal health officials that the veterinary professional who has the knowledge and the skill sets to be able to apply antimicrobials in an appropriate way and an appropriate use for animal health.

Dr. DUNHAM. I think it is very true, the training that our veterinarians go through to practice medicine, they are the ones that you turn to. They are the ones that understand disease process and then, based upon the products that are approved, that they can reach for in their armamentarium, to be able to appropriately use those is the way it should be. So with the veterinarian's discretion, they are the ones that can decide when to intervene, to treat, prevent or control a disease.

Mr. KAGEN. And I will agree with you to the extent that you stay within veterinary medicine and don't go over to the human side because my natural inclination is to disagree with that.

What would be the three most critical problems that you are facing in APHIS that you think need to be addressed? If I just was able to wave a wand or if my name was Secretary Hank Paulson, I could come up with $2 billion, forget the money, what are the three most critical problems that you are facing in APHIS that you think need to be addressed? It is a softball question. You didn't expect that.

Dr. CLIFFORD. No, I really didn't.

Mr. KAGEN. I have only got a couple minutes, so you have thought about this for your whole career, now you are here, your agency is counting on you right now, Dr. Clifford.

Dr. CLIFFORD. Well, it would be, I think in three areas. One, I think it is critically important that we use new technology and techniques to help us address animal health issues in this nation. I think it is important we be able to move toward a system where we can effectively eliminate disease or control disease through other methods other than massive depopulation in the future. Because, for one, the cost to taxpayers; two, really the waste of protein that that does. So that is through the research and development of new technology.

Second, I think it is critically important as we look at animal health threats and issues that we have good continuity of operation planning within the United States so that we can keep producers viable and healthy, even in the face of an outbreak situation. So, that we can allow animals to move safely through mitigation measures and good biosecurity.

Third, traceability, and that is part of our animal ID program that we are moving forward in. Traceability is critically important to animal health and to be able to effectively eliminate disease quickly. Thank you.

Mr. KAGEN. Dr. Dunham?

Dr. DUNHAM. Thank you. I would also agree. I think one of the challenges we are facing now is being able to embrace the exciting field of where we are going with our biotechnology. Science is at the heart of everything we do for our decisions and we need to embrace the new science, and at the same time develop some new

ways of intervening, as we just discussed, to keep the health of both people and animals moving forward. New technology will open those doors for us. Being able to adapt that means we need to have an opportunity to sustain the science and the research that is going to bring those to us. We do the review, so it is what is coming in the pipeline. So anything that continues to advance the research to allow our companies, universities to break through into new technologies and bring those forward to us is going to be very, very, very helpful.

I think also we can try to harmonize. We talked earlier that, internationally, we are meeting with Codex this afternoon. We are one world, and we said before, people travel, animals travel and microbes travel. The more that we are aware of what is happening internationally, it is going to be quintessential as we try to get our hands around these issues because we don't know what is going to walk in the door. Veterinary students used to have a textbook and be told if you don't travel to country X, don't worry, you will never see this disease. That is not true anymore. So we as the agencies have to embrace the idea that what will be walking in our front door could impact the health of people and animals. That would be another venue of how we work internationally together. Also, with regards to methodologies, how we get to a standardization, where it is possible, that our labs can talk, not only within the state but across the states, so we know what is moving in the country, and we can really track appropriately. You are no longer having to compare apples to oranges; you can compare apples to apples. So all of that comes back down to a combination of technologies.

Mr. KAGEN. Thank you for your comments, and before I go too far over, I just have to make a comment about the disinterest of my constituents in northeast Wisconsin of being faced with the possibility of paying for the inspection of the quality and health of foreign food products that might be shipped into this country. We don't want to have to pay for somebody else's mistakes here, and along those lines, if I could just beg the Chairman for a minute to get your comments on what your agencies are doing to make sure that other countries who seek to ship their product here are doing to move up to our quality.

Dr. CLIFFORD. Congressman, at APHIS we have negotiations, bilateral negotiations with countries with the movement of live animals and animal products, and there are certain mitigations and certifications that are required for the movement of those products. Our agency as well as in cooperation with other organizations and Customs and Border Protection are there to assure that those products and animals that enter into the United States meet those conditions.

Mr. KAGEN. Does that mean that they are having anything to do with our standards about the use of antibiotics?

Dr. CLIFFORD. With regards to antibiotic use, I would have to defer that to those that are authorized or have the authority over that particular area. With our area though, they have certain standards relative to disease issues and threats.

Dr. DUNHAM. Regarding again the harmonization that many of us are looking at with VICH that we have similar to the human side of ICH—where we understand what the review processes are

within other countries and how they go through to decide the safety and effectiveness of the drugs that they approve and how they are being utilized—that open dialog helps a tremendous amount. Codex Alimentarius is one program that allows us to go through that, take a look at MRLs within various drugs and now most recently, as I mentioned, this afternoon there will be the second follow-up of the Codex group taking a look specifically at what countries are doing to address antimicrobial resistance. So what are the standards, what are the methodologies? The more we understand how each country is approving and utilizing those drugs in the practice, in this case, of agriculture, the more it will make it easy for us to work together and have that transparency.

Mr. KAGEN. Thank you very much. I look forward to working with you and making certain that consumers have an easy way of identifying what is in their food and where it comes from. Thank you for your work.

I yield back my time.

The CHAIRMAN. Thank you, Mr. Kagen.

The chair recognizes the gentleman from Nebraska, Mr. Smith, for 5 minutes.

Mr. SMITH. Thank you, Mr. Chairman, and thank you to the witnesses.

We know that the marketplace has high expectations and therefore producers want to meet those expectations. Otherwise they don't have a product that will sell and hopefully a commensurate profit. As we do look at this, we know that some groups are advocating a legislative ban on the use of antimicrobials for growth promotion and feed efficiency. What do you think would be the impact this legislative ban would have on development of antimicrobial resistance, and what impact would you believe the legislative ban would have on the actual animal health?

Dr. CLIFFORD. It would be a very devastating effect upon animal health if we did not have the ability and the use of antibiotics for therapeutic and prophylactic use to prevent a number of diseases. So from an animal health perspective, this is something that we would not support. This needs to be in the hands of professionals and veterinary professionals within the field to be able to handle it. We do agree that we need good data to be able to do proper analysis with regards to antibiotic resistance both in the protection of animal health as well as human health. I think we should rely upon the science to dictate the direction that we go *versus* legislation.

Mr. SMITH. Dr. Dunham?

Dr. DUNHAM. We haven't taken any specific position on any legislation, as you well know, but separate from all of that, in general, it is absolutely true, with FDA having the opportunity to do the scientific review of any of the products coming through for us to look at to decide their safety and effectiveness in animals, our standards are very high and we hold to those. That being said, once a product has been approved and you have that claim on the label indicating its use—dosage, species, indication—the veterinarian is the one who then takes hold of that and, with their training, is therefore the capable person to indicate how to use that drug. At the same time, that is what we do when we embrace the use, the judicious

use, of any antimicrobial. So there is an appropriate workup to decide when to treat, prevent or control a disease. This is done on a scientific basis and through the training that the veterinarians have to do that.

Mr. SMITH. Thank you very much. I will say that to be honest with you, I think for humans sometimes, the use of antibiotics and so forth might be a little overused and I say that for myself personally, but I don't really go to the doctor always looking for an antibiotic as often as it might be offered. It had never crossed my mind to seek a legislative ban on that because I might share some personal feelings about that. But it does, I think, speak to the larger issue of what the role of government is here, so I appreciate your input and I yield back.

The CHAIRMAN. Thank you, Mr. Smith.

Dr. Dunham, I would like to pursue a couple more questions. Would you please describe the process a food-animal drug must go through before it can be used on the market, and if you can, average how much time and money is invested?

Dr. DUNHAM. Yes, sir. A company will give us a product to take a look at. We assess all the scientific information they provide to determine the safety of that drug, the target-animal safety, the effectiveness of that drug in that target animal. We take a look at environmental impact. We take a look at the chemistry and manufacturing surrounding that product to ensure it is stable and does exactly what it is supposed to do. We take a look at any toxicology that is involved, and when it is for use in a food-producing animal, then we have to also take a look at it with our human food safety group. They will then take a look to decide, for example, would there be any residues, and if so, what is an acceptable level, and that has to be reviewed as well. And when we have done all of that, we will then be able to decide if this product is safe and effective. So there are multiple teams that get pulled together in our Office of New Animal Drug Evaluation to take a look at all aspects of that package in order to have all of those various sections reviewed and completed before we can finally say yes, this drug is approved. And it depends upon the drug, depends upon the class, use, *et cetera,* as to how long that may or may not take and the data sets that are being provided for us to have that rigorous scientific review. So that is a very short overview of the procedure that is required for them to go through.

And as you hear on the human side or veterinary side, there are a number of years that go into that when you are developing the first molecule and bringing it all the way through to what you can call molecules to miracles, when you have that drug in hand to be able to effectively use that to prevent or treat that disease that you are looking at. And companies then take all of that under consideration when they are developing that product and give us the data sets that we look at. If we have questions, if there is further data that we need, we dialogue that with the company and they usually work very well with us so that we absolutely make sure the i's are dotted and t's are crossed. So we have the confidence when we finally say it is approved that we can follow that through. Then we follow with post-surveillance to see whether or not, when it is finally out being utilized, we are seeing any adverse effects. At that

time, based upon what we are seeing in the science again, we can take a look and make any potential changes to that label, a warning box or make any further changes that are appropriate. It is all based on the science and the data that we collect as we monitor this.

The CHAIRMAN. That is pretty extensive. Do you have some kind of an idea what it costs to do this, maybe compare what it costs to get a drug on the market for human use?

Dr. DUNHAM. I wouldn't be able to give you a direct cost of that. I think each one depends—the pharmaceutical companies usually have a pretty good idea and they can tell you how much it costs them to do the research, the developing, gathering the data that they then give to us for that review. I think those numbers are available but I can't give them to you off the top of my head. I would be happy to obtain that information and submit that to you.

The CHAIRMAN. Okay. Is it true that if a food-animal drug has any risk to humans, the drug can't be used?

Dr. DUNHAM. No. I think we go through the review process to assess how that drug will be used and we are able to decide limitations if that is appropriate, if we decide that. We do have, as you know, a guidance that has been developed. It is referred to as Guidance #152. And that allows us to take a look at a lot of the risk issues and it is one of our tools that can be utilized when we are going to be looking at the development and approval of an antimicrobial. At that point we do have a scenario, working with our counterparts in human medicine as well, to take a look at those drugs' very important use in humans. Sometimes that will be a limitation as to whether or not we have a green light to say whether that same drug can be used or not used in animal medicine. But for the most part, there are opportunities to take a look at this and decide when and where and how much we can use that drug for an approved use in animals, and that has been a very good guidance. It has worked very well and we have had a chance to have advisory committees work with us as well on that.

The CHAIRMAN. In your testimony, you outline human public health numbers. How many livestock bacterial infections are there in the United States?

Dr. DUNHAM. I don't think I have that on the tip of my tongue, but I could certainly take a look and work with John and get some information back to you.

Dr. CLIFFORD. I was just going to say, Mr. Chairman, we will work with FDA to provide that for the record.

The CHAIRMAN. Okay. I appreciate that. All right. What are the four areas that FDA approves antimicrobial use in food animals? I understand there are four areas that FDA approves antimicrobial use in food animals.

Dr. DUNHAM. They, again, are based upon the claim that is being requested by the company. We would be looking to see what the disease is that is being requested for us to take a look at, and approve that product to be utilized. I am not sure if I am looking exactly——

Dr. CLIFFORD. Mr. Chairman, just to clarify, are you referring to therapeutic, control, prevention and for feed efficiency?

The CHAIRMAN. Yes.

Dr. DUNHAM. In that case, based upon the claim that is coming through, if it is going to be used, we will then review that indication on the claim and approve that, just as you said, if it is going to be for therapeutic use, at what dose and what species. Then at the same time, if you are looking at this for control or intervention, we do have that. Those are in the claims.

The CHAIRMAN. Mr. Hayes.

Mr. HAYES. No questions.

The CHAIRMAN. Mr. Smith.

Mr. SMITH. I do have one. I came across this advertisement in I think *CongressDaily*, Pew Charitable Trust, "Bigger Beef, Tougher Bugs: Antibiotics in Livestock Feed Are Making Our Drugs Less Effective." Dr. Dunham, have you seen this ad? Would you say that that is an accurate portrayal of the scenario here?

Dr. DUNHAM. No, I have not seen the ad, but I just think in general, all of us, as you have heard discussed today, it is very important that any of us, be it medicine for humans or medicines for animals, that we constantly embrace judicious use of these antimicrobials. The more that you put pressure on these pathogens, the pressure is just going to have the potential to enhance resistance. So that is why we do embrace, all of us, judicious use of these antimicrobials. We want to make sure that we have access to them. We need them to keep people and animals healthy. So if we have abuse, we would have a problem, but people aren't doing that. They are very conscientious because we do need those. At the same time, just how many do we have? So you want to treat them very carefully. So I do believe that, again, the responsible profession is approaching that in the best manner.

Mr. SMITH. Thank you.

Dr. Clifford, would you care to comment on this ad? The Pew Charitable Trust ran the ad.

Dr. CLIFFORD. I haven't seen the ad. I have read some of their testimony before, but as far as my position that I have already stated stands. We need to not present the issues on fear and concern but on science.

Mr. SMITH. Thank you, Mr. Chairman.

The CHAIRMAN. Well, thank you both. Do either of you have any further comment that you would like to make while you are at the table?

Dr. DUNHAM. No, sir, I am fine, and I will get you the answers to the questions that you did ask. Thank you very much for the opportunity to attend.

The CHAIRMAN. Thank you.

Dr. Clifford.

Dr. CLIFFORD. Mr. Chairman, actually I would just like to make a comment. As Dr. Dunham talked about one world, this goes back to one world, one health. I think it is critically important in the scenario of one world, one health that the human health side and the animal health side work very closely using science, but remembering that while public health is important first and foremost to all of us, it is critically important that we maintain animal health and that animal health be heard. It is critically important for our livestock production in this country. Thank you.

The CHAIRMAN. Well, thank you for that comment I will just add to that from my perspective, speaking for myself, I do believe in the science. I think healthy animals is healthy food and we have to look to the science of this to assure that, particularly in this growing, world population, the demand is going to continue to grow to provide adequate food. It is a big challenge for us, the science, but that is the way I think we go. So I appreciate your comments and thank you very much. You are both excused.

We would like to—as quick as we can—call the second panel to the table.

I would like to welcome you to the table. Thank you for being here. I will just recognize each one and then we will start with Dr. Rowles shortly.

Dr. Craig Rowles, Doctor of Veterinary Medicine, pork producer, is here on behalf of the National Pork Producers Council from Carroll, Iowa. Dr. Michael Rybolt, Director, Scientific and Regulatory Affairs, National Turkey Federation, Washington, D.C. Dr. Robert Byrne, Ph.D., Senior Vice President, Scientific and Regulatory Affairs, National Milk Producers Federation, Arlington, Virginia. Dr. Spangler Klopp, Doctor of Veterinary Medicine, Diplomat, American College of Poultry Veterinarians, Corporate Veterinarian, Townsends, Inc., on behalf of National Chicken Council, Georgetown, Delaware. Mr. Blair Van Zetten, President, Oskaloosa Food Products, on behalf of United Egg Producers from Oskaloosa, Iowa. Dr. Michael Apley, Doctor of Veterinary Medicine, Ph.D., DACVCP, Director, PharmCATS Bioanalytical Laboratory, and Associate Professor, Department of Clinical Sciences, Kansas State University, on behalf of the National Cattlemen's Beef Association from Manhattan, Kansas.

Thank you all for being here. We appreciate it. Dr. Rowles, please begin when you are ready.

STATEMENT OF CRAIG ROWLES, D.V.M., GENERAL MANAGER AND PARTNER, ELITE PORK PARTNERSHIP, CARROLL, IA; ON BEHALF OF NATIONAL PORK PRODUCERS COUNCIL

Dr. ROWLES. Good morning, Chairman Boswell, Ranking Member Hayes and Members of the Subcommittee. My name is Craig Rowles. I am a Doctor of Veterinary Medicine and I have spent 25 years in the pork industry as a pork producer and a veterinarian. I have spent the last 12 years as General Manager and Partner of Elite Pork, and prior to that I was in mixed animal practice in Carroll serving pork producers.

I am testifying on behalf of the National Pork Producers Council, an association of 43 state producer organizations that represent the country's 67,000 pork producers. In providing pork to the world, producers operate under a set of ethical principles which broadly include humane and compassionate care for their pigs. Specific to animal health products, producers use antibiotics judiciously and responsibly to protect pig health and to produce safe pork and to manage antibiotic use and to protect public health. The health and well-being of our pigs is critical to the success of the U.S. pork industry and pork producers. Antibiotics are only one tool that help producers keep their animals healthy, their produce safe, wholesome and nutritious.

Today, the FDA Center for Veterinary Medicine approves antibiotics for four uses: disease treatment, disease control, disease prevention and nutritional efficiency. Pork producers work in collaboration with their veterinarians to design herd health programs. These programs may include diagnostics for determining the best time to vaccinate for diseases or the best time to use antibiotics for preventing a disease outbreak. The health management plans may also include information on ventilation, balanced feed rations or parasite control. These plans are about total system health management, not just about what antibiotic to use to treat a specific illness.

U.S. pork producers take the use of antibiotics very seriously. After 4 years of development and tests, the pork industry rolled out the first producer responsible antibiotic use program called Take Care—Use Antibiotics Responsibly. The program outlines principles and guidelines that protect public health, animal health and animal well-being through the responsible use of antibiotics. During the development of Take Care, the pork industry worked with Federal public health agencies including CDC and the FDA as well as numerous stakeholders such as the American Association of Swine Veterinarians, AVMA, AHI, the American Feed Industry Association and McDonald's. The pork industry's responsible use program has been praised by many Federal agencies, legislators, consumer organizations and food supply companies. The U.S. pork industry developed this program because it was the right thing to do. Producers care about animal health and we care about public health.

Initially a voluntary program, Take Care is now incorporated into our Pork Quality Assurance Plus program, which includes on-farm assessments including reviews of whether antibiotic use principles are being practiced. Producer PQA Plus certification is required by U.S. packing plants as a condition of sale.

Denmark's ban on antibiotic growth promoters, or AGPs, for pigs is often cited as an example of why there should be restrictions on the use of antibiotics in pork production. However, the reality of the impacts of that ban are seldom discussed. After the ban was put in place in 1999 for all swine, Danish pork producers saw an immediate increase in post-weaning diarrhea and an increase in nursery pig mortality that has had long-lasting impacts on the Danish pig industry. In 2002, two Iowa State economists estimated the effect of a ban on antibiotic use in the U.S. similar to Denmark's would increase the cost of pork production by $4.50 per pig in the first year. After 10 years, the ban's cumulative cost to the pork industry would be greater than $700 million, and that was back when corn was listed as $2.50. Denmark would not be a wise course of action for the U.S. pork industry.

Upon graduation from veterinary school, I swore an oath to use my scientific knowledge and skill for the benefit of society through the protection of animal health, the relief of animal suffering, the conservation of animal resources, the promotion of public health and advancement of medical knowledge. As a swine veterinarian, I need all the tools available to live up to that oath. Legislative attempts to ban certain antibiotics will compromise the oath that every veterinarian took on his graduation day.

In summary, pork producers and veterinarians have a moral obligation to use antibiotics responsibly to protect human health and provide safe food. Producers also have an ethical obligation to maintain the health of their pigs. Antibiotics are merely one piece of that healthcare system that pigs need. The U.S. pork industry has a long history of being proactive and doing the right thing for its pigs and consumers. Pork producers developed Take Care and PQA Plus not because they had to, but because it was the right thing to do.

Thank you for the opportunity to share the views of the U.S. swine industry, and I would be happy to take your questions.

[The prepared statement of Dr. Rowles follows:]

PREPARED STATEMENT OF CRAIG ROWLES, D.V.M., GENERAL MANAGER AND PARTNER, ELITE PORK PARTNERSHIP, CARROLL, IA; ON BEHALF OF NATIONAL PORK PRODUCERS COUNCIL

Introduction

The National Pork Producers Council is an association of 43 state pork producer organizations and serves as their voice in Washington, D.C.

The U.S. pork industry represents a significant value-added activity in the agriculture economy and the overall U.S. economy. Nationwide, more than 67,000 pork producers marketed more than 104 million hogs in 2007, and those animals provided total gross receipts of $15 billion. Overall, an estimated $21 billion of personal income from sales of more than $97 billion and $34.5 billion of gross national product are supported by the U.S. hog industry. Iowa State University economists Dan Otto and John Lawrence estimate that the U.S. pork industry is directly responsible for the creation of nearly 35,000 full-time equivalent jobs and helps generate 515,000 indirect jobs. All told, the U.S. pork industry is responsible for more than 550,000 mostly rural jobs in the U.S.

The U.S. pork industry today provides 21 billion pounds of safe, wholesome and nutritious meat protein to consumers worldwide. In fact, 2007 was the sixth consecutive year of record pork production in the United States.

Exports of U.S. pork also continue to grow. New technologies have been adopted and productivity has been increased to maintain the U.S. pork industry's international competitiveness. As a result, pork exports have hit new records for the past 16 years. In 2007, exports represented nearly 15 percent of production. This year, approximately 2.8 billion pounds of pork and pork products are expected to be exported at a value of $4.1 billion.

In providing pork to the world, producers operate under a set of ethical principles, which broadly include humane and compassionate care for their pigs. Specific to animal-health products, producers use antibiotics judiciously and responsibly to protect pig health, to produce safe pork and manage antibiotic use to protect public health.

To meet the tremendous demands for pork in the domestic and export markets, pork producers have designed systems that maximize animal health and production. Pig barns are built to protect animal health by providing pigs a controlled climate and protection from the elements and predators. These barns help ensure that producers can observe animals daily and that each animal has access to ample water and feed, which is formulated to provide optimum nutrition for their life stage.

To better manage disease challenges, modern U.S. pork production uses the practices of multisite production and all-in-all-out pig flow. Simply stated, that means that after baby pigs are weaned they are moved to barns that are geographically separated from the breeding animals. Pork producers strive to keep pigs together in groups that are the same age and come from the same breeding herd. Pork producers implement this to minimize disease. Before a new group of pigs is placed, the barns are completely emptied, cleaned and disinfected.

Antibiotics Used To Protect Pigs, Provide Safe Food

The health and well-being of their pigs is critical to the success of the U.S. pork industry and pork producers. The prudent use of antibiotics in the pork industry is essential to providing consumers safe foods and to ensuring animal health. Antibiotics are only one tool to help producers do this. Today, the Food and Drug Administration's (FDA) Center for Veterinary Medicine (CVM) approves antibiotics for four uses:

1. Disease Treatment: antibiotics used to treat animals after they are clinically ill.

2. Disease Control: antibiotics used to reduce a specific disease after the animal has been exposed to the infectious agent.

3. Disease Prevention: antibiotics administered to animals prior to or directly following exposure to an infectious agent.

4. Nutritional Efficiency: antibiotics used in feed at low concentrations allow the animals to more efficiently utilize the feed they eat.

CVM allows antibiotics to be given to pigs through feed or water. Pigs can also be injected with antibiotics. Producers and veterinarians work together to make the decisions on how, when and which antibiotics should be administered.

Pork producers and veterinarians take numerous steps to maximize animal health and reduce the need to use antibiotics. In addition to current U.S. pork industry production practices of multisite production, herd health management programs have been created and tailored to each production system and often to individual farms.

Pork producers work in collaboration with their veterinarians to design herd health programs. These programs may include diagnostics for determining the best time to vaccinate for diseases or the best time to use antibiotics for preventing a disease outbreak. The health management plans also may include information on ventilation of the barns, balanced feed rations and parasite control. The plans are about total system health management, not just about what antibiotic to treat a specific illness.

Diagnostics are used when pigs are sick. A producer calls his or her veterinarian who takes and submits samples to a veterinary diagnostic laboratory. The results of these tests isolate the bug or bugs causing the disease, as well as give an indication of the best way to treat the pigs and prevent the bug from making other groups of pigs sick.

Pork Industry Developed Guidelines on Antibiotic Use

U.S. pork producers take the use of antibiotics very seriously. After 4 years of development and tests, the pork industry rolled out the first producer responsible antibiotic use program, "Take Care—Use Antibiotics Responsibly," in 2005. The program outlines principles and guidelines that protect public health, animal health and animal well-being through the responsible use of antibiotics. During the development of "Take Care," the pork industry worked with Federal public health agencies, including the Centers for Disease Control (CDC) and the FDA, as well as numerous stakeholders such as the American Association of Swine Veterinarians (AASV), the American Veterinary Medical Association (AVMA), the Animal Health Institute (AHI), the American Feed Industry Association (AFIA) and McDonald's. The pork industry's responsible-use program has been praised by many Federal agencies, legislators, consumer organizations and food supply companies. The U.S. pork industry developed this program because it was the right thing to do. Like all Americans, pork producers care about animal health and public health.

The guiding principles in "Take Care" are:

- Take appropriate steps to decrease the need for the application of antibiotics.
- Assess the advantages and disadvantages of all uses of antibiotics.
- Use antibiotics only when they provide measurable benefits.
- Complete the Pork Quality Assurance (PQA) Plus Program and fully implement the management practices prescribed for responsible use of animal health products into daily operations.
  - Use professional veterinary input as the basis for all medication decision-making.
  - Antibiotics should be used for treatment only when there is an appropriate clinical diagnosis.
  - Limit antibiotic treatment to ill or at-risk animals, treating the fewest animals indicated.
  - Antibiotics that are important in treating antibiotic-resistant infections in human or veterinary medicine should be used in animals only after careful review and reasonable justification.
  - Mixing together injectable or water medications, including antibiotics, by producers is illegal.
  - Minimize environmental exposure through proper handling and disposal of all animal health products, including antibiotics.

Initially, "Take Care" started as a voluntary program, and many producers participated. Today, however, the pork industry understands how important it is to use antibiotics responsibly, and "Take Care" is the way the U.S. pork industry does business. It's good for our pigs, it's good for our producers and families, and it's good for the bottom line. "Take Care" has been incorporated into the industry's Pork Quality Assurance (PQA) Plus program, which includes on-farm assessments, including reviews of whether the antibiotic-use principles are being practiced. Producer PQA Plus certification is required by U.S. packing plants as a condition of sale. Through 4–H and FFA, PQA Plus, including "Take Care," is also taught to the next generation of pork producers, as the young producers have an obligation to use antibiotics responsibly.

The veterinarians working in the U.S. pork industry also have been proactive in the responsible use of antibiotics. AASV was the first species-specific veterinary organization to collaborate with FDA and AVMA to create and endorse judicious-use guidelines for antibiotics.

Addressing Critics' Concerns

There are some who believe that the use of antibiotics in pork production adversely affects public health. There is ample evidence to suggest that not only does the responsible use of antibiotics in pork production protect animal health and welfare, but it may actually protect public health.

Denmark's ban on antibiotic growth promoters (AGPs) is often cited as an example of why there should be restrictions on the use of antibiotics in pork production. However, the reality of the impacts of the ban on antibiotic growth promoters in Denmark is seldom discussed. In 1998, Denmark banned the use of AGPs in finishing swine and in all swine in 1999. It should be noted that this ban was **only** on the use of AGPs, not all antibiotics in feed or water. Danish pork producers saw an immediate increase in post-weaning diarrhea and an increase in baby pig mortality that has had long lasting impacts on the Danish pig industry. [1]

These increases in baby pig mortality and the overall impact on animal welfare might be acceptable if there were improvements to public health. But public health improvements have not materialized. In fact, even with intensive surveillance of the public health impacts, the only demonstrable change to public health could be considered potentially damaging. The Danes observed an increase in the number of human *Salmonella* infections that were resistant to the antibiotic tetracycline. They believe it was due to an increase in the use of tetracycline in pigs to combat the post-weaning diarrhea. [2]

Proponents of imposing a similar ban on antibiotic use in the U.S. cite the drop in total tons of antibiotics used in pork production in Denmark. While overall use of antibiotics has declined, there has been a marked increase in the therapeutic use of antibiotics—antibiotics used for treatment, prevention and control of disease. Today, the use of therapeutic antibiotics in Danish pigs now surpasses what was used to promote growth prior to the ban in 1999 and continues to rise each year. [3] The therapeutic antibiotics used are more modern molecules considered to be more important in human medicine than the older drugs used to promote growth. In 2002, two Iowa State economists used an economic model to estimate the effect that the Denmark ban would have on U.S. pork production, finding that the cost of production would rise by $4.50 per pig in the first year after a ban. Over 10 years, a ban's cumulative cost to the pork industry would be greater than $700 million. (In this model, the economists assumed the price of corn to be $2.50 per bushel.) Clearly, implementing a ban on antibiotic use similar to that in Denmark would not be a wise course of action for U.S. pork producers. [4]

The Danish experience illustrates that if a ban were put in place in the United States on the use of antibiotics as feed additives, pig health and well-being would decline. More pigs would suffer, and more pigs would die.

An Iowa State University study conducted by Dr. Scott Hurd, who now is USDA Deputy Under Secretary of Food Safety, demonstrated that when pigs have been sick during their life, those pigs will have a greater presence of food safety pathogens on carcasses. [5] This study reinforces the importance of using all of the tools available to protect the health of animals.

Another study also answers the critics who suggest that raising animals in large groups inside barns using modern production methods, including the use of antibiotics, presents a human health threat. Dr. Wondwossen Gebreyes from the Ohio State University found that pork from pigs produced in modern, conventional systems had levels of three foodborne pathogens lower than pigs raised in outdoor systems without the use of antibiotics. [6]

According to the AVMA, risk assessments on antibiotic use demonstrate a very low risk to human health from the use of antimicrobials in food animals, and some

models predict an increased human health burden if antibiotic use in food animals were withheld.

A final word on the issue of AGPs: Contrary to the untruths spread by some organizations, AGPs represent only 4.6 percent of all antibiotics given to animals and even the overwhelming majority of those antibiotics prevents and controls diseases. [7] Additionally, very few of them are important to human medicine.

Producers Work With Veterinarians

Pork producers work very closely with their veterinarians. Those swine veterinarians, upon graduation from veterinary school, take an oath stating that they solemnly swear to uphold their "scientific knowledge and skill for the benefit of society through the protection of animal health, the relief of animal suffering, the conservation of animal resources, the promotion of public health, and the advancement of medical knowledge." Swine veterinarians need all the tools available to live up to that oath. Legislative attempts to ban certain antibiotics will compromise the oath that every veterinarian took on his or her graduation day.

In summary, pork producers and veterinarians have a moral obligation to use antibiotics responsibly to protect human health and provide safe food, both of which are paramount concerns to America's pork producers. Producers also have an ethical obligation to maintain the health of their pigs. Antibiotics are merely one piece to the health care system that pigs need. The U.S. pork industry has a long history of being proactive and doing the right thing for its pigs and consumers. Pork producer developed "Take Care" and PQA Plus not because they had to but because it was the right thing to do. The U.S. pork industry continues to adopt better techniques and new technologies, but it cannot lose the tools it already has developed, including antibiotics, to protect the well-being of producers' animals and the safety of pork.

Notes:

[1] Agence France-Presse. *World-leading pork exporter Denmark sees sharp increase in pig mortality.* COPENHAGEN BUSINESS Online. 2005. *http://archive.wn.com/2005/09/06/1400/copenhagenbusiness/.*

[2] World Health Organization. *Impacts of antimicrobial growth promoter termination in Denmark.* Online. 2002. *http://whqlibdoc.who.int/hq/2003/WHO_CDS_CPE_ZFK_2003.1.pdf.*

[3] Danmap 2006. *www.Danmap.org.*

[4] Hayes, Jensen, Fabios. *Technology choice and the economic effects of a ban on the use of antimicrobial feed additives in swine rations.* FOOD CONTROL, 2002.

[5] Hurd H.S., Brudvig J., Dickson J, *et al.* 2008. *Swine health impact on carcass contamination and human foodborne risk.* PUBLIC HEALTH REPORTS: (123) pp. 343–351.

[6] Gebreyes W., Bahnson P., Funk J., *et al.* 2008. *Seroprevalence of* ***Trichinella, Toxoplasma*** and ***Salmonella*** in antimicrobial-free and conventional swine production systems. FOODBORNE PATHOGENS AND DISEASE: (5) pp. 199–203.

[7] Animal Health Institute. 2007. *www.AHI.org.*

The CHAIRMAN. Thank you, Dr. Rowles.

I think we will go right down the table and then we will come back to questions, so Dr. Rybolt, please.

STATEMENT OF MICHAEL L. RYBOLT, PH.D., DIRECTOR, SCIENTIFIC AND REGULATORY AFFAIRS, NATIONAL TURKEY FEDERATION, WASHINGTON, D.C.

Dr. RYBOLT. Good morning, Chairman Boswell, Congressman Hayes and other Members of the Subcommittee. Thank you for the opportunity to be here to talk about the advancements in animal health in the poultry industry. My name is Dr. Michael Rybolt. I am with the National Turkey Federation. I am the Director of Scientific and Regulatory Affairs and I also oversee the Turkey Health and Welfare Committee. NTF, which represents more than 98 percent of the U.S. turkey industry, greatly appreciates the opportunity to be here to talk about the advances in animal health within the U.S. turkey industry.

In the United States, turkeys are raised on small family farms, around 227 acres in size. The advances the turkey industry has made has allowed these farms to produce large volumes of safe, wholesome product more efficiently. The advances have allowed the industry to raise more than 260 million turkeys at an average weight of around 28 pounds. After processing, this has yielded 6 billion pounds of turkey products for human consumption. By contrast, in 1970, the industry only raised 105 million birds with an average live weight of 17 pounds, which equated to about 1.5 billion pounds of product for human consumption. The advances the industry has made in the past 30 plus years have been driven by science and the dedication of the turkey industry experts with the goal to produce the safest, highest-quality, nutritious products at an affordable price for the consuming public. In order to meet that goal, maintaining the health and welfare of the flock is paramount. The industry accomplishes this through a variety of means including raising the birds in environmentally controlled houses or barns, increased biosecurity on the farms, various animal health monitoring programs, the use of vaccination programs and using approved animal drugs or antimicrobials. All of these tools are important for the industry, and when used together help the industry meet its goal.

Arguably, one of the most significant advances in the turkey industry that has played an essential role in improving the health of the turkey flock is the use of environmentally controlled houses or barns. Raising birds indoors helps protect them from predatory wildlife and inclement weather. In turn, this not only prevents the birds from becoming prey but also reduces the risk of a flock becoming exposed to disease agents. Raising turkeys indoors also creates a less stressful environment for the birds, which research from the University of Minnesota has shown leads to better production. A well-treated turkey will grow to its full potential and provide the consumer with a low-fat, high-protein source.

Likewise, increased biosecurity is also important to mitigate exposure of the flocks to potential disease-causing agents. By limiting access to only authorized personnel and/or ensuring proper sanitation of footwear and clothing, strict biosecurity is essential to maintain the health and well-being of our birds. Biosecurity programs have been implemented for many years and are continually updated and strengthened as needed, taking into account the latest scientific data.

Additionally, the turkey industry has made significant advances in the animal disease-monitoring arena. Various programs exist that have benefited the industry and allowed for increased production gains. Such programs include the USDA's National Poultry Improvement Plan, or NPIP. The use of these programs has allowed the industry to monitor various diseases and to control and eradicate them before they spread, thereby allowing for increased livability and more food for humans to consume.

Unfortunately, like humans, turkeys occasionally will become ill and will require medication. For some diseases, the industry has the ability to use prophylactic programs. However, there are also times when the flocks need to be treated with antimicrobials for controlling bacterial diseases. The use of antimicrobials for disease

control, prevention and treatment is necessary for the health and welfare of the turkey flocks.

To raise turkeys without antibiotics would increase the incidence of illness within the flocks. This would result in a decrease in density or an increase in the amount of land needed to raise the additional turkeys to meet the needs of the consuming public. This would also lead to a decrease in livability, an estimated ten percent reduction in gain per day, and a decrease of 0.05 percent in feed conversion.

To compensate for the higher increased illness rates, a decrease in the feed conversion and to meet the growing need of the consuming public, we would require 175,550 tons more feed to feed the turkeys. This increased requirement would equate to about 3.7 million bushels of corn and 1.7 million bushels of soybeans just for the turkey industry alone. In order to fill this need, obviously there would need to be more acreage planted for crop production or an increase in crop yields. Obviously there is an economic impact with increased feed requirements. However, there is also an environmental impact. The decreased feed conversion leads to less efficiency in digestion and utilization of the nutrients in that feed and this will ultimately result in an increase in manure.

With regard to the antibiotic use, each turkey veterinarian follows a set of prudent use guidelines that were adopted in 1998 by AVMA in conjunction with FDA and CDC for prescribing and administering antimicrobials to turkey flocks. Additionally, the flocks that are treated are also required to undergo a withdrawal period prior to processing to ensure all antimicrobials have been eliminated from the bird and ensuring the consumer is not indirectly exposed to the antimicrobials. USDA's Food Safety and Inspection Service also maintains a monitoring program that tests for the antibiotic residue levels in turkey meats to ensure the industry is following the required withdrawal period. Current data indicates that virtually all turkeys are free of unsafe residues.

The tools discussed previously have allowed the industry to make significant improvements in turkey health over the past decade which has allowed for increased production in a more efficient manner. Without these tools, the industry would not be in a position to supply the nearly 6 billion pounds of safe, wholesome, nutritious turkey products for the consumer. If the industry were not able to maintain its current status, there would without a doubt be a decrease in production and an increase in production costs which would inevitably be passed onto the consumer.

The increased costs to raise turkeys without antibiotics is real. One can quickly see the impact on the consumer by walking into the grocery store and doing a price comparison between two similar products, one raised conventionally and one raised without antibiotics. Today at retail outlets here in the D.C. market, a conventionally raised turkey costs $1.29 per pound. A similar whole turkey that was produced without antibiotics costs $2.29 per pound. With the average consumer purchasing a 15 pound whole turkey, that would mean there would be $15 tacked on to their grocery bill. This increased cost to the consumer is a result of more advanced production practices. While some consumers are willing and able to afford the increase, not all Americans have that ability or luxury.

Mr. Chairman and other Members of the Subcommittee, again let me thank you for the opportunity for the National Turkey Federation to provide testimony today. The number one goal of the U.S. turkey industry is to provide safe, wholesome, nutritious quality turkey products at an affordable cost to the consumer. All of the advances discussed previously have allowed the industry to meet its goals. Thank you very much, and I will be happy to answer any questions.

[The prepared statement of Dr. Rybolt follows:]

PREPARED STATEMENT OF MICHAEL L. RYBOLT, PH.D., DIRECTOR, SCIENTIFIC AND REGULATORY AFFAIRS, NATIONAL TURKEY FEDERATION, WASHINGTON, D.C.

Good morning Chairman Boswell, Congressman Hayes and Members of the Subcommittee. Thank you for the opportunity to participate in today's hearing on the advances of animal health with the livestock and poultry industry. My name is Dr. Michael Rybolt and I am the Director for Scientific and Regulatory Affairs for the National Turkey Federation and staff the Federation's Turkey Health and Welfare Committee. NTF, which represents more than 98% of the U.S. turkey industry, greatly appreciates the opportunity to provide comments on the advances in animal health within the U.S. turkey industry.

In the United States, turkeys are raised on small farms of an average size around 227 acres. There have been many advances in turkey production that have allowed the industry to produce a larger volume of safe, wholesome product more efficiently. These advances allowed the industry to raise more than 260 million turkeys in 2007, with an average live weight per bird at 28 pounds. After processing, this yielded nearly 6 billion pounds of turkey products for human consumption. By contrast, in 1970, the industry only raised 105 million birds, with an average live weight of 17 pounds, which provided 1.5 billion pounds of product for human consumption.

The advances the industry has made in the last 30 plus years has been driven by science and the dedication of turkey industry experts with the goal to produce the safest, highest quality, nutritious products at an affordable price. In order to meet that goal, maintaining the health and well being of the turkey flocks is paramount. The industry accomplishes this through a variety of means, including raising the birds in environmentally controlled houses or barns, increased biosecurity on farms, various animal health monitoring programs, the use of vaccination programs, and using approved animal drugs or antimicrobials. All of these tools are important for the industry and when used together help the industry meet its goal.

Arguably, one of the most significant advances in the turkey industry that has played an essential role in improving the health of turkeys flocks is the use of environmentally controlled houses or barns. Raising birds indoors helps protect them from predatory wildlife and inclement weather. This in turn not only prevents the birds from becoming prey but also reduces the risk of the flocks being exposed to disease agents. Raising turkeys indoors also creates a less stressful environment for the birds, which research from the University of Minnesota has demonstrated leads to better production. A well-treated turkey will grow to its full potential and provide consumers with a low-fat and high-protein source.

Likewise, increased biosecurity is also important to mitigate exposure of the flocks to potential disease causing agents. By limiting access to only authorized personnel and/or ensuring proper sanitation of footwear and clothing, strict biosecurity is essential to maintain the health and well being of our birds. Biosecurity programs have been implemented for many years and are continually updated and strengthened as needed, taking into account the latest scientific data.

Additionally, the turkey industry has made significant advances in the animal disease monitoring arena. Various programs exist that have benefited the industry and allowed for increase production gains. Such programs include the USDA National Poultry Improvement Plan. The use of these programs has allowed the industry to monitor for various diseases and to control and eradicate them before they spread, thereby allowing for increased livability and more food for human consumption.

Unfortunately, like humans, turkeys occasionally will become ill and will require medication. For some diseases, the industry has the ability to use prophylactic programs; however, there are also times when a flocks needs to be treated with antimicrobials for controlling bacterial diseases. Use of antimicrobials for disease

control, prevention and treatment is necessary for the health and welfare of the turkey flocks.

To raise turkeys without antibiotics would increase the incidence of illness in turkey flocks. This would result in a decrease in density or an increase in the amount of land needed to raise the additional turkeys needed to meet the consumer demand. This would also lead to decreased livability, an anticipated 10% reduction in gain per day and a decrease of 0.05% in feed conversion.

To compensate for the higher illness rate and resulting decrease in feed conversion and to meet the growing needs of the consuming public, an additional 175,500 tons of feed would be required for the turkey industry. This increase in feed requirement would equate to about 3.7 million bushels of corn and 1.7 million bushels of soybeans, for the turkey industry alone. In order to fill this need, there would need to be either more acreage placed into crop production or an increase in crop yield.

Obviously, there is an economic impact with the increased feed requirement. However, there is also an environmental impact. The decrease in feed conversion leads to less efficiency in digestion and utilization of nutrients, and this ultimately results in an increase in manure.

With regard to antibiotic use, each turkey veterinarian follows a set of prudent use guidelines that were adopted in 1998 by the American Veterinary Medical Association in conjunction with FDA and CDC for prescribing and administering antimicrobials to the turkey flocks. Additionally, the turkey flocks that are treated are also required to undergo a withdrawal period prior to processing to ensure all the antimicrobial has been eliminated from the birds, ensuring the consumer is not indirectly exposed to the antimicrobials. The USDA Food Safety Inspection Service also maintains a monitoring program that test for antibiotic residues levels in turkey meat to ensure the industry is following the required withdrawal period. Current USDA data indicates that 99.9% of samples are free of unsafe residues.

The tools discussed previously have allowed the turkey industry to make significant improvements in turkey health over the past decades, which have allowed for the increase in production in a more efficient manner. Without these tools, the industry would not be in a position to supply nearly 6 billion pounds of safe, wholesome, nutritious turkey products for human consumption. If the industry was not able to maintain its current status, there would without a doubt be decreases in production and an increase in production cost, which would inevitably be passed on to the consumer.

The increased costs to raise turkeys without antibiotics are real. One can quickly see the impact on cost to the consumer by walking into a grocery store and looking at the price comparison between two similar products, one that is antibiotic free and the other that is not. Today, at retail outlets here in the D.C. market, a conventionally raised whole turkey costs $1.29 per pound. A similar whole turkey that was produced from antibiotic-free birds costs $2.29 per pound. With the average consumer purchasing a 15 pound whole bird, that is a $15 increase in the grocery bill. This increase cost to the consumer is a result of the more advanced production practices. While some consumers are willing and able to afford the increased cost, not all Americans have that luxury.

Mr. Chairman and other Members of the Subcommittee, again, let me thank you for allowing the National Turkey Federation the opportunity to provide this testimony today. The number one goal of the U.S. turkey industry is to provide safe, wholesome, nutritious quality products at an affordable cost to the consumer. All the advances discussed previously have allowed the industry to meet this goal. Thank you very much and I will be happy to answer any questions.

The CHAIRMAN. Thank you.

Dr. Byrne.

STATEMENT OF ROBERT D. BYRNE, PH.D., SENIOR VICE PRESIDENT, SCIENTIFIC AND REGULATORY AFFAIRS, NATIONAL MILK PRODUCERS FEDERATION, ARLINGTON, VA

Dr. BYRNE. Good morning. Thank you, Chairman Boswell, Ranking Member Hayes and Members of the Subcommittee. My name is Rob Byrne. I am Senior Vice President of Scientific and Regulatory Affairs for the National Milk Producers Federation. The National Milk Producers Federation, based in Arlington, Virginia, develops and carries out policies that advance the well-being of dairy producers and cooperatives they own. The members of NMPF's 31

cooperatives produce the majority of the U.S. milk supply, making NMPF the voice of more than 40,000 dairy producers on Capitol Hill and with government agencies.

I am very grateful that the Committee is holding this hearing to review the advances in animal health within the livestock industry and am pleased to discuss some of these as they relate to the dairy industry with you. There have been many advances in animal health in the dairy industry over the years and these have enabled the industry to become even more efficient in milk production. As an example of this efficiency, the dairy industry has changed dramatically in the last 50 years. In 1960, there were 17.6 million dairy cows on 1.8 million dairy farms. In 2008, there were 9.3 million dairy cows on 59,000 commercial dairy farms in all 50 states. During the same time, milk production has actually increased from 123 billion pounds per year to almost 190 billion pounds per year. from these numbers, it is clear that the dairy industry is producing more milk with many fewer cows on many fewer farms. At the same time, milk safety and quality have continued to increase, resulting in the assurance that the dairy industry provides an abundant supply of high-quality, safe milk for consumers.

Providing proper care to animals is the best means to ensure their health and this is of utmost importance to our members and dairy producers across the country. This is accomplished on dairy farms through a variety of measures starting with good herd management. Proper management and handling of animals keeps them healthy, producing an abundant supply of high-quality milk. Attention to animal nutrition and feeding for cows is also important, both to ensure they receive diets appropriate to their stage in life to keep them healthy and to ensure that the milk they produce is safe and wholesome. Last, the veterinary-client-patient relationship is one of the most important means to make sure that the health of dairy cows is constantly monitored. A veterinary-client-patient relationship demonstrates that the dairy farm uses a veterinarian for health and disease issues, allowing the producers to use medications appropriately for sick or injured animals. All of these items are very important in maintaining a healthy and productive dairy cow.

To address animal care, NMPF is currently completing the purchase of the Dairy Quality Assurance Center in Stratford, Iowa, and assuming it within NMPF. The DQA program is widely recognized throughout the dairy industry as an excellent educational tool for dairy producers regarding animal care practices. Through a comprehensive set of best management practices, the program provides measurable and verifiable components to allow the industry to prove the good practices being conducted at the farm. While this program currently exists as a separate facility, housing it within NMPF will enable us to create a National Dairy Quality Assurance Program to assist dairy producers across the country in maintaining a viable, up-to-date, quality assurance program. This will provide us an appropriate vehicle to best implement future advances in animal health within our industry.

Despite all these measures to address animal care and health, dairy cows occasionally do get sick and sometimes they must be treated with appropriate medications. When this happens, there

are many safeguards in place to ensure that residues of these medications do not end up in the milk supply. I would like to address a few of these areas in a little more detail to describe how the dairy industry ensures that any animal health treatments that are given do not have a negative impact on the quality or safety of milk.

On-farm therapeutic use of animal healthcare products occurs to cure animals from illness across all stages of their life. A recent survey of dairy farms in Pennsylvania showed the therapeutic use of medications on dairy farms for several illnesses of dairy animals. These illnesses include pneumonia, metritis, foot rot, enteritis and mastitis. It is important to note that the majority of animals are actually not treated with medications, rather, therapeutic usage is reserved for clinical cases of disease.

The first step in deciding to treat a dairy cow is to use only medications that are approved by the Food and Drug Administration's Center for Veterinary Medicine for use in lactating animals. The process for animal drug approval that we heard about earlier involves safety assessments and providing withdrawal times to allow the animal drug to clear the animal's system. In the case of lactating animals, there are specific withdrawal times established to ensure that milk is not contaminated. The milk from any animals that are treated must be held out of the commercial supply until these withdrawal times are met. The approval process is very rigorous and assures that the product is safe both for animals and for the food supply and consumers.

To reduce the level of potentially harmful bacteria which result in infections and sickness to animals, dairy cows may also be treated prophylactically. On-farm prophylactic use of animal medications occurs in two areas in the dairy industry: the use of medicated milk replacers fed to calves and the use of dry cow treatments to prevent mastitis infection during the dry cow period. Medicated milk replacers are used because studies have shown an improvement in animal performance and reduction of scours in dairy calves. Reported usage of medicated milk replacers on dairy farms ranges from 22 to 70 percent, and the use of medicated milk replacers assists with the overall health of dairy calves in this important developmental stage of their life.

Dry cow treatment often involves the use of a long-acting intramammary infusion given to cows between lactation cycles with the intention of treating existing infections and preventing new infections. The use of dry cow treatment is near universal. For example, in a survey in Washington State, 82 percent of the dairy farms reporting using dry cow treatment on all of their cows. While dry cow treatment is near universal, two surveys of antimicrobial resistance of mastitis bacteria in dairy cattle found no consistent change in the prevalence of resistance.

Recognizing that lactating dairy cows are occasionally treated for diseases and to ensure that no animal medications remain in milk, all milk is screened before it is accepted into a processing plant. This is a very important control step in the process, and it is part of a system that the dairy industry, in cooperation with the states and FDA, established in the early 1990s.

As part of this regulatory program, a sample from every tanker of milk that arrives at a processing plant is tested before milk is unloaded using screening tests that have been evaluated and approved for use by FDA. Milk that tests positive is rejected for human consumption and is appropriately discarded. The dairy farmer causing the positive result must then pay for the entire load of milk. This costs approximately $12,000, so there is a large financial incentive to make sure that no treated dairy cows end up being milked. In addition, all milk from the dairy farm is then withheld until a negative farm test is obtained. In 2007, less than .032 percent of all milk tanker samples tested positive for residues of animal medications. Milk tanker samples testing positive declined nearly 70 percent from 1997 to the present, indicating that the program is effective at detecting and deterring animal medications in milk.

Proper animal healthcare is the first step in the assurance that dairy products remain safe and wholesome. In fact, due largely to the part of the animal healthcare practices, and milk being the most highly regulated food product in the United States, dairy foods are lowest among major food groups as the cause of foodborne illness. Clean conditions, good manufacturing practices and the adoption of pasteurization have all enabled dairy products to maintain an excellent safety record. Of the 2,700 foodborne disease outbreaks summarized by CDC from 1993 to 1997, only ten were attributed to milk consumption and seven to cheese consumption. Most foodborne disease outbreaks associated with milk and cheese are due to the consumption of raw or unpasteurized milk and raw milk cheeses that have not been properly aged.

As a result of the entire range of activities at the dairy farm which start with providing excellent care for animal health, to the measures taken at the processing plant, the dairy industry consistently provides a safe, wholesome and nutritious product for all consumers to enjoy.

Thank you again for the opportunity to appear as part of this important hearing, and I would be happy to answer any questions you may have about advances in animal health within the dairy industry.

[The prepared statement of Dr. Byrne follows:]

PREPARED STATEMENT OF ROBERT D. BYRNE, PH.D., SENIOR VICE PRESIDENT, SCIENTIFIC AND REGULATORY AFFAIRS, NATIONAL MILK PRODUCERS FEDERATION, ARLINGTON, VA

Thank you Chairman Boswell, Ranking Member Hayes, and Members of the Committee. My name is Rob Byrne and I am Senior Vice President of Scientific & Regulatory Affairs for the National Milk Producers Federation. The National Milk Producers Federation (NMPF), based in Arlington, VA, develops and carries out policies that advance the well being of dairy producers and the cooperatives they own. The members of NMPF's 31 cooperatives produce the majority of the U.S. milk supply, making NMPF the voice of more than 40,000 dairy producers on Capitol Hill and with government agencies.

I am grateful that the Committee is holding this hearing to review the advances of animal health within the livestock industry and am pleased to discuss some of these as they relate to the dairy industry. There have been many advances in animal health in the dairy industry over the years and these have enabled the industry to become even more efficient in milk production. As an example of this efficiency, the dairy industry has changed dramatically in the past 50 years. In 1960, there were 17.6 million dairy cows on 1.8 million dairy farms. In 2008, there are 9.3 mil-

lion cows on 59,000 commercial dairy farms in all fifty states. During this same time, milk production has increased from 123 billion pounds to almost 190 billion pounds. from these numbers, it is clear that the dairy industry is producing more milk with many fewer cows on many fewer farms. At the same time, milk safety and quality have continued to increase, resulting in the assurance that the dairy industry provides an abundant supply of high quality, safe milk for consumers.

Providing proper care to animals is the best means to ensure their health and this is of the utmost importance to our members and dairy producers across the county. This is accomplished on dairy farms through a variety of measures, starting with good herd management. Proper management and handling of animals keeps them healthy and producing an abundant supply of high quality milk. Attention to animal nutrition and feeding for cows is also important, both to ensure they receive diets appropriate to their stage in life, to keep them healthy, and to ensure that the milk they produce is safe and wholesome. Lastly, the veterinary-client-patient relationship is one of the most important means to make sure that the health of dairy cows is constantly monitored. A veterinary-client-patient relationship demonstrates that the dairy farm uses a veterinarian for health and disease issues allowing the producer to use medications appropriately for sick or injured animals. All of these items are very important in maintaining a healthy and productive dairy cow.

To address animal care, NMPF is currently completing the purchase of the Dairy Quality Assurance (DQA) Center in Stratford, Iowa and assuming it within NMPF. The DQA program is widely recognized throughout the dairy industry as an excellent educational tool for dairy producers regarding animal care practices. Through a comprehensive set of Best Management Practices, the program provides measurable and verifiable components to allow the industry to prove the good practices being conducted at the farm. While this program currently exists as a separate entity, housing it within NMPF will enable us to create a National Dairy Quality Assurance Program to assist dairy producers across the country in maintaining a viable, up-to-date quality assurance program. This will provide us an appropriate vehicle to best implement future advances in animal health in our industry.

Despite all of these measures to address animal care and health, dairy cows occasionally get sick and sometimes must then be treated with appropriate medications. When this happens, there are many safeguards in place to ensure that residues of these medications do not end up in the milk supply. I'd like to address a few areas in more detail to describe how the dairy industry ensures that any animal health treatments that are given do not have a negative impact on the safety or quality of milk.

On-farm therapeutic use of animal health care products occurs to cure animals from illness across all ages of dairy animals. A recent survey of dairy farms in Pennsylvania [1] showed the therapeutic use of medications on dairy farms for several illnesses of dairy animals. These illnesses include pneumonia, metritis, foot rot, enteritis, and mastitis. It is important to note that the majority of animals are actually not treated with medications; rather therapeutic usage is reserved for clinical cases of disease.

The first step in deciding to treat a dairy cow is to use only medications that are approved by the Food and Drug Administration's (FDA) Center for Veterinary Medicine (CVM) for use in lactating animals. The process for animal drug approval involves safety assessments and providing withdrawal times to allow the animal drug to clear the animal's system. In the case of lactating animals, there are specific withdrawal times established to ensure that milk is not contaminated. The milk from any animals that are treated must held out of the commercial supply until these withdrawal times are met. The approval process is very rigorous and assures that the product is safe both for animals and the food supply.

To reduce the level of potentially harmful bacteria, which can result in infections and sickness to animals, dairy cows may also be treated prophylactically. On-farm prophylactic use of animal medications occurs in two areas: (1) use of medicated milk replacers fed to calves and (2) use of dry cow treatments to prevent mastitis infection during the dry period.

Medicated milk replacers are used because studies have shown an improvement in animal performance and reduction of scours in dairy calves.[2] Reported usage of

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[1] Sawant, A.A., L.M. Sordillo, and B.M. Jayarao. 2005. *A survey on antibiotic usage in dairy herds in Pennsylvania.* J. DAIRY SCI. 88:2991–2999.

[2] Quigley, J.D., J.J. Drewry, L.M. Murray, and S.J. Ivey. 1997. *Body weight gain, feed efficiency, and fecal scores of dairy calves in response to galactosyl-lactose or antibiotics in milk replacers.* J. DAIRY SCI. 80:1751–1754.

medicated milk replacers on dairy farms ranges from 22 to 70%.[3 4] The use of medicated milk replacers assists with the overall health of dairy calves in this important developmental stage of their life.

Dry cow treatment often involves the use of "a long-acting intramammary infusion given to cows between lactation cycles with the intention of treating existing infections and preventing new infections."[5] The use of dry cow treatment is near universal. For example in a survey from Washington State, 82% of dairy farms reported using dry cow treatment on all of their cows.[6] While dry cow treatment is near universal, two surveys of antimicrobial resistance of mastitis bacteria in dairy cattle found no consistent change in the prevalence of resistance.[7 8]

Recognizing that lactating dairy cows are occasionally treated for diseases and to ensure that no animal medications remain in milk, all milk is screened before it is accepted into a processing plant. This is a very important control step in the process and is part of a system that the dairy industry, in cooperation with the states and FDA, established in the early 1990's. As part of this regulatory program, a sample from every tanker of milk that arrives at a processing plant is tested before milk is unloaded using screening tests that have been evaluated and approved for use by FDA. Milk that tests positive is rejected for human consumption and appropriately discarded. The dairy farmer causing the positive result must then pay for the entire load of milk. This costs approximately $12,000, so there is a large financial incentive to make sure that no treated dairy cows are milked. In addition, all milk from the dairy farm is then withheld until a negative farm test result is obtained. In 2007 less than 0.032% of all milk tanker samples tested positive for residues of animal medications.[9] Milk tanker samples testing positive declined by nearly 70% from 1996–2005 indicating that the program is effective at detecting and deterring animal medications in milk.[10 11]

Proper animal health care is the first step in the assurance that dairy products remain safe and wholesome. In fact, due largely in part to these animal health care practices, and milk being the most highly regulated food product in the United States,[12] dairy foods are lowest among major food groups in the cause of foodborne illness. Clean conditions, good manufacturing practices, and the adoption of pasteurization have all enabled dairy products to maintain an excellent safety record. Of 2,751 foodborne disease outbreaks summarized by the Center for Disease Control (CDC) from 1993–1997, ten were attributed to milk consumption (0.36%) and seven to cheese consumption (0.25%).[13] Most foodborne disease outbreaks associated with milk or cheese consumption is due to the consumption of raw (unpasteurized) milk or raw milk cheeses that have not been properly aged.

As a result of the entire range of activities at the dairy farm, which start with providing excellent care for animal health, to the measures taken at the processing plant, the dairy industry consistently provides a safe, wholesome, and nutritious range of products for all consumers to enjoy.

Thank you again for the opportunity to appear as part of this important hearing. I will be happy to answer any questions you may have about advances in animal health within the dairy industry.

The CHAIRMAN. Thank you.

Dr. Klopp.

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[3] Raymond, M.J., R.D. Wohrle, and D.R. Call. 2006. *Assessment and promotion of judicious antibiotic use on dairy farms in Washington State.* J. DAIRY SCI. 89:3228–3240.

[4] Sawant, A.A., L.M. Sordillo, and B.M. Jayarao. 2005. *A survey on antibiotic usage in dairy herds in Pennsylvania.* J. DAIRY SCI. 88:2991–2999.

[5] *Ibid.*

[6] *Ibid.*

[7] Erskine, R.J., R.D. Walker, C.A. Bolin, P.C. Bartlett, and D.G. White. 2002. *Trends in antibacterial susceptibility of mastitis pathogens during a seven-year period.* J. DAIRY SCI. 85:1111–1118.

[8] Makovec, J.A., and P.L. Ruegg. 2003. *Antimicrobial resistance of bacteria isolated from dairy cow milk samples submitted for bacterial culture: 8,905 samples (1994–2001).* J. AM. VET. MED. ASSOC. 222:1582–1589.

[9] National Milk Drug Residue Database: Fiscal Year 2007 Annual Report. Available online at: *http://www.cfsan.fda.gov/~acrobat/milkrp07.pdf.*

[10] *Ibid.*

[11] National Milk Drug Residue Database: Fiscal Year 1996 Annual Report. Available online at: *http://www.cfsan.fda.gov/~ear/milkrp96.html*

[12] Milk production is regulated under the Grade "A" Pasteurized Milk Ordinance.

[13] S.J. Olsen, L.C. MacKinnon, J.S. Goulding, N.H. Bean, L. Slutsker. 2000. *Surveillance for foodborne-disease outbreaks—United States, 1993–1997.* MMWR CDC SURVEILL. SUMM. Mar. 17;49(1):1–62 (*Most recent summary*).

STATEMENT OF SPANGLER KLOPP, D.V.M., D.A.C.P.V.; CORPORATE VETERINARIAN, TOWNSENDS, INC., GEORGETOWN, DE; ON BEHALF OF NATIONAL CHICKEN COUNCIL

Dr. KLOPP. Good morning, Chairman Boswell, Congressman Hayes. I thank you for the opportunity to be here to speak on behalf of the National Chicken Council. My name is Buzz Klopp. I am a practicing poultry veterinarian and have been so for 36 years.

For the past 14 years, I have worked for Townsends Incorporated, which is an integrated broiler chicken growing and processing company. We grow and process chickens in the States of North Carolina and Arkansas. The chicken industry itself has made exceptional advances over the decades and this is due in large part to the lead of science and just a lot of hard work and a lot of smart thinking by a lot of different people. Today's industry grows approximately nine billion chickens a year. We grow these chickens on approximately 34,000 independently owned and operated farms. Now, chickens are like anything else. They are a business, and the health of chickens is very important to the business, and maintaining the health of chickens is predicated on prevention of disease. We do this principally through vaccination, appropriate use of antibiotics and other antimicrobials, and good old sound poultry husbandry, or chicken house management, as we call it.

We have some basic parameters that we use for measuring health and performance of chickens. One of these is average daily gain. This is nothing more than how fast does the chicken grow, how much does it grow every day. Another basic parameter that we use is livability: of the number of chicks we place on a farm, how many of them do we take to the processing plant to process for food. The third parameter we use is condemnation at processing. The USDA has a presence in every one of our plants and they reject and discard carcasses that are unfit for human consumption. These are referred to as condemned carcasses, percentage condemnation rates.

We use vaccines to control diseases that cannot be controlled by antibiotics and husbandry. Antibiotics are used for control of specific types of bacterial and parasitic diseases. Now, I want to go back to the three parameters that we use in measuring chicken health and performance: average daily gain, or ADG, is the acronym. Back in the early 1970s when I came in the industry, we talked about a 4 pound chicken at 8 weeks of age. Today we talk about a 5½ pound chicken at 50 days of age. If we had to go back to the previous rates of average daily gain, we would need approximately 2,484,000,000 more chickens to be grown and processed in this country.

If we look at livability, livability percentages in the early 1980s were approximately 93½ percent. For today, the approximate livability is 95.6 percent. This is a real improvement of approximately 2.1 percent. Again, based on the nine billion chickens, if we do not have the appropriate interventions, we would have to have another 190,800,000 day old chicks placed to meet today's needs of the American public.

If we look at condemnation at processing and the improvement here, I have actually put a percentage to this, it is 456 percent over

42 years, and I have broken it down in a chart that is on the page. I am not going to bore you with all of the details of what those are. If you want to know, I will be happy to answer your questions. But again, without the interventions that we have available to us today, we would have to place and produce another 155,700,000 chickens to meet the needs of the American public.

Collectively, without the usage of the appropriate interventions that we have, this would total up to the need to raise approximately 2,830,500,000 more chickens to meet today's need. I think we all know that the population of the world is not holding on a steady line, it is not declining, it is increasing. So it is more food we need, not less food.

It is important to remember when we talk about chickens and a lot of other animals that these are free-roaming animals, and chickens are like dogs, cows, pigs, a lot of animals. They pick at the ground. That is just their nature. So they are very prone for the development of diseases of the gastrointestinal tract, and the occurrence of antibiotic resistance is not due to us in the chicken industry. We have been concerned about it. Like I said, I have been a practicing veterinarian for 36 years. We have been concerned with antibiotic resistance from that very time, and we manage this through the proper and sound usage of the products available to us through rotation programs, through dosage selections, through the proper selection of the given intervention available to us.

Good chicken health is maintained through the responsible use of vaccines and antibiotics, and this is important not just to me, not just to my industry, but it is important to the American public. The adage that I use a lot of times is, hungry people are not happy people, and if you want to see a person that fits that mold, be around me if I don't each lunch. My whole personality changes.

Now, in today's day, we end up producing a lot of different types of chickens, and we do produce some antibiotic-free chickens, and we have found, shock, shock, exactly what we would expect. We had 2.91 percent lower livability. We had basically 33 points lower average daily gain and over a quarter percent higher condemnation at processing. What this results in is not only less food but it results in food at a higher cost to the American consumer. The other thing that should be addressed here, and some of my colleagues have mentioned is, there are environmental impacts to growing more animals, and if we are going to do this, we are going to have a whole side range of aspects that are going to have to be evaluated.

So in conclusion, I say to you, and I really do appreciate the opportunity to be here, that antibiotics are important to the industry as far as disease control is concerned and the phrase of today is "animal welfare." In my years, we always talked about chicken house management or poultry husbandry or animal husbandry but today it is animal welfare, and the use of antibiotics is very important in that aspect as well as to the sustainability of American agriculture. I want to go back to the fact that we grow our chickens on approximately 34,000 independently owned and operated farms, and the other part that is important, and I think that is why we are here, is that the appropriate use of antibiotics and interventions, it is important to the American public, yes, in terms of anti-

biotic resistance and sensitivity, but also in terms of producing a good, sound, nutritious, economically affordable food product.

I thank you very much for the opportunity to be here, and I will be happy to entertain any questions.

[The prepared statement of Dr. Klopp follows:]

PREPARED STATEMENT OF SPANGLER KLOPP, D.V.M., D.A.C.P.V.; CORPORATE VETERINARIAN, TOWNSENDS, INC., GEORGETOWN, DE; ON BEHALF OF NATIONAL CHICKEN COUNCIL

Good morning Chairman Boswell, Congressman Hayes, and Members of the Subcommittee. Thank you, Chairman Boswell for the opportunity to participate in this important hearing on the advances of animal health with the livestock industry. On behalf of the National Chicken Council, I appreciate your invitation to provide comments on the advances in chicken health in the U.S. chicken industry.

My name is Spangler Klopp and I am the Corporate Veterinarian at Townsends, Inc. and former Chairman of the National Chicken Council Poultry Health Committee.

The raising of chickens to produce food for human consumption has made exceptional advances over the decades due in large part to ingenuity and intelligence in following the lead of the sciences and a great deal of hard work. Today's broiler chicken industry processes approximately nine billion chickens/year, representing over $37 billion dollars in value. These chickens are raised to an average live weight of 5.53 lbs with a 75% yield at processing resulting in approximately 37.5 billion pounds of chicken meat, valued at over $37 billion, for human consumption. The broiler industry contributes to sustainable agriculture by raising its chickens on approximately 34,000 independently owned and operated farms.

Maintaining the health of chicken flocks is predicated on disease prevention through vaccination, appropriate use of antibiotics and other antimicrobials and sound poultry husbandry. Critical measurement parameters for chicken performance are rate of gain, (Average Daily Gain or ADG), percentage livability, (number of chicks placed divided by number moved to processing), percentage condemnation at processing, (number of carcasses deemed unfit by USDA for human consumption divided by the number of chickens processed).

Vaccines control diseases that cannot be controlled by antibiotics and husbandry. Antibiotics are used for control of specific bacterial and parasitic diseases especially those of the gastrointestinal tract. Such usages allow for improved health as indicated by improved livability, average daily gain and carcass condemnation at processing.

ADG in the early 1970's was defined as 4 pound live weight at 56 days of age or .0714 pound ADG. Today, the approximate figure for ADG is .1139 based on an average processing weight of 5.53 pounds. This represents a 160% increase in efficiency and that much more meat per chicken. Without today's technologies, approximately 2,484,000,000 more chickens would be required annually to meet the food demands of the American public.

Percentage livability was approximately 93.52 in the early 1980s and the figure for today is approximately 95.64. This represents a real improvement of 2.12% and that much more meat per flock. Based on the national figure of nine billion chickens processed, without this improvement in livability, an additional 190,800,000 day old chicks would have to be placed annually to meet the needs of the American public.

Condemnation percentage improvement, shown below, in the past 42 years is 456% and represents improved meat quality, from taste, nutritional and microbiological aspects. If condemnations were at the level of earlier years, another 155,700,000 chickens would have to be grown annually to meet the needs of the American Public. Collectively, if the industry was not allowed use of appropriate interventions, an additional 2,830,500,000 chickens would have to be grown and processed annually to meet the needs of the American public.

Percentage Field Related USDA Carcass Condemnation of Broiler Chickens for Two Selected Years

Category	1965 *	2007 **
Leukosis	.512	.028
Septicemia/Toxemia	.563	.238
Airsacculitis	.922	.109
Inflammatory process (IP)	.128	.113

Percentage Field Related USDA Carcass Condemnation of Broiler Chickens for Two Selected Years—Continued

Category	1965 *	2007 **
Synovitis	.102	.0003
Total Field	2.227	0.4883

* Dr. L.V. Sanders, USDA, National meeting on Poultry Condemnations, Salisbury, MD, October 18–19, 1966.
** NASS/USDA/Slaughter Report, January–December, 2007, converted to percentages.

It is important to remember that broiler chickens are free roaming and have certain natural tendencies, which include "picking at the ground or litter." Thus disease control becomes a function of maintaining a balance between the chicken and its environment. Vaccines and antibiotics have played significant roles in the improvement of the health parameters cited above and are valued accordingly. Their usage is rigidly monitored by educated and trained professionals.

The development of antibiotic resistant bacteria has been a concern of the industry long before the subject became popular with others and is viewed even more importantly today. Sound usage/rotational programs, proper pharmaceutical selection for use and use of proper dosage regimes have allowed for the continued effectiveness of antibiotics, some of which have been in use for over 25 years. Maintenance of antibiotic sensitivity at the chicken house level is an important issue.

Good chicken health through the responsible use of vaccines and antibiotics is obviously important in feeding the American Public and is equally important in enhancing the quality of the environment and socioeconomic style of life in rural America. Healthy chickens require less feed while using less housing space, produce less manure and produce more meat as compared to the option of not having these important interventions for our use.

In my current experience of producing chickens raised without antibiotics, those flocks have a 2.91% lower livability, 0.0033 lower ADG and a 0.275% higher condemnation. This may be fine for niche markets that cater to consumers who can afford to pay higher prices for chicken. But as I previously noted, without the use of appropriate interventions, an additional 2,830,500,000 chickens would have to be grown each year to meet the needs of the American public. Additionally, this loss would result not only in less food but also at a higher cost with more potential issues to the environment and to the way of life in rural America.

In conclusion, it is apparent that antibiotics are important in disease control or as described in today's vernacular—animal welfare—as well as to the sustainability of American Agriculture and to the American public in general.

The CHAIRMAN. As long as it doesn't get into lunchtime. Thank you.

Mr. Van Zetten.

STATEMENT OF BLAIR VAN ZETTEN, PRESIDENT, OSKALOOSA FOOD PRODUCTS CORP., OSKALOOSA, IA; ON BEHALF OF UNITED EGG PRODUCERS

Mr. VAN ZETTEN. Mr. Chairman, Mr. Vice Chairman, thank you for the opportunity to testify. My name is Blair Van Zetten. I am a proud member of the Iowa egg industry. We are the nation's number one egg-producing state. My company, Oskaloosa Food Products, produces liquid, frozen and dried egg products for the food industry.

I am a member of the United Egg Producers. I am also a member of the Further Processors Division of United Egg Association. Animal healthcare is a critical concern for both of these organizations. UEP and UEA's Further Processor Divisions have taken a leadership role in animal health, and here are just a few examples.

We supported the development of USDA'S Low Pathogenic Avian Influenza Program, a voluntary effort through the National Poultry Improvement Plan to prevent, control and identify LPAI through-

out the poultry industry. We participated in the original design of the program and the private sector participants in NPIP, and worked with the Department of Agriculture and Congress to develop regulations for the program to secure adequate funding. Fortunately, the highly pathogenic H5N1 strain of avian influenza has never been found in North America. However, we all know that we have a responsibility to guard against this threat to both animal and human health. We have worked with respected academic and veterinarian experts to develop procedures for safe movement of eggs and egg products into and out of the quarantine zones in the event of an outbreak of highly pathogenic avian influenza.

We presented our findings and recommendations to USDA veterinary experts and worked closely with them to ensure the maximum protection of both human and animal health. Just this week, UEP in conjunction with USDA and other animal health officials hosted a national conference to advance the egg industry's program that will ensure the containment of highly pathogenic avian influenza, should it be found, as well as the continuity of the nation's egg supply.

We have worked to encourage all egg producers to register their premises under USDA's voluntary National Animal Identification System. If there is a disease outbreak, it is critical for USDA and the public health authorities to be able to locate and contact all producers in the affected area as soon as possible. The NAIS will make this easier.

Nearly all egg producers have implemented quality assurance programs on their farms. These QA programs are primarily aimed at preventing *Salmonella enteritidis*, but they also provide important benefits for animal health, and because of the way they are designed, in particular, producers enforce strict biosecurity programs and take other steps that not only help bird health but have human health benefits as well.

As part of our quality assurance and animal health programs, we routinely vaccinate for various infectious diseases of foodborne pathogens. Early in a bird's life, often on the first day of age, we administer vaccines for respiratory and immunosuppressive diseases. Some producers also vaccinate for *Salmonella enteritidis.* These vaccines may be live, inactivated or a combination, depending on the disease and the producer's own management practices.

Nowadays we often get questions about antibiotics. Antibiotics aren't considered a food safety issue for eggs. Low levels of antibiotics are occasionally used to prevent or treat disease and ensure the health of the laying hens, just as for humans. Few antibiotics are permitted in commercial layers by regulations, and there is an economic incentive not to use them due to the additional cost. Because so few antibiotics are used and are used to such a small degree, they aren't likely to contribute to the problem of antibiotic resistance.

In our own operations, we use antibiotics only for treatment. In my written statement, I have listed examples of several antibiotics that might be used in our industry and the disease which they treat. Through careful and appropriate regulations, the animal agriculture industry's ability to use antibiotics when necessary can and should be preserved. As a relatively small industry, we are a

less lucrative market for veterinary drug makers than other larger segments of animal agriculture. Therefore, we are sensitive to whether the drug makers have incentives to develop new products.

It is important to us that the regulation of antibiotics be based on sound science, not emotions, politics or popular press. We think science is the best basis on which to make highly technical public policy decisions. It is critical that regulators have the resources to do their jobs efficiently and thoroughly, and we hope Congress will continue to address FDA resource needs.

Beyond the availability of veterinary products, it is also important that Congress find more resources for research in animal health issues. The work that our scientists do provides many benefits to the public and to our industry. Unfortunately, the funding for animal agricultural research has been stagnant for many years. There are many reasons to increase this research but one of them is surely to advance animal health. That will improve the welfare of animals under our care and also benefit consumers.

Mr. Chairman, I thank the Subcommittee for its oversight in these matters, and I will be happy to try and answer any questions you may have.

[The prepared statement of Mr. Van Zetten follows:]

PREPARED STATEMENT OF BLAIR VAN ZETTEN, PRESIDENT, OSKALOOSA FOOD PRODUCTS CORP., OSKALOOSA, IA; ON BEHALF OF UNITED EGG PRODUCERS

Mr. Chairman and Members of the Subcommittee, thank you very much for the opportunity to testify today. My name is Blair Van Zetten and I am a proud member of Iowa's egg industry. We are the nation's number-one egg-producing state. My company, Oskaloosa Foods, produces liquid, frozen and dried egg products for the food industry.

About ⅓ of all the eggs produced in the United States are destined for further processing. In many cases, these eggs will become ingredients in a broad range of foods, bringing high-quality protein and other nutritional advantages as well as a number of functional properties that make the foods better and more convenient.

I am a member of United Egg Producers (UEP), as are the producers of about 98% of the nation's eggs. I am also a member of the Further Processors Division of United Egg Association (UEA). Animal health is a critical concern for both of these organizations.

Our industry pays a great deal of attention to animal health for several reasons.

- As producers, we care about the welfare of the birds under our care.
- Healthier birds are more productive and animal health is directly related to our ability to stay in business as producers.
- Good animal health leads to a better, safer, more affordable product for our ultimate customer, the consumer.

I am proud to say that UEP and UEA's Further Processor Division have taken a leadership role in animal health. Here are just a few examples of what we and our industry have been doing in recent years:

- We supported the development of USDA's **Low-Pathogenic Avian Influenza Program—**a voluntary effort through the National Poultry Improvement Plan to prevent, control and indemnify LPAI throughout the poultry industry. We participated in the original design of this program as private-sector participants in NPIP, and worked with the Department of Agriculture and Congress to develop regulations for the program and secure adequate funding. Virtually all of our membership participates in this program.
- Fortunately, the highly pathogenic Asian H5N1 strain of avian influenza has never been found in North America, not even among wild birds, much less domesticated poultry. However, we all know that we have a responsibility to guard against this threat to both animal and human health. We have worked with respected academic and veterinary experts to develop procedures for the safe movement of eggs and egg products into and out of quarantine zones in

the event of an outbreak of **highly pathogenic avian influenza.** We've presented our findings and recommendations to USDA veterinary experts and worked closely with them to ensure the maximum protection for both human and animal health. Just this week UEP, in conjunction with USDA and other animal health officials, hosted a national conference to advance an egg industry program that will assure the containment of highly pathogenic avian influenza should it be found anywhere in the United States and the continuity of the nation's egg supply in such an event.

- We have worked to encourage all egg producers to register their premises under USDA's voluntary **National Animal Identification System.** If there is a disease outbreak, it is critical for USDA and public health authorities to be able to locate and contact all producers in the affected area as soon as possible. The NAIS will make this easier, and minimize the time during which producers' ability to market their products is restricted.
- Nearly all egg producers have implemented **quality assurance programs** on their farms, either through state programs or as part of programs designed by their own companies or their customers. These quality assurance programs are primarily aimed at preventing *Salmonella enteritidis,* but they also provide important benefits for animal health because of the way they are designed. In particular, producers enforce strict biosecurity programs, control for disease vectors like rodents, and take other steps that not only help bird health but have human health benefits as well.
- As part of our quality assurance and animal health programs, we routinely **vaccinate for various infectious diseases or foodborne pathogens.** Early in a bird's life—often on the first day of age—we administer vaccines for respiratory diseases such as Newcastle disease and infectious bronchitis; and immunosuppressive diseases such as Marek's disease and infectious bursal disease. Some producers also vaccinate for *Salmonella enteritidis.* These vaccines may be live, inactivated or a combination, depending on the disease and the producer's own management practices. We encourage support for USDA's biologics division, which has been understaffed, to improve the development and timeliness of vaccine availability.

Nowadays, we often get questions about antibiotics. Antibiotics aren't considered a food safety issue for eggs. Low levels of antibiotics are occasionally used to prevent or treat disease and ensure the health of laying hens, just as for humans. Very few antibiotics are permitted in commercial layers by regulations, and there is an economic incentive not to use them due to the additional cost. Because so few antibiotics are used, and are used to such a small degree, they aren't likely to contribute to the problem of antibiotic resistance.

In our own operations, we use antibiotics only to treat diseases. Examples of some antibiotics that might be used in our industry would be tylosin to treat mycoplasma infections, chlortetracycline to treat *E. coli* respiratory infections, and bacitracin to treat necrotic enteritis and other enteric diseases.

Through careful and appropriate regulation, the animal agriculture industry's ability to use antibiotics when necessary can and should be preserved. As a relatively small industry, we are a less lucrative market for veterinary drug makers than other, larger segments of animal agriculture. Therefore, we are sensitive to whether the drug makers have incentives to develop new products.

It is important to us that the regulation of antibiotics be based on sound science, not emotions, politics or the popular press. We think science is the best basis on which to make highly technical public policy decisions. It is critical that regulators, in this case the Food and Drug Administration, have adequate resources to do their jobs efficiently and thoroughly, and we hope Congress will continue to address FDA's resource needs.

Beyond the availability of veterinary products, it is also important that Congress find more resources for research in animal health issues. The work that our scientists do provides many benefits to the public and to our industry. As just one example, USDA's Agricultural Research Service demonstrated conclusively that the low-pathogenic avian influenza virus is inactivated through pasteurization, a process that all processed egg products undergo. Not only did this work give important reassurance to consumers, and inform industry practice, but it has also been enormously helpful to us in communicating to our overseas trading partners the safety of our products. Unfortunately, the funding for agricultural research has been stagnant for many years. There are many reasons to increase this research, but one of them is surely to advance animal health: That will improve the welfare of the animals under our care, and also benefit consumers.

Mr. Chairman, I thank the Subcommittee for its oversight in these matters, and will be happy to try and answer any questions you may have.

The CHAIRMAN. Thank you.

Dr. Apley.

STATEMENT OF MICHAEL D. APLEY, D.V.M., PH.D., D.A.C.V.C.P., ASSOCIATE PROFESSOR OF BEEF PRODUCTION MEDICINE, CLINICAL PHARMACOLOGIST, AND DIRECTOR, PHARMCATS BIOANALYTICAL LABORATORY, KANSAS STATE UNIVERSITY; MEMBER, CATTLE HEALTH AND WELL BEING COMMITTEE, NATIONAL CATTLEMEN'S BEEF ASSOCIATION, MANHATTAN, KS

Dr. APLEY. Mr. Chairman, Ranking Member Hayes, other Members of the Subcommittee, my name is Mike Apley and I am an Associate Professor of Beef Production Medicine and a Clinical Pharmacologist at Kansas State University.

I think one of the most important pieces of information that should come out of today's hearing is consumers need to know that by law, no meat sold in the United States is allowed to contain drug residues that violate FDA standards and additionally, all products approved by the FDA for use in food-producing animals must first pass significant human food safety benchmarks.

Animal drugs are important in treating disease, but more important is prevention, utilizing cattle management and vaccines. An example is the increasing availability of backgrounded cattle which have been immunized for bovine respiratory disease and held in local environments to overcome the stress of weaning prior to being shipped to a feeding facility. Another example of management practice is reducing the need for therapeutic intervention. It is a system which involves periodically moving cows which have not yet calved away to new calving areas and leaving behind the cows which recently calved. In this way, any shedding of disease organisms and related disease outbreaks are isolated within a subset of the animals and is prevented from spreading to the entire herd.

However, when we can't prevent disease, we do need animal drugs to control it. An example is the use of an antimicrobial in controlling anaplasmosis in cattle. You may be familiar with this disease. It is a bloodborne parasite for which we do not have an adequate vaccine. In older cattle, this disease is often fatal. Chlortetracycline may be fed to cattle at risk for the disease during and immediately after the vector season to control clinical signs.

This disease is a good example for examining the use of the term "subtherapeutic," which is often interpreted to mean low dosage. In the case of anaplasmosis, a relatively low dose of the antimicrobial is effective in controlling a disease that can result in suffering and death of the cattle as well as economic devastation to the producer. The subtherapeutic categorization attempts to cast all antimicrobial regimens below an undefined threshold as inappropriate due to potential selection for resistant pathogens. In reality, resistant organism selection pressure is much, much more complicated than just a high concentration for a short term is good or a lower concentration for a longer exposure is bad. The use of the term "subtherapeutic" to me indicates a cursory knowledge of the effects of antimicrobials in food animals relating to animal well-being, dis-

ease control and food safety. Each application of an antimicrobial is different and the attempts to supersede the regulatory process with blanket legislation prohibiting subtherapeutic uses will result in instances where a decreased ability to address disease pressures in cattle production will not be offset by a benefit in antimicrobial resistant selection. Circumventing the approval process and making leaps from effect back to cause will undermine the ability of the cattle industry to address disease challenges and in many cases may result in no benefit to human therapeutics.

As Congress continues to have an interest in this issue, we recommend that the focus be put on the tools already in place rather than imposing new rules, regulations and prohibitions on animal agriculture. One way to do this would be to ensure that the National Antimicrobial Resistance Monitoring System, or NARMS, and the Food Animal Residue Avoidance Databank, or FARAD, be fully supported and funded. NARMS was developed to monitor changes in susceptibility of select bacteria to antimicrobial agents of human and veterinary importance. FARAD is another valuable tool that Congress and the Administration neglected. FARAD is a computer-based system that is invaluable in helping to avoid drug residue problems and keeping the food supply safe. Unfortunately, the funding for FARAD runs out next week, and unless Congress adds funding to the CR, the valuable information it holds will be gone.

Finally, I would like to talk about the steps the industry has taken to police themselves. The Beef Quality Assurance, or BQA program, has set forth recommendations for how cattle producers should use antibiotics to protect and maintain the health of their animals. BQA was established in 1987 to provide cattle producers with the principles and tools to use every day to ensure animals are given proper care and attention.

In conclusion, we find that in today's cattle industry, the need for animal health interventions that focus on prevention of disease, control of disease pressure and therapy of animals with disease is critical to the success of cattle producers across the country, as well as helping to keep our food supply safe. Antimicrobial drugs are a very important part of our carefully selected tools and should not be removed from use without definitive proof of a benefit to human health that overrides the increased suffering and economic losses that would be experienced in the cattle industry.

Thank you for the opportunity to testify.

[The prepared statement of Dr. Apley follows:]

PREPARED STATEMENT OF MICHAEL D. APLEY, D.V.M., PH.D., D.A.C.V.C.P., ASSOCIATE PROFESSOR OF BEEF PRODUCTION MEDICINE, CLINICAL PHARMACOLOGIST, AND DIRECTOR, PHARMCATS BIOANALYTICAL LABORATORY, KANSAS STATE UNIVERSITY; MEMBER, CATTLE HEALTH AND WELL BEING COMMITTEE, NATIONAL CATTLEMEN'S BEEF ASSOCIATION, MANHATTAN, KS

Chairman Boswell, Ranking Member Hayes, and Members of the Committee, my name is Mike Apley. I am an Associate Professor of Beef Production Medicine, a Clinical Pharmacologist, and the Director of the PharmCATS Bioanalytical Laboratory located at Kansas State University. I am also a Member of the National Cattlemen's Beef Association's (NCBA) Cattle Health and Well Being Committee. I appreciate the opportunity to be here today to talk about the use of drugs to prevent and treat disease within the cattle industry.

Animal health and well-being are top priorities for cattle producers across the country. Without healthy animals, we do not have a healthy industry, so we utilize important tools like vaccines, antimicrobials, and other drugs to control disease, treat disease, and provide a higher quality of life for our cattle while keeping the food supply safe. Ongoing activist and media reports, however, suggest that the use of drugs in animal agriculture is often inappropriate and that the use of drugs is poorly controlled. Misleading statements such as these have put an undue spotlight on animal drugs and threatens to undermine the science-based approval process we have for these products. One of the most important pieces of information that should come out of today's hearing is that consumers need to know that, by law, no meat sold in the United States is allowed to contain drug residues that violate Food and Drug Administration (FDA) standards. Additionally, all products approved by FDA for use in food producing animals must first pass significant human food safety benchmarks.

It is also important to recognize that animal drugs go through a rigorous, science-based testing process before they are approved for use. FDA, the U.S. Department of Agriculture (USDA), veterinarians, animal health companies, producer organizations, and other stakeholders have implemented several layers of human health protections during the past decade to reduce any risks associated with antibiotic use in animals.

FDA approves antibiotics and the specific dosage rates to treat specific diseases or conditions, and producers are legally required to follow these precise label directions. This rigorous approval process was made more stringent in 2003 when FDA finalized an additional safety measure requiring an antibiotic resistance risk assessment for all new and existing antibiotics known as Guidance #152 (Guidance for Industry Part 152).

FDA's Center for Veterinary Medicine (CVM) is responsible for ensuring that animal drugs are safe, effective, and manufactured to the highest quality standards. The standards and processes for reviewing an antibiotic used to treat animals is essentially the same as that for an antibiotic used to treat humans, except for the fact that animal drugs have to go through additional food safety assessments that human drugs do not. Every drug is subject to a safety assessment, efficacy assessment, and quality or manufacturing assessment before it is approved.

The safety assessment layer of the approval process requires sponsors to submit data showing use of the antibiotic is safe for the human or animal in which it is to be used. The safety assessment for food animals is more stringent than that for human antibiotics in three respects:

1. While FDA conducts a risk-benefit assessment for human antibiotics in which it weighs benefits against risks, there is no consideration of benefits in the review of antibiotics used in food animals. This means any animal or human health risks for products under review must be extremely low since FDA does not consider any benefits to offset the risks.

2. The safety assessment for food animal antibiotics requires sponsors to submit human food safety studies to ensure meat from animals treated with the antibiotic will be safe for human consumption. Data from these studies are used to establish withdrawal periods, or the amount of time prior to processing during which antibiotics cannot be used in order to ensure there are no residues above tolerance levels in the final food product.

3. In 2003, FDA implemented an additional safety measure that "outlines a comprehensive, evidence-based approach to preventing antimicrobial resistance that may result from the use of antimicrobial drugs in animals." This risk assessment process was a priority action item in the U.S. Public Health Action Plan and is required for all newly proposed antibiotics. Significantly, CVM is working with animal health companies to also examine all existing, approved products using this new methodology.

Both the animal and human drug approval processes require efficacy assessments. This means the submitting company must provide data from geographically diverse, statistically-designed studies that show the product will work in the way it is intended to provide a clinical improvement or cure.

Finally, approval of animal and human drug products require a quality or manufacturing assessment consisting of facility inspections, assurance of product stability, adherence to good manufacturing practices and other procedures to assure FDA the sponsor can manufacture the product in the approved form.

In addition, USDA's Food Safety and Inspection Service (FSIS) conducts tests to ensure withdrawal periods are being followed and beef products entering the food supply do not contain antibiotic levels that violate FDA standards. The testing pro-

tocol for the FSIS National Residue Testing Program has been updated continuously since its inception in 1967.

Once the products have been approved, many are used to prevent animal disease. There are some who will claim that the cattle industry is dependent on drugs to fix the problems associated with our production methods. While we prefer to prevent diseases, animal drugs are just one tool we utilize to control disease. The cattle industry strives to invent and improve production practices that help minimize the use of drugs and prevent diseases.

An example of an advance in disease prevention management is the increasing availability of "backgrounded" cattle which have received appropriate immunizations for bovine respiratory disease and are then held in local environments to overcome the stress of weaning prior to being shipped to a feeding facility. These cattle are sold at a premium due to their reputation for decreased disease occurrence at the feeding facility.

Another example of management practices reducing the need for therapeutic intervention is the "Sandhills Calving System". Named for the intense cow/calf production area in the sandhills of Nebraska, this system involves periodically moving cows which have not yet calved away to new calving areas and leaving behind the cows and calves which have recently calved. In this way any shedding of disease organisms and related disease outbreaks are isolated within a subset of the animals and prevented from spreading to the entire herd.

The importance of assuring adequate colostrum intake in newborn calves has been demonstrated repeatedly, including data showing that inadequate intake can result in differences in health performance as far removed as in the feedlot phase of beef production. The economic incentive to pay attention to colostrum intake is now based on more than just neonatal health on the farm of origin in an industry where source identity of cattle throughout the production cycle becomes more common place through alliance programs, retained ownership, and branded beef programs.

Despite continually advancing management practices, vaccines remain a staple of preventive programs in cattle. While there are vaccines with demonstrated field efficacy for some pathogens related to bovine respiratory disease, we still await vaccines with consistent, proven efficacy for diseases such as systemic or enteric salmonellosis, infectious pododermatitis (foot rot), *Mycoplasma bovis* involved in the bovine respiratory disease complex, infectious bovine keratoconjunctivitis (pinkeye), and anaplasmosis. It is crucial that funding be provided for basic and applied research leading to increased vaccine availability.

Once a disease has taken hold, we must utilize animal drugs to control the disease and prevent its spread. Treatments for control of some cattle diseases have been approved by FDA/CVM. For example, there are five antimicrobials approved for control of bovine respiratory disease. When appropriate, these applications are very effective in decreasing morbidity and death.

Another example of using antimicrobials to control disease is the occurrence of clinical anaplasmosis in cattle. *Anaplasma marginale* is a blood cell parasite that causes loss of red blood cells in cattle due to infected cells being cleared from the body. In cattle less than 1 year old, the clinical signs are mild due to the animal's ability to regenerate red blood cells while mounting an immune response. As animals age, the severity of the disease worsens to include death as a likely outcome. Chlortetracycline may be fed to cattle at risk for the disease during and immediately after the vector season to control clinical signs while allowing infection that results in a carrier status and immunity to the disease.

Anaplasmosis is a good example in examining the use of the term "subtherapeutic." Chlortetracycline is effective for controlling the effects of anaplasmosis. The approved in-feed dose for this application is 0.5 to 2.0 mg/lb of body weight per day in beef and non-lactating dairy cattle over 700 lbs, and 350 mg per animal per day in beef cattle less than 700 lbs. In comparison, A dose of 10 mg/lb per day may be used in the feed for treatment of bacterial pneumonia caused by *Pasteurella multocida* organisms susceptible to chlortetracycline.

The point is that the term "subtherapeutic" is often interpreted to mean "low concentrations" or "low dosage". In the case of anaplasmosis, a relatively low dose of the antimicrobial is effective in controlling a disease that can result in suffering and death of the cattle as well as economic devastation to the producer. The term "subtherapeutic" has been defined by some to include growth promotion and disease prevention claims. I would challenge these groups to define exactly where a drug becomes "subtherapeutic" and therefore incapable of having an effect on disease. The appropriate use of terms would be to address the drug use by the label claim of treatment, control, or increase in rate of weight gain and/or feed efficiency. Where appropriate, a relatively low dose of an antimicrobial may effectively control disease

signs along with the resulting adverse animal welfare and economic effects. This relatively low antimicrobial exposure also minimizes the total exposure of normal and pathogenic bacterial flora to antimicrobials over time.

The "subtherapeutic" categorization attempts to cast all antimicrobial regimens below an undefined threshold as inappropriate due to selection of resistant pathogens. In reality, resistant organism selection pressure is much more complicated than just "*a high concentration for a short term is good, a lower concentration or a longer exposure is bad*". The use of the term "subtherapeutic" indicates a cursory knowledge of the effects of antimicrobials in food animals as they relate to the combination of effects on animal well being, disease control, and food safety. Each application is different, and the attempts to supersede the regulatory process with blanket legislation prohibiting "subtherapeutic" uses, however well intentioned, will result in instances where a decreased ability to address disease pressures in cattle production will not be offset by a benefit in antimicrobial resistance selection.

I would not propose that the bacterial pathogens in humans and cattle exist in total isolation from each other, nor would I claim that there are no possible links between antimicrobial use in cattle and therapy in humans. However, I would caution that circumventing the approval process in making leaps from effect back to cause will undermine the ability of the cattle industry to address disease challenges and in many cases may result in no benefit to human therapeutics.

Separate scientific risk assessments have been conducted on the uses of virginiamycin and macrolides in food animals.[1 2] The former supported by the FDA/CVM and the latter supported by a pharmaceutical company. Neither risk assessment defined a risk which any reasonable reviewer would classify as significant. It is absolutely essential to the wellbeing of animals and humans in the United States that discussions on antimicrobial resistance be focused on specific drugs, uses, and pathogens with appropriate data supporting the discussion. Efforts to cast all food animal antimicrobial uses in the same light are both misguided and dangerous.

As Congress continues to have an interest in this issue, we recommend that the focus be put on the tools already in place rather than imposing new rules, regulations, and prohibitions on animal agriculture. One way to do this would be to ensure that the National Antimicrobial Resistance Monitoring System (NARMS) and the Food Animal Residue Avoidance Databank (FARAD) be fully supported and funded.

NARMS was developed in 1996 to monitor changes in susceptibility of select bacteria to antimicrobial agents of human and veterinary importance and is a collaboration between three Federal agencies including FDA's CVM, the Centers for Disease Control and Prevention (CDC), and USDA. NARMS also collaborates with antimicrobial resistance monitoring systems in other countries, including Canada, Denmark, France, the Netherlands, Norway, Sweden, and Mexico so that information can be shared on the global dissemination of antimicrobial resistant foodborne pathogens.

The NARMS program monitors changes in antimicrobial drug susceptibilities of selected enteric bacterial organisms in humans, animals, and retail meats to a panel of antimicrobial drugs important in human and animal medicine. Bacterial isolates are collected from human and animal clinical specimens, from healthy farm animals, and raw product from food animals. Retail meats collected from grocery stores were recently added to NARMS sampling. A pilot study of animal feed ingredients collected at rendering plants across the country was also started in 2002. The CDC and USDA provide the NARMS results annually in comprehensive summary reports.

The stated goal of NARMS activities is to prolong the lifespan of approved drugs by promoting prudent and judicious use of antimicrobial drugs and to identify areas for more detailed investigation.

NCBA feels the program could be improved if the FDA, USDA and CDC worked more collaboratively; this includes, among other things, division of funds as well as evaluation of the data. NCBA especially has concerns in how CDC analyzes and utilizes data. Data analysis should be purely science-based and without preconceived agendas. There are various examples of the damage that can be done to industry when Federal agencies do not cooperatively work together. The cattle industry cannot afford for Federal agencies to have an unscientific mis-step that can remove valuable animal health options from our producers.

The issue of antimicrobial resistance is very concerning to cattle producers. We encourage and advocate for judicious use of all medications. In fact, NCBA policy supports the *Producer Guidelines for Judicious Use of Antimicrobials* which have been in place since 1987. In addition, NCBA participates in the Codex Alimentarius task for on antimicrobial resistance.

Antimicrobial resistance is not a black and white issue. It is a multi-faceted and extremely complex issue that cannot be solely focused on the use of drugs in animal

agriculture. Unfortunately, animal agriculture has been a primary target in this fight, with little or no consideration given by the public to the use, misuse, and mishandling of human drugs by the general population. To ensure that the issue of antimicrobial resistance is properly addressed, it is imperative that we gather accurate, appropriate, and complete data to identify any problems and all contributing factors. To date, only limited data exists. These data need to be gathered and scientifically evaluated without bias or a pre-determined agenda before any further action is taken by Congress. We need to have strong information on which to base any action that can impact the use of drugs in animal agriculture.

Related to preventing selection for resistant pathogens is the need to know the optimal duration of antimicrobial therapy that balances initial treatment successes, subsequent relapses, and antimicrobial selection pressure in favor of resistant pathogens. In both human and veterinary medicine we are lacking critical studies that define optimal duration of therapy.

FARAD is another valuable tool that Congress and the Administration have neglected.

Operating since 1982, FARAD is a computer-based system designed to be utilized by veterinarians and livestock producers in finding information on drug use and residue problems. During the drug approval process, FDA establishes drug residue tolerances in order to help keep food safe. They also establish waiting periods and withdrawal times to determine how long you must wait for the animal to process and eliminate the drug from their systems before they can be harvested for food. The information in this database is invaluable in helping to avoid drug residue problems and keeping the food supply safe. FARAD also looks at pesticide and environmental contaminant residue issues. Unfortunately, the funding for FARAD runs out next week, and unless Congress adds funding to the continuing resolution, the valuable information it holds will be gone.

Finally, I would like to talk about the steps the industry has taken to police ourselves. The Beef Quality Assurance (BQA) program has set forth recommendations for how cattle producers should use antibiotics to protect and maintain the health of their animals. BQA was established in 1987 to provide cattle producers with the principles and tools to use every day to ensure animals are given proper care and attention.

BQA unites producers with experts (animal scientists, veterinarians, feed suppliers, animal health companies, meatpackers, retailers and state and Federal regulators) to develop management programs using the latest science and technology to assure proper animal care, beef quality, and safety. The BQA program provides guidelines for livestock care and handling, nutrition and veterinary treatment and incorporates current FDA, Environmental Protection Agency (EPA), and USDA regulations as well as Hazard Analysis Critical Control Point (HACCP) principles.

Cattlemen can become BQA certified when they meet criteria for quality beef production set forth in the BQA guidelines. Producers also undergo continuous training to remain certified. The BQA Manual is the overarching guideline that provides consistency across the nation, but states can go beyond national standards to meet state needs and opportunities. Most states have individual BQA programs that are tailored to the needs of their particular state beef industry, and can offer their own certification standards. State certification requirements vary, but may include third party verification and testing procedures to ensure good management practices.

Today, BQA influences more than ninety percent of U.S. cattle. Approximately 185,000 copies of the brochure of NCBA's Care and Handling Guidelines have been sent to producers, veterinarians, Departments of Agriculture, and Universities. BQA is not a static program. An advisory board made up of cattle producers, beef and dairy veterinarians, University and Extension scientists, meat scientists, auction markets, and the transportation industry continually work to update and strengthen the program. NCBA continues to improve this scientifically based program in order to meet current and future needs of our industry in order to maintain a healthy cattle population and a safe beef supply for our consumers.

In conclusion, we find that in today's cattle industry, the need for animal health interventions that focus on prevention of disease, control of disease pressure, and therapy of animals with disease is critical to the success of cattle producers across this country, as well as helping to keep our food supply safe. However, our industry believes that the use of these drugs comes with much responsibility, and that is why we have worked together with our partners in industry to educate and train cattle producers. The success of programs such as BQA shows our industry's commitment. This commitment cannot be overlooked by those who want to end or restrict the use of animal drugs without having any credible information to base their accusations. That is why we urge Congress to turn their efforts towards proven tools such as NARMS and FARAD in helping to keep our animal and human populations healthy,

and to continue to support the established scientific methods for drug approval and review as the forum in which to evaluate antimicrobial use in food animals. Thank you for the opportunity to testify today and we look forward to working with you in the future.

Endnotes

[1] Virginiamycin risk assessment. FDA Center for Veterinary Medicine website, *http://www.fda.gov/cvm/CVM_Updates/virginiamycinup1.htm.* Accessed 9–23–08.

[2] Hurd H.S., Doores S., Hayes D., *et al. Public health consequences of macrolide use in food animals: a deterministic risk assessment.* J. FOOD PROT. 2004:67(5):980–992.

The CHAIRMAN. Thank you. I wish the whole country could have heard the testimony that you have given this morning, all of you. I think there will be a lot of comfort and satisfaction that you are doing your very best to not only have healthy animals but healthy, safe food.

Somebody may comment, what safeguards do you have to combat antibiotic residue; anybody? What safeguards do you have?

Dr. KLOPP. I will be happy to respond to that one first. There has been a lot of focus placed on a national animal ID system. In the chicken industry, we have had an animal ID system for over 30 years through vertical integration. So the way we monitor residues is by reports that are in black and white as far as the use of any antibiotic or intervention that we use. We document the dates, the dosages, when we started treatment, when we ended treatment, and this is all documented in relation to processing and also to make sure that the appropriate dosages are used. We also, as I am sure every industry does, we participate through the FSIS residue testing program, and I also want to compliment Dr. Apley on the fact that he mentioned the need for funding especially for FARAD. That needs to happen.

The CHAIRMAN. I agree.

Please, go ahead, Dr. Byrne.

Dr. BYRNE. Certainly in the dairy industry, we do a very active job to prevent antibiotic residue starting with treatment records, much like the rest of the livestock industry, following appropriate withdrawal times and then testing every tanker of milk that arrives at a processing plant to ensure that it doesn't contain animal drug residues. So all those systems are there to ensure that we do not end up with any residues in the milk supply.

The CHAIRMAN. Thank you.

Anybody else? Dr. Rowles?

Dr. ROWLES. I can't speak for every producer, but I can say that in our operation, we are very, very cognizant of residues. We have to think about not only U.S. residues but we also have to think about Japanese residues because we ship about 40 percent of our product overseas. And so we are very, very cognizant of those issues and make sure that we are physically removing those products from the site so that there is no chance of a mistake.

Dr. RYBOLT. Mr. Chairman, I would just add that as mentioned in my testimony, we follow our residue avoidance program that was developed by the National Turkey Federation and we also ensure that we follow the prescribed withdrawal timeframes for the particular antimicrobial to ensure that there is no residue.

The CHAIRMAN. Thank you.

Dr. Apley?

Dr. APLEY. Yes. Mr. Chairman, in the feedlot industry, we routinely work with written treatment protocols that have withdrawal times incorporated then into them and at the majority of the feedlots, we have computerized individual animal records that record the drug given to that animal, the withdrawal time, and before penned-up cattle can be shipped, those records are checked, and if we cannot—if we have an animal that still has a withdrawal in effect and we cannot identify it, that pen is not shipped until that animal is identified or clears its withdrawal time.

The CHAIRMAN. Anybody else? Well, thank you very much.

I'll just welcome our Committee Chairman to join us here, Mr. Peterson from Minnesota.

Mr. PETERSON. I just want to say, I want to thank you and the Ranking Member for the outstanding job you are doing keeping on top of this.

The CHAIRMAN. Well, we are trying. Thank you.

Robin?

Mr. HAYES. Gentlemen, I don't know how you could have been any more thorough. The questions that I was contemplating have been answered in tremendous detail. Thank you for your attention to this important subject.

The CHAIRMAN. I recognize the gentlelady from North Carolina, Ms. Foxx.

Ms. FOXX. Thank you. I agree with our Ranking Member, Mr. Hayes, and I too thank the Chairman and the Ranking Member for staying on top of this issue.

The CHAIRMAN. Well, I appreciate it. Your testimony has been good. Blair, I have seen your operation and I know that you go to a great extent, great means, besides the cleanliness, the way you do things. I think that the public ought to know that as well, and I am sure that throughout the industry that you represent that you do that. I have been to several other locations over the years.

I would like to just throw this question out for any of you again. If antibiotic medication were prohibited, could current food demands be met? Dr. Klopp, you kind of made me suspicious of that in your testimony, but anyway, does anybody want to make a comment? Do you think we can do it without the antibiotics?

Dr. KLOPP. Well, this industry didn't get where it is, the only way we get things done is because we get it done. So, yes, but there would be a huge price to pay both in the availability of the amount of meat, the cost of the chicken meat, and the other part that gets a lot of attention is on the microbial quality of the meat because bacteria are a fact of life. And the given food safety aspects that would suffer from the lack of antibiotic interventions would increase, and I do want to make a comment. There has been a lot of negative statements made about growth promotion and it has been mentioned here about subtherapeutics, and the way I look at antibiotics in feed is, that it is a dosage range for disease prevention. I don't look at growth promotion. I don't look at subtherapeutics. I look at a dosage range, and this is how you control disease. But yes, you don't want to overstate anything, but there would be tremendous negative implications for the American public.

The CHAIRMAN. I appreciate that.

I think both you and, I believe it was Dr. Rybolt, made a comment that if we didn't have antibiotics, the volume of manure and what to do with it environmentally would just skyrocket. Any comment about that?

Dr. RYBOLT. Yes, sir. In my written statement, I stated that if we did not have the use of antimicrobials in the turkey industry specifically, what would happen is, we would have a decrease in feed efficiency so we would have a decrease in utilization of the nutrients. You would have increased manure coming out of the birds, to put it bluntly, so therefore you would have that environmental impact as well and would have to deal with that.

The CHAIRMAN. I appreciate that.

Ms. FOXX. Mr. Chairman, your question has prompted me to think of one. Could I——

The CHAIRMAN. I will get right back to you. I have a line of thought here and I want to stick with it and I will come right back to you, Ms. Foxx.

Dr. Rowles, based on your practice of veterinary medicine, as well as a producer, maybe you could make a comment for us that we can have in the record about how a veterinarian sits with a producer and works out their health plan.

Dr. ROWLES. Certainly. In the swine industry, the veterinary profession is very, very actively involved in developing herd health plans for their operations. First of all, they look at issues of housing, they look at issues of biosecurity, they look at issues of management, nutrition, parasite control. All of those things are taken into account when decisions are made on how to handle, grow, raise and manage pigs. The antibiotics that we referred to today are only one of those tools, but it is a very, very important tool that we need to make sure that we maintain in that animal health program development.

The CHAIRMAN. Thank you.

Ms. Foxx.

Ms. FOXX. Thank you, Mr. Chairman.

Now, I grew up where we raised chickens running wild, and I am a huge consumer of eggs and chickens and so is my family. But, it occurred to me as somebody who tries to think about how things have changed over time and how we have to weigh the cost and benefits of change, in 1937, our average lifespan was 59 years. That sticks in my mind because I often talk about Social Security being implemented. Our average lifespan now is almost 80. So in a very short period of time, our lifespan has changed dramatically in this country. I don't think—I mean, I am a social scientist, so I know you can't attribute it to any one thing. It would seem to me that we have seen a tremendous change in the way we get our food and the way our food is processed, the way it is grown. Do any of you know of studies that have been done, any obscure dissertations out there, that have looked at causes of illness and death that used to be created by eating bad meat, eating bad food, and comparing that with what our situation is now? Was there something done in years past not even thought about to be compared with now? I am just not familiar with the literature in this area.

Dr. ROWLES. If I may, I may not be answering your question directly but I think this may speak toward what you are trying to

address. Recently Ohio State did a study where they were comparing conventionally raised pigs *versus* antibiotic-raised pigs, and one of the findings that they found was that the incidence of things like trichonella, toxoplasmosis, which are true human potential problems, was higher in the antibiotic-free pigs, and I should add, *Salmonella* as well. And so in the antibiotic-free-raised pigs, the incidence, the percentage of infected carcasses was higher in antibiotic-free *versus* conventionally. We would argue that the conventional production practices that we are using today are providing a much safer product than what we produced 10, 15, 20 or 40 years ago.

Ms. FOXX. And Dr. Klopp indicated that also in the comments that he made about chickens, so I was just curious if there had been any real extensive work done. Thank you very much.

The CHAIRMAN. I would like to offer the opportunity to all of you on the panel to make any additional comments you would like to make if you care to at this time.

Dr. ROWLES. I would like to add just one further comment. We talked about the issue of manure, but one other factor in the efficiency discussions is also the input side on the corn. Right now we have corn prices that are extremely high, and industries are struggling in terms of a profitability standpoint. Not only is there an increase in manure but there also would be an increased need and demand for corn and/or soybean meal to produce that extra product at a time when those prices are at a premium.

The CHAIRMAN. Your point is well taken. We are going through a transition period, but every producer out there that I know in the corn, soybean production side, I was hoping some day they might be able to get a better price and now we have to figure out how to work with it, and we will. I think we are. But I appreciate your comment. Your point is well taken. Anybody else? Please.

Mr. VAN ZETTEN. Mr. Chairman, obviously from the testimony you have heard, to the entire livestock industry, animal health is very important, and thank you for holding this hearing in order to allow us to talk about the advances in animal health and the importance of being able to maintain animal health for high-quality, safe products for all consumers. Thank you.

The CHAIRMAN. You are welcome.

Anybody else?

Dr. APLEY. Mr. Chairman, one of the things I would like to make sure the public realizes is the sophistication with which we monitor our antibiotic use and treatment results in food animals. For example, I mentioned the feedlots, and ones that I work with, with the individually identified animals, we routinely monitor treatment success, treatment failure rate, relapses. We look at the case fatality rate, the numbers of those treated that die. We work on the case definitions for those and we go back and concentrate very aggressively on how early we are able to identify cattle with disease to minimize the need for further treatment. It is really very sophisticated and I think in the swine industry, I am very familiar with this and I am sure it is that way in the other industries that are here today. The level of monitoring that we are at and our ability to tell you on a daily basis what is going on in our herds or flocks has come to a point that I am not sure the public appreciates. I

think we would all say we are really proud of the way we are able to monitor what we are doing with the tools we have.

The CHAIRMAN. I appreciate that comment very much and I think that what you have done today is a good step in that direction or an additional step, I might say, and I would encourage you to keep it up.

We will dismiss the panel at this time and thank you very much for your testimonies. We appreciate it, and we will take the liberty to come back to you for further information if we need it. You are excused at this time and we would invite the third panel to come to the table.

Mr. PETERSON [presiding.] Mr. Boswell had to step out for a minute, so there is no reason we can't get the panel going, and welcome to the Subcommittee. I want to welcome Dr. Singer, who is from my home State of Minnesota. They do an outstanding job there at the university in monitoring animal health and a lot of other things, so welcome to the panel. Dr. Carnevale, I guess you are first. You have 5 minutes, and your full statement will be made part of the record, so feel free to summarize.

STATEMENT OF RICHARD A. CARNEVALE, V.M.D., VICE PRESIDENT, SCIENTIFIC, REGULATORY AND INTERNATIONAL AFFAIRS, ANIMAL HEALTH INSTITUTE, WASHINGTON, D.C.

Dr. CARNEVALE. Thank you, Mr. Chairman and Members of the Subcommittee. Thank you very much for the opportunity to appear before you today. My name is Dr. Richard Carnevale and I am a Veterinarian by training. I am also a Vice President of the Animal Health Institute, Scientific, Regulatory and International Affairs. The Animal Health Institute is a trade association here in Washington that represents the companies that make medicines and vaccines for animals. Before I worked for AHI, I spent nearly 20 years with both the Food and Drug Administration and the U.S. Department of Agriculture working on animal drugs and food safety.

While I have submitted extensive comments for the record, I would like to talk to you today about one simple truth, and you have heard this a number of times on the panel before me: animals need medicine, including antimicrobials. Without safe and effective medications to treat, control and prevent diseases, suffering and death would increase. Additionally, since healthy farm animals are one of the pillars of safe food, human health would be threatened by increased animal disease and increased bacterial loads in foods.

Research-based animal health companies work hard to provide livestock and poultry producers, and the veterinarians who work with them, the products needed to keep food animals healthy. These products must go through stringent science-based review processes. All products including antimicrobials are required to meet the same standards as medicines approved for humans, meaning they must be shown to be safe and effective.

Now, there are several benefits to animals, producers and consumers from the use of antimicrobials in animal agriculture, and you have heard this theme before this morning. Animal welfare is improved as a result of veterinarians and producers having the

tools to protect animal health and keep them healthy. Producers are more efficient because they can produce more food with fewer animals. This is especially important in this market environment that has seen escalating feed costs, and fewer animals mean less land mass is needed to raise the number of livestock and poultry to meet current demands. I think you have heard some very interesting statistics from some of the producer groups this morning to support that.

There are also benefits to global food markets. Antimicrobials and other animal drugs that improve animal health and productivity are critical to American agriculture's ability to feed the world's growing population. The Food and Agriculture Organization, FAO, estimates that 75 million more people worldwide were below the hunger threshold in 2007 as a result of rising food prices. They propose that one solution is to help producers raise their output. Finally, consumers benefit because healthy animals produce safe food. Published peer-review studies have shown that carcasses from chickens without subclinical disease that are prevented by antibiotics are more likely to be free of human foodborne pathogens such as *Salmonella* and *Campylobacter*.

Now, for more than 40 years, there has been an active debate over the potential for antimicrobial use in animals to contribute to the human burden of antimicrobial resistance. Antimicrobial resistance is a serious public health threat, but I would emphasize that resistance is not a single problem. It is a problem comprised of several different bacteria-drug combinations. For instance, some of the most widely recognized antimicrobial resistance problems in humans are respiratory tract infections and venereal diseases like gonorrhea. In neither of these cases is there any evidence that antimicrobial use in animals is associated with these problems. In a survey published in 2000, a group of medical experts estimated that the animal contribution to the overall resistance problem is likely to be less than four percent. This small contribution was attributed to the potential for antimicrobials used in food animals to transfer certain resistant foodborne bacteria like *Salmonella* and *Campylobacter* to humans.

Because of the potential for both antimicrobial-resistant and antimicrobial-susceptible bacteria to contaminate foods, our food safety systems are comprised of multiple layers of protection to guard against this transfer taking place. The first layer of protection is a stringent regulatory review process at FDA that you heard Dr. Dunham speak of this morning. Antimicrobials for use in animals must meet all the same requirements as antimicrobials used in humans with two additional important requirements. First, sponsors must show the drug residues left in meat, milk and eggs are safe for human consumption. Second, FDA instituted what is called Guidance #152 several years ago, which outlines a qualitative risk assessment process that is applied to all antimicrobials approved for use in animals. The process is designed to estimate and manage the risk of antimicrobial-resistant bacteria being transferred from animals to humans.

In addition to the FDA process, there have been several quantitative risk assessments that have been conducted on antimicrobial compounds, and they have resulted in findings that show

an extremely low level of risk. A quantitative assessment is a more detailed review of each step along the food production continuum from farm to table that could increase or decrease risks from a hazard such as resistant bacteria. We believe that risk assessment is the proper tool for making policy decisions about the use of antimicrobials in animals. Without this scientific basis for decision-making, we do run the real risk of making decisions that have unintended consequences that are damaging to both human and animal health.

A second layer of protection, and one of the most important, is reducing bacteria contamination in slaughter in processing plants. Antimicrobial-resistant bacteria represent only a small subset of bacteria that could contaminate meat and poultry products. USDA through implementation of the Hazard Analysis and Critical Control Point system, or HACCP, and pathogen reduction regulations assures that slaughter plants are following hygienic procedures to minimize bacterial contamination. Results have shown that HACCP has worked to reduce bacterial contamination of meat and poultry products, and therefore, has reduced antimicrobial-resistant bacteria as well.

A third layer of protection is comprised of several monitoring programs established by FDA and USDA to assure antimicrobials are being used properly and according to labels. We heard mention of the National Antimicrobial Resistance Monitoring System, which is a multi-agency program between USDA, CDC and FDA to monitor antimicrobial-resistant bacteria in humans, animals and meat products.

A fourth layer of protection is the responsible or judicious use guidelines. Generally, these guidelines have been prepared collaboratively between the Federal agencies and veterinary groups to help assure there is no unnecessary use of antimicrobials in agriculture. Members of the panel discussed this previously.

Before I close, I want to note that Congress twice this year passed legislation dealing with the use of antimicrobials in animals. The farm bill, passed by this Committee, included a mandate for additional research on the development of resistant bacteria in animals and its potential transfer to humans. Then in the recently enacted Animal Drug User Fee Act, Congress required FDA to collect data from sponsors on the amounts of antimicrobials sold for food-producing animals. Our member companies will of course cooperate with FDA in this endeavor.

Mr. Chairman, there are clear benefits to using antimicrobials to keep animals healthy including attending to animal welfare and assuring food safety. FDA has a stringent review process to assure that antimicrobials used to keep food animals healthy do not significantly contribute to the burden of antimicrobial resistance in humans. Monitoring data from NARMS and several private and public risk assessments demonstrate that this process is working and that utilizing important medicines like antimicrobials to protect animal health provide far more benefits than risk to public health overall.

Thank you for the opportunity to appear here today and I welcome any questions from the Subcommittee.

[The prepared statement of Dr. Carnevale follows:]

PREPARED STATEMENT OF RICHARD A. CARNEVALE, V.M.D., VICE PRESIDENT, SCIENTIFIC, REGULATORY AND INTERNATIONAL AFFAIRS, ANIMAL HEALTH INSTITUTE, WASHINGTON, D.C.

Mr. Chairman and Members of the Subcommittee:

Thank you for holding this hearing on recent developments in animal health. I am Dr. Richard Carnevale. I am a veterinarian by training with a degree from the University of Pennsylvania and I am here today on behalf of the Animal Health Institute, a trade association that represents companies that make medicines for animals. Prior to joining AHI about 12 years ago, I served as Deputy Director for the Office of New Animal Drug Evaluation at FDA's Center for Veterinary Medicine and later as Assistant Deputy Administrator for the Office of Science at USDA's Food Safety & Inspection Service. AHI companies work to provide products to livestock and poultry producers that help keep their animals healthy. By doing this, companies contribute to public health and food safety. Research shows that the first link in the chain of producing safe meat, milk and eggs is keeping animals free from disease.

Food safety starts on the farm, and our companies spend millions of research and development dollars to find new and innovative products to keep farm animals healthy. Some animal health products are used to treat and prevent or control disease in animals. Others help increase animal productivity, allowing producers to meet the growing world food demand while minimizing the use of natural resources. More recently, products are being developed that will contribute to food safety by reducing bacteria that do not make animals sick but have the potential to make people sick.

Animal health products are subject to stringent, science-based review processes at two Federal agencies: pharmaceutical products are reviewed by the Food and Drug Administration under the Federal Food, Drug and Cosmetic Act, and biologic products, or vaccines, are regulated by USDA under the virus, Serum, Toxins and Analogous Products Act. All products are reviewed for safety and efficacy: Efficacy, which protects producers by ensuring the products deliver the benefits they promise; and safety, to ensure the products are safe for the animal being administered the drug or vaccine and to ensure the meat from the animal is safe for human consumption and safe for the environment.

One class of products important to the health of food animals is antibiotics. Antibiotics are used by livestock producers, poultry producers and the veterinarians who work with them to prevent, control and treat often fatal bacterial infections. There are many benefits to animals, producers and consumers that come from the use of antibiotics in animal agriculture:

1. Animal welfare is improved as a result of veterinarians and producers having the tools to be able to maintain the animal's health.

2. Producers are more efficient because they can produce more food from fewer animals. Without antibiotics to prevent and control diseases, more animals get sick and die with producers losing not only the animal but all the input costs, including feed, that have gone into the animal.

3. There are ecologic benefits. Without antibiotics that improve weight gains and feed conversion, more land and feed are necessary to maintain the same herd and flock sizes. Moreover, some studies have shown that certain antimicrobials used in cattle feeds reduce levels of methane emissions important as greenhouse gases.

4. Benefits to global food markets. With the concern over food costs and availability in today's economic climate, antimicrobials and other animal drugs that improve animal health and productivity are critical to American agriculture's ability to feed the world's growing population. The Food and Agriculture Organization (FAO) of the United Nations estimates that 75 million more people worldwide were below the hunger threshold in 2007 due to increasing food prices. They propose that one solution is to help producers to raise their output.

5. Consumers benefit because healthy animals are needed to produce safe food. Over the past 5 years, published, peer-reviewed studies have indicated that carcasses from chickens without subclinical diseases are more likely to be free of human foodborne pathogens.[1–4] Research shows this is due in part to more standardized carcass size, reducing the potential for intestinal breakage during mechanical evisceration.

Antibiotics are approved and labeled for four specific purposes.

1. Disease treatment.

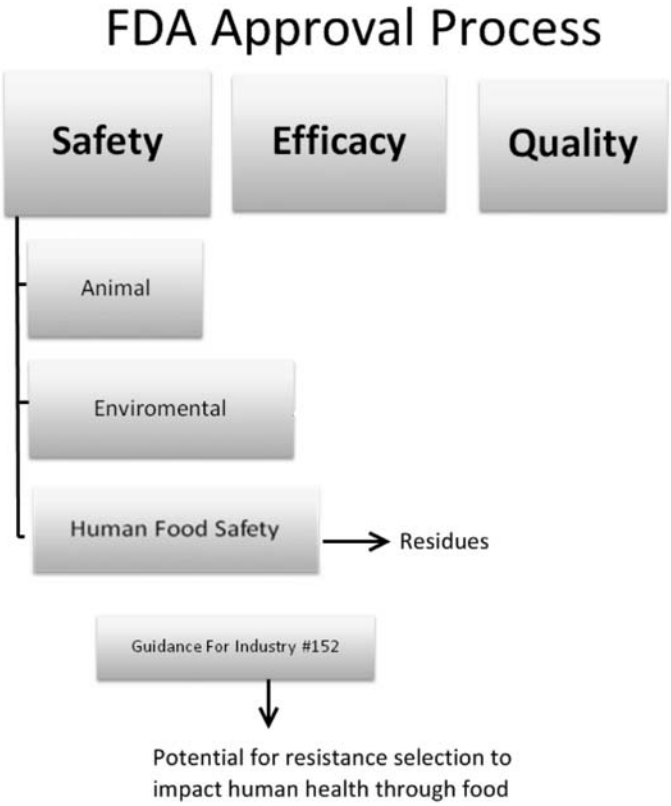
2. Disease prevention.
3. Disease control.
4. Growth promotion, as measured by the amount of feed needed to produce a pound of animal weight or increased rate of weight gain.

The first three uses—disease treatment, prevention and control—are considered to be therapeutic uses by FDA, the American Veterinary Medical Association (AVMA) and such international bodies as Codex Alimentarius and the OIE. While critics of antibiotic use like to use the term "nontherapeutic" to refer to disease prevention, disease control and growth promotion, this term is not used nor recognized in national or international regulation.

Many assume in-feed uses equate to growth promotion, but this confuses the use with the route of administration. In fact, any of the four uses, including therapeutic, can be administered via feed or water, as that is under certain circumstances the only practical way to administer medication to large flocks or herds. In most cases, a veterinarian is involved in this process, recommending feed that is specifically formulated for the health management system used for the flock or herd.

How are antibiotics regulated?

Animal health companies rely on a rigorous, efficient, predictable and science-based review process at the Food and Drug Administration's Center for Veterinary Medicine (CVM) to provide these products. The standard for the approval of antibiotics used in animals is the same as that for antibiotics used in human medicine: They must be shown to be safe and effective.



The rigorous review process and monitoring systems in place are at the heart of a broad system of protections that ensure that all medicines, including antibiotics, are safe for animals and humans. Antibiotics for use in animals must meet all the same requirements as antibiotics used in humans, with two additional requirements: first, sponsors must show the meat, edible tissues, milk and or eggs from

animals in which the medicine is used is safe for human consumption. Second, beginning in 2003, CVM instituted Guidance for Industry (GFI) #152, which outlines a qualitative risk assessment process that is applied to all antibiotics approved for use in animals. This guidance process is designed to measure the risk of antibiotic resistant bacteria being transferred from animals to humans if the product is approved. Based on this risk, FDA makes decisions to either deny or approve the drug with certain restrictions to significantly reduce risk. Restrictions can include requiring a veterinary prescription, prohibiting extra-label use in certain species or restricting the antibiotic to individual animals. In most cases antimicrobial resistance monitoring is required post approval. The methodology is very conservative—meaning it is very difficult to get an antibiotic approved. Further, the guidance is sufficiently broad so that if new, previously unidentified or undescribed, resistant organisms or genes were to become of concern, the agency can act swiftly to take this information into account. The existing guidance allows the agency sufficient flexibility to allocate resources appropriately to changing issues of safety related to resistance emergence.

The GFI #152 process applies not only to new submissions, but to all existing products as well. FDA has established a priority list for the re-evaluation of all antibiotics currently approved and marketed. Most of the drugs on the list are antibiotics administered in animal feed for the prevention and control of animal diseases or to increased the weight gains and improve feed efficiency. The re-review under Guidance #152 was stimulated by new funding that FDA received and continues to receive via annual appropriated money specifically earmarked for these reviews. Bear in mind, though, the evaluation of these products did not begin with Guidance #152. In response to concerns raised some 30 years ago, the Bureau of Veterinary Medicine in FDA, in the 1970's, required sponsors of these products to conduct tests to determine the potential for resistance to be selected in the animals and to be transferred to bacteria that could cause human disease. While the standards and science may have changed over the years, the safety of these products has been an ongoing exercise at FDA. Moreover, published quantitative risk assessments performed by both the agency and individual product sponsors have generally affirmed that the risks to human health from these antibiotics in animal feed under approved conditions of use are quite low.

We fully support efforts by the agency to continue to evaluate the safety of these products using all available scientific data under a sound risk assessment approach in order to determine the true risk to public health and guide appropriate risk management interventions to protect public health.

FDA/CVM has a great deal of authority to act when data or risk assessments indicate a threat to public health. CVM can—and has—successfully asked companies to withdraw products voluntarily or to modify their conditions of use, including restricting extra label use. The agency can also undertake a notice of proposed rulemaking against a product, setting in motion a process to rigorously review the science and determine if a product should continue to be marketed. This authority has been used to remove antibiotics from the market. Finally, if the agency determines there is an imminent hazard to public health, it can immediately remove a product from the market.

In addition to the rigorous review process and the additional public and private risk assessments that have been conducted, there are other post-approval layers of protection to ensure the safe use of antibiotics.

Monitoring programs

USDA's Food Safety and Inspection Service monitor meat samples for the presence of antibiotic residues as a check on the observance of the withdrawal times set by FDA. It is very uncommon for FSIS to find an unsafe residue, an indication that products are being used according to label directions.

The National Antibiotic Resistance Monitoring System (NARMS) is a multi-agency program coordinated by FDA to monitor antibiotic resistant bacteria and allow for implementation of management and control measures if needed. The three agencies involved are:

- The USDA Agricultural Research Service (ARS), which analyzes *Salmonella* and *Campylobacter* isolates collected from carcasses and meat samples in the USDA FSIS HACCP/Pathogen Reduction Program for antibiotic resistance;
- The FDA, which monitors for resistant bacteria in retail meats; and
- The Centers for Disease Control and Prevention (CDC), which collects isolates from public health laboratories to monitor for the emergence of antibiotic resistant enteric pathogens in humans.

To date, the program has produced 7 years of data representing over 19,000 *Salmonella* isolates from livestock and poultry carcasses and meats and 12,000 human *Salmonella* isolates. Most bacterial species isolated from humans and tested for resistance against drug classes potentially related to animal usage have shown stable or declining resistance to most antimicrobials. Most of the multiple-drug resistance types, such as *Salmonella typhimurium* DT104 show stable or declining prevalence in both food animals and humans since 1996, according to an expert report issued in 2006 by the Institute of Food Technologists entitled "Antibiotic Resistance: Implications for the Food System."

While AHI strongly supports continued funding of the NARMS program we would point out that there are inherent weaknesses in the sampling strategies that prevent the data from estimating a true national prevalence of resistance and yearly trends. The FDA Science Board has identified these weaknesses as well and has encouraged the agencies involved in NARMS to work to improve the data.[5]

Judicious Use Guidelines

Responsible, or judicious, use programs that are specific to different livestock species give veterinarians and producers specific guidelines to help them safely and properly use of antibiotics in their health management systems. Generally, these guidelines have been prepared collaboratively by FDA, CDC and veterinary groups. These guidelines help ensure there is no unnecessary use of antibiotics in animal agriculture. Others testifying today will provide additional detail on how these principles are used by veterinarians and producers.

There are two additional layers of scrutiny that antibiotic use receives.

First, at the international level, Codex Alimentarius is responsible for protecting the health of consumers and ensuring fair practices in food trade. Codex has established a committee on antibiotic resistance. Chaired by Korea, this committee is currently working to establish an internationally recognized process for risk analysis of antibiotics used in animals. International standards are important, because bacteria know no borders and actions taken here can be nullified if there is not concerted international action. It is also important that the international community establishes a sound scientific basis for countries to assess the risk of antibiotic use. Otherwise, government regulators are left open to outside pressure to take overly zealous precautionary measures that may be unjustified and in the long term harmful to animal health and food safety.

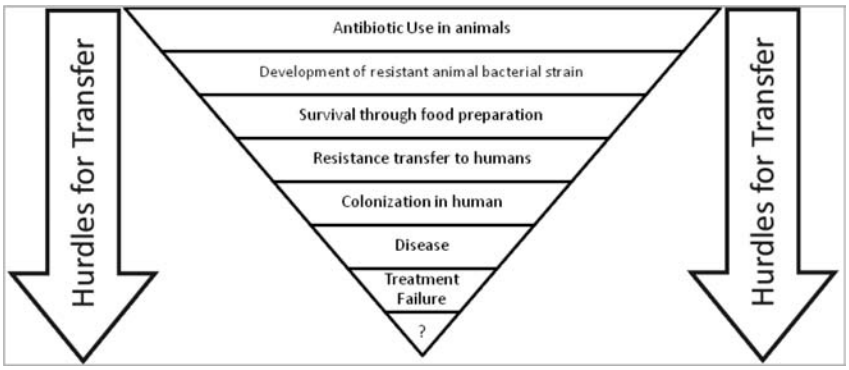
Second, several risk assessments have been conducted on antibiotic compounds, and have uniformly found extremely low levels of risk. Some of these have been conducted and published by the sponsors, some by independent authorities, and some by FDA. In particular, the FDA risk assessment on virginiamycin found there were significant differences between the resistant enterococci bacteria found in animals and those found in humans. Even after they assumed an association for purposes of conducting the risk assessment, the levels of risk they estimated were quite small.

We firmly believe that risk assessment is the proper tool for making policy decisions about the use of antibiotics in animals. Without this scientific basis for decision making, we run the very real risk of making decisions that have unintended consequences that are damaging for both human and animal health.

Does the Use of Antibiotics in Animals Contribute to Human Antibiotic Resistance?

There is no question that antibiotic resistance is a serious public health threat. But resistance is not a single problem: it is a problem comprised of several different bacteria-drug combinations. For instance, some of the most widely recognized antibiotic resistance problems in humans are in respiratory tract infections and venereal diseases like gonorrhea. In neither of these cases is there any evidence that antibiotics used in animals are associated with these problems. In fact, in a survey published in 2000 a group of medical experts estimated the animal contribution to the overall human resistance problem is less than four percent.[6]

That small contribution was attributed to the potential for antibiotics used in food animals to contribute to resistance in certain bacteria which can be transferred from animal food products to humans. However, there is a chain of events from the "farm to the fork" that must be traversed by bacteria that develop resistance in animals as outlined in the accompanying chart:



In order for this to happen, the antibiotic must be used in the animal, resulting in the selection of resistant bacteria in the animal. Those bacteria then must survive the slaughtering and processing of the animal. Remember, we have successfully reduced the number of bacteria—both resistant and not resistant—that survive this process through the implementation of controls like HACCP. The bacteria must then survive the normal cooking process. If enough resistant bacteria survive to this point and are ingested in a large enough quantity, they can make an individual sick with a common foodborne illness. As you know, most foodborne illnesses are self-limiting—they resolve themselves in most cases without antibiotics being necessary. In the event that an antibiotic is necessary, the illness could be treated with the antibiotic that the bacteria is resistant to, and the treatment could fail, prolonging the illness.

While we know this can happen, the question is, how often does this happen and how severe are the consequences? The answer to this much-studied question is that it does not happen enough that we can find it and measure it. So, scientifically, we cannot say it does not happen, but we can say it is rare.

Finally, there are some recurring questions in the debate about antibiotic use I would like to address.

First, what is the quantity of antibiotics used in animal agriculture? Critics have charged that we don't know how big the problem is because we don't have reliable data about the use of antibiotics in animal agriculture. However, levels of antibiotic resistance are not correlated to the amount of use. Not all antibiotics are alike. Nevertheless, each year AHI surveys its members for the amount of antibiotics sold for use in animals. Attached to my testimony are the 2006 results. Note that there are large groupings of products. This grouping is done because of the small number of companies in the market and the need to protect confidential business information. The information is not species specific, because many of the compounds sold are used in more than one species. While critics have demanded species specific information, this would only be available if it comes from producers, adding to their costs and paperwork burden. About 7 years ago CVM began work on a rule to require data collection but dropped the effort as a result of these difficulties. Congress recognized this just this summer when antimicrobial sales and distribution data reporting requirements were included in the Animal Drug User Fee Amendments of 2008. We are appreciative of the cooperation we received from Members and staff in working with the Animal Health Industry to craft appropriate legislative language for these reporting requirements.

Notably, Congress also acted on this issue in the farm bill that was signed into law earlier this year. That legislation contained an authorization for USDA's Agriculture Research Service to conduct additional research to study the development of antibiotic resistant bacteria in livestock on how judicious use principles can help producers use these products to protect both human and animal health.

Also, note that we ask sponsors to estimate the amount of antibiotics used for growth promotion. This estimate dropped to less than five percent of the total in 2006.

What happens if producers lose access to these products? This question can be answered with data from the European experiment. In the late 1990s, the European Union phased out one particular use—the use of antibiotics for growth promotion. Data from the Danish Government, which you see on the accompanying chart, shows that use of antibiotics to treat disease has doubled since the ban.

Trends in the estimated total consumption (kg active compound) of prescribed antimicrobials for production animals, Denmark

DANMAP 2007

Therapeutic group	1990	1992	1994	1996	1998	2000	2002	2004	2006	2007
Tetracyclines	9,300 b)	22,000	36,500	12,900	12,100	24,000	24,500	29,500	32,650	38,200
Penicillins, β–lactamase sensitive	5,000	6,700	9,400	7,200	14,300	15,100	17,400	20,900	22,600	23,850
Other penicillins, cephalosporins	1,200	2,500	4,400	5,800	6,700	7,300	9,900	12,900	11,550	11,500
Sulfonamides + trimethoprim c)	3,800	7,900	9,500	4,800	7,700	7,000	10,600	11,500	13,800	13,850
Sulfonamides	8,700	5,900	5,600	2,100	1,000	1,000	900	850	750	750
Macrolides, lincosamides, pleuromutilins	10,900	12,900	11,400	7,600	7,100	15,600	19,200	24,200	22,050	23,800
Aminoglycosides	7,700	8,500	8,600	7,100	7,800	10,400	11,700	11,600	10,500	8,150
Others c)	6,700	6,800	4,400	600	650	300	1,600	1,000	1,250	1,100
Total	53,400	73,200	89,900	48,000	57,300	80,700	95,900	112,500	115,150	121,100

This data, along with the discussion in the Danish report, clearly indicates the ban led to additional animal disease and death. The important question is what impact did it have on public health? There is some evidence to indicate resistance declined in animals and humans in certain bacteria. However, there is no evidence that this has resulted in reducing the public health burden of resistant bacterial infections in humans. The list of references at the end of my testimony includes published papers on the results of the ban.

In summary, Mr. Chairman, antibiotics are vitally important to the health of our nation's livestock and poultry herds and flocks. Antibiotics are highly and vigorously regulated and are used carefully by veterinarians and livestock and poultry producers. The many regulatory layers of protection that have been put in place allow us to use antibiotics to protect both human and animal health and not add to the burden of antibiotic resistant infections in humans. The FDA regulatory process and risk assessment are the proper tools for making decisions about the use of these products, and to make decisions without these tools we place unwarranted risks on both human and animal health.

Notes

[1] Russell S.M. *The effect of airsacculitis on bird weights, uniformity, fecal contamination, processing errors and populations of* ***Campylobacter spp.*** and ***Escherichia coli.*** POULT. SCI. 2003; 82:1326–31.

[2] Cox, Jr., L.A. *Potential human health benefits of antibiotics used in food animals: a case study of virginiamycin.* ENVIRON. INT. 2005;31:549–63.

[3] Hurd H.S., *et al. Swine Health Impact on Carcass Contamination and Human Foodborne Risk.* PUBLIC HEALTH REPORTS, May–June 2008; 123: 343–351.

[4] Berrang M.E., *et al. Subtherapeutic Tylosin Phosphate in Broiler Feed Affects* ***Campylobacter*** *on Carcasses During Processing.* POULT. SCI. 2007;86:1229–1233.

[5] *http://www.fda.gov/cvm/Documents/NARMSExecSum03.pdf.*

[6] Bywater, R.J. and Casewell M. *An assessment of the impact of antibiotic resistance in different bacterial species and of the contribution of animal sources to resistance in human infections.* J. ANTIMICROB. CHEMOTHER. 2000;46:643–635.

Additional References

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ATTACHMENT

News Release

Contact: Ron Phillips

Trends in Sales of Lifesaving Animal Medicines Continue

Washington, D.C., October 3, 2007—U.S. animal health companies responded to the increased demand for medicine to treat and control animal disease in 2006,

increasing the volume of antibiotics sold for use in animals in the United States. Antibiotics are critical disease-fighting medicines used to treat diseases in dogs, cats and other companion animals, and in farm animals to improve their well-being and ensure the production of safe and wholesome food.

Continuing a trend observed the past 2 years, the volume of antibiotics sold to treat, prevent and control disease in animals rose in 2006, while the percentage sold to promote growth dropped. Total production for use in animals rose 8.2 percent, according to data provided by the research-based companies that produce animal medicines. One factor that may have contributed to the increase was a 2 billion pound increase in U.S. meat production

The antibiotic data were collected from a survey of members of the Animal Health Institute (AHI), consisting of companies that make medicines for pets and farm animals.

"All animal owners rely on these important medicines to fight disease and keep their animals healthy, whether those animals are cats and dogs or farm animals," said AHI President and CEO Alexander S. Mathews. "The careful use of these products contributes to human health by extending the life of our pets and by helping to provide a safe food supply."

Again this year, two classes of compounds, ionophores and tetracyclines, accounted for most of the increase. Ionophores are compounds not used in human medicine. All antibiotics undergo a rigorous approval process at the Food and Drug Administration that includes an assessment of safety of the product for the treated animal and safety of the milk and meat produced. In addition, all proposed antibiotic products as well as those previously approved undergo a risk assessment procedure, called Guidance #152, to scientifically measure the safety of the product with respect to health hazards resulting from the spread of antibiotic resistance.

In 2006, 26.4 million pounds of antibiotics were sold for use in farm and companion animals, an increase from 24.4 million pounds sold in 2005. The small percentage of overall production used to enhance growth dropped slightly to 4.6 percent, down from 4.7 percent the previous year.

The Food and Drug Administration (FDA) approves antibiotics used in animals for four purposes: Disease treatment, disease control and disease prevention, which are considered by FDA and the American Veterinary Medical Association to be therapeutic, and for growth promotion.

2006 AHI Survey

Active Antibacterial Ingredients Sold by AHI Members

Antibiotic Class	2004 Pounds	2005 Pounds	2006 Pounds
Ionophores, Arsenicals, Bambermycin, Carbadox and Tiamulin*	9,602,121	10,293,627	11,149,502
Tetracyclines	6,486,207	8,420,250	9,281,703
Cephalosporins, macrolides, lincosamides, polypeptides, streptogramins, fluoroquinolones and other minor classes of antibiotics**	4,176,088	4,417,316	4,496,522
Sulfonamides and Penicillins	1,117,815	1,043,645	1,198,478
Aminoglycosides	357,077	267,600	327,901
Total	21,761,128	24,442,438	26,454,107

*Ionophores and arsenicals are unique drug products developed for animal production and not related to traditional antibiotics. Others in this grouping are therapeutic drugs with limited or no use in human medicine.

**Grouping necessary to abide by disclosure agreements.

The CHAIRMAN [presiding.] Thank you.

Dr. Hoang.

STATEMENT OF CHRISTINE N. HOANG, D.V.M., M.P.H., ASSISTANT DIRECTOR, SCIENTIFIC ACTIVITIES DIVISION, AMERICAN VETERINARY MEDICAL ASSOCIATION, SCHAUMBURG, IL

Dr. HOANG. Thank you, Mr. Chairman and Members of the Subcommittee for providing the American Veterinary Medical Associa-

tion with the opportunity to speak about the advances in animal health within the livestock industry. My name is Christine Hoang and I work as an Assistant Director in the Scientific Activities Division of the AVMA. In addition to holding a doctorate in veterinary medicine, I also hold a master of public health with concentrations in veterinary public health policy as well as epidemiology.

The AVMA as a whole, with nearly 77,000 member veterinarians, is highly focused on issues related to animal health, animal agriculture and public health and has committed extensive resources to their research and evaluation. Veterinarians are actively involved in research, continually looking for new and better ways to improve animal and human health. It is through this same process of careful study that veterinarians evaluate and determine the efficacy of products and interventions that safeguard our nation's food supply. With limited tools, our profession has made many advances in animal health and food safety in areas such as the development and implementation of animal disease control programs, interventions to minimize bacterial contamination, and biotechnology. Our successes include a decline in foodborne illness associated with meat and poultry products as well as a decline in the prevalence of associated foodborne pathogens including *Salmonella* and the decreased resistance of these organisms.

The AVMA supports the use of multidisciplinary and integrated approaches to address issues affecting public health and food safety. For instance, in addition to supporting improved animal husbandry and management practices, we also support hazard controls in processing and the continued availability and judicious use of antimicrobials to safeguard the nation's food supply. Veterinarians also strongly encourage a veterinarian-client-patient relationship and veterinary consultation when implementing any treatment regimen.

Dispensing or prescribing a prescription product including antimicrobials requires a veterinarian-client-patient relationship. Although there are critical shortages in the veterinary workforce, veterinarians provide oversight and advice on the use of medications including over-the-counter antimicrobials on a significant percentage of animal farms. We believe that further studies should appropriately address the availability of veterinary services and that the use of veterinary services can be improved through the resolution of the critical shortage of the veterinary workforce.

With the large number of animals produced for food in this country, the topic of antimicrobial use in food production often becomes a topic of debate. By controlling and preventing disease through the judicious use of antibiotics and other therapeutic agents, veterinarians assist producers in maintaining and improving animal welfare, the health of the herd and ensuring a safe food supply.

While the end goal is the same for all medical professionals—good health—veterinarians are severely limited in our tools for disease control and prevention. Regulations for drug approvals are more stringent. Therapeutic agents can be more difficult to develop, and there are fewer treatments available. Thus, veterinarians must rely on their knowledge of clinical medicine to determine the best course of treatment. Given the numbers of food animal species, in addition to the diversity of disease conditions that affect animals,

a relative scarcity of labeled indications accompanying FDA-approved drugs exists. Though the FDA, the AVMA and others have, and continue, to make significant strides in enhancing drug availability including legislative initiatives such as the Minor Use and Minor Species Act, the numbers of FDA-approved drugs are inadequate to meet veterinary medical needs, placing animal health and welfare, and potentially human health, at significant risk.

The Food Animal Residue Avoidance Database, or FARAD, has been a chronically under-funded program used by veterinarians, livestock producers, as well as state and Federal regulatory and extension specialists, to ensure that drug, environmental and pesticide contaminants are not in milk, eggs and meat that are consumed by Americans. FARAD serves as an informational resource for withdrawal times. Withdrawal times are periods of time when animals and animal products such as milk and eggs are not to be used for food, allowing time for the animals to metabolize and eliminate the drugs that had been used for treatment. The funding lapses of FARAD in 2007, and the continued lack of recurring support for FARAD, places the entire program in jeopardy. If funding is not appropriated before the end of this month, this vitally important asset to ensure food safety may be forced to close its doors indefinitely.

The American Veterinarian Medical Association is committed to ensuring a safe, healthy and abundant food supply and supports the ongoing scientific efforts and funding for monitoring and surveillance of foodborne disease and resistant pathogens, education, development of new antimicrobials, biologics and other treatment options, and other research to advance animal health and to better define the challenges presented by animal agriculture.

Thank you for the opportunity to appear before you today.

[The prepared statement of Dr. Hoang follows:]

PREPARED STATEMENT OF CHRISTINE N. HOANG, D.V.M., M.P.H., ASSISTANT DIRECTOR, SCIENTIFIC ACTIVITIES DIVISION, AMERICAN VETERINARY MEDICAL ASSOCIATION, SCHAUMBURG, IL

Thank you, Mister Chairman and Members of the Subcommittee on Livestock, Dairy, and Poultry, for providing the American Veterinary Medical Association (AVMA) with the opportunity to speak about the advances in animal health within the livestock industry.

My name is Dr. Christine Hoang, and I work as an Assistant Director in the Scientific Activities Division of the American Veterinary Medical Association. In addition to holding a doctorate in veterinary medicine, I also hold a master of public health degree with concentrations in veterinary public health policy, both national and international, as well as epidemiology.[a] The majority of my work focuses upon food safety, zoonotic disease,[b] and antimicrobial resistance. As a result, issues related to animal health, animal agriculture, and human health have not only become topics of interest, but are topics that require a great deal of intensive research and evaluation.

The AVMA represents nearly 77,000 U.S. veterinarians engaged in every aspect of veterinary medicine and public health. As veterinarians, our oath ethically charges us with promoting public health and protecting animal health and welfare. Thus, we share many of the same concerns as our human health counterparts. Among other things, our members protect the health and welfare of our nation's animals, help ensure food safety, and protect animal and human health through prevention and control of zoonotic diseases.

The AVMA supports the use of multidisciplinary and multi-hurdle[c] approaches[1] to address issues affecting public health and food safety. For instance, in addition to supporting improved animal husbandry and management practices, we also sup-

port the continued availability and judicious use of antimicrobials to safeguard the nation's food supply.

The veterinary profession strives to achieve optimal animal health as well as animal welfare and human health. The fundamentals of food animal medicine and population medicine[d] are the same as the fundamentals of public heath—control and prevention of disease. While the end goal is the same for all medical professionals—good health—veterinarians are severely limited in our tools for disease control and prevention. Regulations for drug approvals are more stringent, therapeutic agents can be more difficult to develop, and there are fewer treatments available. Thus, veterinarians must rely on their knowledge of clinical medicine to determine the best course of treatment. Given the numbers of food animal species, in addition to the diversity of disease conditions that affect animals, a relative scarcity of labeled indications accompanying FDA approved drugs exists. Though the FDA, the AVMA and others have made and continue to make significant strides in enhancing drug availability, including legislative initiatives (such as the Minor Use and Minor Species Act), the numbers of FDA approved drugs are inadequate to meet veterinary medical needs, placing both animal health and welfare—and, potentially, human health—at significant risk.

While it may seem intuitive to some that healthy animals are critically important for safe food, there are few who understand the intricacies of why. As an example, it is fairly intuitive that an effective antibiotic will help decrease the bacterial load in food. What many do not understand is that it is extremely difficult to ascertain whether or not a particular animal is carrying certain bacteria. Many bacteria, such as *Salmonella*, are shed intermittently, and cannot be easily detected by routine testing procedures. Animals can harbor types of bacteria in their intestinal tracts that have no effect on their health, but can cause illness in humans. Thus, we must rely on the combination of many different types of interventions to protect our food supply. These interventions would range from prevention and control of disease before it occurs in animals to post harvest interventions such as carcass rinsing to further minimize bacterial contamination in food. Another concept that is often misunderstood or overlooked is how seemingly unrelated illness, such as respiratory disease in a food animal, can affect the presence of enteric bacterial pathogens in the meat. For example, air sacculitis is a respiratory disease that affects poultry. It is a fairly common disease that can spread rapidly and often go undetected until slaughter. The disease causes tissues to become more friable[e] and difficult to remove during food processing. The increased handling and difficulty in processing increases the potential for damaging the intestines and contaminating the carcass with enteric pathogens that can be harmful to humans.[2] By controlling this disease through the use of antibiotics and/or other therapeutic agents, veterinarians assist producers in maintaining a healthy flock and a safe food supply. This example further illustrates the necessity to continually maintain and improve animal health in the preservation of food safety.

Veterinarian's Role

Veterinarians evaluate whether a therapy's benefits would outweigh its risks to both the patient and to public health. Veterinarians have been trained to "do no harm" as they make therapy recommendations, and they have the duty to utilize such agents to promote animal health and welfare in such a way that safeguards the public health. In addition, veterinarians protect America's food supply by ensuring food animal health from "farm to fork," including their work in clinical practice, in state public health agencies, in the Federal Government, and in the corporate sector. Healthy animals make healthy food; for veterinarians to be effective in protecting our food supply, the appropriate tools for preventing, mitigating, and treating disease, which include antimicrobials, are paramount for veterinarians to be able to utilize.

Veterinarians are actively involved in research, continually looking for new and better ways to improve animal and human health. Some veterinarians work in research through universities, private corporations, or through government projects, and many are actively involved in field research. It is through this process that we have learned so much about the nature of infectious diseases. It is through this same process of careful study that veterinarians evaluate and determine the efficacy of products and interventions that safeguard our nation's food supply. With limited tools, our profession has made many advances in animal health and food safety, including the development and implementation of animal disease control programs, pre- and post harvest interventions, and areas of biotechnology. Other successes through collaborative efforts include a decline in foodborne illness from meat and poultry products[3] as well as a decline in the prevalence of foodborne pathogens (including *Salmonella*) associated with meat and poultry[4] and resistance of those orga-

nisms.[5] These are all a result of improvements in animal health and the joint efforts of stakeholders.

Veterinarians are in the best position to prescribe and administer the most appropriate therapies for their patients. Veterinarians are licensed by state authorities to practice veterinary medicine and are authorized by both state and Federal Government entities to handle potent medical agents in the course of their professional practice. While there is governmental and regulatory oversight, veterinarians use professional judgment to determine the best therapy for their patients:

- Specifically, the Drug Enforcement Administration (DEA) entrusts registered veterinarians to prescribe controlled substances for animals, i.e., those drugs that are not available to the general public due to the potential for abuse and addiction.
- The Environmental Protection Agency (EPA) allows veterinarians to use both restricted-use and conventional pesticides in the course of their professional practice.
- The United States Department of Agriculture (USDA) recognizes veterinarians as professionals who may vaccinate animals to advance national animal disease control and eradication programs.

Of the tools that are available to veterinarians, one of the most important tools that veterinarians use to protect animal health and human health is the judicious use of antimicrobials. The continued availability of safe, effective antimicrobials for veterinary medicine, including the retention of currently approved drugs and future approvals of new drugs, are critical components of ensuring a safe food supply and essential to the improvement of animal health and welfare.

The exact quantity of antimicrobials that are used in animal agriculture remains unknown and estimates vary greatly depending upon the source and the classification of antimicrobials. The Union of Concerned Scientists (UCS) estimates 24.6 million pounds of antimicrobials were used for non-therapeutic uses (defined by UCS to include uses for prevention and control of disease as well as for growth promotion) in cattle, swine, and poultry in 1999.[6] However, The Animal Health Institute (AHI) has reported a general downward trend in total antibiotic use between 1999 and 2004, and estimates 95% therapeutic use (which includes disease control and prevention),[7] and therefore about 1.2 million pounds for growth promotion or feed efficiency. Antibiotic use estimates are equally confusing and inconsistent when evaluating human use data. AHI reported in 2000 that 32.2 million pounds of antibiotics are used annually in human medicine.[8] However, the UCS estimate for human use (for inpatient and outpatient disease treatment and as topical creams, soaps, and disinfectants) was 4.5 million pounds. But the real issue is not the quantity of antimicrobials that are used but the outcomes of use.

Despite all of these figures and other available data, no one knows for certain what role animal agriculture plays in the ecology of antimicrobial resistance. What we do know is that we need to be able to have as many tools as possible to uphold our oath.

The number and supply of animals that is necessary to keep up with human demands for animal protein is rapidly increasing. The world's population is growing, and expected to increase by a third exceeding nine billion by 2050.[9] With that population growth, comes an increased demand for a safe, healthy supply of food. Ban Ki-Moon, the United Nation's Secretary General, has noted in multiple venues that global food production must increase by 50% by 2030 to meet those demands.[10]

In 2000, 9.7 billion animals were slaughtered for human consumption in the United States. In that same year, the U.S. Census Bureau reported a population of approximately 281 million. The U.S. population today is well over 300 million, and the world's population is rapidly approaching seven billion.[11] Red meat production alone in the U.S. totaled 48.8 billion pounds last year.[12] Today, the European Union's population is nearly 500 million, but in 2007 slaughtered only 42 million animals for food[13] compared to the U.S.'s nearly ten billion animals slaughtered annually. While the United States is often compared to the European Union in the discussion of differing husbandry and management practices, few recognize the vast difference in per capita production and that the United States has the most affordable, abundant, safe, and healthy food supply in the world.

With the large number of animals produced for food in this country, the topic of antimicrobial use in food production often becomes a topic of debate. Much of the discussion revolves around a category of antimicrobial use commonly known as growth promotion or a group of antimicrobial uses that are poorly categorized as "non-therapeutic." The term "non-therapeutic" has no meaning in Federal regulation or common usage. The FDA approves antimicrobials for four purposes: disease treat-

ment, disease prevention, disease control, and growth promotion/feed efficiency. The FDA does not approve antimicrobials for "non-therapeutic" uses. Also, the various organizations and people who use the term "non-therapeutic," use it inconsistently. For example, the Pew Commission on Industrial Farm Animal Production (PCIFAP) provides an unclear definition of "non-therapeutic" that is different than H.R. 962, the Preservation of Antibiotics for Medical Treatment Act of 2007 (PAMTA). Additionally, the definitions use terms that are undefined, such as "routine preventive uses and other routine uses." As a result, the term is not commonly understood. The use of exclusionary terms, such as "non-therapeutic", that are ill-defined serves to further confuse the issue. We caution against the use of this term.

Instead, we believe the FDA labeled uses of antimicrobials should be used as the terminology, i.e., treatment, prevention, control, or growth promotion/feed efficiency. Alternatively, we advocate using the definitions of the Codex Alimentarius Commission (an organization of the World Health Organization and the Food and Agricultural Organization of the United Nations), the FDA, and AVMA. All three organizations classify treatment, prevention, and control of disease as therapeutic uses.

Not all antimicrobials or all their uses are equal in their probability of developing resistance or creating a risk to human health. The EU's Scientific Committee on Animal Nutrition has agreed that *possible* theoretical human health concerns related to animal agricultural use of antimicrobials continue to be the focus while *probable* and scientifically based benefits to human and animal health are largely ignored.[14]

There is little debate on the use of antimicrobials for treatment of disease in animals. However, few understand the importance of disease control and prevention, and even fewer have a clear understanding of growth promotants. Prevention and control of disease are key elements in the practice of veterinary medicine, particularly in animal agriculture, where the focus is on population health. This concept of disease prevention and control through herd health is analogous to public health efforts. Additionally, some of the growth promoting antimicrobials have no human health equivalent and thus no human health impact. In fact, studies show a potential health benefit from the use of growth promoting antimicrobials.[15–22]

Danish Experience

The Danish experience has taught us that there can be serious negative consequences in animal health and welfare following the withdrawal of growth promoting antimicrobials and few, if any, improvements or positive human health impact.

In the late 1990s, Denmark instituted a voluntary ban on the use of antimicrobials for growth promotion (AGPs). (A complete ban of AGPs was initiated in 2000.) The use of antimicrobials in feed and water for controlling and treating disease was not banned. The following has been observed as a result of the ban on the use of antibiotics for growth promotion in Denmark:

- There is little evidence to demonstrate a general decline in antimicrobial resistance in humans and there is no evidence of an improvement in clinical outcomes of antimicrobial treatment of humans, the desired consequence of the antibiotic ban in livestock. The results have been mixed. In fact, resistance in humans to some of the banned drugs has increased dramatically.
- There has been increased death and disease in the swine herds, especially at the weaning stage (information inferred from DANMAP 2005 and other reports on pigs). According to published news reports, there was a relative increase of 25% in the number of pigs that died from illnesses from 1995 to 2005.
- While the total quantity of antimicrobials used in food animals has decreased by 27%, the increase in disease has resulted in a 143% increase in the quantity of antimicrobials used for therapeutic purposes. And the antimicrobials now used are classes such as tetracyclines that are also used in humans.[23]
- Resistance to some antibiotics has decreased in some animals while resistance to other antibiotics has increased

The ban on antibiotic growth promoters in Denmark has not resulted in a significant reduction of antibiotic resistance patterns in humans. It has, however, resulted in an increase in disease and death in the swine herds and an increase in the use of antimicrobials for therapeutic uses in swine herds that discontinued the use of antibiotic growth promoters.

Some important resistance trends reported by DANMAP:

- *Salmonella typhimurium* from human isolates[f] has shown 34–49% *increase* in resistance to tetracycline, sulfonamides, and ampicillin from 1997–2006; in-

creases in resistance to nalidixic acid and ciprofloxacin were 3.8% from 1997–2006

- In contrast, during the same period of time, poultry isolates have shown only minimal increases (2–6%) in resistance to the same antimicrobials.
- Isolates from pigs have also shown a lesser increase (25–27%) in resistance to tetracycline and ampicillin than human isolates during that time.

- *Campylobacter jejuni* from human isolates[f] has shown 5–11% increase in resistance to tetracycline, nalidixic acid, and ciprofloxacin from 1997–2006.
  - In contrast, during the same period of time, poultry isolates have shown lesser increases (4–6%) in resistance to the same antimicrobials.
- *Enterococcus faecium* isolates from healthy human volunteers has shown no increase in resistance to vancomycin (the equivalent of avoparcin) from 1997–2006, and remains at 0%.
- However, resistance to virginiamycin (quinupristin/dalfopristin, e.g., Synercid) had been steadily increasing (up to 25%) from 1997 to 2005 until the definition of resistance was changed in 2006, bringing the level of resistance down to 0%.[g]
  - When the definition of resistance is standardized to the United States definition used by CDC and the level of resistance in humans in Denmark to Synercid is compared to the United States, we find that the level is ten times higher in Denmark in spite of the Danish ban in 1998 of use in animals and the continued use in the United States.
- During the same period of time, *Enterococcus faecium* isolates from pigs and poultry has shown 8–20% *decrease* in resistance to avoparcin,[h] virginiamycin, erythromycin and tetracycline from 1997–2006 (using the same definition of resistance as the human isolates from 1997–2005)

Even though the results of the Danish experiment with antimicrobial growth promotant drug bans is very mixed, proposals within the United States go far beyond the Danish example by proposing to ban uses for the prevention and control of disease in addition to uses to promote growth and feed efficiency. Evidence shows that the Danish ban has caused animal health and welfare problems, without improving human health.

Based on the results of a limited ban enacted in Denmark (i.e., the banning of growth promotants, not uses to prevent and control disease), we do not believe the public would benefit from such limitations on the use of antimicrobials. The loss of approved uses of antimicrobials will negatively impact animal health and welfare without significantly or predictably improving public health. Non-science based, broad bans of preventive uses of antimicrobials have the potential to harm public health, such as through increased foodborne disease.

Significant decisions regarding animal health need to be science- and risk-based decisions. Decisions made without the benefit of veterinary input as well as a thorough evaluation of risks and benefits have the potential to further divert resources away from more appropriate disease control measures.

Actions Advancing Livestock Animal Health

AVMA's Efforts

The AVMA has acted with three objectives in mind:

1. Safeguarding public health,
2. Safeguarding animal health, and the
3. Continued availability of effective therapeutic agents, including antimicrobials for veterinary medicine and the retention of currently approved, safe drugs and biologics as well as future approvals of new therapeutic agents.

Veterinary Oversight, Judicious Use, and VCPRs

Since 1998, the AVMA has actively worked to mitigate the development of antimicrobial resistance related to the use of antimicrobials in food animals. The AVMA Guidelines for the Judicious Therapeutic Use of Antimicrobials were developed to safeguard public health by providing specific recommendations for responsible and prudent therapeutic use of antimicrobials. With support and input from the CDC, Infectious Diseases Society of America, the FDA, and the USDA, the guidelines were developed in collaboration with our species specific allied veterinary organizations. These guidelines were based upon carefully reviewed, scientifically sound research, and we believe that our members conscientiously adhere to the principles of judi-

cious therapeutic use of antimicrobials to ensure the protection of human health, as well as animal health and welfare.

We have actively encouraged and assisted our allied veterinary organizations to use the AVMA general principles as a template to develop more detailed guidelines appropriate to each species, disease and type of client. The AVMA also worked with these groups to develop and deliver a continuing education program to raise awareness within the profession and to encourage utilization of the principles. Fundamentally, the guidelines encourage scientifically based therapeutic practices, the use of antimicrobials only when needed, and compliance with all existing regulatory requirements when antimicrobials are used.

Veterinarians also strongly encourage a veterinarian-client-patient relationship (VCPR) and veterinary consultation when implementing any treatment regimen. Dispensing or prescribing a prescription product (including antimicrobials) requires a VCPR. The VCPR is the basis for interaction among veterinarians, their clients, and their patients.

The veterinarian must have sufficient knowledge of the animal(s) to initiate at least a general or preliminary diagnosis of the medical condition of the animal(s). This means that the veterinarian has recently seen and is personally acquainted with the keeping and care of the animal(s) by virtue of an examination of the animal(s), or by medically appropriate and timely visits to the premises where the animal(s) are kept.

Veterinarians making treatment decisions must use sound clinical judgment and current medical information and must be in compliance with Federal, state, and local laws and regulations. The veterinarian must also include consideration of: judicious use principles; food safety and public health; and producer education as a part of the treatment plan. After considerations have been made for animal, human, and the environmental health impact, veterinary authorization is required prior to dispensing of the prescription product.

There are older antimicrobials that are available in medicated feeds that can be purchased without a veterinary prescription. These are called over-the-counter or OTC drugs. OTC drugs have been approved for marketing without a veterinary prescription and include adequate directions for use under which a lay person can use the drugs safely and effectively. To our knowledge, no new classes of antimicrobials have been approved by the FDA as an OTC drug since the 1980s. A newer category of drugs, the Veterinary Feed Directive (VFD) Drug category, was created by the Animal Drug Availability Act of 1996 to provide veterinary control for certain animal pharmaceuticals for use in feed that are not suitable for OTC status. Any animal feed bearing or containing a VFD drug shall be fed to animals only by or upon a lawful VFD issued by a licensed veterinarian in the course of the veterinarian's professional practice.

Veterinarians must balance the need for animal health and welfare with the need of human health. We are supportive of measures to mitigate risks to human health. Risk management measures can include any of the following: advisory committee review of an existing approval or application for a new animal drug approval; post-approval monitoring through systems such as the National Antimicrobial Resistance Monitoring System (NARMS); limitations on the extent of use (e.g., individual animals only for short duration of use); limited or broad extra-label use restrictions in some cases or all cases; antimicrobial use through prescription or VFD drugs only; and, finally, non-approval or withdrawal of a previously approved antimicrobial.

Although there are critical shortages in the veterinary workforce, particularly in food supply veterinary medicine and veterinary public health, veterinarians provide oversight and advice on the use of medications, including OTC antimicrobials, on a significant percentage of animal operations. *Feedlot '99* reports that all large operations and nearly all (96.5%) small operations used the services of a veterinarian. Large operations were more likely to use a veterinarian that made regular or routine visits or employ a full-time veterinarian on staff than small operations. Conversely, small operations were more likely to use a veterinarian when the need for one arose. Veterinarian recommendations had strong or moderate influence on selection of an antimicrobial for nearly 100% of feedlots. Laboratory test results influenced 58.8% of feedlots strongly or moderately. Veterinarian recommendations and laboratory test results were more likely to strongly influence selection of antimicrobials on large feedlots than small feedlots. Almost three out of four feedlots provided formal training in areas related to antimicrobial use.[24]

The *USDA Swine 2006* reports approximately seven of ten sites (69.1%) used a veterinarian during the previous year. A higher percentage of large and medium sites (88.1 and 85.0%, respectively) used a veterinarian during the previous year compared to small sites (60.8%). Nearly five of ten large sites (46.8%) used an on-staff veterinarian. A similar percentage of large sites (42.5%) used a local practi-

tioner. Overall, approximately half of the sites (49.5%) used a local veterinarian during the previous 12 months. About one of four sites (24.7%) was visited by a veterinarian five or more times. Producers used the services of a veterinarian for many purposes during the previous 12 months. A higher percentage of large sites used a veterinarian for blood testing, production record analysis, employee education, and quality assurance compared to small sites. For sites that had at least one veterinary visit during the previous 12 months, the highest percentage of sites used a veterinarian to treat individual pigs (63.8%) and to provide drugs or vaccines (62.6%). These are followed by vaccination consultation (48.6%), quality assurance (47.9%), blood testing (47.6%), nutritional consultation (19.8%), environmental consultation (19.0%), and employee training/education (18.0%).[25]

We believe that these numbers can be improved through the resolution of the critical shortage of the veterinary workforce by identifying resources and developing solutions in collaboration with key stakeholders to ensure that veterinary needs are met. Further studies should appropriately address the availability of veterinary services.

Data Collection and Review; Monitoring and Surveillance Systems

The AVMA has also continually advocated for improved, more robust monitoring and feedback systems for foodborne disease and antimicrobial resistance such as FoodNet and NARMS. It is unfortunate that reporting by NARMS is not timelier. For example, the most recent Centers for Disease Control and Prevention NARMS report that is available to the public is for 2004—4 years ago.

NARMS data, when combined with FoodNet data, demonstrates that the case rate of human infections with multi-drug resistant *Salmonella* spp. has decreased 49% between the NARMS baseline years of 1996–98 and 2004 (the most current, publicly available human data from NARMS). In addition, there has been a 65% reduction in the case rate of penta-resistant *Salmonella typhimurium* infections. The case rate for *Campylobacter* infections in humans that are resistant to ciprofloxacin have remained constant over that period.[26]

Additional important resistance trends[i] reported by NARMS[27] (Isolates from humans with clinical disease):

- *Salmonella* spp. (non-Typhi)—½ as likely to be resistant in 2004 as in 1996
  - ➢ a highly significant[j] improvement in susceptibility[k] (20% relative increase in susceptibility, from 66.2% in 1996 to 79.6% in 2004)
- *Salmonella typhimurium*—less than ½ as likely to be resistant in 2004 as in 1996
  - ➢ a highly significant[j] improvement in susceptibility[k] (60% relative increase in susceptibility[k] from 37.9% in 1996 to 60.7% in 2004)
- *Campylobacter*—only 0.03 times more likely to be resistant in 2004 compared to 1997
  - ➢ a marginally significant[j] increase in resistance (2% relative increase in resistance from 53% in 1997 to 54% in 2004)
  - ➢ However, *Campylobacter* was significantly less likely to be resistant in 2003 when compared to 1997; there was a significant[j] improvement in relative resistance (8.2% decrease from 53% in 1997 to 49% in 2003)
- *E. coli O157*—⅓ as likely to be resistant in 2004 compared to 1996
  - ➢ a highly significant[j] improvement in susceptibility[k] (10% relative increase in susceptibility)

In addition to trends of improved susceptibility, trends[i] regarding multi-drug resistance[l] also showed improvement:

- *Salmonella* spp. (non-Typhi)—nearly ½ as likely to be multi-drug resistant[l] in 2004 when compared to 1996
  - ➢ a highly significant[j] improvement (44% relative decrease) in multi-drug resistance[l] (decreased from 27.0% in 1996 to 15.0% in 2004)
- *Salmonella typhimurium*—nearly ½ as likely to be multi-drug resistant[l] in 2004 when compared to 1996
  - ➢ a highly significant[j] improvement (34% relative decrease) in multi-drug resistance[l] (decreased from 56.2% in 1996 to 37.2% in 2004)
- *Campylobacter*—slightly less likely to be multi-drug resistant[l] in 2004 when compared to 1997

- a marginally significant[j] improvement (10% relative decrease) in multi-drug resistance[1] (decreased from 15.7% in 1997 to 14.1% in 2004)
- However, when comparing 1997 to 2003, isolates were half as likely to be multi-drug resistant[1] and there was a highly significant[j] improvement (46% relative decrease) in multi-drug resistance[1] (decreased from 15.7% in 1997 to 8.5% in 2003)

Most foodborne infections do not require treatment with antimicrobials. Information shows that there is a decreasing trend of foodborne diseases, thereby decreasing the potential numbers of treatments.[28] The trends of increasing susceptibility/decreasing resistance mean more successful treatments when needed. This information indicates that there is not a public health crisis related to human pathogens that are thought to originate in animals.

We have also advocated for more research to support scientifically based therapeutic practices, such as epidemiological studies, that assess the effects of antimicrobial use. In addition, we advocate for increased resources for the FDA's Center for Veterinary Medicine (CVM) so the agency can adequately implement its regulatory authority.

We support the scientifically valid and meaningful collection and review of data for all uses of antimicrobials and other pharmaceuticals used in humans and animals. We urge that such data be collected in concert with other data necessary to explain or inform fluctuations in use, e.g., disease prevalence, regional data, populations of animals, etc. An example is the USDA program, Collaboration for Animal Health, Food Safety and Epidemiology, that is attempting to study the use of antimicrobials on farms correlated with disease occurrence, and the effects of antimicrobial use on antimicrobial resistance as measured both on the farm and during processing of the meat from the specific farm. Unfortunately, the program has not received adequate funding and is therefore not completed or ongoing.

The AVMA provided start-up funding for projects to create a nationally coordinated laboratory system to test for and report on resistance in animal pathogens and to create a decision support system to assist veterinarians when making antimicrobial use decisions. Unfortunately, while this project received follow-on funding by the FDA, it has not been sustained or completed.

The FDA Role and Actions

The FDA approves antimicrobials for four purposes:

1. Treatment of disease,
2. Prevention of disease,
3. Control of disease, and
4. Growth promotion or feed efficiency.

The first three uses are classified as therapeutic uses by the FDA, the AVMA, and Codex Alimentarius Commission (an organization of the World Health Organization and the Food and Agricultural Organization of the United Nations), and the fourth has also been shown to have health-promoting effects.

The FDA process for the evaluation of food animal antimicrobials is at least as stringent as, and often more stringent than, the approval process for human antimicrobials. In addition to the testing for efficacy and safety to the individual (human or animal) receiving the drug that is common to the human and animal drug approval process, each food animal antimicrobial undergoes an assessment for human and environmental safety as part of the review by the FDA. The FDA's Center for Veterinary Medicine uses a very strict safety assessment approval process that requires sponsors to submit data proving the antibiotic is safe for both humans and animals. This is a zero-risk procedure for human safety—benefits to animals are not weighed to offset risks to humans, but rather, drugs that possess risks beyond "a reasonable certainty of no harm" to human health are rejected.

Another safety measure was instituted in 2003 (Guidance for Industry #152, "Evaluating the Safety of Antimicrobial New Animal Drugs with Regard to Their Microbiological Effects on Bacteria of Human Health Concern,") that outlines a comprehensive, evidence-based approach to preventing the emergence and selection of antimicrobial-resistant bacteria that may adversely affect human health. The Guidance requires antimicrobial manufacturers to provide information to the FDA showing that a proposed animal drug will not harm public health. The current FDA risk assessment on a drug-by-drug basis provides a scientifically sound process to protect human health. In the event that a determination is made that human health is jeopardized, FDA will not approve the antimicrobial or may limit the use of the antimicrobial in order to mitigate the adverse effect.

We support GFI #152 while recognizing that it is very conservative in ensuring that preference is given to protection of human health without consideration of benefits to animal health and welfare. We also recognize that the ranking of antimicrobial drugs according to their importance in human medicine adds additional difficulty for approving animal drugs because the ranking design includes treatment of human diseases that are not in any manner associated with food animals. These diseases include gonorrhea, tuberculosis caused by *Mycobacterium tuberculosis*, neurosyphillis, meningitis, neutropenic fever, and Legionnaire's disease.

In addition, we also recognize that the design of GFI #152 makes it extremely difficult or impossible for FDA to approve antibiotics for use in feed or water for treatment of groups of animals if those antibiotics are also used in humans. This is because the extent-of-use limitations table assigns a high ranking for intended administration to flocks or herds of animals regardless if the duration of use is short (less than 6 days) or long (more than 21 days).

Since the mid-1990s, the FDA has coordinated the NARMS in cooperation with the CDC and the USDA. NARMS is a multi-agency program that includes monitoring for resistant bacteria in retail meats by the FDA, monitoring for resistant foodborne pathogens in humans by the CDC, and monitoring for resistant bacteria in animals on farms and animal products in slaughter and processing facilities by the USDA. NARMS has provided a great deal of useful information since 1996.

Therefore, the AVMA does not believe that the FDA needs new authority to regulate the human safety of animal drugs. Instead, the FDA needs additional resources to fulfill its existing mission.

The USDA Role and Actions

USDA Animal and Plant Health Inspection Services (APHIS) regulates veterinary biologics (vaccines, bacterins, antisera, diagnostic kits, and other products of biological origin) to ensure that the veterinary biologics available for the diagnosis, prevention, and treatment of animal diseases are pure, safe, potent, and effective. According to the USDA, which regulates vaccines and other biologics for animals, over 80 billion doses of approved vaccine were produced last year.[29]

USDA also has oversight over many national programs for animal health monitoring and surveillance. Veterinarians in both public and private practice actively participate in these national programs and AVMA has consistently advocated for funding to maintain and continually improve all of these programs.

National Programs

National Animal Health Surveillance System (NAHSS) (*http://www.aphis.usda.gov/vs/nahss/*)—NAHSS integrates animal health monitoring and surveillance activities conducted by many Federal and state government agencies into a comprehensive and coordinated system.

- *U.S. status for reportable diseases* (*http://www.aphis.usda.gov/vs/nahss/disease_status.htm*) as reported to the World Organization for Animal Health (OIE)
- *NAHSS Outlook* (*http://www.aphis.usda.gov/vs/ceah/ncahs/nsu/outlook/index.htm*)—Articles on U.S. animal health surveillance issues and developments.

National Animal Health Monitoring System (NAHMS) (*http://www.aphis.usda.gov/vs/ceah/ncahs/nahms/*)—National studies on animal health and health management practices of U.S. livestock and poultry.

National Animal Health Reporting System (NAHRS) (*http://www.aphis.usda.gov/vs/ceah/ncahs/nahrs/*)—Information on the presence of reportable animal diseases in the United States.

National Animal Identification System (NAIS) (*http://animalid.aphis.usda.gov/nais/index.shtml*)—This program coordinates and expands animal identification programs and practices in livestock and poultry.

National Animal Health Laboratory Network (NAHLN) (*http://www.aphis.usda.gov/vs/nahln/*)—This network of state animal health laboratories provides, among other things, laboratory data to meet epidemiological and disease reporting needs.

National Poultry Improvement Program (NPIP) (*http://www.aphis.usda.gov/animal_health/animal_dis_spec/poultry/index.shtml*)—National poultry health monitoring and surveillance.

National Aquaculture Program (NAP) (*http://www.aphis.usda.gov/animal_health/animal_dis_spec/aquaculture/index.shtml*)—National aquaculture health monitoring and surveillance.

U.S. Animal Health and Productivity Surveillance Inventory (*http://www.aphis.usda.gov/vs/nahss/inventory.htm*)—Search for surveillance programs, studies, and related information.

Impact Assessments on Animal Health Events (*http://www.aphis.usda.gov/vs/ceah/cei/taf/current_iw.htm*)—Reports on trade and production impact of animal disease occurrences in the U.S. and foreign countries.

Emerging Animal Disease Notices (*http://www.aphis.usda.gov/vs/ceah/cei/taf/emergingdiseasenotice_files/notices.htm*)—Information sheets on new and emerging animal diseases.

National Surveillance Unit (*http://www.aphis.usda.gov/vs/ceah/ncahs/nsu/index.htm*)—organization within APHIS tasked with coordinating activities related to animal health surveillance.[30]

FARAD Role and Actions

The Food Animal Residue Avoidance Databank (FARAD) program was developed by pharmacologists and toxicologists at the university of California, Davis, University of Florida, North Carolina State University and the University of Illinois as a complement to the USDA Food Safety and Inspection Service (FSIS) Residue Avoidance Program (RAP) to reduce the rate of animal residue violations through education, and residue mitigation rather than enforcement.

Whenever drugs are used to treat sick animals or prevent disease or when animals are exposed to chemicals in the environment, there is a potential that remnants of the drugs can be found in the meat or other animal products (often known as residues). The FDA establishes tolerances for drug residues to insure food safety. The FDA also establishes "withdrawal times" or "withholding periods" which are times after drug treatment when milk and eggs are not to be used for food, and during which animals are not to be slaughtered. This allows time for the animals to metabolize and eliminate the drugs that had been used for treatment.

FARAD personnel collate residue avoidance information from many sources. These data are then reviewed by residue experts to insure accuracy and consistency, and further analysis is done by FARAD personnel at North Carolina State University to explore novel ways in which the data may be used to prevent residue problems. FARAD maintains an up-to-date computerized compilation of:

- Current label information including withdrawal times on all drugs approved for use in food animals in the United States and on hundreds of products used in Canada, Europe and Australia.
- Official tolerances for drugs and pesticides in meat, milk, and eggs.
- Descriptions and sensitivities of rapid screening tests for detecting chemical residues in meat, milk, and eggs.
- Data on the fate of chemicals in food animals.

FARAD has been a chronically under-funded resource used by veterinarians, livestock producers, and state and Federal regulatory and extension specialists to ensure that drug, environmental, and pesticide contaminants do not end up in meat, milk, and eggs. AVMA has been a strong supporter of FARAD and has worked diligently with Congress on the 2008 Farm Bill to include authorization for a $2.5 million annual appropriation for the Food Animal Residue Avoidance Databank from 2008 through 2012.[31] However, if funding is not appropriated before September 30, 2008, this vitally important asset to ensure food safety may be forced to close its doors—permanently. Not only does FARAD ensure the safety of our meat, milk, and eggs, but the U.S. researchers from FARAD launched a global FARAD (gFARAD) initiative in response to an increasing need from foreign countries for residue data and requests made to FARAD to duplicate this successful program in other countries.

FARAD's efforts in establishing gFARAD have, to date, been financed entirely by local funds in participating countries, and in the U.S. by private donations and use of facilities made available by the three U.S. Universities housing the FARAD program. These exciting developments, which have attracted collaborations (but no funding) from the Food and Agricultural Organization (FAO) and Commonwealth Agricultural Bureaux International (CABI), have far reaching implications for the safety of foods imported into the United States as well as upon global food safety and the harmonization of standards and procedures. Since 2003, the United Kingdom, France, and Spain have initiated gFARAD sites. The Canadian gFARAD became fully operational with significant, recurring support from the government of Canada in 2003. In recent years, FARAD has provided training in gFARAD techniques and databases for China, as well as hosted the Taiwanese gFARAD consortium and South Korean delegate visits to FARAD.

The funding lapses of U.S. FARAD in 2007 and the continued lack of recurring support for U.S. FARAD places the entire program in jeopardy. In addition, the lack of continued funding and support compromises U.S. leadership in the continued development of a program initiated by our own researchers. In 2007, gFARAD may have been able to assist in mitigating the Chinese melamine crisis, however, it was a necessity for funds to be utilized to maintain essential personnel and no funds were available for U.S. FARAD to leverage the gFARAD consortium. Global food safety and security will continue to be a concern for decades to come. Support for a strong U.S. FARAD is a critical investment in continuing relationships with our trading partners and global information sharing between governments to mitigate agroterrorism concerns and ensure a safe, abundant food supply.

Risk Assessments/Human Health Impact

Antibiotics as a Tool To Prevent and Control Disease in Animals and Humans

The use of drugs in animals is fundamental to animal health and well-being. Antibiotics are needed for the relief of pain and suffering in animals. For food animals, drugs additionally contribute to the public health by helping keep animals healthy and thereby keeping bacteria from entering the food supply. The hypothesis, supported by scientific information, is that a reduction in the incidence of food animal illness will reduce bacterial contamination on meat, thereby reducing the risk of human illness.[32–39]

Several risk assessments have been performed that demonstrate a very low risk to human health from the use of antimicrobials in food animals, and some of the models predict an increased human health burden if the use is withdrawn. The unique farm-to-patient risk assessment performed by Hurd demonstrates that the use of tylosin and tilmicosin in food animals presents a very low risk of human treatment failure because of macrolide resistance, with an approximate annual probability of less than 1 in 10 million with *Campylobacter* infections and approximately 1 in 3 billion *E. faecium* infections.[40] Cox performed a quantitative human health risks and benefits assessment for virginiamycin and concluded that there would be a significant human health risk if virginiamycin use is withdrawn. There would be 6,660 excess cases per year of *campylobacteriosis*, which far outweighs the 0.27 per year reduction of cases of streptogramin-resistant and vancomycin-resistant *E. faecium* (VREF) resulting from the withdrawal.[41] Cox also performed a risk assessment regarding macrolide and fluoroquinolone use and concluded that withdrawal is estimated to cause significantly more illness days than it would prevent.[42] Cox also examined the impact of the use of penicillin-based drugs in food animals on penicillin/aminopenicillin resistant enterococcal infections and concluded that not more than 0.04 excess mortalities per year (under conservative assumptions) to 0.18 excess mortalities per year (under very conservative assumptions) might be prevented in the whole U.S. population by discontinuing current use of penicillin-based drugs in food animals. The true risk could be as low as zero.[43] This equates to one potentially preventable mortality in the U.S. population roughly every 7–25 years. Alban's risk assessment concluded that the risk associated with veterinary use of macrolides in Danish pigs resulted in a low risk to human health.[44]

Others have estimated that risk management strategies that focus on eliminating resistance are expected to create < 1% of the public health benefit of strategies that focus on reducing microbial loads in animals or on foods.[45] In another paper, the authors concluded, "We came to some surprising conclusions that were robust to many uncertainties. Among these were that antimicrobials that benefit animal health may benefit human health, while regulatory interventions that seek to reduce antimicrobial resistance in animals may unintentionally increase illness rates (and hence antimicrobial use and resistance rates) in humans. . . . In conclusion, our analysis suggests that the precautionary-principle approach to regulatory risk management may itself be too risky."[46]

Information derived from studies of organic or antibiotic-free production practices compared to traditional production practices is inconclusive, but there are indications that organically grown meat may have less-resistant organisms but greater prevalence and quantities of pathogens on the meat. Therefore, the greater risk of foodborne illness is somewhat offset by an increased likelihood of treatment success if treatment is necessary.[47–50]

The question of what the nature and magnitude of the risk to humans is can only be answered by performing systematic risk assessments. Such risk assessments must include identification of the endpoints of concern (e.g., increased illness or mortality caused by bacteria resistant to antibiotics used to treat the disease in humans), the nature of the treatment protocols in food animals, the potential routes of exposure, characterization of the population at risk, and the probability of occurrence.

Just as in humans, resistant bacteria can and do develop in animals. However, many of the important details regarding the transfer of that resistant bacteria, or even resistance genes—to the environment or humans—still remains in question. Simply because resistance exists in animals, it does not necessarily equate to a human health risk. First, the bacteria or its resistance determinants may not effectively transfer to humans through the food chain. Second, the pathogen may not colonize in humans to create a foodborne disease. Third, if a disease does occur, antimicrobial therapy may not be needed, and the disease resulting from the resistant bacteria is in effect no different than any other bacteria. In the majority of cases, treatment is not needed. Supportive therapy, such as fluids, is the only treatment that is needed for most *Salmonella, Campylobacter* and *E. coli* infections. In fact, antimicrobial therapy of *E. coli O157* infections is contra-indicated because such treatment makes the effects of the disease worse. Last, if antimicrobial therapy is needed, the pathogen may be susceptible to the drug of first choice. The Therapy Guidelines for Enteric Infections for non-typhi *Salmonella* are, "In uncomplicated infections antimicrobial therapy is not indicated because it has no effect on clinical illness and prolongs carriage and excretion of the organism. . . . Treatment recommended only for young infants (< or = 6 m) and immunocompromised individuals. Resistance is common. Agents that can be used include a fluoroquinolone or a third-generation cephalosporin such as ceftriaxone for 5–7 days. Ampicillin and co-trimoxazole can be used if the infecting organism remains susceptible."[51] NARMS[52] reports the following resistance percentages of non-typhi *Salmonella* to fluoroquinolone (ciprofloxacin)—0.2%, third-generation cephalosporin (ceftriaxone)—0.6%, ampicillin—12.0%, and co-trimoxazole (trimethoprim-sulfamethoxazole)—1.8%. These resistance levels do not indicate a public health crisis associated with foodborne *Salmonella*.

Conclusion

The American Veterinary Medical Association is committed to ensuring a safe and healthy abundant food supply. Among other things, our profession is dedicated to improving animal health, further safeguarding public health and food safety, and to maintaining the long-term effectiveness of antibiotics. The AVMA established a profession-wide initiative to create and implement judicious use guidelines for the therapeutic use of antimicrobials by veterinarians, and we launched an educational campaign to raise the awareness of the profession to the issue. Today, we continue to review and update those guidelines to reflect current practices and actively encourage compliance.

Foodborne illness and the spread of antibiotic resistance is a public and animal health concern. There is no question that the public demands a safe food supply and that the human medical profession is facing extreme challenges because of hospital- and community-acquired resistant human pathogens. The human medical problem with resistant nosocomial and community-acquired infections has increased the concern of possible development of resistant pathogens in animals that could be transferred to humans through the food supply or environment.

The AVMA shares the concerns of the human medical community, the public health community, governmental agencies, and the public regarding the potential problem of resistant foodborne pathogens developing in animals and then being transferred to humans. However, we emphasize the importance and primacy of using these medicines to prevent and treat diseases before they enter our food supply. Pre-emptive bans of veterinary antimicrobials before science-based studies and risk-based evaluations are performed would be detrimental to animal and human health. Inappropriate reactions to a perceived problem could have unknown and unintended consequences that negatively affect animal health and welfare, and ultimately, could create other public health risks, such as increased foodborne illness.

The AVMA does not believe that additional regulation of the uses of antimicrobials or other therapeutic agents in veterinary medicine and animal agriculture are necessary. Additional legislation and further regulation can put animal health and welfare and public health at risk. The FDA has adequate authority for oversight but lacks the resources to accomplish its many priorities.

An analysis that compared the regulatory strategy of the European Union to ban or restrict animal antibiotic uses with the United States' approach of continued prudent use to prevent and control animal infections, together with measures to improve food safety, has some pertinent conclusions. Among these, prudent use of animal antibiotics may actually improve human health, while bans on animal antibiotics, intended to be precautionary, inadvertently may harm human health.[53]

The AVMA supports the ongoing scientific efforts of monitoring and surveillance of foodborne disease and resistant foodborne pathogens; education; development of new antimicrobials, biologics, and other treatment options; and other research to

better define the challenges presented by animal agriculture. Increased data collection and surveillance of disease, as well as continued veterinary input (including the appropriate use of pre- and post-harvest interventions, and compliance with judicious use guidelines for veterinarians and producers), may be sufficient to protect human health against the current small risks without compromising the health of food animals.

We also support adequate funding for all efforts to improve animal health and food safety, including efforts to combat antimicrobial resistance. These efforts were high-priority tasks in the 2001 version of the *Public Health Action Plan to Combat Antimicrobial Resistance* that was created by a Federal Interagency Task Force on Antimicrobial Resistance. The Action Plan reflected a broad-based consensus of Federal agencies and stakeholders on actions needed to address antimicrobial resistance and provided a blueprint for specific, coordinated Federal actions that included the full spectrum of antimicrobial use: human medicine, veterinary medicine and animal agriculture. We are disappointed that the Action Plan was not adequately funded and prioritized by Congress. We are also concerned that the new Action Plan under development appears to not be as collaborative, broad-based or acceptable to the diverse community of stakeholders.

The AVMA is committed to working in concert with the CDC, FDA, and USDA to provide consumers—not only in the United States, but all over the world—with the safest food possible. The judicious use of antimicrobials is but one of the essential components of the process that enables animal agriculture to meet that demand. Other components include veterinary care, good management practices, biosecurity, proper nutrition and good husbandry.

Thank you for the opportunity to appear before you today and speak on behalf of our profession.

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[a] Epidemiology is a medical discipline that is the study of the causes, distribution, and control of disease in populations and serves as the foundation and *logic* of interventions made in the interest of *public health* and *preventive medicine.*

[b] Zoonotic diseases are diseases that can be transmitted from animals to humans. CDC estimates at least 60 percent of all human diseases and 75 percent of all newly emerging diseases are zoonotic.

[c] The multi-hurdle concept refers to the interaction of factors that affect microbial behavior in foods. Under some circumstances these effects are additive. Under others the implication is that synergistic interactions lead to a combined effect of greater magnitude than the sum of constraints applied individually.

[d] Population medicine is a medical discipline focusing on the concepts of public health and epidemiology. In veterinary medicine, these concepts are incorporated to make strategic decisions to advance animal and herd health.

[e] Friable is a term used in pathology to describe tissues that are brittle, fragile, and easily damaged.

[f] Domestically acquired clinical cases.

[g] The rationale for this change is unknown, but appears to introduce bias in reporting. DANMAP decided to use a preliminary European Committee on Antimicrobial Susceptibility Testing breakpoint instead of the previously used breakpoint established by the Clinical and Laboratory Standards Institute.

[h] Avoparcin has never been approved for use in the United States.

[i] Odds ratios were calculated based upon available data from NARMS assuming the reported isolates were representative of the bacterial population.

[j] "Marginally significant" indicates a p-value between 0.05 and 0.10; "significant" indicates a p-value between 0.01 and 0.05; "highly significant" indicates a p-value of less than 0.01.

[k] No resistance detected to any of five subclasses of antibiotics.

[l] Resistant to two or more antibiotic subclasses.

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The CHAIRMAN. Thank you.

Dr. Singer.

STATEMENT OF RANDALL S. SINGER, D.V.M., M.P.V.M, PH.D., ASSOCIATE PROFESSOR OF EPIDEMIOLOGY, DEPARTMENT OF VETERINARY AND BIOMEDICAL SCIENCES, COLLEGE OF VETERINARY MEDICINE, AND DIVISION OF ENVIRONMENTAL HEALTH, SCHOOL OF PUBLIC HEALTH, UNIVERSITY OF MINNESOTA, ST. PAUL, MN

Dr. SINGER. Mr. Chairman, Members of the Subcommittee, I would like to thank you for giving me the opportunity to discuss the role of antibiotics in animal agriculture. My name is Randall Singer. I am Associate Professor of infectious disease epidemiology at the University of Minnesota, both in the College of Veterinary Medicine and in the School of Public Health. I received both my veterinary degree and my Ph.D. in Epidemiology from the University of California at Davis.

To begin, let me restate the issue as I see it. What we are really discussing is risk, and specifically, the potential that the use of antibiotics in animal agriculture might result in more antibiotic-resistant bacteria that can subsequently infect humans and that then lead to either treatment failures or prolonged illness due to that resistance. Given this definition, I want to focus on two points. First, how should we assess and manage these potential risks, and second, are there actually any benefits to human health associated with the use of antibiotics in animals?

So how do we assess and manage these potential risks to human health? One approach is to employ the precautionary principle, which states that if there is a perceived potential for serious negative consequences, it is deemed better to avoid an action entirely rather than to suffer the potential consequences. The precautionary principle approach to managing antibiotic use in animal agriculture has only one real option: ban the antibiotic. But a more objective way to assess and manage the risks of animal antibiotic use is to develop scientifically based predictions using methods such as risk assessment. The FDA Center for Veterinary Medicine uses a science-based approach to decision-making, and in 1999 assessed the human health risk of an antibiotic in chickens. Based on the risk assessment model, FDA withdrew a very important antibiotic to poultry veterinarians. Now, even though this decision was science-based, I still had a major concern with the model. It did not evaluate any intervention strategies for reducing the risk to human

health. Withdrawing the antibiotic was the only option. For risk assessments to be useful, they should evaluate strategies for reducing risk. Many potential interventions could have been explored in the FDA model such as processing chickens from treated and untreated flocks separately or cooking the chicken meat from treated flocks prior to distribution.

This leads to my final point. Let me ask a rhetorical question. Let us say we start banning various antibiotics used in animal agriculture, either because of the precautionary principle or because our models do not evaluate risk reduction strategies. Will there be any unintended consequences from these actions? Stated another way, are there any potential benefits to human health associated with antibiotic use in animals? We have already heard about the animal health benefits. Research shows that animals that have experienced illness can lead to a meat product that has higher levels of harmful bacteria on it including *Salmonella* and *Campylobacter*. So healthier animals lead to a healthier food supply and therefore healthier people. Antibiotics improve animal health which under this argument leads to improved food safety and improved human health.

Recently I was part of a team that developed a mathematical model that related animal health to human health and, simultaneously, evaluated the human health risks and benefits associated with the use of antibiotics in animal agriculture. The model showed that under certain circumstances, the potential benefits to human health of antibiotic use in animals far outweigh the potential risks.

So in conclusion, Mr. Chairman, Members of the Subcommittee, I thank you again for the opportunity to speak today. Antibiotics are an integral component of animal health. All responsible uses of antibiotics improve animal health and these improvements can substantially improve human health. All uses of antibiotics also pose a risk mainly associated with increases in antibiotic resistance. Simply removing antibiotics from use in animal agriculture may help reduce some of the antibiotic resistance circulating today but it might also have severe unintended consequences. The key is to identify strategies that maximize the benefits and minimize the risks. The best way to manage antibiotic uses in animal agriculture is through sound, rational, science-based policy. Thank you.

[The prepared statement of Dr. Singer follows:]

PREPARED STATEMENT OF RANDALL S. SINGER, D.V.M., M.P.V.M, PH.D., ASSOCIATE PROFESSOR OF EPIDEMIOLOGY, DEPARTMENT OF VETERINARY AND BIOMEDICAL SCIENCES, COLLEGE OF VETERINARY MEDICINE, AND DIVISION OF ENVIRONMENTAL HEALTH, SCHOOL OF PUBLIC HEALTH, UNIVERSITY OF MINNESOTA, ST. PAUL, MN

Mr. Chairman and Members of the Subcommittee:

Thank you for providing me with the opportunity to discuss the role of antibiotics in animal agriculture and the potential risks and benefits to animal and public health associated with these antibiotic uses. I am an Associate Professor of Infectious Disease Epidemiology and Ecology at the University of Minnesota. I have a dual appointment at the university, both in the College of Veterinary Medicine and the School of Public Health. I am a veterinarian by training with a degree from the University of California at Davis. Following my veterinary degree, I obtained a Ph.D. in epidemiology from the University of California at Davis. I have worked as a professor of epidemiology since 1999, first at the University of Illinois, Urbana-Champaign and now at the University of Minnesota. I have spent the past 10 years engaged in research, teaching and service activities related to antibiotic use and an-

tibiotic resistance in human and animal health. I will focus my discussion on four questions that I think are critically important:

1. What are antibiotics and how are they used in animal agriculture?
2. What is antibiotic resistance and how is it selected?
3. How do we assess and manage the risks of antibiotic use in animal agriculture?
4. Are there benefits to antibiotic use in animal agriculture?

What are antibiotics and how are they used in animal agriculture?

Although many people assume that antibiotics are human-made compounds, antibiotics are actually small molecules that are naturally produced by microorganisms in the environment. Humans have created synthetic analogs to these naturally occurring compounds to improve their efficacy. The function of these molecules in nature is still not entirely understood. Because bacteria in the environment have been exposed to these antibiotics for eons, they have developed mechanisms for survival in the presence of these compounds. These mechanisms are what we refer to as antibiotic resistance, or a way for the bacterium to resist the action of the antibiotic. The presence of naturally produced antibiotics in the environment is rarely considered as a contributor to the amount of resistance that is found in bacteria around the world, and yet it is this environmental pool of resistance, lately termed the resistome [5], that is the basis for the resistance observed today. Antibiotic resistant microorganisms can be found in areas with little to no obvious human influence or impact, emphasizing that there is a large background reservoir of resistance that exists in the natural world.

Antibiotics are used in animal agriculture in four major ways: disease treatment, disease control, disease prevention, and growth promotion. Briefly, disease treatment refers to the use of the antibiotic in an ill animal. Disease control refers to the use of the antibiotic in a population of animals during a time of illness. Not all of the animals receiving the antibiotic are necessarily ill at the time of antibiotic administration. Disease prevention refers to the use of the antibiotic in an animal or in a population of animals at a time when it is known that the animals are susceptible to disease. Finally, growth promotion refers to the use of the antibiotic in a low-dose fashion to improve the weight gain and feed efficiency of the animal. All four of these uses result in an improved health of the animal receiving the antibiotic, and as will be discussed later, can thereby improve the safety of the food supply.

Even though all four of these uses can improve the health of the animal, there has still been confusion about them. One area of confusion is related to the amount of antibiotic that is administered. Because disease control, disease prevention and growth promotion can use smaller amounts of the antibiotic than is given to the sick animal during disease treatment, these uses have sometimes been labeled as "subtherapeutic" or "nontherapeutic". Given that animals receiving an antibiotic in this manner are healthier than if they had not received the antibiotic, these terms are misnomers. Another area of confusion is related to the route of administration. Uses of antibiotics that are "in-feed" are often equated with growth promotion uses and are assumed to be long-term low-dose regimens of antibiotic administration for the sole purpose of improving weight gain. In fact, all of these uses can be applied via the feed or the water because the only realistic way to give antibiotic to populations of animals, such as a flock of chickens, is through the feed or the water. Antibiotics used for disease treatment and disease control are often given via the drinking water because sick animals may stop eating but often continue to consume water.

What is antibiotic resistance and how does it develop?

Antibiotic resistance refers to the ability of a microorganism to survive the effects of an antibiotic. As stated previously, antibiotics are naturally produced by environmental microorganisms, and as a result, many microorganisms possess mechanisms that enable them to resist the action of the antibiotic. Some microorganisms are intrinsically resistant to the action of certain antibiotics, meaning that the antibiotic has no function on the organism. This type of resistance can not be spread and is not of concern when considering antibiotic uses. Instead, we are typically concerned about antibiotic resistance that is acquired by the microorganism. The two major mechanisms by which the microorganism can acquire resistance are through random changes in the genetic makeup, known as mutation, or through the sharing of genetic material with other microorganisms.

When an antibiotic is applied to a population of bacteria, those bacteria that are not intrinsically resistant to its action must find a way to survive. The antibiotic will either kill or suppress the bacteria that are susceptible to the antibiotic. For

this reason, the antibiotic is said to select for resistant bacteria because only the resistant ones can withstand the pressure imposed by the antibiotic. During the course of the antibiotic, the rates at which bacteria can acquire resistance might increase, and consequently, the use of the antibiotic may pose a risk to human and animal health through the selection of a more resistant bacterial population. The problem, stated simply, is how do we ensure that the human and animal health benefits of antibiotic use in animal agriculture outweigh the risks?

How do we assess and manage the risks of antibiotic use?

There are two primary approaches for assessing and managing the potential risks associated with antibiotic use in animal agriculture. One approach is to employ the precautionary principle. In this argument, the precise public health risks associated with animal antibiotic use might not be known. Because there is a perceived potential for serious negative consequences, it is deemed better to avoid the action entirely rather than to suffer the potential consequences. Europe has used this principle to withdraw certain antibiotic uses from animal agriculture [1]. One reason why this approach is often relied upon, especially in the case of antibiotic use and resistance, is the belief that antibiotic use is negatively impacting human health. It is extremely difficult to design, implement and analyze the decisive study that will prove or disprove this theory. Caution would dictate that by the time such a study is complete, any negative effects associated with continued antibiotic use might be irreversible. Consequently, the precautionary principle approach to managing antibiotic use in animal agriculture has only one real option: withdraw the antibiotic use that might result in a negative human health consequence. Unfortunately, there can be negative unintended consequences associated with a precautionary measure [4] as will be discussed later.

A more objective way to evaluate the potential consequences of antibiotic use in livestock and poultry is to develop scientifically-based predictions, and through these models, evaluate interventions that reduce potential human and animal health risks associated with certain antibiotic uses in animal agriculture. This approach includes the methodology known as risk assessment. For example, in 2003 the FDA Center for Veterinary Medicine (FDA–CVM), which uses a scientific approach to regulatory decisions, issued a Guidance for Industry document #152 that described a qualitative risk assessment process that is utilized in the approval of all applications for new animal antibiotics and the reassessment of existing animal antibiotics. I was recently part of a team that conducted a risk assessment following the document #152 approach. Specifically, we assessed the risk that the agricultural use of a family of antibiotics known as macrolide antibiotics poses to human health [7]. The concern is that macrolide antibiotics are also used in human medicine, and therefore, the use of macrolide antibiotics in animal agriculture could compromise the efficacy of these antibiotics in human medicine and potentially increase the number of macrolide-resistant bacterial infections in people. We developed a semi-quantitative risk assessment model following the format of document #152. We found that all macrolide antibiotic uses in animal agriculture in the U.S. posed a very low risk to human health. The highest risk was associated with macrolide-resistant *Campylobacter* infections acquired from poultry, but this risk was still estimated to be less than 1 in 10 million and would thus meet the standard of "reasonable certainty of no harm" employed by FDA–CVM.

Currently, the international body Codex Alimentarius has formed a Task Force to delineate international standards for the conduct of risk assessment and risk management in the context of antibiotic use in animal agriculture. The main purposes of the Codex Alimentarius are "protecting health of the consumers and ensuring fair trade practices in the food trade, and promoting coordination of all food standards work undertaken by international governmental and non-governmental organizations." Once this Task Force has completed its objective, there will be a set of accepted, scientifically-based approaches for determining if antibiotic uses in animal agriculture pose a risk to human health, and if so, how these risks should be managed. Perhaps most important, the final document of this Task Force will outline procedures for assessing whether interventions that are used to mitigate risk have succeeded or whether they have been counter-productive.

Unfortunately, most risk assessments conducted to date in antibiotic resistance that have been used for regulatory purposes have not included specific interventions that can be implemented to reduce the human and animal health risks. Instead, the assessments seem to have been designed for the sole purpose of making the dichotomous decision of whether or not to withdraw an antibiotic from use. For risk assessments to be useful, they must include evaluations of potential interventions for reducing the risks to human and animal health. In the U.S. FDA–CVM risk assessment of fluoroquinolone use in chickens [2], the model only estimated the potential

human health impact of this antibiotic use and did not evaluate ways for minimizing the risk associated with fluoroquinolone use in poultry. For example, the model could have examined the possibility of processing chickens from treated poultry flocks separately from chickens from untreated flocks as a potential risk reduction strategy. This separated processing could help reduce the chance of cross-contamination of chicken meat from non-treated poultry flocks with the bacteria from treated flocks. The model could have examined a potential intervention in which farms that have received fluoroquinolones are cleaned in a more intensive manner than the normal cleaning, and all litter from these flocks is sterilized. Finally, the model could have assessed an intervention in which flocks that have been treated with antibiotics would have to wait for a longer period of time before processing. This type of approach would resemble the mandatory withdrawal times associated with antibiotic residues. Guidelines could then be developed to determine when specific antibiotic uses should be ceased in flocks before they go to processing in order to reduce the amount of antibiotic resistant bacteria in the birds. Consideration of such risk mitigation interventions rather than complete withdrawal of these drugs would have been very important to poultry veterinarians. Prescription drugs like the fluoroquinolones are a valuable option to control fatal respiratory disease in chickens since other effective therapeutic alternatives are not available.

These types of interventions might sound labor-intensive and costly. They are, and that is the point. Under certain circumstances, it might be cost-effective and ethical for a veterinarian to use a powerful antibiotic to control a severe disease in the herd or flock, but this use would then have major repercussions on how the herd or flock as well as the farm are subsequently managed. Producers might not opt for this intensive measure, but at least they would have a choice that is accepted as scientifically-sound for reducing both the human and animal health risks associated with the antibiotic use on their farm. As we begin to gain a better understanding of the ecology of resistance and its relation to animal and human health, we will need these scientifically-based strategies for minimizing the impacts of antibiotic use on animal, human and environmental health.

Are there benefits to antibiotic use in animals?

The models that we build to assess the potential risks of antibiotic use in livestock and poultry must begin to take a more holistic view of health into consideration. Specifically, these models need to include the potential risks and the potential benefits associated with antibiotic use. Phrased another way, are there potential unintended consequences of removing antibiotics from use in food animals? Recent models have predicted that there might be significant negative human health consequences associated with the removal of certain antibiotics from animal production. This is an instance in which the precautionary principle would lead to an action of banning antibiotics in animal agriculture, but that action could have even worse unintended consequences. It might not be intuitive, however, how an antibiotic that is used in animal agriculture can actually benefit human health.

The health status of animals that are processed for meat can potentially affect food safety in two major ways. First, animals that are less healthy may shed higher levels of harmful bacteria, such as *Salmonella* and *Campylobacter*. Second, groups of animals that have experienced illness, either clinically or subclinically, can be smaller in size and more variable in size. During processing, these factors can contribute to an increased likelihood of the gastrointestinal tract being ruptured, and this processing error can lead to increased contamination and cross-contamination of the meat and thus increase the risk of human foodborne illness. Reducing animal illness likely plays a critical role in reducing the chances of contamination during processing.

I recently was part of a team that developed a mathematical model that relates animal illness to human illness [8]. In our model, there was a large increase in human illness associated with small increases in animal illness, suggesting that agricultural management strategies may have significant impacts on human health. Antibiotics administered in feed at low doses over several weeks raise concern about their potential to increase rates of antibiotic resistance, posing a risk to human health. However, these applications also improve animal health and promote size uniformity among animals in the herd or flock. Antibiotic uses in animals can therefore have potential human health risks and benefits. Our model was able to evaluate simultaneously the human health risks and benefits associated with antibiotic use in animal agriculture. Specifically, the model addressed the relationship between the negative human health impact of increased antibiotic resistance and the positive human health impact of fewer foodborne infections, both of which are due to the use of the antibiotic in animal agriculture. The model showed that the potential benefits to human health associated with the use of antibiotics in animal agri-

culture can far outweigh the potential risks. This finding has now been validated by additional studies [3] [6].

In summary, Mr. Chairman and Members of the Subcommittee, thank you again for the opportunity to discuss the role of antibiotics in animal agriculture. Antibiotics are an integral component of animal health. All uses of antibiotics improve animal health, and these improvements in animal health can substantially improve human health. All uses of antibiotics also pose a risk, mainly associated with increases in antibiotic resistance. The key is to assess the ability of interventions to maximize the benefits and minimize the risks associated with the agricultural use of antibiotics. Simply removing antibiotics from use in animal agriculture may help reduce some of the antibiotic resistance circulating today, but it might also have severe unintended consequences. The best way to manage antibiotic uses in animal agriculture is through sound, rational, science-based policy.

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The CHAIRMAN. Well, thank you very much. You may have heard us pose this question to an earlier group. Give us some idea of what goes into developing an antibiotic in time, cost to bring it to market. Can you give us some feeling for what is involved in all that?

Dr. CARNEVALE. Yes, thank you, Mr. Chairman, for that question. It is a very rigorous process. I think Dr. Dunham explained that the drug has to be shown to be safe and effective to the animal as well as manufactured properly. There is an environmental impact component. Clearly, the human food safety from residues and antibiotics presents a significant amount of research. We have estimated at the Animal Health Institute that for a food-producing animal, it can take 7 to 10 years to develop a product from essentially discovery to final approval, and it costs upwards of $100 million. However, there are some examples of products that have actually cost more than that and taken many more years than 7 to 10 years. But that would be an average. So it is a fairly rigorous time and costly process to get a new animal drug through the process and that would include antibiotics. Antibiotics have a particularly difficult time getting through the system today because of this resistance issue. FDA takes a lot of time and care and data requirements to prove that these antibiotics aren't dangerous to human health, so that adds another several years and probably several million more dollars to the development of those. It is very, very

difficult to get a new compound on the market today because of that.

The CHAIRMAN. Thank you very much. Anybody else?

Mr. Hayes.

Mr. HAYES. Again, very thorough. My only question would be from your perspective as scientists and doctors, is there anything that FDA or anyone in the community that is monitoring what you all are doing, any other testing from your perspective that could be done that would fill in any blank that I haven't seen today, but that in somebody's mind might exist?

Dr. HOANG. Currently the only system that we have for monitoring outbreaks of foodborne illness is FoodNet, and that is the only system that has both a component that monitors the bacteria as well as the epidemiological study behind it. NARMS is a separate system that monitors antimicrobial resistance. However, there really is no link between those two systems to accurately indicate the incidence of foodborne illness of resistant pathogens in humans, and also have it be traced back to consumption of animal products. Thank you, sir.

Mr. HAYES. I guess another thing, and as far as domestic is concerned, the evidence that all of you presented is, in my opinion, irrefutable. But, Mr. Chairman, as you know, we continue to run into artificial trade barriers based around some of these issues too. So, I guess my question was directed at that part of our agricultural economy as well. Any other comments from Dr. Carnevale, Dr. Singer?

Dr. SINGER. In relation to the global food system, I mean, this is part of what the Codex Alimentarius, the task force on antimicrobial resistance, is currently working on. How do we come up with international standards for looking at risks, for conducting risk assessments, and most importantly, for implementing risk management strategies. How do nations and regions interact in this case, and so that pilot process is underway. It is a 4 year process, the specific task force.

Mr. HAYES. I have no further questions, Mr. Chairman. Thank you.

The CHAIRMAN. Thank you, Mr. Hayes. Because of your expertise and background, I wonder if any or all of you would care to make a comment about your analysis of the situation that happened in Denmark and the impact. What would be your analysis of that whole thing that happened there?

Dr. HOANG. Based upon our analysis of the experience in Denmark, we found that there has been no significant human health benefit as a result of that ban. However, we have seen that there has been a decrease in animal welfare and animal health and the increase of therapeutic use of antimicrobials. Unfortunately, some of the therapeutic antimicrobials are in the same classes as human medications, which poses more of a risk to human health. Thank you, sir.

Dr. CARNEVALE. Yes, I would certainly support what Christine said. I think the situation in Denmark was a clear example of the government wanting to take an action based on the idea that there was a perceived risk to human health. What they found is that there was a greater risk to animal health by their action. It was

very interesting to me that a couple of years after that Denmark ban on growth promoters, a Danish official at a meeting here in the United States actually admitted that they did not realize that these growth-promoting antibiotics added to feed were suppressing disease. They thought they were strictly promoting growth, but in fact they found out when they took them out of feed that they had a lot of nursery pig diarrhea and a significant number of nursery pig deaths in the first several years of that program. So I think that that program has been, although they would not admit it, a real failure because it simply increased cost to their pork industry. And as Christine said, there has been no indication that it has improved human health at all.

The CHAIRMAN. Dr. Singer?

Dr. SINGER. While we don't have the perfect example here in the United States, we can use organic meat production and antibiotic-free meat production here in the United States for some indication of what we might expect. Research studies do show that the antibiotic-free and organic meat production, the meat produced in those systems can have higher levels of pathogenic bacteria such as *Salmonella* and *Campylobacter* on it than conventionally reared meat. It also might have less antibiotic resistance. So the key here again is a risk-benefit type of analysis. It is not good enough for us to say that the resistance is the only issue we should be considering. We need to weigh both the risks and the benefits.

The CHAIRMAN. Thank you very much.

Mr. Hayes, do you have any closing remarks?

Mr. HAYES. I appreciate the participation of the witnesses and the willingness of the Chairman and the staff to put this together. I think it is very positive.

The CHAIRMAN. I think it has been very productive today. It has certainly been an educational process. Just since we have been here this morning, Mr. Hayes, I have gotten word that even with the statements made by our first panel, and then the concerns by the second panel that the FARAD program that you and I wrote a letter about is not a priority at USDA, so we may have to pursue that a little more. So I think that probably could be the reason why we haven't received a response to our July letter.

But anyway, I want to thank everyone who has joined us today. I hope everyone found the testimony as informative as I have. We have had the opportunity to hear from our regulatory agencies, actual producers on the ground and numerous veterinarians and researchers. I hope we leave here today with resolve to continue to move forward and ensure that consumers in the United States have the safest, most plentiful and most affordable food supply in the world. I believe that is the case because of the work that has gone into it. It is clear from today's hearing that antimicrobials play an extremely important role in producing healthy animals and even a healthier food supply.

With that, under the rules of the Committee, the record of today's hearing will remain open for 10 days to receive additional material and supplementary written responses from witnesses to any question posed by a Member of the panel.

This hearing of the Subcommittee of Livestock, Dairy, and Poultry is adjourned. Thank you.

[Whereupon, at 12:20 p.m., the Subcommittee was adjourned.]
[Material submitted for inclusion in the record follows:]

SUBMITTED STATEMENT OF HON. LOUISE M. SLAUGHTER, A REPRESENTATIVE IN CONGRESS FROM NEW YORK

Thank you Chairman Boswell and Ranking Member Hayes for allowing me to submit testimony on this important public health topic. With antibiotic resistance growing at an alarming rate, it is becoming harder and more expensive to treat common bacterial infections. The problem has become so significant that it has been labeled a "top concern" by the Centers for Disease Control and Prevention (CDC), and the World Health Organization has called it a "crisis." Therefore, it is critically important that we act now to protect our current stocks of antibiotics.

Two million Americans acquire bacterial infections during their hospital stay every year, and 70 percent of their infections will be resistant to the drugs commonly used to treat them. As a result, every day 38 patients in our hospitals will die of those infections.

Sadly, children and infants are particularly susceptible to infections caused by antibiotic resistant bacteria. For example, *Salmonella* causes 1.4 million illnesses every year. Over ⅓ of all diagnoses occur in children under the age of 10. Infants under the age of one are ten times more likely than the general population to acquire a *Salmonella* infection. In 1995, 19 percent of *Salmonella* strains were found to be multi-drug resistant. That means that our children are left to undergo multiple treatments for otherwise simple infections because we have allowed traditional treatments to become ineffective.

And the cost to our already strained health care system is astronomical. In fact, resistant bacterial infections increase health care costs by $4 billion to $5 billion each year.

We cannot in good conscience stand by while our life-saving antibiotics become obsolete. While overuse of antibiotics among humans is certainly a major cause for increasing resistance, there is evidence that the widespread nontherapeutic use of antibiotics in animal feed is another cause of heightened resistance. A *National Academy of Sciences* report states that, "a decrease in antimicrobial use in human medicine alone will have little effect on the current situation. Substantial efforts must be made to decrease inappropriate overuse in animals and agriculture as well."

Currently, seven classes of antibiotics certified by the Food and Drug Administration (FDA) as "highly" or "critically" important in human medicine are used in agriculture as animal feed additives. Among them are penicillin, tetracyclines, macrolides, lincosamides, streptogramins, aminoglycosides, and sulfonamides. These classes of antibiotics are among the most critically important in our arsenal of defense against potentially fatal human diseases.

Penincillins, for example, are used to treat infections ranging from strep throat to meningitis. Macrolides and Sulfonamides are used to prevent secondary infections in patients with AIDS and to treat pneumonia in HIV-infected patients. Tetracyclines are used to treat to people potentially exposed to anthrax.

Despite their importance in human medicine, these drugs are added to animal feed as growth promotants and for routine disease prevention. Approximately 70 percent of antibiotics and related drugs produced in the U.S. are given to cattle, pigs, and chicken to promote growth and to compensate for crowded, unsanitary, stressful conditions. The nontherapeutic use of antibiotics in poultry skyrocketed from 2 million pounds in 1985 to 10.5 million pounds in the late 1990s.

This kind of habitual, nontherapuetic use of antibiotics has been conclusively linked to a growing number of incidents of antimicrobial-resistant infections in humans, and may be contaminating ground water with resistant bacteria in rural areas.

Resistant bacteria can be transferred from animals to humans in several ways. Antibiotic resistant bacteria can be found in the meat and poultry that we purchase in the grocery store. In fact, a *New England Journal of Medicine* study conducted in Washington, D.C. found that 20 percent of the meat sampled was contaminated with *Salmonella* and 84 percent of those bacteria were resistant to antibiotics used in human medicine and animal agriculture. Bacteria can also be transferred from animals to humans via workers in the livestock industry who handle animals, feed, and manure. Farmers may then transfer the bacteria on to their family. A third method is via the environment. Nearly 2 trillion pounds of manure generated in the U.S. annually contaminate our groundwater, surface water, and soil. Because this manure contains resistant bacteria, the resistant bacteria can then be passed on to humans that come in contact with the water sources or soil.

And the problem has been well documented.

A 2002 analysis of more than 500 scientific articles and published in the journal *Clinical Infectious Diseases* found that "many lines of evidence link antimicrobial resistant human infections to foodborne pathogens of animal origin."

The Institute of Medicine's 2003 report on *Microbial Threats to Health* concluded "Clearly, a decrease in the inappropriate use of antimicrobials in human medicine alone is not enough. Substantial efforts must be made to decrease inappropriate overuse in animals and agriculture as well."

As recently as last November, in *FDA Week*, the article below entitled "Study Fuels Call for FDA to Phase Out Antibiotics In Animal Feed" highlighted how methicillin-resistant Staphylococcus aureus (MRSA) is prevalent in Canadian pig farms and pig farmers.

Study Fuels Call for FDA To Phase Out Antibiotics in Animal Feed

9 November 2007
FDA Week
Vol. 13, No. 45

A new study has found that methicillin-resistant Staphylococcus aureus (MRSA) is prevalent in Canadian pig farms and pig farmers, pointing to animals as a source of the deadly bacteria and raising new questions about the use of human antibiotics in animal feed. Health advocates are using the study's results to drum up support for the Preservation of Antibiotics for Medical Treatment Act, which would phase out the use of antibiotics important in human medicine as animal feed additives within 2 years.

The Veterinary Microbiology study (Khanna *et al.* 2007) is the first to show that North American pig farms and farmers have carried MRSA. The study looked for MRSA in 285 pigs in 20 Ontario farms. It found MRSA at 45 percent of farms (9 of 20) and in nearly one in four pigs (71 of 285). One in five pig farmers studied (5 of 25) also were found to carry MRSA, a much higher rate than in the general North American population, according to the study. The strains of MRSA bacteria found in Ontario pigs and pig farmers included a strain common to human MRSA infections in Canada.

The study stated MRSA colonization in pigs was first reported in the Netherlands and has also been found in pigs in France, Denmark, and Singapore. In all of these countries, farm and pig workers were found to have been infected with MRSA by pigs.

The study was published in October.

Also in October, the *Journal of the American Medical Association* (Klevens *et al.* 2007) published a study that estimated almost 100,000 MRSA infections in 2005, and nearly 19,000 deaths in the United States. In comparison, HIV/AIDS killed 17,000 people that year, according to the study.

A pending bill, The Preservation of Antibiotics for Medical Treatment Act, would phase out the use of antibiotics as animal feed additives within 2 years. The Senate version of the legislation is sponsored by Health Committee Chair Edward Kennedy (D–MA) and Sens. Olympia Snowe (R–ME), Susan Collins (R–ME), Sherrod Brown (D–OH) and Jack Reed (D–RI). The House version is sponsored by Rep. Louise Slaughter (D–NY), the only microbiologist in Congress, and 34 other House Members.

The American Medical Association, the Infectious Diseases Society of America and the American Academy of Pediatrics are among the more than 350 advocacy groups nationwide that have endorsed this bill.

Until recently, scientists believed MRSA was an infection occurring mainly in hospitals. The JAMA study found that even healthy people are developing MRSA infections. The Veterinary Microbiology study points to pig farms as a possible source of these resistant infections, as have earlier European studies.

A recent study in the Netherlands found MRSA transmission among pigs, pig farmers and their families.

Members of the Keep Antibiotics Working coalition, including medical, agriculture and environmental experts, are calling for Congress to compel FDA to study whether the use of human antibiotics in animal agriculture is contributing to the reported surge in MRSA infections and deaths in the United States.

"Identifying and controlling community sources of MRSA is a public health priority of the first order," said Richard Wood, Executive Director of Food Animal Concerns Trust and Steering Committee Chair of Keep Antibiotics Working. "Are livestock farmers and farms in the United States also sources? We don't know for sure, because the U.S. Government is not systematically testing U.S. livestock for MRSA."

> "Last summer, when we raised the MRSA issue, the FDA told us that it had no plans to sample U.S. livestock to see if they carry MRSA," said David Wallinga, Director of the Institute for Agriculture and Trade Policy's Food and Health Program. "Given the latest science that hog farms may generate MRSA, we need Congress to give FDA and other relevant agencies the necessary funding and a sense of urgency. Sampling needs to be done as soon as possible."—Inside OSHA.

As the impact of MRSA continues to unfold, there is little doubt that antibiotic resistant diseases are a growing public health menace demanding a high priority response. Despite increased attention to the issue, the response has been inadequate. Part of the problem has been the FDA's failure to adequately address the effect of the misuse of animal antibiotics on the efficacy of human drugs.

Although the FDA could withdraw its approval for these antibiotics, its record of reviewing currently approved drugs under existing procedures indicate that it would take nearly a century to get these medically important antibiotics out of the feed given to food producing animals. In October 2000, for example, the FDA began consideration of a proposal to withdraw its approval for the therapeutic use of fluoroquinolones in poultry. The review, and eventual withdraw of approval, took 5 years to complete. Under its regulations, the FDA must review each class of antibiotics separately.

In 2003, the Center for Veterinary Medicine at FDA released Guidance 152 which provides safety guidelines on how antibiotics should be used in agriculture. However, the guidance never established a timeframe for FDA to reevaluate existing antibiotics used in animal feed and so has rendered these recommendations useless.

During discussions involving the now-enacted farm bill, I supported language which would have provided the farm industry with sound, scientific information on production practices that could have helped them reduce their dependence on antibiotics and meet the growing consumer demand for meat produced without these drugs. The ability to grow food animals with fewer antibiotics would have also given U.S. exporters an advantage in the international marketplace. This language would have also increased research on the movement of antibiotics and antibiotic-resistant traits in water to aid public health professionals in developing new tools and methods for reducing the spread of resistant diseases. Disappointingly, however, industry successfully lobbied to strip this language out of the farm bill.

I am also the sponsor of H.R. 962, the Preservation of Antibiotics for Medical Treatment Act (PAMTA). This bill requires three actions to accomplish the goal of reducing antibiotic resistance in humans. PAMTA would phase out the use of the seven classes of medically significant antibiotics that are currently approved for nontherapeutic use in animal agriculture. Because the bill defines nontherapeutic use as "in the absence of any clinical sign of disease in the animal for growth promotion, feed efficiency, weight gain, routine disease prevention, or other routine purpose," this bill would in no way infringe upon the use of these drugs to treat a sick animal.

In addition, PAMTA provides that if an antibiotic that is now used only in animals also becomes potentially important in human medicine, the drug would be automatically restricted from nontherapeutic use in agricultural animals unless FDA determines that such use will not contribute to development of resistance affecting humans.

Last, to assist public health officials in tracking implementation of the phase out of antibiotics in animal feed, PAMTA requires producers of agricultural antibiotics to report the quantity of drugs they sell, information on the claimed purpose, and the dosage form of those drugs.

The fundamental solution to the problem of antibiotic resistance is to reduce unnecessary use. Then when antibiotics are required, use them prudently. Most antibiotics in agriculture are used for growth promotion and routine disease prevention—uses that can be reduced, if not eliminated, in properly designed animal production systems. Drastic reduction of antibiotics uses in animal agriculture, as called for in PAMTA, will lessen the encouragement of resistant disease and prolong the longevity of vital human drugs.

As a mother, grandmother, and microbiologist, I cannot stress the urgency of this problem enough. When we go to the grocery store to pick up dinner, we should be able to buy our food without worrying that eating it will expose our family to potentially deadly bacteria that will no longer respond to our medial treatments. Unless we act now, we will unwittingly permit animals to serve as incubators for resistant bacteria.

It is time for Congress to stand with scientists, the World Health Organization, the American Medical Association, and the National Academy of Sciences and do

something to address the spread of resistant bacteria. We cannot afford for our medicines to become obsolete.

Thank you.

SUBMITTED STATEMENT OF KEEP ANTIBIOTICS WORKING

Keep Antibiotics Working appreciates this opportunity to provide the Committee information regarding the relation between antibiotics use in livestock and the growing problem of antibiotic resistance—a major health problem for both humans and animals. Keep Antibiotics Working is a coalition of health, consumer, agricultural, environmental, humane and other advocacy groups with more than ten million members dedicated to eliminating a major cause of antibiotic resistance: the inappropriate use of antibiotics in food animals.

Antibiotic Resistance: A Major Threat to Public Health

Antibiotic-resistant disease has been identified by the Centers for Disease Control as one of the top public health challenges in the United States.[1] Resistant strains are often more virulent than their susceptible counterparts, require longer hospital stays, result in more time away from work, and cause dramatically increased human suffering.[2] Resistant diseases, which are on the upswing, are increasingly costly to treat—by one estimate adding over $4 billion per year to the health care tab in the U.S.[3]

The rise of resistant of resistant bacterial diseases is the result of over- and misuse of antibiotics in *both* human and animal medicine. The crisis will not be alleviated by the arrival of new drugs. There virtually no new drugs in the pipeline. Instead, the solution to the crisis will require action in both human medicine and food animal agriculture to reduce unnecessary and inappropriate use of our existing arsenal. To date, the veterinary and industrial agriculture community lags behind the human medical community in taking steps to respond to this crisis. Instead it has spent its energies in minimizing or denying the problem.

Antibiotic Resistance and Animal Agriculture

As the "one health" concept seeks to emphasize, it is unwise to think of animal and human diseases separately. In fact, 60% of known human diseases can be transmitted from animals to humans.[4] In the case of antibiotic resistance, the use of the same classes of antibiotics in food animal production and human medicine creates populations of antibiotic-resistant bacteria carried in or on food animals.[5] These microorganisms can readily travel back and forth between humans and animals—on food, on workers handling livestock, or through the environment. When resistant bacteria move off the farm, the resistance goes with them.

Currently, animal agriculture uses the lion's share of the antibiotics in the United States—some 13 million pounds of antibiotics every year, about 70 percent of total of all antibiotics used.[6] The majority of these antibiotics are not used for treating sick animals but for purposes like growth promotion and prevention. These antibiotics used in agriculture are the very same as those used in human medicine—penicillin, tetracycline and erythromycin.

As long as this massive use continues, animal agriculture will remain a fountain of resistant organisms, dangerous to both animals and humans. The straightforward solution to the problem is to reduce the use of antibiotics in animal production and thereby the pool of resistant organisms they generate.

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[4] Taylor L.H., Latham S.M., Woolhouse M.E.J. *Risk Factors for Human Disease Emergence.* PHILOS. TRANS. R. SOC. LOND. B. BIOL. SCI. Jul. 29, 2001. 356(1411):991–9.

[5] McEwen, S., Fedorka-Cray P. 2002. *Antimicrobial Use and Resistance in Animals.* CID 34 (Suppl. 3):S93–106. While many factors influence the level of resistance in bacteria in farm animals, the most important factor is the use of antimicrobial drugs (Catry *et al. Antimicrobial resistance in livestock.* J. VET. PHARMACOL. THERAP. 26:81–93, 2003.

[6] Mellon M., Benbrook C., Benbrook K. 2000. *Hogging it!: Estimates of Antimicrobial Abuse in Livestock.* Cambridge, MA: Union of Concerned Scientists, p. 60. Online at *http://www.ucsusa.org/food.*

The Erosion of the Efficacy of Human Use Drugs

A mountain of scientific studies over the last thirty years documents that the overuse of antibiotics in animal agriculture undercuts the efficacy of antibiotics. For example, the CDC has found that half of all human *Campylobacter* infections are resistant as are one in five *Salmonella* infections.[7] These bacteria, which come from livestock and poultry, are the two most common foodborne illnesses in the U.S. from these two pathogens alone, there are well over a million resistant infections in the U.S. each year. Resistance in *Campylobacter* and *Salmonella* are associated with increased bloodstream infections, increased hospitalization, and increased death.[8] Recent outbreaks of foodborne illness in produce like peppers and spinach are likely the result of contamination by animal waste containing these bacteria during the production and processing of crops.

In addition to intestinal food borne illness, urinary tract infections, which can be caused by a number of different bacteria including *E. coli,* have been linked to animal sources.[9]

And the list of resistant diseases of animal origin continues to grow. Just last year, we have learned that livestock can be an important source of life threatening *Methicillin-resistant Staphylococcus aureus* (MRSA). In Europe, a strain of MRSA responsible for 20% of human MRSA infections in the Netherlands,[10] has been shown to be transmitted from pigs to farmers and their families, veterinarians, and hospital staff.[11] The pig associated strain of MRSA has now been found in Canada [12] and in the United States.[13] Small studies to determine whether the pig-associated strain will be found in hospitals and doctors clinics in the U.S. are underway, but larger more comprehensive studies are needed.

The literature is voluminous and diverse, but the overall point is clear; antibiotic overuse in agriculture, just as in human medicine, is undercutting the efficacy of important human therapies and in some cases generating even more virulent pathogens.

- In 2003, the World Health Organization concluded, "*There is clear evidence of the human health consequences [from agricultural use of antibiotics, including] infections that would not have otherwise occurred, increased frequency of treatment failures (in some cases death) and increased severity of infections.*"
- In 2003, National Academy of Sciences' Institute of Medicine came to the same conclusion, stating, "*Clearly, a decrease in antimicrobial use in human medicine alone will have little effect on the current situation. Substantial efforts must be made to decrease inappropriate overuse in animals and agriculture as well.*"
- In 2001, the prestigious NEW ENGLAND JOURNAL OF MEDICINE published a special editorial whose title sums it up well—"*Antimicrobial Use in Animal Feed-Time to Stop.*"

As a result of the mounting evidence, the American Medical Association, American Academy of Pediatrics, American Nurses Association, American Public Health Association, Infectious Diseases Society of America, all endorse Federal legislation curtailing the use of medically important drugs in animal agriculture.

Antibiotic Use in Healthy Animals Does Not Benefit Human Health

Despite the overwhelming concern by the medical community about the human health, some experts associated with the animal industry, have claimed that routine antibiotic use benefits human health by suppressing pathogen levels in meat ani-

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[7] CDC. *National Antimicrobial Resistance Monitoring System for Enteric Bacteria (NARMS): Human Isolates Final Report*, 2004. Atlanta, Georgia: U.S. Department of Health and Human Services, CDC, 2007. Online at *http://www.cdc.gov/NARMS/NARMSAnnualReport2004.pdf.*

[8] Helms M., Simonsen J., Olsen K.E., Mølbak K. *Adverse Health Events Associated with Antimicrobial Drug Resistance in* ***Campylobacter*** *Species: A Registry-based Cohort Study.* J. INFECT. DIS. Apr. 1, 2005;191(7):1050–5; Varma J.K., Mølbak K., Barrett T.J., Beebe J.L., Jones T.F., Rabatsky-Ehr T., Smith K.E., Vugia D.J., Chang H.G., Angulo F.J. *Antimicrobial-resistant Nontyphoidal* ***Salmonella*** *is Associated with Excess Bloodstream Infections and Hospitalizations.* 1: J. INFECT. DIS. Feb 15, 2005;191(4):554–61.

[9] Hooton T., Samadpour M. *Is Acute Uncomplicated Urinary Tract Infection a Foodborne Illness, and Are Animals the Source?* CLINICAL INFECT. DIS. 40, 258–9, 2004.

[10] Van Loo I, *et al.* EMERGING INFECT. DIS. 13, 1834 (2007).

[11] Huijsdens X.W., *et al.,* ANN CLIN. MICROBIOL. ANTIMICROBIALS 5, 26 (2006); Voss A., *et al.* EMERGING INFECT. DIS. 11, 1965. 2005.

[12] Khana T., *et al.* VET. MICROBIOL. 128, 298. 2007.

[13] Smith T., *et al.* Paper presented at the 2008 International Conference on Emerging Infectious Diseases, Centers for Disease Control and Prevention, Council of State and Territorial Epidemiologists, Atlanta, GA. March 2008 and personal communication.

mals.[14] There is simply no evidence that that is the case. European studies have shown that levels of foodborne pathogens in human isolates rise and fall independently of antibiotic use in healthy food animals.[15] U.S. experience that directly contradicts the claim. from 1995 to 2000 there is documented evidence of a significant drop in antimicrobial use on U.S. broiler farms.[16] During this same period, the surveillance by the CDC also found a significant drop in the number of *Campylobacter* infections directly contradicting the claims of antibiotic use proponents that any reduction in antibiotic use will result in disease increases.[17] Finally, an FDA administrative law judge considered a claim of an animal health benefit of antibiotic use made in testimony to the administrative law judge during proceedings adjudicating the cancellation of Baytil. The judge rejected the claim because of lack of evidence.[18]

It Is Possible To Raise Livestock and Poultry With Fewer Antibiotics

The most direct and responsible antibiotic policy is to use antibiotics judiciously where they are needed but eliminate uses that are unnecessary. In human medicine, for example, physicians have established guidelines against the use of antibiotics to treat viral diseases, and aggressively seek to reduce prescriptions for those uses.

Animal agriculture offers an important opportunity to reduce the pressure on the microbial ecosystem that creates resistance to antibiotics used in animal agriculture. Most of the drugs used in animal agriculture are used to promote growth and compensate for crowded, stressful conditions characteristic of today's animal production facilities. These uses can be reduce or eliminated with modern husbandry practices. The viability of these practices has been demonstrated in both industrial and alternative agricultural operations. On the industrial side, Tyson was able to develop systems for all of its retail chicken that used no antibiotics at all. On the niche side, cattle grown out-of-doors and fed primarily grass rarely need antibiotics. Many American producers, like Laura's Lean Beef, Niman Ranch, Colemen are thriving in the market place selling beef and pork produced without antibiotics.

Finally, the Europeans have shown that even industrial-style hog and poultry operations can in ways that dramatically cut antibiotic use.

In 1999, Denmark, the world's leading pork exporter, ended all use of antimicrobial growth promoters. A World Health Organization (WHO) analysis of the Danish experience has shown that ban with little or no impact on agricultural productivity and animal welfare. The comprehensive analysis, published in 2003, showed that there were no appreciable impacts from the antibiotic ban in broiler chickens or older, so-called "finisher" pigs. In young, so-called "weaner" pigs, there was a modest increase in the number of pigs requiring antibiotics for the treatment of diarrhea, but the increase was completely offset by the overall decrease in antibiotic use. According to the WHO report, the overall drop in antibiotic use was 54 percent. In the years following the ban, the Danish pig herd continued to grow and the production losses associated with the ban in weaner pigs have been overcome.[19]

The EU now has EU wide-ban on non-therapeutic antibiotics.[20] Thailand[21] and now Korea[22] also have either enacted or will soon enact bans on certain non-therapeutic antibiotic use.

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[14] Cox L.A., Jr. *Potential Human Health Benefits of Antibiotics Used in Food Animals: A Case Study of Virginiamycin.* Cox L.A., Jr. ENVIRON. INT. May 31, 2005 (4):549–63. There have been some published risk assessments that make this claim. Most of these have as an author Dr. Anthony Cox whose testimony was thrown out by the FDA in hearings related to the withdrawal of the animal antibiotic Baytril because of unreliability and lack of credibility.

[15] Evans M.C., Wegener H.C. *Antimicrobial Growth Promoters and* ***Salmonella*** *spp.,* ***Campylobacter*** *spp. in Poultry and Swine.* DENMARK. EMERG. INFECT DIS. 2003 April 9 (4):489–92.

[16] Chapman H.D., Johnson Z.B. *Use of Antibiotics and Roxarsone in Broiler Chickens in the USA: Analysis for the Years 1995 to 2000.* POULT. SCI. March 2002. 81(3):356–64.

[17] CDC. *Preliminary FoodNet Data on the Incidence of Infection with Pathogens Transmitted Commonly Through Food—10 States, 2006.* MMWR April 13, 2007/56(14); 336–339.

[18] FDA. Final Decision of the Commissioner. Docket Number 2000N–1571. Withdrawal of Approval of the New Animal Drug Application for Enrofloxacin in Poultry. On line at *http://www.fda.gov/oc/antimicrobial/baytril.pdf.*

[19] Wegener. Keynote Presentation. ASM Conferences Antimicrobial Resistance in Zoonotic Bacteria and Foodborne Pathogens. June 15–18, 2008. Copenhagen, Denmark.

[20] *Ban on Antibiotics as Growth Promoters in Animal Feed Enters Into Effect.* EUROPA. December 22, 2005. Online at *http://europa.eu/rapid/pressReleasesAction.do?reference=IP/05/1687&format=HTML&aged=0&language=EN&guiLanguage=en.*

[21] Brooks E. *Reconciling Scarcity and Demand through Innovation*. FBA Issue 21. July/August 2008. Online at *http://www.efeedlink.com/ShowDetail/03c885e3-7852-439a-9ef0-a8a0b66a749c.html.*

[22] Tae-jong K. *Antibiotics to Be Banned for Feeding Animals.* THE KOREA TIMES. August 8, 2008. Online at *http://www.koreatimes.co.kr/www/news/nation/2008/09/117_30326.html.*

The actions taken in other countries are important because they validate the public health problem demonstrate that antibiotic can be reduced in commercially acceptable ways. In addition, the point to potential trade challenges the U.S. may encounter in the future if it fails to limit such uses here in the U.S.

As warned in a GAO report from 2004,[23] these countries also represent potential challenges to the U.S. products in the global marketplace. Under the trade rules, countries can restrict imports that do not conform to certain rules, provided they adhere to those rules themselves. For example, Korea could potentially restrict imports that relied on medicated feed not allowed in Korea. The greater the number of export partners that adopt such bans, the more vulnerable our meat exports in the global marketplace.

And as further noted by the GAO report,[24] if any major importer were to restrict trade from the U.S. because of the use of nontherapeutic antibiotics that would override any economic benefits of this practice. In addition, the U.S. currently is failing to follow Codex recommendations[25] by continuing the use of antibiotics as growth promoters.

The U.S. animal agriculture industry is at risk of following the example of the U.S. auto industry and failing to see where the market is going. Increasingly, consumers are seeking meat from animas raised without these antibiotics. International competitors are beginning to meet this demand. In addition to protecting public health, minimizing antibiotics use in livestock can help U.S. producers add consumer value to their products, and position themselves advantageously in the global marketplace. American producers should be supported in reducing their antibiotics use. KAW believes that research, extension, and outreach are critically important to helping producers adopt livestock management techniques that are less dependant on antibiotic use.

SUBMITTED STATEMENT OF KAREN STEUER, DIRECTOR OF GOVERNMENT OPERATIONS, PEW CAMPAIGN ON HUMAN HEALTH AND INDUSTRIAL FARMING

The Campaign on Human Health and Industrial Farming, of the Pew Charitable Trusts, appreciates this opportunity to submit testimony for the record regarding the use of antimicrobials in the livestock industry and important related human health issues.

As the Subcommittee is aware, food animals in intensive production in the United States are commonly treated with antibiotics to prevent the transfer of bacteria and infections in the crowded and sometimes unhygienic conditions of many industrial farms. Such therapeutic treatment of disease is critical to maintaining animal health. However, antibiotics are also commonly used in livestock to promote growth and rapid weight gain, and to prevent disease in the crowded conditions of industrial farms.

This nontherapeutic administration of antibiotics was studied closely by national health and agricultural experts who served on the Pew Commission on Industrial Farm Animal Production. In April 2008, the Commission issued a final report and called for stricter regulation of antibiotic use in industrial farm animals and articulated serious concerns about the nontherapeutic application of certain drugs in animals. Entire herds or flocks of farm animals are routinely fed antibiotics at low levels in their feed or water—a practice that has been identified as a major contributor to antibiotic resistance by human health professionals and organizations worldwide. For example:

- In the July, 2003, issue of ***Pediatrics: Official Journal of the American Academy of Pediatrics*** Dr. Katherine Shea concludes, "There is a long-standing debate over the exact role that agricultural use of antimicrobials plays in the current antibiotic resistance crisis. Although data gaps complicate the de-

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[23] *Antibiotic Resistance: Federal Agencies Need to Better Focus Efforts to Address Risk to Humans from Antibiotic Use in Animals,* GAO–04–490, April 22, 2004. Online at *http://www.gao.gov/docsearch/locate?to=http%3A%2F%2Fwww.gao.gov%2Fnew.items%2Fd04490.pdf.*

[24] *Antibiotic Resistance: Federal Agencies Need to Better Focus Efforts to Address Risk to Humans from Antibiotic Use in Animals,* GAO–04–490, April 22, 2004. Online at *http://www.gao.gov/docsearch/locate?to=http%3A%2F%2Fwww.gao.gov%2Fnew.items%2Fd04490.pdf.*

[25] *Code of Practice to Minimize and Contain Antimicrobial Resistance.* CAC/RCp 61–2005. Online at *http://www.codexalimentarius.net/download/standards/10213/CXP_061e.pdf.*

bate somewhat, existing evidence proves that part of the crisis is caused by antimicrobial use in livestock."[1]

- In 2000, the **World Health Organization** warned, "National governments should adopt a proactive approach to reduce the need for antimicrobials in animals and their contribution to antimicrobial resistance and to ensure their prudent use (including reducing overuse and misuse), as elements of a national strategy for the containment of antimicrobial resistance," and further recommended that "Use of antimicrobial growth promoters that belong to classes of antimicrobial agents used (or submitted for approval) in humans and animals should be terminated or rapidly phased-out in the absence of risk-based evaluations. The termination or phasing-out should be accomplished preferably by voluntary programmes of food animal producers, but by legislation if necessary."[2]
- The **Centers for Disease Control and Prevention** (CDC) observed, "Resistant bacteria may be transferred to humans through the food supply or direct contact with animals. For example, *Campylobacter* lives in the intestines of chickens. People get *Campylobacter* diarrhea primarily from eating undercooked chicken. In 1989, none of the *Campylobacter* strains from ill persons that CDC tested were resistant to fluoroquinolone antibiotics. In 1995, the FDA approved the use of fluoroquinolones in poultry. Soon afterwards, doctors found *Campylobacter* strains from ill persons that were resistant to fluoroquinolone antibiotics."[3]

Many antibiotics that are used in food animal production belong to the same classes that are used to treat humans. These include tetracyclines, penicillins, cephalosporins, macrolides, and fluoroquinolones, among others.[4] The similarity between human and animal drugs frequently means that bacteria resistant to antibiotics used in animals also are likely to be resistant to those used in humans.

The public health implications of antibiotic-resistant bacteria go far beyond the immediate threat of infection. Because the infection lingers while an effective antibiotic is identified, the potential for more severe illnesses and transmission to others is greatly increased. This is troubling for our already besieged public health care system for a number of reasons. More severe illnesses result in both higher frequency and longer duration of hospitalizations, raising the cost of health care. In 1998, the Institute of Medicine estimated that antibiotic-resistant bacteria generated an estimated $4–$5 billion per year in extra costs to the U.S. health care system,[5] and it is likely these costs have increased over time. There is also an overall higher risk of complications and death as there are fewer effective drugs available to treat serious infections.

Corporate food industry representatives have raised concerns that any change in antibiotic use will contribute to already increasing food prices. However, two recent large-scale studies—one with poultry and one with swine—found that the actual economic benefits were miniscule to nonexistent, and that the same financial benefits could instead be achieved by improving the management of the animals.[6] Even when improvements from growth promoting antibiotics have been observed, their benefits are completely offset if costs from increased resistance are considered: loss of disease treatment options in humans and animals, increased health care costs, and more severe and enduring infections. These costs are unfairly externalized to American consumers and the health care system at a time when neither can afford it.

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[1] Shea, K. (2003). *Antibiotic Resistance: What is the Impact of Agricultural Uses of Antibiotics on Children's Health?* PEDIATRICS, 112 (1), 253–258.

[2] World Health Organization. (2000). *WHO Global Principles for the Containment of Antimicrobial Resistance in Animals Intended for Food.* Geneva. At: *http://www.who.int/salmsurv/links/en/GSSGlobalPrinciples2000.pdf.*

[3] Centers for Disease Control and Prevention (CDC). National Antimicrobial Resistance Monitoring System (NARMS) Frequently Asked Questions (FAQ) About Antibiotic Resistance—How do resistant bacteria spread from animals to humans? At: *http://www.cdc.gov/narms/faq_pages/12.htm.*

[4] FDA Center for Veterinary Medicine, Database of Approved Animal Drugs, at *http://dil.vetmed.vt.edu/NADA/.*

[5] Institute of Medicine. (1998). *Antimicrobial Resistance: Issues and Options. Workshop Report, Forum on Emerging Infections.* (P.F. Harrison, & J. Lederberg, Eds.) Washington, D.C.: National Academy Press.

[6] Graham J.P., Boland J.J., Silbergeld E. "Growth promoting antibiotics in food animal production: an economic analysis." PUBLIC HEALTH REP. 2007; 122:79–87; and Miller G.Y., Algozin K.A., McNamara P.E., Bush E.J. "Productivity and economic effects of antibiotics use for growth promotion in U.S. pork production." JOURNAL OF AGRICULTURAL AND APPLIED ECONOMICS 2003; 35:469–482.

Other countries that are important U.S. trading partners have banned or are currently taking steps to phase out the nontherapeutic use of antimicrobials in animal agriculture, such as the European Union, Denmark, Sweden, and South Korea. Denmark became the first country with a large livestock industry to ban antibiotic growth promoters in 1998. According to a World Health Organization (WHO) 4 year review of the impact of the ban, Denmark achieved its goals: total antibiotic use in pigs and poultry was down 54% in 2001 from its peak in 1994 (despite some initial increase in therapeutic antibiotic use in weaner pigs), and drug-resistant strains of bacteria that are harmful to human health fell sharply in animals and meat.[7] As a result, the WHO concluded, "Under conditions similar to those in Denmark, the use of antimicrobials for the sole purpose of growth promotion can be discontinued."[8]

Action is urgently needed to address emerging antibiotic resistance, and should not be weighed in the context of a few pennies per chicken breast or pork chop against the growing health risks faced by thousands of Americans contracting antibiotic-resistant infections annually. According to the Infectious Diseases Society of America, 90,000 people die each year of a hospital-acquired infectious disease. Of these individuals, an estimated 70% have infections that are resistant to at least one antibiotic drug.[9]

The most critical step to ensure the availability and efficacy of antimicrobial drugs is to create policies that drastically reduce their use where they are being applied most inappropriately and in the greatest numbers: in the production of our food supply. The Pew Campaign on Human Health and Industrial Farming supports the Preserving Antibiotics for Medical Treatment Act (H.R. 962), which would ban the routine, non-therapeutic use of antibiotics in industrial animal production unless drug manufacturers can demonstrate that there is no harm to human health due to the development of antibiotic resistance.

Pew is not alone in this approach.

- In 2007 the **American Public Health Association** (APHA) issued the following policy statement: "APHA recognizes the urgency of transforming our food system to promote environmental sustainability, improve nutritional health, and ensure social justice, and therefore—Urges Congress to . . . Ban nontherapeutic antimicrobial use and arsenic use and increase funding for surveillance and research on antimicrobial resistance in healthy animals and ensure public health oversight of animal feed ingredients."[10] This policy came upon the heels of an earlier recommendation by the APHA that "Urges the Center of Veterinary Medicine of the FDA to work for regulations eliminating the non-medical use of antibiotics and limiting the use of antibiotics in animal feeds."[11]
- In 2006, the **Infectious Diseases Society of America** announced their policy of giving "high priority to the following strategies in the belief that support for these efforts will most rapidly achieve control of the problem of antibiotic resistance and/or provide the scientific basis to manage it in a rational manner. Support for legislation to phase out nontherapeutic use of certain antimicrobial drugs in food animals, including all antimicrobial drugs classified as 'critically important' or 'highly important' for human therapeutic use by the Food and Drug Administration."[12]
- In 2002, the **American College of Preventative Medicine** adopted a resolution endorsing "efforts to curb the growing public health threat of antibiotic resistance by reducing the overuse and misuse of antibiotics in both agriculture and human medicine; phasing out the use in healthy farm animals of antibiotics used in human medicine or closely related to human drugs; efforts to promote

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[7] World Health Organization. (2003.) *Impacts of antimicrobial growth promoter termination in Denmark.* Foulum, Denmark. At: *http://www.who.int/salmsurv/en/Expertsreportgrowthpromoterdenmark.pdf.*

[8] *Ibid*, p. 8.

[9] Infectious Diseases Society of America. (July 2004). *Bad Bugs, No Drugs. As Antibiotic Discovery Stagnates . . . A Public Health Crisis Brews.* Alexandria, VA. At: *http://www.idsociety.org/WorkArea/showcontent.aspx?id=5554.*

[10] American Public Health Association (APHA). (November 6, 2007.) *Toward a Healthy, Sustainable Food System.* At: *http://www.apha.org/advocacy/policy/policysearch/default.htm?id=1361.*

[11] APHA. (January 1, 1999.) *Addressing the Problem of Bacterial Resistance to Antimicrobial Agents and the Need for Surveillance.* At: *http://www.apha.org/advocacy/policy/policysearch/default.htm?id=179.*

[12] Infectious Diseases Society of America. (April 24, 2006.) *Principles and Strategies Intended to Limit the Impact of Antimicrobial Resistance.* At: *http://www.idsociety.org/WorkArea/downloadasset.aspx?id=4042.*

sustainable agricultural production methods that provide alternatives to the use of antibiotics in healthy farm animals," and to "Urge companies involved in the production of meat, poultry and fish to voluntarily agree to stop using nontherapeutic antibiotics (i.e., those used for purposes other than treating sick animals), and we urge companies and individuals that purchase meat, poultry and fish products to seek products that have been produced without nontherapeutic antibiotics." [13]

- In 2001, the **American Medical Association** adopted a policy to "oppose the use of antimicrobials at non-therapeutic levels in agriculture, or as pesticides or growth promoters, and urge that non-therapeutic use in animals of antimicrobials (that are also used in humans) should be terminated or phased out based on scientifically sound risk assessments . . ." [14]
- In 1999 the **Council of State and Territorial Epidemiologists, National Association of State Public Health Veterinarians** adopted a position recommending "the discontinuation of antimicrobials used to promote the growth of food animals if they are also used in human medicine. These uses may increase antimicrobial resistance and no longer meet the food safety criteria of reasonable certainty of no harm." [15]

Given the concerns raised by these and other human health professionals, it is the view of the Pew Charitable Trusts that Congress must address the looming crisis posed by antibiotic resistance, and the contribution to that crisis of nontherapeutic antibiotic use in industrial animal agriculture. Congress should also examine the growing body of evidence indicating that farm workers and farm communities are at risk of exposure to resistant bacteria that either originate on industrial farms or are carried by the animals on those farms.[16–18]

We urge the Agriculture Committee and all Members to take these grave health concerns into account and to address this important issue in the next Congress, in particular during consideration of important legislative initiatives related to food safety and health care reform. The Pew Charitable Trusts looks forward to working with the House Committee on Agriculture Members and staff to find practical, workable solutions to this public health threat, while protecting the necessary and valuable therapeutic uses of antimicrobials in order to maintain animal wellbeing and human health.

For additional information, please feel free to contact me at [Redacted], or at [Redacted].

SUBMITTED STATEMENT OF ROBERT P. MARTIN, EXECUTIVE DIRECTOR, PEW COMMISSION ON INDUSTRIAL FARM ANIMAL PRODUCTION

Mr. Chairman and Members of the House Agriculture Subcommittee on Livestock, Dairy, and Poultry, my name is Robert Martin and I was the Executive Director of the Pew Commission on Industrial Farm Animal Production. I appreciate the opportunity to submit a brief statement on the Commission's recommendations on antimicrobial use in industrial farm animal production.

The Pew Commission on Industrial Farm Animal Production was a 2 year study funded by a grant from The Pew Charitable Trusts to recommend solutions to the public health, environmental, animal welfare, and rural community problems created by industrial animal agriculture.

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[13] American College of Preventive Medicine. (January 23, 2002.) *Policy Resolution #05–02(A): Principles for Combating Antibiotic Resistance.* At: *http://www.acpm.org/pol_winter2002res.htm#Principles%20for%20Combating%20Antibiotic%20Resistance.*

[14] American Medical Association. (June 2001). *Resolution 508: Antimicrobial Use and Resistance,* 2001 Annual Meeting Proceedings. At: *http://www.ama-assn.org/meetings/public/annual01/resolutions.pdf.*

[15] Council of State and Territorial Epidemiologists. (1999.) CSTE Position Statement 1999–ID 7: *Discontinuation of Antimicrobials Used to Promote Growth of Food Animals if they are used in or Select for Cross Resistance to Antimicrobials used in Human Therapy.* At: *http://www.cste.org/ps/1999/1999-id-07.htm.*

[16] Gilchrist, M.J., C. Greko, D.B. Wallinga, G.W. Beran, D.R. Riley, & P.S. Thorne. (February 2007.) *The Potential Role of Concentrated Animal Feeding Operations in Infectious Disease Epidemics and Antibiotic Resistance. Environmental Health Perspectives, 115* (2).

[17] van Rijen, M.M.L., P.H. Van Keulen, & J.A. Kluytmans. (January 2008.) *Increase in a Dutch Hospital of Methicillin-Resistant* ***Staphylococcus aureus*** Related to Animal Farming. CLINICAL INFECTIOUS DISEASES, 46 (2): 261–263.

[18] Price, L.B., J.P. Graham, L.G. Lackey, A. Roess, R. Vailes, & E. Silbergeld. (December 2007.) *Elevated Risk of Carrying Gentamicin-Resistant* ***Escherichia coli*** *among U.S. Poultry Workers.* ENVIRONMENTAL HEALTH PERSPECTIVES 15 (12).

The Commission released its final report in April of 2008 that included 24 primary recommendations, and several secondary recommendations, in the four general areas studied. Of those 24 recommendations, 12 addressed public health problems, and five of those addressed antibiotic use in industrial animal agriculture.

The first recommendation on antimicrobial use is to restrict the use of antimicrobials in food animal production to reduce the risk of antimicrobial resistance to medically important antibiotics. That is to be accomplished by: (1) Phase out and ban use of antimicrobials for nontherapeutic use in food in food animals; (2) Immediately ban any new approvals of antimicrobials for nontherapeutic uses in food animals and retroactively investigate microbials previously approved; (3) Strengthen recommendations in the Federal Drug Administration's Guidance 152; and (4) Educate producers on how to raise animals without the reliance on nontherapeutic use of antibiotics and other antimicrobials.

Perhaps equally important are the Commission's definitions of therapeutic, nontherapeutic, and prophylactic use of antimicrobials. Present definitions used by the animal agriculture industry blur the distinctions between these categories, often calling "nontherapeutic" use "prophylactic" use.

The Commission defines nontherapeutic use as any use of antimicrobials in food animals in the absence of microbial disease or documented (known) microbial disease exposure. Any use of the drug as an additive for growth promotion, feed efficiency, weight gain, routine disease prevention in the absence of documented exposure, or other routine purposes, is considered nontherapeutic.

Therapeutic use is defined by the Commission as the use of antimicrobials in food animals with diagnosed microbial disease, that is, sick animals. This definition is very important given some of the inaccurate comments made during the Subcommittee hearing on September 25, 2008. At no time has the Commission called for banning the use of antibiotics in sick animals, as was claimed by witnesses and some Members of the Subcommittee. A recommendation banning the medical use of antibiotics in food animals would be irresponsible and indefensible.

The Commission defines prophylactic as the use of antimicrobials in healthy animals in advance of an expected exposure to an infectious agent or after such an exposure but before the onset of a laboratory-confirmed clinical disease as determined by a licensed professional.

Claims that the Commission proposed banning the use of all antibiotics in animal agriculture, or that it did not want veterinarians to have access to medicine to treat sick animals, do not add to the serious discussion of the issue. Nothing is further from the truth about the Commission recommendations. The Commission's recommendations on antimicrobial use are an attempt to use these important live saving drugs—for people and animals—in a more appropriate way to help preserve their effectiveness.

It is commonly accepted now that all use of antibiotics adds to the problem of antibiotic resistance. Concern about the prudent, medical use of antibiotics in human medicine began at least 30 years ago. It is time to do the same in animal agriculture, since estimates indicate that as much as 70% of the antibiotics used in the United States are used in food animals.

Thank you.

ROBERT P. MARTIN,
PCIFAP.

SUPPLEMENTAL MATERIAL SUBMITTED BY NATIONAL PORK PRODUCERS COUNCIL

Introduction

The National Pork Producers Council is an association of 43 state pork producer organizations and serves as their voice in Washington, D.C.

U.S. pork producers appreciate the opportunity to reiterate their antibiotic responsible use guidelines and to address statements made about Methicillin-resistant Staphylococcus aureus (MRSA) and animal agriculture.

Pork Industry Developed Guidelines on Antibiotic Use

U.S. pork producers take the use of antibiotics very seriously. Our ethical principles specifically address animal-health products because we believe all producers need to use antibiotics judiciously and responsibly to protect pig health, to produce safe pork and manage antibiotic use to protect public health.

This obligation to protect animal health and public health is why U.S. pork producers developed our responsible antibiotic use program, "Take Care—Use Antibiotics Responsibly." It was the first producer program outlining principles and guidelines that protect public health, animal health and animal well-being through

the responsible use of antibiotics. "Take Care" is the product of cooperation among producers, veterinarians, the feed industry, Federal public health agencies and food companies. The pork industry's responsible-use program has been praised by many Federal agencies, legislators, consumer organizations and food supply companies. The U.S. pork industry developed this program because it was the right thing to do. Like all Americans, pork producers care about animal health and public health.

Initially, "Take Care" started as a voluntary program, and many producers participated. Today, however, the pork industry understands how important it is to use antibiotics responsibly, and "Take Care" is the way the U.S. pork industry does business. It's good for our pigs, it's good for our producers and families, and it's good for the bottom line. "Take Care" has been incorporated into the industry's Pork Quality Assurance (PQA) Plus program, which includes on-farm assessments, including reviews of whether the antibiotic-use principles are being practiced. Producer PQA Plus certification is required by U.S. packing plants as a condition of sale.

The veterinarians working in the U.S. pork industry also have been proactive in the responsible use of antibiotics. The American Association of Swine Veterinarians was the first species-specific veterinary organization to collaborate with FDA and the American Veterinary Medical Association to create and endorse judicious-use guidelines for antibiotics.

MRSA

While MRSA has been found in pigs, it likely has little to do with the human epidemic in the U.S. or the use of antibiotics in pig herds. It be should be noted that Denmark, a country that has banned antibiotics growth promoters in 1999, has a high prevalence of swine herds that are positive for MRSA. According to the Centers for Disease Control and Prevention (CDC), MRSA in the U.S. is largely human health care related. When it comes to community acquired infections, CDC says it has investigated numerous outbreaks of community-associated MRSA infections in the U.S., and in none of these investigations has animal exposure been identified as a risk factor for infection. Although the finding of MRSA in retail meat suggests a possible role for foodborne transmission, it likely accounts for a very small proportion of human infections in the U.S., if the transmission does indeed occur.

The MRSA found in pigs does not cause illness in these animals and does not require pork producers to use antibiotics to control it. The presence and further development of antibiotic-resistant strains of bacteria is a serious concern for society. The scientific community, including physicians and veterinarians, continues to work to understand how antibiotic use for humans and on livestock farms, such as swine operations, contributes to antibiotic resistance. Once again, the pork industry supports judicious use of antibiotics, which are essential to the health and well-being of animals.

A letter from Dr. Julie Gerberding of the CDC to the House Committee on Agriculture is submitted along with this statement. (This document is located on p. 113.)

Summary

Pork producers and veterinarians have a moral obligation to use antibiotics responsibly to protect human health and provide safe food, both of which are paramount concerns to America's pork producers. Producers also have an ethical obligation to maintain the health of their pigs. Antibiotics are merely one piece to the health care system that pigs need. The U.S. pork industry has a long history of being proactive and doing the right thing for its pigs and consumers. Pork producer developed "Take Care" and PQA Plus not because they had to but because it was the right thing to do. The U.S. pork industry continues to adopt better techniques and new technologies, but it cannot lose the tools it already has developed, including antibiotics, to protect the well-being of producers' animals and to produce safe pork.

SUPPLEMENTAL MATERIAL SUBMITTED BY RICHARD A. CARNEVALE, V.M.D., VICE PRESIDENT, SCIENTIFIC, REGULATORY AND INTERNATIONAL AFFAIRS, ANIMAL HEALTH INSTITUTE

October 8, 2008

Hon. LEONARD L. BOSWELL,
Chairman,
Subcommittee on Livestock, Dairy, and Poultry,
Committee on Agriculture,
Washington, D.C.

Dear Mr. Chairman:

I am writing to address testimony presented by Representative Louise M. Slaughter to this Subcommittee at the hearing on Advances in Animal Health within the Livestock Industry on the use of antimicrobials in animal agriculture. I am Dr. Richard Carnevale of the Animal Health Institute and testified before you at this hearing. I greatly appreciated the opportunity to present the views of the animal health industry.

Antibiotic resistance is clearly a public health concern, as Representative Slaughter points out. However, it is widely accepted that the major resistance problems in human medicine are due to human use of antimicrobials and that the contribution from the use of antimicrobials in food animals has been greatly exaggerated. The majority of diseases in human medicine and those Representative Slaughter mentions as important uses for antimicrobials do not come from animals. A survey of medical specialists in Europe and the U.S. concluded that use of antimicrobials in livestock might contribute to only 4–5% of resistance problems encountered in human medicine.[1] Furthermore, we are not aware of any studies that have ". . . *conclusively linked non-therapeutic use to a growing number of incidents of antimicrobial-resistant infections in humans.*" as Ms. Slaughter contends.

AHI surveys of the it's antimicrobial producing member companies every year indicates that about 5% of all antimicrobials sold for food animals are used for "non-therapeutic use" to increase weight gain or decrease feed consumption. The vast majority of antimicrobials are used to prevent, control, and treat animal diseases which are all considered therapeutic uses by the American Veterinary Medical Association and the international food standard setting organization, the Codex Alimentarius.

It is also misleading to suggest that the well publicized infections in schools and athletic facilities caused by Methicillin Resistant Staphylococcus Aureus (MRSA) are due to use of antimicrobials in animals. It is true that a strain of MRSA has been isolated from pigs in Canada and some European countries , but this strain is not the same bacterial pathogen that is responsible for either hospital or community MRSA infections in the United States. Dr. Julie Gerberding, Director of the Centers for Disease Control and Prevention, recently wrote to House Agriculture Committee Chairman Collin Peterson on MRSA and its connection to animal agriculture. In none of the investigations that CDC has conducted on outbreaks of community-associated MRSA infections has animal exposure been identified as a risk factor. Furthermore, they have found ". . . *no documented role for meat consumption or handling in the transmission of MRSA.*" We have attached the CDC letter to the Chairman for your information.

Two other points in her testimony require comment. In fact, language inserted in the farm bill to facilitate research on antimicrobial use and resistance was included in the final version. Section 7521 of P.L. 110–246, the farm bill, requires the Secretary to provide research and education grants to study the development of antibiotic resistant bacteria and to ensure the judicious use of antibiotics in veterinary and human medicine.

Second, the Animal Drug User Fee Act of 2008 included a specific provision that requires FDA to collect from animal drug application sponsors and report on antimicrobial sales data beginning in 2010. The industry supported this amendment and provided technical guidance to the House Energy and Commerce Committee in developing the necessary language in the ADUFA bill.

Mr. Chairman, the bill that Congresswoman Slaughter endorses, H.R. 962, the Preservation of Antibiotics for Medical Treatment Act (PAMTA) would do nothing to curb antimicrobial resistance problems in human medicine but will likely have adverse consequences to animal health and food safety, while increasing feed and food costs. As I testified before your Subcommittee, FDA already has a rigorous science-based process for determining the safety of antimicrobials used in food animals and this process has at its foundation, risk assessment. Risk assessments have and continue to be conducted on several antimicrobials used in food-producing animals. Those assessments have indicated that the risks of antimicrobial resistance being transferred to humans and impacting public are quite low and certainly do not justify wholesale removal of safe and effective products important to animal agriculture.

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[1] Bywater R. and Casewell M. *Assessment of the impact of antimicrobial resistance in different bacterial species and of the contribution of animal sources to resistance in human infection.* JOURNAL OF ANTIMICROBIAL CHEMOTHERAPY 2000; 6: 643–645.

I thank you for the opportunity to provide further comment on this important topic.

Sincerely,

RICHARD A. CARNEVALE, V.M.D.

ATTACHMENT

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Centers for Disease Control
and Prevention (CDC)
Atlanta GA 30333

FEB 4 2008

The Honorable Collin C. Peterson
Chairman
Committee on Agriculture
House of Representatives
Washington, D.C. 20515-6001

Dear Mr. Chairman:

Thank you for your letter regarding the potential public health threat posed by methicillin-resistant Staphylococcus aureus (MRSA) in food-producing animals. As you know, MRSA infections have received significant media attention recently.

A report by the Centers for Disease Control and Prevention (CDC) and others on the scope and magnitude of life-threatening MRSA infections in the United States was published this past fall in the *Journal of the American Medical Association*,[1] coincident with media reports of severe MRSA in high school students. This increased attention also heightened the level of concern about the possible implications of several recent reports describing MRSA in food-producing animals; however, although the finding of MRSA in retail meats suggest a possible role for foodborne transmission, if such transmission occurs, it likely accounts for a very small proportion of human infections in the United States.

The report indicated that more than 20 percent of community-associated MRSA among persons in the Netherlands was caused by a strain that is non-typable by pulsed-field gel electrophoresis (NT-PFGE) and now thought to be of animal (i.e., pigs and cattle) origin.[2] Another strain known to commonly colonize persons in North American hospitals is PFGE type USA 100 and was found in pigs and pig workers in Canada.

We appreciate the opportunity to comment on these findings and how they may relate to the epidemiology of MRSA in the United States. Enclosed are CDC's responses to each of the specific questions outlined in your letter.

I hope this information is helpful. I also will provide this response to Representatives Bob Goodlatte, Leonard Boswell, and Robin Hayes who cosigned your letter.

Sincerely,

Julie Louise Gerberding, M.D., M.P.H.
Director

The Centers for Disease Control and Prevention's (CDC) Responses to Questions on Methicillin-Resistant Staphylococcus aureus (MRSA) in Food-Producing Animals Addressed in the December 14, 2007, Letter From the House Committee on Agriculture

- *What is the public-health risk, if any, from MRSA in pigs, and how does that risk compare to the public-health risk of MRSA acquired in health-care facilities or elsewhere in the community?*

Response:

Several facts provide information on the potential public health risk posed by MRSA in food-producing animals. First, more than 80 percent of life-threatening MRSA infections appear to be the result of patient-to-patient transmission in inpatient healthcare facilities.[1] In addition to the nearly 94,000 life-threatening MRSA infections that occur mostly in healthcare settings each year, several million community-associated skin and soft tissue MRSA infections likely occur.[5, 6] It is reasonable to conclude that the vast majority of these common skin and soft tissue infections result from person-to-person transmission of MRSA in the community.

CDC and others have investigated numerous outbreaks of community-associated MRSA infections in the United States, and in none of these investigations has animal exposure been identified as a risk factor for infection.[7-15] Although the finding of MRSA in retail meats suggests a possible role for foodborne transmission, if such transmission occurs, it likely accounts for a very small proportion of human infections in the United States. Recent reports from the Netherlands and Canada suggest that human infections caused by MRSA strains of animal origin occur predominantly among persons with close proximity to colonized or infected animals.[2, 4] In contrast, all U.S. outbreaks of community-associated MRSA infections have been traced to conditions that facilitate human-to-human transmission.[7-15] Although there has long been a type of S. aureus-induced foodborne disease resulting from the ingestion of pre-formed toxin, antibiotic therapy is not used in the treatment of this toxin-related illness. Therefore, MRSA would pose no greater threat than antibiotic- susceptible strains.

- *What type(s) of surveillance programs for monitoring MRSA does CDC have in place in health care and community settings?*

Response:

CDC surveillance systems used to monitor MRSA include the National Healthcare Safety Network (NHSN), the Active Bacterial Core Surveillance (ABCs) and EMERGEncy ID Net components of the Emerging Infections Program (EIP), the National Health and Nutrition Examination Surveys (NHANES), and FoodNet. NHSN is a voluntary surveillance program used by hospitals to report healthcare-associated infections, including those caused by MRSA. The public health importance of healthcare-associated infections has prompted an increasing number of states to enact laws requiring hospitals to report these infections to the health department or another state agency through NHSN. CDC is working to provide technical support and guidance to states with reporting laws and to those considering similar legislation.

Proposed legislation on reporting of these infections has also been introduced on the federal level. The ABCs/EIP has provided recent population-based estimates of both healthcare- and

community-associated life-threatening MRSA infections.[1] In addition, this system has been the source of thousands of MRSA isolates collected from widely dispersed geographic areas over several years. The EMERGEncy ID Net program has provided a geographically dispersed repository of isolates and associated clinical descriptions of outpatients with community-associated MRSA skin and soft tissue infections.[6] Results from NHANES conducted from 2001 through 2004 suggest that asymptomatic carriage (i.e., colonization) of MRSA is present in less than 2 percent of the U.S. population and that most of these persons are colonized with MRSA strains of healthcare origin.[16] FoodNet provides a venue for a planned survey of stool cultures for MRSA from several hundred persons with diarrhea and from healthy controls.

- *Would CDC surveillance detect MRSA that is not typable by pulsed field gel electrophoresis (PFGE)? Are rare types of MRSA, such as a non-typable by PFGE, followed up with an epidemiological investigation?*

Response:

Through the combination of the above outlined surveillance systems and surveys, as well as outbreak investigations, CDC has characterized several thousand community-associated MRSA infections since 2000. Among these isolates, only one has been found to be NT-PFGE (non-typable by PFGE). The majority of human community-associated MRSA infections in the United States are caused by one particular strain and PFGE subtype (USA 300-0114), which appears clearly of human origin. Because virtually all characterized isolates are subjected to PFGE, all NT-PFGE would be identified as such. Although nearly all isolates collected include some epidemiologic information, whether such information is adequate to determine if an animal source could exist would depend upon the surveillance system, survey, or investigation. In some instances, such as the NHANES, additional information necessary to investigate a rare PFGE type may be virtually impossible to obtain.

- *What is known about the transmission of MRSA from humans to animals?*

Response:

Several studies have suggested that MRSA can be transmitted from humans to companion animals, such as dogs, cats, and horses, and that once these animals become colonized or infected with strains of human origin they can be a source for transmission to other animals or humans.[2, 17-21] However, as described in the above response to the first question, thus far there is no documented role for meat consumption or handling in MRSA transmission.

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SUBMITTED QUESTIONS

Response from John Clifford, D.V.M., Deputy Administrator for Veterinary Services and Chief Veterinarian, Animal and Plant Health Inspection Service, U.S. Department of Agriculture

Question. In your testimony you outlined human public health numbers. How many livestock-bacterial infections are there in the United States? What is the percentage of those infections that are associated with bacterial pathogens displaying antimicrobial resistance?

Answer. This is a challenging question to attempt to answer, as *Salmonellae* are the only animal bacterial pathogens covered by a surveillance program that includes evaluating antimicrobial resistance. The National Animal Health Monitoring System (NAHMS) collects information through periodic (at 5–10 year intervals) national surveys on the occurrence of disease in animal populations on farms. However, these data are normally collected without regard to the etiologic agent causing the disease. Instead, the program collects data on the occurrence of disease syndromes in animal groups (usually specific age groups). For example, national estimates are available on the proportion of dairy calves prior to weaning that experience a digestive disease problem. The program does not differentiate digestive disease caused by bacteria (such as *Escherichia coli* or *Salmonella*) from disease caused by viruses (such as *Rotavirus* or *Corona* virus) from disease caused by parasites (such as *Cryptosporidium*).

So, while we do estimate the number of calves affected by "a digestive disease" we cannot say how many of these are associated with bacterial etiologies let alone how many of these are caused by organisms that are resistant to one or more antimicrobial drugs.

The NAHMS program has some information for *Salmonella* based on samples collected on farm from healthy animals. These samples have been collected for some animal species including cattle (beef cow-calf, feedlot, and dairy) and swine. Data on other commodities and companion animals are lacking. One of the primary benefits of this sampling has been to partially characterize the potential risk to food safety. The sampling of healthy animals (i.e., those that are likely to end up in the food chain) has progressed toward this benefit.

Veterinary diagnostic laboratories also receive samples collected from ill animals on the farm. Which factors affect the decision of the producer and/or veterinarian to submit samples to the diagnostic laboratory is not clear and therefore it is unknown how this population relates to all of the animals that become ill on farms. Factors such as the number of animals affected, the severity of the disease, the availability and interest of a veterinarian and individual animal economic value could all affect the decision to submit a sample to obtain a diagnosis. If a bacterial agent is identified from the case material it may or may not be tested for susceptibility to antimicrobial drugs. The cases from which samples are submitted have frequently (though the extent and history is often unknown) been treated with antimicrobial drugs. from the above it should be clear that the diagnostic laboratory data are not representative of all ill animals on farm (though the extent is not known), representing the worst case scenario, i.e., animals that have failed to respond to standard empirical treatments. In addition to the issues associated with sample representativeness and the decision to test for susceptibility there is no central repository of information for the findings on antimicrobial susceptibility for animal pathogens. Some diagnostic laboratories may publish annual summaries for the clientele but there is no entity that collates the information, validates it and interprets it to produce information for producers, veterinarians or diagnosticians.

Response from Stephen R. Mason, Acting Assistant Commissioner for Legislation, Food and Drug Administration, U.S. Department of Health and Human Services

Nov. 20, 2008

Hon. LEONARD L. BOSWELL,
Chairman,
Subcommittee on Livestock, Dairy, and Poultry,
Committee on Agriculture,
Washington, D.C.

Dear Mr. Chairman:

Thank you for providing an opportunity for the Food and Drug Administration (FDA or the agency) to testify at the September 5,2008, hearing before the House Agriculture Committee's Subcommittee on Livestock, Dairy and Poultry. The hearing addressed advances of animal health within the livestock industry.

This letter provides responses for the record to questions you raised during the hearing. We have reprinted the questions below, followed by the agency's response.

Question 1. What are the costs associated with getting an animal drug approved for market?

Answer. In Fiscal Year (FY) 2007, FDA's organizational components spent $49,588,801 in process costs, as described in the Animal Drug User Fee Act (ADUFA), associated with the review of new animal drug applications. Additional details related to FDA's costs for reviewing animal drug applications are provided on page 9 of the enclosed FY 2007 ADUFA Financial Report.

If your question relates to industry's developmental, application, and other costs associated with animal drug applications, drug sponsors are better able than FDA to provide such data.

Question 2. How many livestock bacterial infections are there in the U.S.? What percentage of those infections is associated with bacterial pathogens displaying antimicrobial resistance?

Answer. FDA considers information on bacterial infections in livestock and on potential resistance to antimicrobial drugs of the pathogens that cause such infections in the context of evaluating specific new animal drug applications (NADA). Such information is generally supplied by the sponsor of the NADA and is specific to the intended use of the drug in question. FDA does not conduct routine national surveys of bacterial diseases in livestock. Therefore, we are unable to provide data on the overall number of bacterial infections in U.S. livestock or on the percentage of those infections displaying antimicrobial resistance.

FDA recognizes that bacterial diseases in livestock are important public and animal health challenges. FDA is taking an increasingly active role with our partners at the United States Department of Agriculture and the Centers for Disease Control and Prevention to study livestock bacterial diseases, including *Escherichia coli.* It is hoped that these joint efforts can lead to a greater understanding of the diseases themselves and how best to address and control them.

Thank you again for the opportunity to appear before the Subcommittee. Please let us know if you have any further questions or concerns.

Sincerely,

STEPHEN R. MASON,
Acting Assistant Commissioner for Legislation.

ATTACHMENT 1

FY 2007 MDUFMA FINANCIAL REPORT

REQUIRED BY THE

MEDICAL DEVICE USER FEE AND MODERNIZATION ACT OF 2002

AMENDED BY THE

MEDICAL DEVICE USER FEE STABILIZATION ACT OF 2005

FOOD AND DRUG ADMINISTRATION
DEPARTMENT OF HEALTH AND HUMAN SERVICES

DATE: 6/24/08

Andrew C. von Eschenbach, M.D.
Commissioner of Food and Drugs

THE SECRETARY OF HEALTH AND HUMAN SERVICES
WASHINGTON, D.C. 20201

NOV - 7 2008

The Honorable Richard Cheney
President of the Senate
United States Senate
Washington, DC 20510

Dear Mr. President:

The Medical Device User Fee and Modernization Act (MDUFMA) of 2002, as amended, requires an annual financial report to Congress. I have enclosed the fifth annual financial report to Congress which documents how the Food and Drug Administration (FDA) met each of the necessary conditions specified in MDUFMA for continued collection of medical device user fees. Availability of these fees makes FDA better able to strengthen its medical device review process and meet the performance goals established for this program.

I appreciate the timely action of Congress in reauthorizing MDUFMA for an additional five years in the Food and Drug Administration Amendments Act of 2007.

Sincerely,

Michael O. Leavitt

Enclosure

Identical letters to:
Speaker of the House of Representatives
Chairman and Ranking Minority Member, Committee on Health, Education, Labor, and Pensions, United States Senate
Chairman and Ranking Minority Member, Committee on Energy and Commerce, House of Representatives

EXECUTIVE SUMMARY

The Medical Device User Fee and Modernization Act (MDUFMA) of 2002 requires the Food and Drug Administration (FDA) to report annually on the financial aspects of its implementation of MDUFMA. This is the annual financial report to Congress that covers activities for fiscal year (FY) 2007.

MDUFMA, amended by the Medical Device User Fee Stabilization Act (MDUFSA) of 2005, specifies that three conditions must be satisfied in order for FDA to collect and spend MDUFMA fees:

1. Within FDA's salaries and expenses appropriation, the amount appropriated for devices and radiological health after FY 2004 must be at least $205,720,000, excluding fees, adjusted for inflation.
2. The fee amounts that FDA can collect must be specified in the Appropriation Acts.
3. FDA must spend at least as much from appropriated funds, exclusive of user fees, for the review of medical device applications as it spent in FY 2002, adjusted for inflation.

MDUFMA also contains a provision that FDA must spend at least as much on medical device inspections as it spent in FY 2002, increased by 5 percent in each fiscal year.

This report explains how FDA met the four statutory conditions in FY 2007. The report also provides information on user fee collections, expenditures, and carryover balances. In FY 2007, FDA net collections totaled $30 million from fees. FDA obligated $35 million from MDUFMA collections to support FDA's medical device review program. FDA carried forward into FY 2008 a balance of $11 million—about $5.4 million less than the carryover balance at the end of FY 2006. About 66 percent of the total expenses for the medical device review program in FY 2007 went for personnel salary and benefit costs. The remaining 34 percent was spent on operating and the infrastructure costs necessary to support the medical device review program.

MDUFMA fees, along with the increased appropriations from Congress, enabled FDA to dedicate 242 more full-time equivalents (FTEs) to the medical device review program in FY 2007 than in FY 2002—the year before MDUFMA was enacted. An additional 76 contractor staff-years were also dedicated to the device review in FY 2007 compared with FY 2002. These resources have enabled FDA to achieve the performance goals associated with the enactment of MDUFMA and strengthen FDA's medical device review program. FDA looks forward to continued strengthening of the medical device review program in FY 2008.

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APPENDIX D: ALLOWABLE AND EXCLUDED COSTS FOR THE PROCESS FOR THE REVIEW OF MEDICAL DEVICE APPLICATIONS

APPENDIX E: DEVELOPMENT OF COSTS FOR THE PROCESS FOR THE REVIEW OF MEDICAL DEVICE APPLICATIONS

BACKGROUND

MDUFMA authorizes FDA to collect fees from the medical device industry to augment appropriated funds for the medical device review process. MDUFMA also requires additional funding from appropriations. FDA uses the additional funds from fees and appropriations to support the process for the review of medical device applications as defined in MDUFMA, so that safe and effective devices reach the American public more quickly.

Under MDUFMA, companies must pay application fees when submitting certain device applications to FDA. Fee-paying applications include premarket applications (PMAs), product development protocols (PDPs), premarket reports (PMRs), modular PMAs, biologics license applications (BLAs), certain supplements to all of these applications, and premarket notification submissions (510(k)s). A fee for each application type is fixed in statute as a percent of a standard fee for a PMA. The MDUFSA, Public Law 109-43, amended MDUFMA on August 1, 2005. MDUFSA set the standard fee for a premarket application for FY 2007 at $281,600. FDA then established fee rates for all other applications based on the percents specified in the statute. Unlike the Prescription Drug User Fee Act (PDUFA), MDUFMA does not have product or establishment fees in the first 5 years.

MDUFMA requires FDA to submit two reports to Congress each fiscal year: 1) a performance report is to be sent within 60 days after the end of each fiscal year, and 2) a financial report is to be sent within 120 days after the end of each fiscal year. FDA is separately transmitting the FY 2007 MDUFMA Performance Report that discusses FDA's progress in meeting the goals referred to in MDUFMA. This report is FDA's FY 2007 MDUFMA Financial Report covering the period October 1, 2006 through September 30, 2007.

As required by MDUFMA, this report presents the statutory conditions or "triggers" that must be met as a condition for FDA to be able to collect and spend the fees, and explains how they were met in FY 2007. This report describes the process for the review of medical device applications, as defined in MDUFMA and states the total costs of this process in FY 2007, including costs paid from both fee collections and appropriations. The report also presents the FY 2007 fee collections, obligations, and carryover balances.

MEETING THE STATUTORY CONDITIONS FOR USER FEES IN FY 2007

MDUFMA imposes three statutory conditions that FDA must satisfy before it can collect and spend user fees. FDA's calculations show that FDA met these conditions in FY 2007. See summaries set forth below.

The **first condition** is a funding condition that affects FDA's fee collections in FY 2007. MDUFMA, as amended by MDUFSA, specifies a minimum amount that must be appropriated for the Device and Radiological Health line of FDA's appropriation, exclusive of user fees, for FY 2007. That minimum amount is $230,551,000 (rounded to the next whole thousand dollars). In FY 2007, the final appropriation for the Device and Radiological Health line of FDA's appropriation, exclusive of user fees, was $230,682,000. Therefore, FDA met the first condition.

The **second condition** is that the amount of user fees collected by FDA in each fiscal year must be specifically stated in the Appropriation Acts of February 15, 2007. The President signed the FY 2007 Appropriation Act, Public Law 110-5. It states that the amounts collectable from medical device user fees are $43,726,000. Therefore, FDA met the second condition.

The **third condition** is that user fees may only be retained and spent in years when FDA also spends a specified minimum level of appropriated funds, exclusive of user fees, for the review of medical device applications. The minimum level is the appropriations that FDA spent on the process for the review of medical device applications in FY 2002, adjusted for inflation. That adjusted minimum level for FY 2007 is $134,117,560. FDA obligated $173,130,797 from appropriations. Because FDA spent more than the specified minimum level, FDA met the third condition.

MDUFMA also contains a provision that FDA obligations on medical device establishment inspections must be equal to or greater than it spent in FY 2002, increased by 5 percent each fiscal year. If FDA does not satisfy this condition for 2 consecutive years, FDA is not allowed to use accredited third-parties to conduct certain medical device establishment inspections in the future years. FDA spending on medical device establishment inspections exceeded the specified minimum level for each of the most recent fiscal years, so FDA may continue to permit accredited third-parties to conduct certain medical device establishment inspections in the future years.

FDA provides more details on the calculations that show FDA satisfied these statutory conditions in Appendix A.

USER FEE COLLECTIONS

MDUFMA directs FDA to receive fees only from the medical device applications through FY 2007. The statute directs FDA to set the fee rate for each application type as a percentage of the standard fee for a PMA. For FY 2007, MDUFMA, as amended by MDUFSA, specified that the standard fee for a premarket application is $281,600. FDA, then, establishes other application fees based on the specified percents mentioned in MDUFMA. [1]

Under MDUFMA, medical device user fees continue to remain available to FDA for use in future years for the medical device review process if they are not obligated at the end of the fiscal year. The cash balance carried to the next fiscal year is discussed on page 6, section CARRYOVER BALANCES. The table below shows the amount of user fees FDA has collected since MDUFMA began.

FOOD AND DRUG ADMINISTRATION
STATEMENT OF MEDICAL DEVICE FEE COLLECTIONS
AS OF SEPTEMBER 30, 2007

	FY 2003	FY 2004	FY 2005	FY 2006	FY 2007	Total
Total Fees Collected	$21,620,549	$25,280,073	$31,801,091	$35,288,344	$29,342,013	**$143,332,070**
Unearned Fees[1]				$721,156	$2,448,619	**$3,169,774**
Fees Receivables	$32,265				$221,056	**$253,321**

[1]Unearned Fees are fees collected for applications that had not been received by FDA as of September 30, 2007. They are included above in the 'Total Fees Collected' amounts.

Note that user fees collected (the first line above) are initially credited to the year the fee was received. However, the revenues are later reassigned to the year the application is received—referred to as the cohort year. Last year's report showed $35,358,220 of fees collected in FY 2006, of which $2,568,581 was shown as "unearned income" since the application for which the fee was paid had not been received by the end of FY 2006. The FY 2006 total fees collected line is reduced to $35,288,344 in this report, since all but $721,156 of the unearned income reported last year has now been either refunded or credited to FY 2007—the year the application was actually received. The total fees collected line for FY 2007, when seen in next year's FY 2008 report, will also be different from than the figure shown here—reflecting both the refund or reassignment of most of the unearned income to FY 2007, and the refunds that will be made over the next 12 months. Totals reported for each year are net of any refunds for that year, as of

[1] FDA published FY 2007 medical device user fee rates in a Federal Register Notice on August 2, 2006 (pages 43784 through 43786).

September 30, but do not take into account any refunds that may be made after September 30. Information on the number of each type of fee received in FY 2007 is contained in Appendix B.

In addition to the revenue shown in the table above, a total of $32,265 is due from unpaid invoices for fees for applications that were submitted between October 1, 2002, and March 30, 2003. These FY 2003 accounts receivable have been turned over to a collection agency. After April 1, 2003, FDA no longer accepted applications for review unless a fee for the application had been received. Accounts receivable after that date reflect applications that initially paid a lower fee than FDA subsequently determined was appropriate for the submission.

A summary of FY 2007 waivers, reductions, and exemptions is provided in Appendix C.

OBLIGATION OF USER FEE COLLECTIONS

The user fees collected are expended only for costs necessary to support the process for the review of medical device applications, as defined in MDUFMA. The allowable and excludable costs for the process for the review of medical device applications are defined in Appendix D. In FY 2007, FDA obligated $35,202,700 (17 percent of the total) from user fee collections and $173,130,797 (83 percent of the total) from appropriations, as reflected in the table below.

FOOD AND DRUG ADMINISTRATION
FY 2007 MEDICAL DEVICE REVIEW OBLIGATIONS
BY EXPENSE CATEGORY AND REVENUE SOURCE
AS OF SEPTEMBER 30, 2007

Expense Category	From Appropriations	From Fees	Total
Personnel Compensation and Benefits	$112,261,370	$25,312,174	$137,573,544
Travel and Transportation	$2,086,865	$290,248	$2,377,113
GSA Rent	$12,855,664	$2,348,500	$15,204,164
Communications	$3,064,112	$180,859	$3,244,971
Contract Services	$33,938,817	$6,412,302	$40,351,119
Equipment and Supplies	$6,060,452	$419,676	$6,480,128
Other[1]	$2,863,518	$238,941	$3,102,459
Total Obligations	**$173,130,797**	**$35,202,700**	**$208,333,497**

[1]Other includes expense categories like rent payments to others, printing & reproduction, and other miscellaneous expenses.

More information about the costs of the process for device review, as defined in MDUFMA, begins on page 8.

CARRYOVER BALANCES

Under MDUFMA, fees collected, appropriated, and not obligated by the end of a fiscal year remain available to FDA for future fiscal years. They are referred to as carryover balances. Operations in FY 2007 resulted in a reduction of carryover balances of $5,377,746, and reduced the net carryover balance from $16,240,618 to $10,862,872 by the end of the year.

The table below captures FDA's carryover balances at the beginning and each fiscal year since the beginning of MDUFMA in FY 2003.

FOOD AND DRUG ADMINISTRATION
STATEMENT OF CASH, OBLIGATIONS, AND
CARRYOVER BALANCES BY FISCAL YEAR
AS OF SEPTEMBER 30, 2007

Fiscal Year	Beginning Carryover	Net Cash	Obligations	Year-End Carryover
2003	-	$21,936,910	$14,837,600	$7,099,310
2004	$7,099,310	$26,828,534	$23,875,200	$10,052,644
2005	$10,052,644	$31,102,864	$27,171,400	$13,984,108
2006	$13,984,108	$34,325,120	$32,068,610	$16,240,618
2007	$16,240,618	$29,824,954	$35,202,700	$10,862,872
2008	$10,862,872			

The carryover balances in the table reflect the cumulative cash from the beginning to the end of each fiscal year, the net cash collected, and any refunds or other adjustments that occurred during each fiscal year. The net cash amount for FY 2007 is more than the fees credited to FY 2007, shown on page 3. Some of the cash collected in 2007 was for fees owed for previous years, and reflected as previous year collections in the table on page 3. The net collection in FY 2007 also reflects refunds made in FY 2007.

FEE AMOUNTS APPROPRIATED, FEES COLLECTED, AND DIFFERENCES

Under MDUFMA, if fees are collected in excess of the amount of fees appropriated each year, the differences may be kept and used to reduce fees that would otherwise be assessed in a later fiscal year. The following table depicts for each year cumulative net collections, collection ceilings (appropriated amount of fees that may be collected each year), and differences through the end of FY 2007.

FOOD AND DRUG ADMINISTRATION
STATEMENT OF FEES APPROPRIATED, FEES COLLECTED, AND DIFFERENCES
AS OF SEPTEMBER 30, 2007

Fiscal Year	Fees Appropriated	Fees Collected	Differences
2003	$25,125,000	$21,620,549	($3,504,451)
2004	$31,654,000	$26,280,073	($6,373,927)
2005	$33,938,000	$31,801,091	($2,136,909)
2006	$40,300,000	$35,288,344	($5,011,656)
2007	$43,726,000	$29,342,013	($14,383,987)
Total	**$174,743,000**	**$143,332,070**	**($31,410,930)**

As the table shows, the total amount of fees collected in each year always fell short of the amount appropriated for that year, and over the 5 years of MDUFMA, the total fee collections have been $31.4 million less than fee appropriations. As a result, there have been no excess collections in any year that need to be used to reduce future years' collections.

AVAILABILITY OF CARRYOVER BALANCES

Of the FY 2007 carryover balance, $3,169,774 is the unearned fees from applications that are not yet received by FDA. FDA also holds $1,000,000 in reserve for potential refunds in future years. In addition, MDUFMA requires FDA to have at least 1 month of operating expenses from fees in reserve at the end of each fiscal year for use at the beginning of the next fiscal year. All three of these amounts must be held in reserve and are not available for allocation. The table below shows the amounts of carryover that must be held in reserve and the amount available for allocation in FY 2008.

FOOD AND DRUG ADMINISTRATION
PROPOSED ALLOCATIONS OF MEDICAL DEVICE FEE REVENUE
CARRYOVER BALANCE
AS OF SEPTEMBER 30, 2007

Status of Carryover Funds	Amount
Unearned Fees	$3,169,774
Reserve for Future Refunds	$1,000,000
1-Month Reserve for Next Fiscal Year	$4,031,000
Available Cash for Allocation in FY 2008	$2,662,098
Total Carryover Balance	**$10,862,872**

TOTAL COSTS OF THE PROCESS FOR THE REVIEW OF MEDICAL DEVICE APPLICATIONS

FDA uses data from time reporting surveys conducted during four 2-week periods each fiscal year to determine the percent of cost of each organizational component devoted to activities that are included in the process for the review of device applications, as defined in MDUFMA. See Appendix D for the descriptions of the allowable activities and Appendix E for more detail on how FDA develops the costs of the process for the review of medical device applications.

The following table presents the total costs for the review of medical device applications for FY 2006 and FY 2007, by FDA organizational components and by source of funds (appropriations and user fee collections). The amounts are based upon obligations recorded as of the end of each fiscal year. In the past, over 81 percent of obligated funds in FDA were expended within 1 year, and 96 percent within 2 years. Thus, obligations represent an accurate measure of costs.

FOOD AND DRUG ADMINISTRATION
PROCESS FOR THE REVIEW OF MEDICAL DEVICE APPLICATIONS
TOTAL COSTS BY COMPONENTS AND FUNDS
AS OF SEPTEMBER 30, 2007

FDA Organizational Component	FY 2006	FY 2007
Center for Devices and Radiological Health	$155,850,979	$159,387,019
Center for Biologics Evaluation and Research	$20,830,565	$22,889,470
Field Inspection and Investigation	$10,499,258	$11,511,598
Agency General and Administrative Costs	$12,313,468	$14,545,410
Total Process Costs	**$199,494,271**	**$208,333,497**
Obligations from Appropriations	$167,425,661	$173,130,797
Obligations from Medical Device User Fee Collections	$32,068,610	$35,202,700

The costs for all components increased in FY 2007. The increase reflects both the increase in costs for pay and support, and an increase in the total number of FTEs devoted to the process for the review of medical devices in FY 2007.

FULL TIME EQUIVALENTS (FTEs)

The table below presents FTE levels that support the medical device application review process by FDA organizational components. This is a measure of paid staff years devoted to device review. In FY 2007, FDA spent about 60 percent of its total funds for the salaries and benefits of the medical device process FTEs, and the balance of the funds went for support of these employees.

FOOD AND DRUG ADMINISTRATION
PROCESS FOR THE REVIEW OF MEDICAL DEVICE APPLICATIONS
TOTAL FTES
AS OF SEPTEMBER 30, 2007

	FTE Used Each Year				
Organization \ Fiscal Year	**2003**	**2004**	**2005**	**2006**	**2007**
Center for Devices and Radiological Health (CDRH)	662	713	794	765	806
Center for Biologics Evaluation and Research (CBER)	59	70	87	108	105
Office of Regulatory Affairs (ORA)	59	60	64	65	68
Office of the Commissioner (OC)	77	72	89	82	92
Total FTE	**857**	**915**	**1,034**	**1,020**	**1,071**

FTE numbers for FY 2004 through FY 2007 show CDRH, CBER, and ORA staff transferred to the consolidated shared services organization in OC as if they are still in CDRH, CBER, and ORA, to make the numbers comparable to the FY 2002 and FY 2003 numbers.

The increase in CDRH FTEs from FY 2006 to FY 2007 resulted from hiring completed at various times during FY 2006 and FY 2007.

In addition to the FTE numbers shown in the table, CDRH also expended 76 more contractor staff-years on the medical device review process in FY 2007 than it did in FY 2002.

The change in CBER's FTE between FY 2006 and FY 2007 is the result of minor variations in workload.

PERFORMANCE GOALS

In FY 2007, FDA made steady progress in implementing MDUFMA. FDA continued to focus on consulting with its stakeholders, developing guidance documents, and implementing new review processes and process improvements required to meet MDUFMA's progressively challenging performance goals. Among the key activities and accomplishments during FY 2007 were:

- **Steady progress in meeting MDUFMA performance goals**. FDA's overall performance for the FY 2003 through FY 2007 receipt cohorts indicates FDA is meeting or exceeding most MDUFMA performance goals.

- **Guidance Documents.** FDA issued two guidance documents that related to MDUFMA during FY 2007.

- FY 2007 Medical Device Small Business Qualification Worksheet and Certification (replaced guidance for FY 2006), available at: http://www.fda.gov/cdrh/mdufma/guidance/2007.pdf.
- Bundling Multiple Devices or Multiple Indications in a Single Submission (replaced earlier edition), available at: http://www.fda.gov/cdrh/mdufma/guidance/1215.pdf.

- **Stakeholder communication and consultation.** During FY 2007, FDA's consultations with stakeholders focused on reauthorization of medical device user fees and performance goals for FY 2008 through FY 2012. On April 30, 2007, FDA held an open public meeting to discuss proposals for reauthorization.

- **Reports to Congress issued in FY 2007.** During FY 2007, FDA submitted three annual reports required by MDUFMA to Congress: 1) FY 2006 MDUFMA Performance Report, 2) FY 2006 MDUFMA Financial Report, and 3) FY 2006 Office of Combination Products Report. FDA also submitted three topical reports required under MDUFMA:

  1) ***Postmarket Surveillance of Medical Devices Used in Pediatric Populations:*** A report concerning the adequacy of existing postmarket surveillance of implanted devices used in children and devices used in pediatric populations. The report followed, and was based on, a study conducted by the Institute of Medicine under an agreement with FDA. This report was required by section 212(c) of MDUFMA.

  2) ***Effect of the Medical Device User Fee Program on Postmarket Surveillance of Medical Devices:*** A study of the effects of medical device user fees on FDA's ability to conduct postmarket surveillance, the extent to which device companies comply with postmarket surveillance requirements, and improvements needed for adequate postmarket surveillance. This report was required by section 104(b) of MDUFMA.

  3) ***Third-Party Review of Medical Device Premarket Notifications:*** A study of FDA's experience with third-party reviews of 510(k) premarket notifications. This report was required by section 523(d) of the Food, Drug, and Cosmetic (FD&C) Act, a provision added by MDUFMA.

CBER expects to achieve all its FY 2007 MDUFMA performance goals when the cohort is completed. Thus far, CBER has met or exceeded all the FY 2007 MDUFMA decision-performance goals. CBER continues to emphasize the medical device review process oversight, such as focusing on communication with sponsors during the first review cycle and updating 510(k) standard operating procedures and policies to implement process improvements. CBER also continues to harmonize with CDRH on revisions or updates of common device review processes and policies to improve review efficiency, such as review of the Quality System Record section of a PMA, when to file supplements to PMAs and

review of PMA annual reports. During FY 2007, CBER made a number of modifications for information technology systems, Regulatory Management Systems/Biologics Licensing Application, and Blood Logging and Tracking. These changes include updates to fields, forms, views, and reports for payment information and bundled submissions. These enhancements facilitate the transfer of data between CBER and the Office of Financial Management for MDUFMA payments to expedite the start of application review.

MANAGEMENT CHALLENGES FOR FY 2008

On September 27, 2007, the President signed the Food and Drug Act Amendments Act (FDAAA) of 2007, Title II of which reauthorizes medical device user fees for an additional 5 years, for FY 2008 through FY 2012. This reauthorization of MDUFMA (referred to as MDUFMA II) calls for both challenging performance goals and a new fee structure.

During FY 2008, FDA will focus on implementing the Medical Device User Fee Amendments of 2007 (Title II of FDAAA of 2007, P.L. 110-85, enacted September 27, 2007). The 2007 Amendments provides a significantly changed fee structure. All fees established under MDUFMA I have been significantly reduced (for example the standard fee for a 510(k) premarket notification submitted during FY 2008 is 18 percent less than the fee for an FY 2007 submission, and the standard fee for a premarket application submitted during FY 2008 is 34 percent less than the fee for an FY 2007 submission). Small businesses receive more generous discounts than under MDUFMA I (for example the small business fee for a 510(k) premarket notification submitted during FY 2008 is 49 percent less than the fee for an FY 2007 submission, and the small business fee for a premarket application submitted during FY 2008 is 57 percent less than the fee for an FY 2007 submission).

These fee reductions are made possible by new categories of fees, most notably a new annual registration fee that will apply to certain medical device establishments; establishment registration fees are to supply about 45 percent of the anticipated device fee revenue in FY 2008. Implementation of the annual establishment registration fee is a particularly complex challenge, because this new fee should be paid by almost 13,000 establishments worldwide. This is a much larger volume of user fee transactions than FDA has had to process before, and the fee payments are also linked to the on-line registration of these establishments, which is also required by the 2007 Amendments beginning with registrations for FY 2008. To effectively implement and oversee the changes made by the 2007 Amendments, FDA must:

- develop new IT systems to process on-line registrations and associated fee payments;
- develop new IT systems to track FDA's performance against the new set of performance goals for FY 2008 - FY 2012;
- develop new control mechanisms; and
- educate the industry concerning the new provisions.

The performance goals for applications filed or accepted from FY 2008 through FY 2012 are defined in a September 27, 2007, letter from HHS Secretary Michael O. Leavitt to Congress; see the following table for a summary of these goals.

Medical Device Review Performance Goals for FY 2008 through FY 2012			
Application Type	Type of Goal	Review Time Goal	Performance Goal
Premarket approval application (PMA), panel-track PMA supplement, premarket report	FDA Decision	180 days	60%
		295 days	90%
Expedited PMA, expedited panel-track PMA supplement	FDA Decision	180 days	50%
		280 days	90%
PMA module	FDA Action	90 days	75%
		120 days	90%
180-day PMA supplement	FDA Decision	180 days	85%
		210 days	95%
Real-time PMA supplement	FDA Decision	60 days	80%
		90 days	90%
510(k) premarket notification	SE or NSE Decision	90 days	90%
		150 days	98%

An "FDA Decision" is any of the following: a denial order, an approvable letter (including approvable pending GMP inspection), a not approvable letter, a withdrawal, or a denial order.
An "FDA Action" on a PMA module is any of the following: accepting the module, a request for additional information, receipt of the PMA, or withdrawal of the module

These goals are structured in ways that differ from the goals for FY 2003 through FY 2007:

- The FY 2008 – FY 2012 goals do not vary from one fiscal year to the next. Instead, each goal will apply throughout the 5 years from FY 2008 through FY 2012.
- Except for PMA modules, all of FDA's performance goals focus on making an "FDA decision" and FDA will not have any cycle goals. An "FDA decision" is any of the following: a denial order, an approvable letter (including approvable pending Good Manufacturing Practice (GMP) inspection), a not approvable letter, a withdrawal, or a denial order.
- For PMA modules only, FDA's performance goals focus on FDA taking an "action" on the module. An "FDA action" on a PMA module is any of the following: accepting the module, a request for additional information, receipt of the PMA, or withdrawal of the module. PMA modules are not subject to a decision goal, because the modular submission is converted to a PMA upon submission of the final module.
- Each goal has two tiers, and all submissions are measured in both tiers. Compared with the lower tier, the upper tier of each goal provides for additional review time, but requires a higher percentage of reviews to have an FDA decision (or, in the case of PMA modules, an FDA action) within the specified review time.

The new goals are very challenging, and FDA will have to carefully monitor our review processes to ensure we meet each goal.

Appendix A

STATUTORY CONDITIONS FOR COLLECTION AND USE OF FEES

The FD&C Act was amended by MDUFMA, Public Law 107-250, and by MDUFSA, Public Law 109-43. The Act specifies three statutory conditions that must be satisfied before FDA can collect and spend medical device user fees. A summary of these conditions has been introduced on page 2. Appendix A describes each of the conditions and explains how FDA met the conditions in FY 2007 in more detail.

In order to determine whether the statutory conditions are satisfied, FDA must calculate and apply an adjustment factor, defined in section 737(7) of the Act, in the assessments of the first and third conditions. The Act defines the term "adjustment factor" as follows:

> The term 'adjustment factor' applicable to a fiscal year is the Consumer Price Index for all urban consumers (all items; United States city average) for April of the preceding fiscal year divided by such Index for April 2002.

The April preceding FY 2007, which began on October 1, 2006, was April 2006. The Consumer Price Index (CPI) for April 2006 was 201.5. The CPI for April 2002 was 179.8. Dividing the CPI of April 2006 by the CPI of April 2002 yields an adjustment factor of 1.1207 for FY 2007.

The **first condition** is a funding condition that affects the collection of fees in FY 2007.

MDUFMA, amended by MDUFSA, specifies a minimum amount of budget authority that must be appropriated for the Device and Radiological Health line of FDA's appropriation, exclusive of user fees, for FY 2007. That minimum amount for FY 2007 is $205,720,000 multiplied by the adjustment factor (1.1207), or $230,551,000 (rounded to the next whole thousand dollars). In FY 2007, after rescission, the final appropriated budget authority for the Device and Radiological Health line of FDA's Appropriation, exclusive of user fees, was $230,682,000. Since this amount is greater than $230,551,000, FDA's appropriation for FY 2007 met the first condition.

The **second condition** comes from section 738(h)(2)(A)(i). It states that fees "shall be retained in each fiscal year in an amount not to exceed the amount specified in appropriation acts, or otherwise made available for obligation, for such fiscal year…." The second condition means FDA can not collect medical device user fees without an appropriation.

On February 15, 2007, the President signed FY 2007 Appropriation Act, Public Law 110-5, which appropriated $43,726,000 from medical device user fees for FDA in FY 2007. Therefore, FDA met the second condition.

The **third condition** requires a minimum spending from appropriations, exclusive of user fees, on the process for medical device review as defined in MDUFMA. This condition in section 738(h)(2)(A)(ii), states that fees:

> shall only be collected and available to defray increases in the costs of the resources allocated for the process for the review of device applications (including increases in such costs for an additional number of full-time equivalent positions in the Department of Health and Human Services to be engaged in such process) over such costs, excluding costs paid from fees collected under this section, for fiscal year 2002 multiplied by the adjustment factor.

In FY 2002, FDA's obligations for the process for the review of medical device applications totaled $119,673,026, as reported in the FY 2003 MDUFMA Financial Report. The adjustment factor for FY 2007 is 1.1207. Multiplying by the adjustment factor, FDA calculates the minimum spending from appropriations for the medical device review process in FY 2007 must be at least $134,117,560.

As this report documents, FDA obligated $173,130,797 from appropriations for the process for the review of medical device applications in FY 2007. Since this amount is greater than the minimum spending from appropriation required under MDUFMA, FDA met the third condition.

The table below shows FDA obligations on the process for the review of medical device applications in FY 2006 and FY 2007. The table separates the obligations that were funded by appropriations and user fees.

FOOD AND DRUG ADMINISTRATION
OBLIGATIONS FOR THE PROCESS FOR THE REVIEW
OF MEDICAL DEVICE APPLICATIONS
AS OF SEPTEMBER 30, 2007

	FY 2006	FY 2007
From Appropriations	$167,425,661	$173,130,797
From Medical Device Fee Collections	$32,068,610	$35,202,700
Total Obligations	**$199,494,271**	**$208,333,497**

In addition, MDUFMA imposes a provision that FDA obligations on medical device establishment inspections must be equal to or greater than its obligations for this purpose in FY 2002, with a 5 percent increase for each fiscal year. If FDA does not satisfy this condition for two consecutive years, FDA is prohibited from allowing accredited third-parties to conduct device establishment inspections in the future years. This condition is cited in section 704(g)(10) of the Act.

The table below shows the statutory minimum to be obligated for device establishment inspections (2002 level increased by 5 percent each year) and FDA obligations for medical device establishment inspections from FY 2002 to FY 2007. Because FDA has spent more than the statutory minimum for device inspection for each of the past 2 fiscal years, FDA may continue to allow accredited third-parties to conduct certain device establishment inspections in future years.

FOOD AND DRUG ADMINISTRATION
OBLIGATIONS FOR THE INSPECTION OF MEDICAL DEVICE ESTABLISHMENTS
(ROUNDED TO $000)
AS OF SEPTEMBER 30, 2007

Fiscal Year	Minimum--2002 Obligations Increased by 5% per year	Actual Obligations	Excess or Shortfall
FY 2002 Base	$19,425,000	$19,425,000	$0
FY 2003	$20,396,000	$22,576,000	$2,180,000
FY 2004	$21,416,000	$21,430,000	$14,000
FY 2005	$22,487,000	$21,515,000	($972,000)
FY 2006	$23,611,000	$29,230,000	$5,619,000
FY 2007	$24,792,000	$31,926,000	$7,134,000

Appendix B

NUMBER OF FEE PAID APPLICATIONS IN FY 2007

Under MDUFMA, FDA sets four fee rates for full fee applications, 180-day supplements, real-time supplements, and 510(k)s. The full fee application rates cover PMAs, PDPs, BLAs, PMRs, panel track supplements, and efficacy supplements. Under MDUFMA, a fee rate for each application type is a percentage of a standard fee for a PMA or a full fee application. Of a full fee application, 180-day supplement is 21.5 percent; real-time supplement is 7.2 percent; and 510(k) is 1.42 percent in aggregate. A small business rate for each application type, except 510(k), is 38 percent of its rate. A small business rate for 510(k) is 80 percent of $4,158. The table below exhibits the rates for all types in FY 2006 and FY 2007.

FOOD AND DRUG ADMINISTRATION
MEDICAL DEVICE USER FEE RATES
AS OF SEPTEMBER 30, 2007

Application Type	FY 2006	FY 2007
Full Fee Applications	$259,600	$281,600
Small Business Rate	$98,648	$107,008
180-Day Supplements	$55,814	$60,544
Small Business Rate	$21,209	$23,007
Real-Time Supplements	$18,691	$20,275
Small Business Rate	$7,103	$7,705
510(k)s	$3,833	$4,158
Small Business Rate	$3,066	$3,326

The next table summarizes the number of applications received by FDA in FY 2006 and FY 2007. These applications have been paid in full by the companies before September 30.

FOOD AND DRUG ADMINISTRATION
APPLICATIONS RECEIVED AND PAID FEES
AS OF SEPTEMBER 30, 2007

Application Type	FY 2006 Actual	FY 2007 Actual
Full Fee Applications	51	24
Small Business	7	2
180-Day Supplements	76	99
Small Business	25	23
Real-Time Supplements	156	141
Small Business	16	21
510(k)s	2,988	2,849
Small Business	652	652

Please note that the numbers of fees received by FDA should not be used as a surrogate for medical device review workload. Many applications submitted to FDA are not charged fees by FDA for the following reasons:

- first applications submitted by small businesses;
- applications bundled under one fee because of similarity of medical device review issues;
- applications exempted from fees for pediatric indications; and
- applications for investigational device exemptions (IDEs) and PMA supplements other than Real-Time and 180-Day Supplements;
- other applications for which no fee is charged, such as 30 day notices and 513(g) submissions; and
- annual report submissions that must be examined but that have no fees associated with them.

Appendix C

WAIVERS, REDUCTIONS, AND EXEMPTIONS

MDUFMA directs FDA to waive the first premarket application fee from a qualified small business and an application fee submitted solely for pediatric indications. It also directs FDA to reduce premarket application and supplement fees for subsequent applications from qualified small businesses. Beginning in FY 2004, FDA also charged a reduced rate for 510(k)s from qualified small businesses. In addition, FDA does not collect fees for the followings types:

- applications for Humanitarian Device Exemptions (HDE) submitted under section 520(m);
- applications submitted under section 351 of the Public Health Service (PHS) Act for a product licensed for further manufacturing use only;
- applications submitted by a state or federal government entity for devices that are not intended for commercial distribution; and
- 510(k)s submitted to certified third-party reviewers, rather than to FDA.

FDA provides a summary of MDUFMA fee waivers, reductions, and exemptions granted in FY 2007 in this appendix.

FDA responded to thousands of e-mails and phone calls from companies asking for information regarding the small business waiver for MDUFMA fees. After carefully reviewing the requests from companies, FDA granted 782 of 807 written requests for small business status in FY 2007. FDA waived or reduced 664 applications under small business criteria in FY 2007. This is smaller than the number of requests for waiver granted, since some of the parties to whom a request was granted did not submit the applications in FY 2007. The following table portrays the number of small business application fees that were waived or reduced by FDA, and the value of each category in FY 2007.

FOOD AND DRUG ADMINISTRATION
FY 2007 SMALL BUSINESS FEE WAIVERS AND REDUCTIONS GRANTED
AS OF SEPTEMBER 30, 2007

Category	Number	Amount	Total Value
Full Fees Waived	6	$281,600	$1,689,600
Full Fees Reduced	1	$174,592	$174,592
Panel Track Supplements Reduced	0	$174,592	$0
180-Day Supplements Reduced	19	$37,537	$713,203
Real-Time Supplements Reduced	20	$12,570	$252,002
510(k)s Fees Reduced	618	$832	$523,607
Total	**664**		**$3,353,004**

Note: reduced fee rate = full fee rate - small business fee rate

FDA collected $29,824,954 fees or net cash in fiscal year 2007. Had there been no small business waivers and reductions, FDA would have collected an additional $3,353,004, or an additional 11 percent of collections. The value of the 510(k) waivers is not included in the table above because under MDUFMA the fees for 510(k)s from large firms are increased slightly to offset the reduction in 510(k) fees charged to qualifying small businesses.

FDA received 6 HDE applications and 23 supplements in FY 2007. None of these are subject to MDUFMA fees. FDA does not know if any of them would have been submitted had they been subject to a fee. Therefore, FDA does not know the extent to which this exemption resulted in any loss of revenue.

CBER received two exemption requests in FY 2007 for applications submitted under section 351 of the PHS Act for a product licensed for further manufacturing use only. Because these were bundled with other applications, there would not have been a charge for these if they had not been exempt, so in this case there was no financial impact for these two exemptions.

FDA received and granted three requests from State or Federal government entities for exemptions for 510(k)s that were not intended for commercial distribution. Total cost of the exemptions in FY 2007 was $12,474.

FDA granted exemptions for pediatric indications in FY 2007 to 33 510(k)s, 3 180-day supplements, and 2 real-time. Total value of these exemptions was $359,396.

The 510(k) Third-Party Review Program decreased by 18 percent from FY 2006 to FY 2007. FDA received 235 510(k) submissions subject to third-party review in FY 2007 compared to 287 in FY 2006. FDA exempted fees for the 235 submissions. The total value of these exemptions in FY 2007 was $948,010 – assuming that 15 percent of the third-party submissions would have paid the reduced small business fee.

FOOD AND DRUG ADMINISTRATION
SUMMARY AND TOTAL VALUE OF ALL FEE WAIVERS, REDUCTIONS, AND EXEMPTIONS GRANTED
AS OF SEPTEMBER 30, 2007

Reason	FY 2006	FY 2007
Small Business	$4,274,178	$3,353,004
Govt. Sponsored Application not for Commercial Distribution	$15,332	$12,474
Pediatric Indications	$405,254	$359,396
510(k)s Reviewed by Third-Party Review	$996,411	$948,010
Total Value	**$5,691,175**	**$4,672,884**

Appendix D

ALLOWABLE AND EXCLUDED COSTS FOR THE PROCESS FOR THE REVIEW OF DEVICE APPLICATIONS

The Act, as amended by MDUFMA, defines the process for the review of medical device applications and the costs that may be included in that process. Using these definitions (and further refinements identified below) and the methodologies described in this report, the agency identified those activities that were applicable to the "process for the review of device applications."

In the past, over 81 percent of obligated funds in FDA are expended within 1 year, and 96 percent within 2 years. Therefore, obligations represent an accurate measure of costs.

MDUFMA Related Costs

Included Activities

[Section 737(5)(A)] The activities necessary for or in anticipation of the review of premarket applications, premarket reports, supplements, and premarket notification submissions, including, but not limited to, the following:

- 510(k)s -- Traditional/Supplements/Abbreviated/Specials (third-party and non-third-party)
- Evaluation of Automatic Class III Designations
- Traditional and Expedited PMAs (includes amendments, supplements, and annual reports)
- Modular PMAs (shell, modules, amendments, supplements, and annual reports)
- PDPs (including amendments, supplements, and annual reports)
- Premarket Reports (amendments, supplements, annual reports)
- Reclassification Petitions
- Class II Exemption Petitions
- BLAs and BLA Supplements (Applications subject to 351 of the PHS Act)
- Recruitment and use of outside experts during the review process
- Obtaining advisory committee input (e.g., convened meetings, homework assignments)
- Resolution of product jurisdictional issues
- Dispute resolution/appeals
- Information Technology (IT) support for review activities
- Recruitment of review staff

[Section 737(5)(B)] The issuance of action letters that allow marketing of devices or which set forth in detail the specific deficiencies in such applications, reports, supplements, or submissions and, where appropriate, the actions necessary to place them in condition for approval. This includes activities such as the issuance of deficiency letters, meetings with applicants to discuss such letters, and review of the responses.

[Section 737(5)(C)] The inspection of manufacturing establishments and facilities undertaken as part of the review of pending premarket applications, premarket reports, and supplements to include activities such as the review of manufacturing information submitted in premarket applications, pre-approval GMP inspections, and resolution of any identified GMP issues.

[Section 737(5)(D)] Monitoring of research conducted in connection with the review of such applications, reports, supplements, and submissions. For the types of applications identified above, this would include monitoring activities such as:

- conduct of bioresearch monitoring inspections (both "for cause" and pre-approval) of sponsors, institutional review boards, and clinical investigators;
- adverse event and complaint investigations related to on-going clinical trials; and
- Good Laboratory Practice inspections (21 CFR Part 58).

[Section 737(5)(E)] Review of device applications subject to section 351 of the Public Health Service Act for an investigational new drug application (IND) under section 505(i) or for an investigational device exemption (IDE) under section 520(g) and activities conducted in anticipation of the submission of such applications under section 505(i) and 520(g). This would include the review of the IDEs (original, amendments, and supplements) and INDs (amendments, supplements, and safety reports). Also included are pre-IDEs (review of the submission and any meetings or correspondence), significant/non-significant risk determinations, and Determination/Agreement meetings.

[Section 737(5)(F)] The development of guidance, policy documents, or regulations to improve the process for the review of premarket applications, premarket reports, supplements, and premarket notification submissions to include activities such as the development of device-specific, cross-cutting, special control, and program-related guidances as well as "Blue Book Memoranda" and Standard Operating Procedures.

[Section 737(5)(G)] The development of voluntary test methods, consensus standards, or mandatory performance standards under section 514 in connection with the review of applications listed above. This would include national and international standards development and coordination related to the review of premarket applications.

[Section 737(5)(H)] The provision of technical assistance to device manufacturers in connection with the submission of such applications, reports, supplements, or submissions to include activities such as:

- informal consultation via phone, meetings, e-mail, and facsimile;
- meetings between FDA and applicants, such as pre-submission meetings, Determination/Agreement meetings, and meetings to discuss deficiencies in premarket applications;
- use of outside experts in the review of premarket applications;
- review of labeling prior to approval of a premarket application or supplement;
- FDA sponsored conferences/workshops related to premarket submissions; and
- staff participation at non-FDA meetings related to such applications.

[Section 737(5)(I)] Any activity undertaken under section 513 or 515(i) in connection with the initial classification or reclassification of a device or under section 515 (b) in connection with any requirement for approval of a device to include activities such as the review of requests for information submitted under section 513(g) and the "call" for PMAs for pre-amendment devices.

[Section 737(5)(J)] Evaluation of post-market studies required as a condition of approval of a premarket application or premarket report under section 515 or section 351 of the PHS Act. This would include activities such as the review of:

- protocols for the post-market studies;
- modifications to such protocols;
- data collected under the protocol; and
- labeling changes (instructions for use, warnings, precautions, etc.), if needed as a result of the review of the data.

[Section 737(5)(K)] Compiling, developing, and reviewing information on relevant devices to identify safety and effectiveness issues for devices subject to premarket applications, premarket reports, supplements, or premarket notification submissions to include activities such as:

- epidemiology studies; and
- post-marketing problem identification/resolution, including reports filed under the Medical Device Report regulation.

Training related to premarket and post-market approval activities. This would include the following types of training:

- scientific, clinical, and statistical training;
- managerial or other administrative training;
- policy/regulatory training;

- professional development (coursework, attendance at professional meetings, library resources);
- "Vendor Days;" and
- Site Visit Program for premarket reviewers.

User Fee Act implementation to include activities such as:

- guidance/regulation development;
- stakeholder outreach for educational and comment purposes;
- training of agency staff; and
- IT support for implementation.

***All user fee related costs represented by the above activities are collectively referred to in this report as costs for the process for the review of medical device applications.**

Section 737(6) of the Act defines the "costs of resources allocated for the process for the review of medical device applications" as the expenses incurred in connection with this process for:

(A) officers and employees of the FDA, contractors of the FDA, advisory committees, and costs related to such officers, employees, committees and contracts;
(B) management of information, and the acquisition, maintenance, and repair of computer resources;
(C) leasing, maintenance, renovation, and repair of facilities and acquisition, maintenance, and repair of fixtures, furniture, scientific equipment, and other necessary materials and supplies; and
(D) collecting user fees and accounting for resources allocated for the review of premarket applications, premarket reports, supplements, and submissions.

Excluded Activities

- Enforcement policy and regulation development
- Third-party inspection program
- Post-approval compliance actions and activities unrelated to PMA Conditions of Approval and investigations of safety and effectiveness issues for devices subject to FDA regulation
- Post-approval activities relating to:
  - Promotion and advertising
  - International coordination/Mutual Recognition Agreement work
  - International standard development
  - Liaison/outreach and manufacturing assistance
  - Device tracking
- Inspections unrelated to the review of covered applications

- Export/Import activities unrelated to the conduct of a clinical trial
- Research related to future products
- All activities conducted under the Mammography Quality Standards Act (MQSA), radiation safety authorities of the FD&C Act (Sections 531 et. seq.), and the Clinical Laboratories Improvement Amendments.

Appendix E

DEVELOPMENT OF COSTS FOR THE PROCESS FOR THE REVIEW OF DEVICE APPLICATIONS

GENERAL METHODOLOGY

The costs associated with the process for the review of medical device applications are based on obligations recorded within FDA's CDRH, CBER, ORA, and OC. These organizations correspond to the cost categories presented as follows:

Cost Category	FDA Organization
Costs for PMAs, PDPs, PMRs, Modular PMAs, supplements, and 510(k)s	CDRH
Costs for the Review of BLAs, PMAs, supplements, and 510(k)s	CBER
Costs for field inspection and investigation	ORA
Costs for Agency general and administration	OC

The costs were accumulated using a variety of methods. Using the definitions of costs and activities included in the process for the review of device applications in the Act, as expanded in the discussion in Appendix D, the cost categories within each organization listed above were identified as parts of the medical device review process.

CENTER COSTS

Costs of the medical device review program are tracked for each organizational component in CDRH and CBER, usually at the division level. Most FDA components involved in the process perform a mixture of activities – some within the definition of the process for the review of device applications, and some not. FDA groups its organizational components into three categories:

- direct review and laboratory;
- indirect review and support; and
- center-wide costs.

The allocation of costs for each category is discussed below.

Direct Review and Laboratory

Employees in all components of CDRH and CBER other than those noted below as Center indirect review and support components reported their time in activities that could be used to differentiate between time spent on the process for the review of device applications and all other time.

Both CDRH and CBER have existing time reporting systems in place. These time reporting systems were modified after the enactment of MDUFMA, so that time could be reported in categories that could be separated into allowable and excluded activities with respect to the process for the review of device applications, as defined in MDUFMA and as further defined in Appendix D. This process is further explained below.

Ten years prior to the enactment of MDUFMA, CDRH's time reporting system had been used to gather information about employee time for a 2-week period one or two times each year. After the definitions of allowable and excluded costs for the process for the review of device applications under MDUFMA were further refined, as presented in Appendix D, the time reporting categories in the CDRH time-reporting system were modified so that all data captured fit into either allowable or excluded costs. These modifications to the system were completed in mid-June 2003.

Once these modifications were completed, all CDRH employees other than management and administrative personnel reported all of the time they worked against these revised categories for a period of 8 consecutive weeks, from June 29 through August 23, 2003. Whether time categories were counted as allowable or excluded was not apparent to employees as they reported their time.

FDA Centers are very payroll-intensive organizations. In most years over 60 percent of all FDA funds go to pay for employee salaries and benefits. Almost all other costs directly support these employees. Thus the percent of time reported during this 8-week period as having been expended on allowable device review process activities for each cost-center (usually an organization component at the Division level) was then applied to all costs incurred for that cost-center for the entire FY 2003.

Further, since these percentages of allowable costs had never been collected for earlier periods, the percentages of allowable costs reported in this 8-week period were likewise applied to each cost center's direct costs (obligations) incurred in FY 2002, to get the baseline FY 2002 device review process cost data required under MDUFMA.

For FY 2004 and FY 2005, all CDRH employees, other than management and administrative personnel, reported all of the time they worked against these revised categories for one 2-week period during each quarter of the fiscal year. The results from the 8 weeks of time reporting data were then averaged and extrapolated to the entire year. This served as the basis for measuring CDRH costs for the device review process for direct review and laboratory components, and the same pattern has been followed in

subsequent years. In addition, further modifications were made in FY 2005 to be able to break out time for various specific types of application review.

In FY 2006, CDRH modified its time reporting categories to better account for effort on training, guidance document and standards development, and outreach initiatives. Prior to FY 2006, most of these areas were considered part of the MDUFMA process. These changes allowed CDRH to better distinguish between premarket and postmarket efforts.

In FY 2007, CDRH continued to make minor refinements to the CDRH automated time reporting system. Based on requests from staff, CDRH added several reporting activities to improve reporting accuracy. New activity codes were created to further define premarket review activities, reflect organizational transformation initiatives, and differentiate between user fee and appropriated MQSA program management activity. CDRH also added numerous "sub-activities" to the existing activities in all program areas so that staff could easily identify and report their time in the appropriate categories. These enhancements did not have a significant effect on FDA's MDUFMA process calculations.

A similar procedure is used in CBER to measure the direct review and laboratory components costs for the device review process. CBER was able to use the time-reporting system it has had in place for over 10 years prior to the enactment of MDUFMA, and which was validated by studies done just after PDUFA was initiated in 1993. That system collects time reports from all employees other than management and administrative support personnel for a 2-week period during each quarter of the fiscal year.

CBER's existing time-reporting system was also modified to assure that activities against which time was reported could be clearly divided into those activities that were either allowable or excluded in the MDUFMA-defined process for device application review. The results from each 2-week period of time reported are extrapolated for the quarter being reported. The extrapolated results for each quarter are averaged to estimate the full year costs.

CBER's process for determining allowable and excluded costs for MDUFMA direct review and laboratory costs is identical to how costs for the process for the review of human drug applications was validated by Arthur Andersen under PDUFA for 1992 and 1993.

Center Indirect Review and Support

Indirect review and support components provide the infrastructure for the review process. In CDRH, these are the Office of the Center Director and the Office of Management and Operations. In CBER, these components include the Office of the Center Director, Office of Management, Office of Information Technology, and the Office of Communications, Training, and Manufacturers Assistance.

In both CDRH and CBER, the allowable costs for these indirect review and support components were determined by multiplying the average percent of allowable costs for all direct review and laboratory components by the total costs of each of these indirect review and support components.

Center-wide Costs

A number of Center-wide expenses are paid for centrally from agency funds each year rather than from funds allocated to the centers. These costs include rent, utilities, some computer equipment, facilities repair and maintenance, and some extramural and service contracts.

Many of these costs, such as building rent, can be traced back to the specific organization component that generated the cost and were assigned the user fee related percentage calculated for the division to which the expenditure related. For the costs that benefited the Center as a whole and could not be traced to a specific division, a weighted average user fee percentage was calculated based on the level of user fee related costs to total costs in the Center.

FIELD INSPECTION AND INVESTIGATION COSTS

All field inspection and investigation costs are incurred by FDA's ORA. ORA costs are incurred in both district offices (the "field") and headquarters support offices. In FY 2002, the agency began tracking accumulated ORA costs through the use of the Field Accomplishment and Compliance Tracking System (FACTS). FACTS is a time and activity tracking system which captures time in a variety of categories, including pre-approval inspections of manufacturing facilities, investigations of clinical studies, and analytical testing of samples--which are included in the process for the review of device applications.

Total direct hours reported in FACTS are used to calculate the total number of staff-years required by ORA to perform activities in the process for the review of device applications as defined in MDUFMA. In addition to the direct time, an allocation of support time is also included to represent the work done by the ORA administrative and management personnel. The agency then applies the total number of staff years devoted to the process for the review of device applications to the average salary cost in ORA to arrive at the ORA salary costs for the process for the review of device applications as defined in MDUFMA. The final step is to allocate ORA obligations for operations and rent to the device review process based upon the ratio of user fee related staff years to total ORA staff years. The following table summarizes the calculation for the FY 2006 and FY 2007, respectively.

FOOD AND DRUG ADMINISTRATION
OFFICE OF REGULATORY AFFAIRS
COSTS OF THE PROCESS FOR THE REVIEW OF MEDICAL DEVICE APPLICATIONS
AS OF SEPTEMBER 30, 2007

Cost Component	FY 2006	FY 2007
Staff Years Utilized	64	64
ORA Average Salary and Benefits	$99,675	$104,700
Total Salary and Benefits	$6,379,211	$6,700,800
Operating and Other Costs[1]	$4,120,047	$4,810,798
Total	**$10,499,258**	**$11,511,598**

[1]Other costs are central, GSA rent, rent-related, and Shared Services costs that are applicable to the process for the review of device applications.

The ORA costs for the process for the review of medical device applications shown in the table include costs paid from appropriations and user fee collections.

AGENCY GENERAL AND ADMINISTRATIVE COSTS

The agency general and administrative costs are incurred in the FDA's OC. At the end of FY 2007, OC was comprised of the following offices:

- Immediate Office of the Commissioner
- Office of the Chief Counsel
- Office of the Chief of Staff
- Office of the Administrative Law Judge
- Office of Equal Employment and Diversity Management
- Office of International and Special Programs
- Office of Operations
- Office of Policy, Planning and Preparedness
- Office of Scientific and Medical Programs

The OC costs applicable to the process for the review of medical device applications were calculated using a method prescribed in 1993 by the Division of Cost Determination Management, Office of Finance, Office of the Secretary, Department of Health and Human Services. (Today the Office of Finance is under the Office of the Assistant Secretary for Resources and Technology.) This method uses the percentage derived by dividing total Office of the Commissioner costs by the total FDA salary expenses after subtracting the salary expenses from the Office of the Commissioner. The percentage is then multiplied by the sum of salaries applicable to the process for the review of medical devices in CDRH, CBER, and ORA to derive the agency general and administrative costs applicable to the process for the review of medical device applications.

Using this methodology, FDA dedicated $12,313,468 and $14,545,410 in general and administrative expenses to the medical device review process in FYs 2006 and 2007, respectively. The FY 2007 general and administrative obligations from appropriations and user fees combined accounted for about 7 percent of the total cost of the process for the review of device applications

At the beginning of FY 2004, FDA implemented a reorganization and streamlining of its administrative support activities. Many functions and resources from FDA Centers, ORA, and components of the OC were consolidated into the Office of Shared Services under Office of Management – a component of OC. This was done in an effort to achieve greater efficiency in the provision of these services. For reporting comparability purposes, however, resources expended by the Office of Shared Services in FY 2007 supporting the device review process are shown as having been incurred by CDRH, CBER, ORA, or OC, in proportion to the resources allocated from each these components to the Office of Shared Services. This makes the figures shown for FY 2007 comparable with figures prior to FY 2004.

ATTACHMENT 2

Nov. 20, 2008

Hon. LEONARD L. BOSWELL,
Chairman,
Subcommittee on Livestock, Dairy, and Poultry,
Committee on Agriculture,
Washington, D.C.

Dear Mr. Chairman:

Thank you for your letter of July 10, 2008, cosigned by Ranking Member Robin Hayes, Subcommittee on Livestock, Dairy, and Poultry, Committee on Agriculture. You wrote to express your concern about the potential lack of funding for the Food Animal Residue Avoidance Database (FARAD) program. In your letter, you requested that the United States Department of Agriculture (USDA) and the Department of Health and Human Services (HHS) work together to ensure funding for the program's continuation.

As you know, Title 7 of the United States Code, section 7462 gives the Secretary of Agriculture responsibility for the operation of FARAD. USDA operates this program through the Cooperative State Research, Education, and Extension Service. It is our understanding that, in Fiscal Year 2008, there were no appropriated funds available to support this program. USDA and HHS have worked together to provide partial funding. USDA has agreed to contribute $75,000, and the Food and Drug Administration has agreed to contribute $50,000 to support the program.

Thank you again for your letter. Please call me if you have any further questions or concerns. The same letter has been sent to Ranking Member Hayes.

Sincerely,

STEPHEN R. MASON,
Acting Assistant Commissioner for Legislation.

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